FORSIDEN

CONTRIBUTORS AND PARTICIPANTS

Editors:

Hilde Kruse	NORM-VET, The Norwegian Zoonosis Centre
Gunnar Skov Simonsen	NORM, Department of Microbiology, University Hospital of Tromsø

The following persons contributed to the writing of this report:

Hege Salvesen Blix	WHO Collaborating Centre for Drug Statistics Methodology
Kari Grave	VETLIS / The Norwegian School of Veterinary Science
Einar Heldal	The National Health Screening Service / The National Tuberculosis Register
Merete Hofshagen	NORM-VET, The Norwegian Zoonosis Centre
Hilde Kruse	NORM-VET, The Norwegian Zoonosis Centre
Jørgen Lassen	The National Institute of Public Health
Ane Nødtvedt	NORM-VET, The Norwegian Zoonosis Centre
Per Sandven	The National Institute of Public Health
Gunnar Skov Simonsen	NORM, Department of Microbiology, University Hospital of Tromsø
Martin Steinbakk	NORM, Department of Microbiology, University Hospital of Tromsø

The following institutions participate in the NORM-VET surveillance system:

The Municipal Food Control Authorities	
The Norwegian Food Control Authority	
The Norwegian Animal Health Authority	
The National Institute of Public Health	Jørgen Lassen / Trine-Lise Stavnes
The National Veterinary Institute	Gudmund Holstad / Tormod Mørk / Ellen Christensen / Hanne Tharaldsen
The Norwegian Zoonosis Centre	Merete Hofshagen / Hilde Kruse / Ane Nødtvedt

The following institutions participate in the NORM surveillance system:

Laboratory of Enteric Pathogens, The National Institute of Public Health	Jørgen Lassen / Trine-Lise Stavnes
Department of Microbiology, Ullevål University Hospital	Turid Mannsåker / Thea Bergheim
Department of Immunology and Microbiology, Haukeland University Hospital	Asbjørn Digranes / Berit Riksheim
Department of Microbiology, University Hospital of Trondheim	Per Leiv Svarva / Randi Valsø Lyng
Department of Microbiology, University Hospital of Tromsø	Gunnar Skov Simonsen / Merethe Elise Olsen
Department of Microbiology, Central Hospital of Oppland	Rolf Arne Sandnes / Ingunn Haavemoen
Telelab A/S, Skien	Yngvar Tveten / Anne Ragnhild Oseid
Department of Microbiology, Akershus Central Hospital	Martin Steinbakk / Liselotte Buarø
Department of Microbiology, Central Hospital of Rogaland	Elisebet Haarr / Tone Roa
Department of Microbiology, Central Hospital of Nordland	Liisa Mortensen / Karstein Korsvik

The following persons are members of the NORM-VET steering group:

Gunnar Hagen	The Norwegian Animal Health Authority
Nina Krefting Aas	The Norwegian Food Control Authority
Ellen Mari Grande	The National Agricultural Inspection Service
Kåre Fossum	The National Veterinary Institute
Hilde Kruse	The Norwegian Zoonosis Centre

The following persons were members of the NORM reference group in 2000:

E. Arne Høiby	The National Institute of Public Health
Reidar Hjetland	Department of Microbiology, Central Hospital of Sogn og Fjordane
Eirik Holten	Department of Microbiology, Central Hospital of Akershus
Asbjørn Digranes	Department of Immunology and Microbiology, Haukeland University Hospital
Inger Sofie Samdal Vik	Department of Microbiology, County Hospital of Møre og Romsdal, Molde

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I. SAMMENDRAG

Forbruket av antibiotika til dyr i Norge ligger på et moderat nivå sammenlignet med mange andre industrialiserte land, og forbruksmønsteret er i hovedsak gunstig. Det totale salget av veterinære antibakterielle midler godkjent for terapeutisk bruk til dyr i Norge var 5750 kg i 2000, noe som utgjør en 39% reduksjon siden 1995. Andelen penicilliner av det totale forbruket økte fra 36% i 1995 til 44% i 2000. I samme periode sank aminoglykosidenes andel av det totale forbruket fra 27% til 20%. I 2000 utgjorde penicilliner den største andelen av forbruket (44%), fulgt av sulfa (27%), aminoglykosider (20%), tetracykliner (3%), trimetoprim og derivater (3%), og andre antibakterielle midler (4%). Det totale salget av veterinære antibakterielle midler godkjent for terapeutisk bruk til oppdrettsfisk i Norge utgjorde 685 kg i 2000, og kinoloner representerte 76% av dette forbruket. I løpet av de siste 13 årene har forbruket av antibakterielle midler i oppdrettsnæringen blitt redusert med 99% samtidig som produksjonen av oppdrettsfisk er mangedoblet. Denne reduksjonen tilskrives først og fremst innføring av effektive vaksiner, men bedrede miljøforhold i oppdrettsnæringen har også hatt betydning.

Antibakterielle vekstfremmere benyttes ikke lenger i husdyrproduksjonen i Norge. Avoparcin ble forbudt i 1995 og virginiamycin i 1998. Bacitracin er ikke forbudt, men benyttes ikke lenger som fôrtilsetningsstoff. Årlig forbruk av koksidiostatika har vært på samme nivå de siste seks årene, selv om forbruksmønsteret har endret seg. Narasin har dominert bruken siden 1996, mens bruken av andre ionofore koksidiostatika har sunket.

Den relativt gunstige situasjonen med hensyn til bruk av antibiotika i norsk landbruk gjenspeiler seg i en moderat forekomst av antibiotikaresistens blant bakterier isolert fra norske husdyr og animalske produkter.

Noe resistens ble avdekket ved undersøkelse av *Escherichia coli* fra hundefôr. Resistens mot henholdsvis streptomycin, tetracyklin, sulfonamider og ampicillin ble hyppigst observert. Det ble ikke påvist nedsatt følsomhet overfor kinoloner.

Forekomsten av resistens blant *Staphylococcus aureus* fra så vel klinisk som subklinisk mastitt hos ku er fortsatt på et relativt lavt nivå. Forekomsten av resistens var imidlertid høyere blant isolater fra subklinisk mastitt sammenlignet med isolater fra klinisk mastitt. Resistensfrekvensene gjenspeiler antibiotikaforbruket, i og med at terapeutisk vanlig brukte antibiotika som penicillin, streptomycin og trimetoprim/sulfa var de stoffene det oftest ble påvist resistens overfor. Det ble påvist en betydelig høyere forekomst av resistens blant koagulase-negative stafylokokker fra mastitt hos ku sammenlignet med *S. aureus*-isolatene.

S. intermedius fra hudinfeksjoner hos hund var ofte resistente mot sulfonamider, penicillin, fusidinsyre og tetracyklin. En betydelig andel var resistente mot erytromycin, spiramycin, klindamycin og streptomycin. Forekomsten av resistens mot trimetoprim/sulfa er fortsatt meget lav, mens resistens mot cefalosporiner og fluorokinoloner fortsatt ikke påvises. Stafylokokker fra øreinfeksjoner var hyppigere resistente mot fusidinsyre sammenlignet med stafylokokker fra øvrige hudinfeksjoner, mens det motsatte var tilfellet når det gjaldt pencillinresistens.

Til sammen 36% av *E. coli* fra kyllingkjøtt ble klassifisert som resistente mot ett eller flere av de antibiotika som inngikk i undersøkelsen; 16% mot ett, 11% mot to og 9% mot tre eller flere. Resistens mot sulfonamider ble hyppigst observert, etterfulgt av resistens mot henholdsvis streptomycin, tetracyklin, ampicillin, trimetoprim og nalidixinsyre. Til sammen 64 % av enterokokkene fra kyllingkjøtt ble klassifisert som resistente mot ett eller flere av de antibiotika som inngikk. Samlet sett var 38% av isolatene resistente mot kun ett antibiotikum, 22% mot to, og 4% mot fire eller flere antibiotika. Resistens mot bacitracin ble hyppigst observert, etterfulgt av resistens overfor tetracyklin, erytromycin, spiramycin, vankomycin og streptomycin (høygradig). Det er noe terapeutisk bruk av tetracyklin i norsk kyllingproduksjon.

Til sammen 25 % av *E. coli* fra svinekjøtt ble klassifisert som resistente mot ett eller flere av de antibiotika som inngikk i undersøkelsen; 5% mot ett, 7% mot to og 12% mot tre eller flere. Resistens mot streptomycin ble hyppigst observert, etterfulgt av resistens mot sulfonamider, tetracyklin, trimetoprim og ampicillin. Disse antibiotika brukes ofte terapeutisk i norsk svineproduksjonen. Det ble også observert noe resistens mot kloramfenikol, kanamycin og gentamicin. Til sammen 36% av enterokokkene fra svinekjøtt ble klassifisert som resistente mot ett eller flere av de antibiotika som inngikk. Sett under ett var 24% av isolatene resistente mot kun ett antibiotikum, 9% mot to og 2% mot tre eller flere antibiotika. Resistens mot tetracyklin ble hyppigst observert, etterfulgt av resistens mot bacitracin, trimetoprim, streptomycin (høygradig), erytromycin, spiramycin, kloramfenikol og gentamicin.

Resultatene fra resistensundersøkelsene av indikatorbakterier fra norsk kylling- og svinekjøtt var i overensstemmelse med resultatene fra tilsvarende undersøkelser i Norge i 1998. Dataene viser at fekale indikatorbakterier i norsk svine- og kyllingkjøtt kan være resistente mot ulike typer antibiotika. Generelt ble det hyppigst observert resistens mot de antibiotika som er blitt mest benyttet i de respektive næringer. Det synes følgelig å være en sammenheng mellom bruk av antibiotika til matproduserende dyr og forekomst av bakterier som uttrykker resistens mot tilsvarende antibiotika i kjøttprodukter fra slike dyr.

Blant *S. aureus* fra tankmelk i storfe- og geitebesetninger ble det påvist noe resistens mot penicillin og streptomycin. Forekomsten av resistens mot de ulike antibiotika er i overensstemmelse med bildet som er beskrevet for *S. aureus* fra klinisk mastitt hos storfe.

Alle ni *Salmonella*-isolater fra dyrefôr samt alle 14 *S.* Typhimurium-isolater fra norske dyr var følsomme for alle antibiotika som inngikk i undersøkelsen. Det ble ikke gjort funn av *S.* Enteritidis hverken fra dyr eller dyrefôr. Av de 22 *Salmonella*-isolatene fra dyr som ikke var *S.* Typhimurium, ble to klassifisert som

multiresistente – begge fra måker. To *S.* Typhimurium-isolater fra importerte næringsmidler, fra henholdsvis belgisk svinekjøtt og fransk kalkunkjøtt, ble identifisert som multiresistente DT104. Isolatet fra kalkunkjøtt var også resistent mot nalidixinsyre og viste intermediær følsomhet for ciprofloxacin. Øvrige salmonellaisolater fra næringsmidler var følsomme for de fleste antibiotika som inngikk i undersøkelsen, med unntak av at en relativt høy andel viste redusert følsomhet for henholdsvis kloramfenikol og tetracyklin.

Når det gjelder salmonella fra mennesker, var forekomsten av resistens blant *S.* Enteritidis moderat sammenlignet med *S.* Typhimurium og "*Salmonella* andre enn *S.* Enteritidis og *S.* Typhimurium". De rapporterte resistensfrekvensene er dessverre ikke delt inn i importerte tilfeller og tilfeller smittet i Norge. Blant *S.* Enteritidis-isolatene ble det påvist noe resistens mot henholdsvis tetracyklin, kloramfenikol, ampicillin og trimetoprim/sulfa, samt en relativt høy forekomst av resistens mot nalidixinsyre. Blant de øvrige salmonellaisolatene var det en høy forekomst av resistens mot henholdsvis kloramfenikol, tetracyklin, og ampicillin, og i noe mindre grad mot nalidixinsyre og trimetoprim/sulfa. Til sammen 33% av *S.* Typhimurium-isolatene ble identifisert som multiresistente DT104, hvorav 80% fra importerte tilfeller. Av de multiresistente DT104-isolatene var 6% resistente mot nalidixinsyre.

Forekomsten av resistens blant isolater av *Shigella* spp. fra mennesker var relativt høy. En betydelig andel av isolatene var resistente mot tetracyklin, trimetoprim/sulfa, kloramfenikol, ampicillin og nalidixinsyre. Andelen av salmonella- og shigella-isolater som var resistente mot ciprofloxacin var lav. Imidlertid uttrykte en betydelig andel intermediær følsomhet for ciprofloxacin, og mange av disse var også resistente mot nalidixinsyre.

Blant isolater av *Yersinia enterocolitica* fra mennesker ble det påvist noe resistens mot kloramfenikol. Ett isolat var resistent mot nalidixinsyre, mens 13% var intermediært følsomme for ciprofloxacin.

Isolater av *Campylobacter jejuni* og *C. upsaliensis* fra katt og hund var stort sett følsomme for de antibiotika som inngikk, med unntak av streptomycin, hvor 5% av *C. jejuni* og 90% av *C. upsaliensis* var resistente. Ett isolat av *C. upsaliensis* fra hund var resistent mot nalidixinsyre og intermediært følsomt for ciprofloxacin. Campylobacter-isolatene fra kyllingkjøtt var i hovedsak følsomme for de antibiotika som inngikk, bortsett fra ett isolat som var resistent mot nalixidinsyre og gentamicin. En betydelig andel av campylobacter-isolatene fra mennesker var resistente mot tetracyklin samt mot nalidixinsyre og ciprofloxacin. For alle disse var andelen resistente isolater høyere for *C. coli* enn for *C. jejuni*. En relativt stor andel av *C. coli* isolatene var resistente mot erytromycin.

Norsk Overvåkingssystem for Antibiotikaresistens hos Mikrober (NORM) ble etablert på bakgrunn av økende antibiotikaresistens i mange land. Enkelttilfeller av meticillinresistente *S. aureus* (MRSA), pneumokokker med nedsatt følsomhet for penicillin (PNSP), Enterobacteriaceae med utvidet β-laktamaseproduksjon (ESBL), vankomycinresistente enterokokker (VRE) og multiresistente *Mycobacterium tuberculosis* har også blitt rapportert fra Norge. Den foreliggende rapport dokumenterer imidlertid at antibiotikaresistens fortsatt var et begrenset problem i norsk helsevesen i år 2000. Kun ett enkelt MRSA-isolat ble påvist blant 158 *S. aureus* blodkulturisolater. Fire av 127 *Klebsiella* spp. blodkulturisolater produserte ESBL (3.2%), ingen av 168 *E. coli* blodkulturisolater hadde denne fenotypen. 2.6% av 340 pneumokkisolater fra luftvegsprøver ble kategorisert som intermediært følsomme for penicillin G, men alle disse isolatene hadde MIC-verdier (minste hemmende konsentrasjon) på 0.125 mg/L som er det laveste trinn i den ikke-følsomme kategorien. Blant 167 pneumokokk-isolater fra blodkulturer ble det påvist to stammer som ikke var fullt følsomme for penicillin G. Disse isolatene hadde MIC-verdier på henholdsvis 1 og 2 mg/L. Alle pneumokokkisolater fra blodkulturer ble kategorisert som følsomme for cefotaxim, det klinisk mest brukte cefalosporinet ved mistanke om systemisk pneumokokk- infeksjon. Det ble ikke funnet noen tilfeller av VRE. Som tidligere rapportert gjennom Meldesystemet for infeksjonssykdommer (MSIS) og Det norske tuberkuloseregisteret ble det i år 2000 påvist tre tilfeller av multiresistent *M. tuberculosis* blant 160 isolater (1.9%) fra pasienter som ikke tidligere er blitt behandlet for tuberkulose (MSIS rapport 2001. 29:18-19). Multiresistens er i denne sammenheng definert som resistens mot minst rifampicin og isoniazid.

I tillegg til effektiv overvåkning av disse spesielt viktige resistensfenomenene inneholder NORM 2000 detaljert informasjon om mange av de vanligst brukte antibiotika i Norge og de vanligste humanpatogene bakterier i daglig klinisk praksis. Majoriteten av *S. aureus* blodkultur-isolater produserer β-laktamase (74.5% av 158) mens kun 7.4% av 355 *H. influenzae* luftvegsisolater har denne egenskapen. Det er fortsatt høy grad av følsomhet for aminoglykosider blant Enterobacteriaceae (98.8% i *E. coli* og 99.2% i *Klebsiella* spp. blodkulturisolater), men 7.4% høygradig gentamicinresistens blant 121 *Enterococcus* spp. blodkulturisolater gir grunn til bekymring. 12.4% av enterokokkisolatene har nedsatt følsomhet for ampicillin. Man har grunn til å frykte at nedsatt ampicillinfølsomhet hos enterokokker kan bli et utbredt problem i norsk helsevesen slik det allerede har vist seg å være ved enkelte sykehus. Det høye nivået av nedsatt følsomhet for ampicillin og cefuroxim hos *E. coli* (98.2% nedsatt følsomhet for eller resistens mot ampicillin og 94.7% nedsatt følsomhet for eller resistens mot cefuroxim) og *Klebsiella* spp. (99.2% nedsatt følsomhet for eller resistens mot ampicillin og 82.6% nedsatt følsomhet for eller resistens mot cefuroxim) må sees i sammenheng med brytningspunktene som er definert av Den norske arbeidsgruppen for antibiotikaspørsmål (AFA). Det samme kan være tilfelle for makrolid-resistens i *H. influenzae* (18.9% nedsatt følsomhet for, og 78.3% resistens mot erytromycin blant 355 luftvegs-isolater), mens utviklingen av erytromycinresistens hos *S. pneumoniae* (2.4% i blodkulturisolater og 2.1% i luftvegsisolater) bør følges nøye. Makrolidresistens i *Streptococcus pyogenes* ble ikke undersøkt i NORM 2000, men vil bli inkludert i overvåkningsprogrammet på et senere tidspunkt. En annen resistensmekanisme som bør være gjenstand for

spesiell oppmerksomhet er forekomsten av fluorokinolonresistens i *E. coli* og *Klebsiella* spp. Problemet var fortsatt begrenset i NORM 2000 (henholdsvis 4.2% og 7.1% nedsatt følsomhet for ciprofloxacin i *E. coli* og *Klebsiella* spp. blodkultur-isolater), men forekomsten av høygradig nalidixinsyre-resistens i urinvegsisolater (3.2% blant 729 *E. coli* og 1.7% blant 58 *Klebsiella* spp.) antyder et potensiale for videre utvikling av kinolonresistens. Når man vurderer resultatene fra undersøkelsen av urinvegsisolater er det viktig å huske på at de fleste isolatene kommer fra forholdsvis banale infeksjoner. Flertallet av pasienter er trolig blitt empirisk behandlet med førstelinje-preparater, og forekomsten av resistens er derfor sannsynligvis ikke representativ for bakteriepopulasjon ved nydiagnostisert urinvegsinfeksjon.

Det er antagelig mange årsaker til den lave forekomsten av antibiotikaresistens i Norge, men totalforbruket av antibiotika og fordelingen av forbruk mellom ulike antibiotikagrupper så vel i sykehus som i allmenn-medisinen er utvilsomt en viktig faktor. Totalforbruket av antibiotika til systemisk bruk (ATC gruppe J01) hos mennesker var 16.3 DDD/1000 innbyggere/dag hvilket er sammenlignbart med nivået i resten av Skandinavia, men lavt i forhold til mange andre europeiske land (Cars *et al*., Lancet 2001;1851-53) (DDD=definerte døgn-doser). Salget av antibiotika har vært forholdsvis stabilt gjennom mange år. Det høyeste totalsalget av antibiotika ble registrert i 1993 med 17.8 DDD/1000 innbyggere/ dag, siden da har salget sunket jevnt. I år 2000 ble det påvist en svak reduksjon på 1% målt i DDD. Penicillinene (ATC gruppe J01C) utgjorde 43% av totalforbruket. De β-laktamase følsomme penicillinene (J01CE) og de bredspektrede penicillinene (J01CA) utgjorde henholdsvis 28.6% og 12.4% av totalsalget. Salget av penicilliner har vært stabilt over de siste 5 år. Det har imidlertid vært en endring i forbruket fra β-laktamase følsomme penicillinene (fra 31% J01CE i 1995 til 28% i 2000) til bredspektrede penicilliner (henholdsvis 10 og 12%). Tetracykliner utgjorde 19% av totalforbruket, salget har sunket med 34% siden 1993. Makrolidene (J01FA) utgjorde 9% av totalforbruket. Methenamine, som brukes til profylakse mot urinvegsinfeksjoner, utgjorde 12% av totalforbruket; salget har økt med 50% siden 1995. Salget av cefalosporiner er begrenset (3% av totalforbruket) men har økt jevnt over de siste år. Salget av makrolider og aminoglykosider har vært stabilt, mens salget av sulfonamider og trimetoprim har sunket med 34% siden 1995. Salget av disse stoffene utgjorde 7% av totalforbruket i år 2000. Det har vært en svak men jevn stigning i forbruket av fluorokinoloner. Forbruket utgjør fortsatt kun 2% av totalforbruket, men økningen har vært på hele 35% siden 1995.

Den lave forekomsten av antibiotikaresistens vist for år 2000 må ikke føre til selvtilfredshet. Årsakene til antibiotikaresistens er fortsatt kun delvis avdekket, og det gjenstår mye arbeid med hensyn til å definere en forsvarlig antibiotikapolitikk. Mange mikrobearter er enda ikke inkludert i NORM/NORM-VET og bør undersøkes nærmere i kommende år. Nye antimikrobielle midler blir regelmessig introdusert på markedet, og mulig resistensutvikling mot disse stoffene bør overvåkes nøye. For å bevare den gunstige situasjonen vi for øyeblikket har i Norge, må alle deler av samfunnet bidra slik det er beskrevet i "Regjeringens tiltakssplan for å motvirke antibiotikaresistens (2000-2004)". NORM og NORM-VET har viktige roller å spille i både overvåkning og forebyggelse av antibiotikaresistens. Utdanning og økt bevissthet omkring resistensproblemer vil føre til at kvaliteten i det diagnostiske arbeidet blir hevet på mange laboratorier. Standardisering av lokale resistensdata muliggjør sammenlikning av resultatene mellom ulike sykehus og regioner. Data innsamlet i NORM kan brukes lokalt slik at spesifikke tiltak kan settes i verk før resistensproblemer kommer ut av kontroll. På det nasjonale plan bør resultatene fra NORM/NORM-VET brukes når brytningspunkter for følsomhet og resistens skal defineres og retningslinjer for antibiotikabruk skal utformes. Den foreliggende rapport er derfor kun et utgangspunkt i det videre arbeidet for å forebygge og motvirke utvikling og spredning av antibiotikaresistens.

II. SUMMARY

The use of antimicrobial agents in animals in Norway is low compared to many other industrialized countries, and the consumption pattern is rather favourable. The total sale of veterinary antibacterial drugs approved in Norway for therapeutic use in animals was 5 750 kg in 2000, a 39% decrease since 1995. The proportion of penicillins of the total use increased from 36% in 1995 to 44% in 2000. In the same period, the proportion accounted for by aminoglycosides decreased from 27% to 20 %. In 2000, penicillins represented the most frequently used drugs, followed by sulfonamides (27%), aminoglycosides (20%), tetracyclines (3%), trimethoprim and derivatives (3%), and others (4%). The total sale in Norway of veterinary antibacterial drugs for therapeutic use in farmed fish was 685 kg active substance in 2000, of which quinolones accounted for 76%. During the past 13 years, the total use of antibacterial drugs in farmed fish has decreased by 99%. In the same period, the total production has increased manifold. This decrease in antibacterial consumption is mainly attributed to the introduction of effective vaccines, although improved management and husbandry in aquaculture also play a role.

Antibacterial growth promoters are no longer used in Norwegian animal production. Avoparcin was banned in 1995 and virginiamycin in 1998. Bacitracin has not been banned, but is no longer in use as a growth promoter. The annual consumption of coccidiostats has remained stable through the past six years. Since 1996, narasin has been the most commonly used coccidiostat, and the sale of the other substances in this group has been decreasing.

The relatively favourable situation with regard to usage of antimicrobials in Norwegian animal food production is reflected in a moderate occurrence of antimicrobial resistance among bacteria from Norwegian animals and animal products.

Antimicrobial susceptibility testing of *E. coli* from commercially available meat by-products intended for canine consumption revealed some resistance. Resistance to streptomycin, tetracycline, sulphonamides and ampicillin, respectively, were most common. No reduced susceptibility to quinolones was observed.

The occurrence of resistance among *Staphylococcus aureus* from clinical and subclinical mastitis in cows remained quite low. However, the occurrence was relatively higher among isolates from subclinical mastitis as compared to those from clinical mastitis. The resistance frequencies for the various antimicrobials reflect the usage; penicillin, streptomycin, and sulfonamides/trimethoprim being commonly used for clinical purposes. Resistance in coagulase negative staphylococci from mastitis in cows was considerably more abundant as compared to *S. aureus* isolates.

S. intermedius from skin infections in dogs were frequently resistant to sulfonamides, penicillin, fucidic acid, and tetracycline. Also, a considerable proportion of the isolates were resistant to erythromycin, spiramycin, clindamycin, and streptomycin, respectively. Resistance to trimethoprim/sulfonamides has remained very low, whereas resistance to cephalosporins as well as to fluoroquinolones has remained negligible. Staphylococci from ear infections tend to be more frequently resistant than staphylococci from other skin infections.

A total of 36% of *E. coli* from poultry meat were classified as resistant to one or more of the antimicrobials included; 16% to one, 11% to two, and 9% to three or more antimicrobials. Resistance to sulfonamides was most common, followed by resistance to streptomycin, tetracycline, ampicillin, trimethoprim, and nalidixic acid. A total of 64% of the enterococci from poultry meat were classified as resistant to one or more of the antimicrobials included. In total, 38% of the isolates were resistant to only one antimicrobial, 22% to two, and 4% to three or more antimicrobials. Resistance to bacitracin was most common, followed by resistance to tetracycline, erythromycin, spiramycin, vancomycin, and streptomycin (high-level). There is some use of tetracycline for clinical purposes in Norwegian poultry production.

A total of 25% of *E. coli* from pork were classified as resistant to one or more of the antimicrobials included; 5% to one, 7% to two, and 12% to three or more antimicrobials. Resistance to streptomycin was most common, followed by resistance to sulfonamides, tetracycline, trimethoprim, and ampicillin - all these antimicrobials being commonly used for clinical purposes in swine production. Some resistance to chloramphenicol, kanamycin, and gentamicin was also observed. A total of 36% of the enterococci from pork meat were classified as resistant to one or more of the antimicrobials included. In total, 24% of the isolates were resistant to only one antimicrobial, 9% to two, and 2% to three or more antimicrobials. Resistance to tetracycline was most common, followed by resistance to bacitracin, trimethoprim, streptomycin (high-level), erythromycin, spiramycin, chloramphenicol, and gentamicin.

The results from the susceptibility testing of indicator bacteria from pork and poultry meat were in accordance with results from similar surveys of Norwegian poultry and pork in 1998. The results show that faecal indicator bacteria from pork and poultry meat of Norwegian origin may be resistant to various kinds of antimicrobials. In general, resistance was most commonly observed to the antimicrobials most commonly used in the respective productions. Thus, there appears to be an association between the use of antimicrobials in animal production and the occurrence of resistance to the same antimicrobials among bacteria from related food products.

Among *S. aureus* isolates from bulk milk tank samples from dairy cows and goats some resistance to penicillin and streptomycin was detected. The prevalence of resistance to the various antimicrobials is in accordance with what was found for *S. aureus* isolates from clinical mastitis in cows.

All nine isolates of *Salmonella* from animal feeds and all 14 isolates of *S.* Typhimurium from Norwegian animals were susceptible to all antimicrobials included. No *S.*

Enteritidis was isolated from animal feed or animals. Out of the 22 isolates of *Salmonella* other than *S.* Typhimurium from animals, two were multiresistant, both isolated from seagulls. Two of the *S.* Typhimurium isolates from imported food, one from Belgian pork and one from French turkey, were identified as multiresistant *S.* Typhimurium DT104. The isolate from turkey was also resistant to nalidixic acid and intermediately susceptible to ciprofloxacin. The other *Salmonella* isolates from food were susceptible to most antimicrobials included, except for a relatively high proportion showing reduced susceptibility to tetracycline and/or chloramphenicol.

With regard to *Salmonella* isolates from humans, the occurrence of resistance among *S.* Enteritidis was moderate as compared to *S.* Typhimurium and "*Salmonella* other than *S.* Enteritidis and *S.* Typhimurium". Unfortunately, the resistance frequencies reported are not stratified on domestically acquired and imported cases. Among the *S.* Enteritidis isolates, some resistance to tetracycline, chloramphenicol, ampicillin, and trimethoprim/sulfonamides, respectively, was observed, as well as a relatively high occurrence of resistance to nalidixic acid. Among the other salmonella isolates, a high occurrence of resistance to chloramphenicol, tetracycline, and ampicillin, and to a somewhat lesser degree, to nalidixic acid and trimethoprim/sulfonamides, was observed. In total, 33% of the *S.* Typhimurium isolates were identified as multiresistant DT104, 80% of these from imported cases. Of the multiresistant DT104 isolates, 6% were also resistant to nalidixic acid.

The occurrence of resistance among human isolates of *Shigella* spp. was relatively high. A considerable proportion of the isolates were resistant to tetracycline, trimethoprim/sulfonamides, chloramphenicol, ampicillin, and nalidixic acid, respectively. In general, the proportion of *Salmonella* and *Shigella* isolates being resistant to ciprofloxacin was low. However, a considerable proportion expressed intermediate susceptibility to ciprofloxacin, and many of these were also resistant to nalidixic acid.

Some resistance to chloramphenicol was observed among human isolates of *Yersinia enterocolitica*. One isolate was resistant to nalidixic acid, whereas 13% were classified as intermediately susceptible to ciprofloxacin.

The *Campylobacter jejuni* and *C. upsaliensis* isolates from cats and dogs were in general susceptible to the antimicrobials included, except that 90% of the *C. upsaliensis* and 5% of the *C. jejuni* isolates expressed resistance to streptomycin. One *C. upsaliensis* isolate from a dog was resistant to nalidixic acid and intermediately susceptible to ciprofloxacin. The *Campylobacter* spp. isolates from poultry meat were in general susceptible to the antimicrobials included except for one that was resistant to nalidixic acid and gentamicin. A considerable proportion of the *Campylobacter* spp. isolates from human patients were resistant to tetracycline and to the quinolones nalidixic acid and ciprofloxacin, respectively, the proportion being higher for *C. coli* as compared to *C. jejuni* isolates. The proportion of isolates that were resistant to erythromycin was relatively high for *C. coli* isolates.

The NORM surveillance program was established in response to reports from other countries where antimicrobial resistance among human pathogens is now commonplace. Methicillin resistant *S. aureus* (MRSA), penicillin non-susceptible pneumococci (PNSP), Enterobacteriaceae containing extended spectrum β-lactamases (ESBL), vancomycin resistant enterococci (VRE) and multiresistant *Mycobacterium tuberculosis* have also occasionally been reported from Norway. However, the present report documents that antimicrobial resistance was still a limited problem in Norwegian hospitals and general practice in the year 2000. Only a single MRSA isolate was detected among 158 blood culture isolates included in the program. Four out of 127 *Klebsiella* spp. blood culture isolates were ESBL producers (3.2%), none of 168 *E. coli* blood culture isolates displayed this phenotype. 2.6% of 340 respiratory tract pneumococcal isolates were categorized as intermediately susceptible to penicillin G, but these isolates all had MIC (minimal inhibitory concentrations) values of 0.125 mg/L which is the lowest level of non-susceptibility. Among the 167 pneumococcal blood culture isolates, two isolates were non-susceptible to penicillin G with MIC values of 1 and 2 mg/L, respectively. All pneumococcal blood culture isolates were categorized as susceptible to the 3rd generation cephalosporin cefotaxime. No VRE were detected. As previously reported through the Norwegian Surveillance System for Communicable Diseases (MSIS) and the Norwegian Tuberculosis Register, in the year 2000, only three of 160 (1.9%) *M. tuberculosis* isolates from patients not previously treated for tuberculosis were multiresistant when defined as resistant to at least rifampicin and isoniazid (MSIS rapport 2001. 29: 18-19).

In addition to efficient surveillance of these prime examples of antimicrobial resistance problem phenotypes, NORM 2000 provides detailed information about many of the most commonly used antibiotics used in Norway and many of the most important human pathogens seen in daily clinical practice. The majority of *S. aureus* blood cultures isolates produced β-lactamases (74.5% of 158), whereas this capacity was only detected in 7.1% of 355 *H. influenzae* respiratory tract isolates. The susceptibility to aminoglycosides was still very high among Enterobacteriaceae (98.8% in *E. coli* and 99.2% in *Klebsiella* spp. blood culture isolates), but the 7.4% of 121 *Enterococcus* spp. blood culture isolates with high-level resistance to gentamicin gives reason for concern. 12.4% non-susceptibility to ampicillin among these enterococcal isolates may also indicate future problems as have already been experienced in some Norwegian hospitals. The high levels of non-susceptibility to ampicillin and cefuroxime in *E. coli* (98.2% non-susceptibility to ampicillin and 94.7% non-susceptibility to cefuroxime) and *Klebsiella* spp. (99.2% non-susceptibility to ampicillin and 82.6% non-susceptibility to cefuroxime) must be interpreted in context with the breakpoints defined by the Norwegian Reference Group on Antibiotic Susceptibility Testing (AFA). The same may be true for macrolide resistance in *H. influenzae* (18.9% intermediately susceptible and 78.3% resistant to erythromycin among 355 respiratory tract isolates), while the occurrence of erythromycin resistance in *S.*

pneumoniae gives reason for concern (2.4% in blood culture isolates and 2.1% in respiratory tract isolates). Macrolide resistance in *Streptococcus pyogenes* was not monitored in NORM 2000 but will be included in the program on a later date. Another resistance mechanism that deserves further attention is the level of fluoroquinolone resistance in *E. coli* and *Klebsiella* spp. The problem was still limited in NORM 2000 (4.2% and 7.1% non-susceptiblity to ciprofloxacin among blood culture isolates of *E. coli* and *Klebsiella* spp., respectively), but the occurrence of high-level resistance to nalidixic acid in urinary tract isolates (3.2% among 729 *E. coli* and 1.7% among 58 *Klebsiella* spp. isolates) indicates a potential for further development of quinolone resistance. When reading the resistance data on urinary tract pathogens, the reader should keep in mind that most of these isolates originate from infections of limited severity. The majority of patients have presumably been empirically treated with first-line antibiotics, and the rates of resistance are therefore probably not representative for pathogens in newly diagnosed urinary tract infections.

There are probably many reasons for the low level of antimicrobial resistance in Norway, but the level and profile of antimicrobial consumption in both hospitals and general practice is undoubtedly an important factor. The overall consumption of antibacterials for systemic use (ATC group J01) in humans was 16.3 DDD/1000 inhabitants/day, which is comparable to the level in the rest of Scandinavia, but lower than in many other European countries (Cars *et al*., Lancet 2001:1851-53) (DDD=Defined Daily Doses). Sales of antibacterials have remained relatively unchanged for many years. The highest total sale of antibacterials ever was registered in 1993 with 17.8 DDD/1000 inhabitants/day. Since then the sales have been decreasing. In 2000, a small decrease of 1% measured in DDDs was seen. The penicillins (ATC group J01C) represented 43% of the total antimicrobial use. The β-lactamase sensitive penicillins (J01CE) and penicillins with extended spectrum (J01CA) represented 28.6% and 12.4%, respectively. The sales of penicillins have been stable over the past 5 years. There has, however, been a change in use from the β-lactamase sensitive penicillins (31% of J01 in 1995 to 28% in 2000) to penicillins with extended spectrum (10% and 12% respectively). Tetracyclines represented 19% of total use. The sales have decreased by 34% since 1993. The macrolides (J01FA) represented 9% of the total use. The urinary prophylactic agent methenamine represented 12% of total use; the sales have increased by 50% since 1995. The sales of cephalosporins, although limited, have also increased over the years and represented 3% of the total antibacterials in the year 2000. The sales of the macrolides and aminoglycosides are stable, but the sales of sulfonamides and trimethoprim have decreased by 34% since 1995. The sales equal 7% of total sales in 2000. There has been a small, but stable increase in quinolone use over the years. It represented only a minor fraction (2%) of the antibacterials, but the increase has been 35% since 1995.

The low level of antimicrobial resistance revealed in 2000 should not lead to complacency. The causes of antimicrobial resistance are not fully understood, and much work remains to be done in order to define prudent antimicrobial practices. Many bacterial species have not yet been included in NORM/NORM-VET and will need closer attention in the years to come. New antimicrobials are regularly introduced, and possible development of resistance to these compounds should be closely monitored. In order to preserve the favourable situation we presently have in Norway, all parts of society must participate as described in the Plan of Action to Combat Resistance to Antibiotics (2000–2004) (Royal Ministry of Health and Social Affairs, March 7th 2000). NORM and NORM-VET have important roles to play, not only in surveillance, but also in the prevention of anti-microbial resistance. Education and increased awareness of antimicrobial resistance will improve the quality of diagnostic procedures in many laboratories, and standardization of local resistance data will enhance comparability between regions and hospitals. Data generated in NORM can be used locally to specifically target challenges before the situation gets out of control. On the national level, results from NORM and NORM-VET should be used when susceptibility breakpoints are defined and antibiotic guidelines are issued. The present report is therefore only a starting point for further efforts to prevent and contain antimicrobial resistance.

III. INTRODUCTION

Antimicrobial resistance is an increasing problem worldwide. It affects the treatment of infectious diseases in both humans and animals resulting in increased morbidity and mortality, as well as increased costs. It is well established that there is an association between the usage of antimicrobial agents and the occurrence of resistance. The selective pressure of antimicrobial usage is a key issue in the epidemiology of resistance. Moreover, resistance can be disseminated through the spread of resistant pathogenic bacteria themselves or by horizontal transfer of resistance genes from one type of bacteria to another. Such transfer is not limited to closely related bacteria; it can also take place between bacteria of different evolutionary and/or ecological origin. Antimicrobial usage and resistance in one compartment can thus have consequences for the occurrence of resistance in another compartment. When addressing antimicrobial resistance – the occurrences, causes, consequences, and preventive measures – one must therefore take a holistic view encompassing both usage and resistance in human and veterinary medicine, as well as in the food production sector.

In recent years, several countries have implemented surveillance programs for antimicrobial resistance and antimicrobial usage. Many programs focus primarily on human consumption and resistance, but some countries also include data concerning veterinary medicine and food production. This broad approach was supported by the EU in 1998 through the Copenhagen declaration and more recently at the conference in Visby, Sweden 2001. The WHO has published similar guidelines. In response to the growing concern about antimicrobial resistance, the Norwegian Ministry of Health and Social Affairs issued a national action plan against antimicrobial resistance (2000–2004) in March 2000. Again, the importance of monitoring both the human and veterinary sector, including food production, was emphasized. A surveillance program for antimicrobial resistance in human pathogens was established in Norway in 1999 – NORM. Ten medical microbiological laboratories participated in the year 2000, and the program is coordinated by the Microbiological Department at the University Hospital of Tromsø. A continuous monitoring program for antimicrobial resistance in the veterinary and food sector was established in 2000 – NORM-VET. NORM-VET is coordinated by the Norwegian Zoonosis Centre in Oslo. A detailed surveillance system for all drug prescription in Norway including antimicrobials is presently being discussed.

This report presents the results from NORM and NORM-VET for the year 2000. In addition, data on the consumption of antimicrobial agents in humans and animals in Norway are presented. The data will serve as a basis for the interpretation and evaluation of trends in antimicrobial usage and the occurrence of resistance in Norway in the future. The results from this report may not be directly comparable to results from monitoring programs in other countries due to differences in sampling schemes, methodology, and breakpoints for resistance and susceptibility. However, the extensive use of MICs (minimal inhibitory concentrations) and other continuous parameters of resistance will ensure comparability with similarly structured surveillance programs. Standardization of sampling schemes and microbiological methods ensure that repeated investigations can demonstrate changes in resistance levels and patterns and how these changes may be related to usage of antimicrobials. The data from NORM/ NORM-VET 2000 should therefore form a basis for further efforts to prevent and combat antimicrobial resistance.

The editors would like to thank all those who contributed to data collection and writing of this report.

Tromsø / Oslo, December 2001

IV. DEMOGRAPHIC DATA

To facilitate comparison of Norwegian data on consumption of antimicrobial agents and occurrence of resistance with corresponding figures from other countries, basic demographical data concerning both human and animal populations are presented. The data are collected by Norwegian authorities as indicated for each table.

TABLE 1. Human population in Norway as of January 1st, 2000. Data provided by Statistics Norway.

Age group	All	Males	Females
0 to 4 years	302 387	155 258	147 129
5 to 14 years	592 330	304 038	288 292
15 to 24 years	544 122	277 343	266 779
25 to 44 years	1 330 900	678 497	652 403
45 to 64 years	1 025 726	518 169	507 557
65 years and older	683 032	283 835	399 197
All age groups	4 478 497	2 217 140	2 261 357

TABLE 2. Livestock population in Norway as of January 1st, 2000. Data provided by Statistics Norway.

Animal category	Animals	Herds
Cattle, total	1 018 700	29 400
Dairy cows (incl. in above total)	318 000	22 400
Goats, total	71 200	1 400
Dairy goats (incl. in above total)	53 100	700
Sheep, winterfed	1 081 400	21 600
Swine, total	654 000	4 500
Swine, breeding animals > 6 months	93 800	3 400
Egg laying hens (>20 weeks of age)	3 216 800	3 800
Broilers		480
Turkeys		100
Ducks and geese		100

TABLE 3. Number of animals slaughtered in 2000*. Data provided by The Norwegian Food Control Authority (terrestrial animals) and Directorate of Fisheries (fish).

Animal category	Slaughtered animals
Horse	2 300
Cattle	381 300
Goats	21 400
Sheep	1 158 600
Swine	1 366 800
Poultry	39 915 800
Ostrich	300
Reindeer	26 300
Farmed salmon**	432 666
Farmed trout**	45 953

* Rounded to nearest hundred

** Amount in 1 000 kg, ungutted fish

V. CONSUMPTION OF ANTIMICROBIAL AGENTS

A. ANIMAL CONSUMPTION

Antibacterial growth promoters and coccidiostats

Data on the usage of the different substances and categories of feed additives was obtained from the Norwegian Agricultural Inspection Service. Table 4 summarizes the total sales of antibacterial growth promoters and coccidiostats in Norway for the period 1994-2000.

In 1995, the glycopeptide avoparcin that had been on the Norwegian market since 1986 as a growth promoter in poultry production was prohibited because an association between the use of this antibacterial feed additive and the occurrence of vancomycin resistant enterococci in animal husbandry was reported. The same year the Norwegian food animal production industries voluntarily abandoned the use of all antibacterial growth promoters. Since then, there has been almost no use of antibacterial growth promoters in Norwegian food animal production. In 1998, the streptogramin virginiamycin was officially prohibited due to reports from other countries of an association between the use of this drug and the occurrence of enterococci being resistant to quinupristin-dalfopristin, a combination of streptogramins used in human medicine.

Coccidiostats, however, are still being used in Norwegian poultry production. The total sales, in kg active substance, are at the same level as before the ban of the antibacterial growth promoters was implemented. However, the pattern of use has changed. Narasin has since 1996 dominated the use of coccidiostats, whereas the use of other ionophores has decreased correspondingly.

TABLE 4. Total sales of antibacterial growth promoters and coccidiostats in Norway 1994-2000.

Compound	Total sales in kg active substance						
	1994	1995	1996	1997	1998	1999	2000
Avoparcin	982	419*	Prohibited	Prohibited	Prohibited	Prohibited	Prohibited
Zincbacitracin	234	129	64	27	0	0	0
Virginiamycin	0	0	0	0	0*	Prohibited	Prohibited
Total antibacterial growth promoters	**1 216**	**548**	**64**	**27**	**0**	**0**	**0**
Lasalocid	3 896	996	480	471	193	208	80
Monensin	844	3 422	891	561	485	557	776
Salinomycin	482	214	27	0	0	27	233
Narasin	0	24	3 508	3 343	3 530	4 062	4 486
Total ionophore coccidiostats	**5 222**	**4 656**	**4 906**	**4 375**	**4 208**	**4 854**	**5 575**
Amprolium/etopabat	165	156	116	582	174	201	135
Total other coccidiostats	**165**	**156**	**116**	**582**	**174**	**201**	**135**

* Prohibited part of the year

Usage of veterinary antibacterial drugs for therapeutic use

Data on sales of antibacterial drugs were collected from all the Norwegian drug wholesalers. Although this report primarily presents resistance data for 2000, trends in the prescribing patterns of veterinary antibacterial drugs for the period 1995-2000 are included to show the preceding antibacterial load in the domestic animal population and in Norwegian fish farming.

The majority of the agents included in this report are approved as pharmaceutical formulations both for food producing animals, horses, and/or dogs and cats. Therefore, the sales figures presented represent overall sales data of veterinary antibacterial drugs.

Table 5 summarizes the amount of veterinary antibacterial drugs approved for therapeutic use in domestic animals in Norway delivered by wholesalers in 2000. They are presented according to the main groups of antibacterial agents, and show the usage for the various routes of administration. The total usage for each group of substance is given in Figure 1, while Figure 2 illustrates the proportion of the total sale for the various main groups of antibacterial substances. Both figures present annual sales data for the period 1995-2000.

The total sales of veterinary antibacterial agents approved for therapeutic use in animals in 2000 was 5750 kg active substance, a 39% decrease since 1995. The proportion of penicillins used increased from 36% in 1995 to 44% in 2000. The relative amount of aminoglycosides decreased from 27% to 20% in the same time period,. In 2000, penicillins were the most frequently used drugs (44%), followed by sulfonamides (27%), aminoglycosides (20%), tetracyclines (3%), trimethoprim and derivatives (3%), and others (4%).

In Norway, medicated feeds and premix for farmed fish are approved by the drug authorities and classified as pharmaceutical formulations. Sales figures, in kg active substance, of such products and premixes containing antibacterial drugs are presented in Table 6. In 2000, the total sale of veterinary antibacterial drugs in Norway for therapeutic use in farmed fish was 685 kg. Quinolones accounting for 76% of the use. The annual use of antibacterial drugs declined by 99% during the period 1987-2000. In the same period, the total production of farmed fish increased manifold. This decrease in the use of antibacterial drugs is mainly attributed to the introduction of effective vaccines and improved environmental conditions in aquaculture.

TABLE 5. Sales (in kilograms of active substance) in 2000 of veterinary antibacterial drugs approved in Norway for therapeutic use in animals, fish not included. Data were obtained from the Norwegian drug wholesalers.

Groups of substances	ATCvet code	Active substance or combinations of substances	Gastro-intestinal (QA07)	Uterine (QG01)	Systemic individual (QJ01)	Systemic herds (QJ01)	Intra-mammary (QJ51)
Tetracyclines	QG01AA07	Oxytetracycline		3			
	QJ01AA02	Doxycycline			<0.1		
	QJ01AA06	Oxytetracycline			82	81	
β-lactam	QJ01CA01	Ampicillin			20		
antibacterials	QJ01CA04	Amoxycillin			53	54	
	QJ01CE09	Phenoxymethylpenicillin				< 0.1	
	QJ01CE09	Procaine penicillin*			1 896		
	QJ01CE90/ QJ51CE90	Penethamate hydroiodide*			15		6
	QJ01CR02/ QJ51RV01	Amoxicillin+clavulanic acid			89		6
	QJ51CA51	Ampicillin + cloxacillin					2
Sulfonamides	QJ01EQ03	Sulfadimidine + baquiloprim			0.2		
and trimethoprim or	QJ01EQ09	Sulfadimetoxine + baquiloprim			1		
baquiloprim	QJ01EQ10	Sulfadiazine + trimethoprim			902		
	QJ01EQ13	Sulfadoxine + trimethoprim			123		
	QJ01EQ15	Sulfamethoxypyridazine			485		
Lincosamides	QJ01FF02	Lincomycin			8		
Aminoglycosides	QA07AA01	Neomycin	35				
	QA07AA90	Dihydrostreptomycin (DHS)	162				
Quinolones	QJ01MA90	Enrofloxacin			17		
Others antibacterials	QJ01XX92	Tiamulin			6	171	
Combinations of antibacterials	QG01AE99	Sulfadimidine + procaine penicillin* + DHS		227			
	QJ01RA01	Procaine penicillin* + DHS			645		
	QJ01RA01	Spiramycin+metronidazole			6		
	QJ51RC23	Procaine penicillin* + DHS					604
	QJ51RC25	Penethamate hyd.* + DHS					51
	Total per route of administration:		**197**	**230**	**4 348**	**306**	**669**
						Total:	**5 750**

*Calculated as benzylpenicillin

Table 6. Total sales (in kilograms of active substance) for the period 1995-2000 of veterinary antibacterial drugs for therapeutic use in farmed fish in Norway. Data were obtained from Norwegian wholesalers and feed mills.

Groups of substances	ATCvet code	Active substance	1995	1996	1997	1998	1999	2000
Tetracyclines	QJ01AA06	Oxytetracycline	70	27	42	55	25	15
Amphenicols	QJ01BA90	Florfenicol	64	64	123	135	65	148
Antibacterial quinolones	QJ01MB07	Flumequine	182	105	74	53	7	52
	QJ01MB91	Oxolinic acid	2 800	841	507	436	494	470
Total			**3 116**	**1 037**	**746**	**679**	**591**	**685**

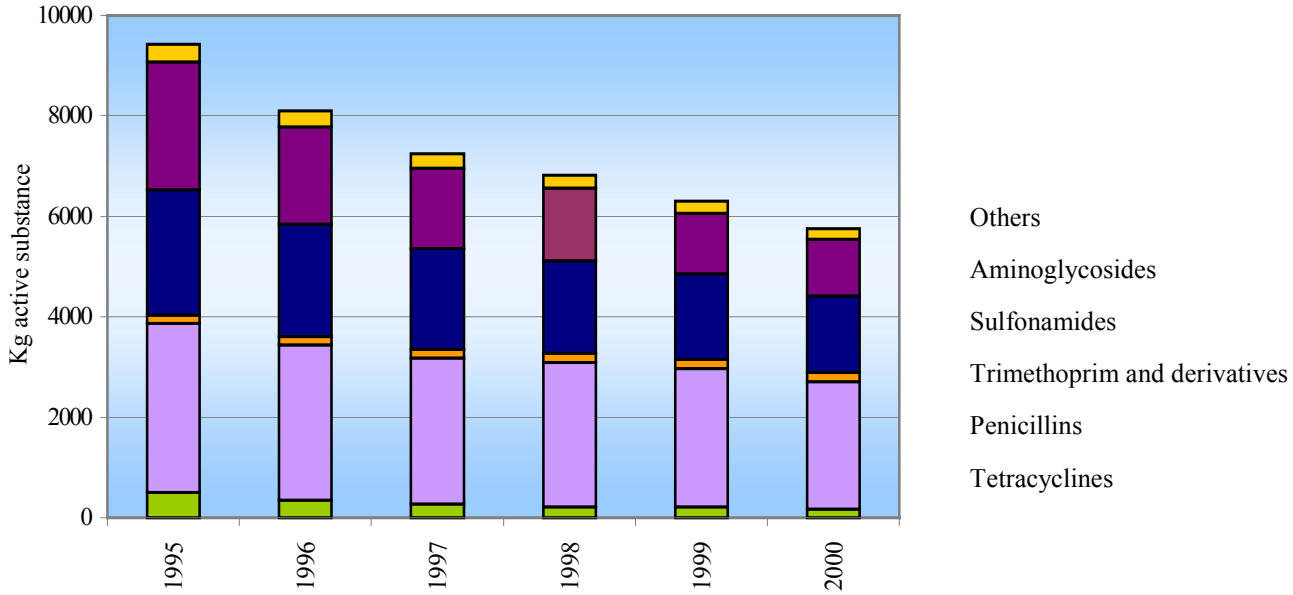


FIGURE 1. Sales (in kg active substance) in 1995–2000 of veterinary antibacterial drugs (QA07AA; QG01AA; QG01AE; QJ01; QJ51) for therapeutic use in Norway, fish not included. (Others: Macrolides, lincosamides, quinolones, and imidazoles).

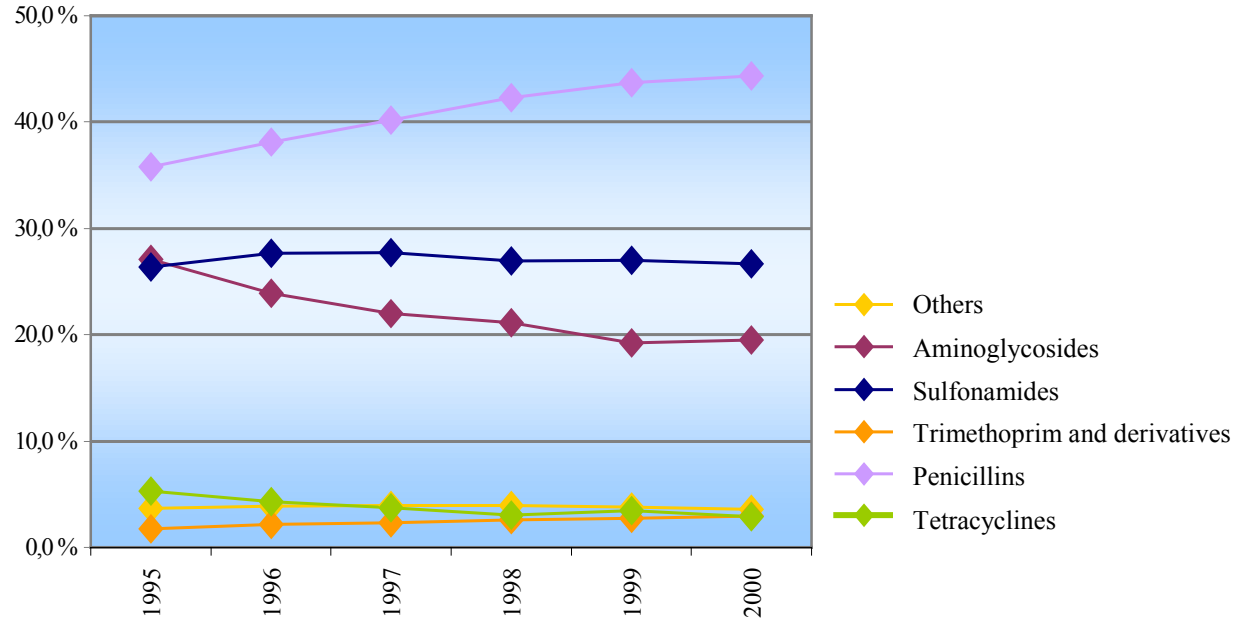


FIGURE 2. Sales (as percentage of total sales) for the period 1995–2000 of veterinary antibacterial drugs (QA07AA; QG01AA; QG01AE; QJ01; QJ51) in Norway, fish not included (Others: Macrolides, lincosamides, quinolones, and imidazoles).

B. HUMAN CONSUMPTION

In 2000, the overall consumption of antibacterials for systemic use (ATC group J01) in humans represented 16.3 DDD/1000 inhab./day. Sales of antibacterials have remained relatively unchanged for many years. The highest total sale of antibacterials ever was registered in 1993; 17.8 DDD/1000 inhabitant/day. Since then the sale has been decreasing. In 2000, a small decrease of 1% measured in DDDs was seen.

TABLE 7. Human consumption of antibacterial agents in Norway 1995-2000 by ATC groups. The consumption is presented as Defined Daily Doses (DDD)/inhabitants/day and % change 1995-2000. Collection of data on human consumption of antimicrobial agents is presented in Appendix 2.

ATC	Groups of substances	1995	1996	1997	1998	1999	2000	Change (%) 1995-2000
J01AA	Tetracyclines	4.14	3.66	3.55	3.37	3.19	3.17	- 23.4
J01BA	Amphenicols	0.01	0.005	0.01	0.00	0.01	0.00	
J01CA	Penicillins with extended spectrum	1.72	1.733	1.87	1.90	1.96	2.01	+ 17.0
J01CE	β-lactamase sensitive penicillins	5.41	5.08	5.32	5.12	5.01	4.66	- 13.8
J01CF	β-lactamase resistant penicillins	0.186	0.21	0.24	0.27	0.32	0.35	+ 88.2
J01CR	Combination of penicillins	0.004	0.01	0.02	0.01	0.01	0.01	+ 122.5
J01DA	Cephalosporins	0.444	0.435	0.41	0.43	0.46	0.50	+ 12.0
J01DF	Monobactams	0.00	0.00	0.00	0.00	0.00	0.00	
J01DH	Carbapenems	0.01	0.006	0.01	0.01	0.01	0.02	
J01EA	Trimethoprim and derivatives	0.986	0.93	0.90	0.87	0.84	0.79	- 19.9
J01EB	Short-acting sulfonamides	0.01	0.001	0.00	0.00	0.00	0.00	
J01EC	Intermediate-acting sulfonamides	0.001	0.003	0.00	0.00	0.00		
J01EE	Comb. of sulfonamides and trimethoprim, incl. derivatives	0.800	0.64	0.55	0.47	0.42	0.38	- 52.5
J01FA	Macrolides	1.48	1.404	1.48	1.50	1.48	1.47	- 0.7
J01FF	Lincosamides	0.10	0.101	0.10	0.11	0.11	0.12	+ 25.8
J01GB	Other aminoglycosides	0.05	0.047	0.05	0.05	0.05	0.04	
J01MA	Fluoroquinolones	0.25	0.259	0.27	0.29	0.32	0.34	+ 38.1
J01MB	Other quinolones	0.02	0.016	0.01	0.01	0.01	0.01	
J01XA	Glycopeptide antibacterials	0.01	0.006	0.01	0.01	0.00	0.01	
J01XB	Polymyxins	0.00	0.002	0.00	0.00	0.00	0.00	
J01XC	Steroid antibacterials	0.002	0.003	0.00	0.00	0.00	0.00	
J01XD	Imidazole derivatives	0.054	0.053	0.06	0.06	0.06	0.06	+ 16.7
J01XE	Nitrofuran derivatives	0.393	0.393	0.38	0.38	0.37	0.37	- 6.4
J01XX	Other antibacterials	1.29	1.44	1.61	1.75	1.91	1.95	+ 51.1
	Total	**17.4**	**16.4**	**16.8**	**16.6**	**16.6**	**16.3**	**- 6.3**

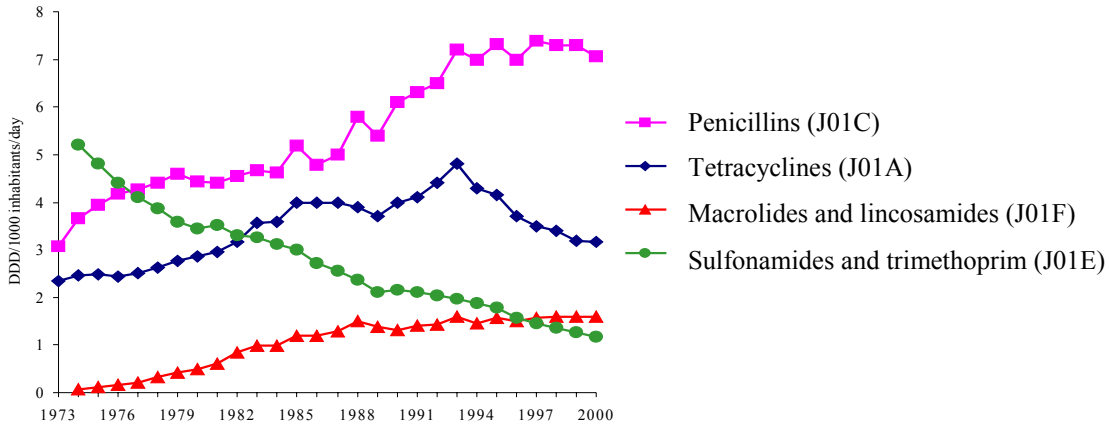


FIGURE 3. Sales of penicillins (J01C), tetracyclines (J01A), macrolides and lincosamides (J01F), and sulfonamides and trimethoprim (J01E) in Norway 1973-2000.

The penicillins (ATC group J01C) represent 43% of the total antimicrobial use. The β-lactamase sensitive penicillins (J01CE) and penicillins with extended spectrum (J01CA) represent 28.6% and 12.4% respectively. The sales of penicillins have been stable over the last 5 years. There has, however, been a shift in use from the β-lactamase-sensitive penicillins (31% of J01 in 1995 to 28% in 2000) to penicillins with extended specter (10% and 12% respectively).

The tetracyclines (J01A) represent 19% of the total use. The sales have been steadily decreasing by 34% since 1993. The macrolides (J01FA) represent 9% of the total use. The urinary prophylactic agent methenamine represents 12% of total use. The sales have increased by 50% since 1995.

The sales of cephalosporins, although little, have also been increasing over the years and now represent 3% of the total sales of antibacterials. The sales of macrolides and amino-glycosides are stable, but the sales of sulfonamides and trimethoprim are decreasing - by 34% since 1995. The sales equals 7% of total sales in 2000. There has been a small, but stable increase in quinolone use over the years. It represents only a minor fraction (2%) of total antibacterial sales. However, the increase has been 35% since 1995.

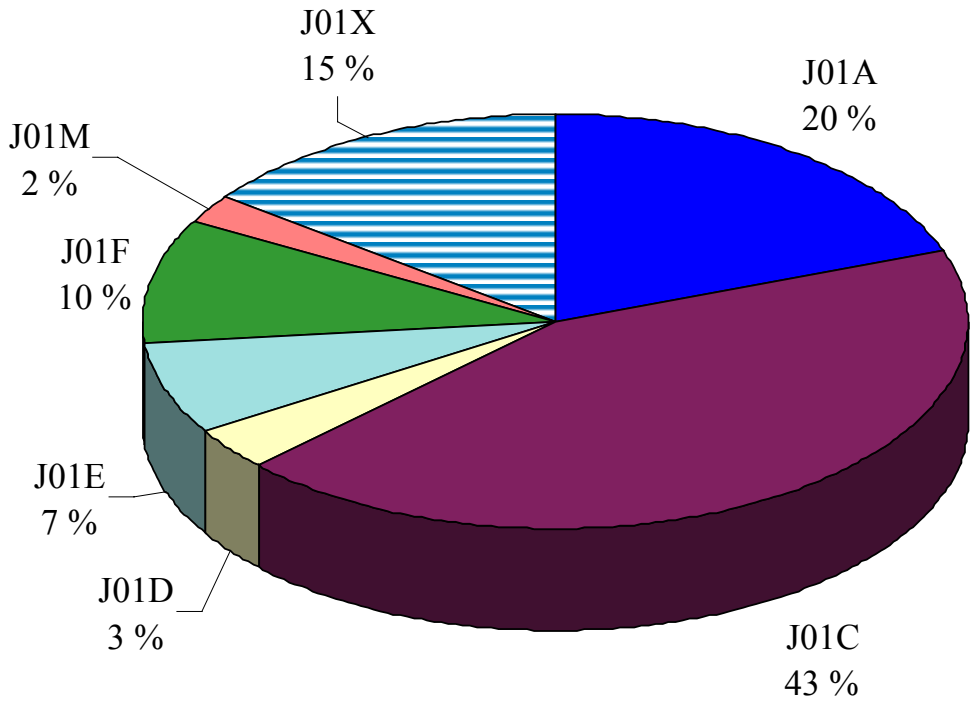


FIGURE 4. Relative amount of antibacterial agents for systemic use in 2000 in Defined Daily Doses (DDD). Groups of antibacterials are represented by ATC numbers as follows: J01A tetracyclines, J01C penicillins, J01D cephalosporins, carbepenems and monobactams, J01E sulfonamides and trimethoprim, J01F macrolides and lincosamides, J01M quinolones, and J01X others.

TABLE 8. Human consumption of single antibacterial agents for systemic use in Norway in 2000 (ATC group J01). Sales given in DDD/1000 inhabitants/day. Collection of data on human consumption of antibacterial agents is presented in Appendix 2.

ATC	Substance	1995	1996	1997	1998	1999	2000
A07AA09	Vancomycin	0.001	0.001	0.001	0.001	0.001	0.001
J01A A02	Doxycycline	2.82	2.49	2.47	2.34	2.20	2.10
J01A A04	Lymecycline	0.14	0.11	0.10	0.09	0.09	0.14
J01A A06	Oxytetracycline	0.43	0.36	0.30	0.27	0.25	0.24
J01A A07	Tetracycline	0.75	0.70	0.68	0.67	0.65	0.69
J01B A01	Chloramphenicol	0.005	0.005	0.005	0.004	0.005	0.004
J01C A01	Ampicillin	0.09	0.09	0.09	0,09	0.09	0.09
J01C A02	Pivampicillin	0.24	0.20	0.17	0.15	0.14	0.13
J01C A04	Amoxicillin	0.79	0.75	0.85	0.85	0.87	0.83

continued …

		1995	1996	1997	1998	1999	2000
J01C A08	Pivmecillinam	0.60	0.69	0.75	0.81	0.86	0.96
J01C A09	Azlocillin	0.0001	0.0001	0.0001			
J01C A11	Mecillinam	0.002	0.003	0.003	0.003	0.004	0.004
J01C E01	Benzylpenicillin	0.20	0.19	0.19	0.21	0.23	0.21
J01C E02	Phenoxymethylpenicillin	5.21	4.89	5.13	4.91	4.78	4.45
J01C F01	Dicloxacillin	0.08	0.13	0.16	0.19	0.22	0.25
J01C F02	Cloxacillin	0.10	0.08	0.08	0.08	0.10	0.10
J01C R02	Amoxicillin and enzyme inhibitor	0.004	0.01	0.02	0.01	0.01	0.01
J01C R05	Piperacillin and enzyme inhibitor						0.0001
J01D A01	Cefalexin	0.26	0.25	0.22	0.22	0.22	0.26
J01D A03	Cefalotin	0.04	0.04	0.04	0.04	0.05	0.05
J01D A05	Cefoxitin	0.0005	0.0004	0.0004	0.0004	0.0004	0.0004
J01D A06	Cefuroxim	0.11	0.11	0.11	0.12	0.13	0.13
J01D A10	Cefotaxim	0.01	0.01	0.02	0.03	0.04	0.04
J01D A11	Ceftazidim	0.02	0.02	0.01	0.01	0.01	0.01
J01D A13	Ceftriaxone		0.001	0.004	0.007	0.008	0.011
J01D A63	Ceftriaxone, combinations		0.00003	0.0001	0.0001	0.0001	
J01D F01	Aztreonam	0.0008	0.0008	0.0007	0.0005	0.0008	0.001
J01D H02	Meropenem			0.002	0.004	0.008	0.012
J01D H51	Imipenem and enzyme inhibitor	0.007	0.006	0.007	0.007	0.006	0.006
J01E A01	Trimethoprim	0.99	0.93	0.90	0.87	0.84	0.79
J01E B02	Sulfamethizole	0.005	0.001		0.0002	0.001	0.002
J01E C20	Sulfonamides, combinations	0.001	0.003	0.003	0.003	0.0004	
J01E E01	Sulfamethoxazol and trimethoprim	0.80	0.64	0.55	0.47	0.42	0.38
J01F A01	Erythromycin	1.18	1.03	1.04	1.06	1.01	1.00
J01F A02	Spiramycin	0.09	0.06	0.05	0.04	0.03	0.02
J01F A09	Clarithromycin	0.06	0.17	0.22	0.24	0.26	0.26
J01F A10	Azithromycin	0.14	0.14	0.17	0.17	0.18	0.19
J01F F01	Clindamycin	0.09	0.10	0.10	0.11	0.11	0.12
J01F F02	Lincomycin	0.003	0.001				
J01G B01	Tobramycin	0.03	0.02	0.03	0.03	0.03	0.02
J01G B03	Gentamicin	0.006	0.007	0.006	0.006	0.006	0.006
J01G B07	Netilmicin	0.02	0.02	0.02	0.02	0.02	0.02
J01M A01	Ofloxacin	0.07	0.07	0.07	0.06	0.06	0.05
J01M A02	Ciprofloxacin	0.18	0.19	0.20	0.23	0.26	0.29
J01M B02	Nalidixic acid	0.02	0.02	0.01	0.01	0.01	0.01
J01X A01	Vancomycin	0.005	0.005	0.005	0.005	0.004	0.005
J01X A02	Teicoplanin	0.0002	0.0009	0.0009	0.001	0.0007	0.0012
J01X B01	Colistin	0.002	0.002	0.004	0.003	0.003	0.003
J01X C01	Fusidic acid	0.002	0.003	0.003	0.003	0.003	0.003
J01X D01	Metronidazole	0.052	0.052	0.056	0.056	0.060	0.063
J01X D02	Tinidazole	0.002	0.001				
J01X E01	Nitrofurantoin	0.39	0.39	0.38	0.38	0.37	0.37
J01X X05	Methenamin	1.29	1.44	1.61	1.75	1.91	1.95
P01AB01	Metronidazole	0.20	0.20	0.18	0.18	0.18	0.18

IV. OCCURRENCE OF ANTIMICROBIAL RESISTANCE

A. BACTERIA FROM FEED, ANIMALS AND FOOD

Bacteria from feed

TABLE 9. *Escherichia coli* isolates from dog food (meat by-products) (n=70). Breakpoints (mg/L), MIC_{50}, MIC_{90}, MIC range (mg/L) and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Tetracycline	≤ 4	≥ 16	86.6	0.0	13.4	0.75 - 256	1	96
Chloramphenicol	≤ 8	≥ 32	94.0	1.5	4.5	1.5 - > 256	4	6
Ampicillin	≤ 8	≥ 32	89.6	0.0	10.4	1 - > 256	3	512
Cefuroxime	≤ 4	≥ 32	95.5	3.0	1.5	1 - 32	2	3
Trimethoprim	≤ 8	≥ 16	95.5	-	4.5	0.19 - > 32	0.5	0.75
Sulfonamides	≤ 256	≥ 512	88.1	0.0	11.9	4 - > 256	64	512
Streptomycin	≤ 4	≥ 8	79.1	-	20.9	1.5 - > 256	3	128
Gentamicin	≤ 4	≥ 16	100.0	0.0	0.0	0.25 - 2	0.75	1
Kanamycin	≤ 16	≥ 64	98.5	0.0	1.5	1 - 256	3	3
Neomycin*	≥ 25	≤ 20	100.0	0.0	0.0	21 - 32		
Nalidixic acid	≤ 16	≥ 32	100.0	-	0.0	1 - 6	2	3
Enrofloxacin	≤ 0.5	≥ 2	100.0	0.0	0.0	0.012 - 0.25	0.047	0.064

***** The susceptibility to neomycin was tested using disk diffusion (Neo-Sensitabs, Rosco).

COMMENTS:

The isolates included were from dog food and treats, either of imported or Norwegian origin, purchased in pet stores in Norway. Dried pig ears, dried skin and penises from cattle as well as other frozen meat by-products were among the products tested.

Seven of the isolates were resistant towards one of the antimicrobial agents included, seven isolates towards two, and five isolates towards five or more anti-microbials. The five multiresistant isolates were from dried swine products, out of which three were from Norway and two were of unknown origin.

The data show that resistance to streptomycin, tetracycline, sulfonamides and ampicillin, respectively, was most common. These antimicrobials have been and/or are still commonly used for clinical purposes in food producing animals in Norway and elsewhere.

All veterinary preparations containing chloramphenicol were withdrawn from the Norwegian market in 1992. However, various studies, including this, have shown that *E. coli* with reduced susceptibility to chloramphenicol still can be isolated from food producing animals in areas where chloramphenicol has been used in the past.

One of the isolates of Norwegian origin was resistant to the cephalosporin cefuroxime, and one was resistant to kanamycin. No antimicrobial preparations containing cephalosporins or kanamycin are approved for veterinary use in Norway.

No reduced susceptibility to the quinolones nalidixic acid and enrofloxacin was observed. Although enrofloxacin is approved for therapeutic use in animals in Norway, the veterinary consumption of this drug is very low.

Bacteria from infections in animals

Staphylococcus spp. from mastitis in cows

TABLE 10. *Staphylococcus aureus* isolates from clinical mastitis in cows (n=123). Breakpoints (mg/L), MIC_{50}, MIC_{90}, MIC range (mg/L) and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)		MIC_{50}	MIC_{90}
	S	R	S	I	R				
Oxytetracycline	≤ 8	≥ 16	99.2	-	0.8	0.25	- 32	1	1
Chloramphenicol	≤ 8	≥ 32	91.1	8.9	0.0	1	- 16	8	8
Penicillin	≤ 0.125	≥ 0.25	95.1	-	4.9	0.032	- 16	0.64	0.125
Oxacillin*	≤ 2	≥ 4	97.6	-	2.4	0.5	- 3	0.5	1
β-lactamase	Neg	Pos	95.1	-	4.9				
Cephalothin	≤ 8	≥ 32	99.2	0.8	0.0	0.125	- 16	0.25	0.25
Trimethoprim	≤ 8	≥ 16	100.0	-	0.0	0.38	- 1.5	0.75	1
Sulfadiazine	≤ 256	≥ 512	90.2	0.0	9.8	48	- 512	96	192
TMS**	≤ 2	≥ 4	100.0	-	0.0	0.125	- 0.25	0.25	0.25
Erythromycin	≤ 1	≥ 4	98.4	1.6	0.0	0.094	- 2	0.5	1
Spiramycin	≤ 16	≥ 32	98.4	-	1.6	8	- 32	16	16
Clindamycin	≤ 1	≥ 4	99.2	0.8	0.0	1	- 2	1	1
Streptomycin	≤ 32	≥ 64	95.9	-	4.1	2	- 512	8	16
Gentamicin	≤ 2	≥ 8	100.0	0.0	0.0	0.25	- 2	0.5	1
Neomycin	≤ 32	≥ 64	100.0	-	0.0	1	- 2	1	1
Ciprofloxacin	≤ 1	≥ 4	100.0	0.0	0.0	0.094	- 0.38	0.19	0.25
Vancomycin	≤ 4	≥ 32	100.0	0.0	0.0	1	- 4	1	2
Fucidic acid	≤ 0.5	≥ 1	98.4	-	1.6	0.064	- 16	0.19	0.19
Avilamycin	≤ 16	≥ 32	99.2	-	0.8	4	- 32	8	16
Virginiamycin	≤ 2	≥ 4	100.0	-	0.0	0.5	- 1	0.5	1

* Three isolates were resistant to oxacillin. These were tested for the presence of the *mecA* gene and found to be negative.

**TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 11. *Staphylococcus aureus* isolates from clinical mastitis in cows (n=123). Distribution (%) of MIC values (mg/L). Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey).

	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline				1	25	67	7				1				
Chloramphenicol						4		7	80	9					
Penicillin	2	85	8	1					1	3					
Oxacillin					73	22	2	2							
Cephalothin			42	51	5				1	1					
Trimethoprim					33	65	3								
Sulfadiazine												32	47	12	10
TMS*			2	98											
Erythromycin			2	1	81	14	2								
Spiramycin									17	81	2				
Clindamycin						99	1								
Streptomycin							2	30	47	15	2			1	3
Gentamicin				11	60	25	3								
Neomycin						94	7								
Ciprofloxacin			38	55	7										
Vancomycin						61	37	2							
Fucidic acid		4	43	51		1				1					
Avilamycin								36	49	15	1				
Virginiamycin					73	27									

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 12. *Staphylococcus aureus* isolates from subclinical mastitis in cows (n=118). Breakpoints (mg/L), MIC_{50}, MIC_{90}, MIC range (mg/L) and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Oxytetracycline	≤ 8	≥ 16	100.0	-	0.0	0.5 - 4	1	1
Chloramphenicol	≤ 8	≥ 32	97.5	2.5	0.0	3 - 16	8	8
Penicillin	≤ 0.125	≥ 0.25	91.5	-	8.5	0.032 - 16	0.064	0.125
Oxacillin	≤ 2	≥ 4	100.0	-	0.0	0.19 - 1	0.5	1
β-lactamase	Neg	Pos	92.4	-	7.6			
Cephalothin	≤ 8	≥ 32	100.0	0.0	0.0	0.125 - 1	0.25	0.25
Trimethoprim	≤ 8	≥ 16	100.0	-	0.0	0.38 - 1.5	0.75	1
Sulfadiazine	≤ 256	≥ 512	76.3	-	23.7	16 - 512	128	512
TMS*	≤ 2	≥ 4	100.0	-	0.0	0.125 - 0.25	0.25	0.25
Erythromycin	≤ 1	≥ 4	100.0	0.0	0.0	0.094 - 1	0.5	0.5
Spiramycin	≤ 16	≥ 32	97.5	-	2.5	0.25 - 64	16	16
Clindamycin	≤ 1	≥ 4	100.0	0.0	0.0	0.5 - 1	1	1
Streptomycin	≤ 32	≥ 64	96.6	-	3.4	2 - 512	8	16
Gentamicin	≤ 2	≥ 8	100.0	0.0	0.0	0.25 - 2	0.5	1
Neomycin	≤ 32	≥ 64	100.0	-	0.0	1 - 2	1	1
Ciprofloxacin	≤ 1	≥ 4	100.0	0.0	0.0	0.032 - 0.25	0.125	0.19
Vancomycin	≤ 4	≥ 32	100.0	0.0	0.0	1 - 4	1	2
Fucidic acid	≤ 0.5	≥ 1	99.2	-	0.8	0.032 - 3	0.125	0.19
Avilamycin	≤ 16	≥ 32	100.0	-	0.0	2 - 16	4	8
Virginiamycin	≤ 2	≥ 4	100.0	-	0.0	0.5 - 1	0.5	1

*For footnote, see Table 11.

TABLE 13. *Staphylococcus aureus* isolates from subclinical mastitis in cows (n=118). Distribution (%) of MIC values (mg/L). Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey).

	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥ 512
Oxytetracycline					28	70	2	1							
Chloramphenicol								14	84	3					
Penicillin	3	82	6	1		1	1		2	4					
Oxacillin				1	72	27									
Cephalothin			45	48	6	1									
Trimethoprim					29	69	3								
Sulfadiazine										1		11	43	21	24
TMS*			3	98											
Erythromycin			2	4	86	9									
Spiramycin				1					22	75	1	2			
Clindamycin					2	98									
Streptomycin							8	38	36	14	1		2		2
Gentamicin				19	48	28	5								
Neomycin						92	8								
Ciprofloxacin	1	2	58	40											
Vancomycin						66	31	3							
Fucidic acid	1	3	56	39	1			1							
Avilamycin							3	50	42	6					
Virginiamycin					84	16									

*For footnote, see Table 11.

TABLE 14. Coagulase negative staphylococci (CNS) isolates from mastitis in cows (n=48). Breakpoints (mg/L), MIC_{50}, MIC_{90}, MIC range (mg/L) and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)			MIC_{50}	MIC_{90}
	S	R	S	I	R					
Oxytetracycline	≤ 8	≥ 16	93.8	-	6.2	0.5	-	64	1	2
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	0.0	2	-	8	8	8
Penicillin	≤ 0.125	≥ 0.25	70.8	-	29.2	0.016	-	16	0.064	4
Oxacillin*	≤ 2	≥ 4	100.0	-	0.0	0.19	-	1.5	0.5	1
β-lactamase	Neg	Pos	70.8	-	29.2					
Cephalothin	≤ 8	≥ 32	100.0	0.0	0.0	0.125	-	1	0.25	1
Trimethoprim	≤ 8	≥ 16	62.5	-	37.5	0.25	-	64	2	24
Sulfadiazine	≤ 256	≥ 512	18.8	-	81.2	24	-	>512	512	512
TMS*	≤ 2	≥ 4	89.6	-	1.4	0.25	-	64	0.25	16
Erythromycin	≤ 1	≥ 4	91.7	2.1	4.2	0.064	-	512	0.5	1
Spiramycin	≤ 16	≥ 32	79.2	-	20.8	4	-	64	16	32
Clindamycin	≤ 1	≥ 4	97.9	2.1	0.0	1	-	2	1	1
Streptomycin	≤ 32	≥ 64	72.9	-	27.1	2	-	512	4	512
Gentamicin	≤ 2	≥ 8	100.0	0.0	0.0	0.25	-	0.5	0.25	0.5
Neomycin	≤ 32	≥ 64	100.0	-	0.0	1	-	1	1	1
Ciprofloxacin	≤ 1	≥ 4	100.0	0.0	0.0	0.047	-	0.38	0.094	0.19
Vancomycin	≤ 4	≥ 32	100.0	0.0	0.0	1	-	2	1	2
Fucidic acid	≤ 0.5	≥ 1	89.6	-	10.4	0.032	-	16	0.19	1.5
Avilamycin	≤ 16	≥ 32	91.7	-	8.3	2	-	128	8	16
Virginiamycin	≤ 2	≥ 4	95.8	-	4.2	0.5	-	4	0.5	2

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 15. Coagulase negative staphylococci (CNS) isolates from mastitis in cows (n=48). Distribution (%) of MIC values (mg/L). Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey).

	0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥512
Oxytetracycline						38	52	2	2			4	2			
Chloramphenicol								4	29	67						
Penicillin	2	10	54	4	2	6	6	4	2	6	2					
Oxacillin					8	65	23	4								
Cephalothin				33	46	10	10									
Trimethoprim					2	15	23	12	2	4	26	4	8			
Sulfadiazine												6	8	2	2	81
TMS*					77	8	2	2			6		4			
Erythromycin			6		8	63	17	2	2							2
Spiramycin									2	35	42	15	6			
Clindamycin							98	2								
Streptomycin								31	29	8	2	2	8	4	4	10
Gentamicin					85	15										
Neomycin							100									
Ciprofloxacin			33	48	16	2										
Vancomycin							88	13								
Fucidic acid		2	6	32	34	17		4	2		4					
Avilamycin								4	38	10	40	4	2	2		
Virginiamycin						83	6	6	4							

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS:

The occurrence of resistance among *S. aureus* from clinical and subclinical mastitis in cows was quite low. However, the occurrence was relatively higher among isolates from subclinical mastitis as compared to those from clinical mastitis. The resistance frequencies for the various antimicrobial agents reflect the usage; penicillin, streptomycin, and to a lesser extent sulfonamides/ trimethoprim being commonly used for clinical purposes in dairy cattle. The prevalence of resistance has remained at the same level during the 1990s, and this picture also applies to the data from 2000. However, the inclusion criteria differed between the isolates included in this report and previous years. Before 2000, the prevalence of antimicrobial resistance in staphylococci isolated from cases of mastitis was estimated using all isolates submitted to the diagnostic laboratories. For the results reported in NORM-VET 2000, only one isolate per herd was included to avoid the effect of clustering at the herd level due to frequent submissions from "problem herds".

The veterinary usage of fluoroquinolones has been very low. No cephalosporins are approved for use in animals in Norway, and this is reflected by the lack of resistance to these classes of antimicrobials. A few isolates were resistant to oxacillin, but these isolates were tested for the presence of the *mecA* gene and found to be negative. A limited number of *S. aureus* isolates from both clinical and subclinical mastitis cases showed resistance towards spiramycin. Neither spiramycin nor other macrolides or lincosamides are approved for use in food producing animals in Norway. Information on whether human formulations have been applied to cattle or other animals is currently unavailable.

Resistance in CNS isolates from mastitis in cows was considerably more abundant as compared to isolates of *S. aureus*. The occurrence of penicillin resistance in CNS remained at the same level throughout the 1990s and this picture also applies to the data from 2000.

Staphylococcus intermedius from skin infections in dogs

TABLE 16. *Staphylococcus intermedius* isolates from skin, dogs (n=94). Breakpoints (mg/L), MIC_{50}, MIC_{90}, MIC range (mg/L) and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)		MIC_{50}	MIC_{90}
	S	R	S	I	R				
Oxytetracycline	≤ 8	≥ 16	63.8	-	36.2	0.5	- 64	0.5	64
Chloramphenicol	≤ 8	≥ 32	98.9	0.0	1.1	2	- 48	4	8
Penicillin	≤ 0.125	≥ 0.25	23.4	-	76.6	0.032	- 16	2	16
Oxacillin	≤ 2	≥ 4	100.0	-	0.0	0.5	- 1	0.5	0.5
β-lactamase	Neg	Pos	22.3	-	77.7				
Cephalothin	≤ 8	≥ 32	100.0	0.0	0.0	0.12	- 0.25	0.125	0.125
Trimethoprim	≤ 8	≥ 16	95.7	-	4.3	0.75	- 64	2	4
Sulfadiazine	≤ 256	≥ 512	1.1	-	98.9	192	- >512	512	512
TMS*	≤ 2	≥ 4	97.9	-	2.1	0.25	- 16	0.5	1
Erythromycin	≤ 1	≥ 4	88.3	1.1	10.6	0.125	- 512	0.5	512
Spiramycin	≤ 16	≥ 32	89.4	-	10.6	4	- 64	8	64
Clindamycin	≤ 1	≥ 4	92.6	0.0	7.4	1	- 512	1	1
Streptomycin	≤ 32	≥ 64	91.5	-	8.5	2	- 512	2	8
Gentamicin	≤ 2	≥ 8	100.0	0.0	0.0	0.25	- 1	0.25	0.25
Neomycin	≤ 32	≥ 64	100.0	-	0.0	1	- 8	1	1
Ciprofloxacin	≤ 1	≥ 4	100.0	0.0	0.0	0.032	- 0.25	0.094	0.125
Vancomycin	≤ 4	≥ 32	100.0	0.0	0.0	0.5	- 2	1	2
Fucidic acid	≤ 0.5	≥ 1	54.3	-	45.7	0.064	- 512	0.19	32
Avilamycin	≤ 16	≥ 32	100.0	-	0.0	0.5	- 8	2	4
Virginiamycin	≤ 2	≥ 4	100.0	-	0.0	0.5	- 0.5	0.5	0.5

**TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 17. *Staphylococcus intermedius* isolates from skin, dogs (n=94). Distribution (%) of MIC values (mg/L). Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey).

	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥512
Oxytetracycline					55	5	3				9	28			
Chloramphenicol							7	77	15			1			
Penicillin	1	22		3	9	12	3	2	6	42					
Oxacillin					96	4									
Cephalothin			99	1											
Trimethoprim						6	65	22	2	1		3			
Sulfadiazine														1	99
TMS*				42	39	15	2	1		1					
Erythromycin			1	33	51	3	1						11		
Spiramycin								27	60	3		11			
Clindamycin						93							7		
Streptomycin							67	20	3	1			3	4	1
Gentamicin				92	7	1									
Neomycin						92	2	3	3						
Ciprofloxacin	1	37	59	4											
Vancomycin					1	86	13								
Fucidic acid		5	37	13		1	3	6	4	14	12	2	2		
Avilamycin					3	42	34	20	1						
Virginiamycin					100										

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS:

The data show that *Staphylococcus intermedius* from skin infections in dogs were frequently resistant to sulfonamides, penicillin G, fucidic acid, and tetracycline, respectively. A considerable proportion of the isolates were resistant to the macrolides erythromycin and spiramycin, the lincosamide clindamycin, and the aminoglycoside streptomycin. All seven clindamycin resistant isolates were also resistant to erythromycin and spiramycin.

Resistance to the trimethoprim/sulfamethoxazole combination has remained at a very low level, although this combination is commonly used for therapeutical purposes in dogs. However, the prevalence of resistance to sulfadiazine alone was very high. Due to the low prevalence of resistance to the trimethoprim/ sulfamethoxazole combination, such formulations remain the drug of choice when treating skin infections in dogs.

Resistance to cephalosporins as well as resistance to fluoroquinolones has remained negligible. The usage of fluoroquinolones to pets in Norway is limited, probably explaining the high susceptibility to this class of drugs. No veterinary preparations containing cephalosporins are approved for use in animals in Norway. There is reason to believe that there is some therapeutic use in pets of cephalosporins approved for humans, but the amount of such use is unknown.

Stratifying the isolates by anatomical origin revealed that the 18 isolates from ears (otitis externa) expressed higher levels of resistance towards fucidic acid than the isolates from other skin lesions (61% versus 42%). However, the latter skin isolates were more frequently resistant to penicillin than the isolates from ears (79% versus 61%). These trends were also seen for skin and ear isolates that were analysed using disk diffusion as part of the routine diagnostic services at the National Veterinary Institute in 2000 and in previous years.

Bacteria from food

Escherichia coli from Norwegian poultry and pork

TABLE 18: The proportion of *E. coli* isolates from Norwegian meat products that were classified as susceptible (S), intermediately susceptible (I) and resistant (R) towards various antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 3.

			Poultry (N=205, n=204)			Pork (N=387, n=158)		
	Breakpoints		Proportion of isolates (%)			Proportion of isolates (%)		
	S	R	S	I	R	S	I	R
Tetracycline	≤ 4	≥ 16	88.2	0.0	11.8	89.9	0.0	10.1
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	0.0	96.2	0.0	3.8
Ampicillin	≤ 8	≥ 32	89.2	0.0	10.8	9.5	0.6	8.9
Cefuroxime	≤ 4	≥ 32	97.1	2.9	0.0	97.5	0.6	1.9
Trimethoprim	≤ 8	≥ 16	92.2	-	7.8	9.5	0.0	9.5
Sulfonamides	≤ 256	≥ 512	74.0	-	26.0	85.4	0.0	14.6
Streptomycin	≤ 4	≥ 8	87.7	-	12.3	76.6	0.0	23.4
Gentamicin	≤ 4	≥ 16	99.5	0.0	0.5	99.4	0.0	0.6
Kanamycin	≤ 16	≥ 64	100.0	0.0	0.0	96.8	0.0	3.2
Neomycin*	≥ 25	≤ 20	100.0	0.0	0.0	97	2.0	1.0
Nalidixic acid	≤ 16	≥ 32	95.1	-	4.9	100.0	0.0	0.0
Enrofloxacin	≤ 0.5	≥ 2	99.5	0.5	0.0	100.0	0.0	0.0

N=total number of samples, n=number of samples from which *E. coli* was isolated .
***** The susceptibility to neomycin was tested using disk diffusion (Neo-Sensitabs, Rosco).

COMMENTS:

Of the 204 *E. coli* isolates from poultry meat, 36% were classified as resistant to one or more of the antimicrobials included. In total, 16% of the isolates were resistant to only one antimicrobial, 11% to two, and 9% of the isolates to three or more antimicrobials. Resistance to sulfonamides was most common, followed by resistance to streptomycin, tetracycline, ampicillin, and trimethoprim. A total of 4.9% of the isolates were resistant to nalidixic acid, out of which 0.5% also showed reduced susceptibility to enrofloxacin. Sulfonamides are rarely used in Norwegian poultry production today, but were commonly used in earlier years. There is some use of tetracycline and amoxicillin (cross-resistance with ampicillin) for clinical purposes, whereas streptomycin and trimethoprim have not officially been used in Norwegian poultry production. No quinolones are approved for use in poultry. However, flumequine (cross-resistance with nalidixic acid) was used for clinical purposes to a very limited extent in the 1980s and early 1990s.

Of the 158 *E. coli* isolates from pork, 25% were classified as resistant to one or more of the antimicrobials included. In total, 5% of the isolates were resistant to only one antimicrobial, 7% to two, and 12% of the isolates to three or more antimicrobials. Resistance to streptomycin was most common, followed by resistance to sulfonamides, tetracycline, trimethoprim, and ampicillin. All these antimicrobials are commonly used for clinical purposes in swine production (sulfonamides and trimethoprim in combination). Some resistance to chloramphenicol, kanamycin, and gentamicin was observed. Veterinary drugs containing chloramphenicol were withdrawn from the Norwegian market in 1992. However, various studies, including this, have shown that *E. coli* with reduced susceptibility to chloramphenicol can still be isolated from swine production. The aminoglycosides gentamicin and kanamycin are not approved for use in food producing animals in Norway. The aminoglycoside neomycin has historically been used for treatment of diarrhoea. No veterinary preparations containing cephalosporins are approved in Norway.

The results obtained in NORM-VET 2000 are in accordance with results from similar surveys of Norwegian poultry and pork in 1998.

Enterococcus spp. from Norwegian poultry and pork

TABLE 19: The number of Norwegian meat samples where *Enterococcus faecalis* was used as an indicator bacterium and the proportion of isolates classified as susceptible (S), intermediately susceptible (I) and resistant (R) towards various antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 3.

	Breakpoints		Poultry (N=204, n=59) Proportion of isolates			Pork (N=387, n=107) Proportion of isolates		
	S	R	S	I	R	S	I	R
Tetracycline	≤ 4	≥ 16	67.8	0.0	32.2	78.5	1.9	19.6
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	0.0	98.1	0.0	1.9
Ampicillin	≤ 8	≥ 32	100.0	0.0	0.0	100.0	0.0	0.0
Trimethoprim	≤ 8	≥ 16	100.0	-	0.0	99.1	0.0	0.9
Erythromycin	≤ 4	≥ 8	91.5	-	8.5	97.2	0.0	2.8
Spiramycin*	≥ 26	≤ 22	88.1	6.8	5.1	97.2	0.0	2.8
Streptomycin**	≤ 512	≥ 1024	96.6	-	3.4	83.2	0.0	16.8
Gentamicin**	≤ 256	≥ 512	100.0	-	0.0	99.1	0.0	0.9
Vancomycin	≤ 4	≥ 32	71.2	28.8	0.0	68.2	31.8	0.0
Bacitracin	≤ 64	≥ 128	78.0	-	22.0	92.5	0.0	7.5
Virginiamycin*[1]	≥ 23	≤ 19	0.0	1.7	98.3	9.3	1.9	88.8

N=total number of meat samples, n=number of samples where *E. faecalis* was used as an indicator bacterium. *Analysed using agar disk diffusion (Neo-Sensitabs, Rosco). **Analysed for high-level resistance.

TABLE 20: The number of Norwegian meat samples where *Enterococcus faecium* was used as an indicator bacterium and the proportion of isolates classified as susceptible (S), intermediately susceptible (I) and resistant (R) towards various antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 3.

	Breakpoints		Poultry (N=204, n=145) Proportion of isolates			Pork (N=387, n=99) Proportion of isolates		
	S	R	S	I	R	S	I	R
Tetracycline	≤ 4	≥ 16	73.1	0.0	26.9	99.0	0.0	1.0
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	0.0	100.0	0.0	0.0
Ampicillin	≤ 8	≥ 32	99.3	0.7	0.0	100.0	0.0	0.0
Trimethoprim	≤ 8	≥ 16	100.0	-	0.0	99.0	0.0	1.0
Erythromycin	≤ 4	≥ 8	93.1	0.0	6.9	100.0	0.0	0.0
Spiramycin*	≥ 26	≤ 22	97.2	0.0	2.8	100.0	0.0	0.0
Streptomycin**	≤ 512	≥ 1024	99.3	-	0.7	100.0	0.0	0.0
Gentamicin**	≤ 256	≥ 512	100.0	-	0.0	100.0	0.0	0.0
Vancomycin	≤ 4	≥ 32	95.2	0.0	4.8	100.0	0.0	0.0
Bacitracin	≤ 64	≥ 128	48.3	-	51.7	92.9	0.0	7.1
Virginiamycin*	≥ 23	≤ 19	91.0	6.9	2.1	100.0	0.0	0.0

N=total number of meat samples, n=number of samples where *E. faecium* was used as an indicator bacterium. *Analysed using agar disk diffusion (Neo-Sensitabs, Rosco). **Analysed for high-level resistance.

TABLE 21: The number of Norwegian meat samples where *Enterococcus* spp. (other than *E. faecalis* and *E. faecium*) were used as indicator bacteria and the proportion of isolates classified as susceptible (S), intermediately susceptible (I) and resistant (R) towards various antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 3.

			Poultry (N=204, n=1)			Pork (N=387, n=48)		
	Breakpoints		Proportion of isolates			Proportion of isolates		
	S	R	S	I	R	S	I	R
Tetracycline	≤ 4	≥ 16	100.0	0.0	0.0	81.2	0.0	18.8
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	0.0	100.0	0.0	0.0
Ampicillin	≤ 8	≥ 32	100.0	0.0	0.0	100.0	0.0	0.0
Trimethoprim	≤ 8	≥ 16	100.0	0.0	0.0	62.5	0.0	37.5
Erythromycin	≤ 4	≥ 8	100.0	-	0.0	100.0	0.0	0.0
Spiramycin**	≥ 26	≤ 22	100.0	0.0	0.0	100.0	0.0	0.0
Streptomycin*	≤ 512	≥ 1024	100.0	-	0.0	95.8	0.0	4.2
Gentamicin*	≤ 256	≥ 512	100.0	-	0.0	100.0	0.0	0.0
Vancomycin	≤ 4	≥ 32	100.0	0.0	0.0	91.7	8.3	0.0
Bacitracin	≤ 64	≥ 128	100.0	-	0.0	79.2	0.0	20.8
Virginiamycin**	≥ 23	≤ 19	100.0	0.0	0.0	100.0	0.0	0.0

N=total number of meat samples, n=number of samples where *Enterococcus* spp. were used as indicator bacteria. *Analysed using agar disk diffusion (Neo-Sensitabs, Rosco). **Analysed for high-level resistance

COMMENTS:

E. faecalis is reported to express a naturally low susceptibility to the streptogramin virginiamycin, whereas *E. faecium* is reported to be susceptible. The same phenomenon was observed in this material. The usage of virginiamycin in animal production in Norway has been negligible, and the substance was banned in 1999. Resistance to virginiamycin is not included in the following discussion.

Of the 204 enterococci from poultry meat, 64% were classified as resistant to one or more of the following antimicrobial agents; tetracycline, erythromycin, spiramycin, streptomycin, vancomycin, and bacitracin. In total, 38% of the isolates were resistant to only one antimicrobial, 22% to two, and 4% to three or more antimicrobials. Resistance to bacitracin was most common, followed by resistance to tetracycline, erythromycin, spiramycin, vancomycin, and streptomycin (high-level). There is some use of tetracycline for clinical purposes in the Norwegian poultry industry. In the 1990s, there was some use of spiramycin for clinical purposes in Norwegian poultry production. Cross-resistance between erythromycin and spiramycin is common. In Norway, avoparcin was used as a growth promoter for broilers and turkeys from 1986 until it was banned in 1995. Studies have shown that this use has selected for an extensive occurrence of vancomycin resistant enterococci (VRE) in Norwegian poultry production, and that VRE were still prevalent 3-4 years after the ban was implemented. Finding a total of 3% VRE in this material probably reflects this persistence of VRE. Streptomycin is not known to be used in Norwegian poultry production, but has commonly been used for clinical purposes in other food producing animals.

Of the 253 enterococci from pork meat, 36% were classified as resistant to one or more of the following antimicrobial agents; tetracycline, chloramphenicol, trimethoprim, erythromycin, spiramycin, streptomycin, gentamicin, vancomycin, and bacitracin. In total, 24% of the isolates were resistant to only one antimicrobial, 9% to two, and 2% to three or more antimicrobials. Resistance to tetracycline was most common, followed by resistance to bacitracin, trimethoprim, streptomycin (high-level), erythromycin, spiramycin, chloramphenicol, and gentamicin. Tetracycline, trimethoprim (in combination with sulfonamides), and streptomycin are commonly used for clinical purposes in Norwegian swine production. All veterinary preparations containing chloramphenicol were withdrawn from the Norwegian market in 1992 and no veterinary preparations containing gentamicin are available in Norway.

The data included in NORM-VET 2000 are in accordance with data from similar surveys of Norwegian pork and poultry in 1998.

For both poultry and pork the MIC values for bacitracin among enterococci were distributed widely. Resistant enterococci (MIC ≥128 mg/L) were isolated more frequently from poultry meat as compared to pork (43% versus 9.8%), and *E. faecium* dominated among the resistant isolates. During the 1990s the usage of bacitracin as a growth promoter has been negligible, and since 1997 no such use has been recorded in animal production in Norway.

Staphylococcus aureus in bulk tank milk

TABLE 22. *Staphylococcus aureus* isolates from bulk milk samples from dairy cattle herds (n=121). Breakpoints (mg/L), MIC_{50}, MIC_{90}, MIC range (mg/L) and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents are shown.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)		MIC_{50}	MIC_{90}
	S	R	S	I	R				
Tetracycline	≤ 8	≥ 16	99.2	0.0	0.8	0.094	- 12	0.19	0.38
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	0.0	2	- 6	4	4
Penicillin G*	≤ 0.125	≥ 0.25	95.9	-	4.1	0.016	- 32	0.047	0.064
Oxacillin	≤ 2	≥ 4	100.0	-	0.0	0.125	- 2	0.5	0.75
β-lactamase	Neg	Pos	95.0	-	5.0				
Cephalothin	≤ 8	≥ 32	100.0	0.0	0.0	0.047	- 0.75	0.25	0.38
Trimethoprim	≤ 8	≥ 16	100.0	-	0.0	0.38	- 2	1	1.5
Sulfonamides	≤ 256	≥ 512	100.0	-	0.0	32	- 256	64	128
Erythromycin	≤ 1	≥ 4	100.0	0.0	0.0	0.094	- 0.25	0.19	0.25
Clindamycin	≤ 1	≥ 4	100.0	0.0	0.0	0.094	- 0.19	0.125	0.19
Streptomycin	≤ 32	≥ 64	94.2	-	5.8	0.3	- 256	3	4
Gentamicin	≤ 2	≥ 8	100.0	0.0	0.0	0.125	- 0.75	0.25	0.38
Enrofloxacin	≤ 0.5	≥ 2	100.0	0.0	0.0	0.064	- 0.38	0.125	0.19
Fucidic acid	≤ 0.5	≥ 1	94.2	-	5.8	0.125	- 1	0.38	0.5

*Penicillin G=Benzylpenicillin.

TABLE 23. *Staphylococcus aureus* isolates from bulk milk samples from dairy goat herds (n=96). Breakpoints (mg/L), MIC_{50}, MIC_{90}, MIC range (mg/L) and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 3.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)		MIC_{50}	MIC_{90}
	S	R	S	I	R				
Tetracycline	≤ 8	≥ 16	100.0	-	0.0	0.094	- 0.25	0.19	0.25
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	0.0	2	- 6	3	4
Penicillin G	≤ 0.125	≥ 0.25	99.0	-	1.0	0.023	- 6	0.047	0.064
Oxacillin	≤ 2	≥ 4	100.0	-	0.0	0.025	- 1.5	0.38	0.75
β-lactamase	Neg	Pos	99.0	-	1.0				
Cephalothin	≤ 8	≥ 32	100.0	0.0	0.0	0.047	- 0.75	0.19	0.25
Trimethoprim	≤ 8	≥ 16	100.0	-	0.0	0.5	- 3	1	1
Sulfonamides	≤ 256	≥ 512	100.0	-	0.0	32	- 256	64	96
Erythromycin	≤ 1	≥ 4	100.0	0.0	0.0	0.094	- 0.25	0.19	0.19
Clindamycin	≤ 1	≥ 4	100.0	0.0	0.0	0.064	- 0.19	0.125	0.125
Streptomycin	≤ 32	≥ 64	100.0	-	0.0	3	- 8	4	4
Gentamicin	≤ 2	≥ 8	100.0	0.0	0.0	0.125	- 1	0.38	0.5
Enrofloxacin	≤ 0.5	≥ 2	100.0	0.0	0.0	0.094	- 0.25	0.125	0.19
Fucidic acid	≤ 0.5	≥ 1	100.0	-	0.0	0.094	- 0.75	0.25	0.38

COMMENTS:

Some resistance to penicillin and streptomycin was detected among *S. aureus* isolates from bulk milk samples from dairy cows. This probably reflects the fact that these antimicrobials are commonly used in the treatment of mastitis in cows. There is also some clinical use of tetracycline. Some isolates expressed resistance towards fucidic acid, although the MIC values recorded were not particularly high (range 0.125-1 mg/L). Fucidic acid has been used to some degree in cattle through a number of years. The prevalence of resistance towards the various antimicrobial agents is in accordance with those found for *S. aureus* isolates from clinical mastitis in cows (Table 10).

Only one of the tested *S. aureus* isolates from goat bulk milk was resistant to penicillin. Overall, the prevalence of resistance in *S. aureus* from goat bulk milk samples was very low.

B. ZOONOTIC AND OTHER FOOD BORNE ENTERIC BACTERIA

Salmonella from animal feed

TABLE 24. *Salmonella* isolates from animal feed (n=9). Breakpoints (mg/L), MIC range and proportion of isolates susceptible (S) and resistant (R) to various antimicrobial agents. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mg/l)		Proportion of isolates		MIC range (mg/l)	
	S	R	S	R		
Oxytetracycline	≤ 8	≥ 16	100.0	0.0	2	- 4
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	4	- 8
Florfenicol	≤ 16	≥ 32	100.0	0.0	4	- 8
Ampicillin	≤ 8	≥ 32	100.0	0.0	0.5	- 1
Amoxi./Clav.*	≤ 8	≥ 32	100.0	0.0	2	- 4
Ceftiofur	≤ 2	≥ 8	100.0	0.0	0.5	- 1
Trimethoprim	≤ 8	≥ 16	100.0	0.0	0.125	- 0.5
Sulfamethoxazole	≤ 256	≥ 512	100.0	0.0	64	- 64
Streptomycin	≤ 32	≥ 64	100.0	0.0	8	- 32
Gentamicin	≤ 4	≥ 16	100.0	0.0	1	- 4
Neomycin	≤ 32	≥ 64	100.0	0.0	1	- 2
Apramycin	≤ 32	≥ 64	100.0	0.0	4	- 8
Enrofloxacin	≤ 0.25	≥ 2	100.0	0.0	0.06	- 0.12
Nalidixic acid	≤ 16	≥ 32	100.0	0.0	4	- 16

*Amoxi./Clav.=Amoxicillin/clavulanic acid.

TABLE 25. *Salmonella* isolates from animal feed (n=9). Distribution (%) of MIC values (mg/L). Shaded areas in each row indicate susceptibility (no shade), intermediate resistance (light grey) and resistance (dark grey).

	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥256
Oxytetracycline							89	11							
Chloramphenicol								44	56						
Florfenicol							44	56							
Ampicillin					11	89									
Amoxi./Clav.*							78	22							
Ceftiofur					11	89									
Trimethoprim			11	78	11										
Sulfamethoxazole												100			
Streptomycin									22	67	11				
Gentamicin						56	33	11							
Neomycin						11	89								
Apramycin								56	44						
Enrofloxacin		89	11												
Nalidixic acid								22	67	11					

*Amoxi./Clav.=Amoxicillin/clavulanic acid.

COMMENTS:

The material included six isolates from fish feed and three from commercially available dog food. None of the isolates were *S.* Enteritidis or *S.* Typhimurium. The fish feed samples were all from Norwegian feed mills, however, the origin of the material included in the feed was not known. One of the samples of dog food was imported from the US. For the remaining two samples the country of origin was not known.

All isolates from animal feeds were susceptible to all antimicrobials included.

Salmonella from animals

TABLE 26. *Salmonella* Typhimurium, isolates from animals in Norway (n=14). Breakpoints (mg/L), MIC range and proportion of isolates susceptible (S) and resistant (R) to antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mg/L)		Proportion of isolates		MIC range (mg/L)
	S	R	S	R	
Oxytetracycline	≤ 8	≥ 16	100.0	0.0	1 - 4
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	2 - 4
Florfenicol	≤ 16	≥ 32	100.0	0.0	2 - 4
Ampicillin	≤ 8	≥ 32	100.0	0.0	0.5 - 2
Amoxi./Clav.*	≤ 8	≥ 32	100.0	0.0	1 - 4
Ceftiofur	≤ 2	≥ 8	100.0	0.0	0.25 - 1
Trimethoprim	≤ 8	≥ 16	100.0	0.0	0.125 - 0.5
Sulfamethoxazole	≤ 256	≥ 512	100.0	0.0	64 - 128
Streptomycin	≤ 32	≥ 64	100.0	0.0	8 - 32
Gentamicin	≤ 4	≥ 16	100.0	0.0	0.5 - 4
Neomycin	≤ 32	≥ 64	100.0	0.0	1 - 4
Apramycin	≤ 32	≥ 64	100.0	0.0	4 - 16
Enrofloxacin	≤ 0.25	≥ 2	100.0	0.0	0.03 - 0.06
Nalidixic acid	≤ 16	≥ 32	100.0	0.0	4 - 8

*Amoxi./Clav.=Amoxicillin/Clavulanic acid.

TABLE 27. *Salmonella* Typhimurium, isolates from animals (n=14). Distribution (%) of MIC values (mg/L). Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey).

	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥256
Oxytetracycline						14	79	7							
Chloramphenicol							64	36							
Florfenicol							64	36							
Ampicillin					7	86	7								
Amoxi./Clav.*						7	79	14							
Ceftiofur				7	79	14									
Trimethoprim			57	29	14										
Sulfamethoxazole												93	7		
Streptomycin									43	50	7				
Gentamicin					29	50	14	7							
Neomycin						64	29	7							
Apramycin								79	14	7					
Enrofloxacin	64	36													
Nalidixic acid								71	29						

*Amoxi./Clav.=Amoxicillin/Clavulanic acid.

TABLE 28. *Salmonella* other than *S.* Enteritidis and *S.* Typhimurium, isolates from animals (n=22). Breakpoints (mg/L), MIC range and proportion of isolates susceptible (S) and resistant (R) to various antimicrobial agents. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mg/L)		Proportion of isolates		MIC range (mg/L)		
	S	R	S	R			
Oxytetracycline	≤ 8	≥ 16	90.9	9.1	1	-	128
Chloramphenicol	≤ 8	≥ 32	95.5	4.5	2	-	32
Florfenicol	≤ 16	≥ 32	100.0	0.0	2	-	8
Ampicillin	≤ 8	≥ 32	95.5	4.5	0.5	-	64
Amoxi./Clav.*	≤ 8	≥ 32	95.5	4.5	2	-	32
Ceftiofur	≤ 2	≥ 8	100.0	0.0	0.25	-	2
Trimethoprim	≤ 8	≥ 16	100.0	0.0	0.125	-	0.5
Sulfamethoxazole	≤ 256	≥ 512	95.5	4.5	64	-	1024
Streptomycin	≤ 32	≥ 64	90.9	9.1	4	-	128
Gentamicin	≤ 4	≥ 16	100.0	0.0	0.5	-	2
Neomycin	≤ 32	≥ 64	95.5	4.5	1	-	64
Apramycin	≤ 32	≥ 64	100.0	0.0	2	-	8
Enrofloxacin	≤ 0.25	≥ 2	95.5	4.5	0.03	-	2
Nalidixic acid	≤ 16	≥ 32	95.5	4.5	4	-	256

*Amoxi./Clav.=Amoxicillin/Clavulanic acid.

TABLE 29. *Salmonella* other than *S.* Enteritidis and *S.* Typhimurium, isolates from animals (n=22). Distribution (%) of MIC values (mg/L). Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey).

	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	≥256
Oxytetracycline						18	64	9					9		
Chloramphenicol							27	59	9		5				
Florfenicol							23	68	9						
Ampicillin					18	68	9					5			
Amoxi./Clav.*							86	9			5				
Ceftiofur				18	68	9	5								
Trimethoprim			32	36	32										
Sulfamethoxazole												96			5
Streptomycin								5	18	46	23	5	5		
Gentamicin					23	50	27								
Neomycin						55	41					5			
Apramycin							14	41	46						
Enrofloxacin	46	46	5				5								
Nalidixic acid								55	41						5

*Amoxi./Clav.=Amoxicillin/Clavulanic acid.

COMMENTS:

The samples included originated from wild, farmed, and exotic animals in Norway. Almost one third of the samples (31%) were from wild birds, 28% were from reptiles, and 13% were from sheep. The remaining samples were of bovine, equine, feline, porcine, turkey, or hedgehog origin. All five isolates from sheep belonged to the sub-species *Salmonella enterica* subsp. *diarizonae*. No *S.* Enteritidis was detected.

All isolates of *S.* Typhimurium from Norwegian animals were susceptible to all antimicrobials included.

Out of the 22 isolates of *Salmonella,* two were multi-resistant, both from seagulls. One isolate, a *S.* Hadar, was resistant to five antimicrobials including enrofloxacin and nalidixic acid. Both *S.* Hadar and resistance to fluoroquinolones are unusual findings in Norway. In 2000, 34 cases of *S.* Hadar infections in humans were registered in Norway, 27 of which were acquired abroad. One might speculate that the seagull has picked up the isolate abroad or indirectly from a human patient within Norway. The other multiresistant isolate, a *S.* Blockley, was resistant to four of the antimicrobials in the panel; chloramphenicol, neomycin, oxytetracycline, and streptomycin. *S.* Blockley is also an unusual finding in Norway.

One isolate from sheep was resistant to sulfamethoxazole, which is commonly used for clinical purposes in Norwegian sheep production.

Salmonella from food

TABLE 30. *Salmonella* Typhimurium isolates from imported meat of pork (n=3) and poultry (n=3). Breakpoints (mm), range (mm) and proportion of isolates susceptible (S), intermediately susceptible (I), and resistant (R) to various antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	16.7	50.0	33.3	10 - 28
Chloramphenicol	≥ 32	≤ 24	0.0	66.7	33.3	6 - 29
Ampicillin	≥ 25	≤ 8	66.7	0.0	33.3	6 - 29
TMS*	≥ 26	≤ 15	100.0	0.0	0.0	28 - 36
Ciprofloxacin	≥ 29	≤ 17	83.3	16.7	0.0	28 - 42
Nalidixic acid	≥ 14	≤ 13	83.3	-	16.7	6 - 26

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 31. *Salmonella* other than *S.* Enteritidis and *S.* Typhimurium, isolates from various food products of animal origin (n=28). Breakpoints (mm), range (mm) and proportion of isolates susceptible (S), intermediately susceptible (I), and resistant (R) to various antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	50.0	46.4	3.6	6 - 32
Chloramphenicol	≥ 32	≤ 24	0.0	82.1	17.9	22 - 31
Ampicillin	≥ 25	≤ 8	100.0	0.0	0.0	25 - 30
TMS*	≥ 26	≤ 15	100.0	0.0	0.0	26 - 37
Ciprofloxacin	≥ 29	≤ 17	100.0	0.0	0.0	31 - 39
Nalidixic acid	≥ 14	≤ 13	100.0	-	0.0	22 - 28

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 32. *Salmonella* other than *S.* Enteritidis and *S.* Typhimurium, isolates from various food products of animal origin (n=28). Distribution (%) of zone diameters (mm). Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey).

	6	7/8	9/10	11/12	13	14/15	16/17	18/19	20/21	22/24	25	26/27	28	29/30	31	32/33	34/35	36/37	≥ 38
Tetracycline	4									4	18	25	29	18	4				
Chloramph.										18	25	36	14	4	4				
Ampicillin											4	29	36	32					
TMS*												4	4	29		36	25	4	
Ciprofloxacin															4	25	29	32	11
Nalidixic acid										36	21	32	11						

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS:

Two of the *S.* Typhimurium isolates, one from Belgian pork and one from French turkey, were identified as multiresistant *S.* Typhimurium DT104 (ACSSuT from pork and ACNSSuT from turkey). The isolate that was resistant to nalidixic acid was also intermediately susceptible to ciprofloxacin.

All *Salmonella* isolates other than *S.* Typhimurium and *S.* Enteritidis, except three, were from imported food. The isolates were in general susceptible to most antimicrobials included, except for an overall low susceptibility to chloramphenicol (see comment on p.35).

Salmonella from human clinical specimens

TABLE 33. *Salmonella* Enteritidis, human clinical isolates (n=768). Breakpoints, proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents, and range of zone diameters (mm) are shown. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	48.0	43.8	8.2	6 - 36
Chloramphenicol	≥ 32	≤ 24	2.9	89.2	7.9	6 - ≥ 40
Ampicillin	≥ 25	≤ 8	90.5	3.1	6.4	6 - ≥ 40
TMS*	≥ 26	≤ 15	95.2	0.7	4.2	6 - ≥ 40
Ciprofloxacin	≥ 29	≤ 17	86.3	13.5	0.1	15 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	80.1	-	19.9	6 - ≥ 40

TABLE 34. *Salmonella* Enteritidis, human clinical isolates (n=768). Distribution (%) of zone diameters (mm). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility.

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	3	4	1													
Chloramph.	1															
Ampicillin	6															
TMS*	4															
Ciprofloxacin																
Nalidixic acid	20															1

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	≥ 37
Tetracycline		2	4	9	14	15	23	7	13	1	2	1	1			
Chloramph.		1	6	21	23	17	15	5	8	1	1					
Ampicillin			3	6	10	18	26	10	16	2	3					
TMS*						1	2	4	10	9	17	15	22	5	8	1
Ciprofloxacin				1	3	3	6	3	4	2	6	6	16	13	15	21
Nalidixic acid	2	8	23	23	15	4	2		1							

TABLE 35. *Salmonella* Typhimurium, human clinical isolates (n=214). Breakpoints, proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents, and range of zone diameters (mm) are shown. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	11.3	37.7	50.9	6 - 31
Chloramphenicol	≥ 32	≤ 24	2.3	37.9	59.8	6 - ≥ 40
Ampicillin	≥ 25	≤ 8	52.3	0.9	46.7	6 - 32
TMS*	≥ 26	≤ 15	85.4	0.5	14.2	6 - ≥ 40
Ciprofloxacin	≥ 29	≤ 17	94.4	4.7	0.9	6 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	92.1	-	7.9	6 - 30

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 36. *Salmonella* Typhimurium, human clinical isolates (n=214). Distribution (%) of zone diameters (mm). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility.

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	10	4	4	12	15	5	1									
Chloramph.	42	1	1												1	
Ampicillin	47															
TMS*	14							1								
Ciprofloxacin	1															
Nalidixic acid	8											1			1	1

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	≥ 37
Tetracycline	2	3	6	9	10	7	7	1	2	1						
Chloramph.	1	4	12	12	9	8	6	1	1		1			1	1	1
Ampicillin	1		1	3	11	11	16	3	6	1	1					
TMS				1	1	3	9	13	16	9	13	4	10	2	5	
Ciprofloxacin			1	1	1	1	1	1	2	2	5	10	13	19	18	26
Nalidixic acid	3	10	20	28	19	8	2		1							

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 37. *Salmonella* other than *S.* Enteritidis and *S.* Typhimurium, human clinical isolates (n=443). Breakpoints, proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents, and range of zone diameters (mm) are shown. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	23.7	49.4	26.9	6 - 37
Chloramphenicol	≥ 32	≤ 24	3.8	65.5	30.7	6 - ≥ 40
Ampicillin	≥ 25	≤ 8	81.9	4.7	13.3	6 - 38
TMS*	≥ 26	≤ 15	89.1	2.7	8.2	6 - 38
Ciprofloxacin	≥ 29	≤ 17	79.9	19.9	0.2	9 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	76.1	-	23.7	6 - 31

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 38. *Salmonella* other than *S.* Enteritidis and *S.* Typhimurium, human clinical isolates (n=443). Distribution (%) of zone diameters (mm). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility.

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	7	6	7	2	2										1	1
Chloramph.	7	1									1			1	1	1
Ampicillin	13															
TMS*	8															
Ciprofloxacin																1
Nalidixic acid	23						1								1	1

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	≥ 37
Tetracycline	1	4	7	11	14	12	13	4	4	1	1					
Chloramph.	1	5	14	19	15	14	9	3	3	2	2	1	1			
Ampicillin		1	2	3	9	10	28	11	14	3	2	1	1		1	1
TMS*	1		1	1	1	2	2	6	11	9	18	12	18	5	5	2
Ciprofloxacin		1	2	3	5	3	4	2	3	3	7	10	16	9	14	18
Nalidixic acid	4	9	17	18	14	5	4	1	1							1

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS:

It is emphasized that the vast majority of cases of *Salmonella* infections in Norway are acquired abroad. In 2000, 89% of the *S.* Enteritidis cases, 62% of the *S.* Typhimurium cases, and 83% of the other *Salmonella* infections reported were classified as imported. Thus, the resistance frequencies reported here predominantly relate to isolates that originated from countries other than Norway. Unfortunately, the resistance frequencies reported were not stratified on domestically acquired and imported cases.

In general, a high proportion of the *Salmonella* isolates were classified as intermediately susceptible to chloramphenicol. This phenomenon, however, is a result of that breakpoints were set to assure the clinical effect of chloramphenicol in meningitis cases.

The occurrence of resistance among *S.* Enteritidis isolates was moderate as compared to isolates of *S.* Typhimurium and "*Salmonella* other than *S.* Enteritidis and *S.* Typhimurium". Among the *S.* Enteritidis isolates, some resistance to tetracycline, chloramphenicol, ampicillin, and trimethoprim/sulfonamides, respectively, was observed, as well as a relatively high occurrence of resistance to nalidixic acid. Among the other salmonella isolates, a high occurrence of resistance to chloramphenicol, tetracycline, and ampicillin, and to a somewhat lesser degree, to nalidixic acid and trimethoprim/sulfonamides, was observed. All these drugs are used for various clinical purposes within human medicine around the world. In total, 70 (33%) of the *S.* Typhimurium isolates were identified as multi-resistant DT104, out of which 56 (80%) were isolated from imported cases. The multiresistant DT104 isolates were also resistant to streptomycin. Four (6%) of the multiresistant DT104 isolates were in addition resistant to nalidixic acid, of which three were isolated from imported cases and one from a case with unknown origin of infection. One of these nalidixic acid-resistant isolates was also intermediately susceptible to ciprofloxacin.

Although the proportion of isolates for all *Salmonella* categories that were resistant to ciprofloxacin was low, a considerable proportion expressed intermediate susceptibility indicating that resistance could be developing. This corresponds with the fact that a relatively high proportion of these isolates were resistant to nalidixic acid.

Shigella spp. from human clinical specimens

TABLE 39. *Shigella* spp., human clinical isolates (n=125). Breakpoints, proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents, and range of zone diameters (mm) are shown. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	12.8	8.0	79.2	6 - 32
Chloramphenicol	≥ 32	≤ 24	13.6	40.8	45.6	6 - 36
Ampicillin	≥ 25	≤ 8	13.6	43.2	43.2	6 - 32
TMS*	≥ 26	≤ 15	24.8	4.0	71.2	6 - ≥ 40
Ciprofloxacin	≥ 29	≤ 17	90.4	8.8	0.8	12 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	85.6	-	14.4	6 - 34

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 40. *Shigella* spp., human clinical isolates (n=125). Distribution (%) of zone diameters (mm). Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey).

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline	71	4	3		1											
Chloramph.	26	2	2	1	2											
Ampicillin	42	1									1		1	1	9	7
TMS*	70				1											
Ciprofloxacin							1									
Nalidixic acid	10	1	2	2												1

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	≥ 37
Tetracycline		1	1	3	2	1	5	2	5	1	1					
Chloramph.		3	9	9	10	10	2	3	5	1	4	2	4	1	3	
Ampicillin	13	6	6	4	2	2	1		2	1	2					
TMS*	1	1		2	2	2		2	2	3	3	1	2	1	6	3
Ciprofloxacin				3	2	2	2	1	2	1	3	2	8	10	14	47
Nalidixic acid	1			1	6	14	20	15	18	5	2	3	1			

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS:

It is emphasized that almost all reported cases of *Shigella* infection in Norway have been acquired while the patient was abroad. In 2000, 89% of the cases were reported as imported. Thus, the resistance frequencies reported here predominantly relate to isolates that originated from other countries.

The distribution of *Shigella* species was as follows*: S. sonnei* 64 (51%), *S. flexneri* 47 (38%), *S. boydii* 10 (8%), and *S. dysenteriae* 4 (3%). Two of the *S. dysenteriae* isolates were of serotype 1.

As is the case in reports from other countries, the occurrence of resistance among *Shigella* isolates is relatively high. A considerable proportion of the isolates were resistant to tetracycline, trimethoprim/sulfonamide, chloramphenicol, and ampicillin - drugs that are quite commonly used for various clinical purposes within human medicine around the world. Although the proportion of isolates that were resistant to ciprofloxacin was low, a significant proportion expressed intermediate susceptibility indicating that resistance could be developing. This corresponds with the finding that 14.4% of these isolates also were resistant to nalidixic acid.

Yersinia enterocolitica from human clinical specimens

TABLE 41. *Yersinia enterocolitica* serogroup 0:3, human clinical isolates (n=91). Breakpoints, proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents, and range of zone diameters (mm) are shown. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mm)		Proportion of isolates (%)			Range (mm)
	S	R	S	I	R	
Tetracycline	≥ 28	≤ 21	79.3	20.7	0.0	22 - ≥ 40
Chloramphenicol	≥ 32	≤ 24	25.0	67.4	7.6	6 - ≥ 40
Ampicillin	≥ 25	≤ 8	0.0	44.4	55.6	6 - 13
TMS*	≥ 26	≤ 15	83.7	16.3	0.0	18 - ≥ 40
Ciprofloxacin	≥ 29	≤ 17	87.0	13.0	0.0	23 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	98.9	-	1.1	6 - ≥ 40

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 42. *Yersinia enterocolitica* serogroup 0:3, human clinical isolates (n=91). Distribution (%) of zone diameters (mm). Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey).

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Tetracycline																
Chloramph.	2															
Ampicillin	17	14	24	12	20	6	6	1								
TMS*													1	1	1	
Ciprofloxacin																
Nalidixic acid	1															2

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	≥ 37
Tetracycline	2		5	5	4	3	11	13	20	1	12	1	7	3	10	2
Chloramph.		1	4	5	5	8	16	3	25	4	16	1	2			5
Ampicillin									1							
TMS*	3	3	1	5	3	3	11	7	21	2	9	7	5	3	4	8
Ciprofloxacin		1	1	1	2	1	7	2	11	8	12	9	9	1	11	25
Nalidixic acid	4	4	5	13	16	11	5	5	13	4	4	2	2		3	2

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS:

Most cases of *Yersinia enterocolitica* infection in Norway have acquired the infection within Norway. In 2000, 60% of the cases were reported as indigenous. No resistance to tetracycline or trimethoprim/sulfonamides was observed, while there was some resistance to chloramphenicol. One isolate was resistant to nalidixic acid, whereas some were classified as intermediately susceptible to ciprofloxacin. All isolates showed reduced susceptibility to ampicillin, an intrinsic resistance trait which is governed by the production by serogroup O:3 isolates of two chromosomally mediated β–lactamases designated A and B.

Campylobacter spp. from animals

TABLE 43. *Campylobacter jejuni,* faecal isolates from cats (n=9) and dogs (n=13). Breakpoints, MIC range and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)		
	S	R	S	I	R			
Tetracycline	≤ 4	≥ 16	100.0	0.0	0.0	0.023	-	0.38
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	0.0	0.25	-	1
Ampicillin	≤ 8	≥ 32	95.5	4.5	0.0	0.25	-	12
Erythromycin	≤ 1	≥ 4	100.0	0.0	0.0	0.19	-	1
Streptomycin	≤ 8	≥ 16	95.5	-	4.5	1	-	≥ 512
Gentamicin	≤ 4	≥ 16	100.0	0.0	0.0	0.25	-	1.5
Ciprofloxacin	≤ 0.125	≥ 4	100.0	0.0	0.0	0.023	-	0.125
Nalidixic acid	≤ 16	≥ 32	100.0	-	0.0	0.75	-	3

TABLE 44. *Campylobacter jejuni,* faecal isolates from cats (n=9) and dogs (n=13). Distribution (%) of MIC values. Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey).

	0.023	0.032	0.047	0.064	0.094	0.125	0.19	0.25	0.38	0.5	0.75	1	1.5	2	3	4	6	8	12	16	≥32
Tetracycline	5	5	27	23	9		5	18	9												
Chloramph.								5	14	9	50	23									
Ampicillin								5					46	32	9	5			5		
Erythromycin							5	14	18	23	36	5									
Streptomycin												18	36	27	14						5
Gentamicin								5	9	27	23	23	14								
Ciprofloxacin	5		18	36	36	5															
Nalidixic acid											9	23	36	27	5						

TABLE 45. *Campylobacter upsaliensis*, faecal isolates from cats (n=5) and dogs (n=15). Breakpoints, MIC range and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to antimicrobial agents are shown. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)		
	S	R	S	I	R			
Tetracycline	≤ 4	≥ 16	100.0	0.0	0.0	0.008	-	0.064
Chloramphenicol	≤ 8	≥ 32	100.0	0.0	0.0	0.125	-	1
Ampicillin	≤ 8	≥ 32	75.0	25.0	0.0	0.19	-	12
Erythromycin	≤ 1	≥ 4	95.0	5.0	0.0	0.19	-	1.5
Streptomycin	≤ 8	≥ 16	10.0	-	90.0	0.125	-	≥ 512
Gentamicin	≤ 4	≥ 16	100.0	0.0	0.0	0.064	-	0.5
Ciprofloxacin	≤ 0.125	≥ 4	90.0	10.0	0.0	0.023	-	1
Nalidixic acid	≤ 16	≥ 32	95.0	-	5.0	0.75	-	≥ 512

TABLE 46. *Campylobacter upsaliensis* faecal isolates from cats (n=5) and dogs (n=15). Distribution (%) of MIC values. Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey).

	≤ 0.023	0.032	0.047	0.064	0.094	0.125	0.19	0.25	0.38	0.5	0.75	1	1.5	2	3	4	6	8	12	16	≥32
Tetracycline	45	20	25	10																	
Chloramph.						10	5		15	35	30	5									
Ampicillin							5	10	30	5	5			5			10	5	25		
Erythromycin							5	20	20	5	25	20	5								
Streptomycin						5			5										5		85
Gentamicin				5		5	20	25	15	30											
Ciprofloxacin	15		25	25	20	5				5		5									
Nalidixic acid											15	30	30	15	5						

COMMENTS:

The *C. jejuni* isolates tested were in general susceptible to the antimicrobials included, except for one isolate from a cat expressing streptomycin resistance.

The *C. upsaliensis* isolates tested were in general susceptible to the antimicrobials included, except that 90% of them expressed resistance to streptomycin. This is in contrast to the results for *C. jejuni* where only 5% were resistant (Figures 5 and 6). Resistance to streptomycin might be an intrinsic trait in *C. upsaliensis*.

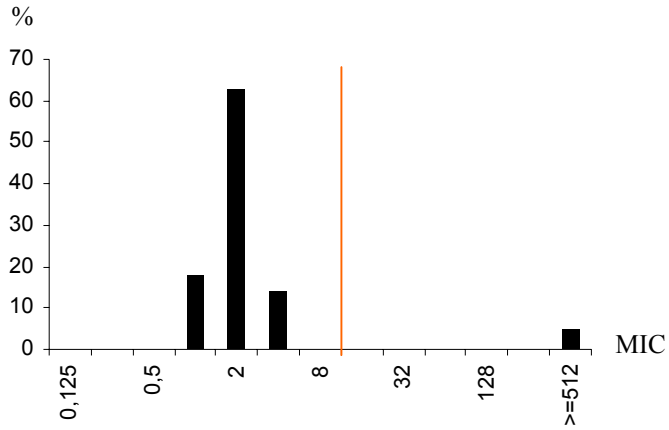


FIGURE 5. Minimal inhibitory concentrations (MIC) of streptomycin for *C. jejuni* from animals. The DANMAP breakpoint is shown in red.

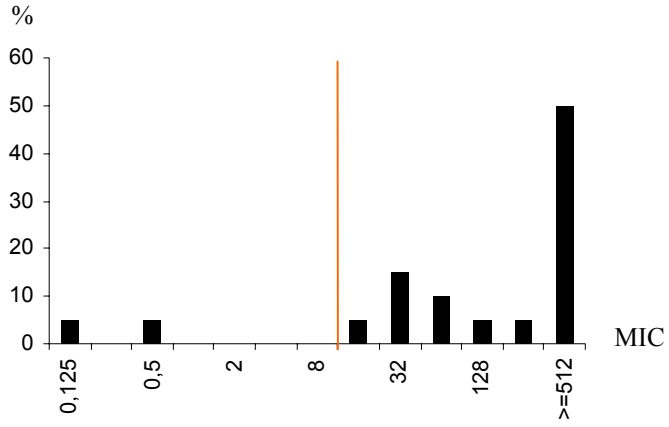


FIGURE 6. Minimal inhibitory concentrations (MIC) of streptomycin for *C. upsaliensis* from animals. The DANMAP breakpoint is shown in red.

One *C. upsaliensis* isolate from a dog was resistant to nalidixic acid, and this isolate also expressed reduced susceptibility to ciprofloxacin. The fluoroquinolone enrofloxacin is approved for clinical use in pets. The clinical importance of *C. upsaliensis* in humans and animals is still unclear.

Campylobacter spp. from food

TABLE 47. *Campylobacter jejuni* (n=10) and *C. coli* (n=2), isolates from poultry meat. Breakpoints, MIC range and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)
	S	R	S	I	R	
Doxycycline	≤ 1	≥ 4	91.7	8.3	0.0	0.125 - 2
Erythromycin	≤ 1	≥ 4	91.7	8.3	0.0	0.5 - 1.5
Gentamicin	≤ 2	≥ 8	83.4	8.3	8.3	0.38 - 12
Ciprofloxacin	≤ 0.125	≥ 4	41.7	58.3	0.0	0.094 - 1.5
Nalidixic acid	≤ 16	≥ 32	91.7	-	8.3	1.5 - ≥ 256

COMMENTS:

The samples included were from Norwegian poultry meat, except for one isolate that was imported from an unknown country. One of the *C. jejuni* isolates from Norwegian poultry meat was resistant to both nalidixic acid and gentamicin. This isolate also expressed a higher level of reduced susceptibility to ciprofloxacin (MIC=1.5 mg/L) than the rest of the isolates that were classified as intermediately susceptible towards this substance (MIC range 0.19 – 0.38 mg/L).

Campylobacter spp. from human clinical specimens

TABLE 48. *Campylobacter jejuni,* human clinical isolates (n=380). Breakpoints, proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents, MIC range, MIC_{50}, and MIC_{90} are shown. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	71.3	2.9	25.8	0.063 - ≥ 256	0.25	32
Erythromycin	≤ 1	≥ 4	80.3	15.5	4.2	0.016 - ≥ 256	1	2
Gentamicin	≤ 2	≥ 8	96.8	1.1	2.1	0.016 - 64	0,5	2
Ciprofloxacin	≤ 0.125	≥ 4	38.2	31.3	30.5	0.032 - ≥ 32	0.25	≥ 32
Nalidixic acid	≤ 16	≥ 32	68.5	-	31.5	0.125 - ≥ 256	4	≥ 256

TABLE 49. *Campylobacter jejuni*, human clinical isolates (n=380). Distribution (%) of MIC values (mg/l). Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey). Hatched areas indicate MIC values above the range of the respective Etest strips.

	≤ 0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline					1	26	33	9	2	3	3	3	6	9	4	2	1
Erythromycin			1				4	28	47	16	2	2					1
Gentamicin				2	5	7	9	32	32	11	1	2					
Ciprofloxacin					2	37	25	4	1	1				30			
Nalidixic acid									1	12	42	10	2				31

TABLE 50. *Campylobacter coli,* human clinical isolates (n=50). Breakpoints, proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to various antimicrobial agents, MIC range, MIC_{50}, and MIC_{90} are shown. Sampling, laboratory methods, and data handling are described in Appendix 4.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	52.0	8.0	40.0	0.063 - 128	0,5	64
Erythromycin	≤ 1	≥ 4	48.0	22.0	30.0	0.125 - ≥ 256	2	8
Gentamicin	≤ 2	≥ 8	98.0	0.0	2.0	0.063 - 8	1	2
Ciprofloxacin	≤ 0.125	≥ 4	28.0	4.0	68.0	0.063 - ≥ 32	≥ 32	≥ 32
Nalidixic acid	≤ 16	≥ 32	32.0	-	68.0	2 - ≥ 256	≥ 256	≥ 256

TABLE 51. *Campylobacter coli*, human clinical isolates (n=50). Distribution (%) of MIC values (mg/l). Shaded areas in each row indicate susceptibility (no shade), intermediate susceptibility (light grey) and resistance (dark grey). Hatched areas indicate MIC values above the range of the respective Etest strips.

	≤ 0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline					6	12	20	12	2	8	2		12	8	14	4	
Erythromycin						2	12	20	14	22	18	2		2		2	6
Gentamicin					6	2	8	20	40	22		2					
Ciprofloxacin					10	18	4					2	2	64			
Nalidixic acid										4	18	10					68

COMMENTS:

For 55% of the reported cases of campylobacteriosis in Norway in 2000, the infection was acquired abroad. Unfortunately, the resistance frequencies are not stratified in indigenous and imported cases. The data show that a considerable proportion of the isolates were resistant to the quinolones nalidixic acid and ciprofloxacin, and that this proportion was higher for *C. coli* isolates as compared to *C. jejuni* isolates. Also, the proportion of isolates that were resistant to the tetracycline doxycycline was rather high, and higher for *C. coli* isolates as compared to *C. jejuni* isolates. The proportion of isolates that were resistant to erythromycin was relatively high for the *C. coli* isolates, but rather low for the *C. jejuni* isolates. The proportion of isolates that were resistant to gentamicin was relatively low for both species.

C. BACTERIA FROM HUMAN CLINICAL SPECIMENS

Escherichia coli in blood cultures

TABLE 52. *Escherichia coli* blood culture isolates (n=168). MIC_{50}, MIC_{90}, MIC range, and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to antimicrobial agents. Sampling, microbiological methods and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	7.7	26.2	66.1	0.25 - ≥ 256	4	≥ 256
Ampicillin	≤ 1	≥ 32	1.8	70.2	28.0	0.5 - ≥ 256	4	≥ 256
Amoxi./Clav.*	-	-	-	-	-	0.5 - 32	4	8
Cefuroxime	≤ 1	≥ 32	5.4	92.3	2.4	0.25 - 64	2	8
Ceftazidime	≤ 1	≥ 32	97.0	3.0	0.0	0.032 - ≥ 8	0.125	0.25
Cefpirome	≤ 1	≥ 32	98.2	1.8	0.0	0.016 - 8	0.063	0.125
Meropenem	≤ 4	≥ 16	100.0	0.0	0.0	0.004 - 0.25	0.016	0.032
TMS**	≤ 2	≥ 16	85.1	0.0	14.9	0.002 - ≥ 32	0.063	≥ 32
Gentamicin	≤ 2	≥ 8	98.8	0.0	1.2	0.125 - 32	0.5	1
Ciprofloxacin	≤ 0.125	≥ 4	95.8	2.4	1.8	0.002 - 32	0.008	0.032

*Amoxi./Clav.=Amoxicillin/Clavulanic acid. Breakpoints for Amoxicillin/Clavulanic acid have not been defined by AFA. **TMS=Trimethoprim/Sulfamethoxa-zole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 53. *Escherichia coli* blood culture isolates (n=168). Distribution (%) of MIC values (mg/L). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility. Hatched areas indicate MIC values above the range of the respective Etest strips.

	≤ 0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline							1	1	7	26	20	11	7	6	1	2	18
Ampicillin								1	2	30	33	6	1	1			28
Amoxi./Clav.*								1	1	20	50	21	5	2	1		
Cefuroxime							1		5	53	35	3	2	1	1		
Ceftazidime				1	13	55	26	2	0	1	1	1					1
Cefpirome			4	38	44	10	1	2		2		1					
Meropenem	1	6	81	12		1	1										
TMS**	1		2	19	37	17	9	2						15			
Gentamicin						12	26	36	19	7		1		1			
Ciprofloxacin	7	50	27	11	1	1	2	1	1		2			1			

*Amoxi./Clav.=Amoxicillin/Clavulanic acid. Breakpoints for Amoxicillin/Clavulanic acid have not been defined by the AFA group. **TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS:

The isolates are generally susceptible to all classes of broad-spectrum antimicrobial agents including amino-glycosides (gentamicin), quinolones (ciprofloxacin) and carbapenems (meropenem). A large proportion of isolates are not fully susceptible to ampicillin and cefuroxime according to the Norwegian AFA breakpoints. As can be seen in Table 52 and Figures 7 and 8, many of these isolates would be categorized as susceptible by use of the NCCLS breakpoint of S ≤ 8 mg/L. A significant proportion of *E. coli* isolates is resistant to ampicillin (MIC ≥ 32 mg/L) by both AFA and NCCLS criteria.

FIGURE 7. Minimal inhibitory concentrations (MIC) of ampicillin for *E. coli* blood culture isolates. AFA breakpoints are red, the lower NCCLS breakpoint is blue.

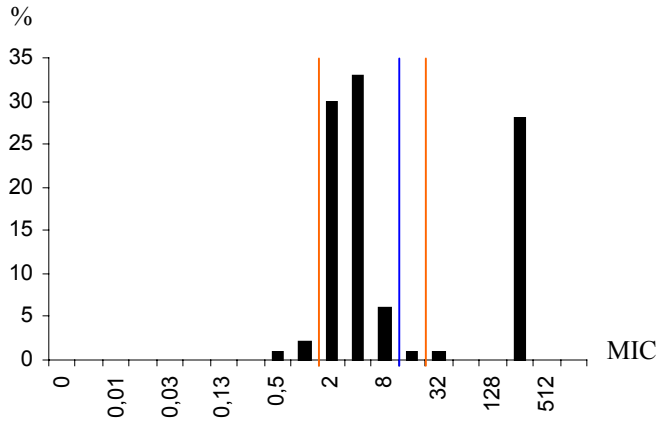
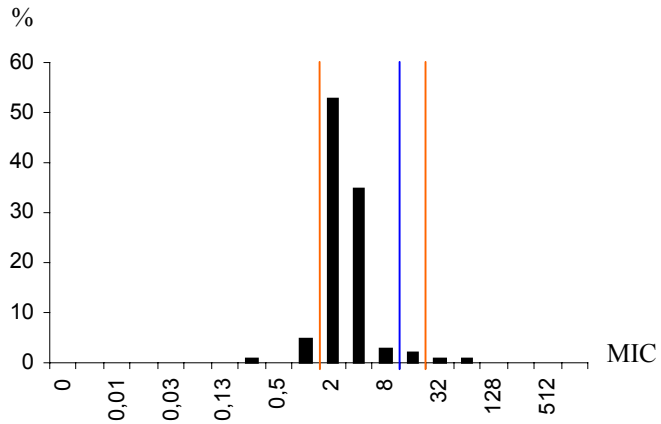


FIGURE 8. Minimal inhibitory concentrations (MIC) of cefuroxime for *E. coli* blood culture isolates. AFA breakpoints are red, the lower NCCLS breakpoint is blue.



Single isolates were reported with elevated MIC values for 3rd (ceftazidime) and 4th (cefpirome) generation cephalosporins indicating possible extended spectrum β-lactamase production, however this could not be confirmed by further examinations including use of the ESBL E-test strip.

Klebsiella spp. in blood cultures

TABLE 54. *Klebsiella* spp. blood culture isolates (n=127). MIC_{50}, MIC_{90}, MIC range, and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to antimicrobial agents. Sampling, microbiological methods and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	3.1	17.3	79.5	1 - ≥ 256	8	≥ 256
Ampicillin	≤ 1	≥ 32	0.8	33.1	66.1	1 - ≥ 256	32	≥ 256
Amoxi./Clav.*	-	-	-	-	-	1 - 32	2	4
Cefuroxime	≤ 1	≥ 32	17.3	78.7	3.9	0.25 - ≥ 256	2	8
Ceftazidime	≤ 1	≥ 32	96.9	1.6	1.6	0.032 - 32	0.125	0.5
Cefpirome	≤ 1	≥ 32	97.6	0.8	1.6	0.016 - ≥ 256	0.063	0.125
Meropenem	≤ 4	≥ 16	100.0	0.0	0.0	0.008 - 0.25	0.032	0.032
TMS**	≤ 2	≥ 16	93.7	1.6	4.7	0.016 - ≥ 32	0.125	0.5
Gentamicin	≤ 2	≥ 8	99.2	0.0	0.8	0.063 - 64	0.5	1
Ciprofloxacin	≤ 0.125	≥ 4	92.9	7.1	0.0	0.004 - 2	0.032	0.125

*Amoxi./Clav.=Amoxicillin/Clavulanic acid. Breakpoints for Amoxicillin/Clavulanic acid have not been defined by AFA.
**TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 55. *Klebsiella* spp. blood culture isolates (n=127). Distribution (%) of MIC values (mg/L). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility. Hatched areas indicate MIC values above the range of the respective Etest strips.

	≤ 0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline									3	17	18	12	16	14	5	3	12
Ampicillin									1	1	3	14	17	27	15	11	14
Amoxi./Clav.*									11	63	20	3	4	1			
Cefuroxime							1	4	14	54	15	5	4	1	1		2
Ceftazidime				4	28	30	24	8	3	1			1	2			
Cefpirome			1	28	46	18	3	3		1				1			1
Meropenem		1	31	63	3	2	1										
TMS**			1	3	20	41	23	4	1	2		2	1	4			
Gentamicin					1	7	24	46	17	5					1		
Ciprofloxacin	1	7	27	40	9	9	1	4	2	1							

*See footnote Table 54. **See footnote Table 54.

COMMENTS:

As for *E. coli*, *Klebsiella* spp. blood culture isolates are generally susceptible to broad-spectrum antimicrobial agents of the aminoglycoside (gentamicin), quinolone (ciprofloxacin) and carbapenem (meropenem) classes. There is a wide range of MIC values for ampicillin with an MIC_{50} of 32 mg/L. The β-lactamase mechanism of ampicillin resistance in *Klebsiella* spp. is demonstrated by the β-lactamase/β-lactamase inhibitor combination amoxicillin/clavulanic acid with MICs between 1 and 32 mg/L and MIC_{90} of 8 mg/L. Norwegian breakpoints for amoxicillin/clavulanic acid have not been defined.

FIGURE 9. Minimal inhibitory concentrations (MIC) of ampicillin for *Klebsiella* spp. blood culture isolates. AFA breakpoints are red, the lower NCCLS breakpoint is blue.

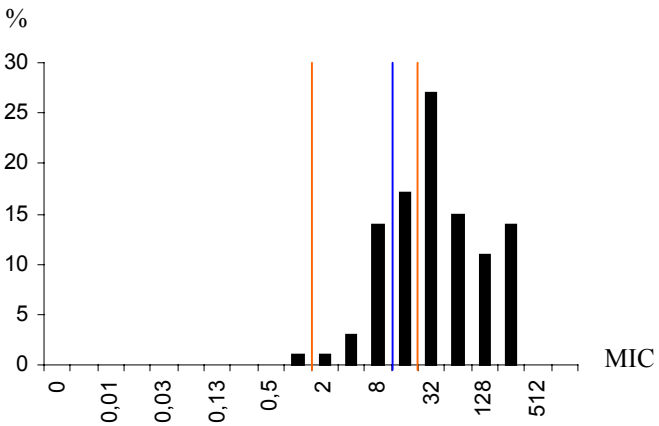
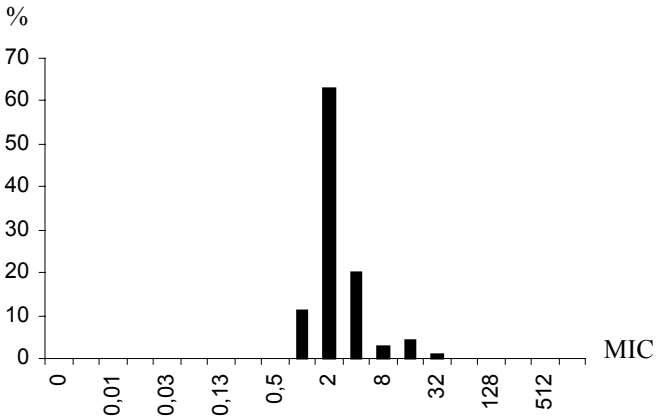


FIGURE 10. Minimal inhibitory concentrations (MIC) of amoxicillin/clavulanic acid for *Klebsiella* spp. blood culture isolates. AFA breakpoints have not been defined.



A total of 4 *Klebsiella* spp. isolates (3.2%) had elevated MICs for 3rd and/or 4th generation cephalosporins, and production of extended-spectrum β-lactamases were confirmed by use of ESBL E-test strips. Genotyping has not been performed, but the isolates originated from 3 different hospitals without obvious epidemiological links.

Enterococcus spp. in blood cultures

TABLE 56. *Enterococcus* spp. blood culture isolates (n=121). MIC_{50}, MIC_{90}, MIC range, and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to antimicrobial agents. Sampling, microbiological methods and data handling are described in Appendix 5.

	Breakpoints mg/L		Proportion of isolates (%)			MIC range	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Ampicillin	≤ 1	≥ 32	87.6	7.4	5.0	0.063 - ≥ 256	0.5	2
Penicillin G	≤ 1	≥ 32	38.0	53.7	8.3	0.032 - ≥ 256	2	16
β-lactamase	Neg	Pos	100.0	-	0.0			
TMS*	≤ 2	≥ 16	86.8	0.0	13.2	0.002 - ≥ 32	0.063	≥ 32
Streptomycin	≤ 512	≥ 1024	85.1	-	14.9	2 - ≥ 1024	32	≥ 1024
Gentamicin	≤ 512	≥ 1024	92.6	-	7.4	0.125 - ≥ 1024	4	16
Vancomycin	≤ 4	≥ 16	83.3	12.5	4.2	0.5 - 16	2	8
Teicoplanin	≤ 4	≥ 16	100.0	0.0	0.0	0.032 - 2	0.5	2
Vancomycin Agar Screen			100.0	-	0.0			

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 57. *Enterococcus* spp. blood culture isolates (n=121). Distribution (%) of MIC values (mg/L). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility. Hatched areas indicate MIC values above the range of the respective Etest strips.

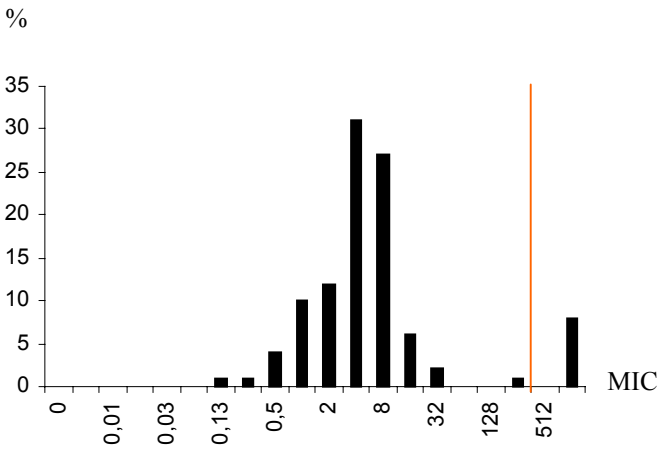
	≤ 0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512	≥ 1024
Ampicillin			3	2	20	35	28	3	3	2	1	3	1		2		
Penicillin G		1	1		5	7	25	39	11	2	3	6	1	1	1		
TMS*	3	16	37	17	10	3	2				1	12					
Streptomycin								1	7	6	17	27	19	5	2	3	15
Gentamicin				1	1	4	10	12	31	27	6	2			1		8
Vancomycin						3	15	35	33	12	4						
Teicoplanin		2		10	31	23	18	17									

*TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS:

The data for *Enterococcus* spp. include *E. faecalis* (75%), *E. faecium* (10%) and unspecified (15%). This may influence the results as *E. faecium* isolates are generally less susceptible to ampicillin whereas a higher proportion of *E. faecalis* isolates will display high-level resistance to aminoglycosides. As a group, *Enterococcus* spp. is generally susceptible to the traditional combination therapy of ampicillin and gentamicin. β-lactamase production was not detected.

FIGURE 11. Minimal inhibitory concentrations (MIC) of gentamicin for *Enterococcus* spp. blood culture isolates. The AFA/ NCCLS breakpoint for high level resistance is shown in red.



16.7% of *Enterococcus* spp. isolates were non-susceptible (MIC ≥ 8) to vancomycin by Etest. This contradicts the results of the vancomycin screening agar where 100% of the isolates were susceptible to vancomycin. As shown in Figure 12, the MIC results for vancomycin are normally distributed which would not be expected if Van-type resistance was present in the population, and *van*-genes were not detected in the non-susceptible isolates. We therefore suggest that MICs are overestimates by the present Etest methodology for vancomycin in enterococci using 200 microlitres of 2.0 McFarland on brain heart infusion (BHI) agar.

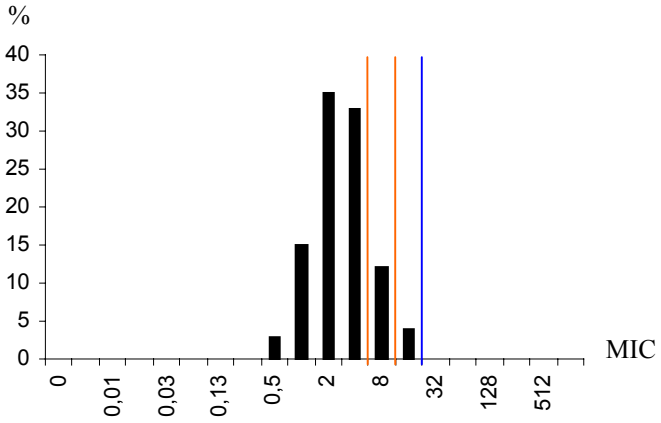


FIGURE 12. Minimal inhibitory concentrations (MIC) of vancomycin for *Enterococcus* spp. blood culture isolates. AFA breakpoints are red, the upper NCCLS breakpoint is blue.

The high level of susceptibility to trimethoprim/ sulfamethoxazole (TMS) does not indicate that TMS may be useful in the treatment of systemic enterococcal infections. The TMS combination may appear active against enterococci *in vitro*, but the clinical efficacy in serious enterococcal infections is uncertain.

Streptococcus pneumoniae in blood cultures

TABLE 58. *Streptococcus pneumoniae* blood culture isolates (n=167). MIC_{50}, MIC_{90}, MIC range, and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to antimicrobial agents. Sampling, microbiological methods and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	99.4	0.0	0.6	0.032 - 16	0.25	0.5
Chloramph.	≤ 2	≥ 8	92.8	6.0	1.2	0.25 - 32	2	2
Penicillin G*	≤ 0.063	≥ 2	98.8	0.6	0.6	0.002 - 2	0.016	0.016
Cefuroxime	≤ 1	≥ 32	98.8	1.2	0.0	0.016 - 2	0.016	0.016
Cefotaxime	≤ 1	≥ 32	100.0	0.0	0.0	0.002 - 1	0.016	0.016
Oxacillin screen	≥ 20 mm	≤ 19 mm	100.0	-	0.0			
TMS**	≤ 2	≥ 16	98.2	0.6	1.2	0.016 - ≥ 32	0.125	0.25
Erythromycin	≤ 1	≥ 4	97.6	0.0	2.4	0.016 - 16	0.125	0.125
Clindamycin	≤ 1	≥ 4	100.0	0.0	0.0	0.016 - 0.25	0.125	0.25
Ciprofloxacin	≤ 0.125	≥ 4	1.2	98.2	0.6	0.125 - 4	1	2
Vancomycin	≤ 4	≥ 16	100.0	0.0	0.0	0.25 - 4	0.5	2

*Penicillin G=Benzylpenicillin. **TMS= Trimethoprim/ Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 59. *Streptococcus pneumoniae* blood culture isolates (n=167). Distribution (%) of MIC values (mg/L) and mm disc diffusion (oxacillin). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility. Hatched areas indicate MIC values above the range of the respective Etest strips.

	≤ 0.002	0.004	0.008	0.016	0.032	0.063	0.125	0,25	0,5	1	2	4	8	16	32	64	≥ 128
Doxycycline					1	2	33	52	12					1			
Chloramph.								1	3	17	72	6		1	1		
Penicillin G*	2	4	23	64	6					1	1						
Cefuroxime				90	9						1						
Cefotaxime	3	7	26	56	7					1							
TMS**				1	1	2	49	42	3	1		1		1	1		
Erythromycin				1	8	38	49	1				1		1			
Clindamycin				2	8	16	57	17									
Ciprofloxacin							1	4	32	40	21	1					
Vancomycin								3	50	28	19	1					

	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	≥ 35
Oxacillin disc		13		1	3	7	16	13	15	7	8	13	2	2	1		

*Penicillin G=Benzylpenicillin. **TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

COMMENTS:

Non-susceptibility to β-lactams in *Streptococcus pneumoniae* is an increasing problem in many countries. Except for a few isolates with MICs of 1 – 2 mg/L, all *S. pneumoniae* blood culture isolates are susceptible to penicillin G. They are also fully susceptible to cefotaxim, the cephalosporin most relevant for treatment of systemic pneumococcal infections. The oxacillin disk screen is routinely used for detecting reduced susceptibility to penicillin G in Norway. The results confirm that this method is suitable to diagnose susceptibility to β-lactams, but the paucity of non-susceptible isolates precludes any conclusions concerning the ability to detect intermediately susceptible and resistant isolates.

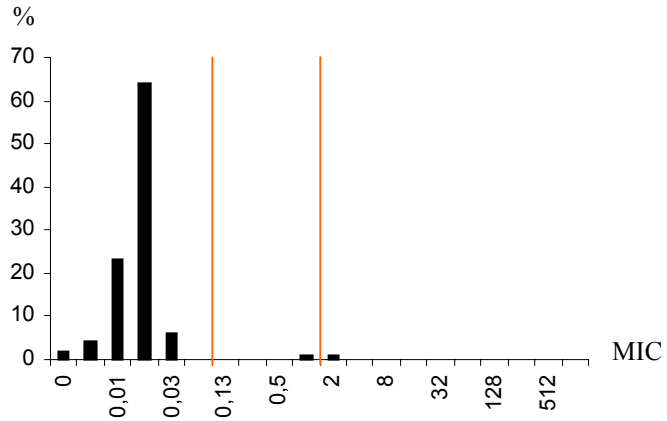
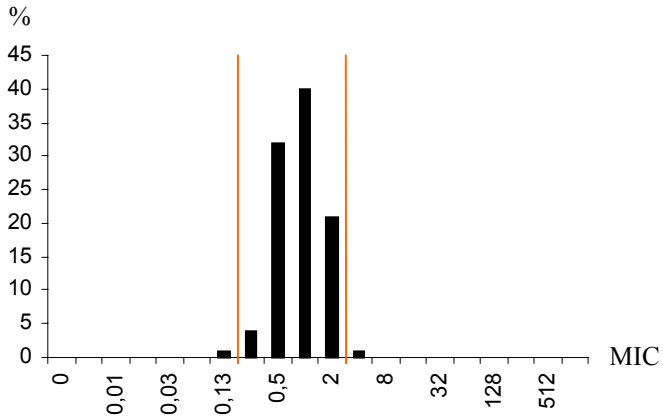


FIGURE 13. Minimal inhibitory concentrations (MIC) of penicillin G for *S. pneumoniae* blood culture isolates. The AFA/NCCLS breakpoints are shown in red.

Macrolide resistance is uncommon with only 2.4% of isolates displaying MICs ≥ 4 mg/L. According to the AFA ciprofloxacin breakpoints of 0.125 and 4 mg/L, the majority of isolates are categorized as intermediately susceptible to this substance (see Figure 14). The fluoroquinolones available in Norway thus have a limited activity against the primary pathogen in community-acquired bacterial respiratory tract infections.

FIGURE 14. Minimal inhibitory concentrations (MIC) of ciprofloxacin for *S. pneumoniae* blood culture isolates. The AFA/NCCLS breakpoints are shown in red.



Staphylococcus aureus in blood cultures

TABLE 60. *Staphylococcus aureus* blood culture isolates (n=158). MIC_{50}, MIC_{90}, MIC range, and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to antimicrobial agents. Sampling, microbiological methods and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	91.8	1.3	7.0	0.063 - 64	0.25	0.5
Penicillin G*	≤ 0.125	≥ 0.25	29.3	-	70.7	0.016 - ≥ 256	1	8
Oxacillin	≤ 1	≥ 4	94.9	3.8	1.3	0.063 - 32	0,5	1
Cefuroxime	≤ 1	≥ 32	94.9	5.1	0.0	0.125 - 4	1	1
β-lactamase	Neg	Pos	25.5	-	74.5			
Oxacillin screen	≤ 2	≥ 4	96.3	-	3.7			
Erythromycin	≤ 1	≥ 4	98.7	0.0	1.3	0.063 - ≥ 256	0.25	0.5
Clindamycin	≤ 1	≥ 4	100.0	0.0	0.0	0.016 - 0.25	0.125	0.25
Gentamicin	≤ 2	≥ 8	100.0	0.0	0.0	0.063 - 2	0.25	1
Vancomycin	≤ 4	≥ 16	97.5	1.9	0.6	0.25 - 8	1	4
Fucidic acid	≤ 0.5	≥ 1	98.1	-	1.9	0.016 - 8	0.063	0.125

*Penicillin G=Benzylpenicillin.

TABLE 61. *Staphylococcus aureus* blood culture isolates (n=158). Distribution (%) of MIC values (mg/L). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility.

	≤ 0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline					9	38	35	9	1	2	5		1	1	1		
Penicillin G*			12	13	4	2	1	14	23	12	7	6	3	4	1		2
Oxacillin					2	16	32	33	13	4		1		1			
Cefuroxime						1	7	34	54	5	1						
Erythromycin					3	42	42	13									1
Clindamycin			1	2	47	41	10										
Gentamicin					1	21	40	19	17	3							
Vancomycin							1	3	53	26	15	2					
Fucidic acid			1	12	43	37	6	1		1	1	1					

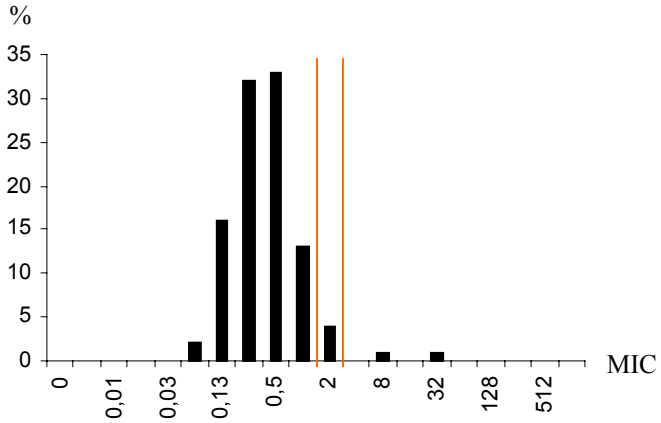
*Penicillin G=Benzylpenicillin.

COMMENTS:

74.5% of *S. aureus* blood culture isolates are β-lactamase producers. The percentage of resistance to penicillin G in the MIC test is slightly lower (70.7%), but the specific assay for β-lactamase production is more reliable for determination of true penicillin G resistance. Resistance to oxacillin indicates resistance to all β-lactam antibiotics including all penicillins and cephalosporins. Such strains are commonly referred to as methicillin-resistant *S. aureus* (MRSA). 5.1% of the isolates are non-susceptible to oxacillin by Etest, and 3.7% display growth on the oxacillin screening agar. However, the intermediately susceptible isolates (3.8%, n=6) had MIC of 2 mg/L and are probably clinically susceptible to oxacillin as they were all *mecA* PCR negative. The remaining two isolates (1.3%) with MICs of 8 and 32 mg/L are MRSA as defined by the MIC, but only the 32 mg/L isolate was *mecA* PCR positive. The 8 mg/L isolate was *mecA* PCR negative and may represent a β-lactamase hyper-producing strain.

The low level of oxacillin resistance is in accordance with data from the Norwegian Surveillance System for Communicable Diseases (MSIS). 67 cases of MRSA infections were reported in 2000, and only two of these were septicaemic patients. No patients died from MRSA infections in Norway in 2000 (MSIS).

FIGURE 15. Minimal inhibitory concentrations (MIC) of oxacillin for *S. aureus* blood culture isolates. AFA breakpoints are shown in red. The NCCL uses only a single breakpoint of S ≤ 2 / R ≥ 4 for *S. aureus*.



The isolates are generally susceptible to other classes of antimicrobial agents used for staphylococcal infections including macrolides (erythromycin), lincosamides (clindamycin) and fucidic acid. Three isolates (2%) had vancomycin MICs of 8 mg/L and were thus categorized as intermediately susceptible. Population-based analysis of these isolates has not been performed. However, reduced susceptibility to vancomycin in *S. aureus* has primarily been demonstrated in MRSA strains, and our isolates were all fully susceptible to oxacillin. We therefore suggest that the vancomycin MIC has been overestimated by the Etest methodology as previously discussed for enterococci.

Haemophilus influenzae in respiratory tract specimens

TABLE 62. *Haemophilus influenzae* respiratory tract isolates (n=355). MIC_{50}, MIC_{90}, MIC range, and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to antimicrobial agents. Sampling, microbiological methods and data handling are described in Appendix 5.

	Breakpoints mg/L		Proportion of isolates (%)			MIC range	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	35.2	48.2	16.6	0.125 - 8	2	4
Ampicillin	≤ 2	≥ 8	94.6	0.0	5.4	0.032 - ≥ 256	0.25	0.5
Penicillin G*	≤ 1	≥ 8	90.1	3.1	6.8	0.016 - 32	0.5	1
Penicillin V**	≤ 1	≥ 4	21.4	37.9	40.8	0.008 - ≥ 256	2	8
Amoxi./Clav.***	≤ 2	≥ 8	98.9	0.6	0.6	0.064 - 32	0.5	1
β-lactamase	Neg	Pos	92.9	-	7.1			
TMS****	≤ 2	≥ 16	94.1	3.4	2.5	0.004 - ≥ 32	0.063	0.25
Erythromycin	≤ 1	≥ 4	2.8	18.9	78.3	0.032 - 32	4	8

*Penicillin G=Benzylpenicillin. **PenicillinV=Phenoxymethylpenicillin. ***Amoxi./Clav.=Amoxicillin/Clavulanic acid. ****TMS=Trimethoprim/Sulfa-methoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 63. *Haemophilus influenzae* respiratory tract isolates (n=355). Distribution (%) of MIC values (mg/L). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility. Hatched areas indicate MIC values above the range of the respective Etest strips.

	≤ 0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥ 256
Doxycycline							3	8	24	49	15	1					
Ampicillin				1	2	25	54	10	2	1							4
Penicillin G				1	2	8	36	39	5	3		1		6			
Penicillin V						1	1	4	16	38	27	5	2	1		1	6
Amoxi./Clav.					1	6	20	55	13	2							
TMS	1	2	12	30	30	13	4		1	1	2	1	1	3			
Erythromycin									2	19	43	29	5				

See footnotes Table 62.

COMMENTS:

Resistance to penicillins in *H. influenzae* may be mediated by β-lactamase production or structural changes in the penicillin-binding proteins reducing the affinity for the substance. 9.9% of respiratory tract *H. influenzae* isolates are non-susceptible to penicillin G, and the vast majority are resistant on the basis of β-lactamase production (7.1%). This is confirmed by the low level of resistance to the combination of amoxicillin and the β-lactamase inhibitor clavulanic acid (0.6% intermediately susceptible and 0.6% resistant). The data further demonstrate the differences in MIC when using penicillin G and penicillin V. As shown in Figures 16 and 17, these two substances cannot be used interchangeably in resistance determination of *H. influenzae*. As shown in Table 62, the majority of *H. influenzae* isolates are non-susceptible to erythromycin by the AFA criteria.

FIGURE 16. Minimal inhibitory concentrations (MIC) of penicillin G (benzyl-penicillin) for *H. influenzae* respiratory tract isolates. AFA breakpoints are shown in red.

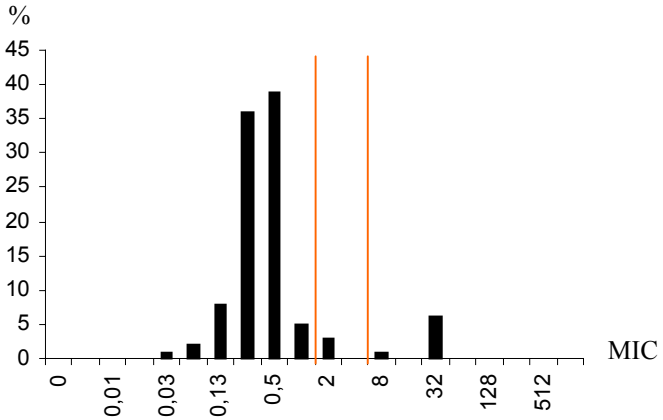
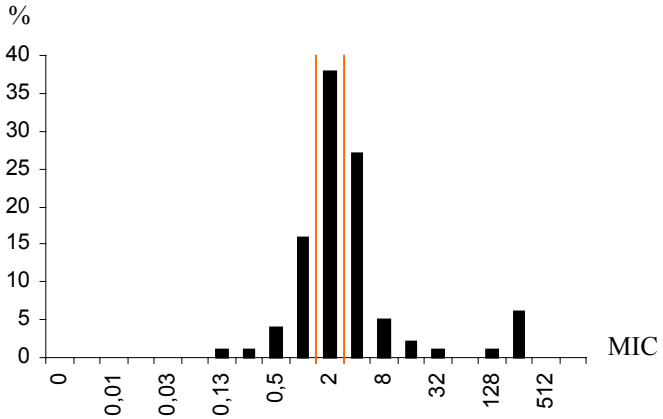


FIGURE 17. Minimal inhibitory concentrations (MIC) of penicillin V (phenoxy-methylpenicillin) for *H. influenzae* respiratory tract isolates. AFA breakpoints are shown in red.



Streptococcus pneumoniae in respiratory tract specimens

TABLE 64. *Streptococcus pneumoniae* respiratory tract isolates (n=340). MIC_{50}, MIC_{90}, MIC range, and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to antimicrobial agents. Sampling, microbiological methods and data handling are described in Appendix 5.

	Breakpoints (mg/L)		Proportion of isolates (%)			MIC range (mg/L)	MIC_{50}	MIC_{90}
	S	R	S	I	R			
Doxycycline	≤ 1	≥ 4	94.4	2.6	2.9	0.016 - 16	0.125	0.5
Penicillin G*	≤ 0.063	≥ 2	97.4	2.6	0.0	0.004 - 0.5	0.016	0.032
Oxacillin screen	≥ 20 mm	≤ 19 mm	98.0	-	2.0			
TMS**	≤ 2	≥ 16	97.6	1.2	1.2	0.016 - ≥ 32	0.25	0.5
Erythromycin	≤ 1	≥ 4	97.9	0.0	2.1	0.032 - ≥ 256	0.125	0.125
Clindamycin	≤ 1	≥ 4	99.1	0.6	0.3	0.008 - ≥ 256	0.125	0.25

Penicillin G=Benzylpenicillin. **TMS=Trimethoprim/Sulfamethoxazole. The breakpoints for the TMS combination are given for the trimethoprim component only.

TABLE 65. *Streptococcus pneumoniae* respiratory tract isolates (n=340). Distribution (%) of MIC values (mg/L) and mm disc diffusion (oxacillin). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility. Hatched areas indicate MIC values above the range of the respective Etest strips.

	≤ 0.002	0.004	0.008	0.016	0.032	0.063	0.125	0.25	0.5	1	2	4	8	16	32	64	≥ 128
Doxycycline					1	10	50	24	7	2	3	1	1	1			
Penicillin G			31	58	7	2	3										
TMS*					1	1	31	54	9	1		1	1		2		
Erythromycin					2	30	62	4						1			
Clindamycin					2	19	61	17									

	≤ 19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	≥ 35
Oxacillin disc	2		1	1	1	1	8	8	16	11	11	13	7	4	5	3	6

See footnotes Table 64.

COMMENTS:

The low level of non-susceptibility to penicillin in *S. pneumoniae* respiratory tract isolates is in accordance with the blood culture data (Table 58). A total of 2.6% (n=9) of the isolates are categorized as intermediately susceptible to penicillin, and all these isolates have a MIC of only 0.125 mg/L, which is the first MIC step above the susceptibility breakpoint (Figure 18). The oxacillin screening test is again demonstrated as a useful tool for detection of *S. pneumoniae* strains with reduced susceptibility to penicillin in a predominantly susceptible strain collection (Figure 19).

The isolates are generally susceptible to all other agents used for the treatment of upper respiratory tract infections in Norway, including tetracycline (doxycycline), macrolides (erythromycin), lincosamides (clindamycin) and trimethoprim/sulfamethoxazole.

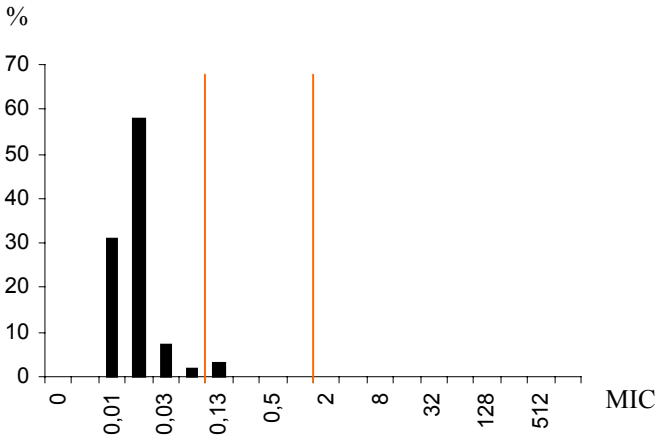
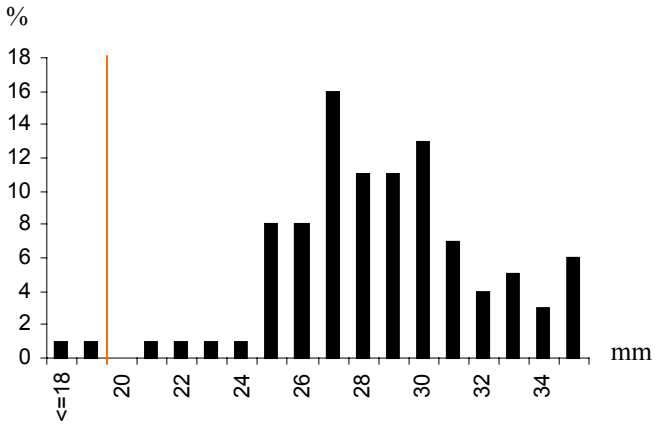


FIGURE 18. Minimal inhibitory concentrations (MIC) of penicillin G for *S.pneumoniae* respiratory tract isolates. AFA breakpoints are shown in red.

FIGURE 19. Oxacillin disk screening test for penicillin resistance in *S. pneumoniae* respiratory tract isolates. Zone diameters ≤ 19 mm indicate reduced susceptibility to penicillin.



Escherichia coli in urine

TABLE 66. *Escherichia coli* urinary tract isolates (n=729). Susceptibility range (mm) and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to antimicrobial agents. Sampling, microbiological methods and data handling are described in Appendix 5.

	Breakpoints (mm)		Proportion of isolates (%)			Range (mm)
	S	R	S	I	R	
Ampicillin	≥ 25	≤ 8	10.2	64.8	25.0	6 - 34
Mecillinam	≥ 24	≤ 13	87.5	10.3	2.2	6 - ≥ 40
Trimethoprim	≥ 22	≤ 16	80.5	0.3	19.2	6 - ≥ 40
Sulfonamide	≥ 26	≤ 11	54.0	18.7	27.3	6 - 39
Ciprofloxacin	≥ 29	≤ 17	96.6	2.5	1.0	6 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	96.8	-	3.2	6 - 37
Nitrofurantoin	≥ 19	≤ 18	95.6	-	4.4	6 - ≥ 40

TABLE 67. *Escherichia coli* urinary tract isolates (n=729). Distribution (%) of zone diameters (mm). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility.

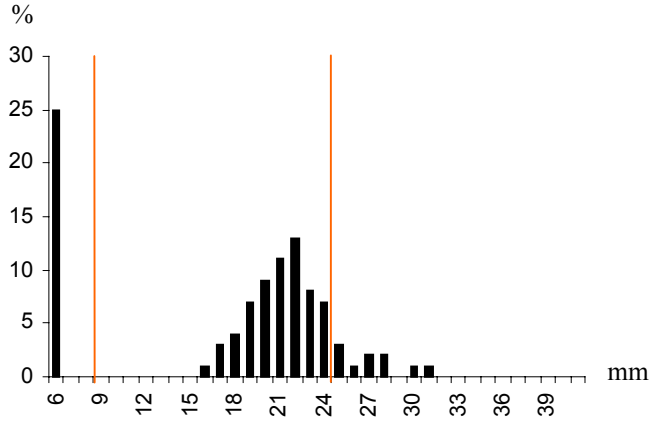
	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Ampicillin	25										1	3	4	7	9	11
Mecillinam	2									1		2		1	1	1
Trimethoprim	19															
Sulfonamide	27													1	1	1
Ciprofloxacin																
Nalidixic acid	3													1	1	1
Nitrofurantoin											1	1	1	2	2	3

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	≥ 37
Ampicillin	13	8	7	3	1	2	2		1	1						
Mecillinam	2	2	3	4	3	3	3	5	12	9	12	11	9	6	4	3
Trimethoprim			1	1	2	3	6	8	13	10	12	8	7	5	3	3
Sulfonamide	2	2	6	6	7	8	7	7	7	4	5	3	2	2	1	2
Ciprofloxacin					1		1	1	3	5	8	10	15	16	14	24
Nalidixic acid	2	3	6	10	14	17	16	8	11	3	3		1			
Nitrofurantoin	6	9	11	14	16	12	10	5	3	2		1			1	

COMMENTS:

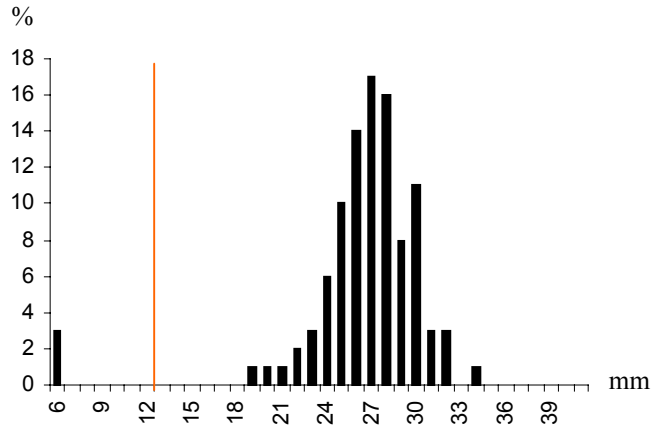
According to Norwegian guidelines, uncomplicated infections of the lower urinary tract in adult women should be treated empirically. The data presented here are primarily from complicated infections in adult women as well as positive cultures from men and children. The majority of isolates represent re-infections or treatment failures, and the level of resistance is probably higher than in uncomplicated infections in adult women. The data may therefore not be suitable for defining primary treatment strategies in uncomplicated cases. A relatively high level of susceptibility is seen for trimethoprim (80.5%), mecillinam (87.5%) and especially nitrofurantoin (95.6%). The majority of isolates are intermediately susceptible to ampicillin, but the separation between susceptible and intermediately susceptible isolates is obviously problematic (Figure 20). The resistant population of 25 % has no inhibition zone around the 6 mm antibiotic disk.

FIGURE 20. Disk diffusion test of ampicillin for *E. coli* urinary tract isolates using 10 µg disks. AFA breakpoints are shown in red. A small zone indicates resistance whereas a large zone indicates susceptibility.



Most strains (96.6%) are fully susceptible to ciprofloxacin, but the occurrence of 3.2% resistance to nalidixic acid is an indication of possible emerging quinolone resistance in this species.

FIGURE 21. Disk diffusion test of nalidixic acid for *E. coli* urinary tract isolates using 30 µg disks. The AFA breakpoint is shown in red. A small zone indicates resistance whereas a large zone indicates susceptibility.



Klebsiella spp. in urine

TABLE 68. *Klebsiella* spp. urinary tract isolates (n=58). Susceptibility range (mm) and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to antimicrobial agents. Sampling, microbiological methods and data handling are described in Appendix 5.

	Breakpoints (mm)		Proportion of isolates (%)			Range (mm)
	S	R	S	I	R	
Ampicillin	≥ 25	≤ 8	0.0	62.5	37.5	6 - 22
Mecillinam	≥ 24	≤ 13	91.2	1.8	7.0	6 - 38
Trimethoprim	≥ 22	≤ 16	91.2	5.3	3.5	6 - 34
Sulfonamide	≥ 26	≤ 11	63.2	33.3	3.5	6 - 33
Ciprofloxacin	≥ 29	≤ 17	91.4	8.6	0.0	25 - ≥ 40
Nalidixic acid	≥ 14	≤ 13	98.3	-	1.7	11 - 34
Nitrofurantoin	≥ 19	≤ 18	75.9	-	24.1	6 - 38

TABLE 69. *Klebsiella* spp. urinary tract isolates (n=58). Distribution (%) of zone diameters (mm). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility.

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Ampicillin	29	9		9	7	7	18	4		2	5	2	2	2		2
Mecillinam	5					2								2		
Trimethoprim	4												2	2		2
Sulfonamide	4											2		4		4
Ciprofloxacin																
Nalidixic acid						2				2	2					3
Nitrofurantoin	2					3	2	3	2	2	3	2	5	9	12	7

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	≥ 37
Ampicillin	4															
Mecillinam			5	2	5	7	12	9	16	5	12	7	9			2
Trimethoprim			2	7	7	12	18	12	11	11	7	4	2			
Sulfonamide	4	2	12	7	9	12	9	7	14	5	5	2				
Ciprofloxacin				2	2	2	3	7	7	14	19	12	12	5	5	11
Nalidixic acid	12	10	17	12	16	10	9	2			2		2			
Nitrofurantoin	10	5	7	3	9		7	3							2	2

COMMENTS:

A limited number of urinary tract *Klebsiella* spp. isolates were included in the analysis (n=58), and further data are needed to draw any firm conclusions with regard to antimicrobial susceptibility in this genus. As for blood culture isolates, *Klebsiella* spp. is less susceptible to ampicillin than *E. coli*. However, most isolates are still susceptible to primary choices for initial therapy such as trimethoprim and mecillinam (Figures 22 and 23). Specific tests for detection of extended spectrum β-lactamase production in urinary tract *Klebsiella* spp. were not included in NORM 2000.

FIGURE 22. Disk diffusion test of trimethoprim for *Klebsiella* spp. urinary tract isolates using 5 µg disks. AFA breakpoints are shown in red. A small zone indicates resistance whereas a large zone indicates susceptibility.

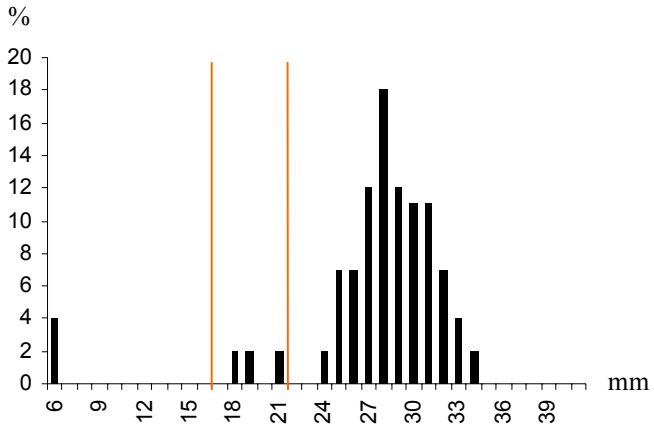
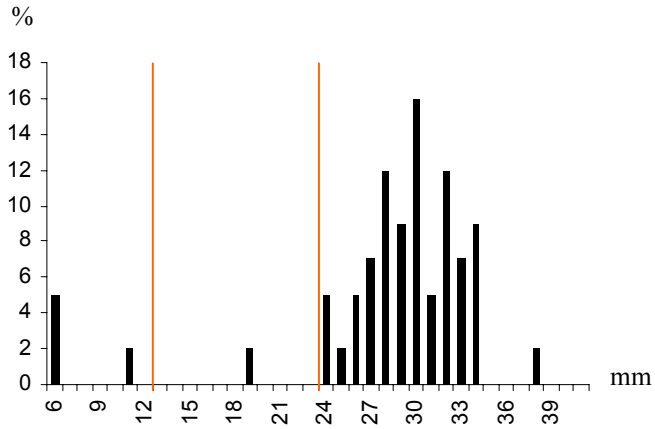


FIGURE 23. Disk diffusion test of mecillinam for *Klebsiella* spp. urinary tract isolates using 10 µg disks. The AFA breakpoint is shown in red. A small zone indicates resistance whereas a large zone indicates susceptibility.



Enterococcus spp. in urine

TABLE 70. *Enterococcus* spp. urinary tract isolates (n=76). Susceptibility range (mm) and proportion of isolates susceptible (S), intermediately susceptible (I) and resistant (R) to antimicrobial agents. Sampling, microbiological methods and data handling are described in Appendix 5.

	Breakpoints (mm)		Proportion of isolates (%)			Range (mm)
	S	R	S	I	R	
Ampicillin	≥ 25	≤ 8	97.4	1.3	1.3	6 - 36
Mecillinam	≥ 24	≤ 13	0.0	0.0	100.0	6 - 6
β-lactamase			100.0	-	0.0	
Trimethoprim	≥ 22	≤ 16	78.9	1.3	19.7	6 - ≥ 40
Sulfonamide	≥ 26	≤ 11	0.0	0.0	100.0	6 - 6
Ciprofloxacin	≥ 29	≤ 17	2.6	81.6	15.8	6 - 33
Nalidixic acid	≥ 14	≤ 13	0.0	-	100.0	6 - 6
Nitrofurantoin	≥ 19	≤ 18	100.0	-	0.0	23 - 36

TABLE 71. *Enterococcus* spp. urinary tract isolates (n=76). Distribution (%) of zone diameters (mm). Dark grey squares indicate resistance, light grey squares indicate intermediate susceptibility, and white squares indicate susceptibility.

	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Ampicillin	1															
Mecillinam	100															
Trimethoprim	18							1					1			
Sulfonamide	100															
Ciprofloxacin	15						1						1	9	15	12
Nalidixic acid	100															
Nitrofurantoin																

	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	≥ 37
Ampicillin		1		3	11	11	11	17	25	11	4	3	3		1	
Mecillinam																
Trimethoprim		1				3	13	5	8	7	8	9	11	8	1	4
Sulfonamide																
Ciprofloxacin	15	12	11	1	4	3			1			1				
Nalidixic acid																
Nitrofurantoin		3	4	4	5	4	3	8	11	13	16	12	12	3	4	

COMMENTS:

As for *Klebsiella* spp., the number of *Enterococcus* spp. included in NORM 2000 is limited (n=76). While nitrofurantoin (100% S) is a good alternative and trimethoprim may be useful in this setting (78.9% S and uncertain bypass of folate metabolism in urine), enterococci are naturally resistant to other typical urinary tract antimicrobials such as mecillinam and sulfonamides. Nalidixic acid has no activity against enterococci, and 15.8% of the isolates are completely resistant to ciprofloxacin. No isolates with β-lactamase production were detected.

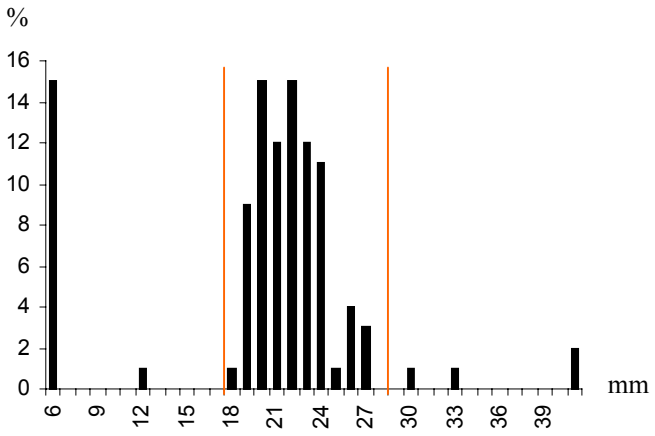


FIGURE 24. Disk diffusion test of ciprofloxacin for *Enterococcus* spp. urinary tract isolates using 10 µg disks. AFA breakpoints are shown in red. A small zone indicates resistance whereas a large zone indicates susceptibility.

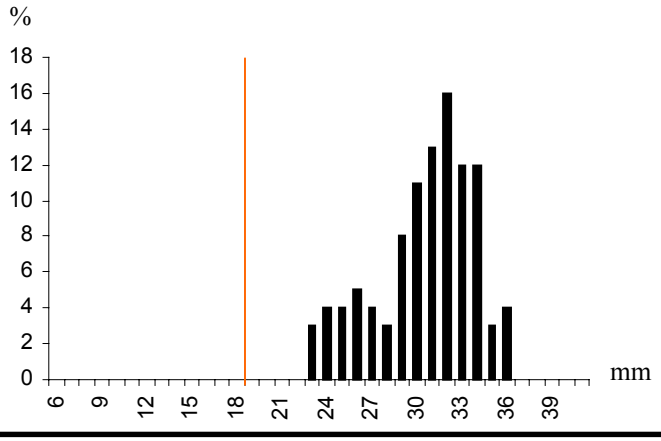


FIGURE 25. Disk diffusion test of nitrofurantoin for *Enterococcus* spp. urinary tract isolates using 100 µg disks. The AFA breakpoint is shown in red. A small zone indicates resistance whereas a large zone indicates susceptibility.

Mycobacterium tuberculosis

A total of 238 new cases of tuberculosis were reported to the Norwegian Surveillance System for Communicable Diseases (MSIS) and the Norwegian Tuberculosis Register in the year 2000 (MSIS rapport 2001. 29: 18-19). *Mycobacterium tuberculosis* was isolated from 170 of these patients. The antimicrobials susceptibility test results for *M. tuberculosis* isolates from 160 patients not previously treated for tuberculosis are shown in Table 71.

TABLE 72. Antimicrobial susceptibility of 160 *Mycobacterium tuberculosis* isolates from patients not previously treated for tuberculosis (ref. MSIS Rapport, 2001, 29:19). Sampling, microbiological methods and data handling are described in Appendix 5.

Geographic origin of patients	No. of isolates	Resistance to antimicrobial agents (isolates)				
		Isoniazid	Rifampicin	Ethambutol	Streptomycin[1]	Multi – resistance[2]
Norway	42	1	0	3	3	0
Europe outside Norway	15	0	0	0	1	0
Asia	41	8	1	5	7	1
Africa	57	10	2	3	6	1
America	1	0	0	0	0	0
2nd generation immigrants	4	2	1	0	1	1
Total	160	21	4	11	18	3
Proportion of isolates resistant (%)		13	3	7	12	2

[1] Isolates from 10 patients were not tested for susceptibility to streptomycin.
[2] Multiresistance is defined as resistance to at least rifampicin and isoniazid.

Twelve patients have been diagnosed with mulitresistant *M. tuberculosis* isolates in Norway in the last five years. All patients except one have been of immigrant descent. However, infection control investigations and finger-printing by RFLP-typing of *M. tuberculosis* isolates indicate that several patients may have acquired their infection in Norway.

Appendix 1:
Collection of data on animal consumption of antimicrobial agents

Data sources

Feed additives

The approval and monitoring of sale of feed additives; i.e. antibacterial growth promoters and coccidiostats, in Norway is in charge of the Norwegian Agricultural Inspection Service (NAIS). Reliable data on the usage of the different substances and categories of feed additives can be obtained from NAIS.

Antibacterial drugs for therapeutic use

In Norway, veterinary antibacterial drugs for therapeutic use in domestic animals or farmed fish are prescription drugs only. Moreover, veterinary antibacterial drugs have to be dispensed through pharmacies, which are supplied solely by drug wholesalers. An exemption from the pharmacy/wholesalers monopoly has been granted for medicated feed (i.e. feeds into which drugs for therapeutic use are mixed prior to sale). Medicated feed have to be prescribed by veterinarians, and are produced and delivered by feed mills authorised by the Norwegian Medicines Agency. In Norway, medicated feeds produced and supplied by feed mills are used only in farmed fish. The reason why feed mill production of medicated feed for use in livestock is not practiced in Norway is the small size of livestock herds compared to most other European countries. Herd/flock treatment of livestock with antibacterial drugs is, however, possible, but such practice is subjected to veterinary prescription, drugs being administered either through drinking water or in medicated feed prepared on the farm.

The sales figures of veterinary antibacterial drugs from wholesalers and feed mills are thought to roughly equal the use of these drugs. Veterinary antibacterial drug use and usage are therefore used as synonyms of sales figures of veterinary antibacterial drugs.

On behalf of the Ministry of Health and Social Welfare, overall sales data, representing sales from the Norwegian drug wholesalers to pharmacies and from feed mills to fish farms, are recorded by the WHO Collaborating Centre for Drug Statistics Methodology. This centre is situated in Oslo and is also responsible for collecting drug sales data on a national level.

The feed mills and the drug wholesalers have to report their sales figures of drugs for therapeutic use to the WHO Collaborating Centre of Drug Statistics Methodology. This reporting was made mandatory from July 2001 to ensure that the data will be complete.

Drug classification system

In Norway, the Anatomical Therapeutic Chemical (ATC) classification system is used to classify veterinary medicinal products (ATCvet).

Unit of measurement

Amount of active substance, in kg, was chosen as the unit of measurement. The amounts, in kg active substance, of veterinary antibacterial specialities supplied by wholesalers to pharmacies and by feed mills, were calculated from sales figures. The data for benzyl penicillin salts and esters (procaine penicillin and penethamate hydriodide) were converted to the corresponding values for benzyl penicillin.

Inclusion criteria

All veterinary antibacterial specialities included in this report belong to the following ATCvet groups: gastrointestinal infections (QA07AA), uterine infections (QG01AA+AE), and antibacterial drugs for systemic use (QJ), including intramammary dose applicators (QJ51). The QJ-group also includes medicated feed and premix for farmed fish that are approved by the drug authorities and classified as pharmaceutical specialities (QJ01).

Dermatological preparations (QD) and preparations intended for sensory organs (QS) are not included in the material. In small animal practice, human antibacterial drugs are also prescribed. However, data about usage of these drugs in animals are not included in the material as such use cannot be separated from use in humans.

Appendix 2:
Collection of data on human consumption of antimicrobial agents

In Norway, antibacterials are prescription drugs only (POM), and only allowed sold by pharmacies. Drug statistics on consumption of antibacterials for human use are based on sale of medicaments from drug wholesalers to pharmacies and hospitals in Norway. This data cover total sale of antibacterials for humans in Norway. Sale to hospitals and nursing homes represents around 7.5% of the total use of antibacterials for human use.
The figures presented should be regarded as maximum figures with the assumption that all medicaments sold from the wholesalers are actually consumed. The actual drug consumption will probably be somewhat lower.

The data are collected on behalf of the Ministry of Health and Social Welfare, by the WHO Collaborating Centre for Drug Statistics Methodology. Data on drug use has been collected since the beginning of the seventies.

The statistical data is sorted according to the ATC classification system and Defined Daily Doses (DDDs) are employed as units of measurement.
The ATC/DDD system is recommended by the WHO to serve as a tool for drug utilisation research in order to improve quality of drug use. One component of this is the presentation and comparison of drug consumption statistics at international and other levels.

The use of defined daily dose, DDD, as a unit of measurement, simplifies and improves the evaluation of drug consumption over time, nationally and internationally. The DDD is a theoretical unit of measurement, and does not necessarily reflect the recommended or Prescribed Daily Dose.

The basic **definition** of the unit is:

The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults.

The DDDs for the antiinfectives are as a main rule based on the use in infections of moderate severity. Some antiinfectives are only used in severe infections and their DDDs are assigned accordingly. The DDDs assigned are based on daily treatment.

Inclusion criteria
The antibacterials for human use included in this report belong to ATC J01 antibacterials for systemic use. Oral vancomycin (A07AA09) and oral and rectal metronidazole (P01AB01) are also included. The ATC/ DDD index version 2001 is used.
Antibacterials used in dermatological preparations (ATC group D) and preparations intended for sensory organs (ATC group S) are not included in the material.

Appendix 3:
Sampling, microbiological methods and data handling in NORM-VET

Bacteria from feed

Escherichia coli

Sampling strategy
Samples from dog feed (chewing bones, frozen offal products, and dried offal products (pig ears, ox penises etc.) were collected by District Veterinary Officers as part of a survey conducted by the Norwegian Animal Health Authority.

Isolation and identification of bacteria
Bacteria were isolated and identified at the National Veterinary Institute. Five gram of material was incubated with 45 ml of MacConkey broth (Oxoid). After incubation at 44°C for 24h a small amount of broth was plated onto the surface of lactose agar (Difco). After incubation at 37°C for 24h, a typical colony was plated onto blood agar. Colonies were identified as *E. coli* if they had a typical colony appearance, were lactose fermenting and indole positive. One isolate per sample was tested for antimicrobial susceptibility.

Susceptibility testing
The isolates were tested for their antimicrobial susceptibility at the National Veterinary Institute. MIC (minimal inhibitory concentration) values were obtained using Mueller-Hinton agar plates and Etest (AB Biodisk). For those antimicrobial agents for which Etest was not available, a disk diffusion method using Neo-Sensitabs (Rosco) was applied.

Bacteria from animals

***Staphylococcus* spp. from mastitis in cows**

Sampling strategy
Milk samples were collected by veterinary practitioners (clinical mastitis) or by consultants from the National Production Recording Scheme (subclinical mastitis). Information about the animals such as health status was given on a standardized scheme.

Isolation and identification of bacteria
Isolates were obtained at the National Veterinary Institute or the Mastitis Laboratory in Molde by plating secretions (0.01 ml) on blood agar (Heart infusion agar (Difco) containing 5 % washed bovine erythrocytes). The plates were incubated in 5% CO_2 atmosphere at 37°C for 24 and 48 h. If no growth was detected after incubation for 24 h, the original secretion sample was preincubated for 4 h at 37°C, and an increased inoculum (0.05 ml) was cultivated on another blood agar as described above.
Species identification of typical isolates was based on the occurrence of haemolytic zones, Gram stain, catalase-, coagulase-, acetoin- and β-galactocidase production, fermentation of D-mannitol and use of the Staph-Zym® system (Rosco). Isolation and identification was performed at the National Veterinary Institute.

Susceptibility testing
Only one isolate from each herd was included. The isolates were tested for antimicrobial susceptibility at the National Veterinary Institute. MIC values were obtained using a microdilution method, VetMIC™ (Dept. of Antibiotics, National Veterinary Institute, Sweden).

***S. intermedius* from skin infections in dogs**

Sampling strategy
Veterinary practitioners provided samples from skin and ear lesions from animals with a history of furunculosis, other skin infections, or otitis externa. The samples were examined within three days after sampling.

Isolation and identification of bacteria
The samples were submitted to the National Veterinary Institute and cultivated on two blood agar plates (heart infusion agar (Difco) containing 5 % washed bovine erythrocytes). The plates were incubated in 5% CO_2 atmosphere and anaerobically respectively at 37°C for 16-24 hrs. Greyish white colonies with a beta-haemolytic zone on blood agar were isolated and tested for cell morphology and Gram stain, production of catalase, coagulase, β-galactosidase and acetoin, and fermentation of D-mannitol.

Susceptibility testing
The isolates were tested for their antimicrobial susceptibility at the National Veterinary Institute. MIC values were obtained using a microdilution method, VetMIC™ (Dept. of Antibiotics, National Veterinary Institute, Sweden) was utilized. For those antimicrobial agents for which VetMIC™ was not available, Mueller-Hinton agar plates and Etest (AB Biodisk) were used.

Bacteria from food

Escherichia coli

Sampling strategy
Samples from Norwegian food products were collected as a part of official monitoring activities run by the Norwegian Food Control Authority. The samples were collected by the Municipal Food Control Authorities.

Isolation and identification of bacteria
Bacteria were isolated and identified at the National Veterinary Institute. Five gram of material was incubated with 45 ml of MacConkey broth (Oxoid). After incubation at 44°C for 24h a small amount of broth was plated onto the surface of lactose agar (Difco). After incubation at 37°C for 24h, a typical colony was plated onto blood agar. Colonies were identified as *E. coli* if they had a typical colony appearance, were lactose fermenting and indole positive. One isolate per sample was tested for antimicrobial susceptibility.

Susceptibility testing
The isolates were tested for their antimicrobial susceptibility at the National Veterinary Institute. MIC values were obtained using Mueller-Hinton agar plates and Etest (AB Biodisk). For those antimicrobial agents for which Etest was not available, a disk diffusion method using Neo-Sensitabs (Rosco) was applied.

Coagulase positive *Staphylococcus* spp.

Sampling strategy
Bulk milk samples from cattle and goat dairy herds from different parts of Norway were collected by the dairy industry.

Isolation and identification of bacteria
Coagulase positive *Staphylococcus* spp. from bulk milk samples were isolated and identified at the National Veterinary Institute by plating 0.1 ml bulk milk on blood agar (Heart infusion agar (Difco) containing 5 % washed bovine erythrocytes). The plates were incubated in 5 % CO_2 atmosphere at 37 ^{o}C for 24 and 48 h. Species identification of typical isolates was based on the occurrence of haemolytic zones and production of coagulase (Monostaph®, Bionor AS). One isolate per bulk milk sample was tested for antimicrobial susceptibility.

Susceptibility testing
The isolates were tested for their antimicrobial susceptibility at the National Veterinary Institute. MIC values were obtained using Mueller-Hinton agar plates and Etest (AB Biodisk). For those antimicrobial agents for which Etest was not available, a disk diffusion method using Neo-Sensitabs (Rosco) was applied.

***Enterococcus* spp.**

Sampling strategy
Samples from Norwegian food products were collected as a part of official monitoring activities run by the Norwegian Food Control Authority. The samples were collected by the Municipal Food Control Authorities.

Isolation and identification of bacteria
Bacteria were isolated and identified at the National Veterinary Institute. Five gram of material was incubated with 45 ml of Azide dextrose broth (Oxoid). After incubation at 44°C for 24h a small amount of broth was plated onto the surface of Slanetz & Bartley agar (Oxoid). After incubation at 37°C for 48h, a typical colony was plated onto blood agar. Colonies were identified as *Enterococcus* sp. if they had a typical colony appearance and were catalase negative. The enterococci were further identified using either ddlID-PCR (multiplex PCR) or rapid ID32 STREP-kit. The bacteria's ability to produce pigment and their motility were also considered. One isolate per sample was tested for antimicrobial susceptibility.

Susceptibility testing
The isolates were tested for their antimicrobial susceptibility at the National Veterinary Institute. MIC values were obtained using Mueller-Hinton agar plates and Etest (AB Biodisk). For those antimicrobial agents for which Etest was not available, a disk diffusion method using Neo-Sensitabs (Rosco) was applied. When testing for vancomycin resistance in enterococci, Brain Heart Infusion agar (Difco) was used instead of Mueller-Hinton agar.

Quality assurance systems
The laboratories at the National Veterinary Institute have a quality assurance system according ISO 17025.
The following bacteria were included as quality controls on a weekly basis: *Staphylococcus aureus* ATCC 29213, *Escherichia coli* ATCC 25923, *Enterococcus faecalis* ATCC 29212, *Campylobacter jejuni* subsp. *jejuni* ATCC 33291. The results were approved according to reference values given by NCCLS.

Data handling
Susceptibility data are in most instances recorded in WHONET5, a programme developed by the World Health Organization (WHO) for analysis of antimicrobial resistance data (ftp.who.int/data/cds/csreph).

Range of dilutions used for staphylococci isolated from mastitis in cows and skin infections in dogs

	VetMIC plate range (mg/L)		
Oxytetracycline	0.5	-	4
Chloramphenicol	2	-	16
Penicillin	0.06	-	8
Oxacillin	0.5	-	4
Cephalothin	0.12	-	1
TMS	0.25/4.75	-	8/152
Erythromycin	0.25	-	2
Spiramycin	4	-	32

	VetMIC plate range (mg/L)		
Clindamycin	1	-	8
Streptomycin	2	-	256
Gentamycin	0.25	-	32
Neomycin	1	-	128
Vancomycin	1	-	128
Avilamycin	0.5	-	64
Virginiamycin	0.5	-	64

Appendix 4:
Sampling, microbiological methods and data handling of zoonotic infections

Salmonella **(isolates from feed, animals, food and humans),** ***Yersinia enterocolitica*** **(isolates from humans) and** ***Shigella*** **spp. (isolates from humans)**

Sampling strategy
Feedstuff from both terrestrial animals and fish were collected according to the official surveillance programs, internal control procedures, and import control legislation.
Samples from animals were collected according to *The Norwegian Salmonella control program for live animals, eggs and meat*. Additionally, faecal samples were obtained from live animals in relation to clinical examinations, and samples from organs were obtained at autopsy at the National Veterinary Institute.
Samples from food were collected in relation to official surveys, routine controls, and outbreak investigations.
Human clinical isolates are isolates obtained from clinical specimens from humans and referred to the Reference Laboratory for Enteropathogenic Bacteria at the National Institute of Public Health.

Isolation and identification of bacteria
For samples from feed and animals, and from food, isolation and identification of bacteria was carried out at the National Veterinary Institute or at the Municipal Food Control Authorities, respectively, according to the Nordic Committee on Food Analyses (NMKL), method no. 71, or ISO no. 6579.
Isolation and identification of bacteria from humans was performed according to conventional methods described in standard reference litterature (e.g. the ASM Manual of Clinical Microbiology).
Confirmation, including typing, was performed at the National Institute of Public Health.

Susceptibility testing
The isolates from feed and animals were tested for antimicrobial susceptibility at the National Veterinary Institute. MIC values were obtained using a microdilution method, VetMIC™ (Dept. of Antibiotics, National Veterinary Institute, Sweden). Range of dilutions for the VetMIC plates are shown in the table on page 63. Only one isolate of each serovar per outbreak or herd was included.
The isolates from food and human clinical cases were tested for antimicrobial susceptibility at the National Institute of Public Health by an agar disk diffusion test using PDM II agar plates and PDM disks (AB Biodisk). Only one isolate of each serovar from one batch of food was included. Only one isolate per patient and infectious episode was included.

Campylobacter **spp. (isolates from animals, food and humans)**

Sampling strategy
Samples from animals were collected as part of a research project at the National Veterinary Institute in collaboration with the Norwegian Zoonosis Centre addressing the occurrence of *Campylobacter* spp. in healthy dogs and cats. Samples were collected at six veterinary clinics located in various parts of Norway.
Samples from food were collected by the Municipal Food Control Authorities in relation to official surveys, routine controls, and outbreak investigations.
Human clinical isolates are isolates obtained from clinical specimens from humans and referred to the Reference Laboratory for Enteropathogenic Bacteria at the National Institute of Public Health.

Isolation and identification of bacteria
Samples from dogs and cats were plated on Campylobacter blood-free agar (Oxoid) supplemented with cephoperazone, amphotericin B and teicoplanin (Oxoid). The plates were incubated at 37°C for 72-96 hours in a microaerobic atmosphere. The isolates were typed according to their susceptibility to nalidixic acid and cephoperazone and their cultural and biochemical characteristics. Confirmation, including typing, was performed at the National Veterinary Institute.
Isolates from food were isolated according to the NMKL, method no. 119.
Isolation and identificationm of bacteria from humans was performed according to conventional methods described in standard reference litterature (e.g. the ASM Manual of Clinical Microbiology). Confirmation was performed at the National Institute of Public Health.

Susceptibility testing
The isolates were tested for antimicrobial susceptibility (MIC values) using Mueller-Hinton agar plates (Difco) and Etest (AB Biodisk) at the National Veterinary Institute (isolates from animals) or at the National Institute of Public Health (isolates from food and humans). For humans, only one isolate per patient and infectious episode was included.

Quality assurance systems

The at the National Veterinary Institute and the Reference Laboratory for Enteropathogenic Bacteria at the National Institute of Public Health have a quality assurance system according to ISO 17025. The National Institute of Public Health is takes part in the external quality assessment programme for *Salmonella* organized by Enter-Net. At the National Veterinary Institute, the following bacteria were included as quality controls on a weekly basis: *Staphylococcus aureus* ATCC 29213, *Escherichia coli* ATCC 25923, *Enterococcus faecalis* ATCC 29212, *Campylobacter jejuni* subsp. *jejuni* ATCC 33291. The results were approved according to reference values given by NCCLS.

Data handling

Susceptibility data are in most instances recorded in WHONET5, a programme developed by the World Health Organization (WHO) for analysis of antimicrobial resistance data (ftp.who.int/data/cds/csreph).

Range of dilutions used for *Salmonella*

	VetMIC plate range (mg/L)		
Oxytetracycline	0.5	-	64
Chloramphenicol	2	-	16
Florfenicol	2	-	16
Ampicillin	0.25	-	32
Amoxi./Clav.*	2/1	-	16/8
Ceftiofur	0.25	-	2
Trimethoprim	0.12	-	16

	VetMIC plate range (mg/L)		
Sulfamethoxazole	64	-	512
Streptomycin	2	-	256
Gentamycin	0.25	-	32
Neomycin	1	-	128
Apramycin	0.25	-	32
Enrofloxacin	0.5	-	64
Nalidixic acid	1	-	128

Appendix 5:
Sampling, microbiological methods and data handling in NORM

General considerations

NORM is based upon periodic sampling of bacteria from patients with respiratory tract infections, urinary tract infections and blood culture isolates. This first year, nine laboratories from all over Norway participated in the surveillance system in addition to the National Institute of Public Health.

The surveillance strategy is based on sampling and local testing bacterial isolates from defined clinical conditions. All laboratories follow the same sampling strategy and use identical criteria for the inclusion of bacterial strains. Only one isolate per patient and infectious episode is included. All bacteria were identified using conventional methods as described in the ASM Manual of Clinical Microbiology.

The surveillance period started in the beginning of January, and consecutive bacterial isolates were included up to a defined maximum of isolates for each surveillance category. The surveillance categories in 2000 were: *E. coli*, *Klebsiella* spp., *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Enterococcus* spp. from blood cultures; *Streptococcus pneumoniae* and *Haemophilus influenzae* from respiratory tract infections and *E. coli*, *Klebsiella* spp. and *Enterococcus* spp. from urinary tract infections.

Blood culture isolates and isolates from respiratory tract infections were tested using E-test, while isolates from urinary tract infections were examined by a disk diffusion method according to the method described by the Norwegian Reference Group on Antibiotic Susceptibility Testing (AFA). In order to follow trends in the occurrence of resistance, all resistance values were recorded either as MICs or mm inhibition zone sizes. Suspected MRSA (*S. aureus* with oxacillin MIC $\geq$ 4 mg/L) were to be confirmed with a *mecA* PCR, and suspected VRE (enterococci growing on BHI with 6 mg/L of vancomycin) were to be confirmed with PCR for the *van* gene complex.

A computer program was developed for the registration of patient data, sample data and resistance data. The data was analysed by WHONET5 with the aid of a special program (NORMlink developed by John Stelling) converting the data base structure of NORM to a single file format and then using Baclink to convert data to the WHONET format.

Blood culture isolates

All participating laboratories keep blood cultures isolates frozen. Consecutive isolates of up to 20 each of *E. coli*, *Klebsiella* spp., pneumococci, *S. aureus* and enterococci from January until testing time in September to October were included in the surveillance. All isolates were identified to genus or preferably to species level using conventional bacteriological methods. All isolates were tested using Etest (AB Biodisk, Solna, Sweden). A total of 168 isolates of *E. coli*, 127 isolates of *Klebsiella* spp, 158 isolates of *S. aureus* and 121 isolates of enterococci were tested on PDM agar at 35ºC in ambient air, while the 167 isolates of pneumococci were tested on PDM agar supplemented with 5% lysed horse blood at 35ºC in 5% CO_2.

Respiratory tract infections (RTIs)

Consecutive isolates of *S. pneumoniae* and *H. influenzae* from patients with RTIs were to be collected in each laboratory during February and March. All isolates were kept in a freezer and tested in batch with Etest (AB Biodisk, Solna Sweden). The total number of pneumococci were 340 (38 isolates per lab with a range of 7-54) and 355 *H. influenzae* (39 isolates per lab with a range of 12 to 54). Most of the isolates were collected during the given time frame, but 30% of the pneumococci and 23% of *H. influenzae* were collected during April through June.

S. pneumoniae were tested on PDM agar supplemented with 5% lysed horse blood at 35ºC in 5% CO_2. *H. influenzae* were tested on PDM agar supplemented with 1% haemoglobin and 1% isovitalex at 35ºC in 5% CO_2.

Urinary tract infections (UTIs)

A total of 100 consecutive isolates of *E. coli*, *Klebsiella* spp. and *Enterococcus* spp. from patients with UTIs were to be collected during March through June. All isolates were either kept on bench or in a freezer until tested in batch with a disk diffusion method using PDM agar and paper disk (AB Biodisk, Solna Sweden) at 35ºC in ambient air. The total number of *E. coli* was 729 isolates, *Klebsiella* spp. 58 isolates and enterococci 76 isolates.

Mycobacterium tuberculosis

In the year 2000, antimicrobial susceptibility testing of *M. tuberculosis* was performed at the following laboratories: Department of Microbiology, National Institute of Public Health, Oslo, Department of Microbiology, Ullevål University Hospital, Oslo, and Department of Immunology and Microbiology, Haukeland University Hospital, Bergen. The majority of isolates were tested using the BACTEC system (both laboratories in Oslo). All three laboratories participate in an external quality control program organized by the WHO.

Appendix 6:
Table of breakpoints

	MIC values, µg/ml		Values from*	Used in**	MIC values, µg/ml		Values from*	Used in**	MIC values, µg/ml		Values from*	Used in**	MIC values, µg/ml		Values from*	Used in**
	S	R			S	R			S	R			S	R		
Amoxi./clav.	≤ 8	≥ 32	A	ae	≤ 2	≥ 8	B	j								
Ampicillin	≤ 8	≥ 32	A	abdf	≤ 8	≥ 16	F	d	≤ 2	≥ 8	B	j	≤ 1	≥ 32	B	kl
Apramycin	≤ 32	≥ 64	E	a												
Avilamycin	≤ 16	≥ 32	F	e												
Bacitracin	≤ 64	≥ 128	C	d												
Cefotaxime	≤ 1	≥ 32	B	h												
Cefpirome	≤ 1	≥ 32	B	l												
Ceftazidime	≤ 1	≥ 32	B	l												
Ceftiofur	≤ 2	≥ 8	A	a												
Cefuroxime	≤ 1	≥ 32	B	ghl	≤ 4	≥ 32	F	f								
Cephalothin	≤ 8	≥ 32	A	e												
Chloramphenicol	≤ 8	≥ 32	A	abdef	≤ 2	≥ 8	B	h								
Ciprofloxacin	≤ 0.125	≥ 4	B	bchl	≤ 1	≥ 4	A	e								
Clindamycin	≤ 1	≥ 4	B	eghi												
Doxycycline	≤ 1	≥ 4	B	cghijl												
Enrofloxacin	≤ 0.25	≥ 2	A	a	≤ 0.5	≥ 2	F	f								
Erythromycin	≤ 1	≥ 4	B	bceghij	≤ 4	≥ 8	C	d								
Florfenicol	≤ 16	≥ 32	E	a												
Fucidic acid	≤ 0.5	≥ 1	B	eg												
Gentamicin	≤ 4	≥ 16	A	abf	≤ 2	≥ 8	B	cegl	≤ 256	≥ 512	C	d	≤ 500	≥ 1000	B	k
Kanamycin	≤ 16	≥ 64	A	f												
Meropenem	≤ 4	≥ 16	B	l												
Nalidixic acid	≤ 16	≥ 32	A	ac												
Neomycin	≤ 32	≥ 64	E	ae												
Oxacillin	≤ 2	≥ 4	C	e	≤ 1	≥ 4	B	g								
Oxytetracycline	≤ 8	≥ 16	C	ae	≤ 4	≥ 16	A	bdf								
Penicillin	≤ 0.125	≥ 0.25	B	e												
Penicillin G	≤ 0.125	≥ 0.25	B	g	≤ 0.063	≥ 2	B	hi	≤ 1	≥ 8	B	j	≤ 1	≥ 32	B	k
Penicillin V	≤ 1	≥ 4	B	j												
Spiramycin	≤ 16	≥ 32	E	e												
Streptomycin	≤ 32	≥ 64	E	ae	≤ 4	≥ 8	F	f	≤ 512	≥ 1024	BC	dk	≤ 8	≥ 16	C	b
Sulfamethoxazole	≤ 256	≥ 512	C	a												
Sulfonamides	≤ 256	≥ 512	C	ef												
TMS	≤ 2	≥ 16	B	hijkl	≤ 2	≥ 4	A	e								
Teicoplanin	≤ 4	≥ 16	B	k												
Trimethoprim	≤ 8	≥ 16	A	adef												
Vancomycin	≤ 4	≥ 32	A	de	≤ 4	≥ 16	B	hk								
Virginiamycin	≤ 2	≥ 4	C	e												

Antimicrobials (amount in disks/tablets)	Breakpoints (mm) S	R	Values from *	Used in **
Ampicillin (10 µg)	≥ 25	≤ 8	B	mn
Chloramphenicol (30 µg)	≥ 32	≤ 24	B	n
Ciprofloxacin (10 µg)	≥ 29	≤ 17	B	mn
Mecillinam (10 µg)	≥ 24	≤ 13	B	m
Nalidixic acid (30 µg)	≥ 14	≤ 13	B	mn
Neomycin (30 µg)	≥ 25	≤ 20	D	f
Nitrofurantoin (100 µg)	≥ 19	≤ 18	B	m
Tetracycline (30 µg)	≥ 28	≤ 21	B	n
Sulfisoxazole (250 µg)	≥ 26	≤ 11	B	m
TMS (1.2 + 23.8 µg)	≥ 26	≤ 15	B	mn
Trimethoprim (5 µg)	≥ 22	≤ 16	B	m
Virginiamycin (30 µg)	≥ 23	≤ 19	D	d

* A NCCLS 1999/2000
B AFA 2000
C DANMAP 2000
D Rosco 2000
E SVARM
F Based on Norwegian isolates

** a *Salmonella* spp. feed, animals (MIC)
b *Campylobacter* spp. animals
c *Campylobacter* spp. food, humans
d *Enterococcus* spp. food
e *Staphylococcus* spp. animals, food
f *E. coli* feed, food
g *Staphylococcus aureus* humans, blood culture
h *Streptococcus pneumoniae* humans, blood culture
i *Streptococcus pneumoniae* humans, respiratory tract
j *Haemophilus influenzae* humans, respiratory tract
k *Enterococcus* spp. humans, blood culture
l *E. coli* and *Klebsiella* spp. humans, blood culture
m *E. coli*, *Klebsiella* spp., and *Enterococcus* spp. humans, urinary tract
n *Salmonella* spp. food, humans (mm)