Usage of Antibiotics and
Occurrence of Antibiotic Resistance
in Bacteria from Humans and
Animals in Switzerland

Swiss Antibiotic Resistance Report 2016

anresis.ch
ARCH-Vet

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Swiss Confederation

Federal Department of Home Affairs FDHA
Federal Office of Public Health FOPH
Communicable Diseases

Federal Food Safety and Veterinary Office FSVO
Animal Health

Strategy on Antibiotic Resistance
StAR

Publishing details

Published by Federal Office of Public Health FOPH
Publication date: November 2016
Editors: Homa Attar Cohen, Division of Communicable Diseases, Federal Office of Public Health (FOPH), and Dagmar Heim, Veterinary Medicinal Products and Antibiotics, Federal Food Safety and Veterinary Office (FSVO)
Design and layout: diff. Kommunikation AG, Bern
FOPH publication number: 2016-OEG-30
Source: SFBL, Distribution of Publications, CH-3003 Bern
www.bundespublikationen.admin.ch
Order number: 316.402.16eng
www.star.admin.ch

Please cite this publication as:
Federal Office of Public Health and Federal Food Safety and Veterinary Office. Swiss Antibiotic Resistance Report 2016. Usage of Antibiotics and Occurrence of Antibiotic Resistance in Bacteria from Humans and Animals in Switzerland. November 2016. FOPH publication number: 2016-OEG-30

Table of contents

1

Foreword

1 Foreword

The "Swiss Antibiotic Resistance Report 2016" is the second combined national report on the comprehensive monitoring of antibiotic resistance and antibiotic consumption in human and veterinary medicine. It reports data from the monitoring systems of anresis.ch and ARCH-Vet for the years 2014 and 2015.

Following a One Health approach, the Federal Department of Home Affairs and the Federal Department of Economic Affairs, Education and Research have mandated the responsible Federal Office of Public Health (FOPH), the Federal Food Safety and Veterinary Office (FSVO), the Federal Office for Agriculture (FOA) and the Federal Office for the Environment (FOEN) to develop a National Strategy on Antibiotic Resistance (StAR). One year after the beginning of implementation, a large number of strategic measures have already been initiated in all four domains. The One Health approach as well as the coordination during the implementation are essential objectives of the Swiss strategy in order to adequately counter the complex problems of antibiotic resistance. Comprehensive surveillance and monitoring is a key element in detecting, monitoring and preventing the development of antibiotic resistance. It allows for the identification of mid- and long term trends and forms the basis for the detection, interpretation and evaluation of the antibiotic resistance's situation in Switzerland.

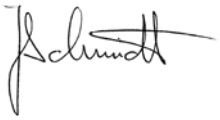
Since 2004, anresis.ch has been gathering data from human microbiological laboratories on antibiotic resistance. The system has since been expanded as to enlarge data collection on antibiotic consumption from hospitals and pharmacies on use in human medicine. The anresis.ch data can be viewed on an interactive database. Specific resistance data are published monthly in the FOPH Bulletin.

Since 2006, the FSVO has been running a monitoring system to assess antibiotic resistance in livestock and in meat. In addition, it collects data on the wholesale sales of antibiotics in veterinary medicine. Since 2009, sales data on veterinary antibiotics and the results of the monitoring of resistances in livestock are published annually in the ARCH-Vet report.

The joint reporting and interpretation of the antibiotic resistance situation in Switzerland is one of the strategic measures of StAR. In future, the "Swiss Antibiotic Resistance Report" will be published every two years. The differences relating to data collection, methodology and interpretation that currently exist in the monitoring systems need to be harmonized and refined to enable a better comparison of the results according to the One Health approach. Also, data from the agriculture and the environment sector should be included.

The FOPH and the FSVO wish to thank the authors of this report for their commitment and outstanding work. We would also like to thank all those who have contributed to the data collection for this report.

Daniel Koch
Division Communicable Diseases
Federal Office of Public Health



Josef Schmidt
Division Animal Health
Federal Food Safety and Veterinary Office

1 Vorwort

Der «Swiss Antibiotic Resistance Report 2016» ist der zweite gemeinsame nationale Bericht über die umfassende Überwachung von Antibiotikaresistenzen und den Antibiotikaverbrauch in der Human- und Veterinärmedizin. Er beinhaltet Daten aus Monitoringsystemen von anresis.ch und ARCH-Vet der Jahre 2014 und 2015.

Im Sinne des One-Health-Ansatzes haben das Eidgenössische Departement des Innern und das Departement für Wirtschaft, Bildung und Forschung die zuständigen Bundesämter für Gesundheit (BAG), Lebensmittelsicherheit und Veterinärwesen (BLV), Landwirtschaft (BLW) und Umwelt (BAFU), beauftragt, eine nationale Strategie Antibiotikaresistenzen (StAR) zu erarbeiten. Heute, ein Jahr nach Beginn der Umsetzung, sind bereits zahlreiche Massnahmen in den vier erwähnten Fachbereichen initiiert worden. Der One-Health-Ansatz und die Koordination in der Umsetzung sind essenzielle Ziele der Schweizer Strategie, um der komplexen Problematik der Antibiotikaresistenzen adäquat zu begegnen. Die umfassende Überwachung ist ein Kernelement zur Erkennung, Überwachung und Bekämpfung der Entwicklung von Antibiotikaresistenzen. Sie erlaubt es, Tendenzen über einen längeren Zeithorizont zu verfolgen, und bildet die Grundlage für Erkennung, Interpretation und Evaluation der Antibiotikaresistenzsituation in der Schweiz.

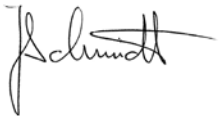
Seit 2004 sammelt anresis.ch Daten zur Antibiotikaresistenzlage aus humanmikrobiologischen Laboratorien. Das System wurde erweitert und erfasst nun ebenfalls Daten zum Antibiotikakonsum in der Humanmedizin aus Spitälern und in Apotheken. Die Daten von anresis.ch können über eine interaktive Datenbank eingesehen werden. Bestimmte Resistenzen werden einmal pro Monat im BAG-Bulletin veröffentlicht.

Seit 2006 führt das BLV ein Monitoringsystem zur Erfassung von Antibiotikaresistenzen bei Nutztieren und Fleisch. Zusätzlich erhebt es Daten zum Vertrieb von Antibiotika in der Veterinärmedizin auf Stufe Grosshandel. Seit 2009 werden die Daten zum Vertrieb von Veterinärantibiotika und die Ergebnisse des Monitorings bei Nutztieren jährlich im ARCH-Vet-Bericht veröffentlicht.

Eine gemeinsame Berichterstattung und Interpretation der Situation in der Schweiz ist eine der strategischen Massnahmen von StAR. Der «Swiss Antibiotic Resistance Report» wird zukünftig alle zwei Jahre publiziert. Die heute bestehenden Unterschiede in den Überwachungssystemen betreffend Datensammlung, Methodik und Interpretation sollen künftig harmonisiert und verfeinert werden, um einen besseren Vergleich der Ergebnisse im One-Health-Ansatz zu erlauben. Auch sollen bestehende Daten der Landwirtschaft und der Umwelt integriert werden.

Das BAG und das BLV danken den Autorinnen und Autoren dieses Berichts für ihr Engagement und für ihre ausgezeichnete Arbeit. Ebenfalls danken wir all denjenigen, die zur Datenerhebung für diesen Bericht beigetragen haben.

Daniel Koch
Abteilung Übertragbare Krankheiten
Bundesamt für Gesundheit



Josef Schmidt
Abteilung Tiergesundheit
Bundesamt für Lebensmittelsicherheit und Veterinärwesen

1 Avant-propos

Le « Swiss Antibiotic Resistance Report 2016 » est le second rapport national sur le suivi global de la résistance aux antibiotiques et la consommation d'antibiotiques en médecine humaine et vétérinaire. Il comporte des données issues des systèmes de surveillance d'anresis.ch et d'ARCH-Vet pour les années 2014 et 2015.

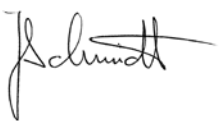
Dans le cadre de l'approche holistique (« One Health ») adoptée dans ce domaine, le Département fédéral de l'intérieur et le Département fédéral de l'économie, de la formation et de la recherche ont chargé l'Office fédéral de la santé publique (OFSP), l'Office fédéral de la sécurité alimentaire et des affaires vétérinaires (OSAV), l'Office fédéral de l'agriculture (OFAG) et l'Office fédéral de l'environnement (OFEV) d'élaborer une stratégie nationale contre la résistance aux antibiotiques (Strategie Antibiotikaresistenzen, StAR). Aujourd'hui, un an après le début de la mise en œuvre de cette stratégie, de nombreuses mesures ont déjà été prises dans les quatre secteurs concernés. L'approche « One Health » et la coordination de la mise en œuvre sont les grands objectifs de la stratégie de la Suisse, afin d'apporter une réponse adéquate au problème de la résistance aux antibiotiques. La surveillance globale est un élément-clé de la détection et du suivi du développement de telles résistances, ainsi que de la lutte contre celui-ci. Elle permet de suivre les tendances sur le long terme, et constitue la base de la définition, de l'interprétation et de l'évaluation de la situation de la Suisse en matière d'antibiorésistance.

Depuis 2004, anresis.ch rassemble des données sur la résistance aux antibiotiques, transmises par des laboratoires de microbiologie humaine. Ces données peuvent être consultées par l'intermédiaire d'une base de données interactive. Le système a été élargi et recueille désormais également des données sur la consommation d'antibiotiques en médecine humaine dans les hôpitaux et les pharmacies. Certaines résistances font l'objet d'articles publiés une fois par mois dans le bulletin de l'OFSP.

Depuis 2006, l'OSAV dispose d'un système de surveillance permettant de déterminer les résistances aux antibiotiques chez les animaux de rente et dans la viande. Il recense également des données sur les ventes d'antibiotiques en médecine vétérinaire au niveau du commerce de gros. Publié chaque année depuis 2009, le rapport ARCH-Vet présente ces données sur les ventes d'antibiotiques et les résultats de la surveillance des résistances chez les animaux de rente. La rédaction d'un rapport commun, présentant une interprétation commune de la situation en Suisse, constitue l'une des mesures stratégiques du programme StAR. Le « Swiss Antibiotic Resistance Report » sera désormais publié tous les deux ans. Les différences existant actuellement entre les modalités de collecte des données, d'analyse et d'interprétation des systèmes de surveillance devront être harmonisées et peaufinées, de façon à permettre de meilleures comparaisons des résultats au sein de l'approche « One Health ». Les données issues des offices de l'agriculture et de l'environnement devront en outre y être intégrées.

L'OFSP et l'OSAV remercient les auteurs du présent rapport pour leur dévouement et le travail remarquable qu'ils ont fourni. Nous tenons également à remercier tous ceux qui ont contribué à la collecte de données pour ce rapport.

Daniel Koch
Division Maladies transmissibles
Office fédéral de la santé publique



Josef Schmidt
Division Santé animale
Office fédéral de la sécurité alimentaire
et des affaires vétérinaires

1 Prefazione

Lo «Swiss Antibiotic Resistance Report 2016» è il secondo rapporto nazionale comune concernente l'ampia sorveglianza delle resistenze agli antibiotici e del consumo di antibiotici nella medicina umana e veterinaria. Esso contiene i dati provenienti da sistemi di monitoraggio di anresis.ch e ARCH-Vet degli anni 2014 e 2015.

Ai sensi dell'approccio One Health, il Dipartimento federale degli interni e il Dipartimento dell'economia, della formazione e della ricerca hanno incaricato i competenti uffici federali della sanità pubblica (UFSP), della sicurezza alimentare e di veterinaria (USAV), dell'agricoltura (UFAG) e dell'ambiente (UFAM) di elaborare una strategia nazionale contro le resistenze agli antibiotici (StAR). Oggi, a un anno dall'attuazione, sono già stati avviati numerosi provvedimenti nei quattro settori specializzati citati. L'approccio One Health e la coordinazione per l'attuazione sono obiettivi essenziali della strategia svizzera per affrontare in maniera adeguata la complessa problematica delle resistenze agli antibiotici. L'ampia sorveglianza è un elemento centrale per riconoscere, osservare e combattere lo sviluppo di resistenze agli antibiotici. Essa permette di seguire le tendenze per un periodo prolungato e costituisce la base per riconoscere, interpretare e valutare la situazione delle resistenze agli antibiotici in Svizzera.

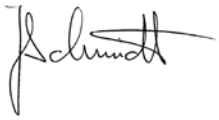
Dal 2004 anresis.ch raccoglie i dati relativi alla situazione delle resistenze agli antibiotici provenienti dai laboratori di microbiologia umana. Il sistema è stato ampliato e comprende ora pure i dati relativi al consumo di antibiotici nella medicina umana provenienti da ospedali e farmacie. I dati di anresis.ch possono essere visionati tramite una banca dati interattiva. La pubblicazione di determinate resistenze avviene una volta al mese nel bollettino UFSP (solamente in tedesco e francese).

Dal 2006 l'USAV gestisce un sistema di monitoraggio per il rilevamento di resistenze agli antibiotici negli animali da reddito e nella carne. Esso rileva inoltre i dati concernenti la vendita di antibiotici nella medicina veterinaria a livello di commercio all'ingrosso. Dal 2009 il rapporto ARCH-Vet pubblica annualmente i dati relativi alla vendita di antibiotici per il settore veterinario e i risultati del monitoraggio degli animali da reddito.

Il resoconto e l'interpretazione comuni della situazione in Svizzera costituiscono una delle misure strategiche del programma StAR. In futuro lo «Swiss Antibiotic Resistance Report» sarà pubblicato ogni due anni. Le differenze odierne nei sistemi di sorveglianza per quanto riguarda la raccolta di dati, la metodologia e l'interpretazione dovranno in futuro essere armonizzate e affinate, al fine di permettere un migliore confronto dei risultati nell'approccio One Health. Occorrerà integrare pure i dati disponibili dell'agricoltura e dell'ambiente.

L'UFSP e l'USAV ringraziano gli autori e le autrici del presente rapporto per il loro impegno e per il loro eccellente lavoro. Ringraziamo pure tutti coloro che hanno contribuito al rilevamento dei dati per il presente rapporto.

Daniel Koch
Divisione Malattie trasmissibili
Ufficio federale della sanità pubblica



Josef Schmidt
Divisione Salute degli animali
Ufficio federale della sicurezza alimentare e di veterinaria

2

Summary

2 Summary

Antibiotic consumption in human medicine

In Swiss acute care hospitals, consumption of antibiotics for systemic use increased by 36% to 62.9 DDD per 100 bed-days between 2004 and 2015, whereas it was relatively stable when expressed in DDD per 100 admissions. This discrepancy can be explained by an increasing number of admissions and a decreasing number of bed-days in hospitals due to shorter length of hospital stay. The most commonly used class of antibiotics was the penicillins (ATC code J01C), followed by the other beta-lactam antibacterials, including cephalosporins (ATC group J01D) and quinolones (ATC group J01M).

In outpatient care, the most commonly used class of antibiotics was the penicillins (ATC group J01C), followed by the quinolones (ATC code J01M) and the macrolides, lincosamides and streptogramins (ATC group J01F). The relative consumption of fluoroquinolones and penicillins, associated with beta-lactamase inhibitors was relatively high in comparison with countries participating in the European Surveillance of Antimicrobial Consumption Network (ESAC-Net). Total consumption of antibacterials for systemic use (ATC group J01) was close to the median in the inpatient setting, but was relatively low in the outpatient setting compared with the countries participating in the ESAC-Net.

Sales of antimicrobials in veterinary medicine

The sales volume of antimicrobials continued to decline in 2015. Overall, 42,188 kg of antimicrobials were sold for veterinary medicine, which was about 10% less compared with the previous year. This amounts to a decline of 40% (28 tonnes) since 2008. The decrease is mainly due to a fall in sales of medicated premixes.

The sales rankings of the various classes of antimicrobials remained unchanged: sulfonamides are in first place, followed by penicillins and tetracyclines. These three classes are often sold as medicated premixes, which account for about 60% of the total volume (24 tonnes). The quantity of antibiotics approved only for pets comprises 2% of the total volume.

Within the highest-priority critically important antibiotic classes for human medicine (WHO 2011), the sales of macrolides have decreased by approximately 40% (–1,655 kg) since 2008. However, the sales of long-acting, single-dose injection products show an upwards trend. The sales of fluoroquinolones and third- and fourth-generation cephalosporins remained unchanged.

The sales volume of colistin, which is of public interest following the discovery of a horizontally transferable resistance mechanism (MCR-1), has declined approximately 70% since 2008 and amounted to 502 kg in the reporting year.

Resistance in bacteria of human clinical isolates

Since 2004, different trends have been observed in gram-positive and gram-negative bacteria. Methicillin-resistant *Staphylococcus aureus* (MRSA) rates have decreased significantly since 2004, mainly in the western part of Switzerland. This trend has also been observed in several other European countries, including the neighboring countries Germany, France and Italy. Penicillin resistance in *Streptococcus pneumoniae* has also decreased over time. This effect was mainly due to a reduction in the prevalence of more resistant serotypes, due to the introduction of pneumococcal vaccines. Vancomycin resistance in enterococci is very low, and has remained stable over the last 10 years.

In contrast, we have observed a steady increase in quinolone resistance and 3rd-generation cephalosporin resistance in *Escherichia coli* and *Klebsiella pneumoniae*. This increase is observed in most European countries and is consistent with the wide distribution of extended-spectrum-beta-lactamase-(ESBL-)producing isolates. In *K. pneumoniae,* resistance rates have not increased any further since 2013. This is probably rather fortuitous than a true change in the epidemic curve, as resistance rates are increasing steadily in most other European countries. Fortunately, carbapenem resistance still is rare in *E. coli* and *K. pneumoniae*. While carbapenem resistance is rare in *E. coli* in most European countries as well, increasing carbapenem resistance is observed in Europe in *K. pneumoniae;* in 2014, resistance rates above 25% have been described in Italy, Greece and Bulgaria. To allow a closer monitoring of the distribution of carbapenemase-producing Enterobacteriaceae, an obligation to report these microorganisms was introduced in Switzerland on 1.1.2016.

In *Pseudomonas aeruginosa,* significant increases in resistance rates since our last report (data 2013) were observed for ceftazidime and aminoglycosides. More detailed analyses are planned. No relevant changes were observed in *Acinetobacter* spp.

Resistance in zoonotic bacteria

In broilers, the resistance rate to ciprofloxacin in *Campylobacter jejuni (C. jejuni)* has increased significantly in the last years. From 15% in 2006, the resistance rate rose to 46% in 2014. In contrast, resistance to erythromycin was rarely found. Fluoroquinolones, which include ciprofloxacin, and macrolides, which include erythromycin, are highest-priority critically important antimicrobials (WHO), because these substance groups represent the treatment of choice for serious forms of campylobacteriosis or salmonellosis in humans.

In fattening pigs, the resistance rate to streptomycin in *Campylobacter coli (C. coli)* decreased from 2006 to 2012. Subsequently, the resistance rate has increased significantly in the last three years, up to 86.5% in 2015. Also the resistance rates of tetracycline (63.5%) and ciprofloxacin (46.8%) has increased significantly in the last years.

Salmonella occur only rarely in livestock in Switzerland. Therefore, the risk of Salmonella transmission to humans from food produced with Swiss animals is considered low. Moreover, their resistance rates are low, especially in *S. enteritidis* and *S. typhimurium*.

Resistance in indicator bacteria in animals

Antimicrobial resistance is generally widespread in enterococci and *E. coli* isolated from livestock in Switzerland.

Resistances to ampicillin, sulfamethoxazole and tetracycline are often found in commensal *E. coli* isolates from broilers, fattening pigs and veal calves. Additional resistance to ciprofloxacin was found in isolates from broilers. Although resistance to these substances increased in isolates from broilers between 2006 and 2012, the trend is clearly decreasing since then. In isolates from calves, the trend is also decreasing since 2006. However, resistances to tetracycline and ampicillin are increasing again since 2013. In fattening pigs, the resistance rates in *E. coli* isolates have not changed significantly much in the last years.

By applying selective enrichment methods, ESBL/pAmpC-producing *E. coli* were detected in 41.8% of broiler flocks, in 25.7% of fattening pigs and in 37.6% of veal calves. The strong increase of the ESBL/pAmpC prevalence in livestock animals might be due to a more sensitive laboratory method. In 73.3% of chicken meat samples and in 1% of pork samples, ESBL/pAmpC-producing *E. coli* have been detected. No ESBL/pAmpC-producing *E. coli* have been found in beef samples. The occurrence in chicken meat of foreign origin (85.6%) was significantly higher than the occurrence in meat from Swiss production (65.5%). The prevalence in beef and pork is very low or even zero. This difference may relate to the distinct slaughtering processes. No carbapenemase-producing *E. coli* were found in species of livestock and meat thereof.

In the enterococcal species *E. faecalis* and *E. faecium* isolated from broilers, veal calves and fattening pigs, resistances to erythromycin and tetracycline are often found. However, in *E. faecalis* isolated from broilers and veal calves, the resistance to these antimicrobials has decreased in the last years. In contrast, resistance rates in enterococci from fattening pigs have generally increased in the last years.

For many years, no vancomycin-resistant enterococci (VRE) have been detected within the frame of the resistance monitoring of livestock in Switzerland. However, in 2013, one *E. faecalis* isolate from a veal calf and in 2015, two *E. faecium* isolates from fattening pigs were resistant to vancomycin.

Among all investigated species, high rates of resistance have been found for *E. faecium* isolates with respect to quinupristin/dalfopristin, a combination that is authorized in the USA as a therapy option for humans infected with vancomycin-resistant enterococci. Quinupristin/dalfopristin are not used in veterinary medicine. They belong to the streptogramins, which show cross-resistance with macrolides and lincosamides that are widely used in livestock.

In Switzerland, the occurrence of methicillin-resistant *S. aureus* (MRSA) in fattening pigs at slaughter increased significantly from 2% in 2009 to 20.8% in 2013. Since then, the prevalence has remained constant. The results reported for MRSA confirm that spa type t034 in particular, and to a lesser extent also spa type t011, are becoming widespread in Switzerland's population of slaughtered pigs. These genotypes belong to the clonal complex CC 398, which is typically livestock associated (LA-MRSA). MRSA can be transmitted between animals and humans. Not only in Switzerland but also in other European countries, most of the detected MRSA spa types in pigs were associated with LA-MRSA CC398.

MRSA was detected in a total of 6.9% of chicken meat samples, although, at 1%, the occurrence in meat from domestic production was much lower than in meat from abroad (16%). Food is not currently regarded as a relevant source of MRSA transmission to humans.

Resistance in diagnostic submissions from animals

Monitoring of antimicrobial resistance in relevant pathogens from diseased livestock and companion animals is not implemented in Switzerland up to now. In the context of One Health these data are important for the comprehensive risk assessment of resistance in the future, hence a pilot project on antimicrobial resistance in veterinary pathogens was launched by the Federal Food Safety and Veterinary Office in 2015. The Center for Zoonoses, Animal Bacterial Diseases and Antimicrobial Resistance (ZOBA) exemplified such data in staphylococci and *E. coli* from dogs and horses in this report. Isolates were derived from clinical submis-

sions at the ZOBA in 2014 and 2015. As clients of the ZOBA are mostly horse and small-animal clinics, these antibiotic resistance data are not representative for Switzerland. However, high detection rates of methicillin-resistant *Staphylococcus pseudintermedius* in dogs as well as methicillin-resistant *Staphylococcus aureus* rates in horses and the occurrence of multidrug resistant isolates are not only a challenge for the attending veterinarians but pose also a risk for humans because of their zoonotic potential. Establishing representative data from a comprehensive spectrum of pathogens will be the task for the future.

2 Zusammenfassung

Antibiotikaverbrauch in der Humanmedizin

In Schweizer Akutspitälern stieg der Verbrauch von Antibiotika zur systemischen Anwendung zwischen 2004 und 2015 um 36% auf 62,9 DDD (Defined Daily Doses, definierte Tagesdosen) pro 100 Bettentage. In DDD pro 100 Einweisungen berechnet, blieb er jedoch relativ stabil. Diese Diskrepanz lässt sich mit einer steigenden Anzahl von Einweisungen und einer sinkenden Anzahl von Bettentagen aufgrund kürzerer Spitalaufenthalte erklären.

Die am häufigsten verwendete Antibiotikagruppe waren die Penicilline (ATC-J01C), gefolgt von den anderen Beta-Laktam-Antibiotika, inkl. Cephalosporine (ATC-J01D), und von den Quinolonen (ATC-J01M). In der ambulanten Versorgung waren die Penicilline (ATC-J01C) die am häufigsten verwendete Antibiotikagruppe, gefolgt von den Quinolonen (ATC-J01M) sowie den Makroliden, Lincosamiden und Streptograminen (ATC-J01F). Der relative Verbrauch von Fluoroquinolonen und Penicillinen inkl. Beta-Laktamase-Inhibitoren war relativ hoch im Vergleich mit Ländern, die sich am European Surveillance of Antimicrobial Consumption Network (ESAC-Net) beteiligen. Im stationären Bereich lag der gesamte Antibiotikaverbrauch zur systemischen Anwendung (ATC-J01) im Vergleich mit den am ESAC-Net beteiligten Ländern nahe am Median.

Vertrieb von Antibiotika in der Veterinärmedizin

Die verkaufte Antibiotikamenge nahm 2015 weiterhin ab. Insgesamt wurden 42 188 kg Antibiotika für die Veterinärmedizin verkauft. Im Vergleich zum Vorjahr entspricht dies einem Minus von 10%. Verglichen mit 2008 beträgt der Rückgang 40% (oder 28 Tonnen), was vor allem auf eine Abnahme der Verkäufe von Arzneimittelvormischungen zurückzuführen ist.

Die Verkaufsrangliste der verschiedenen Antibiotikaklassen blieb unverändert: Sulfonamide an erster Stelle, gefolgt von Penicillinen und Tetracyclinen. Diese drei Kategorien werden sehr oft als Arzneimittelvormischungen angeboten und machen 60% des gesamten Antibiotikavertriebs aus (24 Tonnen). Der Anteil der Menge an Wirkstoffen, die nur für Haustiere zugelassen sind, umfasste 2% der Gesamtmenge. Von den kritischen Antibiotika mit höchster Priorität für die Humanmedizin (WHO 2011) verzeichneten die Makrolide seit 2008 einen Rückgang von rund 40% (–1655 kg). Eine Zunahme erfolgte dafür bei den Verkäufen von langwirksamen, einmalig applizierten Injektionspräparaten. Die Verkäufe von Fluoroquinolonen und von Cephalosporinen der dritten und vierten Generation blieben unverändert.

Das Verkaufsvolumen von Colistin ist seit der Entdeckung eines horizontalen Transfermechanismus in der Resistenz (MCR-1-Gen) von öffentlichem Interesse. Das Volumen ging seit 2008 um rund 70% zurück und betrug im Berichtsjahr 502 kg.

Resistenz bei Bakterien aus klinischen Isolaten vom Menschen

Seit 2004 wurden verschiedene Tendenzen bei grampositiven und gramnegativen Bakterien beobachtet. Die Raten Methicillin-resistenter *Staphylococcus aureus*-Bakterien (MRSA) nahmen seit 2004 bedeutend ab, vor allem in der Westschweiz. Dieser Trend liess sich auch in einigen anderen europäischen Ländern, einschliesslich Deutschland, Frankreich und Italien, feststellen. Die Penicillin-Resistenz bei *Streptococcus pneumoniae* ging im Laufe der Zeit ebenfalls zurück, wahrscheinlich aufgrund der Einführung von Pneumokokken-Impfstoffen, die zu einer Abnahme der resistenteren Serotypen führte. Die Vancomycin-Resistenz bei Enterokokken ist sehr tief und blieb über die letzten zehn Jahre stabil.

Im Gegensatz dazu nahmen die Resistenzen gegen Quinolone und Cephalosporine der dritten Generation bei *Escherichia coli* und *Klebsiella pneumoniae* stetig zu. Dies ist in den meisten europäischen Ländern zu beobachten und passt zur weiten Verbreitung von Extended-Spectrum-Beta-Laktamase-(ESBL-)produzierenden Isolaten. Bei *K. pneumoniae* haben sich die Resistenzen seit 2013 nicht weiter erhöht. Dies ist wahrscheinlich eher dem Zufall zuzuschreiben als ein Hinweis auf eine dauerhafte Änderung der epidemischen Kurve, da die Resistenzraten in den meisten europäischen Ländern weiterhin steigen. Erfreulicherweise bleibt die Carbapenem-Resistenz bei *E. coli* und *K. pneumoniae* selten. Während dies bei *E. coli* auch in den meisten europäischen Ländern so ist, wird in Europa eine zunehmende Resistenz bei *K. pneumoniae* verzeichnet; 2014 wurden Resistenzraten von über 25% in Italien, Griechenland und Bulgarien beschrieben. Seit dem 1. Januar 2016 gilt in der Schweiz deshalb eine Meldepflicht für diese Mikroorganismen. Damit soll eine enge Überwachung der Verteilung von Carbapenemase-produzierenden Enterobacteriaceae sichergestellt werden.

Bei *Pseudomonas aeruginosa* wurde seit unserem letzten Bericht (auf Basis der Daten von 2013) ein markanter Anstieg

bei Ceftazidimen und Aminoglycosiden verzeichnet. Weiterführende Untersuchungen sind geplant. Keine bedeutenden Veränderungen wurden bei *Acinetobacter* spp. beobachtet.

Resistenzen bei Zoonose-Erregern

Bei *Campylobacter jejuni (C. jejuni)* in Mastpoulets hat die mikrobiologische Resistenz gegenüber Ciprofloxacin in den letzten Jahren signifikant zugenommen. Von 15% im Jahr 2006 stieg sie auf über 46% im Jahr 2014. Mikrobiologische Resistenzen gegenüber Erythromycin werden bei *C. jejuni* in Mastpoulets selten festgestellt. Fluoroquinolone, zu denen das Ciprofloxacin gehört, und Makrolide, zu denen das Erythromycin gehört, gelten als kritische Antibiotika höchster Priorität (WHO), weil diese Wirkstoffgruppen bei schweren Verlaufsformen der Campylobacteriose oder der Salmonellose beim Menschen bevorzugt zum Einsatz kommen.

Bei den Mastschweinen ist die Resistenzrate der *Campylobacter coli*-Stämme gegenüber Streptomycin zwischen 2008 und 2012 gesunken. Anschliessend stieg die Resistenzrate in den letzten drei Jahren signifikant, bis auf 86,5% im Jahr 2015. Hohe Resistenzraten gab es ebenfalls gegenüber Tetracyclin (63,5%) und Ciprofloxacin (46,8%).

Salmonellen sind nur selten bei Schweizer Nutztieren zu verzeichnen. Aus diesem Grund darf das Risiko einer Übertragung auf den Menschen von Salmonellen aus Fleisch von Schweizer Nutztieren als gering betrachtet werden. Darüber hinaus fallen ihre Resistenzraten gegenüber *S. enteritidis* und *S. typhimurium* ebenfalls sehr gering aus.

Resistenzen bei Indikatorkeimen in Tieren

Bei Enterokokken und *Escherichia coli-Isolaten* von Nutztieren in der Schweiz sind mikrobiologische Resistenzen weit verbreitet.

In kommensalen *Escherichia coli*-Isolaten von Mastpoulets, Mastschweinen und Mastkälbern wurden häufig Resistenzraten gegenüber Ampicillin, Sulfamethoxazol und Tetracyclin festgestellt. Zudem liessen sich bei *E. coli*-Isolaten von Mastpoulets Resistenzen gegenüber Ciprofloxacin nachweisen. Obschon die Resistenzen gegenüber diesen Substanzen bei Isolaten von Mastpoulets zwischen 2006 und 2012 anstiegen, wird inzwischen eindeutig ein sinkender Trend verzeichnet. Auch in Isolaten von Mastkälbern geht der Trend seit 2006 zurück. Allerdings steigt die Resistenzrate gegenüber Tetracyclin und Ampicillin seit 2013 wieder. Bei den Mastschweinen hat sich die Resistenzsituation gegenüber *E. coli*-Isolaten im Vergleich zu den Vorjahren nicht signifikant verändert.

Über selektive Anreicherungsmethoden wurden in 41,8% der Mastpouletbestände, in 25,7% der Mastschweinbestände und in 37,6% der Mastkälberbestände ESBL/pAmpC-produzierende *E. coli* gefunden. Der starke Anstieg der Prävalenz von ESBL/pAmpC-produzierenden *E. coli* bei Nutztieren könnte möglicherweise auf eine sensiblere Laboranalyse zurückzuführen sein. ESBL/pAmpC-produzierende *E. coli* wurden bei 73,3% der Hühnerfleischproben und bei 1% der Schweinefleischproben entdeckt. Bei keiner Rindfleischprobe konnten ESBL/pAmpC-produzierende *E. coli* nachgewiesen werden. Das Auftreten in Hühnerfleisch ausländischer Herkunft (85,6%) war signifikant höher als der Nachweis in Fleisch aus Schweizer Produktion (65,5%). Bei Rind und Schwein liegt die Prävalenz sehr tief oder bei praktisch null. Dieser Unterschied ist möglicherweise auf die unterschiedlichen Schlachtmethoden zurückzuführen. Bei Nutztieren und ihrem Fleisch wurden keine Carbapenemase-produzierenden *E. coli* gefunden.

Die Untersuchungen der Enterokokkenspezies *E. faecalis* und *E. faecium* zeigten, dass mikrobiologische Resistenzen gegenüber Erythromycin und Tetracyclin sowohl bei Mastpoulets als auch bei Mastkälbern und Mastschweinen häufig vorkommen. In den letzten Jahren sind die Resistenzraten gegenüber diesen antimikrobiellen Stoffen zurückgegangen. Dagegen stiegen im gleichen Zeitraum die Resistenzraten gegenüber Enterokokken bei Mastschweinen.

Während mehrerer Jahre wurden im Rahmen des Antibiotikaresistenzmonitorings bei Nutztieren in der Schweiz keine Vancomycin-resistenten Enterokokken (VRE) entdeckt. 2013 hat man ein mikrobiologisch Vancomycin-resistentes *E. faecalis-Isolat* bei einem Mastkalb und 2015 zwei Vancomycin-resistente *E. faecium*-Isolate bei Mastschweinen isoliert.

Bei allen untersuchten Tierarten wurden hohe Resistenzraten bei *E. faecium*-Isolaten bezüglich Quinupristin/Dalfopristin festgestellt, eine Wirkstoffkombination, die in den USA als mögliche Therapie von humanen Infektionen mit VRE zugelassen ist. Quinupristin/Dalfopristin wird in der Veterinärmedizin nicht eingesetzt. Sie gehören zu der Gruppe der Streptogramine, die gegenüber den bei Nutztieren weit verbreiteten Makroliden und Lincosamiden Kreuzresistenzen aufweisen.

In der Schweiz stieg das Auftreten von Methicillin-resistenten *S. aureus* (MRSA) bei Mastschweinen bei der Schlachtung signifikant von 2% im Jahr 2009 auf 20,8% im Jahr 2013. Seitdem blieb es konstant.

Die Resultate bezüglich MRSA zeigten, dass sich in der Schweizer Schlachtschweinepopulation vor allem der *spa* Typ t034 und in geringerem Masse auch der *spa* Typ t011 stark ausbreiten. Diese Genotypen gehören zur klonalen Linie CC398, die zu den sogenannten Nutztierassoziierten MRSA gehört. MRSA kann vom Tier auf den Menschen übertragen werden. Nicht nur in der Schweiz, sondern auch in anderen europäischen Ländern waren die meisten entdeckten MRSA-*spa* Typen bei Schweinen mit LA-MRSA CC398 verbunden.

MRSA wurde bei insgesamt 6,9% der Hühnerfleischproben nachgewiesen, wobei der Anteil in Fleisch aus Schweizer Produktion mit 1% bedeutend geringer ausfiel als der Anteil

in Fleisch aus dem Ausland (16%). Lebensmittel werden aktuell nicht als massgebliche Quelle für die Übertragung von MRSA auf den Menschen betrachtet.

Resistenz bei klinischen Isolaten von Tieren

Bis heute gibt es in der Schweiz kein Antibiotikaresistenzmonitoring bei relevanten Krankheitserregern von Nutz- oder Heimtieren. Da solche Daten im Rahmen des One-Health-Konzepts für die Risikobewertung von Resistenzen wichtig sind, hat das Bundesamt für Lebensmittelsicherheit und Veterinärwesen 2015 ein Pilotprojekt über die Resistenzsituation von veterinärmedizinischen Infektionserregern lanciert. Das Zentrum für Zoonosen, bakterielle Tierkrankheiten und Antibiotikaresistenz (ZOBA) erläutert im vorliegenden Bericht entsprechende Daten von Staphylokokken und *E. coli* aus Hunden, Katzen und Pferden. Die Isolate stammen von klinischen Untersuchungen beim ZOBA in den Jahren 2014 und 2015. Da diese vorwiegend bei Pferden und Kleintieren vorgenommen werden, sind diese Resistenzraten für die Schweiz nicht repräsentativ. Allerdings zeigen hohe Nachweisraten Methicillin-resistenter *Staphylococcus pseudintermedius* bei Hunden wie auch Methicillin-resistenter *S. aureus* bei Pferden und der Nachweis von multiresistenten Isolaten nicht nur eine Herausforderung für die behandelnden Tierärztinnen und -ärzte auf, sondern aufgrund des zoonotischen Potenzials auch ein Risiko für den Menschen. Die Erarbeitung von zuverlässigen Daten zum vollständigen Erregerspektrum wird in Zukunft eine wichtige Aufgabe darstellen.

2 Synthèse

Consommation d'antibiotiques en médecine humaine

Dans les hôpitaux suisses de soins aigus, la consommation d'antibactériens à usage systémique pour 100 journées d'hospitalisation a crû de 36% à 62,9 DDD entre 2004 et 2015. Elle est en revanche restée relativement stable lorsqu'exprimée en DDD pour 100 admissions : cette différence résulte d'une augmentation du nombre d'admissions, accompagnée d'une diminution du nombre de journées d'hospitalisation due à une réduction de la durée des séjours à l'hôpital. La classe d'antibiotiques les plus fréquemment utilisés était les pénicillines (classe ATC J01C), suivie des autres bêtalactamines qui comprennent notamment les céphalosporines (classe ATC J01D), et des quinolones (classe ATC J01M). En milieu ambulatoire, la classe d'antibiotiques les plus fréquemment utilisés était les pénicillines (classe ATC J01C), suivie des quinolones (classe ATC J01M) et des macrolides, des lincosamides et des streptogramines (classe ATC J01F). La consommation relative de fluoroquinolones et de pénicillines incluant des inhibiteurs de bêtalactamases était relativement élevée par rapport aux pays membres du réseau européen de surveillance de la consommation d'antimicrobiens (ESAC-Net). La consommation totale d'antibactériens à usage systémique (classe ATC J01) en milieu hospitalier était proche de la médiane, mais relativement basse en milieu ambulatoire par rapport aux pays membres du réseau ESAC-Net.

Ventes d'antibiotiques utilisés en médecine vétérinaire

Les ventes d'antibiotiques à usage vétérinaire ont continué à décroître en 2015. De manière globale, 42 188 kg de médicaments de ce type ont été vendus : cela correspond à une baisse d'environ 10% par rapport à l'année précédente, baisse qui atteint même 40% (28 tonnes) en comparaison avec 2008. Ce déclin est principalement dû à une baisse des ventes des prémélanges pour aliments médicamenteux. Le classement des ventes des différentes classes d'antimicrobiens reste inchangé : les sulfonamides sont en tête, suivis des pénicillines et des tétracyclines. Ces trois classes sont souvent vendues sous forme de prémélanges pour aliments médicamenteux, atteignant environ 60% de la quantité totale (24 tonnes). La part des antibiotiques autorisés seulement pour les animaux se monte à 2% de la quantité totale.

Pour ce qui est des antimicrobiens critiques de première priorité en médecine humaine (OMS 2011), la vente des macrolides a diminué d'environ 40% (–1655 kg) depuis 2008. A noter toutefois que les ventes de préparation de macrolides injectables à action prolongée montrent une tendance à la hausse. Les ventes de fluoroquinolones et de céphalosporines de troisième et quatrième génération restent inchangées.

Les ventes de colistine, d'intérêt public depuis la découverte d'un mécanisme de résistance transférable horizontalement (gène MCR-1), ont baissé d'environ 70% depuis 2008, se montant à 502 kg dans l'année sous revue.

Résistance des bactéries dans les isolats cliniques chez l'être humain

Depuis 2004, des tendances différentes se dessinent chez les bactéries à Gram positif et chez les bactéries à Gram négatif : les taux de résistance à la méticilline de *Staphylococcus aureus* (SARM) ont nettement reculé depuis 2004, en particulier en Suisse romande. Cette tendance a également pu être observée dans quelques autres pays européens, comme les pays limitrophes que sont l'Allemagne, la France et l'Italie. La résistance à la pénicilline de *Streptococcus pneumoniae* a également diminué au fil du temps, probablement grâce à l'introduction de vaccins contre les infections invasives à pneumocoques, qui ont pu provoquer un recul des sérotypes les plus résistants. Chez les entérocoques, les taux de résistance à la vancomycine, très faibles, sont restés stables au cours de la décennie écoulée.

En revanche, la résistance aux quinolones et aux céphalosporines de troisième génération croît de façon régulière chez *Escherichia coli* et *Klebsiella pneumoniae.* Cette évolution a également pu être observée dans la plupart des pays européens et coïncide avec la large distribution des isolats producteurs de bêtalactamases à spectre élargi (BLSE). Chez *K. pneumoniae,* les taux de résistance n'ont pas connu de nouvelle augmentation depuis 2013. Il s'agit probablement davantage d'une coïncidence plutôt que d'un réel fléchissement de la courbe épidémique, car les taux de résistance sont en augmentation stable dans la plupart des autres pays européens. Heureusement, la résistance aux carbapénèmes est encore rare chez *E. coli* et *K. pneumoniae.* Dans la majorité des pays européens, on observe toutefois une résistance aux carbapénèmes croissante chez *K. pneumoniae,* alors que la résistance chez *E. coli* reste rare; en 2014, des taux de résistance au-dessus de 25% ont été décrits en Italie, en Grèce et en Bulgarie. Afin d'assurer une surveillance accrue de la distribution d'Enterobacteriaceae productrices de carbapénémases, une obligation de déclaration de ces microorganismes est entrée en vigueur au 1er janvier 2016 en Suisse.

Chez *Pseudomonas aeruginosa,* de fortes progressions dans les taux de résistance ont été observées depuis notre rapport de 2013 pour la ceftazidime et les aminoglycosides. Des analyses plus pointues sont en préparation. Aucune modification significative n'a été observée chez *Acinetobacter* spp.

Résistance des bactéries zoonotiques

Chez les poulets de chair, la résistance de *Campylobacter jejuni (C. jenjuni)* à la ciprofloxacine a augmenté de manière significative ces dernières années. De 15% en 2006, le taux de résistance est passé à 46% en 2014. En revanche, la résistance à l'érythromycine n'a été que rarement constatée. Les fluoroquinolones, dont fait partie la ciprofloxacine, et les macrolides, dont fait partie l'érythromycine, sont classés dans la catégorie des antimicrobiens critiques de première priorité (OMS), ces groupes de principes actifs constituant le traitement de choix en cas de forme sévère de campylobactériose ou de salmonellose chez l'homme.

Chez les porcs d'engraissement, le taux de résistance à la streptomycine des souches de *Campylobacter coli (C. coli)* a baissé entre 2006 et 2012. En conséquence, les taux de résistance ont connu une forte croissance ces trois dernières années, atteignant 86,5% en 2015. Les résistances à la tétracycline (63,5%) et à la ciprofloxacine (46,8%) ont également fortement augmenté ces dernières années.

En Suisse, la salmonellose ne se produit que rarement chez les bovins. Le risque de transmission de salmonelles à l'homme à partir d'aliments produits avec de la viande suisse est considéré comme faible. De plus, leurs taux de résistance sont faibles, en particulier chez *S. enteritidis* et *S. typhimurium*.

Résistance des germes indicateurs chez les animaux

En Suisse, la résistance antimicrobienne est généralement largement répandue chez les entérocoques et *E. coli* isolés à partir de bovins.

Les résistances à l'ampicilline, au sulfaméthoxazole et à la tétracycline sont fréquemment prélevées en flore commensale dans des isolats d'*E. coli* chez les poulets de chair, les porcs et les veaux d'engraissement. Une résistance supplémentaire à la ciprofloxacine a été découverte dans des isolats chez les poulets de chair. Bien que les résistances à ces substances aient augmenté dans les isolats de poulets de chair entre 2006 et 2012, la tendance est en nette diminution depuis. Dans des isolats chez les veaux d'engraissement, la tendance est également à la baisse depuis 2006. Toutefois, les résistances à la tétracycline et à l'ampicilline sont à nouveau en augmentation depuis 2013. Chez les porcs d'engraissement, les taux de résistance dans des isolats d'*E. coli* n'ont pas connu de modification importante ces dernières années.Des méthodes sélectives ont permis d'identifier des *E. coli* producteurs d'BLSE/pAmpC dans 41,8% des cheptels de poulets de chair, chez 25,7% des porcs d'engraissement et chez 37,6% des veaux d'engraissement. La forte croissance de la prévalence de BLSE/AmpC dans les animaux de bétail pourrait s'expliquer par une méthode d'analyse plus précise. Des *E. coli* producteurs de BLSE/AmpC ont été découverts dans 73,3% des échantillons de viande de poulet et dans 1% des échantillons de viande de porc. Aucun *E. coli* producteur de BLSE/AmpC n'a été détecté dans les échantillons de viande de bœuf. La part de viande de poulet d'origine étrangère (85,6%) était nettement plus élevée que la part de viande en provenance de Suisse (65,5%). La prévalence dans la viande de bœuf et de porc est très basse, voire pratiquement à zéro. Cette différence peut s'expliquer par la différence dans les méthodes d'abattage. Aucun *E. coli* producteur de carbapénémases n'a été identifié dans les animaux de rente et leur viande.

L'analyse des entérocoques *Enterococcus faecalis* et *Enterococcus faecium* révèle de fréquentes résistances à la tétracycline et à l'érythromycine chez les poulets de chair ainsi que chez les veaux et les porcs d'engraissement. Ces dernières années, tandis que dans les isolats d'*E. faecalis,* la résistance a diminué chez les poulets de chair et les veaux d'engraissement, chez les porcs, les taux de résistance chez les entérocoques ont généralement augmenté.

Pendant de nombreuses années, aucun entérocoque résistant à la vancomycine n'a été découvert dans le cadre des analyses de résistances du bétail suisse. Un isolat d'*E. faecalis* résistant à la vancomycine a toutefois été détecté chez un veau d'engraissement en 2013, tandis qu'en 2015, ce sont deux isolats d'*E. faecium* chez des porcs d'engraissement qui se sont avérés résistants à la vancomycine.

Parmi toutes les espèces analysées, des taux de résistance élevés ont été découverts dans des isolats d'*E. faecium* en ce qui concerne la quinupristine-dalfopristine, une combinaison d'antibiotiques qui est autorisée aux Etats-Unis comme option thérapeutique pour l'humain en cas d'infection avec des entérocoques résistant microbiologiquement à la vancomycine. La quinutristine-dalfopristine n'est pas utilisée en médecine vétérinaire. Elle fait partie de la classe d'antibiotique des streptogramines, qui montrent des résistances croisées aux macrolides et aux lincosamides largement administrés pour le bétail.

En Suisse, la prévalence des *Staphylococcus aureus* résistants à la méticilline (SARM) chez les porcs d'engraissement au moment de l'abattage a connu une forte croissance, passant de 2% en 2009 à 20,8% en 2013. Depuis, la prévalence est restée constante. Les résultats pour les SARM confirment en particulier que le type *spa* t034, et, dans une moindre mesure, le type *spa* t011, sont en passe de s'étendre largement dans les cheptels de porcs d'abattage. Ces génotypes font partie d'un certain complexe clonal CC398, typiquement associés aux animaux de rente (livestock-associated LA-MRSA). Les SARM peuvent se transmettre de l'animal à l'homme. En Suisse, mais également dans d'autres pays européens, la majorité des SARM de type *spa*

détectés chez les porcs d'engraissement sont associés avec le type LA-MRSA CC398.

Des SARM ont été identifiés dans 6,9% des échantillons de viande de poulets de chair, avec 1% dans la viande en provenance de Suisse et 16% dans la viande d'origine étrangère. A l'heure actuelle, l'alimentation n'est pas considérée comme source pertinente dans la transmission des SARM à l'homme.

Résistance détectée dans les résultats des analyses à visée diagnostique chez l'animal

Actuellement, la Suisse ne dispose de surveillance de l'antibiorésistance des agents pathogènes d'importance clinique ni pour le cheptel vif ni pour les animaux de compagnie. Dans le cadre du concept One Health, ces données sont importantes pour évaluer le risque que des résistances se développent ; c'est pourquoi, l'Office fédéral de la sécurité alimentaire et des affaires vétérinaires a lancé un projet-pilote de surveillance des résistances aux antibiotiques des germes animaux en 2015. Dans le présent rapport, le Centre des zoonoses, des maladies animales bactériennes et de l'antibiorésistance (ZOBA) présente des données relatives à l'antibiorésistance des staphylocoques et des *E. coli* chez les chiens et les chevaux. Des isolats ont été prélevés lors d'analyses cliniques soumises à ZOBA en 2014 et en 2015. Les cas examinés par le ZOBA étant principalement des chevaux et des petits animaux de compagnie, ces données sur les résistances aux antibiotiques ne sont pas représentatives de l'ensemble de la Suisse. Cependant, des taux élevés de résistance à la méticilline de *Staphylococcus* pseudintermedius chez le chien et de *S. aureus* chez le cheval dans les cliniques vétérinaires, de même que la mise en évidence d'isolats multirésistants, représentent non seulement un défi pour les vétérinaires traitants, mais posent aussi le risque que ces bactéries présentent pour l'homme du fait de leur potentiel zoonotique. Il sera important à l'avenir de consolider ces données à partir d'une vue d'ensemble complète d'agents pathogènes.

2 Sintesi

Consumo di antibiotici nella medicina umana

Tra il 2004 e il 2015 il consumo di antibiotici ad uso sistemico negli ospedali svizzeri per cure acute è aumentato del 36 per cento a 62,9 dosi definite giornaliere (DDD) per 100 giorni di degenza, mentre è rimasto relativamente stabile se espresso in DDD per 100 ricoveri. Tale discrepanza può essere spiegata da un tendenziale aumento del numero di ricoveri cui ha fatto fronte una contemporanea riduzione del numero di giorni di degenza dovuta a una minore durata del soggiorno in ospedale. La classe di antibiotici più comunemente usata è stata quella delle penicilline (codice ATC: J01C), seguita dagli altri antibatterici beta-lattamici, comprese le cefalosporine (gruppo ATC: J01D) e i chinoloni (gruppo ATC: J01M).

Nell'ambito delle cure ambulatoriali la classe di antibiotici più comunemente usata è stata quella delle penicilline (gruppo ATC: J01C), seguite da chinoloni (codice ATC: J01M) e da macrolidi, lincosamidi e streptogramine (gruppo ATC: J01F). Il consumo relativo di fluorochinoloni e penicilline associati ad inibitori della beta-lattamasi è risultato comparativamente alto rispetto a quello dei Paesi che partecipano alla Rete di sorveglianza europea sul consumo di antibiotici (ESAC-Net). Il consumo totale di antibatterici ad uso sistemico (gruppo ATC: J01), che si situa in prossimità del valore mediano nell'ambito delle cure residenziali, è invece risultato relativamente basso in confronto a quello dei Paesi dell'ESAC-Net nel settore ambulatoriale.

Vendite di antibiotici nella medicina veterinaria

Il volume di vendita degli antibiotici ha continuato a diminuire anche nel 2015. Nel settore della medicina veterinaria sono stati complessivamente venduti 42 188 chilogrammi di antibiotici, ovvero il 10 per cento in meno rispetto all'anno precedente. Tale riduzione, che equivale a un calo del 40 per cento (28 tonnellate) dal 2008, è prevalentemente dovuta a un calo delle vendite di premiscele di medicamenti.

La classifica di vendita delle diverse classi di antibiotici è rimasta invariata: i sulfonamidi sono al primo posto, seguiti da penicilline e tetracicline. Queste tre classi sono spesso vendute come premiscele di medicamenti, categoria che rappresenta circa il 60 per cento del volume totale (24 tonnellate). La quantità di antibiotici omologati unicamente per gli animali da compagnia costituisce il 2 per cento del volume totale.

Nel quadro delle classi di antibiotici critici di massima priorità per la medicina umana (OMS 2011), le vendite di macrolidi sono diminuite all'incirca del 40 per cento (–1655 kg) dal 2008. Mostrano tuttavia una tendenza ascendente le vendite di prodotti iniettabili monodose a lunga emivita. Sono invece rimaste invariate le vendite di fluorochinoloni e le cefalosporine di terza e quarta generazione.

Il volume di vendita della colistina, divenuta di pubblico interesse in seguito alla scoperta di un meccanismo di resistenza a trasferimento orizzontale (MCR-1), è diminuito approssimativamente del 70 per cento dal 2008, attestandosi sui 502 chilogrammi nell'anno in esame.

Resistenza nei batteri presenti negli isolati clinici umani

Diverse sono le tendenze osservate a livello di batteri gram-positivi e gram-negativi a partire dal 2004. I tassi di *Staphylococcus aureus* resistente alla meticillina (MRSA) sono diminuiti in modo significativo dal 2004, perlopiù nella parte occidentale della Svizzera. La stessa tendenza è stata osservata in numerosi altri Paesi europei, incluso nelle vicine Germania, Francia e Italia. È diminuita nel corso del tempo anche la resistenza alla penicillina in *Streptococcus pneumoniae,* perlopiù a seguito di una riduzione nella prevalenza di sierotipi più resistenti dovuta all'introduzione di vaccini antipneumococchi. La resistenza alla vancomicina negli enterococchi è molto bassa ed è rimasta stabile nell'arco degli ultimi dieci anni.

Si è al contrario riscontrato un costante aumento della resistenza al chinolone e alle cefalosporine di terza generazione in *Escherichia coli* e *Klebsiella pneumoniae*. Lo stesso incremento è osservato nella maggior parte dei Paesi europei ed è in linea con l'ampia distribuzione di isolati produttori di beta-lattamasi a spettro esteso (ESBL). In *K. pneumoniae* i tassi di resistenza non sono più aumentati dal 2013. Più che di una vera e propria evoluzione della curva epidemica si tratta in questo caso di un cambiamento probabilmente fortuito, visto che nella maggior parte degli altri Paesi europei i tassi di resistenza continuano a crescere costantemente. In *E. coli* e *K. pneumoniae* è fortunatamente ancora rara la resistenza ai carbapenemi. Mentre però la resistenza in *E. coli* è rara anche nella maggior parte dei Paesi europei, una crescente resistenza ai carbapenemi si osserva in Europa per *K. pneumoniae;* nel 2014 tassi di resistenza superiori al 25 per cento sono stati descritti in Italia, Grecia e Bulgaria. Per consentire un monitoraggio più preciso della distribuzione di Enterobacteriaceae produttori di carbapenemasi, il 1° gennaio 2016 è stato introdotto in Svizzera l'obbligo di notifica di questi microrganismi.

In *Pseudomonas aeruginosa* aumenti significativi nei tassi di resistenza sono stati osservati dall'ultimo rapporto (stato al 2013) per la ceftazidima e gli aminoglicosidi. Analisi più approfondite sono comunque in programma. Nessun cambiamento rilevante si segnala invece in *Acinetobacter* spp.

Resistenza nei batteri zoonotici

Nel pollame da ingrasso il tasso di resistenza alla ciprofloxacina di *Campylobacter jejuni* è aumentato significativamente negli ultimi anni, passando dal 15 per cento del 2006 al 46 per cento nel 2014. Si è per contro raramente rilevata una resistenza all'eritromicina. I fluorochinoloni, dei quali fa parte la ciprofloxacina, e i macrolidi, dei quali fa parte l'eritromicina, sono considerati antibiotici critici di massima priorità (OMS), poiché questi gruppi di principi attivi costituiscono la terapia elettiva di gravi forme di campilobatteriosi o salmonellosi nell'uomo.

Nei suini da ingrasso il tasso di resistenza alla streptomicina di *Campylobacter coli* è diminuito tra il 2006 e il 2012, per poi aumentare significativamente negli ultimi tre anni fino a toccare l'86,5 per cento nel 2015. Sono aumentati in modo significativo negli ultimi anni anche i tassi di resistenza alla tetraciclina (63,5%) e alla ciprofloxina (46,8%).

Le salmonelle sono presenti solo raramente nel bestiame da reddito in Svizzera. Il rischio di una loro trasmissione all'uomo da alimenti prodotti a partire da animali svizzeri è dunque considerato basso. Le salmonelle mostrano in più tassi di resistenza bassi, specie nel caso di *S. enteritidis* e *S. typhimurium.*

Resistenza nei batteri indicatori negli animali da reddito

L'antibiotico-resistenza è in generale ampiamente diffusa negli isolati di enterococchi ed *E. coli* prelevati da bestiame allevato in Svizzera.

Resistenze ad ampicillina, sulfametoxazolo e tetraciclina sono state spesso riscontate in isolati di *E. coli* commensale provenienti da pollame, suini e vitelli da ingrasso. In isolati provenienti da pollame da ingrasso si è riscontrata, oltre a queste, anche una resistenza alla ciprofloxacina. Sebbene in questi ultimi isolati sia aumentata tra il 2006 e il 2012 la resistenza a questi principi attivi, la tendenza è da allora in fase chiaramente discendente. È in discesa dal 2006 anche negli isolati provenienti da vitelli da ingrasso. Sono tuttavia tornate ad aumentare dal 2013 le resistenze a tetraciclina e ampicillina. Non sono invece cambiati in maniera oltremodo significativa negli ultimi anni i tassi di resistenza riscontrati negli isolati di *E. coli* prelevati da suini da ingrasso.

Applicando metodi di arricchimento selettivo, *E. coli* produttori di ESBL/pAmpC sono stati rilevati nel 41,8 per cento delle batterie di pollame, nel 25,7 per cento dei suini e nel 37,6 per cento dei vitelli da ingrasso. Il forte incremento della prevalenza di ESBL/pAmpC negli animali da reddito potrebbe tuttavia essere dovuto all'impiego di un metodo di laboratorio più sensibile. *E. coli* produttori di ESBL/pAmpC sono stati rilevati nel 73,3 per cento dei campioni di carne di pollo e nell'1 per cento di quelli di maiale. La presenza nella carne di pollo di provenienza estera (85,6%) era significativamente più elevata che nella carne di produzione svizzera (65,5%), con una prevalenza molto bassa se non addirittura pari a zero nel manzo e nel maiale. Tale differenza potrebbe essere correlata ai diversi processi di macellazione. Per il resto nessun *E. coli* produttore di carbapenemasi è stato riscontrato nelle suddette specie di animali da reddito e di carne. Nelle specie di enterococchi *E. faecalis* e *E. faecium* isolati in pollame, vitelli e suini da ingrasso sono state spesso rilevate resistenze all'eritromicina e alla tetraciclina. Negli isolati di *E. faecalis* prelevati da pollame da ingrasso e vitelli da carne la resistenza a questi antibiotici è tuttavia diminuita negli ultimi anni, mentre sono generalmente aumentati nello stesso periodo i tassi di resistenza negli enterococchi provenienti da suini da ingrasso.

Per molti anni nessun enterococco resistente alla vancomicina (VRE) è stato rilevato nel quadro del monitoraggio delle resistenze degli animali da reddito in Svizzera. Nel 2013 un isolato di *E. faecalis* prelevato da un vitello da carne e nel 2015 due isolati di *E. faecium* provenienti da suini da ingrasso sono tuttavia risultati resistenti alla vancomicina.

Tra tutte le specie esaminate, tassi di resistenza elevata sono stati riscontrati in isolati di *E. faecium* nei confronti di quinupristina/dalfopristina, combinazione approvata negli USA in qualità di terapie possibili in caso di infezioni da EVR nell'uomo. Quinupristina/dalfopristina non sono utilizzate nella medicina veterinaria, ma fanno parte delle streptogramine che mostrano una resistenza crociata con macrolidi e lincosamidi largamente usati negli animali da reddito.

In Svizzera la presenza di *S. aureus* resistente alla meticillina (MRSA) nei suini da macello è significativamente aumentata, passando dal 2 per cento del 2009 al 20,8 per cento nel 2013. Da allora la prevalenza è tuttavia rimasta costante. I risultati riportati per MRSA confermano che, specie lo *spa* tipo t034 e sebbene in misura minore anche lo *spa* tipo t011, stanno diventando sempre più diffusi nella popolazione svizzera di suini macellati. Entrambi questi genotipi appartengono al complesso clonale CC 398, tipicamente associato agli animali da reddito (LA-MRSA). MRSA può essere trasmesso dagli animali all'uomo e, non solo in Svizzera ma anche in altri Paesi europei, la maggior parte degli *spa* tipi di MRSA rilevati nei suini erano associati a LA-MRSA CC398. MRSA è stato anche rilevato nel 6,9 per cento di tutti i campioni di carne di pollo, sebbene nell'1 per cento del totale la presenza nella carne di produzione svizzera fosse molto più bassa che in quella di provenienza estera (16%). Attualmente gli alimenti non sono ad ogni buon conto considerati una fonte rilevante di trasmissione di MRSA all'uomo.

Resistenza nei campioni diagnostici provenienti da animali

A tutt'oggi non si è ancora avviato in Svizzera un monitoraggio dell'antibiotico-resistenza nei maggiori agenti patogeni degli animali da reddito o da compagnia malati. Poiché nel quadro dell'iniziativa One Health questi dati sono importanti ai fini di una valutazione esaustiva dei rischi di resistenza futuri, l'Ufficio federale della sicurezza alimentare e di veterinaria (USAV) ha lanciato nel 2015 il progetto pilota «Monitoraggio della resistenza agli antibiotici nei germi patogeni degli animali». Il Centro per le zoonosi, le malattie animali di origine batterica e la resistenza agli antibiotici (ZOBA) ha illustrato nel presente rapporto i dati inerenti quest'ultimo aspetto con particolare riguardo agli stafilococchi ed a *E. coli* di cani e cavalli. Gli isolati sono stati tratti da campioni diagnostici sottoposti allo ZOBA nel 2014 e nel 2015. Poiché i clienti di questo Centro sono perlopiù piccole cliniche per cavalli ed animali domestici, i suoi dati riguardo l'antibiotico-resistenza non sono però rappresentativi a livello svizzero. Gli elevati tassi di resistenza alla meticillina rilevati per *Staphylococcus pseudintermedius* nei cani e per *Staphylococcus aureus* nei cavalli, come pure il rilevamento di isolati multifarmaco resistenti, non costituiscono tuttavia solo una sfida per i veterinari che curano questi animali, ma anche un rischio per l'uomo a causa del loro potenziale zoonotico. Estrapolare dati rappresentativi da uno spettro esaustivo di agenti patogeni sarà dunque il compito per il futuro.

3

Introduction

3 Introduction

3.1 Antibiotic resistance

Antibiotic resistance is responsible for increased morbidity and mortality and increases healthcare costs significantly. Alternative treatments may have more serious side effects, need longer treatments and hospital stays, with increased risk of suffering and death. Physicians in hospitals must increasingly rely on the so-called last-line antibiotics (e.g. carbapenems). Increasing antibiotic resistance, also to these last-line antibiotics, raises a serious concern. Surveillance of antibiotic use and resistance is considered to be the backbone of action plans developed by the different countries, in order to determine the extent of the problem and the effectiveness of the measures taken.

3.2 About anresis.ch

The Swiss Centre for Antibiotic Resistance anresis.ch was established within the frame of the National research program 49 "Antibiotic Resistance" (NRP49). After termination of the NRP49, financing was further guaranteed by the Swiss Federal Office of Public Health, the Swiss Conference of the Cantonal Ministers of Public Health and the University of Bern. Since 2016, the project is financed by the Swiss Federal Office of Public Health and the Institute for Infectious Diseases in Bern; it is supported by the Swiss Society of Infectious Diseases (SSI), the Swiss Society for Microbiology (SSM), the Swiss Association of Public Health Administration and Hospital Pharmacists (GSASA) and PharmaSuisse, the Swiss Society of Pharmacists.

The first microbiology laboratories participated in anresis.ch in 2004. The surveillance system expanded continuously during the following years; it now includes the National Reference Center for Antibiotic Resistance of human clinical isolates (NARC), the bacteremia database (since 2006) and the antibiotic consumption database (since 2006 for inpatients, and since 2015 for outpatients). Data on antibiotic resistance in clinical veterinary isolates are also collected in the anresis.ch database since 2014. The open data structure still allows further developments.

The steering committee of anresis.ch includes specialists from microbiology laboratories and specialists in infectious diseases, hospital epidemiology and veterinary medicine, as well as representatives from the Swiss Federal Office of Public Health and the Swiss Conference of the Cantonal Ministers of Public Health (Annexe IV).

3.2.1 Monitoring of antibiotic consumption in human medicine

For the inpatient setting, the consumption of antibiotics has been monitored since 2006 through a sentinel network of hospital pharmacies. Yearly, data from approximately 60 hospitals are collected on a voluntary basis. These hospitals are distributed all over the geographic territory and represent 54% of the total number of acute somatic care hospitals (excluding psychiatric and rehabilitation centers) and 47% of all beds in this category in Switzerland (33% of all beds) (see Chapter 11.1). The participating hospitals receive a benchmarking report, allowing them to compare their results with those of similar-size hospitals. Data for the outpatient setting are provided by PharmaSuisse. They are based on the prescriptions at the individual level and are obtained from the privately run pharmacies. The coverage is about 65% of all pharmacies in Switzerland.

3.2.2 Monitoring of resistance in human medicine

Anresis.ch collects and analyzes anonymous antibiotic resistance data provided by the participating clinical microbiology laboratories (Annexe IV). These laboratories are homogeneously distributed all over the geographic territory. They include university laboratories, mainly representing isolates from tertiary-care hospitals, as well as cantonal and private laboratories, representing data from smaller hospitals and ambulatories. These send in antimicrobial susceptibility test results (AST) of all routinely performed analyses including isolates from non-sterile sites. Collected data represent at least 60% of annual hospitalization days and about 30% of the practitioners in Switzerland. The epidemiological data provided allow for stratification of resistance results according to "hospital versus outpatients," age groups, and anatomical location of the infection.

Antibiotic resistance data are continuously available on www.anresis.ch. The proportion of the following multiresistance bacteria in invasive isolates is reported and updated on a monthly basis in the weekly Bulletin of the Federal Office of Public Health (BAG Bulletin, available on http://www.bag.admin.ch/dokumentation/publikationen, (in German): fluoroquinolone-resistant *Escherichia coli,* extended-spectrum cephalosporin-resistant (ESCR) *E. coli,* ESCR *Klebsiella pneumoniae,* methicillin-resistant *Staphylococcus aureus* (MRSA), penicillin-resistant *Streptococcus pneumoniae* and vancomycin-resistant enterococci. More detailed data from anresis.ch are published every second year together with veterinary data in this report.

3.2.3 Monitoring of resistance in clinical veterinary isolates

Since 2014 the Center for Zoonoses, Animal Bacterial Diseases and Antimicrobial Resistance (ZOBA) provides antibiotic resistance data of veterinary pathogens from dogs, cats and horses to the anresis database. Only resistance results from diagnostic submissions are included in anresis.ch. In contrast to the human resistance data, all resistance data are generated locally at the ZOBA by standard bacteriological procedures. Clients of the ZOBA are mostly horse and small-animal clinics, so these antibiotic resistance data are not representative for Switzerland up to now. In the future isolates from other veterinary laboratories should be included as well as other relevant pathogens of veterinary interest.

3.3 About ARCH-Vet

The use of antimicrobials in livestock is a subject of public concern, as resistant bacteria can be selected and can enter the food chain and eventually infect people. Hence, a system to enable the continuous monitoring of resistance in livestock animals, meat and dairy products in Switzerland was introduced in 2006 on the basis of article 291d of the Epizootic Diseases Ordinance (EzDO; SR 916.401). Additionally, this system compiles data on sales of antimicrobial agents for veterinary medicine in accordance with article 36 of the Federal Ordinance on Veterinary Medicines (FOVM; SR 812.212.27). Since 2009, data on sales of veterinary antimicrobials and results of the resistance monitoring are published yearly in the ARCH-Vet report. For the second time, the ARCH-Vet data is published together with the anresis.ch data in the present report.

3.3.1 Sales of antimicrobials in veterinary medicine

Sales data is used to estimate the consumption of antimicrobial agents in veterinary medicine. Marketing authorization holders (MAH) report the sales of antimicrobial veterinary medicinal products annually to Swissmedic (Swiss Agency for Therapeutic Products). This data is transmitted to the Food Safety and Veterinary Office (FSVO), where it is processed and analyzed. The data covers 100% of the authorized antimicrobial veterinary medicinal products. The sales data is also transmitted to the European Medicines Agency (EMA) and published within the framework of the European Surveillance of Veterinary Antimicrobial Consumption Project (Sales of veterinary antimicrobial agents in 26 EU/EEA countries in 2013; EMA/387934/2015).

3.3.2 Monitoring of resistance in zoonotic and indicator bacteria from animals

The main goals of the standardized monitoring of antimicrobial resistance in zoonotic and indicator (commensal) bacteria isolated from healthy food animals are to estimate resistance prevalence, to detect trends over years and to produce data for risk assessment. This information provides the basis for policy recommendations to combat the spread of antimicrobial resistance and allows the evaluation of the impact of measures taken.

Species examined

Cattle, pigs and broilers are monitored because of their importance in food production. Samples of cattle and pigs are taken alternately every other year with broilers. Fecal and nasal swab samples are taken at the slaughterhouse and meat samples of the respective animal species in retail businesses by official inspectors. Resistance tests are performed for the zoonotic pathogens *Campylobacter jejuni* and *C. coli* and for the indicator bacteria *Escherichia coli, Enterococcus faecalis* and *E. faecium*. Since 2009, nasal swab samples from fattening pigs and calves have also been tested for methicillin-resistant *Staphylococcus aureus* (MRSA). Since 2011, tests have been carried out to detect ESBL-(extended-spectrum-beta-lactamase-)producing *E. coli* in broilers, pigs and cattle, using a selective enrichment procedure. *Salmonella* isolates available from clinical material from various animal species and from the national control program for *Salmonella* in poultry are also included. Meat samples are tested for MRSA, ESBL and carbapenemase-producing *E. coli*.

Sampling

Stratified random samples of slaughtered animals are taken in slaughterhouses. At least 60% of the slaughtered animals of the concerned species must potentially form part of the sample. Every slaughterhouse taking part in the program collects a number of samples proportional to the number of animals of the species slaughtered per year. In addition, sampling is spread evenly throughout the year. The number of samples tested should allow:

- to estimate the proportion of resistant isolates within +/–8% of an actual resistance prevalence of 50%
- to detect a change of 15% in the proportion of resistant isolates if resistance is widespread (50% resistant isolates)
- to detect a rise of 5% in the proportion of resistant isolates if resistance was previously low (0.1% resistant isolates)

Resistance testing needs to be carried out on 170 isolates in order to reach this accuracy. The sample size must be adjusted to reflect prevalence in previous years for the concerned animal species in order to obtain this number of isolates. As the prevalence of particular pathogens in some animal species is very low in Switzerland, it is not always possible to obtain 170 isolates. 170 isolates is the target for *C. jejuni, E. coli* and *Enterococcus* spp. in broilers, *C. coli* and *E. coli* for fattening pigs and for *E. coli* in cattle.

Meat samples are collected in all Swiss cantons. The number of samples is proportionate to the number of inhabitants per canton. The samples are taken at different retailers proportionate to their market share throughout the country. For beef and pork meat, only domestic meat is collected, as the main part of consumed beef and pork meat is produced in Switzerland. For chicken meat, two thirds of the samples were domestic meat and one third imported meat.

3.4 Guidance for readers

The present report is the result of a cooperation between the Federal Office of Public Health (FOPH), the Food Safety and Veterinary Office (FSVO), anresis.ch and the Center for Zoonoses, Animal Bacterial Diseases and Antimicrobial Resistance (ZOBA). We are glad to present the Swiss data on the consumption of antimicrobials and antimicrobial resistance, both in humans and in animals.

Though these data are presented in one report, it is important to be aware that differences between the monitoring systems for collection, interpretation and reporting hamper direct comparisons of the results.

Antibiotic consumption data
Antimicrobial consumption data from humans are reported as defined daily doses (DDD) per 1,000 inhabitants and per day, or as DDD per 100 occupied bed-days or as DDD per 100 admissions.

In veterinary medicine, sales data on antimicrobials are used to estimate the consumption of these products. They are reported by weight (kg) of active substance per year or by weight of active substance per population correction unit (PCU) and per year. A comparable unit of measurement like the DDD in human medicine is not yet available.

Antibiotic resistance data
The main issues when comparing antimicrobial resistance data originating from humans and food-producing animals are the different sampling strategies, the use of different laboratory methods and different interpretative criteria of resistance.

Sampling strategies:
Resistance in bacteria from humans is determined in isolates from clinical submissions, whereas for animals, bacteria originate from samples taken of healthy food-producing animals in the framework of an active monitoring.

Laboratory methods:
Susceptibility testing in human isolates is done in different laboratories using different methods (diffusion and microdilution methods). Animal isolates are tested at the Swiss national reference laboratory for antimicrobial resistance (the Center for Zoonoses, Animal Bacterial Diseases and Antimicrobial Resistance, ZOBA, Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Bern) using a microdilution method.

Criteria of resistance:
Human clinical isolates are classified as "susceptible," "intermediate" or "resistant" applying clinical breakpoints and quantitative resistance data are not available for most isolates. This interpretation indicates the likelihood of a therapeutic success with a certain antibiotic and thus helps the attending physician to select the best possible treatment. Clinical breakpoints are defined against a background of clinically relevant data such as dosing, method and route of administration, pharmacokinetic and pharmacodynamics. The use of different clinical breakpoints (e.g. EUCAST vs. CLSI) or changing breakpoints over time may therefore influence the results.

The resistance monitoring in animals uses epidemiological cutoff values (ECOFFs) to separate the natural, susceptible wild-type bacterial populations from isolates that have developed reduced susceptibility to a given antimicrobial agent. So called non-wild-type organisms are assumed to exhibit acquired or mutational resistance mechanisms and are referred as "microbiologically resistant." ECOFF values allow no statement on the potential therapeutic success of an antimicrobial, but as they are able to indicate resistance mechanisms at an early stage, they are used for epidemiological monitoring programs that measure resistance development over time.

Clinical breakpoints and ECOFFs may be the same, although it is often the case that the ECOFF is lower than the clinical breakpoint. That means although the bacteria can be "microbiologically resistant," therapeutically the antimicrobial can still be effective.

Cooperation and coordination between the different monitoring networks has to be strengthened and systems have to be refined, to improve comparability, as it is foreseen in the national Strategy against Antibiotic Resistance (StAR).

3.5 Authors and contributions

Main authors
- Andreas Kronenberg, Swiss Centre for Antibiotic Resistance, University of Bern
- Gudrun Overesch, Center for Zoonoses, Animal Bacterial Diseases and Antimicrobial Resistance (ZOBA), University of Bern, Institute of Veterinary Bacteriology
- Catherine Plüss-Suard, Hospital Preventive Medicine, University Hospital of Lausanne
- Kay Torriani, Veterinary Medicinal Products and Antibiotics, Federal Food Safety and Veterinary Office

Contributing authors
- Marisa Dolina, Cantonal Institute of Microbiology, Bellinzona
- Olivier Dubuis, Viollier AG, Basel
- Reno Frei, Division of Clinical Microbiology, University Hospital Basel
- Markus Hilty, Institute for Infectious Diseases, University of Bern
- Patrice Nordmann, Service of Molecular and Medical Microbiology, University of Fribourg
- Vincent Perreten, Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Bern
- Jean-Claude Piffaretti, Interlifescience, Massagno
- Jacques Schrenzel, Service of Infectious Diseases, University Hospital of Geneva
- Giorgio Zanetti, Hospital Preventive Medicine, University Hospital of Lausanne

Authors of the textboxes are named in the concerning textboxes.

Editors
Homa Attar Cohen, Division of Communicable Diseases, Federal Office of Public Health (FOPH), and Dagmar Heim, Veterinary Medicinal Products and Antibiotics, Federal Food Safety and Veterinary Office (FSVO)

Acknowledgements
Anresis.ch would like to thank all participating microbiology laboratories, sentinel network of hospital pharmacies and PharmaSuisse for their important contribution in providing resistance and antibiotic consumption data.

Color code

This is the color code that is used in various figures in this report.

- Ionophore
- Nitrofuran
- Oxazolidone
- Fluoroquinolone
- Glycopeptide
- Aminoglycoside
- Epoxide-AB
- Polypeptide
- Sulfonamide
- Steroidal antibiotics
- Amphenicole
- Ansamycin
- Tetracycline
- Lincosamide
- Streptogramin
- Macrolide
- Penicillin
- Carbapenem
- Cephalosporin

4

Abbreviations

4 Abbreviations

AFSSA	French Food Safety Agency
AGISAR	Advisory Group on Integrated Surveillance of Antimicrobial Resistance
AMR	Antimicrobial resistance
ATC	Anatomical Therapeutic Chemical
CAESAR	Central Asian and Eastern European Surveillance on Antimicrobial Resistance
CC	Clonal complex
CI	Confidence interval
CLSI	Clinical Laboratory Standards Institute
DD	Disc diffusion
DDD	Defined daily doses
DID	Defined daily doses per 1000 inhabitants and per day
EARSS	European Antimicrobial Resistance Surveillance System
ECDC	European Centre for Disease Prevention and Control
ECOFF	epidemiological cutoff value
EEA	European Economic Area
EFSA	European Food Safety Authority
EMA	European Medicines Agency
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESBL	Extended-spectrum beta-lactamase
ESC-R	Extended-spectrum cephalosporin resistance
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	European Union
EUCAST	European Committee on Antimicrobial Resistance Testing
EzDO	Epizootic Diseases Ordinance
FAO	Food and Agriculture Organization
FOAG	Federal Office for Agriculture
FOEN	Federal Office for the Environment
FOPH	Federal Office of Public Health
FSVO	Federal Food Safety and Veterinary Office
GP	General practitioner
GSASA	Swiss Association of Public Health Administration and Hospital Pharmacists
ICU	Intensive care units
MALDI TOF MS	Matrix-assisted laser desorption/ionization time-of-flight mass spectroscopy
mCCDA	Modified charcoal cefoperazone deoxycholate agar
MDR	Multi-drug resistant
MIC	Minimal inhibitory concentration
MRSA	Methicillin-resistant *Staphylococcus aureus*
MRSP	Methicillin-resistant *Staphylococcus pseudintermedius*
MSM	Men who have sex with men
MSSA	Methicillin-susceptible *Staphylococcus aureus*
NRP	National research project
OFAC	Professional cooperative of the Swiss pharmacists
OIE	World organization for animal health
pAmpC	Plasmid-mediated AmpC-beta-lactamase
PBP	Penicillin-binding proteine
PCU	Population correction unit
PNSP	Penicillin-non-susceptible *Streptococcus pneumoniae*
PSSP	Penicillin-susceptible *Streptococcus pneumonia*
SIR	Susceptible – Intermediate – Resistant
SNF	Swiss National Foundation
spp.	species
SSM	Swiss Society for Microbiology
SSP	Swiss Society of Pharmacists, Pharma-Suisse
t	*spa* type
VetCAST	EUCAST Veterinary Subcommittee on Antimicrobial Susceptibility Testing
VMD	Veterinary Medicines Directorate
VRE	Vancomycin-resistant enterococci
WHO	World Health Organization
ZOBA	Center for Zoonoses, Animal Bacterial Diseases and Antimicrobial Resistance

5

Antibacterial consumption in human medicine

5 Antibacterial consumption in human medicine

5.1 Hospital care

5.1.1 Total antibiotic consumption in hospitals participating in anresis.ch

Considering the hospitals that have participated each year since 2004 in the surveillance system anresis.ch (n = 21), the number of DDD has increased by 29% since 2004. The number of admissions increased (+31%), while the number of bed-days was relatively stable (+2%). This means that more patients are admitted to hospitals, but their length of stay is shorter in 2015 than in 2004.

The total consumption of systemic antibiotics in DDD per 100 bed-days increased by 36% from 46.2 (weighted mean, range: 21.0–97.4) in 2004 to 62.9 (range: 34.6–87.0) in 2015 (Figure 5. a). This increasing trend was observed in the three categories of hospital sizes and the total consumption was slightly higher in the large-size hospitals. The antibiotic consumption in DDD per 100 admissions remained stable from 2004 to 2015 (–2%). The total consumption of antibacterial agents for systemic use was approximated at 1.8 DDD per 1,000 inhabitants per day in 2014. In comparison, the median consumption was 1.9 per 1,000 inhabitants per day (range 1.0–2.6) in 2014 in the countries participating in the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) [1].

5.1.2 Antibiotic consumption in hospitals participating in anresis.ch by antibiotic class and by specific antibiotic

In 2015, penicillin consumption (ATC group J01C) ranked first among antibiotic classes, representing 43% of the total consumption (Figure 5. b). It was followed by the consumption of other beta-lactam antibacterials, including cephalosporins (ATC group J01D) and quinolones (ATC group J01M) (26% and 10%, respectively).

Table 5. a shows the consumption of antibiotic classes expressed in DDD per 100 bed-days in sentinel hospitals over the period 2004–2015. The use of four of the 20 antibiotic classes decreased between 2004 and 2015 (fourth-generation cephalosporins, fluoroquinolones, rifamycins and tetracyclines). The most important progression (more than 100%) in consumption between 2004 and 2015 was observed for the polymyxins, the nitrofuran derivates and the antipseudomona penicillins associated with a beta-lactamase inhibitor.

Figure 5. a: Total antibiotic consumption expressed in DDD per 100 bed-days (bright line) and in DDD per 100 admissions (dark line) in the hospitals participating in anresis.ch over the period 2004–2015. The number of hospitals (or hospital networks) participating in anresis.ch (n) is indicated under the corresponding year.

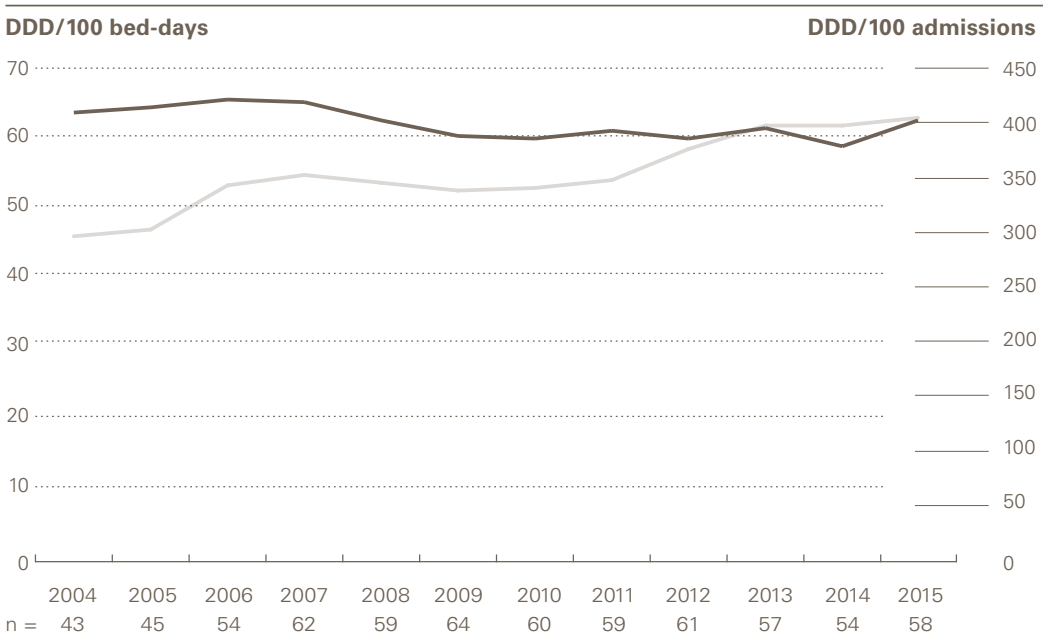


Figure 5. b: Distribution of the total antibiotic consumption per antibiotic class in the inpatient setting in 2015 in Switzerland.

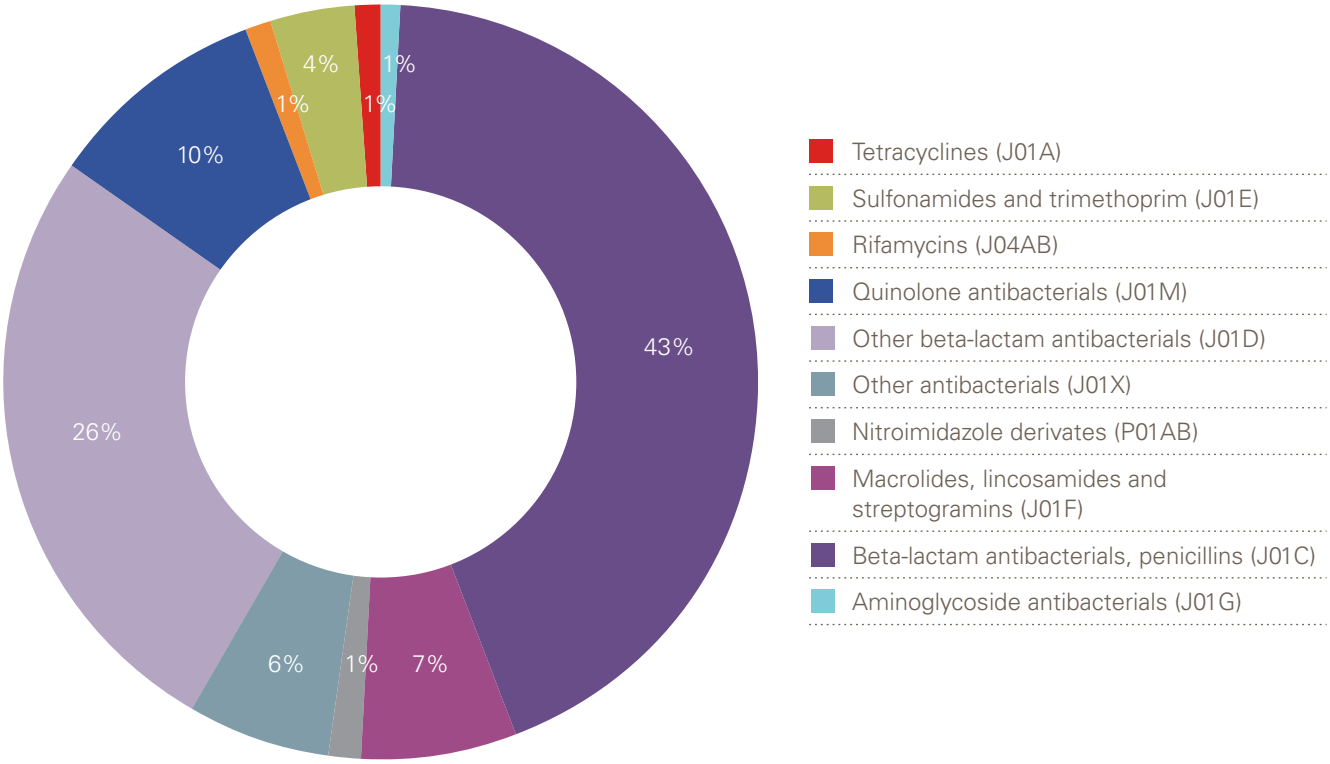


Table 5. a: Consumption of antibiotic classes expressed in DDD per 100 bed-days in hospitals participating in anresis.ch (2004–2015).

ATC Group	Antibiotic class	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
J01G	Aminoglycosides	0.8	0.6	0.9	0.8	0.7	0.7	0.8	0.7	0.7	0.7	0.6	0.6
J01CF	Beta-lactamase-resistant penicillins	1.8	1.7	1.9	1.7	1.6	1.7	1.8	1.9	2.1	2.1	2.4	2.4
J01CE	Beta-lactamase-sensitive penicillins	0.6	0.7	0.8	0.9	0.9	1.1	1.1	1.3	1.5	1.3	1.2	1.3
J01DH	Carbapenems	1.4	1.4	1.7	2.2	2.2	2.4	2.4	2.6	2.8	3.2	3.0	2.9
J01DB	Cephalosporins – first generation	0.9	0.9	1.1	1.2	1.3	1.2	1.1	1.1	1	1	1.1	1.3
J01DC	Cephalosporins – second generation	3.0	3.0	3.6	3.9	3.8	3.6	3.6	3.6	3.8	4.3	4.6	5.0
J01DD	Cephalosporins – third generation	2.4	2.6	3.2	3.7	3.7	3.7	3.8	4.0	4.2	4.9	4.9	5.6
J01DE	Cephalosporins – fourth generation	2.4	2.1	1.8	0.7	1.1	1.0	1.1	1.3	1.5	1.6	1.5	1.7
J01MA	Fluoroquinolones	6.1	6.9	7.8	7.9	7.3	6.7	6.5	6.1	6.1	6.2	6.2	5.9
J01XA	Glycopeptides	0.6	0.5	0.7	0.8	0.9	0.9	1.0	1.1	1.1	1.2	1.3	1.3
J01FF	Lincosamides	0.8	0.7	0.9	0.9	0.9	0.9	0.8	0.8	0.9	0.9	1.0	1.0
J01FA	Macrolides	2.5	2.6	2.7	3.1	2.9	2.7	2.6	2.5	2.7	3.0	3.0	3.1
J01XE	Nitrofuran derivates (nitrofurantoin)	0.1	0.1	0.0	0.1	0.1	0.1	0.1	0.2	0.3	0.4	0.4	0.4
J01CR02	Penicillins & beta-lactamase inhibitors (amoxicillin & clavulanic acid)	15.0	15.0	16.9	16.8	16.0	16.7	16.3	16.5	18.2	18.8	17.9	17.0
J01CR03-05	Penicillins & beta-lact. inhibitors (antipseudomonal)	0.6	0.6	1.1	1.3	1.5	1.6	1.8	1.9	2.3	2.7	2.7	2.8
J01CA	Penicillins with extended spectrum (amoxicillin)	2.1	2.1	2.5	2.5	2.7	2.5	2.5	2.7	2.9	3.4	3.4	3.6
J01XB	Polymyxins (colistin)	0.0	0.0	0.1	0.1	0.2	0.0	0.1	0.1	0.1	0.2	0.2	0.3
J04AB	Rifamycins	0.8	0.8	0.9	1.0	1.0	0.9	1.0	0.9	0.8	0.8	0.9	0.7
J01E	Sulfonamides & trimethoprim	1.9	1.9	1.9	2.1	2.1	1.9	1.9	2.0	2.3	2.3	2.3	2.3
J01A	Tetracyclines	0.7	0.9	0.7	0.7	0.7	0.5	0.6	0.5	0.6	0.6	0.7	0.6
	Others	1.7	1.8	2.2	2.3	2.3	1.8	2.1	2.4	2.6	2.7	2.6	2.8

Figure 5. c: Consumption of penicillins (ATC group J01C) expressed in DDD per 100 bed-days in hospitals participating in anresis.ch (2004–2015).

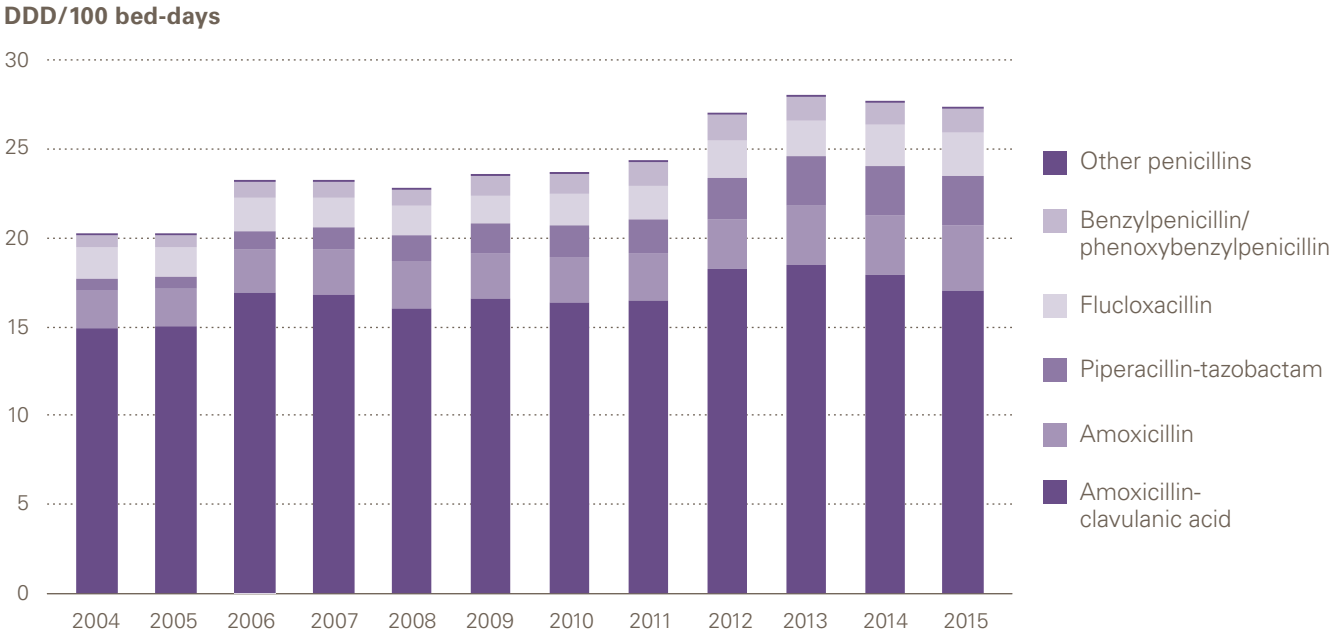
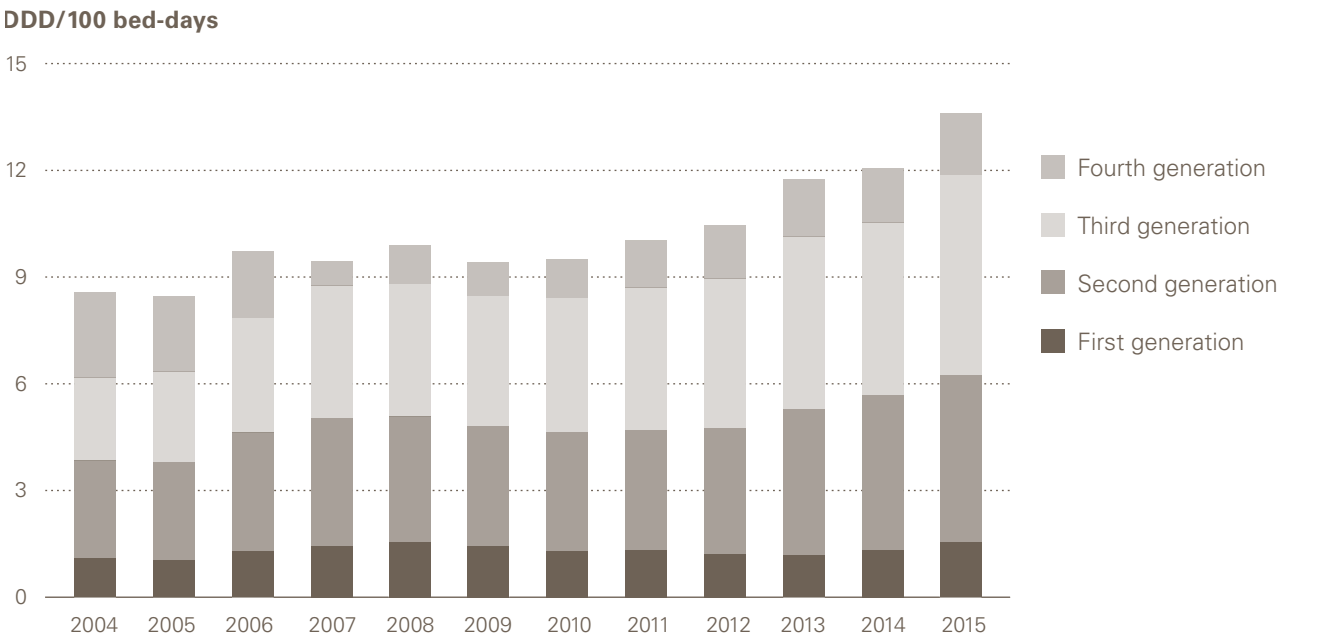


Figure 5. d: Consumption of cephalosporins (first, second, third and fourth generation; ATC group J01DB-DC-DD-DE) expressed in DDD per 100 bed-days in hospitals participating in anresis.ch (2004–2015).



Penicillin consumption increased 35% between 2004 and 2015. Among penicillins, the association of amoxicillin and clavulanic acid was the most frequently prescribed antibiotic and ranged from 15.0 in 2004 to 17.0 DDD per 100 bed-days in 2015 (+14%) (Figure 5. c). Its consumption decreased in 2015 compared to previous years, due to shortage of a widely used parenteral form. The association of piperacillin and tazobactam increased by 340% from 0.6 in 2004 to 2.8 DDD per 100 bed-days in 2015.

The use of second- and third-generation cephalosporins increased markedly from 2004 to 2015 (Figure 5. d). In 2015, cefuroxim (second generation) and ceftriaxon (third generation) were the most widely used cephalosporins overall and in the three hospital size categories.

Figure 5. e: Consumption of carbapenems (ATC group J01DH) expressed in DDD per 100 bed-days by hospital size categories (2004–2015).

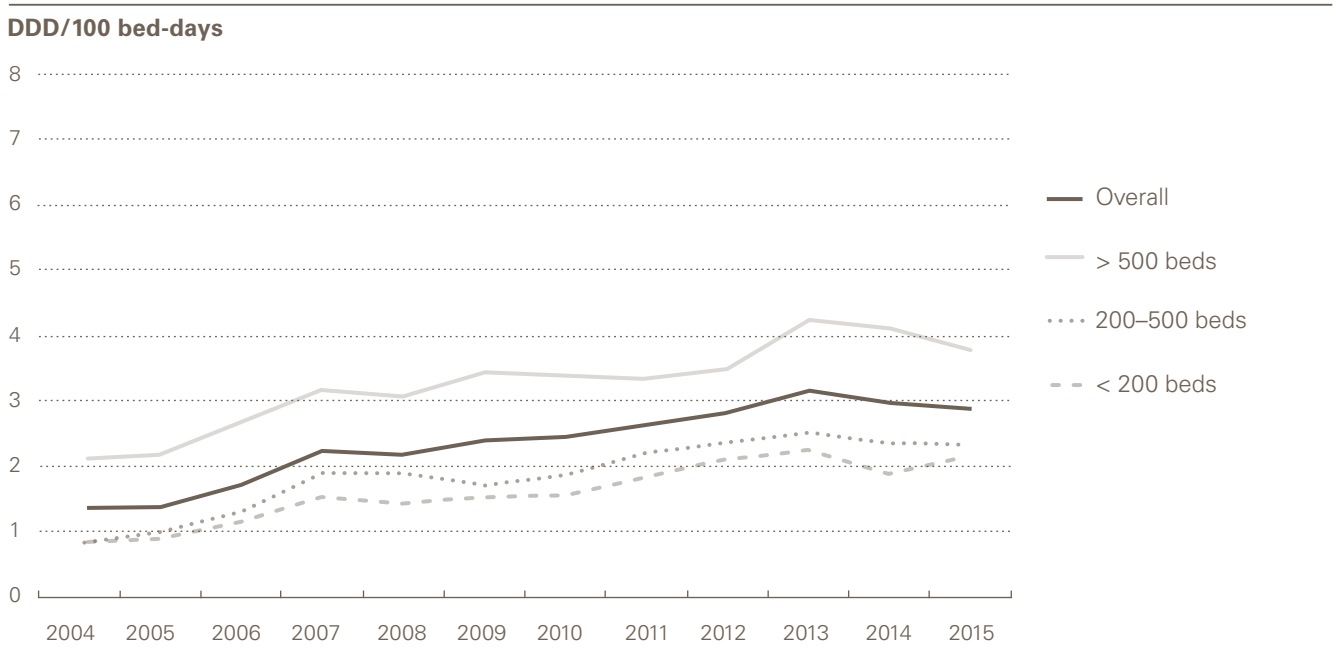
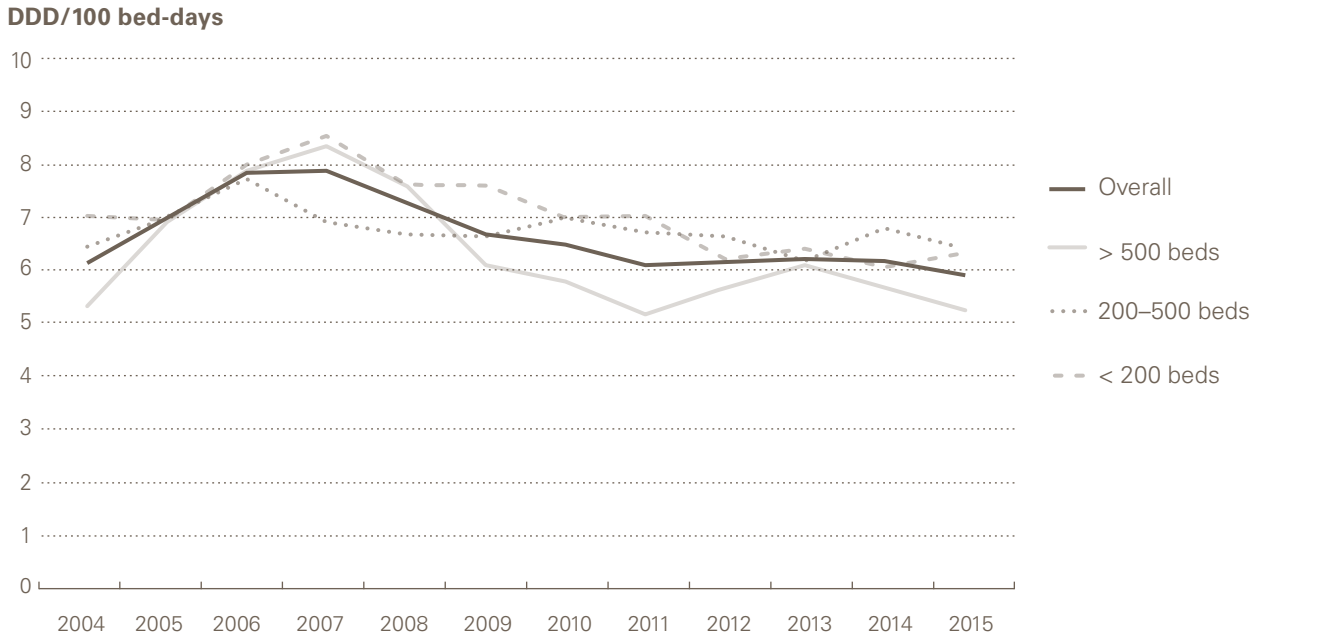


Figure 5. f: Consumption of fluoroquinolones (ATC group J01MA) expressed in DDD per 100 bed-days by hospital size category (2004–2015).



Following a constant increase until 2013, the consumption of carbapenems decreased overall and in the 3 categories of hospital size in 2014 and 2015 (Figure 5. e). Overall, while the consumption of meropenem and ertapenem remained stable (–4% for both between 2013 and 2015), the consumption of imipenem and cilastatin decreased by 18% during the same period.

Fluoroquinolone consumption decreased over the years 2007–2011 and has been stable since 2012 (Figure 5. f). Ciprofloxacin was the most widely used fluoroquinolone overall (4.4 DDD per 100 bed-days, 74% of fluoroquinolone consumption) and in the three hospital size categories in 2015. The consumption of levofloxacin and moxifloxacin was relatively stable over the years 2004 and 2015, accounting for 1.1 and 0.2 DDD per 100 bed-days respectively in 2015. Norfloxacin and ofloxacin use decreased overall and in the three hospital size categories between 2004 and 2015 (–81% and –90%, resp.).

Macrolide consumption (ATC group J01FA) slightly increased from 2.5 DDD per 100 bed-days in 2006 to 3.1 in 2015 (+24%). Clarithromycin was the most widely used macrolide overall (2.5 DDD per 100 bed-days, 80% of macrolide

Figure 5. g: Consumption of vancomycin, teicoplanin, daptomycin and linezolid expressed in DDD per 100 bed-days in hospitals participating in anresis.ch (2004–2015).

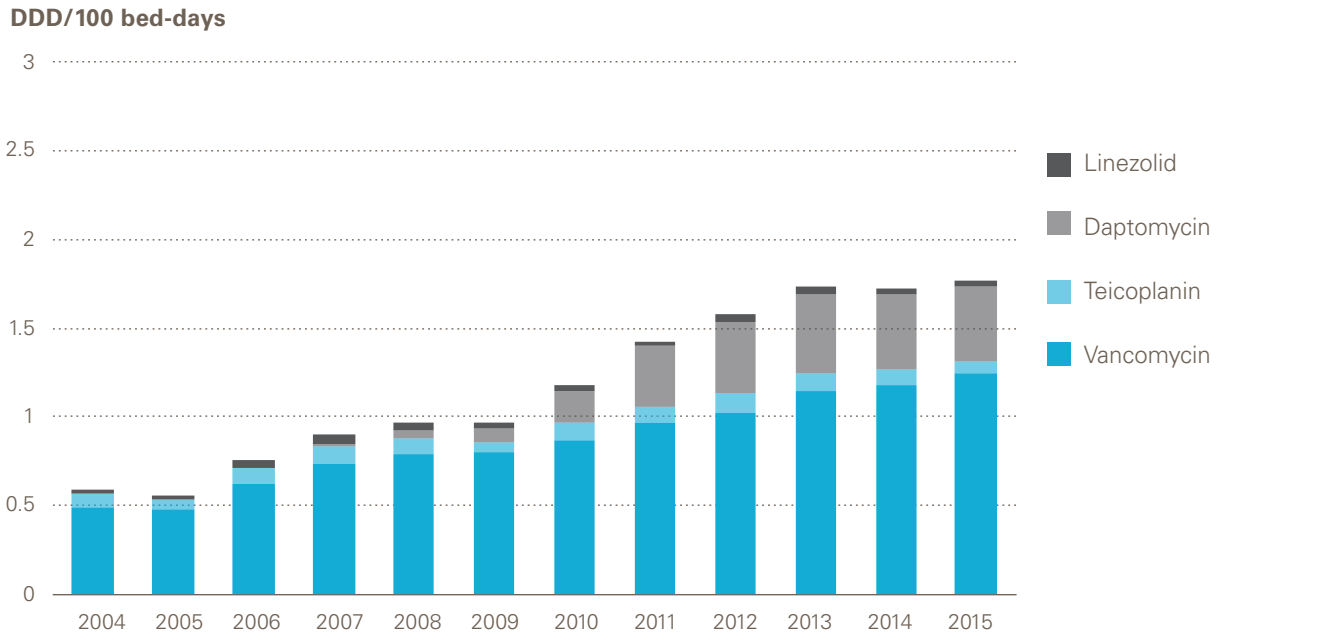
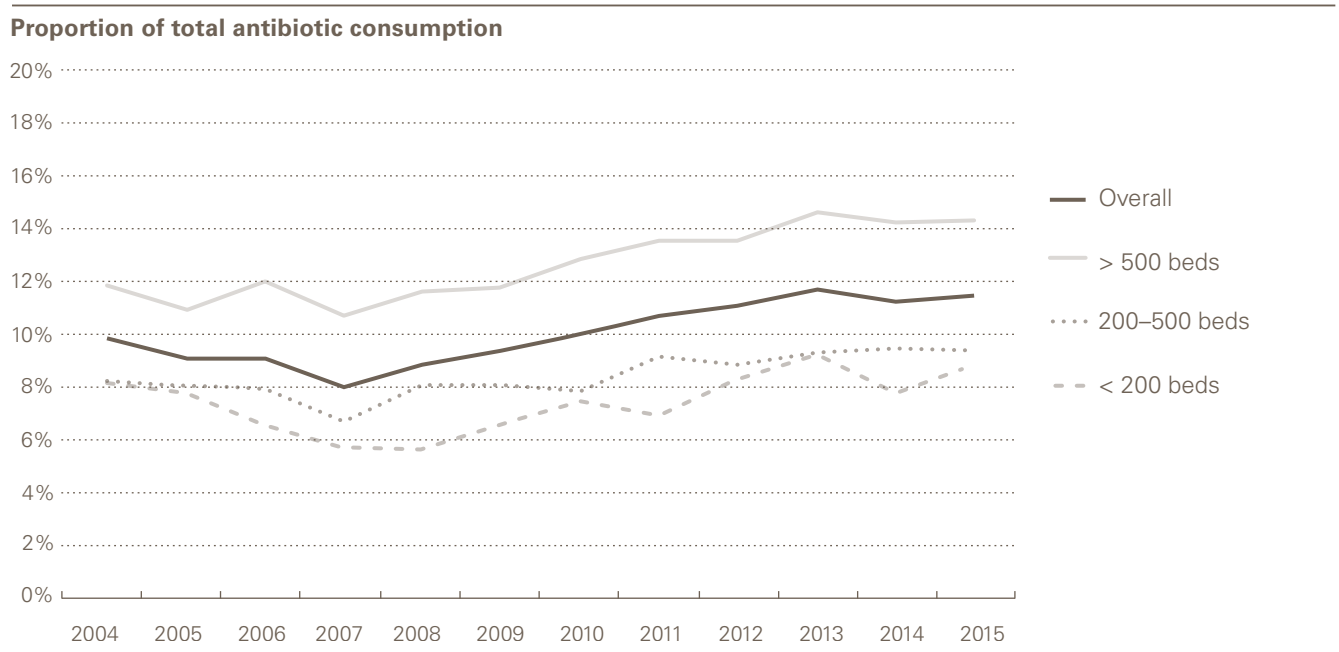


Figure 5. h: Proportion of the broadest-spectrum antibiotics by hospital size categories (2004–2015). The broadest-spectrum antibiotics include: aztreonam, cefepime, ceftazidime, imipenem, meropenem, piperacillin, piperacillin-tazobactam, ticarcillin and ticarcillin-tazobactam.

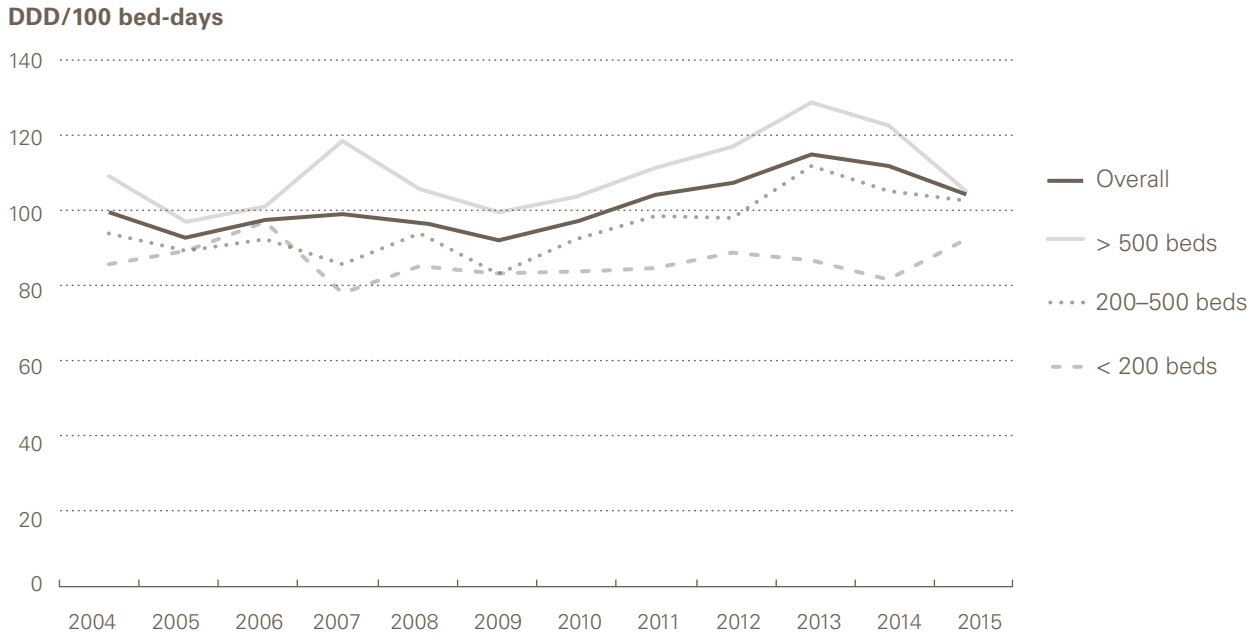


consumption) and in the three hospital size categories in 2015. It was followed by azithromycin (0.4 DDD per 100 bed-days, 12%) and erythromycin (0.2 DDD per 100 bed-days, 8%). The consumption of clindamycin (ATC group J01FF01) remained stable over the period 2004–2015 (1.0 DDD per 100 bed-days in 2015).

Among antibiotics active against resistant gram-positive bacteria, we observed an increase by 152% in consumption of vancomycin between 2004 and 2015 (Figure 5. g). Consumption of daptomycin increased until 2013, but remained stable in 2014 and 2015. Linezolid and teicoplanin remained stable over the years 2004 to 2015.

The proportion of the broadest-spectrum antibiotics has remained stable since 2013 overall and in the three hospital size categories (Figure 5. h). In the present report, aztreonam, cefepime, ceftazidime, imipenem, meropenem, piperacillin, piperacillin-tazobactam, ticarcillin and ticarcillin-tazobactam are considered to be the broadest-spectrum antibiotics. In 2015, piperacillin-tazobactam was the most used of them in the sentinel hospitals (39% of the broadest-spectrum antibiotic use), followed by meropenem (23%), cefepime (23%) and imipenem-cilastatin (11%).

Figure 5. i: Total antibiotic consumption expressed in DDD per 100 bed-days in intensive care units of hospitals participating in anresis.ch over the period 2004–2015.



5.1.3 Total antibiotic consumption in intensive care units of hospitals participating in anresis.ch

Global use of systemic antibiotics remained relatively stable, ranging from 99.4 DDD per 100 bed-days in 2004 to 104.3 in 2015 (+5%) (Figure 5. i). In 2015, total antibiotic consumption was lower in the intensive care units of small-size hospitals (92.3 DDD per 100 bed-days), compared with the ones of medium-size (102.8) and large-size (105.0) hospitals.

5.2 Outpatient care

5.2.1 Total antibiotic consumption in the outpatient setting

In 2015, the total consumption of antibacterial agents for systemic use was approximated (see Chapter 5.3, Discussion) at 5.7 DDD per 1,000 inhabitants per day (DID). It has remained stable since 2013 (6.1 in 2013 and 5.7 in 2014). In comparison, the median consumption was 20.8 DDD per 1,000 inhabitants per day (range between 10.6 in the Netherlands to 34.0 in Greece) in 2014 in the countries participating in the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) [1].

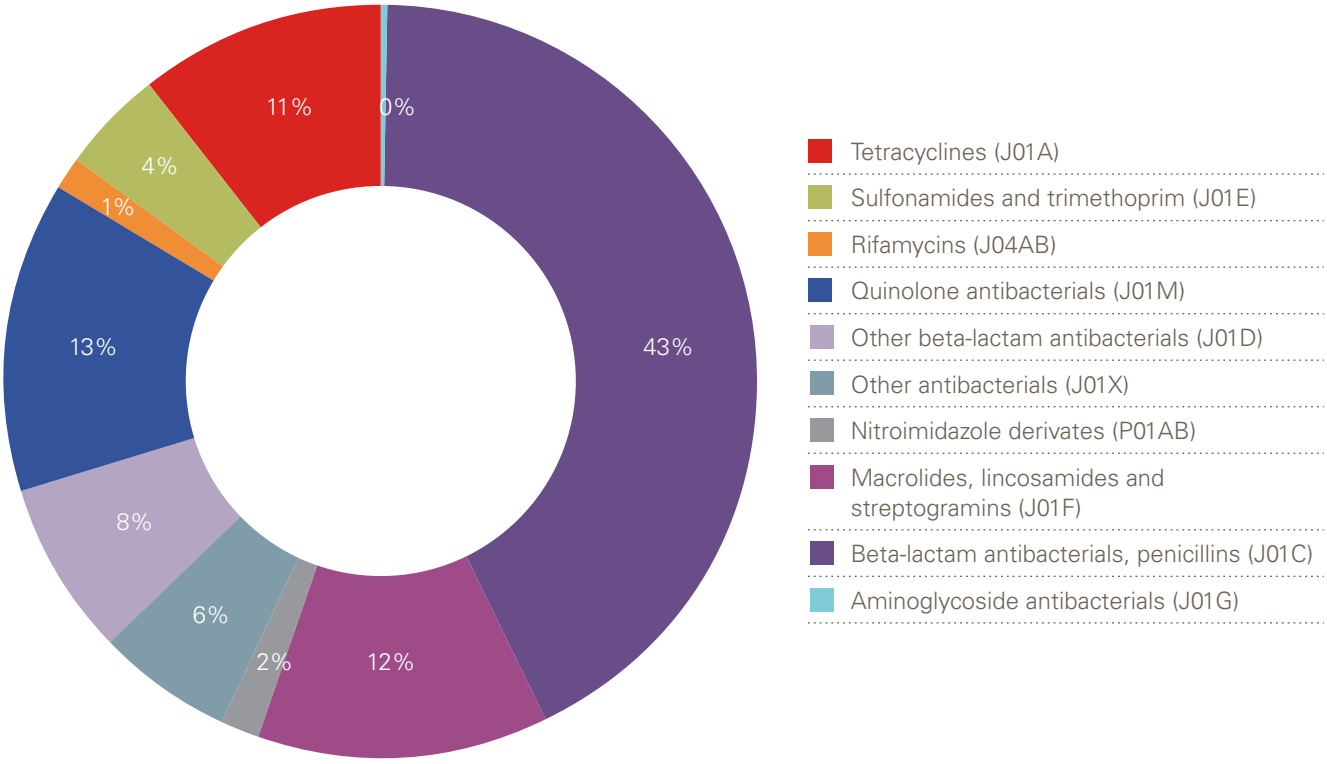
5.2.2 Antibiotic consumption in the outpatient setting by antibiotic class and by specific antibiotic

Consumption of penicillins (including amoxicillin-clavulanic acid, ATC Code J01C) ranked first among antibiotic classes, amounting to 43% of the total antibiotic consumption in 2015 (Figure 5. j). It was followed by the consumption of quinolones (13%, ATC Code J01M), macrolides, lincosamides and streptogramins (12%, ATC Code J01F), tetracyclines (11%, ATC Code J01A), other beta-lactam antibacterials (including cephalosporins, 8%, ATC Code J10D), other antibacterials (6%, ATC Code J01X) and sulfonamides (4%, ATC Code J01E).

The overall consumption of penicillins remained stable in 2015 (2.43 DID, 43% of total antibiotic consumption) compared to 2014 (2.40 DID). Combinations of penicillins including beta-lactamase inhibitors were the most used group of systemic antibiotics in 2015 (1.79 DID, 31% of total antibiotic consumption) and of penicillins (74% of penicillin consumption). Among penicillins, the penicillins with an extended spectrum, namely amoxicillin, were the second most used group (0.55 DID, 23% of penicillin consumption) (Table 5. b). This group was especially used in children aged less than 2 years (66% of penicillin consumption in 2015), whereas penicillins associated with beta-lactamase inhibitors were the most used penicillins in the other age groups (2–11 years: 44%; 12–17: 66%; 18–64: 79%; > 64: 84%) (Figure 5. k). The relative consumption of beta-lactamase-sensitive penicillins was low in Switzerland (1.6% of total antibiotic consumption in 2015), as this indicator ranged from < 0.1% to 26.9% in 2014 in countries participating in the ESAC-Net [1]. However, the relative consumption of penicillins associated with beta-lactamase inhibitors was relatively high (31%) in comparison with countries participating in the ESAC-Net (range: < 0.1%–43.8%) in 2014 [1]. At the substance level, amoxicillin-clavulanic acid and amoxicillin were the most frequent antibiotics in 2015 (1.78 and 0.55 DID, resp.), of which both consumptions remained stable between 2014 and 2015.

The cephalosporins (ATC Code J01DB-DE) remained stable in 2015 (0.43 DID) compared to 2014 (0.43 DID). Cefuroxime, cefpodoxime and cefaclor represented 74%, 17% and 3%

Figure 5. j: Distribution of the total antibiotic consumption per antibiotic class in the outpatient setting in 2015 in Switzerland.



resp. of the cephalosporin consumption in 2015. The relative consumption of third- and fourth-generation cephalosporins (ATC code J01DD-DE) was 2% in 2015, compared with a range of < 0.1% to 7.0% in countries participating in the ESAC-Net in 2014 [1].

Fluoroquinolone consumption was 0.77 DDD per 1,000 inhabitants and per day in 2015 in Switzerland, accounting for 13% of the total antibiotic consumption. Although we have observed a slight downward trend (–4% between 2014 and 2015), their consumption has remained high in comparison with countries participating in the ESAC-Net, where the relative consumption of fluoroquinolones ranged from 2.3% to 14.9% in 2014 [1]. At the substance level, ciprofloxacin was the most used fluoroquinolone (62%), followed by levofloxacin (15%), norfloxacin (13%), moxifloxacin (8%) and ofloxacin (2%) in 2015. Except moxifloxacin, the other fluoroquinolones have shown a slight decrease of use since 2013. Seniors aged 65 and over were relatively high consumers of fluoroquinolones (20% of their total antibiotic consumption).

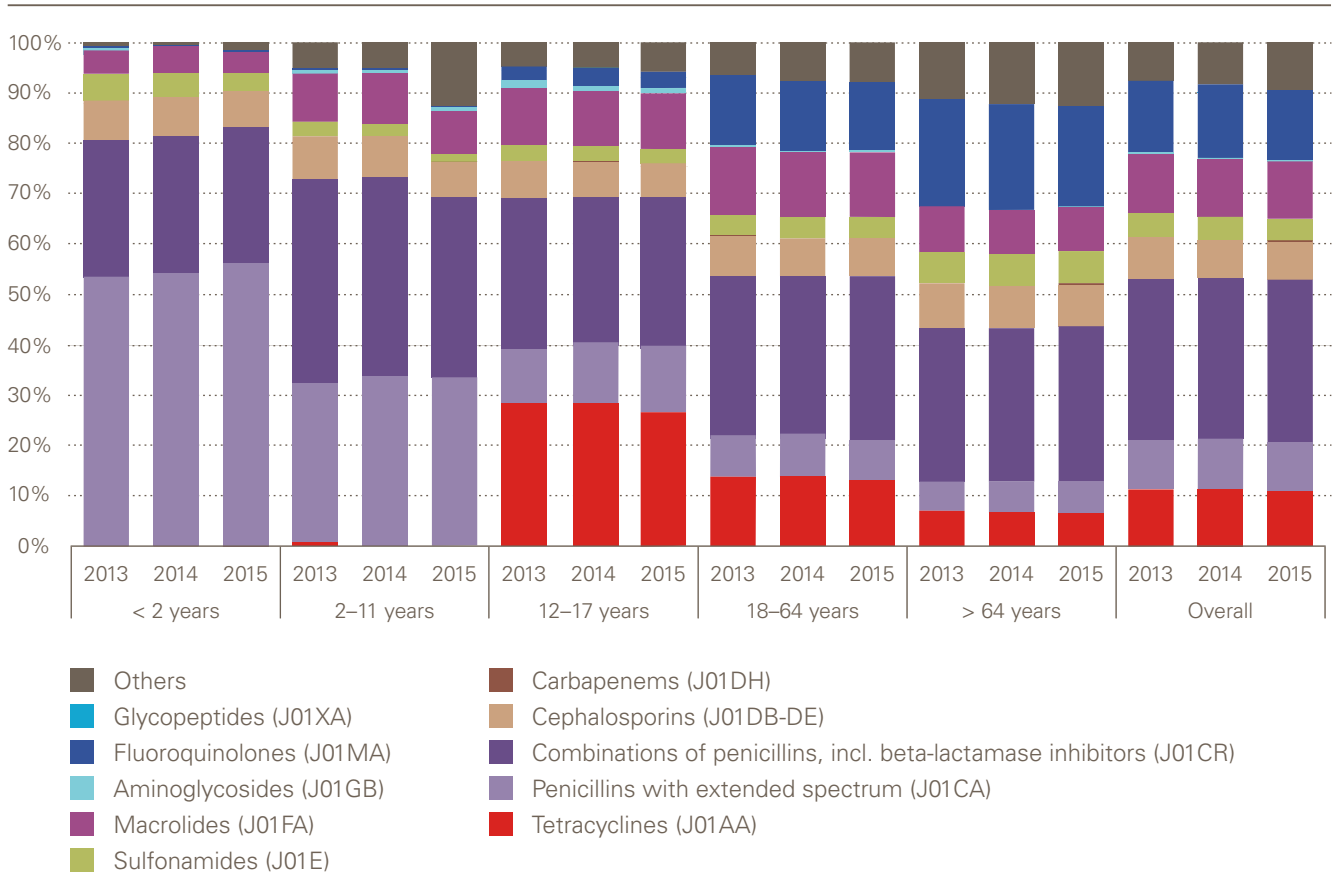
In the group macrolides, lincosamides and streptogramins (ATC code J01F), only macrolides and lincosamides have been used in Switzerland (0.62 and 0.09 DDD per 1,000 inhabitants per day, 2015). Macrolide consumption slightly decreased (–2%) between 2014 and 2015, while lincosamide consumption remained stable. Clarithromycin, azithromycin and erythromycin accounted for 58%, 41% and 1% resp. of the macrolides in 2015. Among lincosamides, clindamycin consumption was 0.09 DDD per 1,000 inhabitants per day in 2015 and has remained stable since 2013.

Tetracycline consumption decreased from 0.63 DDD per 1,000 inhabitants per day in 2014 to 0.60 in 2015 (–6%), accounting for 11% of the total antibiotic consumption. The consumption of all tetracyclines slightly decreased between 2014 and 2015. Doxycycline was the most used tetracycline (71%), followed by limecycline (15%), and minocycline (14%). Limecycline and minocycline were especially used in patients between 12 and 17 years of age (44% and 25% of tetracycline use, resp.).

Table 5. b: Consumption of antibiotic classes expressed in DDD per 1,000 inhabitants per day in the outpatient setting for the years 2013–2015 in Switzerland.

ATC Group	Antibiotic class	2013	2014	2015
J01G	Aminoglycosides	0.02	0.02	0.02
J01CF	Beta-lactamase-resistant penicillins	0.01	0.01	0.01
J01CE	Beta-lactamase-sensitive penicillins	0.06	0.05	0.09
J01DH	Carbapenems	0.00	0.00	0.00
J01DB	Cephalosporins – first generation	0.00	0.00	0.00
J01DC	Cephalosporins – second generation	0.37	0.32	0.32
J01DD	Cephalosporins – third generation	0.12	0.10	0.10
J01DE	Cephalosporins – fourth generation	0.00	0.00	0.00
J01MA	Fluoroquinolones	0.84	0.80	0.76
J01XA	Glycopeptides	0.00	0.00	0.00
J01FF	Lincosamides	0.09	0.09	0.09
J01FA	Macrolides	0.69	0.63	0.62
J01XE	Nitrofuran derivates (nitrofurantoin)	0.23	0.25	0.26
P01AB	Nitroimidazole derivates (metronidazole oral)	0.10	0.10	0.10
J01CR02	Penicillins & beta-lactamase inhibitors (amoxicillin & clavulanic acid)	1.89	1.79	1.78
J01CR03-05	Penicillins & beta-lact. inhibitors (antipseudomonal)	0.00	0.00	0.00
J01CA	Penicillins with extended spectrum (amoxicillin)	0.56	0.54	0.55
J01XB	Polymyxins (colistin)	0.01	0.01	0.01
J04AB	Rifamycins	0.08	0.08	0.08
J01E	Sulfonamides & trimethoprim	0.27	0.26	0.25
J01A	Tetracyclines	0.67	0.63	0.60
	Others	0.04	0.05	0.05

Figure 5. k: Antibiotic classes per age group and overall as a proportion of the total consumption in the outpatient setting over the period 2013–2015 in Switzerland.



5.3 Discussion

In Swiss acute care hospitals, total antibiotic consumption increased from 46.2 to 62.9 DDD per 100 bed-days between 2004 and 2015, whereas it was relatively stable when expressed in DDD per 100 admissions. This discrepancy can be explained by an increasing number of admissions and a decreasing number of bed-days in hospitals due to shorter length of hospital stays. Expressed in DDD per 1,000 inhabitants per day, the total antibiotic consumption (1.8) was close to the median (1.9) obtained in the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) [1]. The most commonly used class of antibiotics was the penicillins (ATC Code J01C), followed by the other beta-lactam antibaterials, including cephalosporins (ATC Code J01D) and quinolones (ATC Code J01M).

In the outpatient setting, the total consumption of antibiotics for systemic use was approximated at 5.7 DDD per 1,000 inhabitants per day in 2015, which was lower than observed in countries participating in the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) [1]. However, comparisons with other countries must be performed with caution, as consumption may have been underestimated in Switzerland (see limitations). The most commonly used class of antibiotics was the penicillins (ATC Code J01C), followed by the quinolones (ATC Code J01M) and the macrolides, lincosamides and streptogramins (ATC Code J01F). The relative consumption of fluoroquinolones and penicillins, including beta-lactamase inhibitors, remained relatively high in comparison with countries participating in the ESAC-Net.

Our methodology has several limitations [2, 3]. The DDD methodology allows comparisons between hospitals or countries, but it may reflect the dosages chosen in some of them inaccurately, thus limiting the qualitative appraisal of different prescribers' profiles [4]. Concerning the inpatient setting, a sentinel network like anresis.ch, which is based on voluntary participation of hospitals in Switzerland, is a surveillance system comprising a non-exhaustive group of hospitals. Nevertheless, the high proportion of all Swiss acute care hospitals included in our surveillance suggests that the data are representative. In this report, we express the antibiotic consumption mostly in DDD per 100 bed-days rather than per admission for the inpatient setting. The definition of bed-days has been set by the Federal Statistical Office, while the number of admissions is not an official indicator and can be subject to different interpretations among hospitals. Concerning the outpatient setting, the data may be slightly underestimated. Indeed, the data from dispensing physicians and partially from nursing homes are missing in the dataset [5].

References

[1] European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe, ESAC-Net interactive database (2016, July 25). Retrieved from http://ecdc.europa.eu/en/activities/surveillance/ESAC-Net/Pages/index.aspx

[2] Filippini M, Masiero G, Moschetti K. Socioeconomic determinants of regional differences in outpatient antibiotic consumption: Evidence from Switzerland. Health Policy. 78 (1)

[3] Plüss-Suard C et al. Hospital antibiotic consumption in Switzerland: comparison of a multicultural country with Europe. J Hosp Inf 2011; 79(2): 166 –171

[4] de With K et al. Comparison of Defined versus Recommended versus Prescribed Daily Doses for Measuring Hospital Antibiotic Consumption. Infection 2009; 37(4): 349 –352

[5] [Kantonal unterschiedliche Dichte von selbst dispensierenden Ärzten und Apotheken]. Interpharma (2016, July 25). Retrieved from http://www.interpharma.ch

6

Sales of antimicrobials in veterinary medicine

6 Sales of antimicrobials in veterinary medicine

6.1 Sales of antimicrobials for use in animals

The sales of antimicrobials continued to decline in 2015 (Table 6 a.). Overall, 42,188 kg of antibiotics were sold for veterinary medicine, which corresponds to a decrease of 10% compared with the previous year. This amounts to a decline of 40% (28 tonnes) since 2008. The decrease is mainly due to a fall in sales of medicated premixes.

The sales rankings of the various classes of antibiotics remained unchanged: sulfonamides come in first place, followed by penicillins and tetracyclines. These three classes

Table 6. a: Sales of antibiotic classes in 2008 to 2015.

Sales (kg)								
	2008	2009	2010	2011	2012	2013	2014	2015
Sulfonamides	29,129	27,261	25,696	23,123	21,556	18,942	17,009	14,959
Penicillins	11,275	10,698	11,272	11,516	11,055	10,930	10,389	10,057
Tetracyclines	16,719	15,559	14,749	13,737	12,043	11,631	10,402	8,683
Aminoglycosides	3,721	3,573	3,222	3,324	3,207	3,124	3,125	3,104
Macrolides	4,384	4,109	3,910	3,551	3,369	3,166	2,858	2,680
Trimethoprim	1,858	1,752	1,704	1,549	1,368	1,148	1,102	904
Polymyxins	1,577	1,544	1,489	1,454	1,058	855	733	503
Cephalosporins	501	520	568	565	542	530	522	495
Fluoroquinolones	433	427	415	394	359	413	404	407
Amphenicols	253	271	258	284	232	202	188	217
Others*	42	52	83	407	262	290	222	179
Total	**69,894**	**65,766**	**63,367**	**59,904**	**55,050**	**51,231**	**46,995**	**42,188**

*Imidazoles, nitrofurans, pleuromutilins, polypeptides excluding polymyxins, steroidal antibiotics, quinolones (until 2014)

Table 6. b: Sales of antimicrobials according to the administration route in 2008–2015.

Sales (kg)	2008	2009	2010	2011	2012	2013	2014	2015
Oral	**55,132**	**51,993**	**50,143**	**46,476**	**42,005**	**38,756**	**34,697**	**30,015**
Premixes	48,794	45,714	44,125	40,606	36,181	33,021	29,079	24,336
Others*	6,338	6,279	6,017	5,871	5,824	5,735	5,618	5,679
Intramammary	**4,505**	**4,015**	**3,595**	**3,734**	**3,655**	**3,482**	**3,375**	**3,193**
Dry cow products	1,439	1,291	1,209	1,323	1,315	1,336	1,343	1,064
Lactating cow products	3,066	2,724	2,386	2,411	2,340	2,146	2,033	2,129
Parenteral	**9,050**	**8,597**	**8,419**	**8,487**	**8,258**	**7,931**	**7,768**	**7,974**
Intrauterin	**870**	**870**	**905**	**857**	**815**	**767**	**864**	**719**
Topical / external	**337**	**291**	**306**	**350**	**318**	**296**	**290**	**286**
Sprays	241	253	280	321	299	278	272	270
Others **	96	38	27	30	18	18	19	16
Total	**69,894**	**65,766**	**63,367**	**59,904**	**55,050**	**51,231**	**46,995**	**41,188**

*tablets, capsules, powders, suspensions, granules
**ointment, drops, gels

are often sold as medicated premixes, which accounted for about 60% of the total volume (24 tonnes). The quantity of antibiotics approved only for companion animals comprises 2% of the total volume.

An error was identified for the conversion factor of all products containing benzathine penicillin and procaine penicillin. This led to an overestimation of sold penicillins of around 20% (about 2,000 kg) in the previous reports. The data has been corrected and is published correctly in the present report.

Regarding the highest-priority critically important antibiotic classes for human medicine [1], the sales of macrolides have decreased by approximately 40% (–1,655 kg) since 2008. But the sales of long-acting, single-dose injection products containing macrolides show an upward trend. The sales of fluoroquinolones and third- and fourth- generation cephalosporins remained unchanged.

Active ingredient groups are listed individually only if at least three different products from three different marketing authorization holders are licensed. All others are summarized in the category "Others".

The distribution of antimicrobials according to the administration route remained unchanged compared to previous years (Table 6. b). The biggest sales volumes are products licensed for oral application (71%), followed by parenteral (18%), intramammary (8%), intrauterine (2%) and topical formulations (1%). Products authorized for oral application were mainly sold in the form of premixes (81% of oral application).

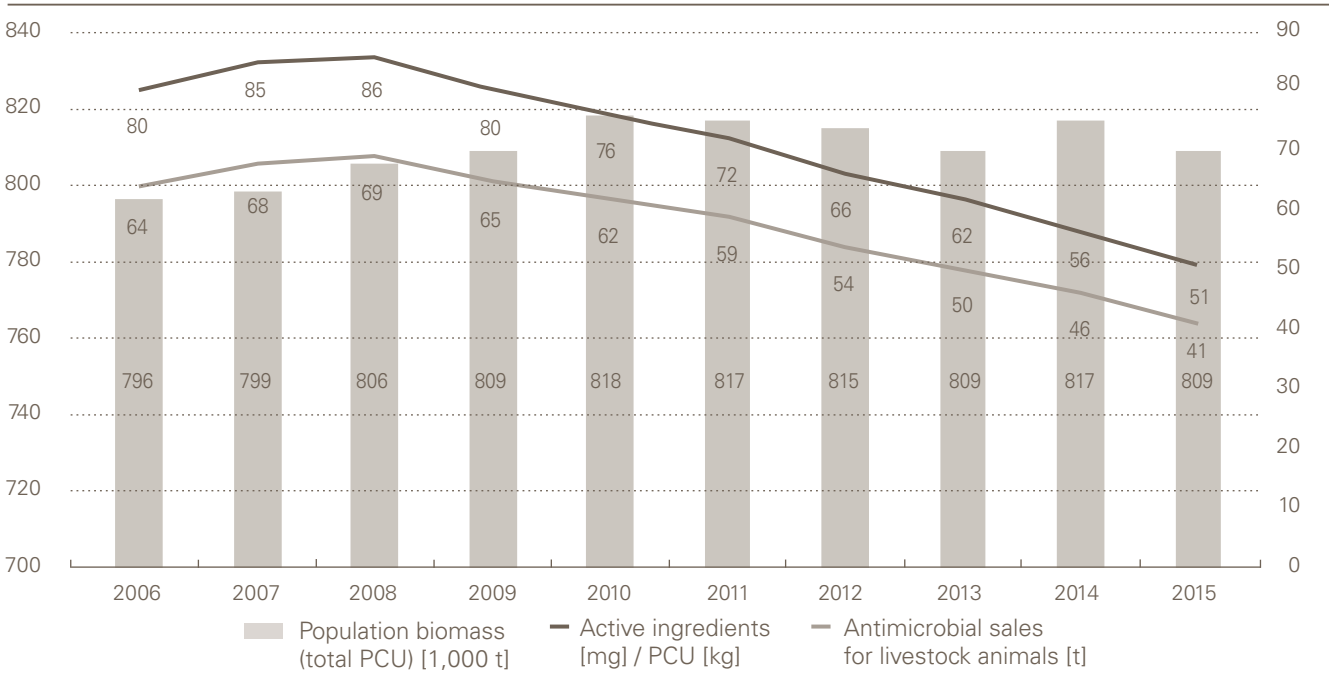
6.2 Sales of antimicrobials for use in livestock animals

6.2.1 General

The amount of sales of antimicrobials for livestock animals includes products approved for livestock animals and products approved for livestock and companion animals (mixed registrations). This is in accordance with the procedure used by the ESVAC project [2]. The amount has decreased continuously since 2008 (–40%). Sulfonamides account for the bulk of agents followed by penicillins and tetracyclines. The sales of macrolides have decreased by approximately 40% since 2008 (Table 6. c). But the sales of long-acting, single-dose injection products containing macrolides show an upward trend. Several such products are available on the market to treat respiratory diseases in calves and pigs. The sales of fluoroquinolones and third- and fourth- generation cephalosporins remained unchanged over the years under investigation.

The sales volume of colistin, which has recently been of public interest following the discovery of a horizontally transferable resistance mechanism (MCR-1), has declined by approximately 70% since 2008 and amounted for 502 kg in 2015. Products containing colistin are mainly authorized for pigs, to treat gram-negative gastrointestinal infections. Expressed in correlation to the biomass under exposure (population correction unit, PCU; see Chapter 6.2.2.), the level is 0.6 mg Colistin / PCU for Switzerland. This is below the European average and in line with the requested reduction of colistin to a level of 1 or below 1 mg / PCU for European countries in order to maintain its efficacy in the treatment of severe infections in humans [3].

Figure 6. a: Antimicrobial sales for livestock animals in the years 2006–2015 compared with the population biomass (total PCU) and the sales of active ingredients per PCU.



6.2.2 Antimicrobial sales in relation to the livestock population weight (Population Correction Unit Method)

The amount of sales of antimicrobials depends on the size of the animal population. To compare sales in individual countries and across countries, the ESVAC-Project (European Surveillance of Veterinary Antimicrobial Consumption, EMA) developed a method to express antimicrobial sales correlated to the weight of an animal livestock population [2]. The amount of active ingredients is divided by the estimated most likely weight at treatment (population correction unit, PCU). Companion animals are not taken into account, as the number is unknown in many countries. PCU is a technical unit of measurement and consists of the number of live (dairy cows, sheep, sows, horses) and slaughtered animals (cattle, pigs, lambs, horses, poultry, turkeys) in the corresponding year multiplied by the estimated weight at the time of treatment (expressed in kg). Imports and exports of live animals are also taken into account. Figure 6. a shows the normalization of antimicrobial sales for livestock animals in Switzerland using the PCU method for the years 2006 to 2015.

The figure shows decreasing sales of antimicrobials in the last 7 years, despite a relatively steady population biomass. The reduction of milligram active ingredients per PCU indicates that the decrease of sales of antimicrobials is not primarily due to a smaller animal livestock population. It can be assumed that the reduction in sales is most probably due to a reduction in the number of treatments performed. The efforts made in the framework of the national strategy on antibiotic resistance (StAR) [4] in Switzerland seem to have a positive effect on the awareness of veterinarians and farmers using antimicrobials in Switzerland.

6.2.3 Medicated premixes

Medicated premixes accounted for 58% of the total sales in 2015, a proportion which was similar to the previous years. A steady decrease in sales of medicated premixes has been observed since 2008 (–24,458 kg). Sulfonamides, tetracyclines and penicillins are the three main classes of active ingredients contained in premixes (Table 6. d). This reduction is the main reason for the decrease in the sales of antimicrobials

Table 6. c: Sales of different antibiotic classes licensed for livestock animals in 2008–2015.

Sales (kg)								
	2008	2009	2010	2011	2012	2013	2014	2015
Sulfonamides	29,088	27,231	25,672	23,118	21,556	18,942	17,009	14,959
Penicillins	10,890	10,286	10,855	11,078	10,640	10,492	9,938	9,614
Tetracyclines	16,704	15,546	14,746	13,731	12,038	11,626	10,398	8,679
Aminoglycosides	3,688	3,549	3,215	3,317	3,199	3,115	3,114	3,095
Macrolides/lincosamides	4,338	4,063	3,864	3,508	3,326	3,125	2,816	2,641
Trimethoprim	1,854	1,749	1,702	1,548	1,368	1,148	1,102	904
Colistin	1,577	1,543	1,489	1,454	1,057	854	773	502
Fluoroquinolones	408	403	388	371	335	384	379	384
Cephalosporins	169	203	237	249	237	228	241	234
Amphenicols						183	169	199
Others*	191	211	245	568	413	274	208	166
Total	**68,906**	**64,784**	**62,413**	**58,942**	**54,169**	**50,370**	**46,147**	**41,378**

*Pleuromutilins, quinolones, amphenicoles (until 2012)

Table 6. d: Sales of antimicrobials licensed as premixes in 2008–2015, according to antibiotic classes.

Sales (kg)								
	2008	2009	2010	2011	2012	2013	2014	2015
Sulfonamides	23,075	21,412	20,236	17,788	16,319	13,931	12,141	10,028
Tetracyclines	15,008	13,880	12,983	12,006	10,359	9,968	8,673	7,038
Penicillins	3,874	3,836	4,610	4,722	4,309	4,461	4,198	3,840
Macrolides/lincosamides	3,815	3,645	3,444	3,097	2,919	2,762	2,423	2,272
Colistin	1,544	1,525	1,472	1,438	1,045	844	763	500
Trimethoprim	1,399	1,320	1,249	1,124	937	740	626	453
Others *	78	96	131	431	293	314	255	205
Totals	**48,794**	**45,714**	**44,125**	**40,606**	**36,181**	**33,021**	**29,079**	**24,336**

*Pleuromutilins, fluoroquinolones, aminoglycosides, quinolones (until 2014)

Figure 6. b: Sales of antimicrobials (in kg) licensed for intramammary use in 2008–2015 separated into dry cow products and products for use during lactation.

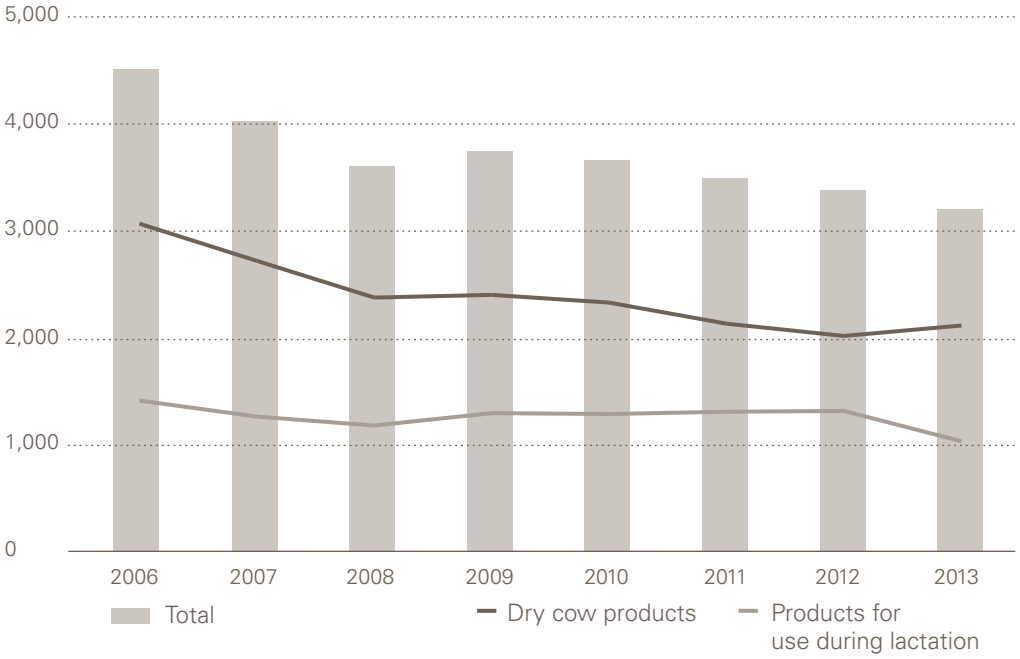


Table 6. e: Sales of antimicrobials licensed for intramammary use in 2008–2015 according to anitbiotic class.

Sales (kg)								
	2008	2009	2010	2011	2012	2013	2014	2015
Dry cow products								
Beta-lactams*	1,170	1,039	963	1,058	1,055	1,070	1,075	896
Aminoglycosides	269	252	245	265	261	266	268	168
Total	**1,439**	**1,291**	**1,209**	**1,323**	**1,315**	**1,336**	**1,343**	**1,064**
Products for use during lactation								
Penicillins	2,326	2,052	1,785	1,813	1,774	1,644	1,545	1,652
Aminoglycosides	558	492	445	436	406	376	370	361
Cephalosporins	35	51	56	60	55	52	56	59
Others**	147	129	101	102	104	74	62	57
Total	**3,066**	**2,724**	**2,386**	**2,411**	**2,340**	**2,146**	**2,033**	**2,129**

*Only penicillins after 2011
**Lincosamides, macrolides, polymyxins

Table 6. f: Sales of antibiotic classes licensed for companion animals in 2008 to 2015.

Sales (kg)								
	2008	2009	2010	2011	2012	2013	2014	2015
Penicillins	385	412	417	438	415	438	450	443
Cephalosporins	332	317	331	316	304	302	281	262
Macrolides/lincosamides	46	45	46	44	43	41	42	38
Others *	125	129	102	129	86	41	38	35
Fluoroquinolones	25	24	27	23	24	29	25	23
Aminoglycosides	33	24	7	7	8	9	10	9
Sulfonamides **	41	30	24	5				
Total	**988**	**982**	**955**	**962**	**881**	**860**	**847**	**810**

*Imidazoles, nitrofurans, polypeptides, steroidal antibiotics, tetracyclines, trimethoprim, amphenicoles
**No licensed products since 2012

for veterinary medicine. Medicated premixes are available in several combinations of active ingredients: products containing a single active ingredient, two active ingredients (usually a sulfonamide combined with trimethoprim) or three active ingredients (a tetracycline combined with a sulfonamide and a macrolide). Products with three active ingredients accounted for 50% of the medicated premixes sold.

6.2.4 Antimicrobials authorized for intramammary use

The sales of products for intramammary use also showed a decrease in 2015. Since 2008, the amount has been reduced by 30%. Two thirds of all antimicrobials licensed for intramammary use are products for the treatment of mastitis during lactation and one third are products for drying off. The sales of the latter products have decreased by 21% compared to the previous year, whereas the sales of products for use during lactation increased slightly, by 5% (Figure 6. b).

The distribution by antibiotic classes shows that penicillins are predominant, accounting for 80% of all active ingredients administered into the udder (Table 6. e). Sales of products containing cephalosporins for the treatment of mastitis during lactation have been increasing since 2014.

6.3 Sales of antimicrobials licensed for companion animals

The quantity of antibiotics approved exclusively for use in companion animals amounts to approximately 2% of the total volume. Since 2012, products licensed for both livestock and companion animals are added to the category "livestock animals", in accordance with the guidelines of the ESVAC project [2]. This is especially relevant for active ingredients for parenteral application, as the major part of these products are licensed for both livestock and companion animals. The consequence is a slight underestimation of the use in companion animals.
The amount sold for companion animals has decreased by 18% (–178 kg) since 2008. Penicillins were the most important active ingredient group, followed by cephalosporins, macrolides, lincosamides and fluoroquinolones (Table 6. f). The slightly decreasing trend of sales of cephalosporins continued in 2015 (–7% compared to 2014). The strong decrease related to aminoglycosides in the year 2010 was due to the withdrawal of a single product containing such an antimicrobial.

6.4 Discussion

The decrease in the volume of antimicrobials sold for use in veterinary medicine is ongoing since 2008.This is mainly due to a fall in the sales of medicated premixes. The reduction of milligram active ingredients per PCU indicates that the reason for the decrease is most likely a reduced number of treatments. However, the data should be interpreted cautiously as it is based on sales figures only. Relevant information about target species (livestock animals, companion animals, mixed), route of administration (parenteral, oral, topical/external, intrauterine, intramammary) and galenics are solely based on the marketing authorization (summary of product characteristics). Therefore, the report does not contain any data about effective use at the species level. Different dosages for different antibiotic classes and target species are not taken into account and can differ widely. Various potencies of antimicrobials can only be corrected using standardized daily doses (in keeping with the defined daily doses "DDD" used in human medicine). Therefore, ESVAC recently published technical units of measurements to report antimicrobial consumption data in animals [5]. Defined daily doses for animals (DDDvet) and defined course doses for animals (DCDvet) take into account differences between species and substances as well as the treatment duration.

Information about treatment intensities, i.e. the number of animals treated in relation to a given population, can only be provided by data at the veterinary or farm level. These data are currently not available in Switzerland. To establish a correlation with the development of resistance to antimicrobials, the reduction of total volumes of antimicrobials sold is less relevant than the number of treatments per animal or the number of animals treated per unit of time. A system to collect veterinary prescription data is currently under construction. The recording of prescription data is crucial to target the introduction of reasonable measures for prevention and prudent use, and to follow up on their effects.

References

[1] WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR). Critically Important Antimicrobials for Human Medicine. 3rd revision, 2011

[2] European Medicines Agency, European Surveillance of Veterinary Antimicrobial Consumption, 2015. Sales of veterinary antimicrobial agents in 26 EU/EEA countries in 2013 (EMA/387934/2015)

[3] European Medicines Agency 2016. Updated advice on the use of colistin products in animals within the European Union: development of resistance and possible impact on human and animal health (EMA/231573/2016).

[4] Swiss Confederation 2015. Strategy on Antibiotic Resistance Switzerland

[5] European Medicines Agency, European Surveillance of Veterinary Antimicrobial Consumption, 2016. Defined daily doses for animals (DDDvet) and defined course doses for animals (DCDvet) (EMA/224954/2016)

7

Resistance in bacteria from human clinical isolates

7 Resistance in bacteria from human clinical isolates

7.1 *Escherichia coli*

Escherichia coli is the most frequent gram-negative microorganism causing bacteremia. It is a colonizer of the intestinal tract and as such the most frequent microorganism causing urinary tract infections. As urinary tract infections are the second most frequent infectious disease in ambulatory care, increasing resistance trends directly affect the hospital as well as the ambulatory settings.

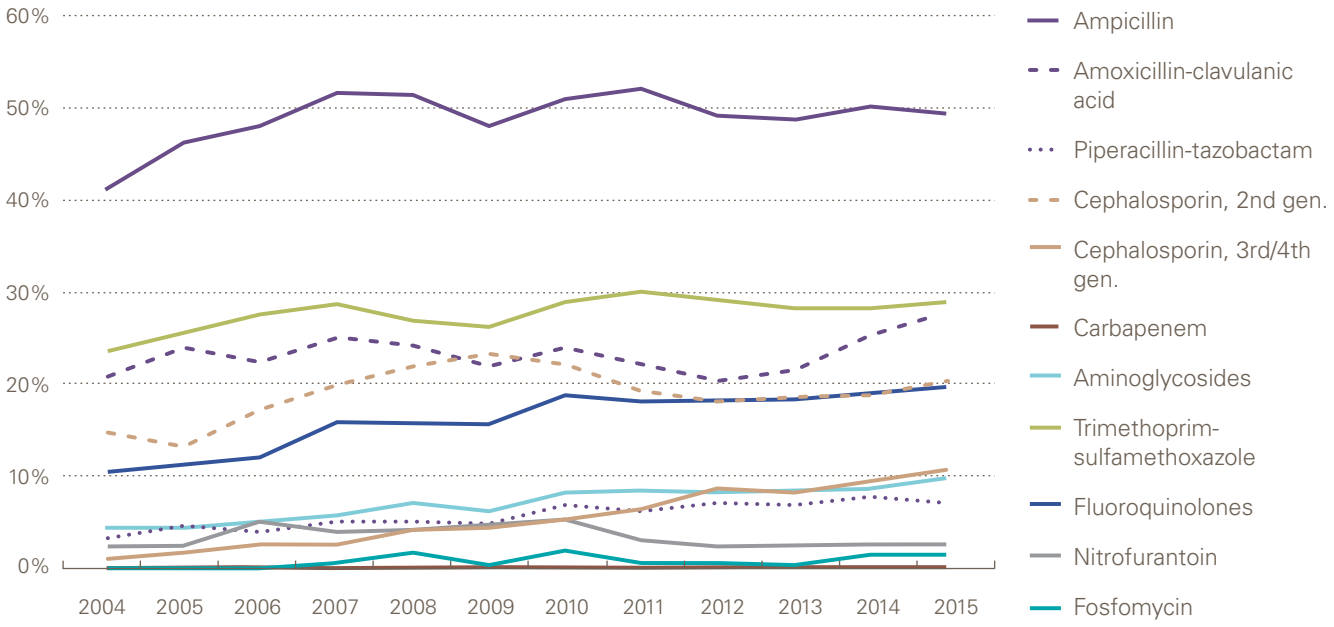
In 2015, resistance to fosfomycin and nitrofurantoin was still very low. These antibiotics can only be used for non-invasive urinary tract infections. Therefore, they represent an important option in ambulatory care. Interestingly, only about one quarter of all isolates are tested routinely against theses antibiotics. Fluoroquinolone non-susceptibility, which increased from 10.3% in 2004 to 18.4% in 2013 further increased (non-significantly) to 19.6% in 2015. This is close to the EU/EEA average of 22.4% in 2014 [1]. Although non-susceptibility to trimethoprim-sulfamethoxazole is even higher (29%), this antibiotic still remains a first-line option in non-invasive ambulatory urinary tract infections [2]. As for quinolones, we also observed a further increase in non-susceptibility to 3rd-/4th-generation cephalosporins from 8.2% in 2013 to 10.7% in 2015 ($p < 0.005$). Significant increase in non-susceptibility rates during the last three years was observed in 12/29 EU/EEA states. The population weighted mean percentage increased from 9.6% in 2011 to 12.0% in 2014 [1]. The parallel increase in aminoglycoside, quinolone and trimethoprim-sulfamethoxazole resistance is at least in part attributable to cross-resistance. As carbapenem resistance in *E. coli* fortunately still is very rare, passive surveillance within anresis is not adequate for early detection of increasing resistance trends. Therefore, an obligation to report carbapenemase-producing *E. coli* and *K. pneumoniae* strains was introduced on 1.1.2016. Results from this new surveillance tool are pending. Colistin – a rather toxic reserve antibiotic from the polymyxin group – might become more important in future as a "last resort antibiotic" for carbapenemase-producing Enterobacteriaceae. Therefore, new reports from China, describing a mobile plasmid-encoding colistin-resistance gene (mcr-1), are worrisome [3]. Several *E. coli* isolates expressing mcr-1 have already been reported from human infections in Switzerland [4,5]. Currently, algorithms for the testing and reporting of colistin resistance in Switzerland are under development.

Table 7. a: Susceptibility rates of invasive *Escherichia coli* isolates in humans in 2015.

Escherichia coli							**2015**
Antibiotic	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Ampicillin	3,076	1,555	50.6%	45	1.5%	1,476	48.0%
Amoxicillin-clavulanic acid	4,868	3,519	72.3%	256	5.3%	1,093	22.5%
Piperacillin-tazobactam	4,772	4,434	92.9%	140	2.9%	198	4.1%
Cephalosporin, 2nd gen.	4,279	3,406	79.6%	320	7.5%	553	12.9%
Cephalosporin, 3rd/4th gen.	4,906	4,382	89.3%	25	0.5%	499	10.2%
Carbapenem	4,920	4,919	100.0%	1	0.0%	0	0.0%
Aminoglycosides	4,904	4,424	90.2%	45	0.9%	435	8.9%
Trimethoprim-sulfamethoxazole	4,553	3,234	71.0%	16	0.4%	1303	28.6%
Fluoroquinolones[1]	4,879	3,919	80.3%	51	1.0%	909	18.6%
Nitrofurantoin	1,268	1,234	97.3%	1	0.1%	33	2.6%
Fosfomycin	1,637	1,614	98.6%	8	0.5%	15	0.9%

[1] Fluoroquinolones: ciprofloxacin, norfloxacin, ofloxacin

Figure 7. a: Non-susceptibility rates in invasive *Escherichia coli* isolates in humans between 2004 and 2015.



7.2 *Klebsiella pneumoniae*

Klebsiella spp. are frequent colonizers of the gastrointestinal tract. Although they may also occur in the outpatient setting, they are more frequently found in the hospital setting, affecting patients with an impaired immune system. Their main focus of infection is urinary tract infections and pneumonia. In contrast to *E. coli,* they are intrinsically resistant to aminopenicillins.

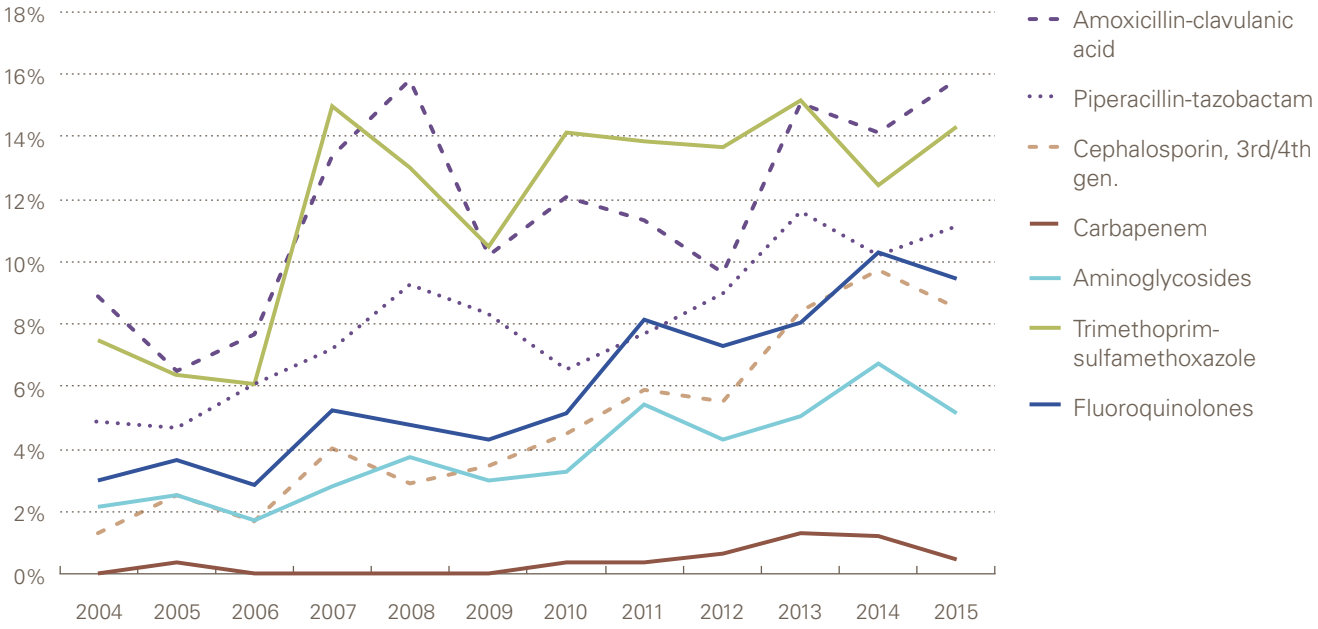
In this report, we only show the data on *K. pneumoniae,* which is the most frequent species of the genus *Klebsiella* isolated in human clinical probes. As was the case for *E. coli,* increasing resistance to 3rd-/4th-generation cephalosporins was the main issue between 2004 (1.3%) and 2013 (8.6%), but in contrast to *E. coli,* resistance rates did not increase further during the last two years (8.5% in 2015). Whether this indeed corresponds to a stabilization period is doubtful, as European data shows a significant increase in 3rd-/4th-generation-cephalosporin-resistance rates from 23.6% in 2011 to 28.0% in 2014. As *K. pneumoniae* is often involved in hospital outbreaks and numbers of isolates are smaller than for *E. coli,* resistance rates between years may vary considerably and trends have to be observed over longer periods of time. Compared to 2013, resistance rates for other antibiotics were also stable in Switzerland, while significant increases in EU/EEA population-weighted mean percentages were observed for fluoroquinolones, aminoglycosides and carbapenems as well [1]. The 0.4% carbapenem-resistance rate in Switzerland is still very low compared to an average of 7.3% in EU/EEA states in 2014 and rates surpassing 25% in Greece, Italy and Romania. As discussed in Chapter 7.1, active surveillance of cabapenemase production is running since 1.1.2016.

Table 7. b: Susceptibility rates of invasive *Klebsiella pneumoniae* isolates in humans in 2015.

Klebsiella pneumoniae							**2015**
Antibiotic	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Amoxicillin-clavulanic acid	905	762	84.2%	24	2.7%	119	13.1%
Piperacillin-tazobactam	889	790	88.9%	41	4.6%	58	6.5%
Cephalosporin, 2nd gen.	789	654	82.9%	49	6.2%	86	10.9%
Cephalosporin, 3rd/4th gen.	908	831	91.5%	9	1.0%	68	7.5%
Carbapenem	910	906	99.6%	1	0.1%	3	0.3%
Aminoglycosides	908	861	94.8%	2	0.2%	45	5.0%
Trimethoprim-sulfamethoxazole	843	722	85.6%	3	0.4%	118	14.0%
Fluoroquinolones[1]	907	821	90.5%	14	1.5%	72	7.9%

[1] Fluoroquinolones: ciprofloxacin, norfloxacin, ofloxacin

Figure 7. b: Non-susceptibility rates in invasive *Klebsiella pneumoniae* isolates in humans between 2004 and 2015.



7.3 *Pseudomonas aeruginosa*

Pseudomonas aeruginosa is a non-fermentative gram-negative rod and the most important human pathogen in this group of bacteria. *P. aeruginosa* is one of the leading causes of nosocomial respiratory tract infections and is also found in hospital-acquired urinary tract, wound and bloodstream infections. It is a feared pathogen, especially in burn units. Mucoid strains frequently infect cystic fibrosis patients and are very difficult to eradicate. The main community-acquired infections in immunocompetent hosts caused by *P. aeruginosa* are external otitis (swimmer's ear) and sinusitis.

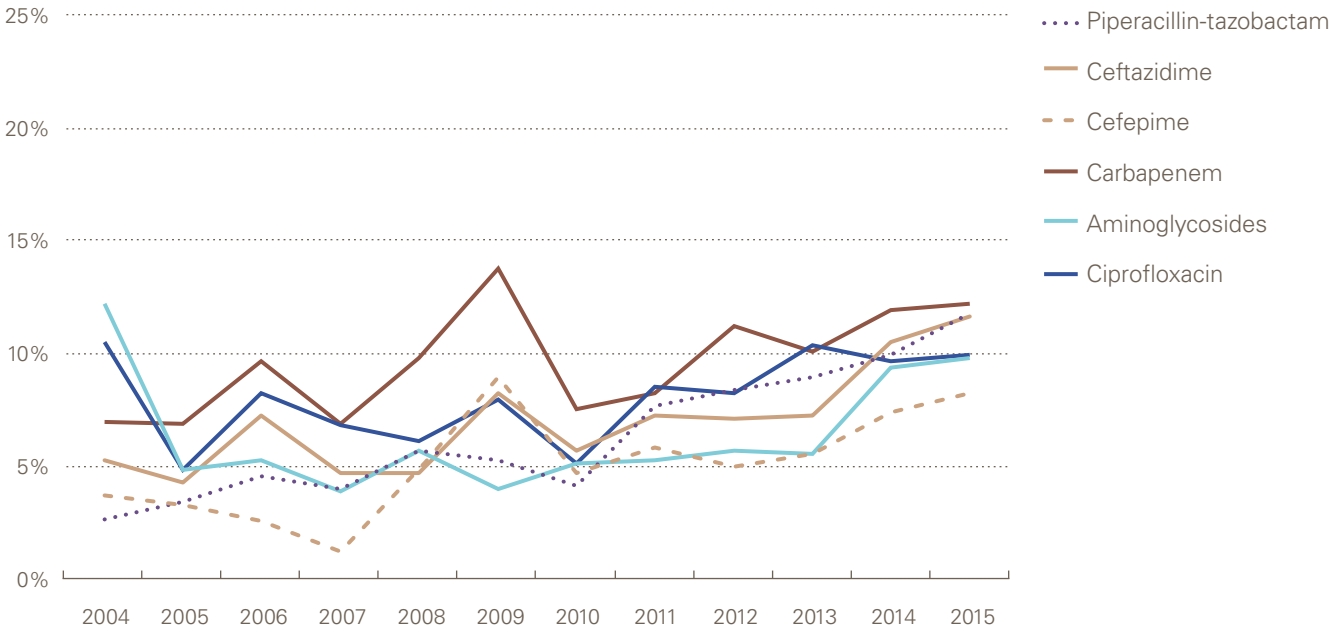
P. aeruginosa is intrinsically resistant to amoxicillin, amoxicillin-clavulanic acid, first- and second-generation cephalosporins, cefixime, cefpodoxime, ceftriaxone, ertapenem, tetracyclines including tigecycline and trimethoprim-sulfamethoxazole. Quinolones are the only orally available antibiotic with activity against *P. aeruginosa*.

Non-susceptibility rates increased since our last report (data 2013) for all antibiotics except ciprofloxacin (significant for ceftazidime, (p = 0.03) and aminoglycosides (p = 0.04) and are above 10% for piperacillin-tazobactam (11.8%), ceftazidime (11.6%) and carbapenems (12.2%) and slightly below 10% for ciprofloxacin (9.9%) and aminoglycosides (9.8%, Table 7. c and Figure 7. c). Increasing trends are also observed in EU/EEA countries for piperacillin-tazobactam (16.9% in 2014) and carbapenems (18.3% in 2014), while decreasing trends are observed for aminoglycosides (14.8% in 2014) and quinolones (19.4% in 2014). In general, resistance rates vary broadly throughout Europe, with higher rates in eastern and southeastern countries. The increase in aminoglycoside resistance observed in Switzerland mainly between 2013 and 2014 is not observed in other European countries. And it cannot be observed if contemplating tobramycin resistance alone (which has the lowest epidemiological cutoff for *P. aeruginosa* of all aminoglycosides), where we even find a slight, statistically non-significant decrease from 3.2% in 2013 to 2.1% (8 out of 376 isolates) in 2015. A more detailed analysis is planned in 2017.

Table 7. c: Susceptibility rates of invasive *Pseudomonas aeruginosa* isolates in humans in 2015.

Pseudomonas aeruginosa							**2015**
Antibiotic	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Piperacillin-tazobactam	476	420	88.2%	1	0.2%	55	11.6%
Ceftazidime	475	420	88.4%	5	1.1%	50	10.5%
Cefepime	465	427	91.8%	3	0.6%	35	7.5%
Carbapenem	485	426	87.8%	10	2.1%	49	10.1%
Aminoglycosides	488	440	90.2%	4	0.8%	44	9.0%
Ciprofloxacin	484	436	90.1%	19	3.9%	29	6.0%

Figure 7. c: Non-susceptibility rates of invasive *Pseudomonas aeruginosa* isolates in humans between 2004 and 2015.



7.4 *Acinetobacter* spp.

Acinetobacter spp. are gram-negative, strictly aerobic coccobacilli. They can be found in soil and water and are opportunistic pathogens. *Acinetobacter* spp. can roughly be divided into two groups: the *Acinetobacter baumannii* group, which is intrinsically resistant to many antibiotic agents and the *Acinetobacter* non-*baumannii* group, including a large number of environmental species with low pathogenicity.

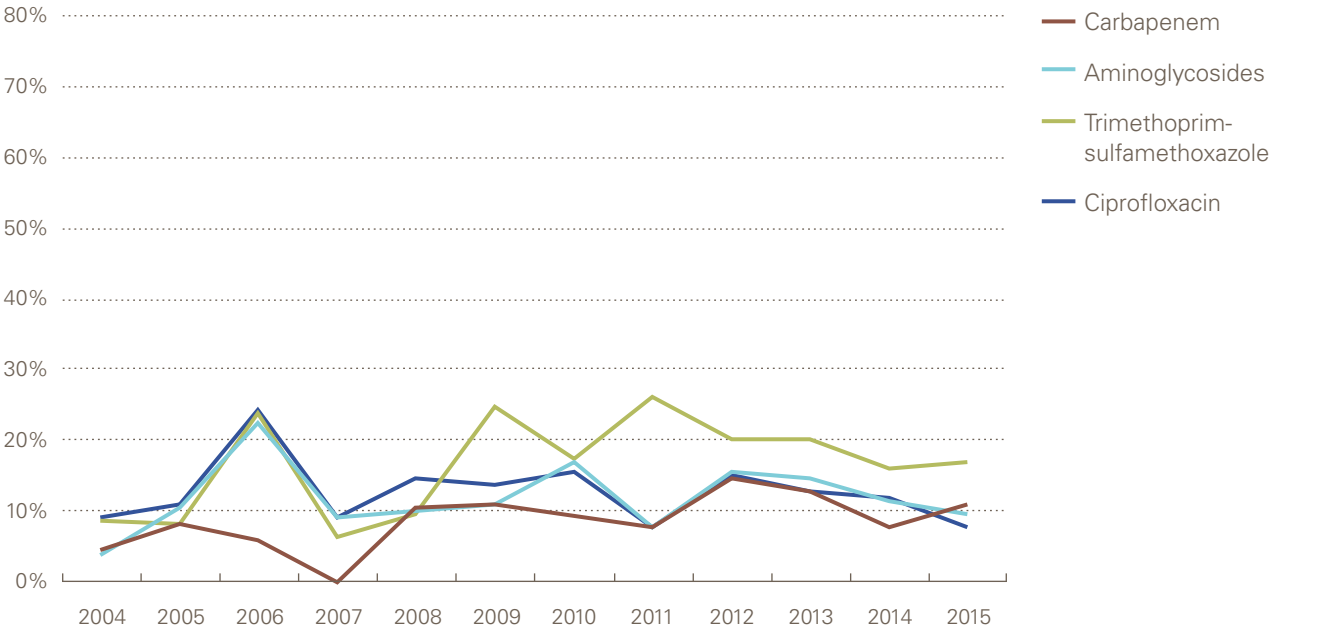
Acinetobacter baumannii infections are a big concern for hospital-acquired infections. They can cause respiratory, urinary, wound infections and septicemia. Meningitis has also been reported. Risk factors for multidrug-resistant *A. baumannii* are severe underlying diseases, prolonged hospital stays especially in ICUs with antibiotic administration, mechanical ventilation and surgical procedures. As species identification is difficult, we show aggregated data on the genus level, as suggested in the ECDC resistance report [1].

About 10% of *Acinetobacter* spp. isolates are not susceptible to the three most important antibiotics carbapenems (10.8%), aminoglycosides (9.8%) and ciprofloxacin (7.8%). Although a north-south gradient in antibiotic resistance can be observed in Europe for nearly all antibiotics, differences are most prominent in *Acinetobacter* spp. In 2014, resistance rates in Denmark were 1.6% for carbapenems, 1.7% for aminoglycosides and 2.9% for quinolones, corresponding numbers for Greece were 93.2%, 88.6% and 95.3% [1]. In Switzerland, no clear trend can be observed since 2004 (Figure 7. d).

Table 7. d: Susceptibility rates of invasive *Acinetobacter* spp. isolates in humans in 2015.

***Acinetobacter* spp.**							**2015**
Antibiotic	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Carbapenem	65	58	89.2%	3	4.6%	4	6.2%
Aminoglycosides	61	55	90.2%	0	0.0%	6	9.8%
Trimethoprim-sulfamethoxazole	53	44	83.0%	0	0.0%	9	17.0%
Ciprofloxacin	64	59	92.2%	0	0.0%	5	7.8%

Figure 7. d: Non-susceptibility rates of invasive *Acinetobacter* spp. isolates in humans between 2004 and 2015.



7.5 *Streptococcus pneumoniae*

Streptococcus pneumoniae is a common cause of upper respiratory tract infections such as sinusitis and otitis media, but is also a common pathogen found in invasive pneumonia, bloodstream infections and meningitis. Since 2002, all invasive isolates of *S. pneumoniae* are sent by the microbiology clinical laboratories to the National Reference Center for invasive *S. pneumoniae,* located at the Institute for Infectious Diseases, University of Bern. For all isolates, serotyping (to survey the impact of vaccinations on serotype distribution) and antibacterial resistance testing is performed. Results of the latter are then sent to anresis.ch. For this Chapter, we analyzed the anresis.ch data of *S. pneumoniae* from this reference center, as these data are complete and AMR testing is standardized. E-tests are performed for all penicillin-non-susceptible isolates (PNSP). PNSP was defined as MIC >= 0.064 mg/l, resistance was defined as >= 2 mg/l. Ceftriaxone testing was performed only for PNSP, penicillin-susceptible isolates (PSSP) are set to ceftriaxone-susceptible.

In 2015, the PNSP rate was 6.1% (Table 7. e). In comparison, PNSP rates in EU/EEA countries ranged from 0% to 46.7% in 2014 [1]. However, data between different countries are not comparable, due to differences in the definitions of breakpoints, depending on national guidelines and site of infection. With 6.6%, the macrolide-non-susceptibility rate is slightly higher than penicillin non-susceptibility. Resistance against levofloxacin is still very rare in Switzerland. As shown in figure 7. e, resistance in PNSP is higher than in PSSP for trimethoprim-sulfamethoxazole and erythromycin, but not for levofloxacin.

Over the last 10 years, a slight decrease in antibiotic resistance in *S. pneumoniae* for penicillin, trimethoprim-sulfamethoxazole and erythromycin was observed (Figure 7. f). A recent study published by the National Reference Center for invasive *S. pneumoniae* showed that this is mainly due to a vaccine-related decrease of the intrinsically more resistant serotypes (see textbox 7. a). So far, it is not known whether the higher trimethoprim-sulfamethoxazole resistance observed in 2015 will be sustained in future years.

Table 7. e: Susceptibility rates of invasive *Streptococcus pneumoniae* isolates in humans in 2015.

Streptococcus pneumoniae							**2015**
Antibiotic	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Penicillin[1]	839	788	93.9%	14	1.7%	37	4.4%
Ceftriaxone[2]	839	48	5.7%	3	0.4%	0	0.0%
Trimethoprim-sulfamethoxazole	839	710	84.6%	11	1.3%	118	14.1%
Erythromycin	839	784	93.4%	0	0.0%	55	6.6%
Levofloxacin	839	837	99.8%	1	0.1%	1	0.1%

[1] Penicillin-non-susceptible defined as MIC >= 0.064 mg/l, penicillin-resistant defined as MIC >= 2 mg/l
[2] Penicillin-susceptible isolates were not tested but set automatically to ceftriaxone-susceptible.

Figure 7. e: Susceptibility rates in invasive PSSP (penicillin-susceptible isolates) and PNSP (penicillin-non-susceptible isolates) in humans in 2015.

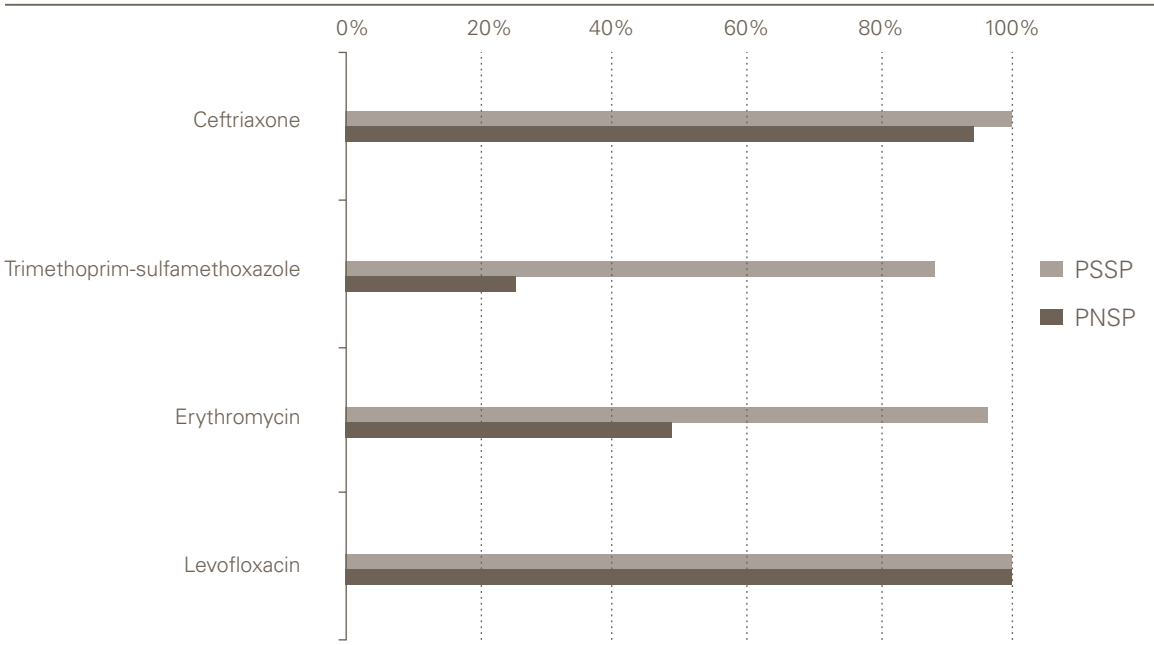
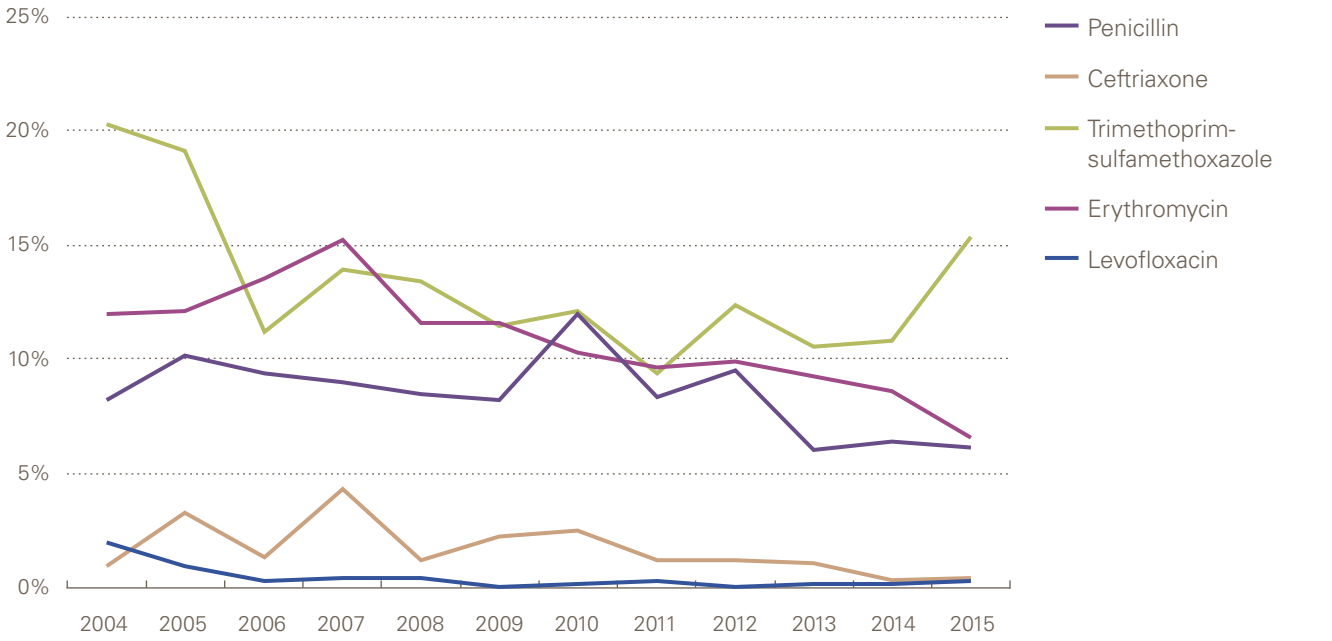


Figure 7. f: Non-susceptibility rates of invasive *Streptococcus pneumoniae* isolates in humans between 2004 and 2015.



Textbox 7. a

Serotype/serogroup-specific antibiotic non-susceptibility of invasive and non-invasive *Streptococcus pneumoniae*, Switzerland, 2004–2014 [1].

M. Hilty[1]

[1] Institute for Infectious Diseases and Department of Infectious Diseases, University of Bern

Introduction

Ideally, antibiotic resistance rates in non-invasive and invasive *S. pneumoniae* are analyzed simultaneously, but such studies of representative size are rare or often not very recent [2]. Switzerland runs two different national surveillance systems, collecting resistance data on *S. pneumoniae:* a) a sentinel surveillance of outpatient non-invasive pneumococci (Sentinella) and b) a comprehensive passive surveillance of all invasive pneumococci in Switzerland [3, 4]. Therefore, the aims of this study were a) to simultaneously describe antimicrobial resistance prevalence in invasive and non-invasive *S. pneumoniae* in different patient populations in Switzerland between 2004 and 2014, b) to analyze possible temporal trends and effects of heptavalent conjugated pneumococcal polysaccharide vaccines (PCV7) and 13-valent conjugated pneumococcal polysaccharide vaccine (PCV-13) on resistance prevalence, c) to detect serotype/serogroup-specific antibiotic resistance and d) to analyze regional differences for the antibiotic resistance rates.

Study design

Between 2004 and 2014, data on colonizing pneumococci were obtained from a nationwide, ongoing, prospective surveillance study within the Swiss Sentinel System which has been described in detail previously [4]. In brief, this network involves a chosen sample of practitioners who represent Switzerland geographically and demographically. The overall number of participants per subspecialty in the Sentinel System is defined as a proportion of all Swiss practitioners in the matching specialty. Therefore, approximately 200 practitioners (general practitioners, internists and paediatricians) took samples of outpatients who were clinically diagnosed with acute otitis media or pneumonia [4]. All received swabs were cultured for *S. pneumoniae* at the Swiss National Reference Center for Pneumococci (NZPn) as described [2].

Reporting of invasive pneumococcal infection has been mandatory in Switzerland since 1999. In March 2002, the NZPn was set up and has since been prospectively collecting clinical pneumococcal isolates from normally sterile body sites (blood, cerebrospinal, joint, pleural, and peritoneal fluid but not middle-ear fluid) sent in by Swiss clinical microbiology laboratories. It is possible to link approximately 90% of all reported IPD cases with a corresponding pneumococcal isolate. Therefore, the completeness of this linkage was very high, indicating a very high participation of involved laboratories [3]. PCV7 followed by PCV13 have been recommended in Switzerland in late 2006 and in 2011 respectively for all children under the age of two.

All isolates were confirmed as *S. pneumoniae* by alpha hemolysis morphology on blood agar plates, bile solubility and optochin sensitivity. Serotypes of all confirmed pneumococcal isolates were determined by the Quellung reaction. Methods for antibiotic resistance testing were identical for non-invasive and invasive isolates and have been described previously [2].

Results and conclusions

From 2004 to 2014, the proportion of non-susceptible isolates significantly decreased within non-invasive and invasive isolates for penicillin, ceftriaxone, erythromycin and co-trimoxazole (TMP-SMX) [1]. This was most apparent in non-invasive diseases of study subjects < 5 years of age (penicillin [p=0.006], erythromycin [p=0.01] and TMP-SMX [p=0.002]). Resistant serotypes/serogroups included in PCV7 and/or PCV13 decreased and were replaced by non-PCV13 serotypes (6C and 15B/C). Serotype/serogroup-specific antibiotic resistance rates were comparable between invasive and non-invasive isolates. Adjusted odds ratios of serotype/serogroup-specific penicillin resistance were significantly higher in the west as compared to the rest of Switzerland for serotype 6B (1.8; 95% confidence interval [CI]: 1.4–4.8), 9V (3.4; 95% CI: 2.0–5.7), 14 (5.3; 95% CI: 3.8–7.5), 19A (2.2; 95% CI: 1.6–3.1) and 19F (3.1; 95% CI: 2.1–4.6), probably due to variations in the antibiotic consumption [1].

References

[1] Hauser C, Kronenberg A, Allemann A, Muhlemann K, Hilty M: Serotype/serogroup-specific antibiotic non-susceptibility of invasive and non-invasive *Streptococcus pneumoniae,* Switzerland, 2004 to 2014. Euro surveillance: bulletin européen sur les maladies transmissibles = European communicable disease bulletin 2016, 21

[2] Kronenberg A, Zucs P, Droz S, Muhlemann K: Distribution and invasiveness of *Streptococcus pneumoniae* serotypes in Switzerland, a country with low antibiotic selection pressure, from 2001 to 2004. J Clin Microbiol 2006, 44:2032–2038

[3] Meichtry J, Born R, Kuffer M, Zwahlen M, Albrich WC, Brugger SD, Muhlemann K, Hilty M: Serotype epidemiology of invasive pneumococcal disease in Swiss adults: A nationwide population-based study. Vaccine 2014, 32:5185–5191

[4] Muhlemann K, Matter HC, Tauber MG, Bodmer T: Nationwide surveillance of nasopharyngeal *Streptococcus pneumoniae* isolates from children with respiratory infection, Switzerland, 1998-1999. J Infect Dis 2003, 187:589–596

7.6 Enterococci

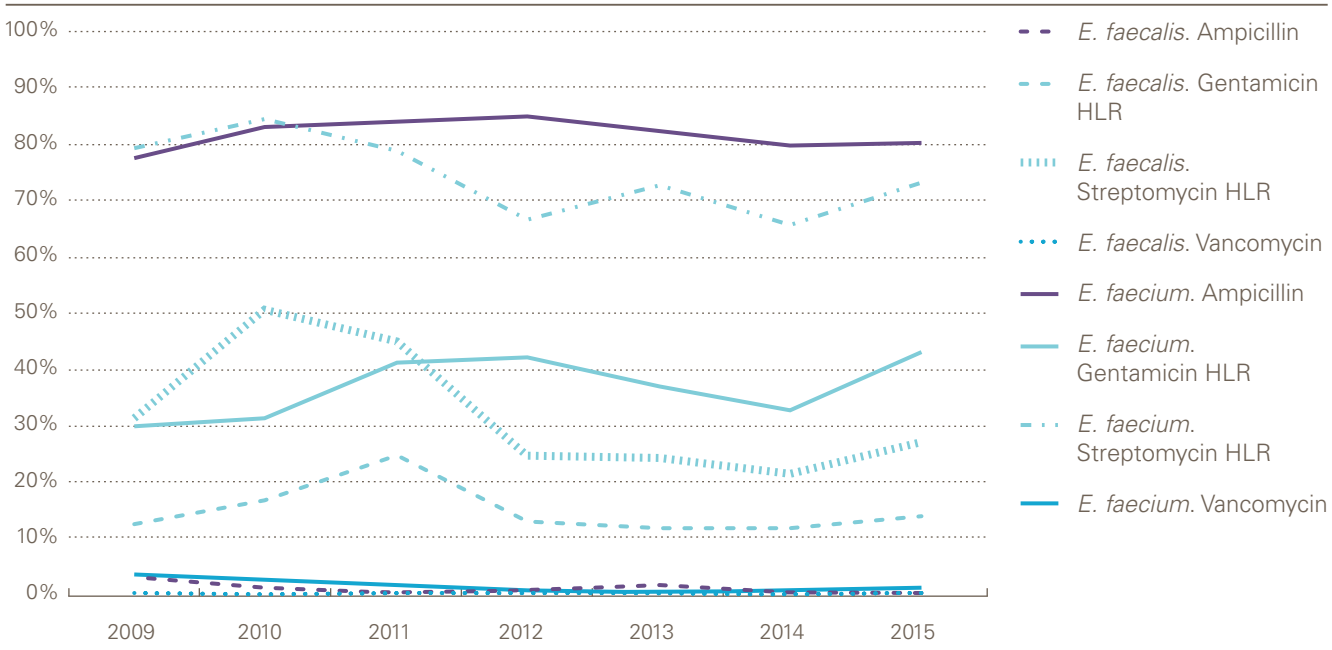
Enterococci belong to the normal gastrointestinal flora of humans and animals. As such, they are often harmless commensals. However, mainly in the hospital setting, they can also cause serious infections such as urinary tract infections, bacteremia, endocarditis, and intra-abdominal infections. The vast majority of enterococcal infections are caused by *Enterococcus faecalis* and *E. faecium*. *E. faecalis* isolates still remain susceptible to many antibiotics, including a 99.8% susceptibility rate to aminopenicillins. In contrast, *E. facium* isolates usually are resistant to aminopenicillin and other beta-lactam agents, including carbapenems. In addition, *E. faecium* shows increased resistance rates to high-level aminoglycosides in comparison to *E. faecalis* (Table 7. f). While resistance to vancomycin is a frequent problem in the United States, it is fortunately not increasing over time in Switzerland and far below the EU/EEA average of 7.9% in *E. faecium* in 2014 [1]. Development of resistance between 2009 and 2015 is shown in figure 7. g. Data before 2008 are not shown, due to low numbers of *E. faecium* isolates.

Table 7. f: Susceptibility rates of invasive *Enterococcus faecalis* and *Enterococcus faecium* isolates in humans in 2015. HLAR, high-level aminoglycoside resistance.

Enterococcus faecalis							2015
Antibiotic	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Ampicillin	542	541	99.8%	0	0.0%	1	0.2%
Gentamicin HLAR	241	207	85.9%	1	0.4%	33	13.7%
Streptomycin HLAR	169	123	72.8%	0	0.0%	46	27.2%
Tetracycline	228	53	23.2%	0	0.0%	175	76.8%
Vancomycin	658	657	99.8%	0	0.0%	1	0.2%
Linezolid	374	373	99.7%	1	0.3%	0	0.0%

Enterococcus faecium							2015
Antibiotic	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Ampicillin	321	64	19.9%	0	0.0%	257	80.1%
Gentamicin HLAR	182	104	57.1%	0	0.0%	78	42.9%
Streptomycin HLAR	127	34	26.8%	0	0.0%	93	73.2%
Tetracycline	91	55	60.4%	2	2.2%	34	37.4%
Vancomycin	433	427	98.6%	0	0.0%	6	1.4%
Linezolid	324	322	99.4%	0	0.0%	2	0.6%

Figure 7. g : Non-susceptibility rates in invasive *Enterococcus faecalis* and *Enterococcus faecium* isolates in humans between 2009 and 2015.



7.7 *Staphylococcus aureus*

Staphylococcus aureus is one of the most important microorganisms in clinical microbiology. Besides bloodstream infections, *S. aureus* frequently causes soft-tissue infections, osteomyelitis, joint infections, and, more rarely, endocarditis and pneumonia. Methicillin-resistant *S. aureus* (MRSA) remains one of the most important causes of antimicrobial-resistant infections worldwide. While initially these infections were mainly hospital acquired, they have successfully spread into the community over the last years.

There are different methods to detect MRSA, and the methods used for screening have changed over time. *Staphylococcus aureus* methicillin/oxacillin resistance can be detected either phenotypically by MIC determination, disk diffusion tests or latex agglutination to detect PBP2a, or genotypically using mecA/mecC detection. Due to poor correlation with the presence of mecA, oxacillin disk testing to detect *S. aureus* methicillin/oxacillin resistance is discouraged by EUCAST and CLSI guidelines (see also Chapter 11). In contrast, cefoxitin susceptibility is a very sensitive and specific marker of mecA/mecC-mediated methicillin resistance and is the agent of choice for disk diffusion testing. *S. aureus* with cefoxitin MIC values > 4 mg/l are methicillin resistant, mostly due to the presence of the mecA gene.

In the anresis.ch database, MRSA is defined as non-susceptibility to at least one of the following: methicillin, oxacillin, flucloxacillin or cefoxitin. Results from confirmation tests such as PBP2a-agglutination or direct detection of the mecA gene are typically not provided to anresis.ch. MRSAs are resistant to all beta-lactams, including combinations with beta-lactam inhibitors (e.g. amoxicillin-clavulanic acid). In 2015, the MRSA rate in Switzerland was 4.2%. This rate is far below the European average of 17.4%, but above MRSA rates in northern countries such as the Netherlands (0.9%), Norway (1.0%), Sweden (1.0%), Denmark (2.5%) and Finland (2.6%) in 2014 [1]. Coresistance in MRSA is frequent and is depicted in figure 7. h.

Development of resistance during the last 10 years is shown in figure 7. i. During the last ten years, we have observed a significant decrease in invasive MRSA rates in Switzerland, from 12.7% in 2004 to 4.2% in 2015. Decreasing trends from 2011 to 2014 were also reported for Europe overall, and in some neighboring countries such as France and Germany, as well as in Belgium, Italy, Ireland, Luxembourg, Portugal and the United Kingdom [1]. The decrease in invasive MRSA rates was more pronounced in the western part of Switzerland (data not shown). The decrease in MRSA rates runs parallel to a decrease in resistance rates (non-susceptibility rates) against ciprofloxacin, macrolides and, to a lesser extent, clindamycin and aminoglycosides in *Staphylococcus aureus* isolates. Further detailed analysis of these trends was published in the "Swiss Medical Weekly" in 2016 (see textbox 7. b).

Table 7. g: Susceptibility rates of invasive *Staphylococcus aureus* isolates in humans in 2015.

Staphylococcus aureus							**2015**
Antibiotic	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Penicillin	1,569	326	20.8%	0	0.0%	1243	79.2%
Aminoglycosides	1,678	1,646	98.1%	0	0.0%	32	1.9%
Trimethoprim-sulfamethoxazole	1,575	1,561	99.1%	1	0.1%	13	0.8%
Tetracycline	1,241	1,211	97.6%	1	0.1%	29	2.3%
Macrolides	1,739	1,572	90.4%	2	0.1%	165	9.5%
Clindamycin	1,738	1,618	93.1%	4	0.2%	116	6.7%
Vancomycin	1,422	1,420	99.9%	0	0.0%	2	0.1%
Ciprofloxacin	1,663	1,521	91.5%	41	2.5%	101	6.1%
Fusidic acid	1,349	1,292	95.8%	0	0.0%	57	4.2%
Linezolid	781	780	99.9%	0	0.0%	1	0.1%
Rifampicin	1,644	1,636	99.5%	2	0.1%	6	0.4%

Figure 7. h: Susceptibility rates of invasive MRSA (methicillin-resistant *Staphylococcus aureus*) and MSSA (methicillin-sensitive *Staphylococcus aureus*) isolates in humans 2015.

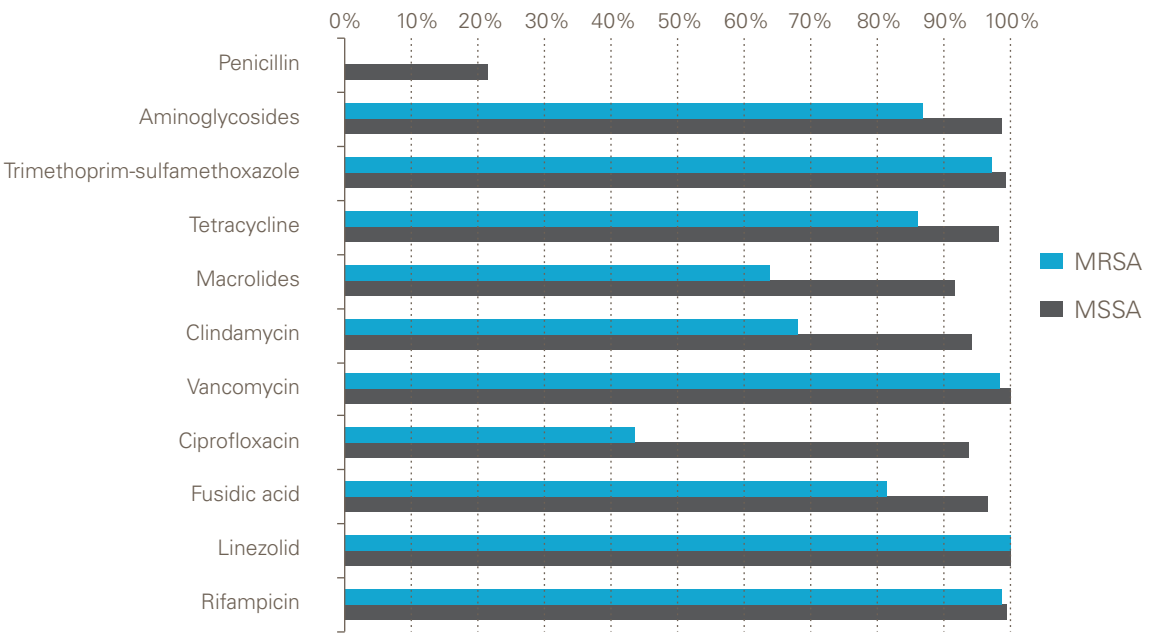
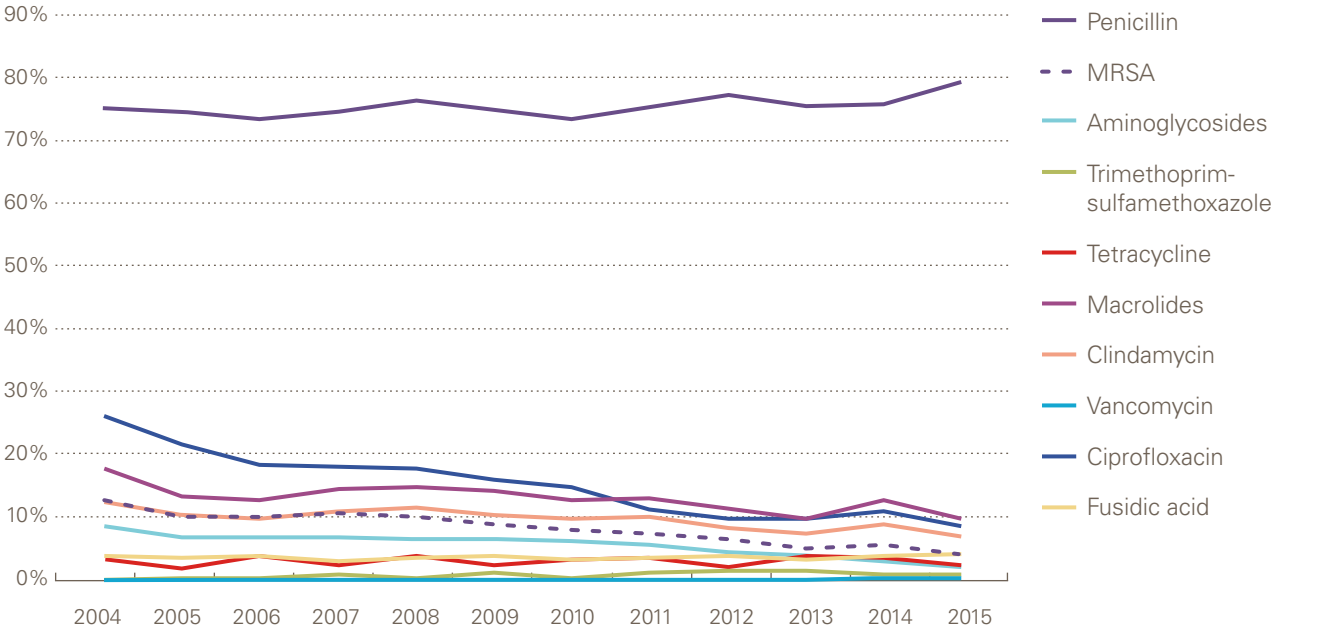


Figure 7. i: Non-susceptibility rates of invasive *Staphylococcus aureus* isolates in humans between 2004 and 2015.



References

[1] European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2014. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2015

[2] B. Hasse, A. Huttner, B. Huttner, M. Egger, G. Zanetti, J. Marschall, K. Mühlemann, S. Harbarth. Behandlung von unkomplizierten Harnwegsinfektionen. from http://www.sginf.ch/ssi/images/ssi/guidelinesnmm/Guidelines_d_HWI_CH_2014_05_22.pdf (in German)

[3] Liu YY, Wang Y, Walsh TR, Yi L-X, Zang R, Spencer J, et al. Emergence of plasmid-mediated colistin-resistance mechanism MCR-1 in animals and human beings in China: a microbiological study and molecular biology study. Lancet Infect Dis 2016. pii:S1473–3099(15)00424-7i

[4] Poirel L., Kieffer N., Liassine N., Than D., Nordmann P. (2016). Plasmid-mediated carbapenem and colistin resistance in a clinical isolate of *Escherichia coli*. Lancet Infect Dis 16:281

[5] Nordmann P., Lienhard R., Kieffer N., Clerc O., Poirel L. (2016). Plasmid-mediated colistin-resistant *Escherichia coli* in bacteremia in Switzerland. Clin Infect Dis. 62:1322-1323

Textbox 7. b

Methicillin-resistant *Staphylococcus aureus* in Switzerland: how the situation has changed in the last decade.

F. Olearo[1], W. Albrich[2], S. Harbarth[1], A. Kronenberg[3]

[1] University Hospital of Geneva and Faculty of Medicine; [2] Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital; St. Gallen; [3] Institute for Infectious Diseases and Department of Infectious Diseases, University of Bern

Staphylococcus aureus is one of the major causes of community and nosocomial infections, determining primarily skin and soft-tissue infections and being responsible for about 12% of bacteraemias in Switzerland [1]. It's main resistance threat is resistance to methicillin (and all other betalactam antibiotics), which was first described in 1961, and led to the acronym MRSA for methicillin-resistant *Staphylococcus aureus*. While MRSA infections were increasing steadily worldwide in the last century, two new main trends were observed during the last decade: first, in contrast to many other resistant microorganisms, incidence of MRSA infections has decreased in several European countries and in North America during the last years. Second a shift from hospital- to community-acquired infections was described in several settings. This is not primarily due to spreading from hospital-acquired MRSA (HA-MRSA) to the community, but due to different clones, circulating primarily in the community (community-acquired MRSA, CA-MRSA), which are characterized by lower resistance rates to other antibiotics and different genetic resistance elements (SCCmec IV cassette). As recent epidemiologic data about MRSA prevalence were missing for Switzerland, F. Olearo and colleagues performed a detailed analysis on the trends in MRSA epidemiology in Switzerland from 2004 to 2014 using data from the Swiss Antibiotic Resistance Centre ANRESIS [2]. As genetic data are not available in ANRESIS, non-multiresistant MRSA (NmMRSA) – defined as MRSA being susceptible to at least 3 of the following agents: ciprofloxacin, clindamycin, tetracycline or trimethoprim-sulfamethoxazole (TMP/SMX) – was used as surrogate marker for CA-MRSA.

The authors analyzed 14,648 MRSA infections and found that – extrapolating to the whole Swiss population – the incidence of mMRSA bacteraemia decreased from 21 to 7 episodes per 100,000 admissions per year. In addition, the overall proportion of MRSA among *S. aureus* decreased from 14% in 2004 to 8% in 2014, with a decreasing trend of –0.08% per quarter per year.

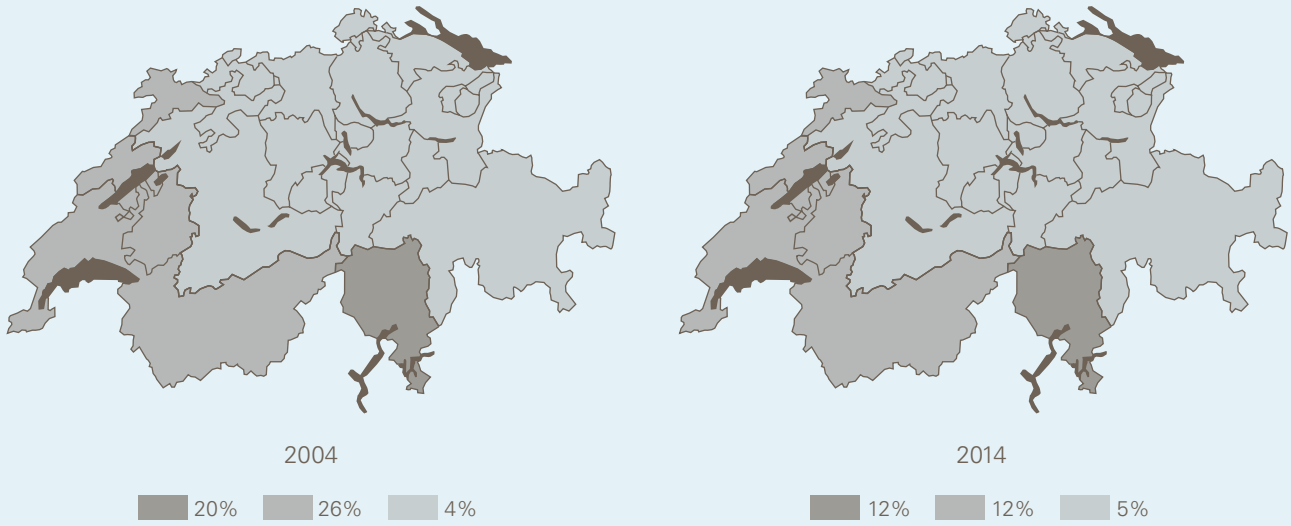
The MRSA epidemiology differed from one linguistic region to another (Figure). In the French- and Italian- speaking regions MRSA proportions among *S. aureus* were decreasing over time, while in the German-speaking region MRSA trends were slightly on an upward trajectory, but still at a very low level. Nevertheless, MRSA rates remained significantly higher in the French- and Italian-speaking regions than in the German part throughout the whole time period. The geographical, cultural and economic ties of the Swiss Italian- and French-speaking regions to Italy and France (where the prevalence of MRSA as reported by ECDC was 36% and 17%, respectively, ECDC 2013) may in part explain the higher MRSA prevalence in these regions compared to the German-speaking region that borders with countries with lower MRSA proportions (Germany, 12.7%; Austria, 9.2% in 2013, ECDC data). Different sociocultural factors as the organization of the healthcare system with reimbursement structures and incentives, diagnostic practices, labora-

tory recognition, antibiotic use, physician and patient attitudes and expectations have been used to explain differences in geographic distribution of antibiotic-resistant microorganisms between countries and continents and may in part also be responsible for the different regional distribution of MRSA in Switzerland.

While in general MRSA proportions were decreasing in Switzerland, increasing MRSA proportions were observed in specific subgroups, namely outpatients and younger patients (< 16 years). Conversely to the MRSA trend and in agreement with observations from other countries, the relative proportion of NmMRSA among all MRSA increased from 8% in 2004 to 43% in 2014 (+0.92% per quarter per year). This increase was observed in all Swiss regions and all subgroups.

In conclusion, this study confirms the low MRSA prevalence in Switzerland compared to the rest of Europe and declining rates of nosocomial MRSA infections throughout Switzerland. At the same time this study illustrates the regional differences and trends which may be affected by surrounding countries and thus cultural influences. This comprehensive dataset mirrors the successful efforts to reduce MRSA incidences observed in many countries worldwide with a simultaneous increase in NmMRSA likely reflecting the concomitant emergence of CA-MRSA.

Figure T 7. b. 1: Proportion of methicillin-resistant *S. aureus* (MRSA) among *S.aureus* isolates by linguistic region (German-, French-, and Italian-speaking).



References

[1] N. Buetti, J. Marschall, A. Atkinson, A. Kronenberg and the Swiss Centre for Antibiotic Resistance (ANRESIS). National Bloodstream Infection Surveillance in Switzerland 2008–2014: Different Patterns and Trends for University and Community Hospitals. Infect Control Hosp Epidemiol 2016; 1–8

[2] F. Olearo, W. Albrich, S. Harbarth, A. Kronenberg and the Swiss Centre for Antibiotic resistance (ANRESIS). *Staphylococcus aureus* and methicillin resistance in Switzerland: regional differences and trends from 2004–2014. Swiss Medical Weekly. In press

Textbox 7. c

Epidemiology of bloodstream infections in Switzerland

N. Buetti[1]

[1] Department of Infectious Diseases, University Hospital Bern, Bern, Switzerland

Bloodstream infections are a major healthcare issue, with a disease burden comparable to that caused by myocardial infarctions, trauma, and major strokes. Bloodstream infections represent a significant cause of mortality worldwide, leading to about 157,000 deaths per year in Northern Europe. Demographic changes and advances in medical technology have changed the epidemiology of bloodstream infections in recent decades and have led to a shift in the pathogen spectrum. While gram-positive bacteria were the predominant agents in bloodstream infections from 1987 to 2000, gram-negative bacteria have constantly increased since then. Because changes in spectrum and antimicrobial resistance patterns have a direct impact on the care of patients and on the choice of empiric antimicrobial therapy, the epidemiology of bloodstream infections needs to be reassessed periodically on a national scale.

Given the limited understanding of the epidemiology of bloodstream infection in Switzerland, we performed an analysis of national data using ANRESIS. Our analysis was divided into three major projects.

Firstly, we performed an extrapolated population-based study describing the incidence of bloodstream infections in Switzerland in different department settings. European studies that reported data which was collected until 2008 showed variable trends, with increasing bacteremia rates in Finland in the period from 2004 to 2007 and in England from 2004 to 2006, but decreasing rates in England between 2006 and 2008 and in Denmark from 2000 to 2008. Using data collected between 2008 and 2014 from a subset of 26 hospitals (representing 33% of all acute hospitals) distributed homogeneously across Switzerland, we observed an increase in the incidence of bloodstream infections from 211 per 100,000 population (in 2008) to 240 (in 2014, Figure). The increase was most pronounced in individuals ≥65 years old and when bloodstream infection was diagnosed in an emergency department. A possible explanation could be the decreasing average duration of hospitalization, with discharge of sicker patients who might be prone to readmission. *E. coli* was found to be the most important microorganism causing bloodstream infections in Switzerland, with a share that is becoming larger and larger. Moreover, bloodstream infections caused by enterococci showed a marked upward trend over the study period. Of note, the incidence of *S. aureus* (the second most important microorganism detected in blood) showed an overall deceleration, with only a marginal increase between 2008 and 2014 [1].

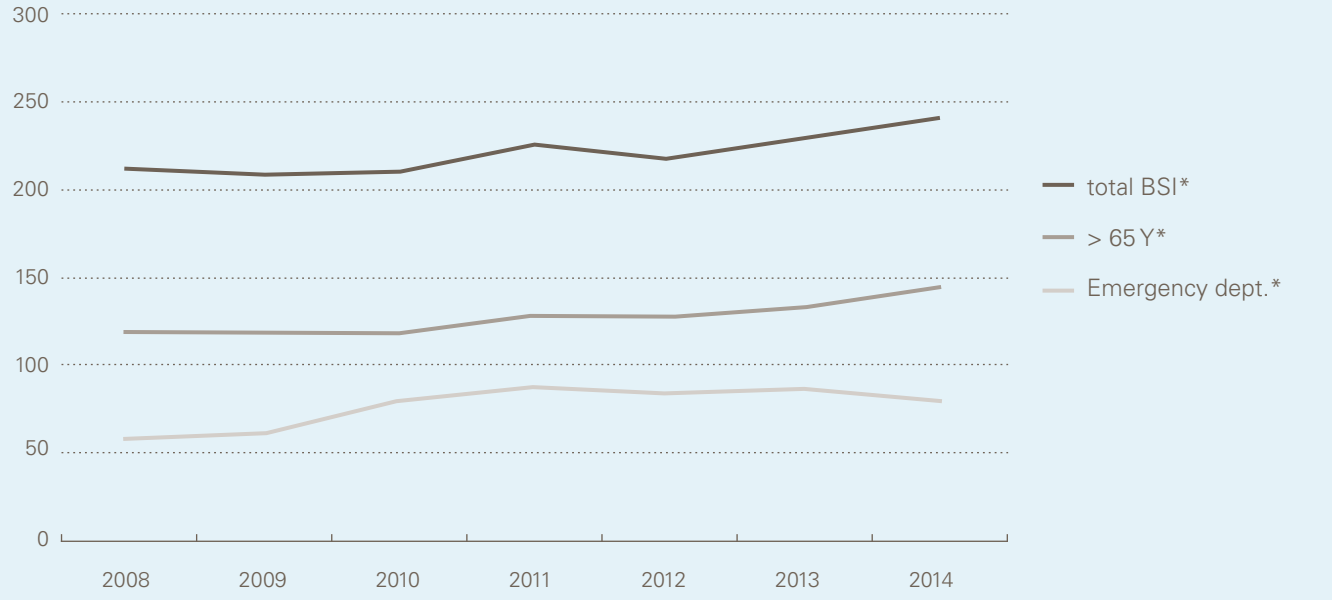
In the second project we analyzed the epidemiology of bloodstream infections in Switzerland between 2008 and 2014 in different hospital settings (university vs community hospitals and in community-acquired vs hospital-acquired infections). Interestingly, we found important differences in patterns and trends of bloodstream infections between community and university hospitals. *E. coli* and *S. aureus* were identified more frequently in community hospitals, whereas difficult-to-treat infections (e.g. coagulase-negative staphylococci and polymicrobial bloodstream infections) were more commonly observed in the university setting. Our findings were further confirmed by divergent trends (from 2008 to 2014) for *E. coli* in the two different hospital settings. The observed disparities could reflect the different populations of patients treated in the two different hospital settings. The differences in patterns and trends of microorganisms causing bloodstream infections in community and university hospitals may affect current and future clinical care. Empiric antibiotic treatment guidelines in Switzerland are often produced by academic centers and distributed to networks of smaller centers. Such protocols are mostly based on the local epidemiology observed in the university hospital setting and their application to community centers may be less appropriate [2].

In the third project, we performed an analysis of bloodstream infections in neonates and children, using data from ANRESIS. While numerous studies addressing the national epidemiology of bloodstream infections have focused on adult populations, only few studies exist for the pediatric population. To our knowledge, no recent Swiss data are available. In data collected in 20 acute hospitals, we identified 1,823 true bloodstream infections in children that occurred between 2008 and 2014. As observed in the adult population, *S. aureus* and *E. coli* remained the most important pathogens among pediatric bloodstream infections in Switzerland. Both microorganisms appeared to be largely independent of the healthcare exposure of children. Resistance rates (e.g. 4.3% MRSA out of *S. aureus,* 7.3% 3rd-/4th-generation cephalosporin resistance out of *E. coli*) remained low over the study period. Coagulase-negative staphylococci increased between 2008 and 2014, possibly reflecting a growing use of vascular access. A decrease in bacteremic pneumococcal infections was observed after the 13-valent conjugate vaccine had been introduced in 2011, documenting the success of achieving high immunization coverage with public health programs [3].

In conclusion, with the results of these three projects we have provided a timely picture of bloodstream infections in our country. The incidence of bloodstream infections is actually increasing, especially in emergency departments. *E. coli* and *S. aureus* remain the most important pathogens in adults and children. The epidemiology of bloodstream

infections differs between community and university hospitals. The described trends and patterns may impact morbidity, mortality and healthcare costs associated with bloodstream infections.

Figure T 7. c. 1: Incidence in bloodstream infections between 2008 and 2014.



* p < 0.001. BSI: bloodstream infections. Dept.: department. y: years old

References

[1] N. Buetti, J. Marschall, A. Atkinson, A. Kronenberg and the Swiss Centre for Antibiotic Resistance (ANRESIS). The Incidence of Bloodstream Infections is Increasing: a Population-based Study in Switzerland 2008–2014. Submitted May 2016

[2] N. Buetti, A. Atkinson, J. Marschall, A. Kronenberg and the Swiss Centre for Antibiotic Resistance (ANRESIS). National Bloodstream Infection Surveillance in Switzerland 2008–2014: Different Patterns and Trends for University and Community Hospitals. Infect Control Hosp Epidemiol. 2016 Jun 28:1–8

[3] N. Buetti, A. Atkinson, L. Kottanattu, J. Bielicki, J. Marschall, A. Kronenberg and the Swiss Centre for Antibiotic Resistance (ANRESIS). Patterns and Trends of Pediatric Bloodstream Infections. A 7-Year Surveillance Study. Submitted May 2016

8

Resistance in zoonotic bacteria

8 Resistance in zoonotic bacteria

Zoonoses are infections and diseases that are transmissible from animals to humans. Infection can be acquired through direct contact with animals or indirectly by contaminated food. The severity of these diseases in humans can vary from mild symptoms to life-threatening conditions. Antimicrobial resistance in zoonotic bacteria from animals is of special concern, since it might compromise the effective treatment of infections in humans.

8.1 *Campylobacter* spp.

Campylobacter is the most commonly reported cause of human food-borne zoonoses in Switzerland as well as in the EU [1], [2]. Infections are mainly caused by *C. jejuni*, but other species such as *C. coli* can also be responsible. While *Campylobacter* causes acute gastroenteritis in humans, infected animals are usually asymptomatic. Reservoir hosts include livestock such as broiler cattle, pigs, sheep and fowl, domestic pets and wild animals [8].

Incorrect handling of raw poultry meat and the consumption of undercooked contaminated poultry meat and poultry liver are the two main causes for contracting human campylobacteriosis. Meat from cattle and pigs and contact with pets is of less importance. A comparison of isolates from humans and animals collected between 2001 and 2012 in Switzerland identified chicken as the main source for human campylobacteriosis (71% of the human cases were attributed to chicken, 19% to cattle, 9% to dogs and 1% to pigs) [9].

Campylobacteriosis is usually self-limiting in humans and does not require antibacterial treatment. However, treatment with antibiotics is necessary for severe cases, whereby resistance to antimicrobials in *Campylobacter* is a source of concern. Resistance can lead to therapy failure and longer treatment duration. Fluoroquinolones, such as ciprofloxacin, and macrolides, such as clarithromycin or azithromycin, represent standard therapies for severe cases of campylobacteriosis and are therefore considered critically important antimicrobials of highest priority [10].

This chapter includes antimicrobial resistances of *Campylobacter jejuni* and *Campylobacter coli* in livestock and humans. Broilers were investigated in 2014 and fattening pigs in 2015.

8.1.1 *Campylobacter* spp. in broilers

At present, only a few antimicrobial products are licensed for use in poultry in Switzerland. More than half of them contain antimicrobial substances that belong to the highest-priority critically important antimicrobials according to the WHO [10]

Table 8. a: Occurrence of resistance in *Campylobacter jejuni* and *Campylobacter coli* from broilers in 2014.

2014	*Campylobacter jejuni* (N = 159)			*Campylobacter coli* (N = 15)		
Antimicrobial	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Chloramphenicol	0	0.0	0.0–2.4	0	0.0	0.0–20.4
Ciprofloxacin	73	45.9	38.4–53.7	6	40.0	19.8–64.3
Erythromycin	1	0.6	0.1–3.5	3	20.0	7.0–45.2
Gentamicin	2	1.3	0.3–4.5	0	0.0	0.0–20.4
Nalidixic acid	74	46.5	39.0–54.3	6	40.0	19.8–64.3
Streptomycin	5	3.1	1.4–7.1	7	46.7	24.8–69.9
Tetracycline	43	27.0	20.7–34.4	5	33.3	15.2–58.3
Number of resistances	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
None	76	47.8	40.2–55.5	4	26.7	10.9–52
1 antimicrobial	9	5.7	3.0–10.4	4	26.7	10.9–52
2 antimicrobials	39	24.5	18.5–31.8	2	13.3	3.7–37.9
3 antimicrobials	31	19.5	14.1–26.3	2	13.3	3.7–37.9
4 antimicrobials	3	1.9	0.6–5.4	2	13.3	3.7–37.9
> 4 antimicrobials	1	0.6	0.1–3.5	1	6.7	1.2–29.8

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

and should be used with caution in view of antimicrobial resistance in human and veterinary medicine. In the absence of authorized products with sulfonamides or tetracyclines, fluoroquinolones (e.g. enrofloxacin) or macrolides are often used as first-line treatments in Swiss broiler production.

In 2014, a random sample of 493 broiler flocks was investigated at slaughter in the framework of the antimicrobial resistance-monitoring program using cloacal swabs (5 pooled swabs per flock). *Campylobacter jejuni* was identified in 163 samples (33.1%) and *Campylobacter coli* in 16 samples (3.2%). Susceptibility testing was performed for 159 *C. jejuni* isolates and 15 *C. coli* isolates (Table 8. a). Complete susceptibility to all tested antimicrobials was found in 47.8% of the *C. jejuni* isolates and in 26.7% of the *C. coli* isolates.

Moderate to high levels of resistance to (fluoro-)quinolones (ciprofloxacin and nalidixic acid) and tetracycline were found in *C. jejuni* as well as in *C. coli* (between 27.0% and 46.5%). High microbiological resistance to streptomycin was found in *C. coli* (46.7%). Slightly more than one fifth of *C. jejuni* isolates (22%) were resistant to at least 3 of the tested antimicrobials. A single *C. jejuni* isolate was resistant to 5 tested antimicrobials: ciprofloxacin, erythromycin, gentamicin, nalidixic acid, streptomycin and tetracycline (Table 8. a).

In 2014, only 15 *C. coli* isolates were available from broilers. This small number of isolates does not allow the detection of statistically significant trends over the years.

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.17 & Table II.18) and multi-resistance patterns are shown in Annexe III (Table III.3 & Table III.4)

8.1.2 *Campylobacter coli* in fattening pigs

In 2015, a random sample of 299 fattening pigs was investigated at slaughter in the framework of the antimicrobial-resistance-monitoring program using caecum samples. *Campylobacter coli* was isolated in 156 out of 299 samples (52.2%). All isolates were subjected to susceptibility testing (Table 8. b).

In *C. coli* from fattening pigs, the highest level of microbiological resistance was found for streptomycin (86.5%). High levels of microbiological resistance were also found for tetracycline (63.5%), ciprofloxacin (46.8%) and nalidixic acid (46.8%). Lower levels of resistance were detected for erythromycin (4.5%) and gentamicin (0.6%). Only 6.4% of the *C. coli* isolates were fully sensitive to all tested antimicrobials, while 30.8% showed resistance to 4 or more antimicrobials (Table 8. b).

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.19).

Table 8. b: Occurrence of resistance in *Campylobacter coli* from fattening pigs in 2015.

2015	*Campylobacter coli* (N = 156)		
Antimicrobial	**n**	**%**	**95% CI**
Ciprofloxacin	73	46.8	39.1–54.6
Erythromycin	7	4.5	2.2–9.0
Gentamicin	1	0.6	0.1–3.5
Nalidixic acid	73	46.8	39.1–54.6
Streptomycin	135	86.5	80.3–91.0
Tetracycline	99	63.5	55.7–70.6
Number of resistances	**n**	**%**	**95% CI**
None	10	6.4	3.5–11.4
1 antimicrobial	27	17.3	12.2–24.0
2 antimicrobials	48	30.8	24.1–38.4
3 antimicrobials	23	14.7	10.0–21.2
4 antimicrobials	44	28.2	21.7–35.7
> 4 antimicrobials	4	2.6	1.0–6.4

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

8.1.3 *Campylobacter* spp. in humans

A total of 7,055 laboratory-confirmed cases of human campylobacteriosis were reported in 2015 (85 per 100,000 inhabitants). *C. jejuni* caused 75% of the cases, while in 13% of all cases no distinction was made between *C. jejuni* and *C. coli*. In anresis.ch, resistance data were available for 2,638 isolates (37.4%). 2,400 were identified as *C. jejuni* (91.0%), 220 as *C. coli* (8.3%). Resistance data for 2015 are shown in Table 8. c. Overall, 58% of the *C. jejuni* isolates were resistant to quinolones but resistance to macrolides was still low (1.2%). For *C. coli* isolates, resistance rates were higher for fluoroquinolones and macrolides. Resistance rates since 2004 were increasing for macrolides and fluoroquinolones in *C. coli* and for fluoroquinolones only in *C. jejuni* (Figure 8. a).

Table 8. c: Occurrence of resistance in *Campylobacter coli* and *Campylobacter jejuni* from human clinical isolates in 2015.

Campylobacter coli							**2015**
Antimicrobials	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Macrolides[1]	220	185	84.1%	0	0.0%	35	15.9%
Fluoroquinolones[2]	220	49	22.3%	0	0.0%	171	77.7%

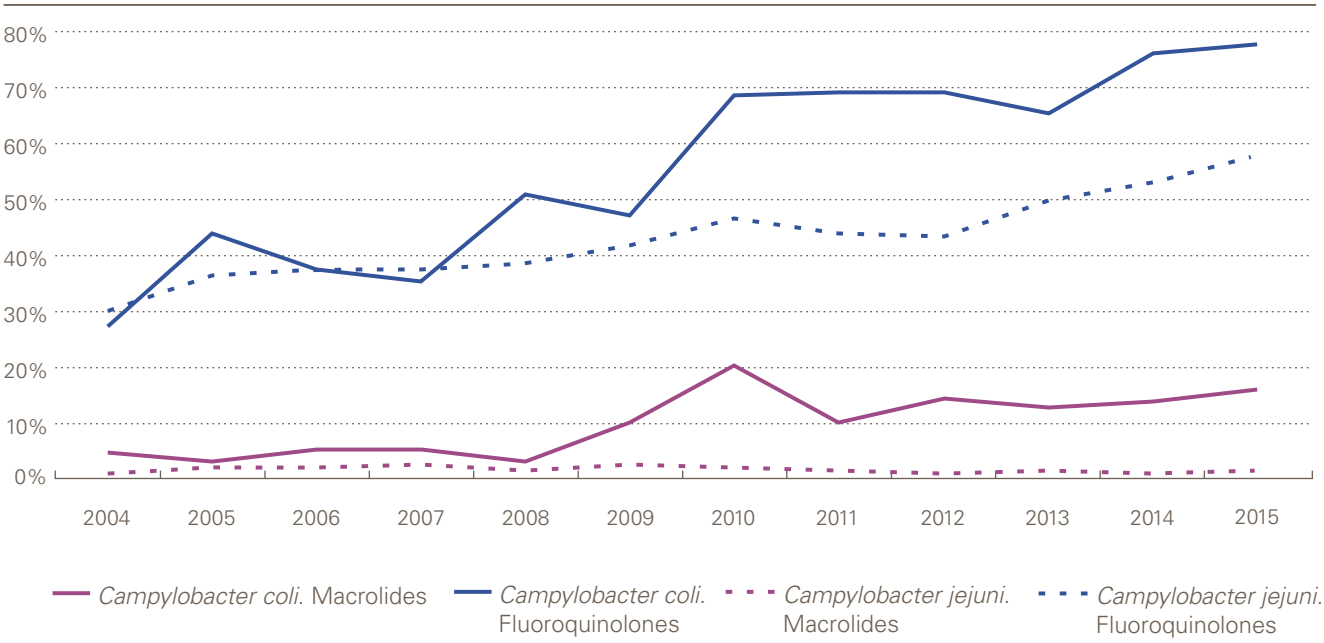
Campylobacter jejuni							**2015**
Antimicrobials	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Macrolides[1]	2,400	2,370	98.8%	1	0.0%	29	1.2%
Fluoroquinolones[2]	2,397	1,005	41.9%	1	0.0%	1391	58.0%

N = total number of tested isolates, S (n) = number of susceptible isolates, S (%) = percentage of susceptible isolates, I (n) = number of intermediate susceptible isolates, I (%) = percentage of intermediate susceptible isolates, R (n) = number of resistant isolates, R (%) = percentage of resistant isolates

[1] Makrolides: erythromycin, clarithromycin, azithromycin

[2] Fluoroquinolones: ciprofloxacin, norfloxacin, ofloxacin

Figure 8. a: Trends in resistance to fluoroquinolones and macrolides in *Campylobacter coli* and *Campylobacter jejuni* from human clinical isolates in Switzerland in 2004–2015.

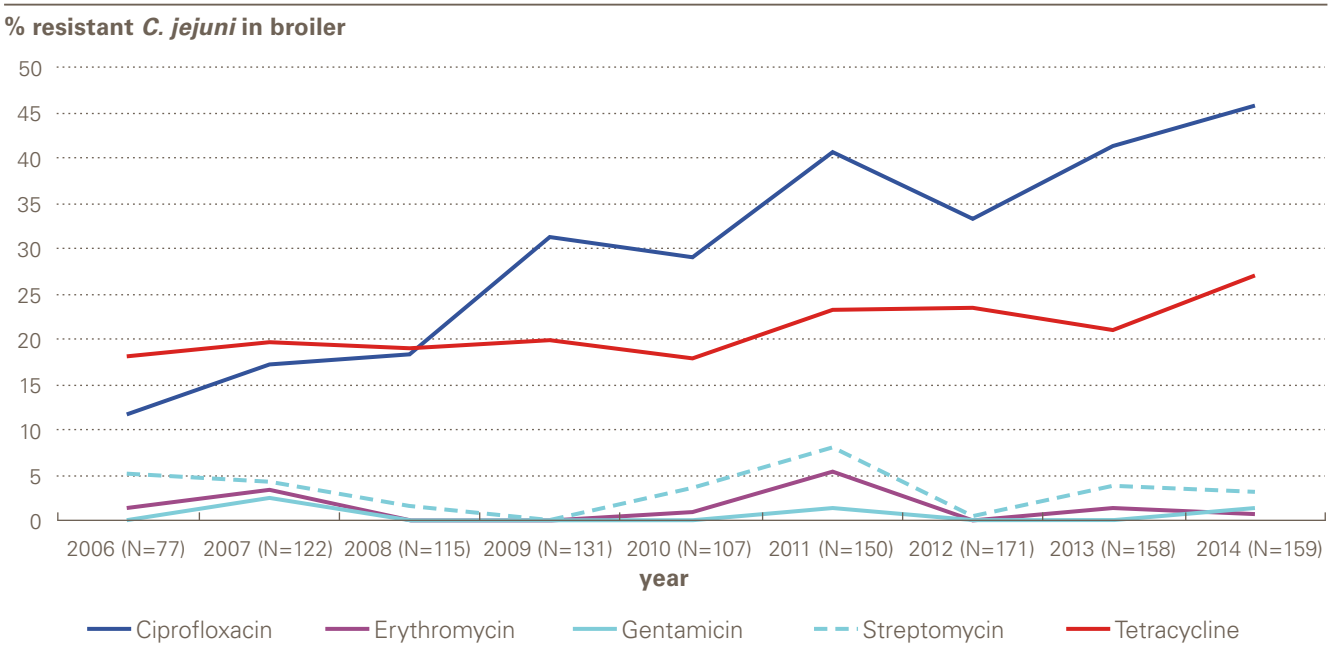


8.1.4 Discussion

The increase of resistance to ciprofloxacin in *C. jejuni* from broilers is of special concern, as fluoroquinolones and macrolides are the drugs of choice for the treatment of severe human campylobacteriosis. Their efficacy for the treatment of *Campylobacter* infections in humans should be preserved. Studies estimate that *Campylobacter* from broilers accounts for 50–80% of human campylobacteriosis cases and hence resistance can be passed on to humans [8], [9], [11].

In *C. jejuni* from broilers, microbiological resistance to ciprofloxacin has displayed a statistically significant increasing trend over the last 8 years. The same trend is observed in human clinical isolates as well. While in broilers an increase from 11.7% resistant isolates in 2006 to 45.9% in 2014 was observed, resistance rates in clinical isolates from humans rose from 37.6% to 53.2% during the same time interval. Also, the resistance rate to tetracycline increased again in 2014 to 27.0%. In Switzerland, there are currently no products licensed for use in broilers containing tetracycline or streptomycin, but tetracycline is widely used in other farm animals, especially in fattening pigs and cattle. Resistance to other tested antimicrobials (erythromycin, gentamicin and streptomycin) remained stable or low (Figure 8. b).

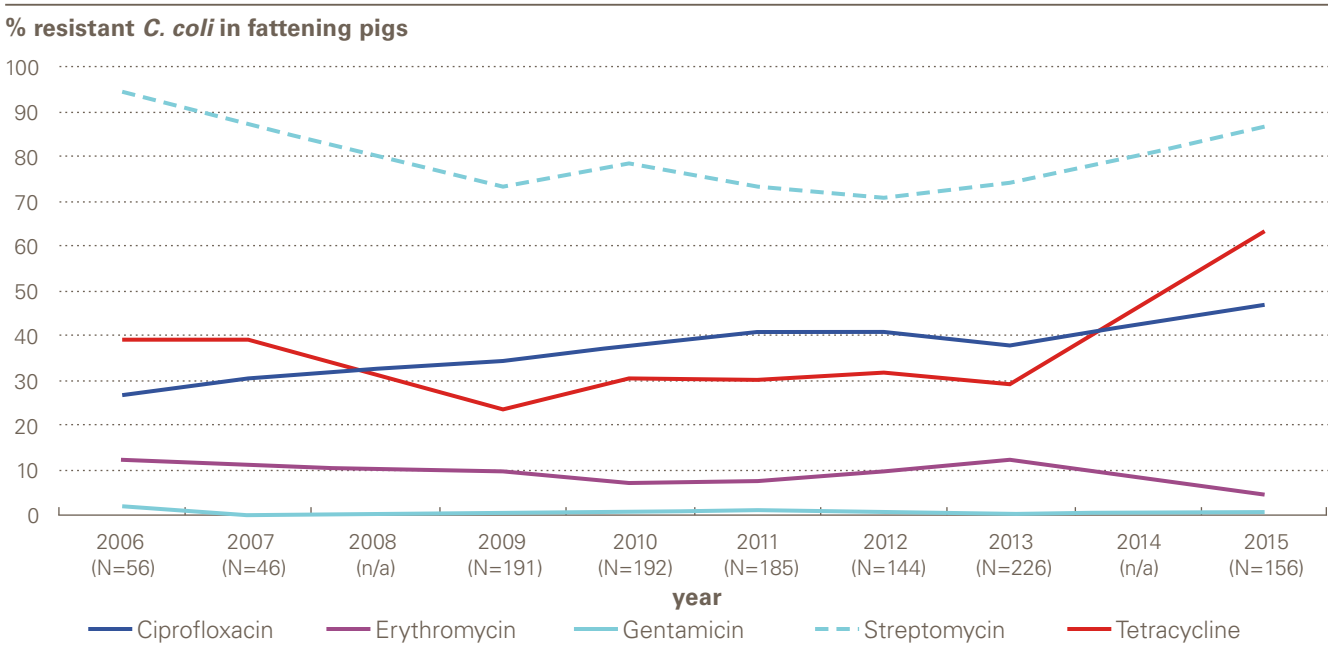
Figure 8. b: Trends in ciprofloxacin, erythromycin, gentamicin, streptomycin and tetracycline resistance in *C. jejuni* from broilers in 2006–2014 (N = total number of tested isolates).



Data on microbiological resistance in *C. jejuni* from broilers from 25 European countries in 2014 showed average levels of resistance of 69.8% to ciprofloxacin, 54.4% to tetracycline, 6.9% to streptomycin and 5.9% to erythromycin [3]. As in previous years, resistance levels varied greatly among countries and were generally much lower in Nordic countries than in other European countries [3]. Levels of resistance for *C. jejuni* in Switzerland were below the European averages, except for streptomycin which was slightly higher. Besides Switzerland, Austria, Finland, France, Hungary and Spain also observed an increasing trend of resistance to ciprofloxacin in *C. jejuni* from broilers [3].

In *C. coli* from fattening pigs, levels of microbiological resistance to streptomycin decreased significantly in past years, but an increasing trend can be observed since 2012. The rate of resistance to tetracycline doubled between 2013 (29.2%) and 2015 (63.5%) after being rather stable from 2010 to 2013. Microbiological resistance levels to ciprofloxacin have increased steadily since 2006, despite a slight fall in 2013. The prevalence of resistance to erythromycin has consistently been around 10% since monitoring began in 2006 and was halved to 4.5% in 2015 (Figure 8. c).

Figure 8. c: Trends in ciprofloxacin, erythromycin, gentamicin, streptomycin and tetracycline resistance in *C. coli* from fattening pigs between 2006 and 2015 (N = total number of tested isolates; values for 2008 and 2014 interpolated [n/a]).



Reasons for the significant increase of the resistance level to tetracycline in *C. coli* from fattening pigs are under investigation. The *tet(O)* gene – located on a self-transmissible plasmid or on the chromosome – is the most common gene known to confer resistance to tetracycline in *Campylobacter* [12]. Therefore, an increasing spread of *tet(O)* among *C. coli* from fattening pigs could be a possible reason for the observed increase of the resistance level to tetracycline.

Information in anresis.ch on antimicrobial resistance was available for more than one third of the reported human *Campylobacter* cases. Resistance levels were reported for fluoroquinolones and macrolides. Resistance levels of fluoroquinolones were very high (above 50%), and the trend has been rising over the last ten years.

Similar average levels of resistance to ciprofloxacin for *C. jejuni* (average 60.2%) and *C. coli* (average 68.9%) isolated form humans were found in 13 EU countries in 2014. Resistance levels varied considerably between different countries, ranging from 50.0% to 97.9% for *C. jejuni* and from 61.4% to 97.0% for *C. coli* [3]. As a result, the European Food Safety Authority and the European Centre for Disease Prevention and Control no longer consider fluoroquinolones appropriate for the routine empirical treatment of human campylobacteriosis due to its high level of resistance [3]. In Switzerland, resistance levels to macrolides (erythromycin) are generally low, whereas in EU countries resistance levels range from 0.0% to 57.6% for *C. jejuni* and *C. coli* [3].

The available data do not allow a direct comparison of resistance in *Campylobacter* isolates from humans and animals. The sampling strategy, methodology and breakpoints used for testing of isolates are not the same for animals and humans. Nevertheless, it must be assumed that the increasing trend in fluoroquinolone resistance in *Campylobacter* isolates from humans over the last ten years is due to the increase of resistance in *Campylobacter* among animals. *Campylobacter* infections may be acquired from domestically produced and imported meat or during foreign travel. A study in Switzerland has shown that resistance levels for ciprofloxacin differ substantially in isolates from domestically produced and imported broiler meat [13], and resistance levels also depend on whether patients have been abroad [14]. Therefore, more information on resistance levels in *Campylobacter* from meat (domestically produced and imported) and on travel status would be necessary to complete the picture.

8.2 *Salmonella* spp.

Salmonella is the second most important zoonotic bacterial pathogen in Switzerland and the EU [1], [2]. Salmonellosis in humans has to be notified (ordinance of the FOPH on laboratory reports), whereas the notification of resistance profiles of these findings is not mandatory.

Human salmonellosis usually does not require antimicrobial treatment. In some patients, *Salmonella* infection can cause serious illness and sepsis. In these cases, effective antimicrobials are essential for treatment and can be lifesaving. The treatment of choice for *Salmonella* infections is fluoroquinolones for adults and third-generation cephalosporins for children.

Information on antimicrobial resistance in anresis.ch was available for more than one third of the reported human *Salmonella* cases. Resistance rates are only available for aminopenicillins, ceftriaxone, trimethoprim-sulfamethoxazole and quinolones (Table 8. d). Serovar typing in human medicine

is only performed for a minority of isolates. Although this information is interesting for epidemiologic purposes – in contrast to susceptibility testing results – it is irrelevant for treatment decisions. As in veterinary medicine. *S. typhimurium* and *S. enteritidis* are the most frequent serovars specified and they differ in their antimicrobial resistance profile.

Animals can be carriers of *Salmonella* without showing any clinical signs. Poultry in particular often show no signs of infection. In cattle, *Salmonella* infection can cause fever, diarrhoea and abortion. Fever and diarrhoea are less common in pigs. Transmission of *Salmonella* from animals to humans usually occurs through food. A wide variety of foodstuff of animal and plant origin can be contaminated with *Salmonella*. *Salmonella* can also be transmitted through direct contact with infected animals.

In Europe, *S. enteritidis* and *S. typhimurium* are the most common serovars in human infections. *S. enteritidis* cases are mostly associated with the consumption of contaminated eggs and poultry meat, whereas *S. typhimurium* cases are mostly associated with the consumption of contaminated pork, beef and poultry meat. Findings of *Salmonella* in animals have to be notified in Switzerland, and antibacterial susceptibility is tested in one isolate from each animal species involved per incident. Isolates obtained from samples of poultry flocks collected within the national control program for *Salmonella* are also included in the data.

8.2.1 *Salmonella* in animals

This chapter includes antimicrobial resistances of *Salmonella enteritidis*, *Salmonella typhimurium* and monophasic *Salmonella typhimurium* in livestock. Poultry and cattle samples were investigated in 2014 and 2015. In those two years, no isolates from pigs were detected.

In 2014, a total of 64 *Salmonella* isolates (28 from poultry, 36 from cattle) were available for susceptibility testing. 42 of these isolates, originating from different holdings or different sampling dates (19 from poultry, 23 from cattle), are presented in Table 8. e and Table 8. f. *S. typhimurium* was identified in 18 (8 from poultry, 10 from cattle), *S. enteritidis* in 11 (9 from poultry, 2 from cattle) and monophasic *Salmonella typhimurium* in 13 (2 from poultry, 11 cattle) of the 42 isolates.

All 11 *S. enteritidis* isolates were fully susceptible to all tested antimicrobials and are included in the column of *Salmonella* spp. in Table 8. e and Table 8. f. Half of the *S. typhimurium* isolates from poultry (4 isolates) and 70% of the *S. typhimurium* isolates from cattle were susceptible to all tested antimicrobials.

Table 8. d: Occurrence of resistance in non-typhoidal *Salmonella* from human clinical isolates 2015.

Salmonella* ser. *enteritidis							**2015**
Antimicrobial	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Aminopenicillin	121	112	92.6%	0	0.0%	9	7.4%
Ceftriaxone	93	92	98.9%	0	0.0%	1	1.1%
Trimethoprim-sulfamethoxazole	116	115	99.1%	0	0.0%	1	0.9%
Fluoroquinolones[1]	117	114	97.4%	1	0.9%	2	1.7%

Salmonella* ser. *typhimurium							**2015**
Antimicrobial	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Aminopenicillin	56	25	44.6%	0	0.0%	31	55.4%
Ceftriaxone	46	44	95.7%	0	0.0%	2	4.3%
Trimethoprim-sulfamethoxazole	52	43	82.7%	0	0.0%	9	17.3%
Fluoroquinolones[1]	57	51	89.5%	0	0.0%	6	10.5%

N = total number of tested isolates, S (n) = number of susceptible isolates, S (%) = percentage of susceptible isolates, I (n) = number of intermediate susceptible isolates, I (%) = percentage of intermediate susceptible isolates, R (n) = number of resistant Isolates, R (%) = percentage of resistant isolates

[1] Fluoroquinolones: ciprofloxacin, norfloxacin, ofloxacin

Four *S. typhimurium* isolates from poultry were microbiologically resistant to colistin and one of them additionally to ampicillin, sulfamethoxazole and tetracycline (Table 8. e). Multidrug-resistance to ampicillin, chloramphenicol, sulfamethoxazole and tetracycline was found in three of the 10 *S. typhimurium* isolates from cattle (Table 8. f).

Eleven of the monophasic *Salmonella typhimurium* isolates (2 from poultry, 9 from cattle) showed microbiological resistance to 3 antimicrobials (ampicillin, sulfamethoxazole, tetracycline) (Table 8. e and Table 8. f). The other 2 monophasic *Salmonella typhimurium* isolates from cattle were resistant to tetracycline only.

The distribution of the minimum inhibitory concentrations (MICs) for *Salmonella* spp. isolates of 2014 is shown in Annexe II (Table II.1 to Table II.8) and multi-resistance patterns are shown in Annexe III (Table III.1 & Table III.2).

In 2015, 31 *Salmonella* isolates from poultry and 32 *Salmonella* isolates from cattle underwent susceptibility testing (Table 8. g and Table 8. h). *S. typhimurium* was identified in 40 (21 from poultry, 19 from cattle), *S. enteritidis* in 14 (9 from poultry, 5 from cattle) and monophasic *Salmonella typhimurium* in 9 (1 from poultry, 8 from cattle) of the 63 isolates.

All 9 *S. enteritidis* isolates from poultry and 4 out of 5 isolates from cattle were fully susceptible to all tested antimicrobials. The remaining *S. enteritidis* isolate from cattle was resistant to colistin. *S. enteritidis* isolates are included in the column of *Salmonella* spp. in Table 8. g and Table 8. h.

The majority of *S. typhimurium* isolates from poultry (81.0%) and from cattle (68.4%) were susceptible to all tested antimicrobials (Table 8. g). Among the other *S. typhimurium* isolates from poultry, 2 were microbiologically resistant to colistin and 2 to ampicillin, chloramphenicol, sulfamethoxazole and tetracycline. Also 1 *S. typhimurium* isolate from cattle showed resistance to ampicillin, chloramphenicol, sulfamethoxazole and tetracycline (Table 8. h). Single resistance to tetracycline was detected in 5 *S. typhimurium* isolates from cattle.

The only monophasic *Salmonella typhimurium* isolate from poultry showed microbiological resistance to 3 antimicrobials (ampicillin, sulfamethoxazole, tetracycline) (Table 8. g). Seven monophasic *Salmonella typhimurium* isolates from cattle were resistant to 3 and 1 to 4 of the tested antimicrobials (Table 8. h).

The distribution of the minimum inhibitory concentrations (MICs) for *Salmonella* spp. isolates of 2015 is shown in Annexe II (Table II.9 to Table II.16).

Table 8. e: Occurrence of resistance in *Salmonella* spp., *Salmonella typhimurium* and monophasic *Salmonella typhimurium* from poultry in 2014.

2014	*Salmonella* spp. (N=19)			*Salmonella typhimurium* (N=8)			Monophasic *Salmonella typhimurium* (N=2)		
Antimicrobial	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Ampicillin	3	15.8	5.5–37.6	1	12.5	2.2–47.1	2	100.0	34.2–100.0
Azithromycin	0	0.0	0.0–16.8	0	0.0	0.0–32.4	0	0.0	0.0–65.8
Cefotaxime	0	0.0	0.0–16.8	0	0.0	0.0–32.4	0	0.0	0.0–65.8
Ceftazidime	0	0.0	0.0–16.8	0	0.0	0.0–32.4	0	0.0	0.0–65.8
Chloramphenicol	0	0.0	0.0–16.8	0	0.0	0.0–32.4	0	0.0	0.0–65.8
Ciprofloxacin	0	0.0	0.0–16.8	0	0.0	0.0–32.4	0	0.0	0.0–65.8
Colistin	4	21.1	8.5–43.3	4	50.0	21.5–78.5	0	0.0	0.0–65.8
Gentamicin	0	0.0	0.0–16.8	0	0.0	0.0–32.4	0	0.0	0.0–65.8
Meropenem	0	0.0	0.0–16.8	0	0.0	0.0–32.4	0	0.0	0.0–65.8
Nalidixic acid	0	0.0	0.0–16.8	0	0.0	0.0–32.4	0	0.0	0.0–65.8
Sulfamethoxazole	3	15.8	5.5–37.6	1	12.5	2.2–47.1	2	100.0	34.2–100.0
Tetracycline	3	15.8	5.5–37.6	1	12.5	2.2–47.1	2	100.0	34.2–100.0
Tigecycline	0	0.0	0.0–16.8	0	0.0	0.0–32.4	0	0.0	0.0–65.8
Trimethoprim	0	0.0	0.0–16.8	0	0.0	0.0–32.4	0	0.0	0.0–65.8
Number of resistances	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
None	13	68.4	46–84.6	4	50.0	21.5–78.5	0	0.0	0.0–65.8
1 antimicrobial	3	15.8	5.5–37.6	3	37.5	13.7–69.4	0	0.0	0.0–65.8
2 antimicrobials	0	0.0	0.0–16.8	0	0.0	0.0–32.4	0	0.0	0.0–65.8
3 antimicrobials	2	10.5	2.9–31.4	0	0.0	0.0–32.4	2	100.0	34.2–100.0
4 antimicrobials	1	5.3	0.9–24.6	1	12.5	2.2–47.1	0	0.0	0.0–65.8
>4 antimicrobials	0	0.0	0.0–16.8	0	0.0	0.0–32.4	0	0.0	0.0–65.8

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

8.2.2 Non-typhoidal *Salmonella* in human clinical isolates

For salmonellosis, 1,375 laboratory-confirmed cases in humans were reported in 2015, which represents a notification rate of 18 cases per 100,000 inhabitants. The most frequently reported serovars were *S. enteritidis* (34%), *S. typhimurium* (13%) and the monophasic strain 4,12,:i:- (10%).

Resistance in non-typhoidal human *Salmonella* isolates was high for aminopenicillin (21.7%), intermediate for fluoroquinolones (12.3%) and low for ceftriaxone and trimethoprim-sulfamethoxazole (2.5% and 4.7% respectively). In 2015, the most frequently isolated serovars were *Salmonella enteritidis* (n = 121) and *Salmonella typhimurium* (n = 57), but 250 isolates were not specified to serovar level. Non-susceptibility rates were higher in *Salmonella typhimurium* than in *Salmonella enteritidis* for aminopenicillins (55% vs. 7.4%), trimethoprim-sulfamethoxazole (17.3% vs. 0.9%) and fluoroquinolones (10.5% vs. 2.6%). Ceftriaxone resistance was rare in both serovars (Table 8.d). Non-susceptibility rates had been stable since 2004 for aminopenicillins, ceftriaxone and trimethoprim-sulfamethoxazole but increased for fluoroquinolones since 2010. Indeed, in 2013 for the first time, non-susceptibility rates for fluoroquinolones were higher than for trimethoprim-sulfamethoxazole (Fig. 8. d).

8.2.3 Discussion

The prevalence of *Salmonella* spp. in food-producing animals in Switzerland is very low as a consequence of long-term control programs. Because of this, only a few *Salmonella* isolates from animals, either from clinical material or from *Salmonella* eradication programs, were available over the last years (Figure 8. e). As a consequence thereof, rates of resistance and their long-term trends should be interpreted with caution.

Between 2014 and 2015, susceptibility of *Salmonella* spp. to all tested antimicrobials increased from 68.4% to 83.9% for isolates from poultry and from 39.1% to 53.1% for isolates from cattle. Overall, the situation regarding antibiotic resistance in poultry and cattle can be considered as good and is comparable with neighboring countries such as Austria, France, Germany and Italy [3].

Fluoroquinolones and third-generation cephalosporins are critically important antimicrobials for the treatment of human salmonellosis. Resistance to ciprofloxacin or third-generation cephalosporins was neither found in *Salmonella* spp. isolates from poultry nor from cattle in 2014 and 2015. Resistances to ampicillin, sulfamethoxazole and tetracycline were high in the last three years, but showed a decreasing trend

Table 8. f: Occurrence of resistance in *Salmonella* spp., *Salmonella typhimurium* and monophasic *Salmonella typhimurium* from cattle in 2014.

2014	*Salmonella* spp. (N=23)			*Salmonella typhimurium* (N=10)			Monophasic *Salmonella typhimurium* (N=11)		
Antimicrobial	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Ampicillin	12	52.2	33.0–70.8	3	30.0	10.8–60.3	9	81.8	52.3–94.9
Azithromycin	0	0.0	0.0–14.3	0	0.0	0.0–27.8	0	0.0	0.0–25.9
Cefotaxime	0	0.0	0.0–14.3	0	0.0	0.0–27.8	0	0.0	0.0–25.9
Ceftazidime	0	0.0	0.0–14.3	0	0.0	0.0–27.8	0	0.0	0.0–25.9
Chloramphenicol	3	13.0	4.5–32.1	3	30.0	10.8–60.3	0	0.0	0.0–25.9
Ciprofloxacin	0	0.0	0.0–14.3	0	0.0	0.0–27.8	0	0.0	0.0–25.9
Colistin	0	0.0	0.0–14.3	0	0.0	0.0–27.8	0	0.0	0.0–25.9
Gentamicin	0	0.0	0.0–14.3	0	0.0	0.0–27.8	0	0.0	0.0–25.9
Meropenem	0	0.0	0.0–14.3	0	0.0	0.0–27.8	0	0.0	0.0–25.9
Nalidixic acid	0	0.0	0.0–14.3	0	0.0	0.0–27.8	0	0.0	0.0–25.9
Sulfamethoxazole	12	52.2	33.0–70.8	3	30.0	10.8–60.3	9	81.8	52.3–94.9
Tetracycline	14	60.9	40.8–77.8	3	30.0	10.8–60.3	11	100.0	74.1–100.0
Tigecycline	0	0.0	0.0–14.3	0	0.0	0.0–27.8	0	0.0	0.0–25.9
Trimethoprim	0	0.0	0.0–14.3	0	0.0	0.0–27.8	0	0.0	0.0–25.9
Number of resistances	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
None	9	39.1	22.2–59.2	7	70.0	39.7–89.2	0	0.0	0.0–25.9
1 antimicrobial	2	8.7	2.4–26.8	0	0.0	0.0–27.8	2	18.2	5.1–47.4
2 antimicrobials	0	0.0	0.0–14.3	0	0.0	0.0–27.8	0	0.0	0.0–25.9
3 antimicrobials	9	39.1	22.2–59.2	0	0.0	0.0–27.8	9	81.8	52.3–94.9
4 antimicrobials	3	13.0	4.5–32.1	3	30.0	10.8–60.3	0	0.0	0.0–25.9
> 4 antimicrobials	0	0.0	0.0–14.3	0	0.0	0.0–27.8	0	0.0	0.0–25.9

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

Table 8. g: Occurrence of resistance in *Salmonella* spp., *Salmonella typhimurium* and monophasic *Salmonella typhimurium* from poultry in 2015.

2015	*Salmonella* spp. (N=31)			*Salmonella typhimurium* (N=21)			Monophasic *Salmonella typhimurium* (N=1)		
Antimicrobial	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Ampicillin	3	9.7	3.3–24.9	2	9.5	2.7–28.9	1	100.0	20.7–100.0
Azithromycin	0	0.0	0.0–11.0	0	0.0	0.0–15.5	0	0.0	0.0–79.3
Cefotaxime	0	0.0	0.0–11.0	0	0.0	0.0–15.5	0	0.0	0.0–79.3
Ceftazidime	0	0.0	0.0–11.0	0	0.0	0.0–15.5	0	0.0	0.0–79.3
Chloramphenicol	2	6.5	1.8–20.7	2	9.5	2.7–28.9	0	0.0	0.0–79.3
Ciprofloxacin	0	0.0	0.0–11.0	0	0.0	0.0–15.5	0	0.0	0.0–79.3
Colistin	2	6.5	1.8–20.7	2	9.5	2.7–28.9	0	0.0	0.0–79.3
Gentamicin	0	0.0	0.0–11.0	0	0.0	0.0–15.5	0	0.0	0.0–79.3
Meropenem	0	0.0	0.0–11.0	0	0.0	0.0–15.5	0	0.0	0.0–79.3
Nalidixic acid	0	0.0	0.0–11.0	0	0.0	0.0–15.5	0	0.0	0.0–79.3
Sulfamethoxazole	3	9.7	3.3–24.9	2	9.5	2.7–28.9	1	100.0	20.7–100.0
Tetracycline	3	9.7	3.3–24.9	2	9.5	2.7–28.9	1	100.0	20.7–100.0
Tigecycline	0	0.0	0.0–11.0	0	0.0	0.0–15.5	0	0.0	0.0–79.3
Trimethoprim	0	0.0	0.0–11.0	0	0.0	0.0–15.5	0	0.0	0.0–79.3
Number of resistances	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
None	26	83.9	67.4–92.9	17	81.0	60.0–92.3	0	0.0	0.0–79.3
1 antimicrobial	2	6.5	1.8–20.7	2	9.5	2.7–28.9	0	0.0	0.0–79.3
2 antimicrobials	0	0.0	0.0–11.0	0	0.0	0.0–15.5	0	0.0	0.0–79.3
3 antimicrobials	1	3.2	0.6–16.2	0	0.0	0.0–15.5	1	100.0	20.7–100.0
4 antimicrobials	2	6.5	1.8–20.7	2	9.5	2.7–28.9	0	0.0	0.0–79.3
>4 antimicrobials	0	0.0	0.0–11.0	0	0.0	0.0–15.5	0	0.0	0.0–79.3

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

Table 8. h: Occurrence of resistance in *Salmonella* spp., *Salmonella typhimurium* and monophasic *Salmonella typhimurium* from cattle, 2015.

2015	*Salmonella* spp. (N=32)			*Salmonella typhimurium* (N=19)			Monophasic *Salmonella typhimurium* (N=8)		
Antimicrobial	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Ampicillin	9	28.1	15.6–45.4	1	5.3	0.9–24.6	8	100.0	67.6–100.0
Azithromycin	0	0.0	0.0–10.7	0	0.0	0.0–16.8	0	0.0	0.0–32.4
Cefotaxime	0	0.0	0.0–10.7	0	0.0	0.0–16.8	0	0.0	0.0–32.4
Ceftazidime	0	0.0	0.0–10.7	0	0.0	0.0–16.8	0	0.0	0.0–32.4
Chloramphenicol	1	3.1	0.6–15.7	1	5.3	0.9–24.6	0	0.0	0.0–32.4
Ciprofloxacin	0	0.0	0.0–10.7	0	0.0	0.0–16.8	0	0.0	0.0–32.4
Colistin	1	3.1	0.6–15.7	0	0.0	0.0–16.8	0	0.0	0.0–32.4
Gentamicin	0	0.0	0.0–10.7	0	0.0	0.0–16.8	0	0.0	0.0–32.4
Meropenem	0	0.0	0.0–10.7	0	0.0	0.0–16.8	0	0.0	0.0–32.4
Nalidixic acid	0	0.0	0.0–10.7	0	0.0	0.0–16.8	0	0.0	0.0–32.4
Sulfamethoxazole	9	28.1	15.6–45.4	1	5.3	0.9–24.6	8	100.0	67.6–100.0
Tetracycline	14	43.8	28.2–60.7	6	31.6	15.4–54.0	8	100.0	67.6–100.0
Tigecycline	0	0.0	0.0–10.7	0	0.0	0.0–16.8	0	0.0	0.0–32.4
Trimethoprim	1	3.1	0.6–15.7	0	0.0	0.0–16.8	1	12.5	2.2–47.1
Number of resistances	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
None	17	53.1	36.4–69.1	13	68.4	16.0–84.6	0	0.0	0.0–32.4
1 antimicrobial	6	18.8	8.9–35.3	5	26.3	11.8–48.8	0	0.0	0.0–32.4
2 antimicrobials	0	0.0	0.0–10.7	0	0.0	0.0–16.8	0	0.0	0.0–32.4
3 antimicrobials	7	21.9	11.0–38.8	0	0.0	0.0–16.8	7	87.5	52.9–97.8
4 antimicrobials	2	6.3	1.7–20.1	1	5.3	0.9–24.6	1	12.5	2.2–47.1
> 4 antimicrobials	0	0.0	0.0–10.7	0	0.0	0.0–16.8	0	0.0	0.0–32.4

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

Figure 8. d: Trends in aminopenicillin, ceftriaxone, trimethoprim-sulfamethoxazole and fluoroquinolone resistance in non-typhoidal *Salmonella* from human clinical isolates between 2004 and 2015.

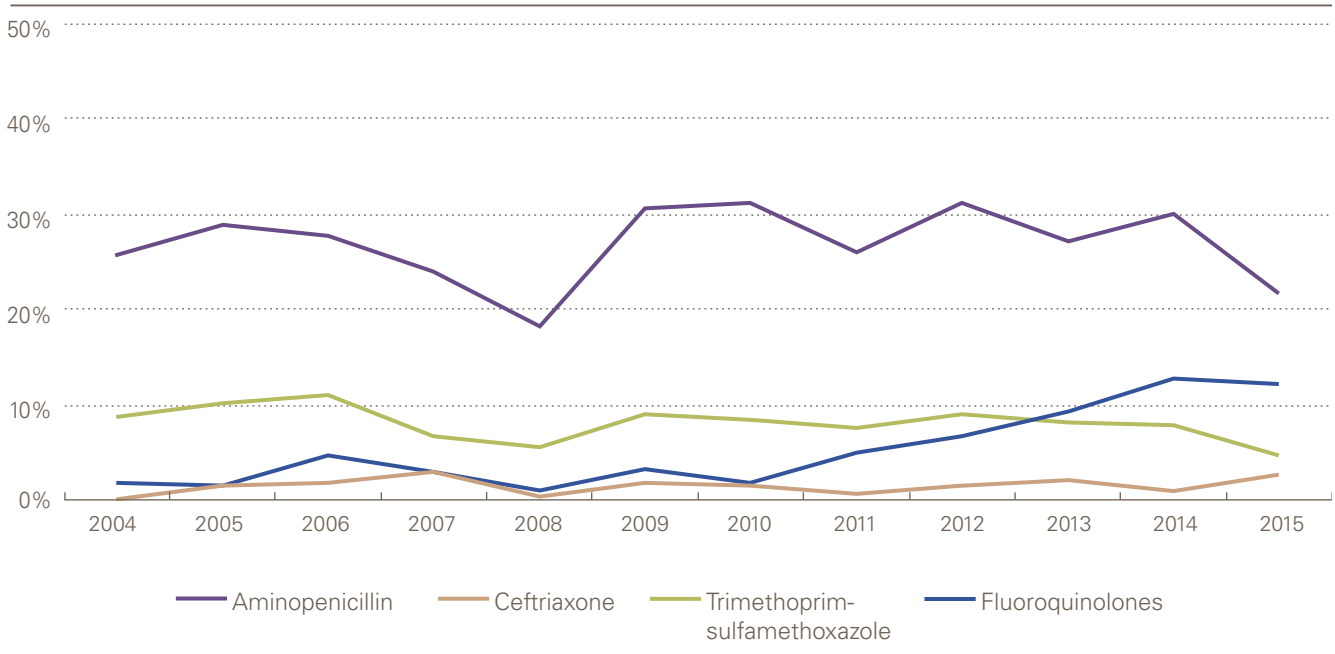
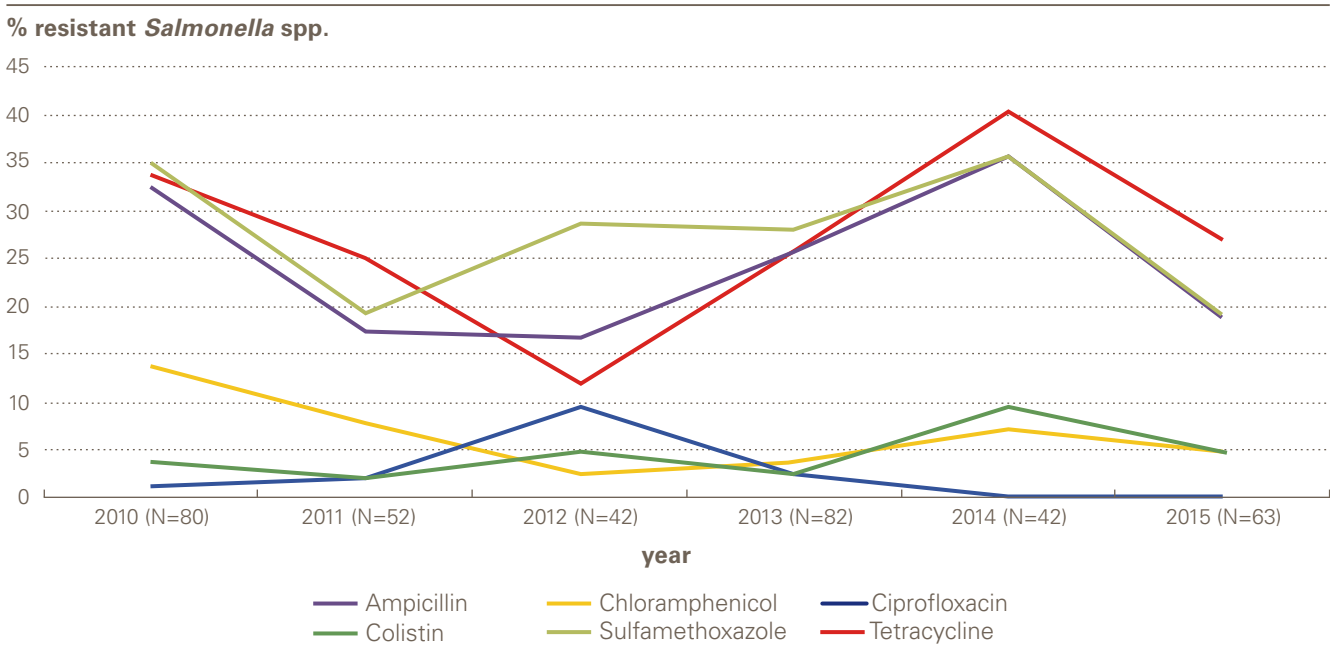


Figure 8. e: Trends in ampicillin, chloramphenicol, ciprofloxacin, colistin, sulfamethoxazole and tetracycline resistance in *Salmonella* spp. from poultry, pigs and cattle between 2010 and 2015 (N = total number of tested isolates).



from 2014 to 2015. These antimicrobials have been used in animal farming for many years and rates of resistance reflect the actual selection pressure.

Microbiological resistance to colistin was detected in 7 of the 105 *Salmonella* spp. isolates from poultry and cattle undergoing susceptibility testing in 2014 and 2015. In the EU, the overall rate of microbiological resistance to colistin among *Salmonella* spp. was 8.3% in 2014 [3]. If the the resistance to colistin of those 7 *Salmonella* spp. isolates in Switzerland is associated with the recently described plasmid-mediated colistin resistance (mcr-1) [4] or with other resistance mechanisms is under investigation. In Switzerland, the mcr-1 gene has so far only been detected in a clinical *E. coli* isolate from a patient with renal deficiency [5] and one *E. coli* from a Swiss slaughter pig in 2015 (textbox 9. a). Furthermore the mcr-1 gene was present in ESBL-producing *E. coli* strains isolated from chicken meat imported from Germany and Italy [6] (textbox 9. b), in one ESBL-producing *E. coli* strain from river water in Switzerland and in 2 ESBL-producing *E. coli* strains isolated from imported vegetables from Vietnam and Thailand [7].

The frequency of resistance to aminopenicillins in human non-typhoidal *Salmonella* spp. isolates in Switzerland (21.7%) was lower than the mean level of resistance to ampicillin in 21 different EU member states in 2014 (28.2%) [3]. Since 2011 in Switzerland, resistance levels to fluoroquinolones increased up to 12.3% in 2015. This is above the mean value for ciprofloxacin resistance in EU member states (8.8%), but variation between member states was high (0.0–50.0% resistant isolates).

A direct comparison of the resistance situation between *Salmonella* in animals and in human clinical isolates is not possible for various reasons. Interpretative criteria (clinical breakpoint in human isolates / epidemiological cutoff in animal isolates) may differ substantially. As the only information available is qualitative data from human isolates, a reinterpretation of the results using the same cutoff values is not possible. Regarding the favorable *Salmonella* situation in Swiss farm animals, it is likely that a substantial part of *Salmonella* infections are acquired through imported food or foreign travel. Data on antimicrobial resistance in *Salmonella* from imported food and information about the origin of the infection (domestic/abroad) would be necessary to complete the picture.

References

[1] Federal Food Safety and Veterinary Office. Bericht zur Überwachung von Zoonosen und Tierseuchen 2014. Bern 2015; 80 pp. German

[2] EFSA (European Food Safety Authority) and ECDC (European Centre for Disease Prevention and Control). The European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2014. EFSA Journal 2015; 13(12): 4329, 191 pp. doi:10.2903/j.efsa.2015.4329

[3] EFSA (European Food Safety Authority) and ECDC (European Centre for Disease Prevention and Control). The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2014. EFSA Journal 2016; 14(2): 4380, 207 pp. doi:10.2903/j.efsa.2016.4380

[4] Liu et al. Emergence of plasmid-mediated colistin

resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. Lancet Infect Dis 2015; 16(2): 161–168. doi: 10.1016/S1473-3099(15)00424-7

[5] Poirel et al. Plasmid-mediated carbapenem and colistin resistance in a clinical isolate of *Escherichia coli*, Lancet Infect Dis 2016; 16(3): 281. doi:10.1016/S1473-3099(16)00006-2

[6] Zogg et al. Characteristics of ESBL-producing Enterobacteriaceae and Methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from Swiss and imported raw poultry meat collected at retail level. Schweizer Archiv für Tierheilkunde 2016; 158(6): 451-456. doi:10.17236/sat00071

[7] Zurfluh K, Poirel L, Nordmann P et al. Occurrence of the plasmid-borne mcr-1 colistin resistance gene in extended-spectrum-B-lactamase producing Enterobacteriaceae in river water and imported vegetable samples in Switzerland. Antimicrob Agents Chemother 2016; 60: 2594–2595

[8] EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards). Scientific Opinion on Quantification of the risk posed by broiler meat to human campylobacteriosis in the EU. EFSA Journal 2010; 8(1):1437, 89 pp., doi:10.2903/j.efsa.2010.1437

[9] Kittl et al. Source attribution of human *Campylobacter* isolates by MLST and *Fla*-Typing and association of genotypes with quinolone resistance. PLoS ONE 2013; 8(11): e81796. doi:10.1371/journal.pone.0081796

[10] WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR). Critically Important Antimicrobials for Human Medicine. 3rd revision, 2011

[11] Kittl et al. Comparison of genotypes and antibiotic resistance of *Campylobacter jejuni* isolated from humans and slaughtered chickens in Switzerland. J Appl Microbiol 2011; 110(2): 513–520. doi:10.1111/j.1365-2672.2010.04906.x

[12] Wieczorek et al. Antimicrobial resistance mechanisms among *Campylobacter*. Biomed Res Int 2013; 340605. doi:10.1155/2013/340605

[13] Kittl et al. Comparison of genotypes and antibiotic resistances of *Campylobacter jejuni* and *Campylobacter coli* on chicken retail meat and at slaughter. Appl Environ Microbiol 2013; 79(12): 3875–3878. doi:10.1128/AEM.00493-13

[14] Niederer et al. Genotypes and antibiotic resistances of *Campylobacter jejuni* and *Campylobacter coli* isolates from domestic and travel-associated human cases. Appl Environ Microbiol 2012, 78(1): 288–291. doi: 10.1128/AEM.06194-11

9

Resistance in indicator bacteria in animals

9 Resistance in indicator bacteria in animals

The prevalence of antimicrobial resistance among certain bacteria of the intestinal flora can be used as an indicator of the selective pressure from use of antimicrobial agents in various populations. These bacteria constitute a reservoir of transferable resistance genes that can be spread horizontally to other bacteria, including zoonotic bacteria. Antimicrobial resistance in indicator bacteria from healthy animals is monitored in order to provide information about the types of resistance present in intestinal bacteria of animal origin. Antimicrobial use leads to a selection pressure for resistant bacteria in the intestinal flora of affected animals. Monitoring allows a comparison of the effects of this selection pressure in different animal species. It also serves as a valuable early warning system to help identify emerging types of resistance in livestock populations and to monitor their potential spread.

9.1 Enterococci

In the context of monitoring antimicrobial resistance, enterococci are indicator bacteria for the occurrence of resistances in gram-positive intestinal bacteria from livestock. Resistance can be transferred from animals to humans either by direct transmission of resistant bacterial strains or by horizontal gene transfer of resistance genes among bacteria [1]. Enterococci are generally found as commensals in the gastrointestinal tract of animals and humans. In a hospital setting, however, they can cause diseases such as urinary tract infections, sepsis or endocarditis in patients with a weakened immune system. Of particular concern in this regard are vancomycin-resistant enterococci (VRE), which can spread rapidly and are difficult to treat. The responsible resistance gene is located on a transposon and can therefore

Table 9. a: Occurrence of resistance in *Enterococcus faecalis* and *Enterococcus faecium* from broilers, 2014.

2014	*Enterococcus faecalis* (N=202)			*Enterococcus faecium* (N=80)		
Antimicrobials	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Ampicillin	1	0.5	0.1–2.8	4	5.0	2.0–12.2
Chloramphenicol	1	0.5	0.1–2.8	0	0.0	0.0–4.6
Ciprofloxacin	0	0.0	0.0–1.9	3	3.8	1.3–10.5
Daptomycin*	1	1.1	0.1–6.1	–	–	–
Erythromycin	34	16.8	12.3–22.6	22	27.5	18.9–38.1
Gentamicin	1	0.5	0.1–2.8	0	0.0	0.0–4.6
Linezolid	0	0.0	0.0–1.9	0	0.0	0.0–4.6
Quinupristin/Dalfopristin**	–	–	–	60	75.0	64.5–83.2
Teicoplanin*	0	0.0	0.0–4.1	–	–	–
Tetracycline	105	52.0	45.1–58.8	24	30.0	21.1–40.8
Tigecycline*	59	66.3	56–75.3	–	–	–
Vancomycin	0	0.0	0.0–1.9	0	0.0	0.0–4.6
Number of resistances	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
None	63	31.2	25.2–37.9	14	17.5	10.7–27.3
1 antimicrobial	88	43.6	36.9–50.5	29	36.3	26.6–47.2
2 antimicrobials	40	19.8	14.9–25.8	29	36.3	26.6–47.2
3 antimicrobials	10	5.0	2.7–8.9	6	7.5	3.5–15.4
4 antimicrobials	1	0.5	0.1–2.8	2	2.5	0.7–8.7
>4 antimicrobials	0	0.0	0.0–1.9	0	0.0	0.0–4.6

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval
* N = 89 *E. faecalis*
** Intrinsic resistance of *E. faecalis*

easily be spread horizontally to other bacteria, prompting particular fears that vancomycin resistance might be passed from enterococci to methicillin-resistant *Staphylococcus aureus* (MRSA).

This chapter includes antimicrobial resistances of *Enterococcus faecalis* and *Enterococcus faecium* in livestock. Broilers were investigated in 2014, veal calves and fattening pigs in 2015.

9.1.1 *Enterococcus* spp. in broilers

In 2014, a random sample of 350 broiler flocks was investigated at slaughter in the framework of the antimicrobial resistance monitoring program using cloacal swabs (5 pooled swabs per flock). *E. faecalis* was identified in 206 samples (58.9%) and *E. faecium* in 81 samples (23.1%). Susceptibility testing was performed for 202 *E. faecalis* and 80 *E. faecium* isolates (Table 9. a).

Not all *Enterococcus* spp. isolates were tested for susceptibility for the entire spectrum of presented antimicrobials because panels of antimicrobial substances were adapted to EU standards during 2014.

Full susceptibility to all tested antimicrobials was observed for 31.2% of *E. faecalis* isolates and for 17.5% of *E. faecium* isolates. Multi-resistance to 4 of the tested antimicrobials was observed for 1 *E. faecalis* (0.5%) and 2 *E. faecium* (2.5%) isolates.

For *E. faecalis,* very high to high levels of microbiological resistance to tigecycline (66.3%) and tetracycline (52%) were found. Additionally, 16.8% of isolates were resistant to erythromycin. *E. faecium* showed a very high level of resistance to quinupristin/dalfopristin (75%) and high resistance to erythromycin (27.5%) and tetracycline (30%).

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.20 to Table II.22) and multi-resistance patterns are shown in Annexe III (Table III.5 & Table III.6).

9.1.2 *Enterococcus* spp. in veal calves

In 2015, a random sample of 298 veal calves was investigated at slaughter in the framework of the antimicrobial resistance monitoring program using caecum samples. 56 *Enterococcus faecalis* strains (18.8%) and 151 *Enterococcus faecium* strains (50.7%) were isolated and subjected to susceptibility testing (Table 9. b).

60.7% of the *E. faecalis* and 10.6% of the *E. faecium* isolates showed microbiological resistance to tetracycline. A high level of resistance was found to erythromycin for both *E. faecium* and *E. faecalis* (35.7%, 31.8%). *E. faecalis* isolates

Table 9. b: Occurrence of resistance in *Enterococcus faecalis* and *Enterococcus faecium* from veal calves, 2015.

2015	*Enterococcus faecalis* (N=56)			*Enterococcus faecium* (N=151)		
Antimicrobial	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Ampicillin	0	0.0	0.0–6.4	1	0.7	0.1–3.7
Chloramphenicol	10	17.9	10.0–29.8	0	0.0	0.0–2.5
Ciprofloxacin	0	0.0	0.0–6.4	3	2.0	0.7–5.7
Daptomycin	0	0.0	0.0–6.4	6	4.0	1.8–8.4
Erythromycin	20	35.7	24.5–48.8	48	31.8	24.9–39.6
Gentamicin	7	12.5	6.2–23.6	0	0.0	0.0–2.5
Linezolid	0	0.0	0.0–6.4	0	0.0	0.0–2.5
Quinupristin/Dalfopristin*	–	–	–	142	94.0	89.1–96.8
Teicoplanin	0	0.0	0.0–6.4	0	0.0	0.0–2.5
Tetracycline	34	60.7	47.6–72.4	16	10.6	6.6–16.5
Tigecycline	0	0.0	0.0–6.4	0	0.0	0.0–2.5
Vancomycin	0	0.0	0.0–6.4	0	0.0	0.0–2.5
Number of resistances	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
None	0	0.0	0.0–6.4	4	2.6	1.0–6.6
1 antimicrobial	20	35.7	24.5–48.8	94	62.3	54.3–69.6
2 antimicrobials	17	30.4	19.9–43.3	39	25.8	19.5–33.3
3 antimicrobials	8	14.3	7.4–25.7	12	7.9	4.6–13.4
4 antimicrobials	6	10.7	5.0–21.5	2	1.3	0.4–4.7
>4 antimicrobials	5	8.9	3.9–19.3	0	0.0	0.0–2.5

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

* Intrinsic resistance of *E. faecalis*

additionally showed moderate levels of resistance to chloramphenicol (17.9%) and gentamicin (12.5%). 94% of the *E. faecium* isolates were microbiologically resistant to quinupristin/dalfopristin. Resistance to linezolid, teicoplanin, tigecycline or vancomycin was observed for neither isolates.

Only 2.6% of the *E. faecium* and none of the *E. faecalis* isolates were fully susceptible to all tested antimicrobials. Multi-resistance to at least 4 of the tested antimicrobials was observed for 11 *E. faecalis* (19.6%) and 2 *E. faecium* (1.3%) isolates.

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.23 & Table II.24).

9.1.3 *Enterococcus* spp. in fattening pigs

In 2015, a random sample of 300 fattening pigs was investigated at slaughter in the framework of the antimicrobial resistance monitoring program using caecum samples. 28 *Enterococcus faecalis* (9.3%) and 53 *Enterococcus faecium* (17.7%) strains were isolated and subjected to susceptibility testing (Table 9. c).

75% of the *E. faecalis* and 34% of the *E. faecium* isolates showed microbiological resistance to tetracycline. A high level of resistance was found to erythromycin for both *E. faecium* and *E. faecalis* (20.8%, 42.9%). *E. faecalis* isolates additionally showed moderate to low levels of resistance to chloramphenicol (17.9%) and gentamicin (7.1%). Of the *E. faecium* isolates, 88.7% were microbiologically resistant to quinupristin/dalfopristin and they showed moderate levels to daptomycin (17%). 2 isolates were microbiologically resistant to vancomycin (3.8%). Resistance to linezolid and tigecycline was found for neither isolates.

Only 5.7% of *E. faecium* and none of the *E. faecalis* isolates were fully susceptible to all tested antimicrobials. Multi-resistance to at least 4 of the tested antimicrobials was observed for 5 *E. faecalis* (17.9%) and 8 *E. faecium* (15.1%) isolates.

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.25 & Table II.26).

9.1.4 Discussion

Resistance to antimicrobials is generally widespread in enterococci isolated from livestock in Switzerland. Resistances to erythromycin and tetracycline are often found in isolates from broilers, pigs and veal calves. Long-term trends of both resistances vary between enterococci and type of animal (Figures 9 a–f). In the past years, a significant decreasing trend of microbiological resistance to tetracycline and erythromycin has been observed for *E. faecalis* isolates from broilers. However, resistance to tetracycline

Table 9. c: Occurrence of resistance in *Enterococcus faecalis* and *Enterococcus faecium* from fattening pigs, 2015.

2015	*Enterococcus faecalis* (N=28)			*Enterococcus faecium* (N=53)		
Antimicrobial	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Ampicillin	0	0.0	0.0–12.1	8	15.1	7.9–27.1
Chloramphenicol	5	17.9	7.9–35.6	4	7.5	3.0–17.9
Ciprofloxacin	0	0.0	0.0–12.1	3	5.7	1.9–15.4
Daptomycin	0	0.0	0.0–12.1	9	17.0	9.2–29.2
Erythromycin	12	42.9	26.5–60.9	11	20.8	12.0–33.5
Gentamicin	2	7.1	2.0–22.6	1	1.9	0.3–9.9
Linezolid	0	0.0	0.0–12.1	0	0.0	0.0–6.8
Quinupristin/Dalfopristin*	–	–	–	47	88.7	77.4–94.7
Teicoplanin	0	0.0	0.0–12.1	2	3.8	1.0–12.8
Tetracycline	21	75.0	56.6–87.3	18	34.0	22.7–47.4
Tigecycline	0	0.0	0.0–12.1	0	0.0	0.0–6.8
Vancomycin	0	0.0	0.0–12.1	2	3.8	1.0–12.8
Number of resistances	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
None	0	0.0	0.0–12.1	3	5.7	1.9–15.4
1 antimicrobial	7	25.0	12.7–43.4	22	41.5	29.3–54.9
2 antimicrobials	9	32.1	17.9–50.7	15	28.3	18.0–41.6
3 antimicrobials	7	25.0	12.7–43.4	5	9.4	4.1–20.3
4 antimicrobials	3	10.7	3.7–27.2	3	5.7	1.9–15.4
>4 antimicrobials	2	7.1	2.0–22.6	5	9.4	4.1–20.3

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval
* Intrinsic resistance of *E. faecalis*

increased from 38.1% in 2013 to 52% in 2014 (Figure 9. a). Resistance to erythromycin increased in both enterococci species from fattening pigs and in *E. faecium* in veal calves (Figures 9. d–f).

Antimicrobial resistances in pigs generally appear to have increased in enterococci isolates compared to 2012 (Figure 9. e & f). However, trends should be interpreted with caution due to low numbers of isolates for *E. faecalis.*

Figure 9. a: Trends in ampicillin, chloramphenicol, erythromycin, gentamicin, tetracycline and vancomycin resistance in *Enterococcus faecalis* from broilers between 2006 and 2014 (N = total number of tested isolates).

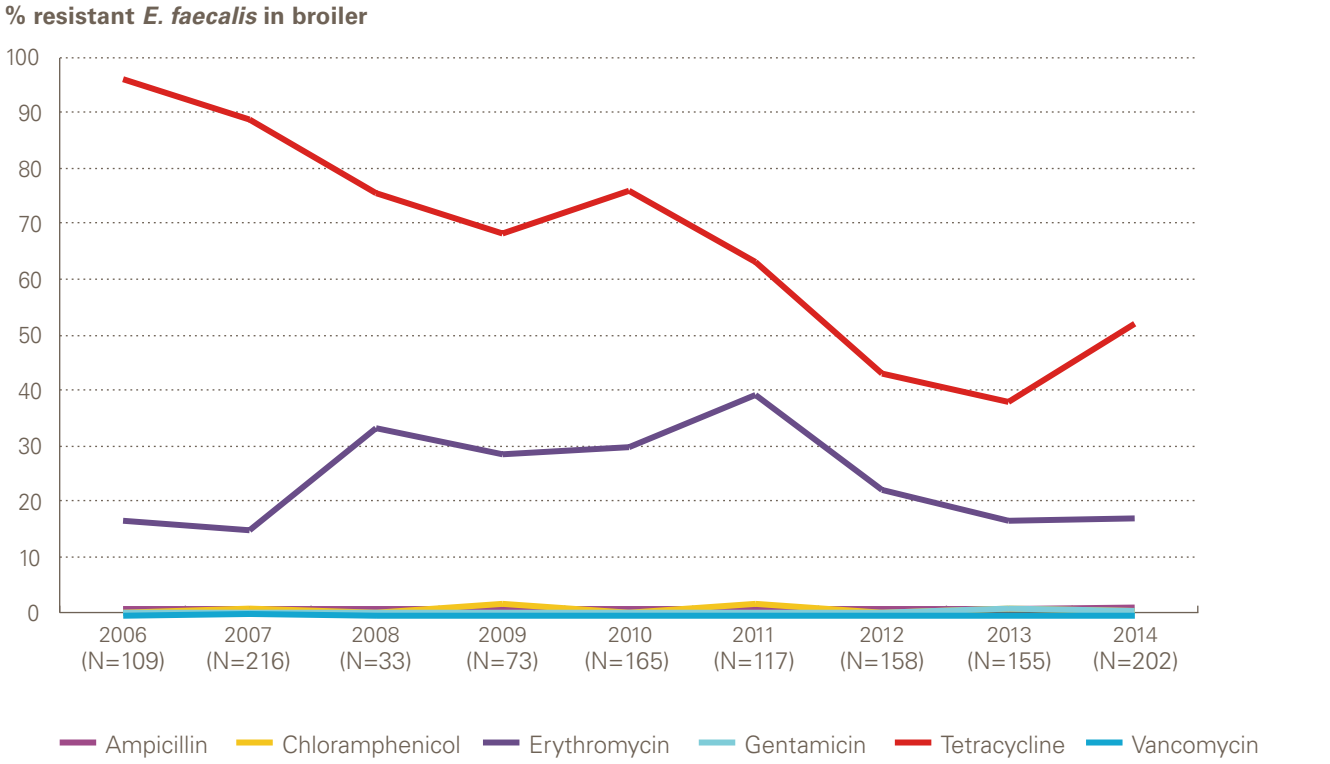


Figure 9. b: Trends in ampicillin, erythromycin, quinupristin/dalfopristin, tetracycline and vancomycin resistance in *Enterococcus faecium* from broilers between 2006 and 2014 (N = total number of tested isolates).

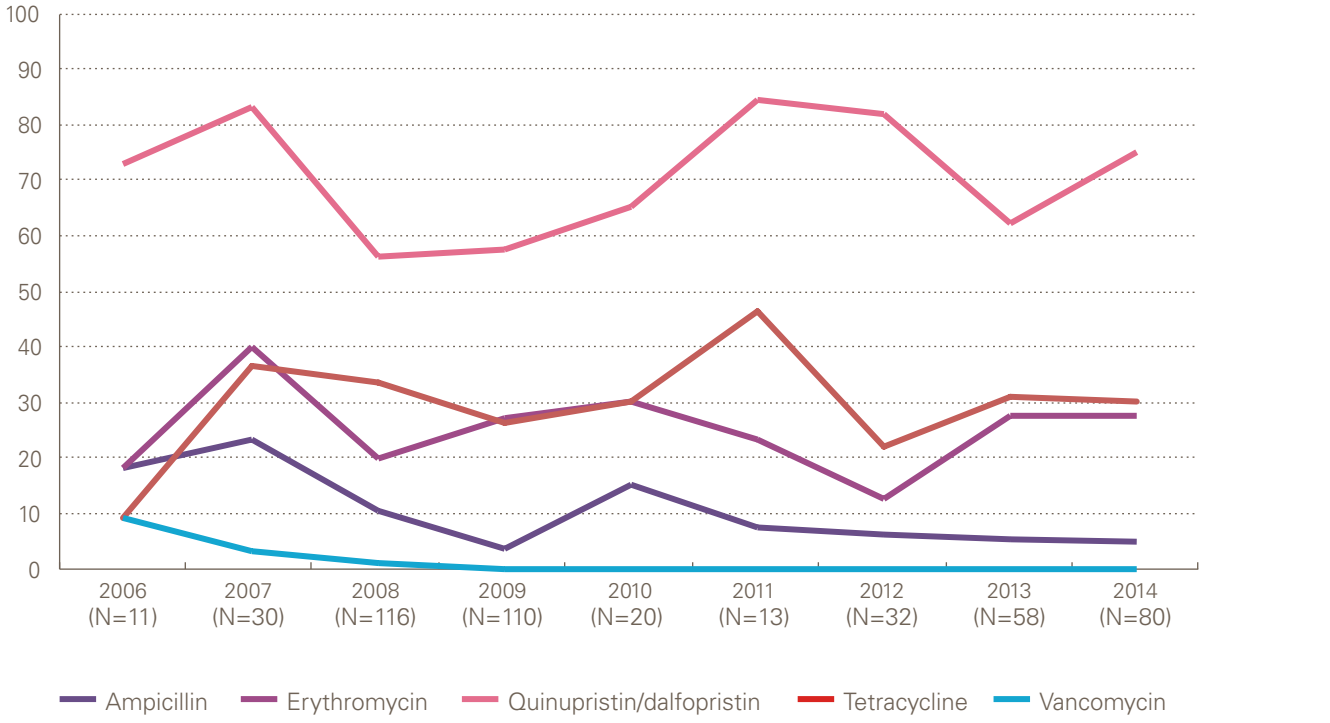


Figure 9. c: Trends in ampicillin, chloramphenicol, erythromycin, gentamicin, tetracycline and vancomycin resistance in *Enterococcus faecalis* from veal calves between 2006 and 2015 (N = total number of tested isolates; values for 2007, 2008, 2009, 2011, 2012 and 2014 interpolated [n/a]).

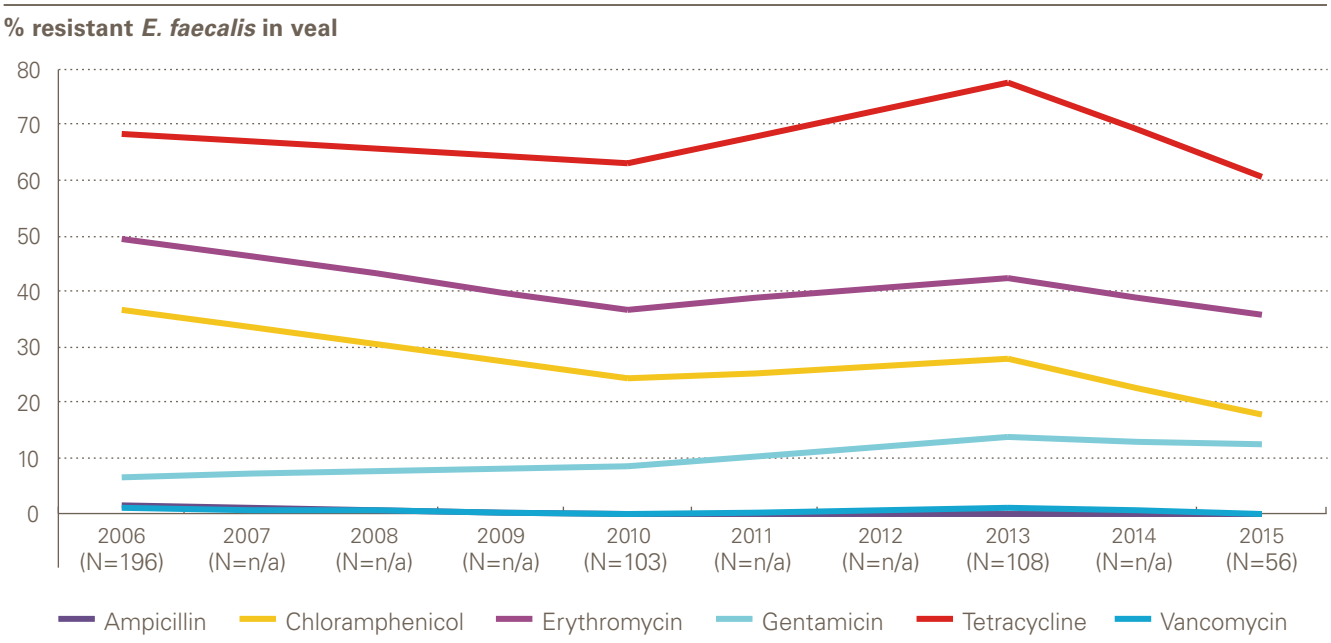
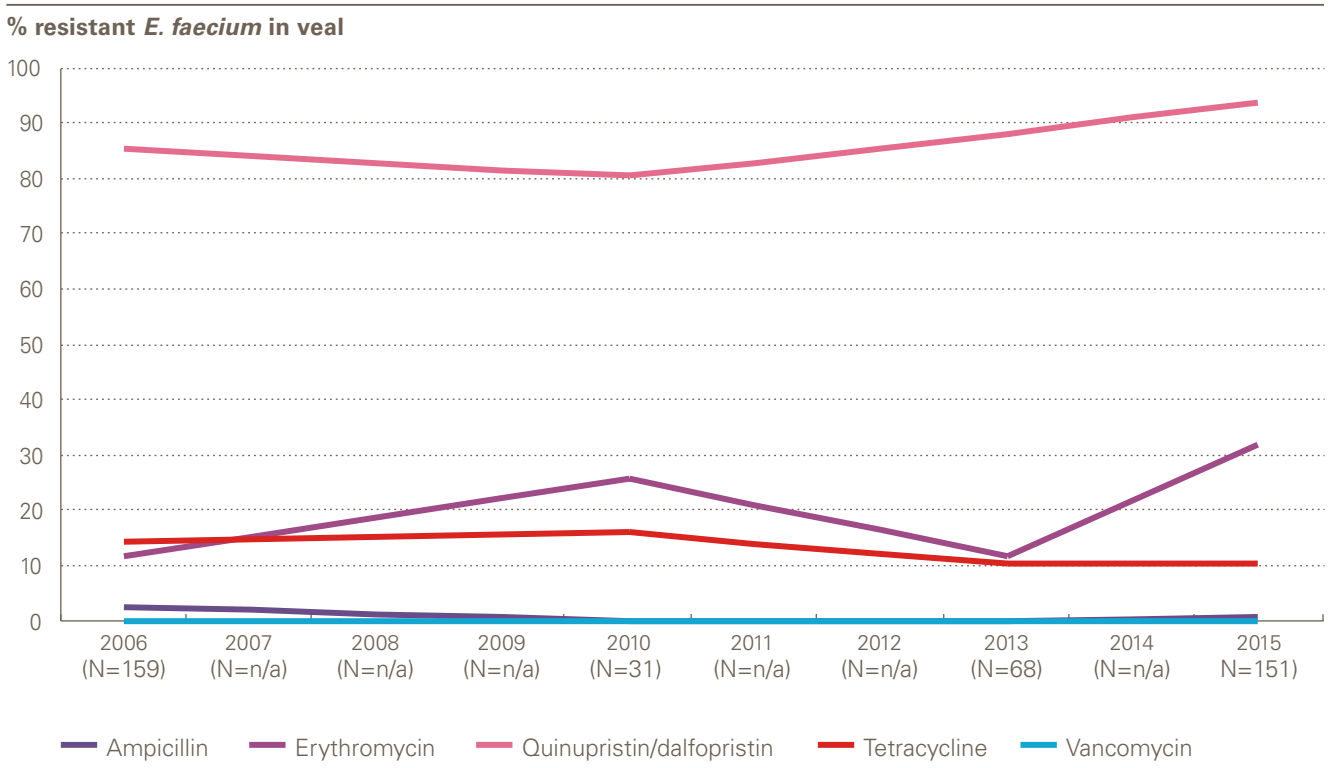


Figure 9. d: Trends in ampicillin, erythromycin, quinupristin/dalfopristin, tetracycline and vancomycin resistance in *Enterococcus faecium* from veal calves between 2006 and 2015 (N = total number of tested isolates; values for 2007, 2008, 2009, 2011, 2012, and 2014 interpolated [n/a]).



Ampicillin is a first-line treatment for infections caused by enterococci in human medicine and is also used in combination with gentamicin for severe infections. Ampicillin resistance is very low or not observable among *E. faecalis* isolates from broilers (5%), fattening pigs and veal calves. An increasing resistance rate to ampicillin (15.1%) is solely observed for *E. faecium* from fattening pigs since 2011. Gentamicin resistance in *E. faecalis* isolates from all tested species is low to very low.

In the current reporting period, resistance to vancomycin was found in 2 *E. faecium* isolates from fattening pigs. No

Figure 9. e: Trends in ampicillin, chloramphenicol, erythromycin, gentamicin, tetracycline and vancomycin resistance in *Enterococcus faecalis* from fattening pigs between 2006 and 2015 (N = total number of tested isolates; values for 2008, 2013 and 2014 interpolated [n/a]).

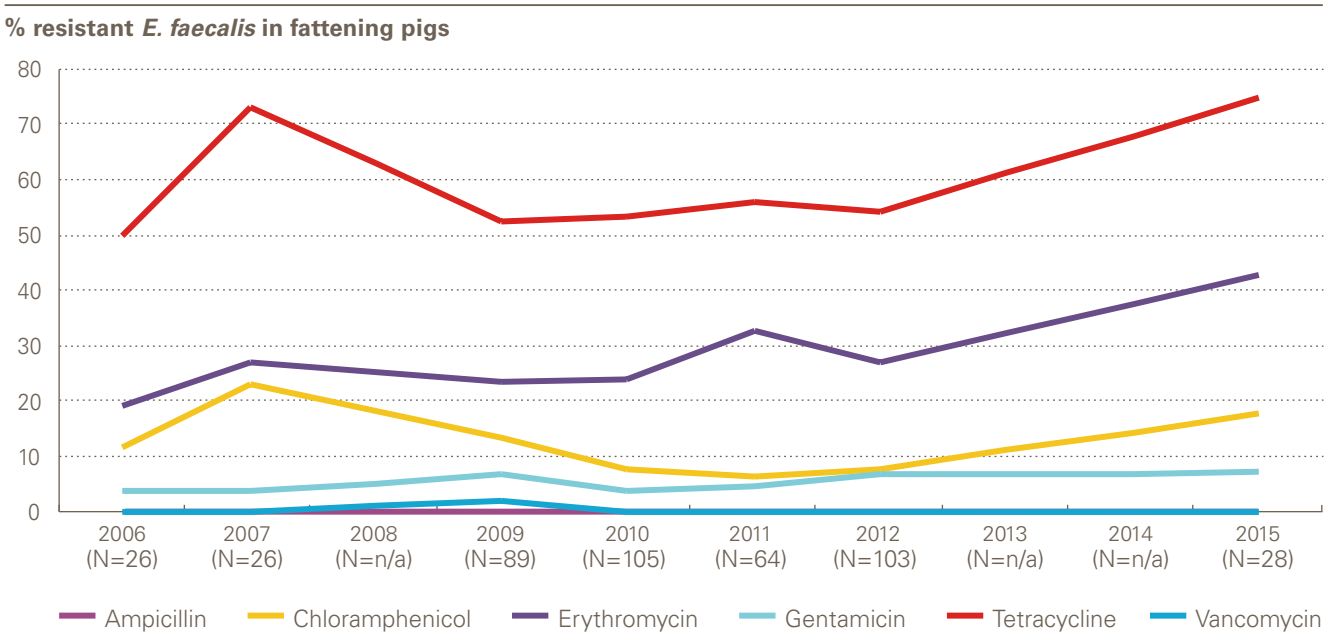
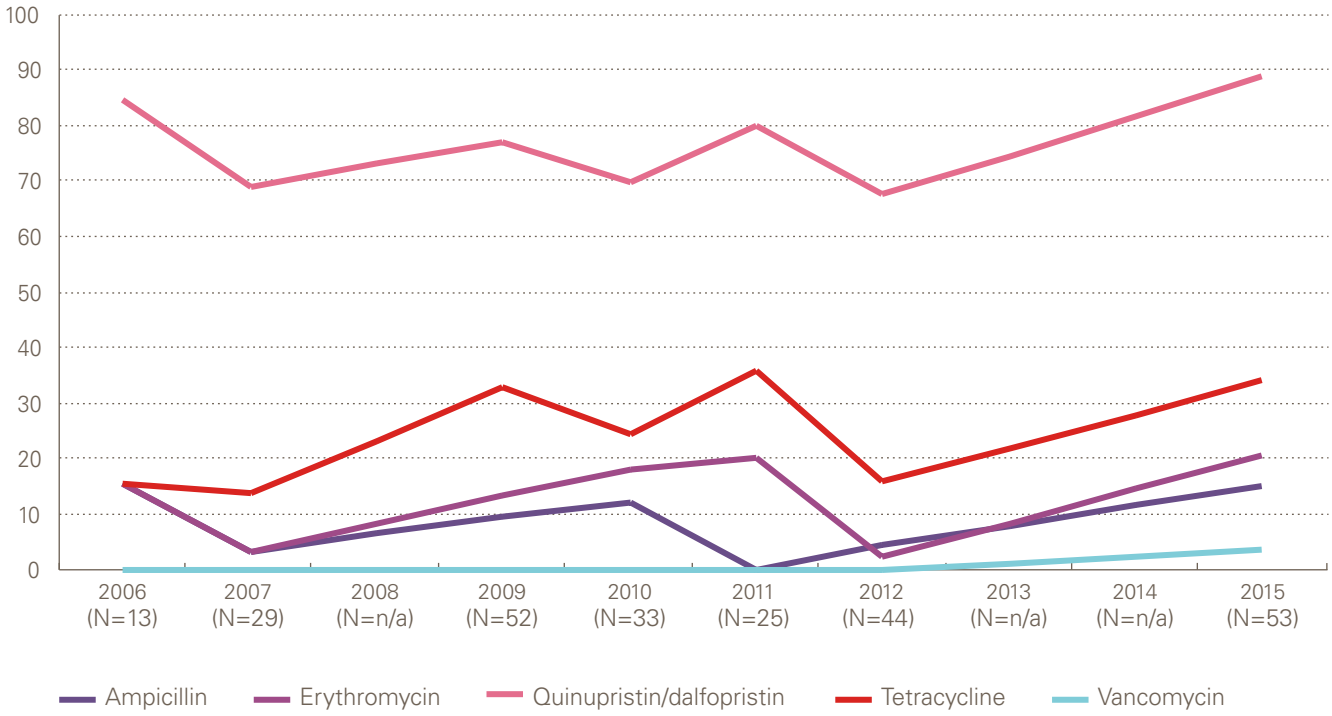


Figure 9. f: Trends in ampicillin, erythromycin, quinupristin/dalfopristin, tetracycline and vancomycin resistance in *Enterococcus faecium* from fattening pigs between 2006 and 2015 (N = total number of tested isolates; values for 2008, 2013 and 2014 interpolated [n/a]).



enterococci isolates were resistant to linezolid. Vancomycin, a glycopeptide antibiotic, is used in combination with gentamicin instead of ampicillin if resistance to ampicillin is present. Linezolid is the drug of choice for the treatment of severe infections with vancomycin-resistant enterococci (VRE).

The emergence of vancomycin resistance in bacteria from livestock is linked to the use of avoparcin as a growth promoter. As a result, avoparcin was prohibited as growth promoter in Europe in 1997. After the ban, a decreased incidence of VRE in the livestock population and a smaller proportion of people with VRE gut colonization could be

verified [2]. Today, rates of resistance are low to very low in all European countries in which the level of vancomycin resistance in enterococci is investigated [3]. Resistance monitoring in livestock in Switzerland has not detected any vancomycin resistance in enterococci for many years. However, resistance was detected in 1 *E. faecalis* isolate from veal calves in 2013 and in 2 *E. faecium* isolates from fattening pigs in 2015.

Very high levels of microbiological resistance to quinupristin/dalfopristin in *E. faecium* from broilers, veal calves and fattening pigs remain widespread. *E. faecalis* is not susceptible to quinupristin/dalfopristin due to its intrinsic resistance. The drug combination was originally recommended as an alternative for the treatment of VRE infections in humans. Nowadays, new antimicrobials such as linezolid or tigecycline are available for the treatment of human VRE infections.
In veterinary medicine, quinoprustin/dalfopristin has never been used. Other streptogramins (e.g. virginiamycin) had been used for prophylactic treatment (although not in Switzerland). But this type of indication has been prohibited throughout Europe since the late 1990s in veterinary medicine.

One explanation for the high resistance levels in isolates from livestock could be cross-resistance of streptogramins, macrolides and lincosamides. Both macrolides and lincosamides are often used as medicated premixes in livestock.

Monitoring of antimicrobial resistance in humans in Switzerland shows that the proportion of clinical infections with vancomycin-resistant enterococci in the past years is at a low level (0.7% in 2015) [4]. VRE remains a widely feared hospital pathogen. However, transmission to humans via animals or food of animal origin plays a minor role due to its low prevalence in animals.

Since 2014, enterococci isolates have been tested for resistance to newer antimicrobials such as daptomycin, teicoplanin and tigecycline, given their importance for human health. In 2014, 89 *E. faecalis* isolates from broilers and all enterococci isolates from veal calves and fattening pigs in 2015 have been tested. Microbiological resistance to daptomycin was found in 1 *E. faecium* isolate from broilers (1.1%), 6 *E. faecium* isolates from veal calves (4%) and 9 *E. faecium* isolates from fattening pigs (17%). Resistance to teicoplanin

Table 9. d: Occurrence of resistance in *Escherichia coli* from broilers

***Escherichia coli* (N=200)**			**2014**
Antimicrobials	**n**	**%**	**95% CI**
Ampicillin	45	22.5	17.3–28.8
Azithromycin	1	0.5	0.1–2.8
Cefepime	5	2.5	1.1–5.7
Cefotaxime	6	3.0	1.4–6.4
Cefoxitin	2	1.0	0.3–3.6
Ceftazidime	5	2.5	1.1–5.7
Chloramphenicol	6	3.0	1.4–6.4
Ciprofloxacin	64	32.0	25.9–38.8
Colistin	0	0.0	0.0–1.9
Ertapenem	0	0.0	0.0–1.9
Gentamicin	2	1.0	0.3–3.6
Imipenem	0	0.0	0.0–1.9
Meropenem	0	0.0	0.0–1.9
Nalidixic acid	67	33.5	27.3–40.3
Sulfamethoxazole	50	25.0	19.5–31.4
Temocillin	0	0.0	0.0–1.9
Tetracycline	45	22.5	17.3–28.8
Tigecycline	0	0.0	0.0–1.9
Trimethoprim	24	12.0	8.2–17.2
Number of resistances	**n**	**%**	**95% CI**
None	87	43.5	36.8–50.4
1 antimicrobial	20	10.0	6.6–14.9
2 antimicrobials	42	21.0	15.9–27.2
3 antimicrobials	18	9.0	5.8–13.8
4 antimicrobials	16	8.0	5.0–12.6
>4 antimicrobials	17	8.5	5.4–13.2

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

was only found in 2 *E. faecium* isolates from fattening pigs (3.8%).

None of the enterococci isolates from veal calves or fattening pigs showed resistance to tigecycline, while 59 *E. faecalis* isolates (66.3%) from broilers did. Tigecycline is not used in veterinary medicine but plays an important role in the treatment of human VRE infections. A coselection of resistance to tigecycline and tetracycline cannot be excluded as they are chemically related to each other. Concomitantly, *E. faecalis* isolates from broilers are also highly resistant to tetracycline [5].

9.2 *Escherichia coli*

9.2.1 *Escherichia coli* from broilers

In 2014, a random sample of 205 broiler flocks was investigated at slaughter in the framework of the antimicrobial resistance monitoring program using cloacal swabs (5 pooled swabs per flock). Two hundred one *Escherichia coli* strains were isolated and 200 were subjected to susceptibility testing (Table 9. d).

Seven isolates were either resistant to cefotaxime or ceftazidime on the first panel (EUVSEC) and were therefore presumptive ESBL/AmpC producers. They were tested on a supplementary panel (EUVSEC2) including following antimicrobials: cefepime, Cefoxitin, ertapenem, imipenem, meropenem and temocillin. Six of those isolates showed phenotypically characteristic MIC values for ESBL/pAmpC producers. One isolate showed no resistance to cefotaxime or ceftazidin on the second panel and was therefore rated ESBL negative. No isolate was resistant to carbapenems.

Of the 200 tested *E. coli* isolates, 43.5% were susceptible to all tested antimicrobials, whereas 8.5% of the tested isolates were microbiological resistant to more than 4 antimicrobials. Microbiological resistance was most frequently detected for ampicillin, ciprofloxacin, nalidixic acid, sulfamethoxazole and tetracycline, with resistance levels

Table 9. e: Occurrence of resistance in *Escherichia coli* from fattening pigs.

***Escherichia coli* (N = 182)**			**2015**
Antimicrobials	**n**	**%**	**95% CI**
Ampicillin	31	17.0	12.3–23.2
Azithromycin	0	0.0	0.0–2.1
Cefepime	0	0.0	0.0–2.1
Cefotaxime	0	0.0	0.0–2.1
Cefoxitin	0	0.0	0.0–2.1
Ceftazidime	0	0.0	0.0–2.1
Chloramphenicol	15	8.2	5.1–13.2
Ciprofloxacin	6	3.3	1.5–7.0
Colistin	0	0.0	0.0–2.1
Ertapenem	0	0.0	0.0–2.1
Gentamicin	3	1.6	0.6–4.7
Imipenem	0	0.0	0.0–2.1
Meropenem	0	0.0	0.0–2.1
Nalidixic acid	6	3.3	1.5–7.0
Sulfamethoxazole	76	41.8	34.8–49.0
Temocillin	0	0.0	0.0–2.1
Tetracycline	54	29.7	23.5–36.7
Tigecycline	0	0.0	0.0–2.1
Trimethoprim	40	22.0	16.6–28.5
Number of resistances	**n**	**%**	**95% CI**
None	85	46.7	39.6–53.9
1 antimicrobial	33	18.1	13.2–24.4
2 antimicrobials	25	13.7	9.5–19.5
3 antimicrobials	18	9.9	6.3–15.1
4 antimicrobials	12	6.6	3.8–11.2
> 4 antimicrobials	9	4.9	2.6–9.1

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

between 22.5% and 33.5%. These are slightly lower levels than in previous years (Figure 9. g)

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.27) and multi-resistance patterns are shown in Annexe III (Table III.7).

9.2.2 *Escherichia coli* from fattening pigs

In 2015, a random sample of 197 fattening pigs was investigated at slaughter in the framework of the antimicrobial resistance monitoring program using caecum samples. *E. coli* was isolated from 182 samples which were subjected to susceptibility testing (Table 9. e).

Susceptibility to all tested antimicrobials was found in 46.7% of the isolates. High levels of resistance to sulfamethoxazole, tetracycline and trimethoprim were found and a moderate level of resistance to ampicillin. Resistance levels in 2015 were generally comparable to those in previous years (Figure 9. e). Four isolates were resistant to either cefotaxime or ceftazidime on the first panel and were therefore presumtive ESBL/AmpC producers. However, none of those showed resistance to cefotaxime or ceftazidime on the supplementary panel (EUVSEC2) and were therefore rated as ESBL/AmpC negative.

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.28 & Table II.29).

9.2.3 *Escherichia coli* from veal calves

In 2015, a random sample of 205 veal calves was investigated at slaughter in the framework of the antimicrobial resistance monitoring program using caecum samples. *E. coli* was isolated from 190 samples which were subjected to susceptibility testing (Table 9. f).

Of the isolates, 47.9% were susceptible to all antimicrobials tested. High levels of resistance to ampicillin, sulfamethoxazole and tetracycline were found and moderate resistance levels to trimethoprim and chloramphenicol. Seven isolates were

Table 9. f: Occurrence of resistance in *Escherichia coli* from veal calves.

***Escherichia coli* (N = 190)**			**2015**
Antimicrobials	**n**	**%**	**95% CI**
Ampicillin	70	36.8	30.3–43.9
Azithromycin	1	0.5	0.1–2.9
Cefepime	4	2.1	0.8–5.3
Cefotaxime	4	2.1	0.8–5.3
Cefoxitin	0	0.0	0.0–2.0
Ceftazidime	4	2.1	0.8–5.3
Chloramphenicol	22	11.6	7.8–16.9
Ciprofloxacin	13	6.8	4.0–11.4
Colistin	1	0.5	0.1–2.9
Ertapenem	0	0.0	0.0–2.0
Gentamicin	11	5.8	3.3–10.1
Imipenem	0	0.0	0.0–2.0
Meropenem	0	0.0	0.0–2.0
Nalidixic acid	12	6.3	3.6–10.7
Sulfamethoxazole	79	41.6	34.8–48.7
Temocillin	0	0.0	0.0–2.0
Tetracycline	77	40.5	33.8–47.6
Tigecycline	0	0.0	0.0–2.0
Trimethoprim	30	15.8	11.3–21.6
Number of resistances	**n**	**%**	**95% CI**
None	91	47.9	40.9–55.0
1 antimicrobial	15	7.9	4.8–12.6
2 antimicrobials	20	10.5	6.9–15.7
3 antimicrobials	27	14.2	10.0–19.9
4 antimicrobials	12	6.3	3.6–10.7
> 4 antimicrobials	25	13.2	9.1–18.7

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

either resistant to cefotaxime, ceftazidime or meropenem on the first panel (EUVSEC) and were therefore presumptive ESBL/AmpC producers. They were tested on the supplementary panel (EUVSEC2). Four of these isolates showed phenotypically characteristic MIC-values for ESBL/pAmpC producers. No isolate was resistant to carbapenems after testing on the second panel.

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.30 & Table II.31).

9.2.4 Discussion

In the context of monitoring antimicrobial resistance, *E. coli* are indicator bacteria for the occurrence of resistances in gram-negative intestinal bacteria from livestock. They constitute a reservoir of resistance genes that can be transferred horizontally to other bacteria including zoonotic agents.

From 2006 to 2012, the prevalence of *E. coli* from broilers in Switzerland exhibiting resistance to ciprofloxacin increased significantly (Figure 9. g). In the following years, the prevalence decreased markedly from 46% in 2012 to 32% in 2014. Also, the rates of resistance to ampicillin, sulfamethoxazole and tetracycline from broilers have been regressive since two years.

In contrast, resistance rates of *E. coli* from fattening pigs and veal calves did not change significantly compared to 2013.

In pigs, resistance rates remained more or less unchanged (Figure 9. h) whereas in veal calves, resistance to ampicillin and tetracycline increased slightly from 27.3% and 38.1% in 2013 to 36.8% and 40.5% respectively in 2015 (Figure 9. i.)

Microbiological resistance is widespread in *E. coli* from livestock in Switzerland. Moderate to high resistance rates to ampicillin, sulfamethoxazole and tetracycline have been found in isolates from all animals. In broilers additionally, the resistance rate to ciprofloxacin is high. Sulfonamides, tetracyclines and penicillins are the most widely used antimicrobials in pigs and calves in Switzerland. In broilers, mostly fluoroquinolones are used. This suggests that the resistance situation found in non-pathogenic *E. coli* from the gastrointestinal tract in livestock actually reflects the selective pressure bacteria are exposed to as a result of using antimicrobials during production.

Although the application of chloramphenicol in livestock was prohibited in 2001, resistance was detected in broilers (3%), fattening pigs (8.2%) and veal calves (11.6%). This could potentially be due to coselection with other antimicrobials. Additionally, cross-resistance between chloramphenicol and florfenicol has been described [6]. Florfenicol is often used in pigs and cattle to treat respiratory tract infections.

Figure 9. g: Trends in ampicillin, ciprofloxacin, gentamicin, sulfamethoxazole and tetracycline resistance in *Escherichia coli* from broilers between 2006 and 2014 (N = total number of tested isolates).

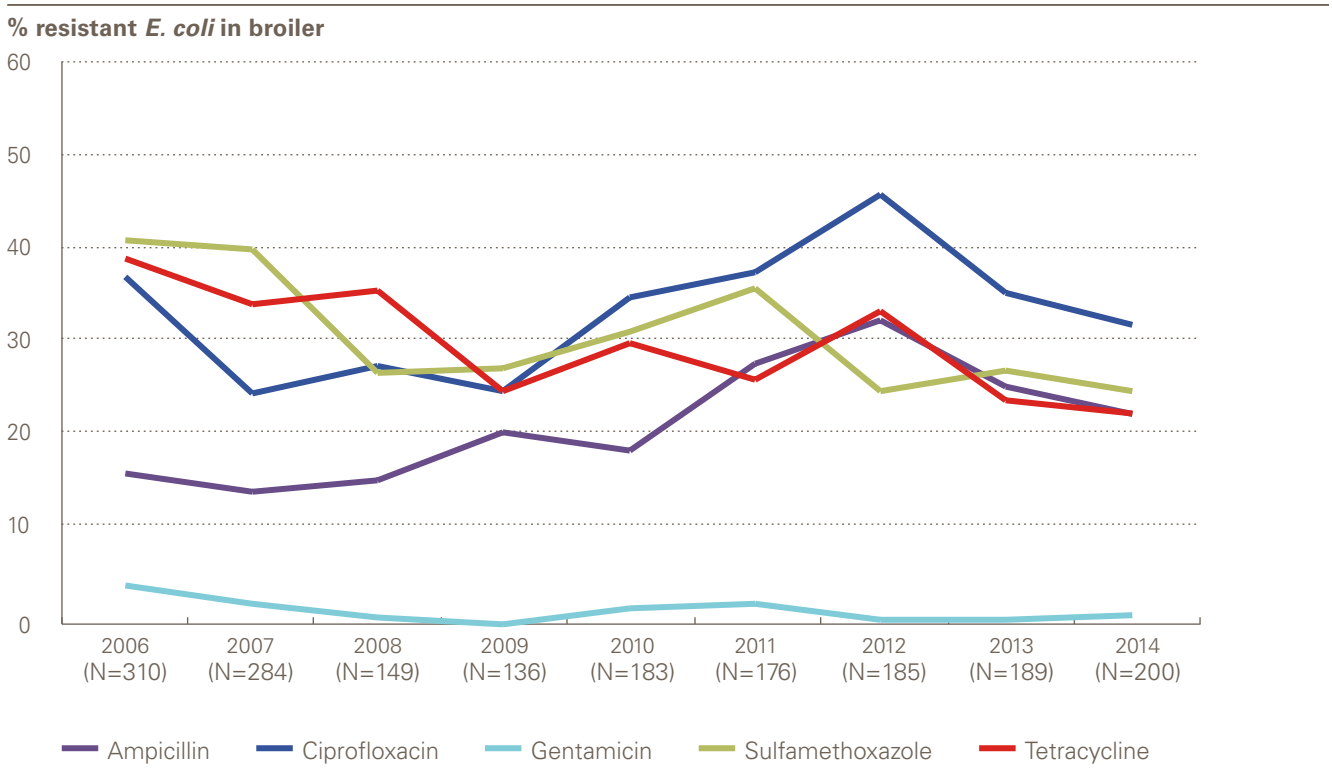


Figure 9. h: Trends in ampicillin, ciprofloxacin, gentamicin, sulfamethoxazole and tetracycline resistance in *Escherichia coli* from fattening pigs between 2006 and 2015 (N = total number of tested isolates, values for 2008 and 2014 interpolated [n/a]).

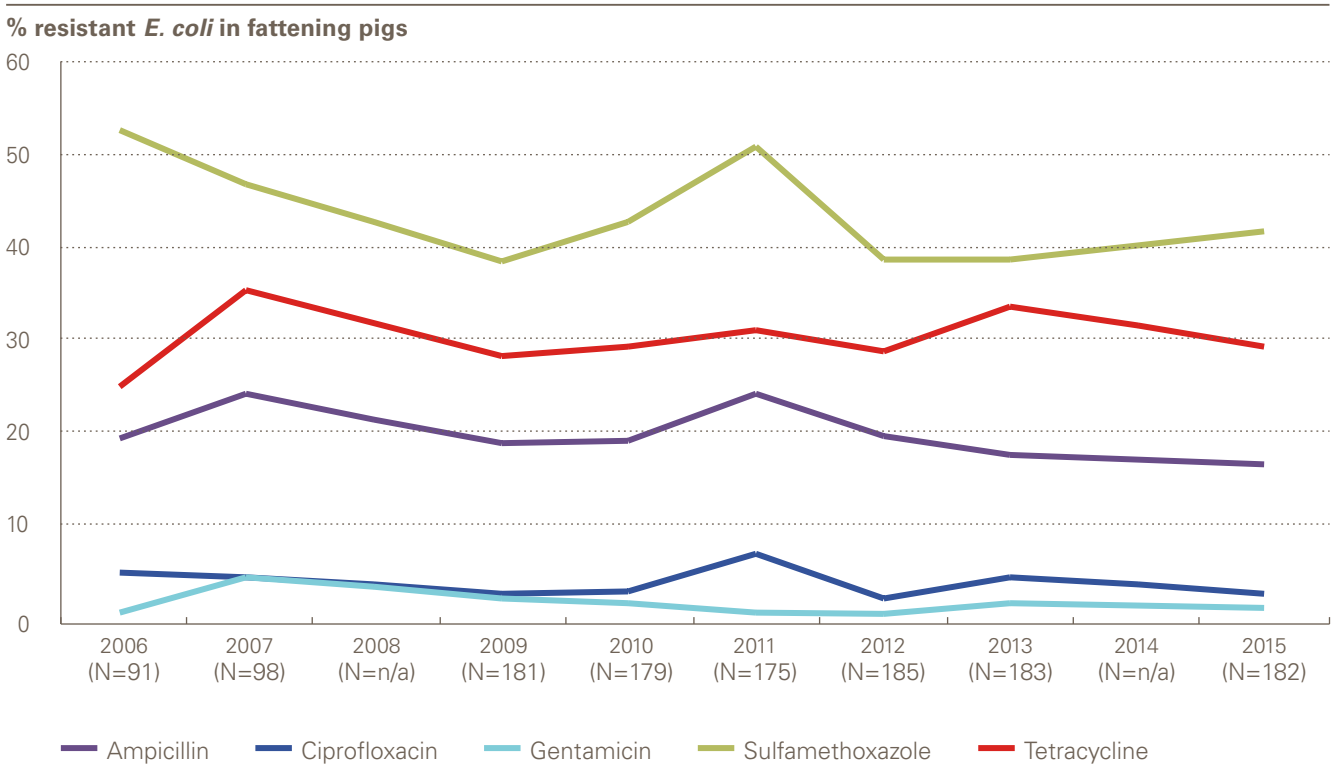
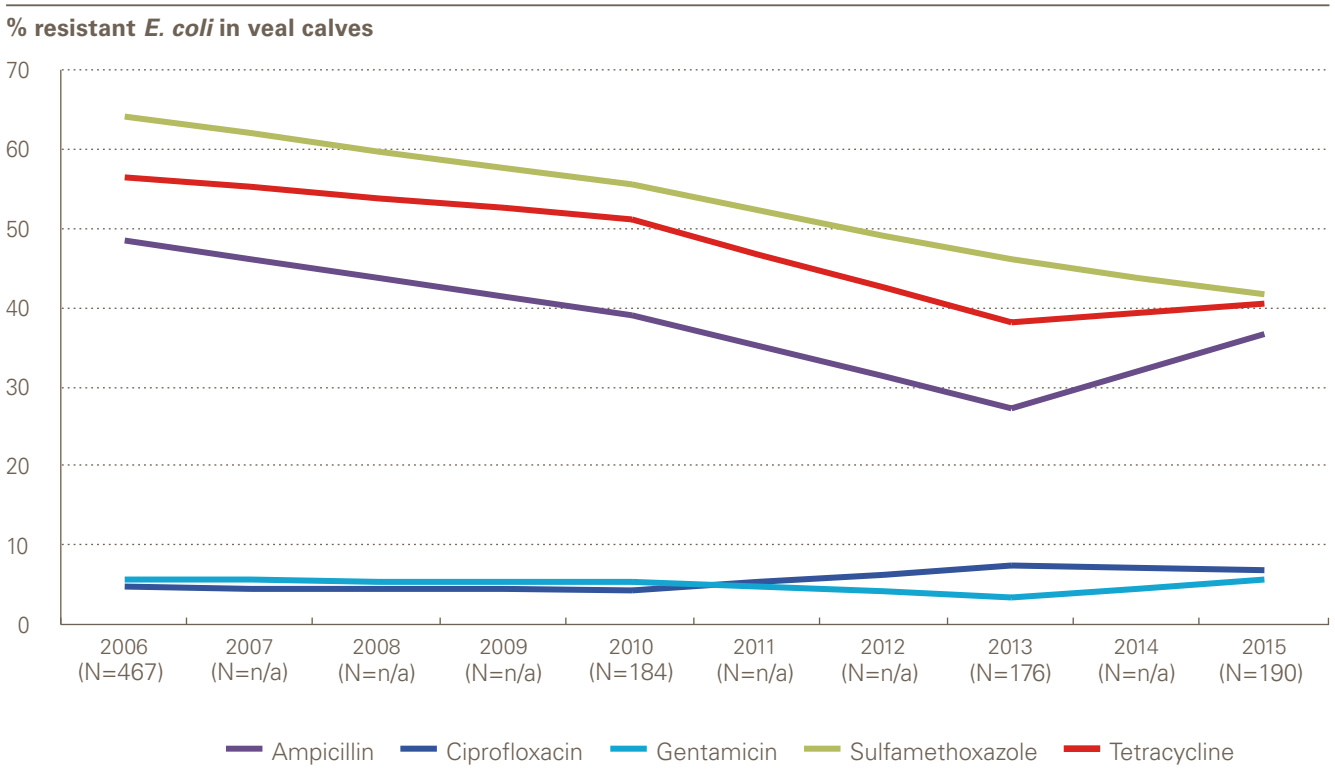


Figure 9. i: Trends in ampicillin, ciprofloxacin, gentamicin, sulfamethoxazole and tetracycline resistance in *Escherichia coli* from veal calves between 2006 and 2015 (N=total number of tested isolates, values for 2007, 2008, 2009, 2011, 2012 and 2014 interpolated [n/a]).



Textbox 9. a

Colistin resistance in pigs and calves, Switzerland 2015.

Vincent Perreten[1], Gudrun Overesch[2]

[1] Molecular Epidemiology and Infectiology; [2] ZOBA, Institute of Veterinary Bacteriology, Vetsuisse Faculty Bern, University of Bern

The discovery of the transferrable plasmid-mediated colistin resistance gene mcr-1 in November 2015 in China [1] and its subsequent detection in animals, humans, vegetables and environment in many different countries around the world has raised the question whether food-producing animals in Switzerland also contain this gene.

Caecum samples of pigs and calves, collected by the Swiss National Monitoring of Antibiotic Resistance using a sampling strategy representative of the slaughtered animals in Switzerland, could retrospectively be screened for the presence of colistin-resistant *Escherichia coli* using a selective enrichment broth and selective plates and tested for the presence of the mcr-1 gene [2].

Colistin-resistant *E. coli* with MIC > 4 µg/ml were found in 2 of 257 caecum samples from pigs and in 5 of 257 caecum samples from calves, corresponding to a prevalence of 0.8% (95% CI 0.2–3%) in pigs and of 2% (95% CI 0.2–3%) in calves. Out of the 8 colistin-resistant *E. coli,* only one from pigs was found to contain the plasmid-mediated colistin resistance gene mcr-1.

Although the prevalence of colistin resistance in *E. coli* from pigs and calves was found to be low in 2015 and mainly not associated with the transferable mcr-1 gene, it is necessary to take advantage of this favorable situation by preventing uncontrolled selection of colistin-resistant bacteria in food-producing animals in Switzerland and to further monitor resistance of clinically important antibiotics in the Swiss animal population. In this regard, selective screening of colistin-resistant Enterobacteriaceae has been implemented into the National Montoring as it is also established for the surveillance of resistance to 3rd-generation cephalosporins and carbapenems.

References

[1] Liu YY, Wang Y, Walsh TR, Yi LX, Zhang R, Spencer J, Doi Y, Tian G, Dong B, Huang X, Yu LF, Gu D, Ren H, Chen X, Lv L, He D, Zhou H, Liang Z, Liu JH, Shen J. 2016. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. Lancet Infect Dis 16: 161–168

[2] Bernasconi OJ, Kuenzli E, Pires J, Tinguely R, Carattoli A, Hatz C, Perreten V, Endimiani A. 2016. Travelers can import colistin-resistant Enterobacteriaceae, including those possessing the plasmid-mediated mcr-1 gene. Antimicrob Agents Chemother. 60: 5080–5084

(These data were obtained with financial support from the Federal Food Safety and Veterinary Office [FSVO] grant no. 1.15.07 within the framework of the Animal Health and Welfare [ANIHWA] ERA-Net project "Prevalence and optimised detection of resistance to antibiotics vital for animal and human health [PRAHAD]".)

9.3 ESBL/pAmpC-producing *Escherichia coli*

In recent years, broad-spectrum beta-lactamase-producing intestinal bacteria have increasingly been detected among livestock in various countries. Not only bacteria producing extended-spectrum beta-lactamase (ESBL) but also bacteria producing plasmid-encoded AmpC (pAmpC) have been frequently found. Beta-lactamases are bacterial enzymes that enable bacteria to inactivate beta-lactam antimicrobials by breaking their beta-lactam ring. ESBL-producing intestinal bacteria are resistant to most beta-lactams, especially aminopenicillins (e.g. ampicillin), cephalosporins (inclusive third and fourth generation) and monobactams. pAmpC beta-lactamases mediate resistance to penicillins, second- and third-generation cephalosporins (including beta-lactama inhibitors such as clavulanic acid) and cephamycins. However, they do not usually mediate resistance to fourth generation cephalosporins and carbapenems.

Both ESBL and pAmpC are produced by intestinal bacteria. Most of them are commensals and do not induce any illness in the host. These bacteria constitute a reservoir for resistance genes that can be transmitted to pathogens by means of mobile genetic elements such as plasmids, integrons and transposons. However, resistance genes may also occur in zoonotic pathogens (e.g. *Salmonella* or enterohaemorrhagic *E. coli*). Although diseases caused by such pathogens usually do not require antimicrobial treatment, the disease may take a severe course in vulnerable patients such as young children, elderly people or patients with a depressed immune system, rendering antimicrobial treatment necessary. Pathogenic bacteria harboring an ESBL or pAmpC resistance are hard to treat, thus prolonging or worsening disease course. The occurrence of such bacteria in the context of severe infections of hospitalized humans in Switzerland has increased from 0.9% in 2004 to 10.8% in 2015 [7].

As a consequence thereof, *E. coli* isolates from animals are also used to gauge the spread of bacteria that produce ESBL or pAmpC.

9.3.1 ESBL/pAmpC-producing *Escherichia coli* in broilers

In 2014, a random sample of 297 broiler flocks was investigated at slaughter using cloacal swabs (5 pooled swabs per flock). By applying selective enrichment methods, 124 isolates of presumptive ESBL/pAmpC-producing *E. coli* were isolated. This corresponds to a flock prevalence of 41.8%. These isolates were then subjected to susceptibility testing (Table 9. g).

Apart from resistance to beta-lactam antimicrobials, recorded resistance levels to sulfonamides (62.1%), tetracycline (53.2%), ciprofloxacin (44.4%), nalidixic acid (39.5%) and trimethoprim (30.6%) were detected. 85.5% of the isolates were resistant to cefepime. Cefepime is a fourth-generation cephalosporin which is more stable to some beta-lactamases. Thus, observed resistance to cefepime serves as an indicator for the presence of ESBL-producers. 44.4% of the isolates were microbiologically resistant to cefoxitin, which is indicative for the presence of AmpC-beta-lactamases. 17.7% of the isolates showed phenotypically reduced susceptibility to ertapenem, whereas microbiological resistances to imipenem and meropenem, azithromycin, colistin, temocillin and tigecycline were not detected.

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.32 & Table II.33) and multi-resistance patterns are shown in Annexe III (Table III.8).

9.3.2 ESBL/pAmpC-producing *Escherichia coli* in chicken meat

In 2014, 319 samples of retail chicken meat were collected (194 domestic samples, i.e. chicken meat produced in Switzerland, and 125 imported samples, i.e. chicken meat produced abroad). By applying selective enrichment methods, 234 presumptive ESBL/pAmpC-producing *E. coli* strains

Table 9. g: Occurrence of resistance in ESBL/pAmpC-producing *Escherichia coli* from broilers.

ESBL/pAmpC-producing *Escherichia coli* (N = 124)			**2014**
Antimicrobials	**n**	**%**	**95% CI**
Ampicillin	124	100.0	97.0–100.0
Azithromycin	0	0.0	0.0–3.0
Cefepime	106	85.5	78.2–90.6
Cefotaxime	124	100.0	97.0–100.0
Cefoxitin	55	44.4	35.9–53.1
Ceftazidime*	113	91.1	83.8–94.4
Chloramphenicol	23	18.5	12.7–26.3
Ciprofloxacin	55	44.4	35.9–53.1
Colistin	0	0.0	0.0–3.0
Ertapenem	22	17.7	12.0–25.4
Gentamicin	0	0.0	0.0–3.0
Imipenem	0	0.0	0.0–3.0
Meropenem	0	0.0	0.0–3.0
Nalidixic acid	49	39.5	31.4–48.3
Sulfamethoxazole	77	62.1	53.3–70.2
Temocillin	0	0.0	0.0–3.0
Tetracycline	66	53.2	44.5–61.8
Tigecycline	0	0.0	0.0–3.0
Trimethoprim	38	30.6	23.2–39.2
Number of resistances	**n**	**%**	**95% CI**
None	0	0.0	0.0–3.0
1 antimicrobial	0	0.0	0.0–3.0
2 antimicrobials	0	0.0	0.0–3.0
3 antimicrobials	3	2.4	0.8–6.9
4 antimicrobials	13	10.5	10.2–17.1
> 4 antimicrobials	108	87.1	80.1–91.9

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval
* Result of EUVSEC plate

were isolated. This corresponds to a prevalence of 73.4%. 232 of these strains were subjected to susceptibility testing (Table 9. h).

Out of 194 domestic samples (chicken meat of Swiss origin), 107 were tested positive (65.5%). In contrast, 107 out of 125 foreign samples were tested positive, corresponding to a prevalence of 85.6%.

Apart from the resistance to beta-lactam antimicrobials, high to very high microbiological resistance levels to sulfonamides (53.4%), fluoroquinolones (48.7%), tetracycline (42.7%), quinolones (40.9%) and trimethoprim (25.4%) were found. The portion of isolates resistant to cefepime was 67.7% and 53% of the isolates were microbiologically resistant to cefoxitin. 8.2% of the isolates displayed phenotypically reduced susceptibility to ertapenem, whereas resistance levels to azithromycin and colistin were low (1.3% and 1.7%). Microbiological resistances to imipenem, meropenem, temocillin and tigecycline were not detected.

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.34 & Table II.35) and multi-resistance patterns are shown in Annexe III (Table III.9).

9.3.3 ESBL/pAmpC-producing *Escherichia coli* in fattening pigs

In 2015, 77 ESBL/pAmpC-producing *E. coli* strains were isolated with selective enrichment methods from a random sample of 300 caecum samples from fattening pigs. This corresponds to a prevalence of 25.7%. All isolates were subjected to susceptibility testing (Table 9. i).

Apart from the resistance to beta-lactam antimicrobials, high to very high microbiological resistance levels to sulfonamides (70.1%), tetracycline (61.0%), trimethoprim (39.0%), ciprofloxacin (35.1%) and nalidixic acid (23.4%) were found. The portion of isolates resistant to cefepime was 74.0%, and 26.0% of the isolates were microbiologically resistant to cefoxitin. Moderate proportions of isolates showed pheno-

Table 9. h: Occurrence of resistance in ESBL/pAmpC-producing *Escherichia coli* from chicken meat.

ESBL/pAmpC-producing *Escherichia coli* (N=232)			**2014**
Antimicrobials	**n**	**%**	**95% CI**
Ampicillin	232	100.0	98.4–100.0
Azithromycin	3	1.3	0.4–3.7
Cefepime	157	67.7	61.4–73.4
Cefotaxime	231	99.6	97.6–99.9
Cefoxitin	123	53.0	46.6–59.3
Ceftazidime*	216	93.1	90.7–0.967
Chloramphenicol	16	6.9	4.3–10.9
Ciprofloxacin	113	48.7	42.3–55.1
Colistin	4	1.7	0.7–4.3
Ertapenem	19	8.2	5.3-12.4
Gentamicin	10	4.3	2.4-7.8
Imipenem	0	0.0	0.0-1.6
Meropenem	0	0.0	0.0-1.6
Nalidixic acid	95	40.9	34.8-47.4
Sulfamethoxazole	124	53.4	47–59.8
Temocillin	0	0.0	0.0–1.6
Tetracycline	99	42.7	36.5–49.1
Tigecycline	0	0.0	0.0–1.6
Trimethoprim	59	25.4	20.3–31.4
Number of resistances	**n**	**%**	**95% CI**
None	0	0.0	0.0–1.6
1 antimicrobial	0	0.0	0.0–1.6
2 antimicrobials	0	0.0	0.0–1.6
3 antimicrobials	13	5.6	3.3–9.3
4 antimicrobials	25	10.8	7.4–15.4
> 4 antimicrobials	194	83.6	78.3–87.8

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval
* Result of EUVSEC plate

typically reduced susceptibility to gentamicin (18.2%) and chloramphenicol (14.3%), whereas the level of resistance to azithromycin (7.8%) was low. Microbiological resistances to colistin, ertapenem, imipenem, meropenem, temocillin and tigecycline were not detected.

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.36 & Table II.37).

9.3.4 ESBL/pAmpC-producing *Escherichia coli* from pork meat

In 2015, 301 pork meat samples were collected from retailers and 3 ESBL/pAmpC-producing *E. coli* were isolated with selective enrichment methods. This corresponds to a prevalence of approximately 1%. Two isolates were subjected to antimicrobial susceptibility testing. Both showed microbiological resistance to all beta-lactam antimicrobials (ampicillin, cefepime, cefoxitin and ceftazidime), sulfamethoxazole and trimethoprim.

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.38 & Table II.39).

9.3.5 ESBL/pAmpC-producing *Escherichia coli* from veal calves

In 2015, 112 ESBL/pAmpC-producing *E. coli* strains were isolated with selective enrichment methods from a random sample of 298 caecum samples from veal calves. This corresponds to a prevalence of 37.6%. All isolates were subjected to susceptibility testing (Table 9. j).

Apart from the resistance to beta-lactam antimicrobials, high to extremely high microbiological resistance levels to sulfonamides (84.8%), tetracycline (83.0%), trimethoprim (55.4%), ciprofloxacin (54.5%) and nalidixic acid (34.8%) were found. The portion of isolates resistant to cefepime was 70.5%, and 33.9% of the isolates were microbiologically resistant to cefoxitin. Moderate proportions of isolates showed phenotypically reduced susceptibility to gentamicin

Table 9. i: Occurrence of resistance in ESBL/pAmpC-producing *Escherichia coli* from fattening pigs.

ESBL/pAmpC-producing *Escherichia coli* (N=77)			**2015**
Antimicrobials	**n**	**%**	**95% CI**
Ampicillin	75	97.4	91.0–99.3
Azithromycin	6	7.8	3.6–16.0
Cefepime	57	74.0	63.3–82.5
Cefotaxime	73	94.8	87.4–98.0
Cefoxitin	20	26.0	17.5–36.7
Ceftazidime	69	89.6	80.8–94.6
Chloramphenicol	11	14.3	8.2–23.8
Ciprofloxacin	27	35.1	25.3–46.2
Colistin	0	0.0	0.0–4.8
Ertapenem	0	0.0	0.0–4.8
Gentamicin	14	18.2	11.2–28.2
Imipenem	0	0.0	0.0–4.8
Meropenem	0	0.0	0.0–4.8
Nalidixic acid	18	23.4	15.3–34.0
Sulfamethoxazole	54	70.1	59.2–79.2
Temocillin	0	0.0	0.0–4.8
Tetracycline	47	61.0	49.9–71.2
Tigecycline	0	0.0	0.0–4.8
Trimethoprim	30	39.0	28.8–50.1
Number of resistances	**n**	**%**	**95% CI**
None	1	1.3	0.2–7.0
1 antimicrobial	2	2.6	0.7–9.0
2 antimicrobials	0	0.0	0.0–4.8
3 antimicrobials	10	13.0	7.2–22.3
4 antimicrobials	9	11.7	6.3–20.7
> 4 antimicrobials	55	71.4	60.5–80.3

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

(38.4%) and chloramphenicol (33.9%), whereas the levels of resistance for azithromycin (7.1%) and ertapenem (2.7%) were low. Microbiological resistances to colistin, imipenem, meropenem, temocillin and tigecycline were not detected.

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.40 & Table II.41).

9.3.6 ESBL/pAmpC-producing *Escherichia coli* from beef meat

In 2015, 298 beef meat samples were collected from retailers and analyzed with selective enrichment methods for ESBL/pAmpC-producing *E. coli.* Only one sample was tested positive for suspected ESBL/pAmpC-producing *E. coli* The isolate was subjected to susceptibility testing and was sensitive to all tested antimicrobials.

The distribution of the minimum inhibitory concentrations (MICs) is shown in Annexe II (Table II.42 & Table II.43).

9.3.7 Carbapenemase-producing *Escherichia coli* from chicken, beef and pork meat

In total, 319 chicken meat, 301 pork meat and 298 beef meat samples were collected from retailers and analyzed with selective enrichment methods for carbapenemase-producing *E. coli.* None of the meat samples tested positive for carbapenemase-producing *E. coli.*

9.3.8 Discussion

Using selective enrichment methods, ESBL/pAmpC-producing *E. coli* were found in 41.8% of broiler flocks, 25.7% of fattening pigs and 37.6% of veal calves. The prevalence of ESBL/pAmpC-producing *E. coli* increased clearly for all investigated animal species compared to 2013 (broilers: 27.7%, fattening pigs: 9.4%, veal calves: 16.6%). A possible explanation is the modification regarding the applied selective growth medium (mid-2014) in accordance with the new EU requirements for the surveillance of antimicrobial

Table 9. j: Occurrence of resistance in ESBL/pAmpC-producing *Escherichia coli* from veal calves.

ESBL/AmpC-producing *Escherichia coli* (N = 112)			**2015**
Antimicrobials	**n**	**%**	**95% CI**
Ampicillin	112	100.0	96.7–100.0
Azithromycin	8	7.1	3.7–13.5
Cefepime	79	70.5	61.5–78.2
Cefotaxime	112	100.0	96.7–100.0
Cefoxitin	38	33.9	25.8–43.1
Ceftazidime	107	95.5	90.0–98.1
Chloramphenicol	38	33.9	25.8–43.1
Ciprofloxacin	61	54.5	45.2–63.4
Colistin	0	0.0	0.0–3.3
Ertapenem	3	2.7	0.9–7.6
Gentamicin	43	38.4	29.9–47.6
Imipenem	0	0.0	0.0–3.3
Meropenem	0	0.0	0.0–3.3
Nalidixic acid	39	34.8	26.6–44.0
Sulfamethoxazole	95	84.8	77.0–90.3
Temocillin	0	0.0	0.0–3.3
Tetracycline	93	83.0	75.0–88.9
Tigecycline	0	0.0	0.0–3.3
Trimethoprim	62	55.4	46.1–64.2
Number of resistances	**n**	**%**	**95% CI**
None	0	0.0	0.0–3.3
1 antimicrobial	0	0.0	0.0–3.3
2 antimicrobials	0	0.0	0.0–3.3
3 antimicrobials	7	6.3	3.1–12.4
4 antimicrobials	7	6.3	3.1–12.4
> 4 antimicrobials	98	87.5	80.1–92.4

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

resistances in zoonotic and commensal bacteria. The new method is more sensitive than the previous. The change from faecal swab samples to caecum samples for fattening pigs and veal calves between 2014 and 2015 might play an additional role. Using the selective method, comparatively lower rates of ESBL/AmpC-producing *E. coli* were found in Switzerland than in other European countries.

Besides microbiological resistance to beta-lactam antimicrobials, the isolates showed high to extremely high rates of resistance to (fluoro-)quinolones, sulfonamides, trimethoprim and tetracycline in all three animal species. Isolates from veal calves and fattening pigs presented moderate to high rates of gentamicin resistance; similarly, isolates of all three animal species showed moderate to high resistance to chloramphenicol. Low levels of resistance to azithromycin were detected in isolates from fattening pigs and veal calves. None of the isolates from all three animal species was resistant to colistin, imipenem, meropenem, temocillin or tigecycline, while low to moderate levels of resistance to ertapenem were found in broiler and veal calves.

An increasing spread of ESBL/pAmpC-producing *E. coli* among food-producing animals has been observed in Europe over the past years, especially among broilers. The prevalence in broiler flocks is influenced by different factors. The prevalence among individual birds increases towards the end of the fattening period. Other influencing factors include flock management, hygiene or use of antimicrobials, especially beta-lactams [8]. ESBL/pAmpC-producing *E. coli* are vertically transmitted along the production chain from grandparents and parents to broilers [9], [10]. Once present in a broiler farm, they spread horizontally from one flock to another. Specific bacteria can also be found in the environment of farms where they are able to survive for extended periods of time and hence are a potential source for further transmission [11]. Another study showed that a horizontal transfer of bacteria from animals to their owners is possible [12].

For the first time, meat samples (chicken, pork, beef) from retailers were tested for ESBL/pAmpC-producing *E. coli* as part of the national antimicrobial resistance monitoring program. The prevalence in chicken meat (73.3%) was extremely high, whereas the prevalence in pork and beef samples was very low (< 1%). For chicken meat, a significant difference could be observed between domestic and imported meat (65.5% vs. 85.6%, Table 9. k).

Table 9. k: Number of samples and number of positive ESBL/pAmpC-producing *E. coli* samples by origin of chicken meat.

Origin	No. of samples	No. of positive samples
Germany	58	48 (82.8)
Slovenia	19	18 (94.7)
Hungary	18	16 (88.9)
France	17	15 (88.2)
Austria	7	6 (85.7)
The Netherlands	3	2 (66.7)
Italy	2	2 (100.0)
Brazil	1	0 (0.0)
Total foreign countries	**125**	**107 (85.6)**
Switzerland	**194**	**127 (65.5)**

Other studies from Switzerland confirm the high prevalence of ESBL/pAmpC-producing *E. coli* observed for chicken meat [13]–[15]. The prevalence of these types of resistance in chicken meat (73.3%) is much higher than the prevalence in broiler flocks (41.8%). This indicates that resistant bacteria are spreading by cross-contamination between animals, processing materials and staff during the slaughter process and/or the subsequent meat processing. ESBL/pAmpC-producing *E. coli* in chicken meat represent a potential source of transmission for humans e.g. by kitchen utensils or hands [16]. As a consequence thereof, adequate kitchen hygiene and proper cooking of raw chicken meat are essential.

The low prevalence of ESBL/pAmpC-producing *E. coli* in pork and beef (< 1%) compared to the prevalence in fattening pigs (25.7%) and veal calves (37.6%) could be attributed to good hygiene measures during slaughtering process.

Until recently, ESBL/pAmpC-producing bacteria were mainly a problem in hospitals. Lately, they have increasingly been found in the general population as well. Here, they either occur harmlessly in the guts of healthy individuals or cause diseases such as urinary tract infections. The incidence of these types of resistance has increased in Switzerland in recent years, both in hospitals and in outpatients [17]. A study carried out in Switzerland with healthy staff of meat-processing plants found ESBL-producing intestinal bacteria in 5.8% of those tested [18]. Another study, which tested 291 faecal swab samples from patients of GP practices, found ESBL-producing bacteria in 5.2% of the samples [19]. Resistance genes of ESBL/pAmpC-producing *E. coli* display a large heterogeneity. The comparison of different genes and resistance patterns from isolates of food producing animals, raw meat and humans shows that the majority of isolates differ considerably [20]–[22]. Food producing animals

and especially chicken meat are seen as an important reservoir for ESBL/pAmpC-producing *E. coli*. Nevertheless, the vast majority of ESBL/pAmpC-producing *E. coli* colonizing humans cannot currently be exclusively attributed to food-producing animals or food.

Textbox 9. b

Acquired colistin resistance gene mcr-1 in imported chicken meat.

Vincent Perreten[1], Gudrun Overesch[2]

[1] Molecular Epidemiology and Infectiology; [2] ZOBA, Institute of Veterinary Bacteriology, Vetsuisse Faculty Bern, University of Bern

Since the first report of the plasmid-mediated colistin resistance gene mcr-1 in November 2015 in China [1], several studies have confirmed its worldwide spread in different animal and human environments and clinical settings. Dissemination of these genes has been associated with travelers and trading of food animals and meat [2, 3].

Retrospective analysis of data from the Swiss National Monitoring of Antibiotic Resistance in food-producing animals and meat revealed the presence of colistin-resistant *E. coli* (MIC > 4 µg/ml) in four samples of chicken meat imported in 2014 and in none of the meat from indigenous production, corresponding to an overall prevalence of 1.3% (95% CI 0.4–3.2%) (ARCH-Vet 2014). The 4 isolates contained the colistin resistance gene mcr-1 and were also resistant to third-generation cephalosporins. They were genetically diverse, indicating different sources of contamination. Further analysis of chicken meat from 2016 confirmed the presence of mcr-1 positive *E. coli* in the imported meat, with 2 of 150 samples being positive for mcr-1 in the first half of the year.

The detection of mcr-1-mediated colistin resistance in *E. coli* from chicken meat emphasizes once again the potential of chicken meat to vehicle bacteria resistant to clinically important antibiotics into households. It should also be noted that 73.5% (95% CI 68.1–78.1%) of the *E. coli* isolated from chicken meat in 2014 exhibited resistance to third-generation cephalosporins. Continuous efforts have to be made at each level of the production, food processing and packaging and surveillance in order to limit the spread of resistant bacteria into the community via the food chain.

References

[1] Liu YY, Wang Y, Walsh TR, Yi LX, Zhang R, Spencer J, Doi Y, Tian G, Dong B, Huang X, Yu LF, Gu D, Ren H, Chen X, Lv L, He D, Zhou H, Liang Z, Liu JH, Shen J. 2016. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. Lancet Infect Dis 16: 161–168

[2] Grami R, Mansour W, Mehri W, Bouallegue O, Boujaafar N, Madec JY, Haenni M. 2016. Impact of food animal trade on the spread of mcr-1-mediated colistin resistance, Tunisia, July 2015. Euro. Surveill. 21

3 Bernasconi OJ, Kuenzli E, Pires J, Tinguely R, Carattoli A, Hatz C, Perreten V, Endimiani A. 2016. Travelers can import colistin-resistant Enterobacteriaceae, including those possessing the plasmid-mediated mcr-1 gene. Antimicrob Agents Chemother. 60:5080-5084

(These data were obtained with financial support from the Federal Food Safety and Veterinary Office [FSVO] grant no. 1.15.07 within the framework of the Animal Health and Welfare [ANIHWA] ERA-Net project "Prevalence and optimised detection of resistance to antibiotics vital for animal and human health [PRAHAD]".)

9.4 Methicillin-resistant *Staphylococcus aureus* (MRSA)

Staphylococcus aureus are skin and mucous membranes colonizing bacteria of humans and animals [23]. Usually, they do not induce any disease. However, in some cases, *S. aureus* bacteria are isolated from infected wounds and inflamed airways. In most cases, infections can be treated without any complications using antimicrobials. However, in the case of methicillin-resistant *S. aureus* (MRSA), an infection is difficult to treat. This kind of bacteria are resistant to all beta-lactams (penicillins and cephalosporins) and some of them are resistant to additional classes of antimicrobials as well. That is why an infection with MRSA may take a severe course.

This chapter includes antimicrobial resistance of MRSA strains in livestock. Broilers and fattening pigs were investigated in 2014, veal calves and fattening pigs in 2015.

9.4.1.1 Fattening pigs

In 2014 and 2015, nasal swabs from fattening pigs at slaughter were used to isolate strains of MRSA, applying selective enrichment methods. Obtained isolates were subjected to *spa* typing and susceptibility testing.

In 2014, 79 isolates were obtained from 298 nasal swabs, corresponding to a prevalence of 26.5%. Fifty-seven isolates belonged to *spa* type t034 (CC398), 19 to spa-type t011 (CC398) and one isolate each belonged to spa-type t208 (CC49), t899 (CC9) and t2741, respectively.

All isolates were microbiologically resistant to beta-lactam antibiotics (cefoxitin, oxacillin and penicillin) and tetracycline (Table 9. l). Very high to extremely high resistance rates were found for macrolides/lincosamides (erythromycin 75.9%, clindamycin 79.7%), tiamulin (78.5%), trimethoprim (74.7%) and streptomycin (59.5%). Low resistance rates were found for kanamycin (8.9%), ciprofloxacin (8.9%), gentamicin (6.3%), sulfamethoxazole (3.8%) and rifampin (1.3%). All isolates were fully susceptible to vancomycin and linezolid, two important antimicrobials for treatment of human patients.

The distribution of the minimum inhibitory concentrations (MICs) are shown in Annexe II (Table II.44 & II.45), the multi-resistance patterns for 2014 data in Annexe III (Table III.10).

In 2015, 77 out of 300 nasal swabs were tested positive for MRSA. This corresponds to a prevalence of 25.7%. Fourty-eight isolates belonged to *spa* type t034 (CC398), 23 to spa-type t011 (CC398) and one each to *spa* type t032, t571 (CC 398), t899, t1145, t1250 and t4475, respectively.

The resistance pattern remained more or less the same compared to previous years. It should be noted that in 2015 another Sensititre custom plate was used, with the consequence that some antimicrobials changed. All isolates were resistant to beta-lactames (cefoxitin, penicillin) and all except one were resistant to tetracycline (Table 9. m). Very high to extremely high resistance rates were found for

Table 9. l: Occurrence of resistance in MRSA from fattening pigs, data of 2014.

Methicillin-resistant *Staphylococcus aureus* (N=79)			**2014**
Antimicrobials	**n**	**%**	**95% CI**
Cefoxitin	79	100.0	95.4–100.0
Chloramphenicol	0	0.0	0.0–4.6
Ciprofloxacin	7	8.9	4.4–17.2
Clindamycin	63	79.7	69.6–87.1
Erythromycin	60	75.9	65.5–84
Fusidic acid	0	0.0	0.0–4.6
Gentamicin	5	6.3	2.7–14
Kanamycin	7	8.9	4.4–17.2
Linezolid	0	0.0	0.0–4.6
Mupirocin	0	0.0	0.0–4.6
Oxacillin	79	100.0	95.4–100.0
Penicillin	79	100.0	95.4–100.0
Rifampin	1	1.3	0.2–6.8
Streptomycin	47	59.5	48.5–69.6
Sulfamethoxazole	3	3.8	1.3–10.6
Tetracycline	79	100.0	95.4–100.0
Tiamulin	62	78.5	68.2–86.1
Trimethoprim	59	74.7	64.1–83
Vancomycin	0	0.0	0.0–4.6
Number of resistances	**n**	**%**	**95% CI**
None	0	0.0	0.0–4.6
1 antimicrobial	0	0.0	0.0–4.6
2 antimicrobials	0	0.0	0.0–4.6
3 antimicrobials	0	0.0	0.0–4.6
4 antimicrobials	7	8.9	4.4–17.2
>4 antimicrobials	72	91.1	82.8–95.6

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

macrolides/lincosamides (erythromycin 70.1%/, clindamycin 72.7%), trimethoprim (71.4%), tiamulin (70.1%), quinupristin/dalfopristin (68.8%) and streptomycin (54.5%). The resistance rate of ciprofloxacin (11.7%) was moderate, while the resistance rates of gentamicin, kanamycin and sulfamethoxazole (5.2%), fusidic acid, linezolid and rifampin (2.6% each), mupirocin and vancomycin (1.3%) were low. No microbiological resistance to chloramphenicol was detected.

9.4.1.2 Veal calves

In 2015, 300 nasal swabs were collected from veal calves. By applying selective enrichment methods, 19 MRSA isolates were obtained from this random sample. Thus, the prevalence was 6.3%. 11 isolates belonged to *spa* type t011 (CC398), 6 to *spa* type t011 (CC398) and 2 to *spa* type t008.

Susceptibility testing revealed that all isolates were microbiologically resistant to beta-lactames and tetracycline. Extremely high levels of microbiological resistance were found for macrolides/lincosamides (erythromycin/clindamycin both 73.7%). The resistance levels for quinupristin/dalfopristin, streptomycin, tiamulin and trimethoprim were high (20–50%). Low resistance levels (1–10%) were found for chloramphenicol, ciprofloxacin, fusidic acid, gentamicin, kanamycin, linezolid, mupirocin, rifampin and vancomycin. Resistance to sulfamethoxazole was not detected (Table 9. n).

The distribution of the minimum inhibitory concentrations (MICs) are shown in Annexe II (Table II.47).

9.4.2 MRSA in meat

9.4.2.1 Chicken meat

Chicken meat was investigated in 2014. By applying selective enrichment methods, 22 MRSA isolates were obtained from 319 samples of retail chicken meat (194 samples of Swiss origin, 125 samples of foreign origin). Thus, the prevalence was 6.9%. The isolates were subjected to *spa* typing and susceptibility testing (Table 9. o). Fourteen isolates were identified as *spa* type t034. Three isolates belonged to spa-type t011 and three isolates to *spa* type t032. The *spa* types t5571 and t899 were each detected once.

Table 9. m: Occurrence of resistance in MRSA from fattening pigs, data of 2015.

Methicillin-resistant *Staphylococcus aureus* (N=77)			**2015**
Antimicrobials	**n**	**%**	**95% CI**
Cefoxitin	77	100.0	95.2–100.0
Chloramphenicol	0	0.0	0.0–4.8
Ciprofloxacin	9	11.7	6.3–20.7
Clindamycin	56	72.7	61.9–81.4
Erythromycin	54	70.1	59.2–79.2
Fusidic acid	2	2.6	0.7–9.0
Gentamicin	4	5.2	2.0–12.6
Kanamycin	4	5.2	2.0–12.6
Linezolid	2	2.6	0.7–9.0
Mupirocin	1	1.3	0.2–7.0
Penicillin	77	100.0	95.2–100.0
Quinupristin/Dalfopristin	53	68.8	57.8–78.1
Rifampin	2	2.6	0.7–9.0
Streptomycin	42	54.5	43.5–65.2
Sulfamethoxazole	4	5.2	2.0–12.6
Tetracycline	76	98.7	93.0–99.8
Tiamulin	54	70.1	59.2–79.2
Trimethoprim	55	71.4	60.5–80.3
Vancomycin	1	1.3	0.2–7.0
Number of resistances	**n**	**%**	**95% CI**
None	0	0.0	0.0–4.8
1 antimicrobial	0	0.0	0.0–4.8
2 antimicrobials	0	0.0	0.0–4.8
3 antimicrobials	14	18.2	11.2–28.2
4 antimicrobials	3	3.9	1.3–10.8
>4 antimicrobials	60	77.9	67.5–85.7

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

Out of 22 MRSA positive samples, 20 samples were chicken meat produced abroad. Two MRSA positive samples were chicken meat of Swiss origin. Consequently, the prevalence in externally produced chicken meat was 16.0%, while the prevalence for Swiss chicken meat was 1%.

Susceptibility testing revealed that all isolates were microbiologically resistant to beta-lactam antibiotics (cefoxitin, oxacillin and penicillin). Extremely high resistance rates were found for tetracyclines (86.4%), macrolides/lincosamides (erythromycin 72.7%, clindamycin 86.4%), tiamulin (77.3%) and trimethoprim (86.4%). High resistance rates were found for ciprofloxacin (22.7%) and moderate resistance rates for sulfamethoxazole (13.6%).

9.4.2.2 Pork

Pork was investigated in 2015. Two out of 301 examined samples tested positive for MRSA, corresponding to a prevalence of 0.7%.

The two MRSA isolates were subjected to susceptibility testing. Both were microbiologically resistant to cefoxitin, clindamycin, erythromycin, penicillin, quinupristin/dalfopristin, streptomycin, tetracycline, tiamulin and trimethoprim. Resistance to ciprofloxacin and fusidic acid was each found in one isolate (Table 9. p).

The distribution of the minimum inhibitory concentrations (MIC's) are shown in Annexe II (Table III. 46), the multi-resistance patterns in Annexe III (Table III. 10).

9.4.2.3 Beef

Beef samples were investigated in 2015. All 298 samples tested negative for MRSA.

Table 9. n: Occurrence of resistance in MRSA from veal calves, 2015 data.

Veal calves: Methicillin-resistant *Staphylococcus aureus* (N = 19)			**2015**
Antibiotic	**n**	**%**	**95% CI**
Cefoxitin	19	100.0	83.2–100.0
Chloramphenicol	1	5.3	0.9–24.6
Ciprofloxacin	3	15.8	5.5–37.6
Clindamycin	14	73.7	51.2–88.2
Erythromycin	14	73.7	51.2–88.2
Fusidic acid	1	5.3	0.9–24.6
Gentamicin	3	15.8	5.5–37.6
Kanamycin	3	15.8	5.5–37.6
Linezolid	1	5.3	0.9–24.6
Mupirocin	1	5.3	0.9–24.6
Penicillin	19	100.0	83.2–100.0
Quinupristin/Dalfopristin	6	31.6	15.4–54.0
Rifampin	1	5.3	0.9–24.6
Streptomycin	8	42.1	23.1–63.7
Sulfamethoxazole	0	0.0	0.0–16.8
Tetracycline	19	100.0	83.2–100.0
Tiamulin	6	31.6	15.4–54.0
Trimethoprim	7	36.8	19.1–59.0
Vancomycin	1	5.3	0.9–24.6
Number of resistances	**n**	**%**	**95% CI**
None	0	0.0	0.0–16.8
1 antimicrobial	0	0.0	0.0–16.8
2 antimicrobials	0	0.0	0.0–16.8
3 antimicrobials	4	21.1	8.5–43.3
4 antimicrobials	0	0.0	0.0–16.8
> 4 antimicrobials	15	78.9	56.7–91.5

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

9.4.3 Discussion

Livestock animals:

In Switzerland, the occurrence of MRSA in fattening pigs at slaughter increased significantly from 2009 to 2013. In 2009, the prevalence was assessed at 2.0%, in 2011 at 5.6% and in 2013 at 20.8% [24, 25]. Since then, the occurrence of MRSA seems stable. In 2014, the prevalence was 26.5% and in 2015 25.7%.

The reported results confirm that *spa* type t034 MRSA in particular and to a lesser extent also *spa* type t011 are becoming widespread in Switzerland's population of slaughtered pigs (Tables 9. l, 9. m). These genotypes belong to the clonal complex CC 398, which is typically livestock-associated (LA-MRSA). MRSA CC398 is mostly found in fattening pigs, cattle and poultry and can be transmitted between animals and humans. Not only in Switzerland but also in other European countries most of the MRSA *spa* types detected were associated with LA-MRSA CC398 [26].

Table 9. o: Occurrence of resistance in MRSA from chicken meat, 2014 data.

Methicillin-resistant *Staphylococcus aureus* (N=22)			**2014**
Antimicrobials	**n**	**%**	**95% CI**
Cefoxitin	22	100.0	85.1–100.0
Chloramphenicol	0	0.0	0.0–14.9
Ciprofloxacin	5	22.7	10.1–43.4
Clindamycin	19	86.4	66.7–95.3
Erythromycin	16	72.7	51.8–86.8
Fusidic acid	0	0.0	0.0–14.9
Gentamicin	0	0.0	0.0–14.9
Kanamycin	0	0.0	0.0–14.9
Linezolid	0	0.0	0.0–14.9
Mupirocin	0	0.0	0.0–14.9
Oxacillin	22	100.0	85.1–100.0
Penicillin	22	100.0	85.1–100.0
Rifampin	0	0.0	0.0–14.9
Streptomycin	4	18.2	7.3–38.5
Sulfamethoxazole	3	13.6	4.7–33.3
Tetracycline	19	86.4	66.7–95.3
Tiamulin	17	77.3	56.6–89.9
Trimethoprim	19	86.4	66.7–95.3
Vancomycin	0	0.0	0.0–14.9
Number of resistances	**n**	**%**	**95% CI**
None	0	0.0	0.0–15.5
1 antimicrobial	0	0.0	0.0–15.5
2 antimicrobials	0	0.0	0.0–15.5
3 antimicrobials	0	0.0	0.0–15.5
4 antimicrobials	0	0.0	0.0–15.5
> 4 antimicrobials	22	100.0	85.1–100.0

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

Table 9. p: Occurrence of resistance in MRSA from pork, 2015 data.

Methicillin-resistant *Staphylococcus aureus* (N=2)			**2015**
Antimicrobials	**n**	**%**	**95% CI**
Cefoxitin	2	100.0	34.2–100.0
Chloramphenicol	0	0.0	0.0–65.8
Ciprofloxacin	1	50.0	9.5–90.5
Clindamycin	2	100.0	34.2–100.0
Erythromycin	2	100.0	34.2–100.0
Fusidic acid	1	50.0	9.5–90.5
Gentamicin	0	0.0	0.0–65.8
Kanamycin	0	0.0	0.0–65.8
Linezolid	0	0.0	0.0–65.8
Mupirocin	0	0.0	0.0–65.8
Penicillin	2	100.0	34.2–100.0
Quinupristin/Dalfopristin	2	100.0	34.2–100.0
Rifampin	0	0.0	0.0–65.8
Streptomycin	2	100.0	34.2–100.0
Sulfamethoxazole	0	0.0	0.0–65.8
Tetracycline	2	100.0	34.2–100.0
Tiamulin	2	100.0	34.2–100.0
Trimethoprim	2	100.0	34.2–100.0
Vancomycin	0	0.0	0.0–65.8
Number of resistances	**n**	**%**	**95% CI**
None	0	0.0	0.0–65.8
1 antimicrobial	0	0.0	0.0–65.8
2 antimicrobials	0	0.0	0.0–65.8
3 antimicrobials	0	0.0	0.0–65.8
4 antimicrobials	0	0.0	0.0–65.8
>4 antimicrobials	2	100.0	34.2–100.0

N = total number of tested isolates, n = number of resistant isolates, % = percentage of resistant isolates, 95% CI: 95% Confidence Interval

In 2014, all MRSA isolates obtained from fattening pigs at slaughter showed microbiological resistance to beta-lactams (cefoxitin, oxacillin and penicillin) and tetracycline. Quite a few had additional resistances to other antimicrobials important for treatment. In 2014, four isolates were resistant to 11 antimicrobials. These findings underline the multi-resistant nature of MRSA.

Colonization of fattening pigs with MRSA may occur during transportation to the slaughterhouse or at slaughter itself (cross-contamination). Due to this fact, the validity of data recorded at the stage of slaughter may be limited with regard to showing the change of MRSA occurrence in fattening pigs [27].

Overall data of 2014 and 2015 illustrate the fact that the occurrence of MRSA in fattening pigs needs to be further investigated. Bangerter et al. [27] conducted comprehensive studies of the individual colonization dynamics of MRSA throughout Swiss pig production [textbox 9. c]. Humans in close contact with livestock are at higher risk of being carriers of livestock-associated MRSA [28]. Although colonization of healthy humans with MRSA usually does not induce disease, MRSA introduced in hospitals may cause infections that are almost impossible to treat. At least the occurrence of MRSA in the context of severe infections in hospitalized humans (septicaemia) has decreased significantly in the past years, with a prevalence of 12.8% in 2004 as opposed to 3.3% in 2015 [29].

The prevalence of MRSA in veal calves increased from 2.1% in 2010 to 6.3% in 2015. These data indicate an increasing trend too. Therefore, the occurrence of MRSA in veal calves needs to be further observed.

Meat

Although food is currently not regarded as a relevant source of MRSA infection or colonization for humans, MRSA can be found in meat. Investigations have revealed that the occurrence of MRSA in chicken meat produced abroad (16.0%) is significantly higher than in chicken meat produced in Switzerland (1%). Looking at the details, it becomes obvious that most MRSA isolates were obtained from chicken meat imported from Germany (Table 9. q).

Figure 9. j: Number of MRSA genotypes from fattening pigs between 2009 and 2015.

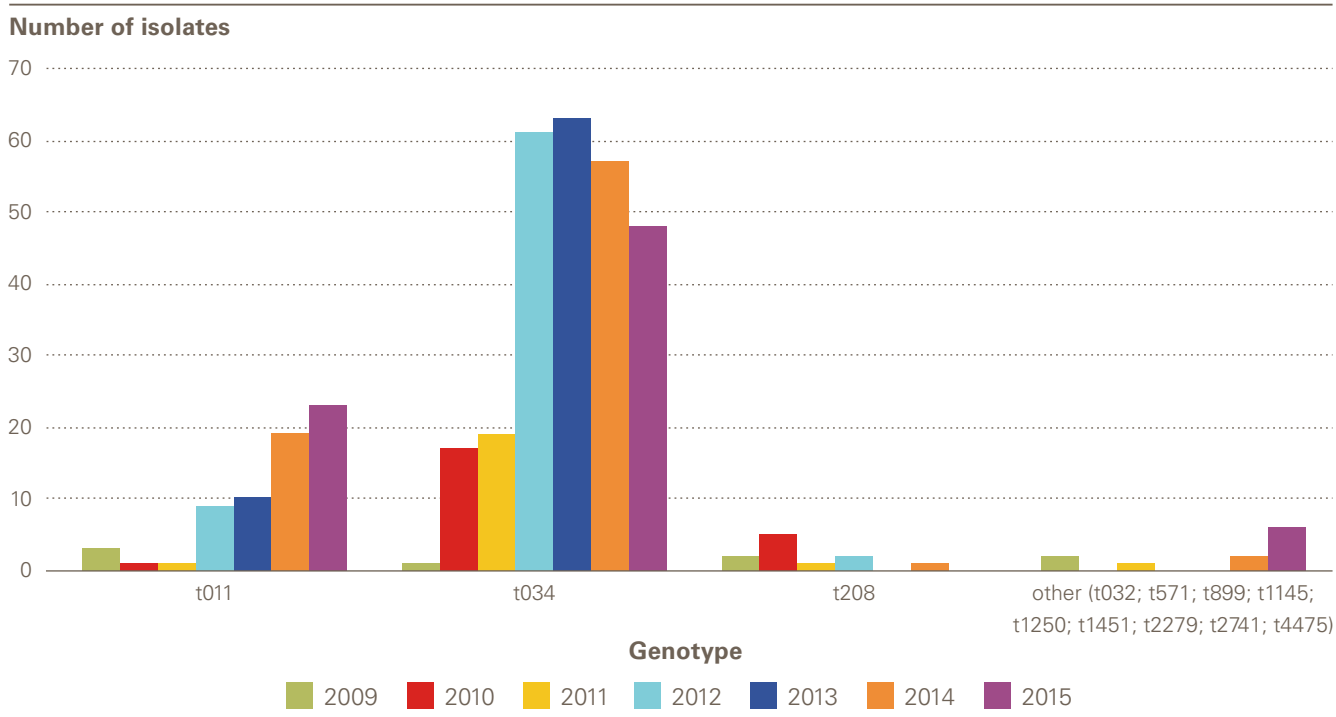


Table 9. q: Number of samples and number of MRSA-positive samples by origin of chicken meat.

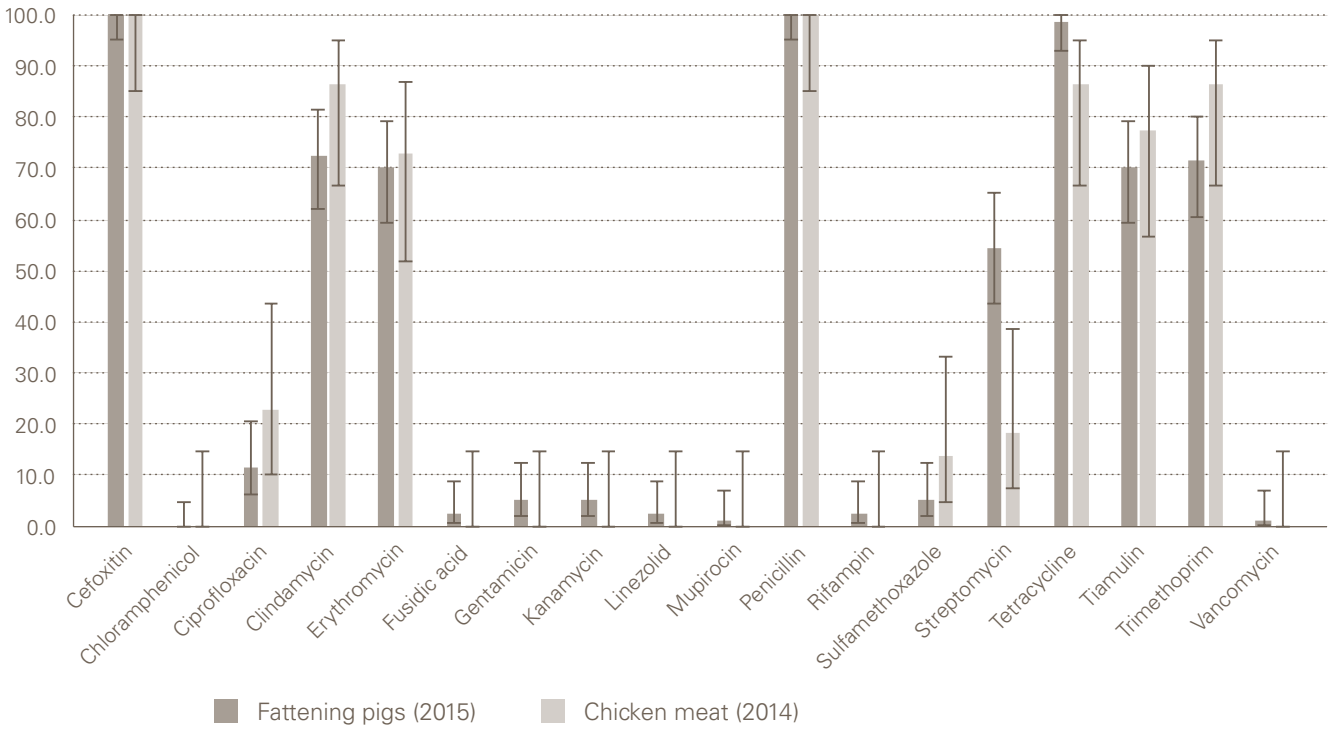
Origin	Number of samples	Number of positive samples (%)
Germany	58	18 (31.0)
France	17	1 (5.9)
Hungary	18	1 (5.6)
Slovenia	19	0 (0.0)
Austria	7	0 (0.0)
The Netherlands	3	0 (0.0)
Italy	2	0 (0.0)
Brazil	1	0 (0.0)
Switzerland	194	2 (1.0)

The two isolates obtained from Swiss chicken meat were identified as *spa* type t032 which is a highly prevalent healthcare-associated MRSA in humans. This might indicate that the contamination with MRSA occurred after slaughter, i.e. during processing or packaging.

The MRSA investigation in pork revealed a prevalence of 0.7% (two isolates out of 301 samples), indicating that MRSA can occur in pork too, albeit at very low levels. No MRSA was found in beef in the reporting period.

Resistance patterns of MRSA isolates differ between isolates from chicken meat and fattening pigs. Resistance to ciprofloxacin was more often found in isolates from chicken meat, whereas resistance to streptomycin and tetracycline was higher in isolates from fattening pigs (Figure 9. k). This might be due to differences in selection pressure. Aminoglycosides such as spectinomycin are used in pigs. One-step mutations are known and can lead to cross-resistance with streptomycin. On the other hand, enrofloxacin, a fluoroquinolone like ciprofloxacin, is more often used in poultry farming.

Figure 9. k: Resistance prevalence of MRSA from pigs and chicken meat.



References

[1] De Leener et al. Molecular analysis of human, porcine, and poultry *Enterococcus faecium* isolates and their erm(B) genes. Appl Environ Microbiol 2005; 71(5): 2766–2770. doi:10.1128/AEM.71.5.2766–2770.2005

[2] Heuer et al. Human health hazard from antimicrobial-resistant enterococci in animals and food. Clin Infect Dis 2006; 43(7): 911–916. doi: 10.1086/507534

[3] EFSA (European Food Safety Authority) and ECDC (European Centre for Disease Prevention and Control), 2015. EU Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2013. EFSA Journal 2015; 13(2): 4036, 178 pp., doi:10.2903/j.efsa.2015.4036

[4] ANRESIS: Antibiotic Resistance Data in Switzerland, University of Bern, www.anresis.ch, last accessed on July 15th, 2016, Bulletin 30/16, Federal Office of Public Health, FOPH, p 462

[5] European Food Safety Authority; Technical specifications on the harmonised monitoring and reporting of antimicrobial resistance in *Salmonella*, *Campylobacter* and indicator *Escherichia coli* and *Enterococcus* spp. bacteria transmitted through food. EFSA Journal 2012; 10(6): 2742. [64 pp.] doi:10.2903/j.efsa.2012.2742

[6] White et al. Characterization of chloramphenicol and florfenicol resistance in *Escherichia coli* associated with bovine diarrhea. J Clin Microbiol 2000; 38(12): 4593-4598

[7] ANRESIS: Antibiotic Resistance Data in Switzerland, University of Bern, www.anresis.ch, last accessed on July 15th, 2016, Bulletin 30/16, Federal Office of Public Health, FOPH, p 462

[8] Laube et al. Longitudinal monitoring of extended-spectrum-beta-lactamase/AmpC-producing *Escherichia coli* at German broiler chicken fattening farms. Appl Environ Microbiol 2013; 79(16): 4815–4820. doi:10.1128/AEM.00856-13

[9] EFSA. Scientific Opinion on the public health risks of bacterial strains producing extended-spectrum beta-lactamases and/or AmpC beta-lactamases in foods and food producing animals. EFSA Journal 2011; 9(8): 2322. doi:10.2903/j.efsa.2011.2322

[10] Zurfluh et al. Vertical transmission of highly similar blaCTX-M-1-harboring IncI1 plasmids in *Escherichia coli* with different MLST types in the poultry production pyramid. Front Microbiol 2014; 5: 519. doi:10.3389/fmicb.2014.00519

[11] Blaak et al. Detection of extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* on flies at poultry farms. Appl Environ Microbiol 2014; 80(1): 239-246. doi: 10.1128/AEM.02616-13

[12] Huijbers et al. Extended-spectrum and AmpC-lactamase-producing *Escherichia coli* in broilers and people living and/or working on broiler farms: prevalence, risk factors and molecular characteristics. Antimicrob Agents Chemother 2014; 69(10): 2669–2675. doi:10.1093/jac/dku178

[13] Seiffert et al. High prevalence of extended-spectrum-cephalosporin-resistant Enterobacteriaceae in poultry meat in Switzerland: Emergence of CMY-2- and VEB-6-possessing Proteus mirabilis. Antimicrob Agents Chemother 2013; 57(12): 6406–6408. doi:10.1128/AAC.01773-13

[14] Abgottspon et al. Characteristics of extended-spectrum cephalosporin-resistant *Escherichia coli* isolated from Swiss and imported poultry meat. J Food Prot 2014; 77(1): 112-115. doi:10.4315/0362-028X.JFP-13-120
[15] Vogt et al. Occurrence and genetic characteristics of third-gerneration cephalosporin-resistant *Escherichia coli* in Swiss retail meat. Microb Drug Resist 2014; 20(5): 485-494. doi:10.1089/mdr.2013.0210
[16] Tschudin-Sutter et al. Extended-spectrum-lactamase-(ESBL-)producing Enterobacteriaceae: A Threat from the Kitchen. Infect Control Hosp Epidemiol 2014; 35(5): 581-584. doi: 10.1086/675831
[17] Kronenberg et al. Temporal trends of extended-spectrum cephalosporin-resistant *Escherichia coli* and *Klebsiella pneumoniae* isolates in in- and outpatients in Switzerland, 2004 to 2011. Euro Surveill 2013; 18(21). pii:20484
[18] Geser et al. Molecular identification of extended-spectrum-beta-lactamase genes from Enterobacteriaceae isolated from healthy human carriers in Switzerland. Antimicrob Agents Chemother 2012; 56(3): 1609–1612. doi:10.1128/AAC.05539-11
[19] Nuesch-Inderbinen et al. Cross-sectional study on fecal carriage of Enterobacteriaceae with resistance to extended-spectrum cephalosporins in primary care patients. Microb Drug Resist 2013; 19(5): 362–369. doi:10.1089/mdr.2013.0013
[20] Geser et al. Occurrence and characteristics of extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae in food producing animals, minced meat and raw milk. BMC Vet Res 2012; 8:21 doi:10.1186/1746-6148-8-21.
[21] Wu G. et al. Comparative analysis of ESBL-positive *Escherichia coli* isolates from animals and humans from the UK, the Netherlands and Germany. PLoS One 2013; 8(9):e75392. doi:10.1371/journal.pone.0075392
[22] Sharp et al. Abschätzung des Transfers von ESBL-bildenden *Escherichia coli* zum Menschen für Deutschland. Berliner und Münchener Tierärztliche Wochenschrift 2014; 127: 446–477. doi:10.2376/0005-936-127-464
[23] den Heijer, C., E. van Bijnen, W. Paget, M. Pringle, H. Goossens, C. Bruggeman, F. Schellevis, E. Stobberingh, 2013: Prevalence and resistance of commensal *Staphylococcus aureus*, including methicillin-resistant *S. aureus*, in nine European countries: a cross-sectional study. Lancet Infectious Diseases 13(5): 409-415
[24] Overesch et al. The increase of methicillin-resistant *Staphylococcus aureus* (MRSA) and the presence of an unusual sequence type ST49 in slaughter fattening pigs in Switzerland. BMC Veterinary Research 2011; 7: 30
[25] Overesch et al. Entwicklung der Prävalenz von MRSA des Sequenztyps ST49. Fleischwirtschaft 2012; 92 (12): 95–97
[26] EFSA (European Food Safety) and ECDC (European Centre for Disease Prevention and Control), 2016: The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2014. EFSA Journal 2016; 14(2): 4380, 207pp. doi:10.2903/j.efsa.2016.4380
[27] Bangerter, P. D., Sidler, X., Perreten, V., Overesch, G., 2016: Longitudinal study on the colonisation and transmission of methicillin-resistant *Staphylococcus aureus* in fattening pig farms. Veterinary Microbiology 183(2016): 125–134
[28] Wettstein Rosenkranz K, E. Rothenanger, I. Brodard, A. Collaud, G. Overesch, B. Bigler, J. Marschall, V. Perreten 2014: Nasal carriage of methicillin-resistant *Staphylococcus aureus* (MRSA) among Swiss veterinary health care providers: detection of livestock- and healthcare-associated clones. Schweizer Archiv für Tierheilkunde, Band 156, Heft 7, Juli, 317–325.
[29] ANRESIS: Antibiotic Resistance Data in Switzerland, Universität Bern, www.anresis.ch, last accessedon July 15th, 2016, Bulletin 30/16, Bundesamt für Gesundheit, p 462
[30] Crombé F, Argudín MA, Vanderhaeghen W, Hermans K, Haesebrouck F and Butaye P, 2013. Transmission dynamics of methicillin-resistant *Staphylococcus aureus* in pigs. Frontiers in Microbiology, 4, 57. doi:10.3389/fmicb.2013.00057

Textbox 9. c

Longitudinal study on the colonization and transmission of methicillin-resistant *Staphylococcus aureus* in fattening pig farms.

Bangerter, P. D.[1], Sidler, X.[2], Perreten, V.[1], Overesch, G.[1]

[1] Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Bern; [2] Department of Farm Animals, Division of Swine Medicine, Vetsuisse Faculty, University of Zurich

The dramatic increase of MRSA in Swiss slaughter pigs during recent years necessitates the introduction of measures to combat the further spread of MRSA in the Swiss pig population. However, until now, there have been no precise studies of the individual colonization dynamics of MRSA throughout each pig production stage. A comprehensive study was therefore performed to determine the colonization status of MRSA in individual pigs throughout each production stage from birth to slaughter, in order to gain a better understanding of the substantial factors involved in transmission. Two farrow-to-finish herds and two grow-to-finish herds were included in the study. A total of 1,728 nasal swabs from 390 pigs and 592 environmental wipes were collected at 11 different time points. Intermittent colonization throughout the entire production cycle was conspicuous in the tracking of MRSA at the level of the individual pig. This strongly implies that pigs are transiently, rather than permanently, colonized, and suggests repeated contamination, possibly at all stages and at all production sites. The MRSA status should therefore be defined at the herd level instead of the level of the individual pig for the establishment of prevention measures against MRSA. As the prevalence in Swiss slaughter pigs is constantly increasing, though still at a moderate level, the further spread of MRSA could feasibly be prevented among Swiss pig producing facilities by defining farms as MRSA positive or negative and by allowing the trade of animals only within herds of the same status. The implementation of these measures could also combat further dissemination of LA-MRSA into healthcare facilities and the community via humans with close contact to these animals, i.e., farmers, veterinarians and slaughterhouse workers.

Reference

Bangerter, P. D., Sidler, X., Perreten, V., Overesch, G., 2016: Longitudinal study on the colonisation and transmission of methicillin-resistant *Staphylococcus aureus* in fattening pig farms. Veterinary Microbiology 183(2016): 125–134

10

Resistance in diagnostic submissions from animals

10 Resistance in diagnostic submissions from animals

Monitoring of antimicrobial resistance for relevant pathogens from diseased livestock and companion animals is important for the assessment of future trends in antimicrobial resistance. International organizations have recently focused on these topics [1]. The establishment of a European Veterinarian Committee on Antimicrobial Susceptibility Testing (VetCAST) in 2015 also proves the importance of these measures.
In its function as the Swiss national reference laboratory for antibacterial resistance, the Center for Zoonoses, Animal Bacterial Diseases and Antimicrobial Resistance (ZOBA) at the Institute of Veterinary Bacteriology, Vetsuisse Faculty of Bern, has provided data for staphylococci and *E. coli* of dogs and horses, isolated from clinical submissions within this report. The relatively low number of isolates is due to the fact that only data from the diagnostic unit of the ZOBA could be implemented. In future, additional data from other Swiss veterinary diagnostic laboratories as well as other relevant bacterial species, i.e. *Acinetobacter* spp., *Pseudomonas* spp. and streptococci should also be included.

10.1 *Staphylococcus* spp.

Staphylococci are gram-positive, non-motile and non-sporulating cocci. About 30 species are found in animals, of which a few are pathogenic. They belong to the normal microbiota in animals and humans, but are occasionally responsible for opportunistic infections. Different *Staphylococcus* species are specifically associated to their hosts. *S. pseudintermedius* is the most relevant *Staphylococcus* species in dogs, whereas *S. aureus* is found more frequently in horses.

10.1.1 *Staphylococcus* spp. in dogs

In dogs, *Staphylococcus pseudintermedius* was the most relevant staphylococcal species, highly prevalent in affected skin and wounds (2014: 21%; 2015: 14%). *S. pseudintermedius* were isolated in about 28% (2014) and 30% (2015) of infected eye/ear and nose samples, whereas this species was found only in 4% (2014) and 3% (2015) of samples collected in connection with urogenital tract complications. *S. pseudintermedius* is a coagulase-positive animal-associated *staphylococcus,* mainly detected in dogs, but it can also occasionally cause infections in other animals. Humans with close contact to animals present a higher risk of becoming colonized with *S. pseudintermedius* [2]. Like other staphylococci, *S. pseudintermedius* is an opportunistic pathogen. First described in 2005 as a novel species, *S. pseudintermedius* has gained more importance in recent years, in both human and veterinary medicine, because of the emergence of methicillin-resistant *S. pseudintermedius* (MRSP) [3]. This is not only a therapeutic challenge for the veterinarians treating the infected animals, but also a risk for pet owners who can become colonized with MRSP.

Other *Staphylococcus* species, such as *S. aureus*, *S. schleiferi* subspecies coagulans, *S. epidermidis* and *S. haemolyticus* were rarely isolated from clinical cases of dogs. Recently, Wipf and Perreten published a study regarding methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from dogs and cats in Switzerland [5]. Canine and feline MRSA exhibit resistances against beta-lactams, trimethoprim and fluoroquinolones, but single strains also exhibited resistance to macrolides, lincosamides, aminoglycosides, tetracycline, chloramphenicol and/or mupirocin. Molecular characterization indicates clonal spread of a human-associated lineage in Swiss companion animals. Maintance of a low level of MRSA infections in animals is therefore important for public health, in order to avoid uncontrolled dissemination of MRSA clones in humans and animals.

Antimicrobial resistance data for *S. pseudintermedius* isolates from 2014 and 2015 are presented in Table 10. a and Table 10. b, respectively. In general, *S. pseudintermedius* isolates present an extremely high percentage of resistance to penicillin (2014: 84%, 2015: 82%). High resistance percentages are detected for kanamycin (2014: 45%, 2015: 35%), tetracycline (2014: 41%, 2015: 45%), erythromycin (2014: 41%, 2015: 34%), clindamycin (2014: 28%, 2015: 23%) and chloramphenicol (2014: 28%, 2015: 21%). Moderate resistance is found for trimethoprim-sulfamethoxazole (2014: 16%, 2015: 18%), gentamicin (2014: 12%, 2015: 11%), enrofloxacin (2014: 14%, 2015: 11%) and marbofloxacin (2014: 14%, 2015: 11%). These data demonstrate the potential therapeutic difficulties in treatment of *S. pseudintermedius* infections in dogs. Resistance percentages for fusidic acid were low (2014: 2%, 2015: 5%), and resistance to nitrofurantoin was not found. Also, resistance to vancomycin and mupirocin was not detected, but 10% of the tested strains (n = 142) in 2015 were intermediately resistant to the latter. In 2015, resistance to rifampicin was found in ten isolates (7%). Attention has to be paid to possible emergence of rifampicin resistance in *S. pseudintermedius,* since resistance can develop rapidly during monotherapy.

About 16% of the *S. pseudintermedius* isolates in 2014 and 15% in 2015 were fully sensitive to all tested antimicrobials. About 42% (2014) and 50% (2015) of the isolates displayed resistance to between one and three antimicrobials, of which about one half showed resistance only to penicillin.

Resistance to more than four and up to nine antibiotics was found in 37% (2104) and 35% (2015) of S. pseudintermedius isolates. Strikingly, 7 isolates in 2014 (6%) and 12 isolates in 2015 (8%) showed antibacterial resistance to nearly all therapeutically relevant veterinary substances, with nitrofurantoin and/or fusidic acid being the only options left. This clearly underlines the necessity for prudent use of antimicrobials and the need to monitor such data to stay aware of future trends.

Table 10. a: Susceptibility rates of *Staphylococcus pseudintermedius* isolates in dogs in 2014.

Staphylococcus pseudintermedius							**2014**
Antimicrobials	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Penicillin	116	18	16%	0	0%	98	84%
Kanamycin	116	64	55%	1	1%	52	45%
Gentamicin	116	112	97%	0	0%	14	12%
Trimethoprim-sulfamethoxazole	116	97	84%	0	0%	19	16%
Tetracycline	116	68	59%	0	0%	48	41%
Erythromycin	116	68	59%	0	0%	48	41%
Clindamycin	116	83	72%	0	0%	33	28%
Vancomycin	116	116	100%	0	0%	0	0%
Mupirocin	116	116	100%	2	3%	0	0%
Fusidic acid	116	114	98%	0	0%	2	2%
Chloramphenicol	116	83	72%	0	0%	33	20%
Enrofloxacin	116	97	84%	3	3%	16	14%
Marbofloxacin	116	99	85%	1	1%	16	14%
Nitrofurantoin	116	116	100%	0	0%	0	0%
Rifampicin	116	116	100%	0	0%	0	0%

n: number of isolates, S (n) and S (%): number and percentage of sensitive isolates, I (n) and I (%): number and percentage of intermediate isolates, R (n) and R (%): number and percentage of resistant isolates

Table 10. b: Susceptibility rates of *Staphylococcus pseudintermedius* isolates in dogs in 2015.

Staphylococcus pseudintermedius							**2015**
Antimicrobials	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Penicillin	142	25	18%	0	0%	117	82%
Kanamycin	142	92	65%	0	0%	50	35%
Gentamicin	142	127	89%	0	0%	15	11%
Trimethoprim-sulfamethoxazole	142	117	82%	0	0%	25	18%
Tetracycline	142	78	55%	0	0%	64	45%
Erythromycin	142	94	66%	0	0%	48	34%
Clindamycin	142	110	77%	0	0%	32	23%
Vancomycin	142	142	100%	0	0%	0	0%
Mupirocin	142	128	90%	1	1%	0	0%
Fusidic acid	142	135	95%	0	0%	7	5%
Chloramphenicol	142	112	79%	0	0%	303	21%
Enrofloxacin	142	123	87%	3	2%	16	11%
Marbofloxacin	142	123	87%	3	2%	16	11%
Nitrofurantoin	142	142	100%	0	0%	0	0%
Rifampicin	142	132	93%	0	0%	10	7%

n: number of isolates, S (n) and S (%): number and percentage of sensitive isolates, I (n) and I (%): number and percentage of intermediate isolates, R (n) and R (%): number and percentage of resistant isolates

Methicillin-resistant *S. pseudintermedius* (MRSP) was frequently detected (2014: 15% [n = 17], 2015: 13% [n = 19]). MRSP is regarded as a nosocomial bacterium in veterinary clinics, comparable to methicillin-resistant *S. aureus* (MRSA) in human settings. The high detection rate of MRSP in our diagnostics is likely due to the disproportionately high rate of submissions from the clinics for small animals at the Vetsuisse Faculty of Bern.

MRSP of canine origin revealed a broad spectrum of multiresistance (Table 10. c). Most of the isolates (n = 10, 28%) displayed resistance to clindamycin, erythromycin, enrofloxacin, kanamycin, marbofloxacin and trimethoprim-sulfamethoxazole. Two MRSP isolates showed an extensive multidrug resistance pattern, with only nitrofurantoin, rifampicin and fusidic acid as possible treatment options left.

Table 10. c: Multi-resistance patterns of methicillin-resistant *Staphylococcus pseudintermedius* isolates in dogs in 2014 and 2015.

Number of resistances	Number of isolates	Bacterial species	Chloramphenicol	Clindamycin	Erythromycin	Enrofloxacin	Gentamicin	Kanamycin	Marbofloxacin	Benzylpenicillin	TMP-sulfameth.	Tetracycline	Rifampicin
10 ABM	2	*S. pseudintermedius*											
9 ABM	2	*S. pseudintermedius*											
9 ABM	1	*S. pseudintermedius*											
8 ABM	1	*S. pseudintermedius*											
8 ABM	2	*S. pseudintermedius*											
8 ABM	1	*S. pseudintermedius*											
7 ABM	1	*S. pseudintermedius*											
7 ABM	10	*S. pseudintermedius*											
7 ABM	4	*S. pseudintermedius*											
6 ABM	1	*S. pseudintermedius*											
6 ABM	1	*S. pseudintermedius*											
6 ABM	2	*S. pseudintermedius*											
6 ABM	1	*S. pseudintermedius*											
6 ABM	1	*S. pseudintermedius*											
5 ABM	2	*S. pseudintermedius*											
5 ABM	1	*S. pseudintermedius*											
4 ABM	1	*S. pseudintermedius*											
3 ABM	1	*S. pseudintermedius*											

ABM: antimicrobial

10.1.2 *Staphylococcus* spp. in horses

In horses, staphylococci play an important role as a pathogen. Particularly *S. aureus* was found in 7% (2014) and 9% (2015) of cases from skin lesions and wound infections. In contrast to dogs and cats, no *S. pseudintermedius* were isolated. Other species such as *S. epidermidis, S. sciuri and S. equorum* were detected only occasionally. Antimicrobial resistance data are therefore only reported for the *S. aureus* isolates (Table 10. d and Table 10. e).

The percentage of resistance to benzylpenicillin is extremely high (2014: 73%, 2015: 82%). Resistance to aminoglycosides is very high for kanamycin (2014: 53%, 2015: 64%) and gentamicin (2014: 53%, 2015: 64%). Also resistance to trimethoprim-sulfamethoxazole (2014: 53%, 2015: 50%) and tetracycline (2014: 53%, 2015: 64%) is very high. In contrast, low resistance level were found for erythromycin (2014: 7%, 2015: 0%) and clindamycin (2014: 7%, 2015: 0%). The resistance level to fluoroquinolones was moderately high in 2014 (enrofloxacin and marbofloxacin: 13% each), and low in 2015 (enrofloxacin and marbofloxacin: 5% each). No resistance to nitrofurantoin, vancomycin, mupirocin and rifamipicin was detected.

The antimicrobial resistance pattern of *S. aureus* isolates clearly demonstrated that the use of antibiotics should be limited as much as possible, in order to maintain therapeutic options for the treatment of infections in the future.

In 2014 methicilin-resistant S. *aureus* (MRSA) were detected in 53% of the isolates in 2014 and in 59% of the isolates in 2015 (2014: n = 8, 2015: n = 13). This worrisome high detection rate of MRSA has to be interpreted carefully. The

total number of isolates is very small, therefore calculated percentages spread in a wide range and the origin of the samples is limited mainly to the horse clinics at the Vetsuisse Faculty of Bern. Schnellmann et al. demonstrated that horses entering the hospital harbor staphylococci carrying antibiotic resistance genes, including new variants of mecA and mph(C) genes. Shortly after hospitalization, horses acquire a specific multidrug-resistant skin flora that is presumably selected for and maintained in the hospital by the use of penicillin [4]. Multidrug resistance patterns are listed in Table 10. f. In contrast to methicillin-resistant *S. pseudintermedius,* MRSA from horses exhibit less broad multi-resistance patterns. The majority of the isolates (n = 15) showed resistance to kanamycin, gentamicin, trimethoprim-sulfamethoxazole and tetracyline. Another three MRSAs additionally displayed resistance to enrofloxacin and marbofloxacin.

In 2014, 27% and in 2015, 18% of the *S. aureus* isolates from horses were fully sensitive to the tested antimicrobials. Of the tested strains, 18% (2014) and 20% (2015) showed resistance to penicillin alone. The vast majority of the isolates (2014: 47%, 2015: 59%), most of them MRSAs, exhibited resistance to up to seven antimicrobials.

Table 10. d: Susceptibility rates of *Staphylococcus aureus* isolates in horses in 2014.

Staphylococcus aureus							**2014**
Antimicrobials	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Penicillin	15	4	27%	0	0%	1	73%
Kanamycin	15	7	47%	0	0%	8	53%
Gentamicin	15	7	47%	0	0%	8	53%
Trimethoprim-sulfamethoxazole	15	7	47%	0	0%	8	53%
Tetracycline	15	7	47%	0	0%	8	53%
Erythromycin	15	14	93%	0	0%	1	7%
Clindamycin	15	14	93%	0	0%	1	7%
Vancomycin	15	15	100%	0	0%	0	0%
Mupirocin	15	15	100%	0	0%	0	0%
Fusidic acid	15	15	100%	0	0%	0	0%
Chloramphenicol	15	15	100%	0	0%	2	0%
Enrofloxacin	15	13	87%	0	0%	2	13%
Marbofloxacin	15	13	87%	0	0%	2	13%
Nitrofurantoin	15	15	100%	0	0%	0	0%
Rifampicin	15	15	100%	0	0%	0	0%

n: number of isolates, S (n) and S (%): number and percentage of sensitive isolates, I (n) and I (%): number and percentage of intermediate isolates, R (n) and R (%): number and percentage of resistant isolates

Table 10. e: Susceptibility rates of *Staphylococcus aureus* isolates in horses in 2015.

Staphylococcus aureus							**2015**
Antimicrobials	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Penicillin	22	4	18%	0	0%	18	82%
Kanamycin	22	8	36%	0	0%	14	64%
Gentamicin	22	8	36%	0	0%	14	64%
Trimethoprim-sulfamethoxazole	22	11	50%	0	0%	11	50%
Tetracycline	22	8	36%	0	0%	14	64%
Erythromycin	22	22	100%	0	0%	0	0%
Clindamycin	22	22	100%	0	0%	0	0%
Vancomycin	22	22	100%	0	0%	0	0%
Mupirocin	22	22	100%	0	0%	0	0%
Fusidic acid	22	22	100%	0	0%	0	0%
Chloramphenicol	22	22	100%	0	0%	0	0%
Enrofloxacin	22	19	86%	2	9%	1	5%
Marbofloxacin	22	21	95%	0	0%	1	5%
Nitrofurantoin	22	22	100%	0	0%	0	0%
Rifampicin	22	22	100%	0	0%	0	0%

n: number of isolates, S (n) and S (%): number and percentage of sensitive isolates, I (n) and I (%): number and percentage of intermediate isolates, R (n) and R (%): number and percentage of resistant isolates

Table 10. f: Multi-resistance patterns of *S. aureus* from horses in 2014 and 2015.

Number of resistances	Number of isolates	Bacterial species	Chloramphenicol	Clindamycin	Erythromycin	Enrofloxacin	Gentamicin	Kanamycin	Marbofloxacin	Benzylpenicillin	TMP-sulfameth.	Tetracycline	Rifampicin
7 ABM	3	*S. aureus*											
5 ABM	15	*S. aureus*											
4 ABM	3	*S. aureus*											

ABM: antimicrobial

10.2 *Escherichia coli*

E. coli was chosen as a representative for gram-negative pathogens. *E. coli* is an important cause of opportunistic infections in veterinary medicine. For infections with pathogenic *E. coli* (e.g. verotoxin-producing *E. coli*), beyond isolation further characterization of virulence markers is necessary. For the identification of opportunistic cases however, it is sufficient to isolate *E. coli* in pure growth from carefully taken samples. In this report, antimicrobial resistances of opportunistic *E. coli* isolated from diseased dogs and horses are presented. *E. coli* was chosen as a representative for gram-negative pathogens.

10.2.1 *E. coli* in dogs

E. coli strains are found in nearly 20% of all urogenital tract infections. Furthermore, *E. coli* is frequently isolated from infected wounds, skin lesions and ear swabs.

Antimicrobial resistance data for *E. coli* strains isolated in 2014 and 2015 are summarized in Table 10. g and Table 10. h. High resistance percentages are reported for ampicillin (2014: 37%, 2015: 40%), chloramphenicol (2014: 38%, 2015: 39%), tetracycline (2014: 24%, 2015: 23%) and piperacillin (2014: 30%, 2015: 23%). Resistance rates for amoxicillin-/clavulanic acid (2014: 18%, 2015: 23%) as well as for trimethoprim-sulfamethoxazole (2014: 16%, 2015: 20%) are moderate to high. Cephalosporine resistance is moderate for cefpodoxime (3rd generation) (2014 and 2015: 15%), cefalexin (1st generation) (2014 and 2015: 15%) and ceftiofur (3rd generation) (2014: 14%, 2015: 12 %). Cefpirome (4th generation) resistance percentage is low (2014: 10%, 2015: 8%). Resistance to aminoglycosides is low to moderate for gentamicin (2014: 8%, 2015: 13%). Two isolates in 2015 exhibited resistance to amikacin, an important antimicrobial for treatment of severe infections with gram-negative bacteria in human medicine. In contrast, resistance to tobramycin, another important aminoglycoside in human medicine, is moderately high (2014: 10%, 2015: 13%). For fluoroquinolones, resistance percentages are moderate as well. For enrofloxacin and marbofloxacin in 2014, 14% of the *E. coli* isolates showed resistance. In 2015, 18% were resistant. No carbapenemase-producing *E. coli* were detected and all strains were susceptible to polymyxin B. Only two isolates in 2014 were resistant to nitrofurantoin (2%). In 2015 all isolates were susceptible to nitrofurantoin.

In 2014, 9 *E. coli* isolates were confirmed to be extended-spectrum-beta-lactamase-producing (ESBL) *E. coli* (10%). In 2015, 15 *E. coli* isolates were ESBLs (8%). These strains exhibit a very broad range of multi-resistance (Table 10. i). Five isolates, resistant to all antimicrobials tested, are particularly alarming. These cases are critical in terms of therapy as well as in terms of their potential to spread within clinics and among owners.

Table 10. g: Susceptibility rates of *E. coli* isolates in dogs in 2014.

E. coli							2014
Antimicrobials	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Ampicillin	87	55	63%	0	0%	32	37%
Amoxicillin-clavulanic acid	87	68	78%	3	3%	16	18%
Gentamicin	87	80	92%	0	0%	7	8%
Trimethoprim-sulfamethoxazole	87	73	84%	0	0%	14	16%
Tetracycline	87	65	75%	1	1%	21	24%
Cefalexin	87	74	85%	0	0%	13	15%
Cefpodoxime	87	74	85%	0	0%	13	15%
Cefpirome	87	78	90%	0	0%	9	10%
Imipenem	87	87	100%	0	0%	0	0%
Polymyxin B	87	87	100%	0	0%	0	0%
Enrofloxacin	87	74	85%	1	1%	12	14%
Amikacin	87	87	100%	0	0%	0	0%
Nitrofurantoin	87	85	96%	0	0%	2	2%
Marbofloxacin	87	75	86%	0	0%	12	14%
Piperacillin	87	61	70%	0	0%	26	30%
Chloramphenicol	87	54	62%	0	0%	33	38%
Ceftiofur	87	75	86%	0	0%	12	14%
Tobramycin	87	78	90%	0	0%	9	10%

n: number of isolates, S (n) and S (%): number and percentage of sensitive isolates, I (n) and I (%): number and percentage of intermediate isolates, R (n) and R (%): number and percentage of resistant isolates

Table 10. h: Susceptibility rates of *E. coli* isolates in dogs in 2015.

E. coli							2015
Antimicrobials	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Ampicillin	192	115	60%	0	0%	77	40%
Amoxicillin-clavulanic acid	192	143	74%	5	3%	44	23%
Gentamicin	192	168	88%	0	0%	24	13%
Trimethoprim-sulfamethoxazole	192	154	80%	0	0%	38	20%
Tetracycline	192	147	77%	0	0%	45	23%
Cefalexin	192	164	85%	0	0%	28	15%
Cefpodoxime	192	164	85%	0	0%	28	15%
Cefpirome	192	177	92%	0	0%	15	8%
Imipenem	192	192	100%	0	0%	0	0%
Polymyxin B	192	192	100%	0	0%	0	0%
Enrofloxacin	192	151	79%	6	3%	35	18%
Amikacin	192	190	99%	0	0%	2	1%
Nitrofurantoin	192	192	100%	0	0%	0	0%
Marbofloxacin	192	157	82%	0	0%	35	18%
Piperacillin	192	148	77%	0	0%	44	23%
Chloramphenicol	192	118	61%	0	0%	74	39%
Ceftiofur	192	165	86%	4	2%	23	12%
Tobramycin	192	168	88%	0	0%	24	13%

n: number of isolates, S (n) and S (%): number and percentage of sensitive isolates, I (n) and I (%): number and percentage of intermediate isolates, R (n) and R (%): number and percentage of resistant isolates

Table 10. i: Multi-resistance patterns of extended-spectrum beta-lactamases producing *E. coli* from dogs in 2014 and 2015.

Number of resistances	Number of isolates	Bacterial species	Tobramycin	TMP-sulfameth.	Tetracycline	Ampicillin	Amox.-clav. acid	Chloramphenicol	Cefalexin	Cefpodoxime	Cefpirome	Enrofloxacin	Gentamicin	Marbofloxacin	Tetracycline	Piperacillin
14 ABM	5	*E. coli*														
13 ABM	2	*E. coli*														
13 ABM	1	*E. coli*														
13 ABM	1	*E. coli*														
13 ABM	1	*E. coli*														
12 ABM	1	*E. coli*														
12 ABM	1	*E. coli*														
12 ABM	1	*E. coli*														
12 ABM	1	*E. coli*														
12 ABM	1	*E. coli*														
11 ABM	1	*E. coli*														
11 ABM	1	*E. coli*														
11 ABM	1	*E. coli*														
10 ABM	1	*E. coli*														
10 ABM	1	*E. coli*														
10 ABM	1	*E. coli*														
9 ABM	1	*E. coli*														
8 ABM	1	*E. coli*														

ABM: antimicrobial

10.2.2 *E. coli* in horses

Only a limited number of *E. coli* strains were isolated from clinical submissions of horses. These strains were derived mainly from infected wounds (2014: 7%, 2015: 14%) and skin lesions (2014: 7%, 2015: 4%). Antimicrobial resistances of the isolates are presented in Tables 10. j and 10. k.

In general, *E. coli* isolates from diseased horses exhibit very high resistance percentages (> 50%) to most of the tested antimicrobials. Very high percentages were detected for ampicillin, gentamicin, tetracycline, 1st-to-4th-generation cephalosporines, trimethoprim-sufamethoxazole, piperacillin, chloramphenicol and tobramycin. Resistance rates to fluoroquinolones are high: 22% to marbofloxacin and enrofloxacin in 2014, 27% to both in 2015. Resistance percentage to amoxicillin-clavulanic acid increased from 22% in 2014 to 41% in 2015. Resistances to polymyxin B, nitrofurantoin and amikacin were not detected in 2014 and 2015. Additionally, no carbapenemase-producing *E. coli* were detected.

Ten *E. coli* isolates were confirmed as ESBLs (63%) in 2014 and 11 *E. coli* isolates in 2015 (50%). These strains exhibit a broad spectrum of multi-resistance (Table 10. l). Five isolates showed resistance to all antimicrobials tested, including critically important antimicrobials such as fluoroquinolones and tobramycin. The vast majority of the isolates were resistant to most of the tested antimicrobials, but showed susceptibility to fluoroquinolones.

Resistance data as well as the extremely high ESBL numbers must be interpreted with caution. The number of isolates was very small (2014: n = 16, 2015 n = 22) and most were derived from the horse clinic Vetsuisse Faculty in Bern. The limited number of resistance patterns within the ESBL-confirmed strains might indicate a limited number of clones circulating in a clinical setting.

Table 10. j: Susceptibility rates of *E. coli* isolates in horses in 2014.

E. coli							2014
Antimicrobials	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Ampicillin	18	6	33%	0	0%	12	67%
Amoxicillin-clavulanic acid	18	7	39%	7	39%	4	22%
Gentamicin	18	7	39%	0	0%	11	61%
Trimethoprim-sulfamethoxazole	18	6	33%	0	0%	12	67%
Tetracycline	18	6	33%	0	0%	12	67%
Cefalexin	18	7	39%	0	0%	11	61%
Cefpodoxime	18	7	39%	0	0%	11	61%
Cefpirome	18	8	44%	0	0%	10	56%
Imipenem	18	18	100%	0	0%	0	0%
Polymyxin B	18	18	100%	0	0%	0	0%
Enrofloxacin	18	1	78%	0	0%	4	22%
Amikacin	18	18	100%	0	0%	0	0%
Nitrofurantoin	18	18	100%	0	0%	0	0%
Marbofloxacin	18	14	78%	0	0%	4	22%
Piperacillin	18	6	33%	0	0%	12	67%
Chloramphenicol	18	6	33%	0	0%	12	67%
Ceftiofur	18	8	44%	0	0%	10	56%
Tobramycin	18	7	39%	0	0%	11	61%

n: number of isolates, S (n) and S (%): number and percentage of sensitive isolates, I (n) and I (%): number and percentage of intermediate isolates, R (n) and R (%): number and percentage of resistant isolates

Table 10. k: Susceptibility rates of *E. coli* isolates in horses in 2015.

E. coli							2015
Antimicrobials	**n**	**S (n)**	**S (%)**	**I (n)**	**I (%)**	**R (n)**	**R (%)**
Ampicillin	22	6	27%	0	0%	16	73%
Amoxicillin-clavulanic acid	22	8	36%	5	23%	9	41%
Gentamicin	22	7	32%	0	0%	15	68%
Trimethoprim-sulfamethoxazole	22	4	18%	0	0%	18	82%
Tetracycline	22	7	32%	0	0%	15	68%
Cefalexin	22	10	45%	0	0%	12	55%
Cefpodoxime	22	10	45%	0	0%	12	55%
Cefpirome	22	11	50%	0	0%	11	50%
Imipenem	22	22	100%	0	0%	0	0%
Polymyxin B	22	22	100%	0	0%	0	0%
Enrofloxacin	22	15	68%	1	5%	6	27%
Amikacin	22	22	100%	0	0%	0	0%
Nitrofurantoin	22	22	100%	0	0%	0	0%
Marbofloxacin	22	16	73%	0	0%	6	27%
Piperacillin	22	6	27%	0	0%	16	73%
Chloramphenicol	22	8	36%	0	0%	14	64%
Ceftiofur	22	10	45%	0	0%	12	55%
Tobramycin	22	10	45%	0	0%	12	55%

n: number of isolates, S (n) and S (%): number and percentage of sensitive isolates, I (n) and I (%): number and percentage of intermediate isolates, R (n) and R (%): number and percentage of resistant isolates

Table 10. I: Multi-resistance patterns of extended-spectrum-beta-lactamases-producing *E. coli* from horses in 2014 and 2015.

Number of resistances	Number of isolates	Bacterial species	Tobramycin	TMP-sulfameth.	Tetracycline	Ampicillin	Amox.-clav. acid	Chloramphenicol	Cefalexin	Cefpodoxime	Cefpirome	Enrofloxacin	Gentamicin	Marbofloxacin	Tetracycline	Piperacillin
14 ABM	5	*E. coli*														
13 ABM	1	*E. coli*														
12 ABM	14	*E. coli*														
11 ABM	1	*E. coli*														

ABM: antimicrobial

10.3 Discussion

The presence of extremely high levels of resistance to important antimicrobials in companion animals highlights the need for a systematic monitoring of antimicrobial resistance. Infections in animals caused by multidrug-resistant pathogens can be expected increasingly for both *S. pseudintermedius* and *E. coli*. As in human medicine, especially clinical settings are faced with the presence of methicillin-resistant staphylococci and extended-spectrum-beta-lactamase-producing Enterobacteriaceae linked with a high risk of nosocomial infections. Possible therapy options for severe infections with multi-resistant bacteria have to strictly follow the guidelines for prudent use, and critically important antimicrobials for human medicine should not be applied to companion animals. The presence of multidrug-resistant bacteria in veterinary medicine does not only constitute a challenge for treatment of the diseased animals, but also represents a risk for humans because of their zoonotic potential.

Our results demonstrate that a significant and sensitive monitoring of antibacterial resistance of bacteria causing diseases in livestock and companion animals is urgently needed. These data will provide an important insight into the occurrence, spread and dynamics of critical antibacterial resistance in animal pathogens in Switzerland.

In this report, antimicrobial resistance data from a limited number of clinical submissions from dogs and horses has been presented. In the future, the data volume should be increased, adding isolates from other laboratories, so as to obtain a more representative overview of the situation in Switzerland. Furthermore, additional bacterial species including other relevant gram-positive and gram-negative pathogens will be reported. Moreover, animal species under observation need to encompass livestock, e.g. pigs and calves, as well, as these animals receive relevant amounts of antimicrobials for prophylactic and/or metaphylactic reasons. In 2015, the Food Safety and Veterinary Office (FSVO) launched a pilot project on the monitoring of antimicrobial resistance for relevant pathogens from diseased livestock and companion animals. As a result, a more representative picture on antimicrobial resistance in relevant veterinarian pathogens will be achieved in the future.

References

[1] Methicillin-resistant *Staphylococcus aureus* and *Staphylococcus pseudintermedius* in veterinary medicine. (2010). Weese JS, van Duijkeren E, Vet Microbiol 2010; 140: 418–429

[2] Reflection paper on the risk of antimicrobial resistance transfer from companion animals (2015). EMA/CVMP/AWP/401740/2013, Committee for Medicinal Products for Veterinary Use (CVMP)

[3] Clonal spread of methicillin-resistant *Staphylococcus pseudintermedius* in Europe and North America: an international multicentre study (2010). Kristina Kadlec, Stefan Schwarz, Ulrika Grönlund Andersson, Maria Finn, Christina Greko, Arshnee Moodley, Stephen A. Kania, Linda A. Frank, David A. Bemis, Alessia Franco, Manuela Iurescia, Antonio Battisti, Birgitta Duim, Jaap A. Wagenaar, Engeline van Duijkeren, J. Scott Weese, J. Ross Fitzgerald, Alexandra Rossano and Luca Guardabassi, J Antimicrob Chemother. 2010, Jun; 65(6): 1145–1154.

[4] Presence of New mecA and mph(C) Variants Conferring Antibiotic Resistance in *Staphylococcus* spp. Isolated from the Skin of Horses before and after Clinic Admission (2006). Christina Schnellmann, Vinzenz Gerber, Alexandra Rossano, Valentine Jaquier, Yann Panchaud, Marcus G. Doherr, Andreas Thomann, Reto Straub, and Vincent Perreten, J Clin Microbiol. 2006, Dec; 44(12): 4444–4454

[5] Methicillin-resistant *Staphylococcus aureus* isolated from dogs and cats in Switzerland (2016). Wipf JR, Perreten V. Schweiz Arch Tierheilkd. 2016 Jun; 158(6): 443–450

Human and veterinary resistance data: a microbiologist's view

Jean-Claude Piffaretti[1]

[1] Interlifescience, 6900 Massagno

This common report provides in a single document an overview of the situation of antibiotics resistance and consumption in human and veterinary medicine. The comparison of the Swiss data with those from the EU, shows that Switzerland is generally in a favorable situation, although much has anyhow to be done, e.g. in regards of the emergence of plasmid-mediated colistin resistance in *Escherichia coli* from animals, meat and humans, the emergence of carbapenem resistance in humans, and the increasing numbers of MRSA in food-producing and companion animals.

An important added value of this common report should be the detection of any possible correlation between resistances in animal and humans, at least for some resistance determinants. Antibiotic resistance in humans is generally considered to be originated and spread mostly by the selective pressure exerted by the antimicrobial use in human medicine. However, antibiotic consumption and antibiotic resistance in animals can play a role in humans, either by promoting the transfer (via direct contact or contaminated food) of resistant strains such as *Campylobacter* or *Salmonella*, or by being a source – or even a reservoir – of bacterial resistance genes having the potential of being transmitted to humans. Thus, the emergence of new resistance determinants or their increase in different settings, including animals, should be considered as an alarm and examined, the relevance for human and veterinary medicine be established, and appropriate measures be taken. This has been very recently exemplified by the sudden finding in gram-negative bacteria of a transmissible plasmid-encoded colistin resistance gene (mcr-1). The avorpacin/vancomycon resistance in enterococci is another example which demonstrates the importance of a One Health perspective in order to timely detect and effectively combat public health threats posed by resistance phenomena.

The present report does not permit yet to reasonably detect possible correlations between resistances in animals and humans. This is due to a number of reasons, among which we can highlight: i) the lack of standardized common antibiotic break-points defining resistance for a number of antibiotics (considering Minimum Inhibitory Concentrations might help to solve this issue); ii) the limited number of clinical isolates of veterinarian origin; iii) the lack of data from healthy humans; iv) the lack of molecular epidemiology data allowing the comparison between human and animal strains. The reports to come in the next years should try to consider and resolve these weaknesses.

Nevertheless, a few observations can already be considered of significant interest and need follow-up or action.

Campylobacter jejuni. Humans are mostly infected by eating poultry meat. Thus, the resistance situation of *C. jejuni* in broilers should have an obvious impact on the resistance situation in humans. Indeed, the increasing resistance trend observed during the past years in broilers for fluoroquinolones – an important antibiotic used to treat severe human *C. jejuni* infections – (11.7% in 2006 to 45.9% in 2014) is correlated to a similar increase in human clinical isolates (37.6% in 2006 to 58.0% in 2015).

Resistance among gram-negative bacteria. Resistance to 3rd-generation cephalosporins in clinical Enterobacteriaceae is challenging therapy in human medicine and leads to the use of carbapenems. In this regard, carbapenem resistance has emerged in human medicine and has to be reported to the Federal Office of Public Health. Up to now, no carbapenem resistance has been observed in animals. This is likely due to the fact that carbapenems are not used in food-producing animals and only rarely used in companion animals.

However, more than 70% of poultry meat contains *E. coli* which are resistant to 3rd-generation cephalosporins. Of note, plasmid-mediated colistin resistance has also been observed in *E. coli* from poultry meat retailed in Switzerland as well as in a few human cases. These alarming data emphasize that adequate measures should be taken to avoid the dissemination of resistance genes or resistant bacteria.

Methicillin-resistant *Staphylococcus aureus* (MRSA). Infections caused by MRSA in Swiss hospitals could be stabilized or even reduced. However, MRSA infections in the ambulatory setting are increasing (see textbox 7. b). Interestingly, a significant increase of MRSA colonization in pigs has been observed for a few years. Similarly, cases of MRSA are also reported in companion animals and horses. So far the connection between these trends has not been analyzed properly, more detailed data on MRSA subtypes (e.g. Clonal Complex) are needed to address these issues. These data strengthen the need to continuously survey the prevalence of resistant bacteria and their potential impact in veterinary

and human therapy, particularly for the persons living in close contact with farm and companion animals.

In conclusion, it should be pointed out that this joint report is well in line with the One Health approach that is currently being implemented in Switzerland (as well in many other countries) to fight increasing and spreading antibiotic resistance. Further reservoirs such as the environment should also be monitored. In addition, molecular data are necessary to demonstrate dissemination of antibiotic-resistant bacteria and their genetic elements between the different human, food and animal environments. This common report should also serve as a baseline for taking action in the existing reservoirs where antibiotic-resistant bacteria are predominant.

11

Materials and methods

11 Materials and methods

11.1 Data on antibacterial consumption in human medicine

11.1.1 The Anatomical Therapeutic Chemical (ATC) classification system and defined daily doses (DDD)

Data are collected regarding antibacterials for systemic consumption (group J01 of the ATC classification), antibiotics for treatment of tuberculosis (ATC group J04AB) and agents against amoebiasis and other protozoal diseases (ATC group P01AB) [1]. Antibiotic consumption (in grams or millions of International Units) was converted into defined daily doses (DDD) using the 2016 release of the DDD by the World Health Organization Collaborating Centre for Drug Statistics Methodology (see Annexe I).

11.1.2 Data sources in the in- and outpatient settings

For the inpatient setting, a voluntary network of acute care hospitals participating in the surveillance system anresis.ch was set up in 2004. Data were collected from the entire hospitals, and separately from the adult intensive care units (ICUs) when possible. Fourty-three hospitals participated in 2004 and 58 in 2015, of which 32 were small-size (< 200 beds), 18 medium-size (200–500 beds) and 8 large-size hospitals (> 500 beds, which includes the five Swiss university hospitals) (Annexe IV, Table IV.1). Initially, the hospital network represented 54% of the total number of acute somatic care hospitals (excluding psychiatric and rehabilitation centers) and 47% of all beds in this category in Switzerland (33% of all beds). Twenty-three hospitals (10 small-, 14 medium- and 5 large-size) also provided data on adult ICUs. This number increased to 40 (17, 16, 7, respectively) in 2015, representing 51% of the hospitals equipped with ICU beds in Switzerland. Data on hospital occupied bed-days and admissions were collected, enabling the expression of the consumption density as DDD per 100 occupied bed-days and as DDD per 100 admissions. Of note, the definition of bed-days given by the Swiss Federal Statistical Office (SFSO) included the day of discharge or transfer in the counting days until 2012 and excludes it since then. This means that there is a bias towards a slightly lower number of bed-days in comparison with the previous years and therefore, for a same number of DDD, towards a slightly higher number of DDD/100 bed- days.

Data on sales of antibiotics in the outpatient setting were provided by PharmaSuisse, the Swiss Society of Pharmacists. The updating of the database is entrusted to the professional cooperative of the Swiss pharmacists (OFAC, Genève) that collects the prescription orders at the individual level from the public pharmacies and produces invoices for health insurance companies on behalf of pharmacies. The coverage is approximately 65% of all pharmacies in Switzerland. All antibiotics are dispensed with a prescription. The data include the quantities of antibiotics sold to a number of individuals per age group (< 2; 2–11; 12–17; 18– 64; > 64 years of age). Prescriptions from self-dispensing physicians are not included in the database. The measurement units for reporting antibiotic consumption are DDD per 1,000 inhabitants per day [1].

References

[1] WHO Collaborating Centre for Drug Statistics Methodology, Guidelines for ATC classification and DDD assignment 2015. Oslo, 2014

11.2 Data on antimicrobial sales in veterinary medicine

The list of veterinary products which were granted marketing authorization during the years under review in this report (2014 & 2015) was extracted semi-automatically from the internal Swissmedic database on the basis of their ATCvet codes [1] and completed by the products which were withdrawn from the market in the period under review. Marketing authorization holders were then asked to report sales figures for their products. Products authorized for export only were excluded. They cannot be used in Switzerland and do not contribute to the development of resistance in Switzerland.

The obtained data was transmitted from Swissmedic to the Federal Food Safety and Veterinary Office (FSVO) where it was entered and assessed in a Microsoft Access database specifically developed for this purpose. The entry of each product consists of a unique identification number, the brand name, the ATCvet code, information on the authorized method of application and the target animal group. Pharmaceutical premixes are indicated separately. The entry additionally includes the number of sold "basic units" (e.g. vials

[incl. volume], tablets, injectors, tubes or pouches/bags [incl. weight]).

Total volumes were then calculated by repeatedly multiplying the volume of active substance in each basic unit by the number of basic units sold. Combinable filters (year, ATCvet code, administration route) were used for specific queries. The volume of active substance contained in each product and each basic unit is recorded. In the case of antimicrobials declared in International Units, conversion factors according to the template of the European Surveillance of Veterinary Antimicrobial Consumption Project (ESVAC) of the European Medicines Agency [2] were used.

The methods of application were selected to reflect those referred to in similar reports in other countries (France, AFSSA and United Kingdom, VMD): oral, parenteral, intramammary and topical/external. Target animal groups are recorded on the basis of marketing authorizations. The only distinction that can be drawn is between "farm animals," "pets" and "mixed group" because specific records on the actual target animals of administered products are not available. Specific animal species or age groups were only recorded if these were clearly mentioned in the marketing authorization (e.g. intramammary injectors for cows or products to treat piglets).

References

[1] WHO Collaborating Centre for Drug Statistics Methodology, Guidelines for ATCvet classification 2015. Oslo, 2014, http://www.whocc.no/atcvet

[2] European Medicines Agency, European Surveillance of Veterinary Antimicrobial Consumption, 2015. Sales of veterinary antimicrobial agents in 26 EU/EEA countries in 2013. EMA/387934/2015

11.3 Bacterial isolates from humans (clinical probes)

Currently, 20 microbiology laboratories are linked to anresis.ch (Annexe IV, Table IV.2). These laboratories send all results from routine testing of all clinical bacteriology cultures to the anresis.ch database on a regular basis (weekly or monthly). In contrast to most other surveillance systems, all antimicrobial resistance results are sent, not restricting the dataset either to invasive isolates or to a predefined set of microorganisms only (please note that nevertheless, most analyses in Chapter 7 are restricted to invasive isolates, due to better comparability with international data). Screening results are labelled specially and do not influence results of this report. Antibiotic resistance test results done as reference laboratory are labelled specifically. It is possible to provide epidemiological information such as sample location, provider of the sample, patient sex and age. In contrast, clinical data regarding diagnosis, therapy or outcome are not available in anresis.ch. Although we prefer quantitative antibiotic resistance testing results, most microbiological laboratories unfortunately send only qualitative, interpreted resistance data (SIR). Resistance data are not validated by anresis.ch but only by the laboratory sending the data. All laboratories participating in anresis.ch are approved and are participants of at least one external quality control program.

11.4 Bacterial isolates from animals (for monitoring: clinical and not clinical probes)

11.4.1 Sampling of healthy animals at the slaughterhouse

Stratified random samples were taken in the years 2014 and 2015 (Table 11. a & b). Sampling was spread evenly throughout each year, on the basis of a sampling plan established for meat inspections. Samples were collected at the five largest poultry, pig and cattle slaughterhouses. Every slaughterhouse taking part in the program collected a number of samples proportional to the number of animals of the species slaughtered per year. This procedure ensured that at least 60% (2014) or 75% (2015) of slaughtered animals belonging to the species in question were part of the sample. In 2014, samples were taken from 493 broiler flocks. Random cloacal swab samples were taken from 5 chickens per flock. During the same year, 298 nasal swab samples from fattening pigs were collected. Analyses were performed at the National Reference Laboratory (ZOBA), where broiler samples were shaken in 1 ml of trypton soya broth to produce one pooled sample per flock. In 2015, 300 caecum and nasal swab samples were collected from fattening pigs and 298 caecum samples and 300 nasal swab samples from calves. Samples were sent to the National Reference Laboratory (ZOBA) for further analyses.

For calves and fattening pigs, the intention was to take samples from one animal selected at random per farm and to avoid taking two samples a year from any particular farm.

The results discussed in this report illustrate the data from 2006 to 2015. Sampling procedures in the previous years were done in a similar way.

11.4.2 Sampling of meat at retailers

In both years, meat samples (min. 50 g) were taken from fresh, skinless, chilled, packed and untreated meat sold at the retail level. Samples were collected in all Swiss cantons throughout each year. The applied sampling scheme considered each canton's population density and market shares of retailers.

In 2015, 301 pork and 298 beef samples of domestic production were collected (Table 11. b). Approximately half of the chicken meat consumed in Switzerland is imported. Hence, imported and domestic chicken meat accounted for

around one third and two thirds respectively of the 319 chicken meat samples in 2014 (Table 11. a).

11.4.3 Samples of clinical isolates from animals

For *Salmonella*, no special monitoring at slaughter was feasible due to the very low prevalence of *Salmonella* spp. in Swiss livestock. Therefore, *Salmonella* isolates sent to ZOBA in 2014/2015 in connection with its function as a reference laboratory and isolates from its own diagnostic activities were included in the monitoring (Table 11. a & Table 11. b). Most of these isolates were from clinical material of various animal species. They also included a small number of isolates derived from samples isolated as part of the national *Salmonella* monitoring program in accordance with articles 257 and 258 of the Epizootic Diseases Ordinance of 27 June 1995 (EzDO; SR 916.401). The results discussed in this report illustrate the data from 2006 to 2015. Sampling procedures in previous years were performed in a similar way.

Staphylococci and *E. coli* strains described in Chapter 10 ("Resistance in diagnostic submissions from animals") were isolated from diagnostic submissions of canine and equine origin, sent to the diagnostic unit of the ZOBA by veterinarian practitioners and clinics in 2014/2015.

Table 11. a: Antimicrobial resistance monitoring program in 2014.

Type of sample	Number of samples	Bacteria tested	Number of resistance tests
Cloacal swab – broilers	493	*Campylobacter* spp.	174
Cloacal swab – broilers	205	*E. coli*	200
Cloacal swab – broilers	350	Enterococci	282
Cloacal swab – broilers	297	ESBL-prod. *E. coli*	124
Nasal swab – fattening pigs	298	MRSA	79
Meat – broilers	319	ESBL-prod. *E. coli*	232
Meat – broilers	319	MRSA	22
Meat – broilers	319	Carbapenemase-prod. *E.coli*	0
Clinical material/all species	–	*S. typhimurium*	18
Clinical material/all species	–	Monophasic *S. typhimurium*	13
Clinical material/all species	–	*S. enteritidis*	11

Table 11. b: Antimicrobial resistance monitoring program in 2015.

Type of sample	Number of samples	Bacteria tested	Number of resistance tests
Caecum – fattening pigs	299	*Campylobacter* spp.	161
Caecum – fattening pigs	197	*E. coli*	182
Caecum – fattening pigs	300	Enterococci	81
Caecum – fattening pigs	300	ESBL-prod. *E. coli*	77
Nasal swab – fattening pigs	300	MRSA	77
Caecum – calves	205	*E. coli*	190
Caecum – calves	298	Enterococci	207
Caecum – calves	298	ESBL-prod. *E. coli*	112
Nasal swab – calves	300	*MRSA*	19
Meat – fattening pigs	301	ESBL-prod. *E. coli*	2
Meat – fattening pigs	301	*MRSA*	2
Meat – fattening pigs	301	Carbapenemase-prod. *E.coli*	0
Meat – beef	298	ESBL-prod. *E. coli*	1
Meat – beef	298	*MRSA*	0
Meat – beef	298	Carbapenemase-prod. *E.coli*	0
Clinical material/all species	–	*S. typhimurium*	40
Clinical material/all species	–	Monophasic *S. typhimurium*	9
Clinical material/all species	–	*S. enteritidis*	14

11.5 Susceptibility testing, breakpoints, processing antibiotic resistance data from human isolates

There are no mandatory Swiss guidelines for antibiotic resistance testing. Most laboratories initially based on CLSI guidelines and changed to EUCAST guidelines between 2011 and 2013. In general use of automated systems increased over years. The Swiss Society of Microbiology encourages the use of EUCAST breakpoints and provides recommendations on their website (http://www.swiss-microbiology.ch). Nevertheless individual laboratories are free to use other guidelines than EUCAST.

Therefore, identification methods used may differ between the different laboratories. In most laboratories validated automated systems – generally based on CLSI guidelines – were introduced during the last couple of years. There is no formal validation of species identification by anresis.ch and no systematic collection of multi-resistant isolates.

The antibiotic resistance data presented in this report were extracted from the database using the analysis tool SAGENT, which is provided to all participating laboratories. For data selection we used the identical methodology like the antibiotic surveillance systems of the ECDC (EARS) and of the WHO Europe (CASEAR), restricting the isolates analyzed to invasive isolates from blood cultures or cerebrospinal fluid. Isolates from foreign countries were excluded. Doubles were defined as identical microorganism from the same patient during the same calendar year and were, therefore, excluded (only first isolate per calendar year analyzed). As patient identifiers are specific for individual laboratories only, it was not possible, to exclude doubles, if isolates from the same patient originated from different laboratories. For *Salmonella* spp. and *Campylobacter* spp. we analyzed isolates from all materials (e.g. stool), doubles were excluded as described above.

For this analysis we used the interpreted, qualitative data (SIR) as delivered from the participating laboratories. An isolate was considered resistant (R) to an antimicrobial agent when tested and interpreted as resistant in accordance with the breakpoint used by the local laboratory. Quantitative resistance data are not provided in most cases and are not used in this analysis (except for *S. pneumoniae*). An isolate was considered non-susceptible to an antimicrobial agent when tested and found resistant or intermediate susceptible to this antibiotic. An isolate was considered resistant/intermediate to an antibiotic group, if it was tested resistant/intermediate to at least one antibiotic of this group.

Changing breakpoints over time may influence resistance data. This especially comes true for *S. pneumoniae,* where in addition to changing breakpoints over time different breakpoints are used for different kinds of infections. Therefore, we decided to use the dataset from the Swiss National Reference Center for invasive Pneumococci, which collects all invasive *S. pneumoniae* isolates, and – besides serotyping – repeats antibiotic-resistance testing on a standardized manner. This means that all isolates are tested for erythromycin, levofloxacin, co-rimoxazole, and oxacillin. Additional e-tests for penicillin G and ceftriaxone are performed for all oxacillin-non-susceptible strains.

11.6 Susceptibility testing, cut-off, processing antimicrobial resistance data from animal isolates

Samples from fattening pigs, calves and broilers were tested for *Campylobacter* spp., *Salmonella* spp., *E. coli, Enterococcus* spp. and *Staphylococcus aureus* at the National Reference Laboratory for Antimicrobial Resistance (ZOBA, University of Bern) using internationally standardised microbiological methods. *Campylobacter* spp., *E. coli* and enterococci from cloacal swabs and caecum samples were isolated by direct detection on selective culture media, using modified charcoal cefoperazone deoxycholate agar (mCCDA), MacConkey agar and Slanetz-Bartley agar, respectively. Identification of suspicious colonies was carried out by the direct transfer method, using matrix-assisted laser desorption/ionization time-of-flight mass spectroscopy (MALDI TOF MS) (Biotyper 3.0, Bruker Daltonics, Bremen, Germany) following the manufacturer's recommendations.

MRSA detection was performed by transferring the nasal swab samples consecutively into two different enrichment broths, following cultivation on chromogenic MRSA-selective agar (method according to the European reference laboratory of the EU, RL for Antimicrobial Resistance, The National Food Institute, Lyngby, Denmark). Confirmation for *S. aureus* was carried out by MALDI TOF MS (Biotyper 3.0, Bruker Daltonics, Bremen, Germany). Methicillin-resistance-gene-mecA detection and determination of the clonal complex (CC) CC398 were carried out by means of multiplex real-time PCR, as previously published [1]. Spa type was determined as previously described and analyzed using the Ridom StaphType software (Ridom StaphType, Ridom GmbH, Würzburg, Germany) [2].

Detection of ESBL/AmpC-forming intestinal bacteria in 2014 was carried out by incubating the pooled cloacal swab samples in a selective enrichment medium MacConkey broth, supplemented with 4 mg/l ceftazidime (Oxoid, Ltd, Basingstoke, England) and by then cultivating them on a selective agar (chromID ESBL, bioMérieux Inc., Marcy l'Etoile, France; modified method described by Endimiani). The selective agar chromID ESBL was replaced by MacConkey agar with 1 µg/ml Cefotaxime (CTX) (Tritium) from 1 June 2014 onwards. Detection of ESBL/AmpC-forming *E. coli* from caecum samples in 2015 and meat samples in 2014 and 2015 was performed by selective enrichment methods, according to the protocol of the European reference laboratory of the

Table 11. c: Epidemiological cutoff values used to interpret MIC results, 2014 & 2015.

		Campylobacter spp.	*E. coli*/ *Salmonella* spp.	*Enterococcus* spp.	MRSA
Substance class	**Antimicrobials**	**ECOFF (µg/ml) WT<**	**ECOFF (µg/ml) WT<**	**ECOFF (µg/ml) WT<**	**ECOFF (µg/ml) WT<**
Penicillins	Ampicillin		8	4	
	Oxacillin				2
	Penicillin				0.125
	Temocillin		32		
Cephalosporins	Cefotaxime		0.25[c]/0.5[d]		
	Cefotaxime-clavulanic acid		*		
	Ceftazidime		0.5[c]/2[d]		
	Ceftazidime-clavulanic acid		*		
	Cefepime		0.125[c]		
	Cefoxitin		8		4
Carbapenems	Ertapenem		0.06		
	Imipenem		0.5[c]/1[d]		
	Meropenem		0.125		
Amphenicols	Chloramphenicol	16[h]	16	32	16[g]
Tetracyclines	Tetracycline	1[a]/2[b]	8	4	1
Glycylcyclines	Tigecycline		1	0.25	
(Fluoro)quinolone	Ciprofloxacin	0.5	0.064	4	1[g]
	Nalidixic acid	16	16		
Sulfonamids	Sulfamethoxazole		64[c]/256[d, k]		128[g]
Lincosamides	Clindamycin				0.25
Aminoglycosides	Gentamicin	2	2	32/512[k]	2
	Kanamycin				8[g]
	Streptomycin	4			16[g]
Polymyxins	Colistin		2		
Macrolides	Erythromycin	4[a]/8[b]		4	1
	Azithromycin		16		
Cyclic lipopeptides	Daptomycin			4	
Glycopeptides	Vancomycin			4	2
	Teicoplanin			2	
Diaminopyrimidins	Trimethoprim		2		2
Oxazolidines	Linezolid			4	4[g]
Streptogramins	Quinupristin/dalfopristin			1[f]	1[g, h]
Ansamycins	Rifampin				0.032
Pleuromutilins	Tiamulin				2[g]
Monocarbolic acid	Mupirocin				1
Fusidans	Fusidic acid				0.5

[a] *C. jejuni,* [b] *C. coli,* [c] *E. coli,* [d] *Salmonella* spp., [e] *E. faecalis,* [f] *E. faecium;* [g] ECOFF for *S. aureus,* [h] Only tested in 2014, [k] EUCAST-clinical breakpoint (ECOFF not defined or outside test-range); CLSI-clinical breakpoint (EUCAST clinical breakpoint not defined or outside test-range)
* Interpretation according to EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/ or epidemiological importance, v. 1.0, 2013

EU (RL for Antimicrobial Resistance, The National Food Institute, Lyngby, Denmark). Suspected *E. coli* colonies were identified by MALDI TOF MS (Biotyper 3.0, Bruker Daltonics, Bremen, Germany). Confirmation of the isolated *E. coli* by beta-lactamase type was carried out phenotypically by MIC determination on an EUVSEC2 plate.

Clinical submissions from dogs and horses were cultured according to standard bacterial culture methods. All isolates derived from ear/eye/nose swabs, urine and skin/wound specimens were included in the analysis. Identification down to the species level was performed by MALDI TOF MS or using the VITEK Compact system with Vitek GD ID card (bioMérieux Inc., Marcy l'Etoile, France).

The minimal inhibitory concentration (MIC) of the antimicrobials was determined by broth microdilution in cation-adjusted Müller-Hinton with (for *Campylobacter*) or without lysed horse blood, using Sensititre susceptibility plates (Trek Diagnostics Systems, East Grinstead, England) according to CLSI guidelines. The MIC was defined as the lowest antimicrobial concentration at which no visible bacterial growth occurred (Table 11. c).

Clinical staphyloccoci isolates were tested for susceptibility using the Vitek Compact 2 system with Vitek AST GP69 cards. For *E. coli,* Vitek AST GN38 cards were used (bioMérieux Inc., Marcy l'Etoile, France). The isolates were subcultured on tryptic soy 5% sheep blood agar plates (BBL Trypticase soy agar [TSA] II; BD Diagnostic Systems) in ambient air at 37°C before testing. Isolates were classified as susceptible or resistant according to clinical breakpoints published in the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (www.eucast.org) or, if not available, the Clinical and Laboratory Standards Institute document M31-A3 (CLSI). Methicillin resistance was screened by cefoxitin and confirmed using a slide latex agglutination test for the detection of Penicillin-Binding Protein (PBP) 2a (Oxoid, Pratteln, Switzerland).

Resistance prevalence rates were described using the following terminology:

Minimal:	< 0.1%
Very low:	0.1% to 1%
Low:	> 1% to 10%
Moderate:	> 10% to 20%
High:	> 20% to 50%
Very high:	> 50% to 70%
Extremely high:	> 70%

Antimicrobial resistance is recommended to be monitored by the assessment of MIC values based on epidemiological cutoff (ECOFF) values. Bacterial strains are considered microbiologically resistant if their MIC value is above the highest MIC value observed in the wild-type population of the bacteria (WT). The ECOFF distinguishes wildtypes from non-wildtypes and is set and published by the European Committee on Antimicrobial Susceptibility Testing (EUCAST). It is sometimes different from the clinical breakpoint. The clinical breakpoint relates primarily to the extent to which the pathogen may respond to treatment by taking into account aspects of pharmacodynamics and pharmacokinetics as well as specific features of the host and the target organ. Wherever possible, the EUCAST ECOFF values were used to interpret the MIC results.

References

[1] M. Stegger, J. A. Lindsay, A. Moodley, R. Skov, E. M. Broens, L. Guardabassi Rapid PCR Detection of *Staphylococcus aureus* Clonal Complex 398 by Targeting the Restriction-Modification System Carrying sau1-hsdS1. J Clin Microbiol, Febr. 2011, p. 732–734

[2] Harmsen D. et al. Typing of methicillin-resistant *Staphylococcus aureus* in a university hospital setting by using novel software for spa repeat determination and database management. J Clin Microbiol 2003; 41(12):5442–5448

Annexe I

Defined daily dose (DDD) of antibiotics for patient treatment

Annexe I: Defined daily dose (DDD) of antibiotics for patient treatment

Table I.1: List of defined daily doses (DDD) according to the WHO for each antibiotic and administration route of antibacterials for systemic use (ATC group J01), antibiotics for treatment of tuberculosis (ATC group J04AB) and antibiotics against amoebiasis and other protozoal diseases (ATC group P01AB).

ATC Group	Antibiotic Name	Administration route	DDD [g]
J01A	Doxycycline	oral	0.1
	Doxycycline	parenteral	0.1
	Lymecycline	oral	0.6
	Minocycline	oral	0.2
	Tetracycline	oral	1
	Tetracycline	parenteral	1
	Tigecycline	parenteral	0.1
J01C	Amoxicillin	oral	1
	Amoxicillin	parenteral	1
	Amoxicillin-clavulanic acid	oral	1
	Amoxicillin-clavulanic acid	parenteral	3
	Flucloxacillin	oral	2
	Flucloxacillin	parenteral	2
	Phenoxymethylpenicillin	oral	2
	Benzathine phenoxymethylpenicillin	oral	2
	Benzathine benzylpenicillin	parenteral	3.6
	Piperacillin	parenteral	14
	Piperacillin-tazobactam	parenteral	14
	Ticarcillin	parenteral	15
	Ticarcillin-clavulanic acid	parenteral	15

ATC Group	Antibiotic Name	Administration route	DDD [g]
J01D	Aztreonam	parenteral	4
	Cefaclor	oral	1
	Cefamandole	parenteral	6
	Cefazolin	parenteral	3
	Cefepime	parenteral	2
	Cefixime	oral	0.4
	Cefotaxime	parenteral	4
	Cefoxitin	parenteral	6
	Cefpodoxime	oral	0.4
	Cefprozil	oral	1
	Ceftaroline	parenteral	1.2
	Ceftazidime	parenteral	4
	Ceftibuten	oral	0.4
	Ceftriaxone	parenteral	2
	Cefuroxime	oral	0.5
	Cefuroxime	parenteral	3
	Ertapenem	parenteral	1
	Imipenem	parenteral	2
	Meropenem	parenteral	2
J01E	Sulfadiazine	oral	0.6
	Sulfadiazine	parenteral	0.6
	Trimethoprim	oral	0.4
	Trimethoprim-sulfamethoxazole	oral	1.92
	Trimethoprim-sulfamethoxazole	parenteral	1.92
J01F	Azithromycin	oral	0.3
	Clarithromycin	oral	0.5
	Clarithromycin	parenteral	1
	Clindamycin	oral	1.2
	Clindamycin	parenteral	1.8
	Erythromycin	oral	2
	Erythromycin	parenteral	1
	Roxithromycin	oral	0.3
	Spiramycin	oral	3
J01G	Amikacin	parenteral	1
	Gentamicin	oral	0.24
	Gentamicin	other	0.24
	Gentamicin	parenteral	0.24
	Neomycin	oral	5
	Netilmicin	oral	0.35
	Netilmicin	parenteral	0.35
	Streptomycin	parenteral	1
	Tobramycin	inhaled	0.3
	Tobramycin	parenteral	0.24

ATC Group	Antibiotic Name	Administration route	DDD [g]
J01M	Ciprofloxacin	oral	1
	Ciprofloxacin	parenteral	0.5
	Levofloxacin	oral	0.5
	Levofloxacin	parenteral	0.5
	Moxifloxacin	oral	0.4
	Moxifloxacin	parenteral	0.4
	Norfloxacin	oral	0.8
	Ofloxacin	oral	0.4
	Ofloxacin	parenteral	0.4
J01X	Colistin	oral	3
	Colistin	inhaled	3
	Colistin	parenteral	3
	Daptomycin	parenteral	0.28
	Fosfomycin	oral	3
	Fosfomycin	parenteral	8
	Fusidic acid	oral	1.5
	Fusidic acid	parenteral	1.5
	Colistin	oral	3
	Colistin	inhaled	3
	Colistin	parenteral	3
	Daptomycin	parenteral	0.28
	Fosfomycin	oral	3
	Fosfomycin	parenteral	8
	Fusidic acid	oral	1.5
	Fusidic acid	parenteral	1.5
	Linezolid	oral	1.2
	Linezolid	parenteral	1.2
	Metronidazole	parenteral	1.5
	Nitrofurantoin	oral	0.2
	Ornidazole	parenteral	1
	Teicoplanin	parenteral	0.4
	Vancomycin	oral	2
	Vancomycin	parenteral	2
J04AB	Rifampicin	oral	0.6
	Rifampicin	parenteral	0.6
	Rifamycin	parenteral	0.6
	Rifabutin	oral	0.15
P01AB	Metronidazole	rectal	2
	Metronidazole	oral	2
	Ornidazole	oral	1.5

Annexe II

Distribution of minimal inhibitory concentrations (MICs) in bacterial isolates from animals

Annexe II: Distribution of minimal inhibitory concentrations (MICs) in bacterial isolates from animals

In all reported tables of Annexe II (distribution of MICs in bacterial isolates from animals), vertical red lines indicate cutoff values for resistance. The white areas indicate the dilution range tested for each antimicrobial agent. Values above this range indicate MIC values > the highest concentration in the range. Values at the lowest concentration tested indicate MIC-values ≤ the lowest concentration in the range. Vertical bars indicate the epidemiological cutoff values, used as breakpoints.

Table II.1: Distribution (n) of MICs (mg/L) in *Salmonella* spp. from poultry in 2014.

Minimal Inhibitory Concentration (MIC) / poultry / *Salmonella* spp. / Number of isolates (N=19)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin								11	5						3					
Azithromycin										11	8									
Cefotaxime						19														
Ceftazidime							19													
Chloramphenicol											19									
Ciprofloxacin		5		12		2														
Colistin								6	9	1	3									
Gentamicin							19													
Meropenem			16		3															
Nalidixic acid										19										
Sulfamethoxazole													6	8	1	1			3	
Tetracycline									16						3					
Tigecycline						15	4													
Trimethoprim						18	1													

Table II.2: Distribution (n) of MICs (mg/L) in *Salmonella typhimurium* from poultry in 2014

Minimal Inhibitory Concentration (MIC) / poultry / *Salmonella typhimurium* / Number of isolates (N=8)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin								5	2						1					
Azithromycin										8										
Cefotaxime						8														
Ceftazidime							8													
Chloramphenicol											8									
Ciprofloxacin		4		3		1														
Colistin								2	2	1	3									
Gentamicin							8													
Meropenem			5		3															
Nalidixic acid										8										
Sulfamethoxazole													1	5		1			1	
Tetracycline									7						1					
Tigecycline						6	2													
Trimethoprim						8														

Table II.3: Distribution (n) of MICs (mg/L) in monophasic *Salmonella typhimurium* from poultry in 2014.

Minimal Inhibitory Concentration (MIC) / poultry / monophasic *Salmonella typhimurium* / Number of isolates (N=2)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin																		2		
Azithromycin										1	1									
Cefotaxime						2														
Ceftazidime							2													
Chloramphenicol											2									
Ciprofloxacin			2																	
Colistin								2												
Gentamicin							2													
Meropenem			2																	
Nalidixic acid										2										
Sulfamethoxazole																			2	
Tetracycline															2					
Tigecycline						1	1													
Trimethoprim						2														

Table II.4: Distribution (n) of MICs (mg/L) in *Salmonella enteritidis* from poultry in 2014.

Minimal Inhibitory Concentration (MIC) / poultry / *Salmonella enteritidis* / Number of isolates (N=9)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin								6	3											
Azithromycin										2	7									
Cefotaxime						9														
Ceftazidime							9													
Chloramphenicol											9									
Ciprofloxacin		1	7	1																
Colistin								2	7											
Gentamicin							9													
Meropenem			9																	
Nalidixic acid										9										
Sulfamethoxazole													5	3	1					
Tetracycline									9											
Tigecycline						8	1													
Trimethoprim						8	1													

Table II.5: Distribution (n) of MICs (mg/L) in *Salmonella* spp. from cattle in 2014.

Minimal Inhibitory Concentration (MIC) / cattle / *Salmonella* spp. / Number of isolates (N=23)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin								8	3						12					
Azithromycin										12	9	2								
Cefotaxime						23														
Ceftazidime							23													
Chloramphenicol											20					3				
Ciprofloxacin		6		16		1														
Colistin								14	9											
Gentamicin							21	2												
Meropenem			23																	
Nalidixic acid										22	1									
Sulfamethoxazole													1	10					12	
Tetracycline									9				1	2	11					
Tigecycline						18	5													
Trimethoprim						22	1													

Table II.6: Distribution (n) of MICs (mg/L) in *Salmonella typhimurium* from cattle in 2014.

Minimal Inhibitory Concentration (MIC) / cattle / *Salmonella typhimurium* / Number of isolates (N=10))																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin								5	2						3					
Azithromycin										4	4	2								
Cefotaxime						10														
Ceftazidime							10													
Chloramphenicol											7					3				
Ciprofloxacin		3		7																
Colistin								5	5											
Gentamicin							9	1												
Meropenem			10																	
Nalidixic acid										9	1									
Sulfamethoxazole														7					3	
Tetracycline									7				1	2						
Tigecycline						8	2													
Trimethoprim						9	1													

Table II.7: Distribution (n) of MICs (mg/L) in monophasic *Salmonella typhimurium* from cattle in 2014.

Minimal Inhibitory Concentration (MIC) / cattle / monophasic *Salmonella typhimurium* / Number of isolates (N=11)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin								2							9					
Azithromycin										8	3									
Cefotaxime						11														
Ceftazidime							11													
Chloramphenicol											11									
Ciprofloxacin		2		9																
Colistin								9	2											
Gentamicin							10	1						1						
Meropenem			11																	
Nalidixic acid										11										
Sulfamethoxazole											2								9	
Tetracycline															11					
Tigecycline						8	3					3								
Trimethoprim						11														

Table II.8: Distribution (n) of MICs (mg/L) in *Salmonella enteritidis* from cattle in 2014.

Minimal Inhibitory Concentration (MIC) / cattle / *Salmonella enteritidis* / Number of isolates (N=2)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin								1	1											
Azithromycin											2									
Cefotaxime						2														
Ceftazidime							2													
Chloramphenicol											2									
Ciprofloxacin		1		1																
Colistin									2											
Gentamicin							2													
Meropenem			2																	
Nalidixic acid										2										
Sulfamethoxazole													1	1						
Tetracycline									2											
Tigecycline						2														
Trimethoprim						2														

Table II.9: Distribution (n) of MICs (mg/L) in *Salmonella* spp. from poultry in 2015.

Minimal Inhibitory Concentration (MIC) / poultry / *Salmonella* spp. / Number of isolates (N=31)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin							9		19						3					
Azithromycin										27	4									
Cefotaxime					31															
Ceftazidime						31														
Chloramphenicol										29						2				
Ciprofloxacin	6		25																	
Colistin							22		7		2									
Gentamicin						28		3												
Meropenem		25		6																
Nalidixic acid									30		1									
Sulfamethoxazole													6	9	13				3	
Tetracycline								22		6			1	1	1					
Tigecycline					21		10													
Trimethoprim					28		3													

Table II.10: Distribution (n) of MICs (mg/L) in *Salmonella typhimurium* from poultry in 2015.

Minimal Inhibitory Concentration (MIC) / poultry / *Salmonella typhimurium* / Number of isolates (N=21)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin							9		10						2					
Azithromycin										20	1									
Cefotaxime					21															
Ceftazidime						21														
Chloramphenicol										19						2				
Ciprofloxacin	3		18																	
Colistin							16		3		2									
Gentamicin						18		3												
Meropenem		15		6																
Nalidixic acid									20		1									
Sulfamethoxazole													6	3	10				2	
Tetracycline								13		6			1	1						
Tigecycline					11		10													
Trimethoprim					19		2													

Table II.11: Distribution (n) of MICs (mg/L) in monophasic *Salmonella typhimurium* from poultry in 2015.

Minimal Inhibitory Concentration (MIC) / poultry / monophasic *Salmonella typhimurium* / Number of isolates (N=1)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin															1					
Azithromycin										1										
Cefotaxime					1															
Ceftazidime						1														
Chloramphenicol										1										
Ciprofloxacin			1																	
Colistin							1													
Gentamicin						1														
Meropenem		1																		
Nalidixic acid									1											
Sulfamethoxazole																			1	
Tetracycline															1					
Tigecycline					1															
Trimethoprim					1															

Table II.12: Distribution (n) of MICs (mg/L) in *Salmonella enteritidis* from poultry in 2015.

Minimal Inhibitory Concentration (MIC) / poultry / *Salmonella enteritidis* / Number of isolates (N=9)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin									9											
Azithromycin										6	3									
Cefotaxime					9															
Ceftazidime						9														
Chloramphenicol										9										
Ciprofloxacin	3		6																	
Colistin							5		4											
Gentamicin						9														
Meropenem		9																		
Nalidixic acid									9											
Sulfamethoxazole														6	3					
Tetracycline								9												
Tigecycline					9															
Trimethoprim					8			1												

Table II.13: Distribution (n) of MICs (mg/L) in *Salmonella* spp. from cattle in 2015.

Minimal Inhibitory Concentration (MIC) / cattle / *Salmonella* spp. / Number of isolates (N=33)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin							17		6						9					
Azithromycin										29	3									
Cefotaxime					32															
Ceftazidime						32														
Chloramphenicol										31						1				
Ciprofloxacin	11		21																	
Colistin							20		11	1										
Gentamicin						29		3												
Meropenem		30		2																
Nalidixic acid									31		1									
Sulfamethoxazole														2	19	2			9	
Tetracycline								17		1			4	2	8					
Tigecycline					13		19													
Trimethoprim					27		4							1						

Table II.14: Distribution (n) of MICs (mg/L) in *Salmonella typhimurium* from cattle in 2015.

Minimal Inhibitory Concentration (MIC) / cattle / *Salmonella typhimurium* / Number of isolates (N=19)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin							16		2						1					
Azithromycin										18	1									
Cefotaxime					19															
Ceftazidime						19														
Chloramphenicol										18						1				
Ciprofloxacin	4		15																	
Colistin							10		9											
Gentamicin						16		3												
Meropenem		19																		
Nalidixic acid									18		1									
Sulfamethoxazole														2	14	2			1	
Tetracycline								12		1			4	2						
Tigecycline					7		12													
Trimethoprim					16		3													

Table II.15: Distribution (n) of MICs (mg/L) in monophasic *Salmonella typhimurium* from cattle in 2015.

Minimal Inhibitory Concentration (MIC) / cattle / monophasic *Salmonella typhimurium* / Number of isolates (N=8)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin															8					
Azithromycin										7	1									
Cefotaxime					8															
Ceftazidime						8														
Chloramphenicol										8										
Ciprofloxacin	3		5																	
Colistin								6	2											
Gentamicin						8														
Meropenem		7		1																
Nalidixic acid									8											
Sulfamethoxazole																			8	
Tetracycline															8					
Tigecycline					2		6													
Trimethoprim					7									1						

Table II.16: Distribution (n) of MICs (mg/L) in *Salmonella enteritidis* from cattle in 2015.

Minimal Inhibitory Concentration (MIC) / cattle / *Salmonella enteritidis* / Number of isolates (N=5)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin							1		4											
Azithromycin										4	1									
Cefotaxime					5															
Ceftazidime						5														
Chloramphenicol										5										
Ciprofloxacin	4		1																	
Colistin							4			1										
Gentamicin						5														
Meropenem		4		1																
Nalidixic acid									5											
Sulfamethoxazole															5					
Tetracycline								5												
Tigecycline					4		1													
Trimethoprim					4		1													

Table II.17: Distribution (n) of MICs (mg/L) in *Campylobacter jejuni* from broilers in 2014.

Minimal Inhibitory Concentration (MIC) / broiler / *Campylobacter jejuni* / Number of isolates (N=159)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Chloramphenicol									32	110	17									
Ciprofloxacin				27	52	6	1	1			72									
Erythromycin							34	61	49	14				1						
Gentamicin					46	82	29			2										
Nalidixic acid									10	61	14				74					
Streptomycin								151	3			1	4							
Tetracycline						62	45	9	2			1	40							

Table II.18: Distribution (n) of MICs (mg/L) in *Campylobacter coli* from broilers in 2014.

Minimal Inhibitory Concentration (MIC) / broiler / *Campylobacter coli* / Number of isolates (N=15)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Chloramphenicol										7	7	1								
Ciprofloxacin				3	4	2				1	5									
Erythromycin							4	1	5	2		1		2						
Gentamicin					1	5	9													
Nalidixic acid										3	5	1			6					
Streptomycin								3	5			1	6							
Tetracycline						1	6	1	2				5							

Table II.19: Distribution (n) of MICs (mg/L) in *Campylobacter coli* from fattening pigs in 2015.

Minimal Inhibitory Concentration (MIC) / fattening pigs / *Campylobacter coli* / Number of isolates (N=156))																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ciprofloxacin				55		25	3			9	27	32	5							
Erythromycin							102		31	14	2		1	2	1	3				
Gentamicin				8		20	95	32					1							
Nalidixic acid									1	26	44	12		2	71					
Streptomycin							1	4	12	4	5	34	96							
Tetracycline						39		12	6	3	3	7	38	33	15					

Table II.20: Distribution (n) of MICs (mg/L) in *Enterococcus faecalis* from broilers, NLV plate, in 2014.

Minimal Inhibitory Concentration (MIC) / broiler / *Enterococcus faecalis* / Number of isolates (N=113)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin									110	2	1									
Chloramphenicol										9	87	16		1						
Ciprofloxacin							33	57	23											
Erythromycin							22	45	19	7	1		19							
Gentamicin															113					
Linezolid								18	92	3										
Tetracycline									1	7	42	18	6							
Vancomycin								45	8					60						

Table II.21: Distribution (n) of MICs (mg/L) in *Enterococcus faecalis* from broilers, EUVENC plate, in 2014.

MinimMinimal Inhibitory Concentration (MIC) / broiler / *Enterococcus faecalis* / Number of isolates (N=89)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin							2	31	52	4										
Chloramphenicol											60	26	1							
Ciprofloxacin					2	7	6	45	28	3										
Daptomycin								7	26	55	1									
Erythromycin								46	21	8										
Gentamicin											35	53							1	
Linezolid								1	53	35										
Teicoplanin							88	1												
Tetracycline								28	16			2	1	15	27					
Tigecycline						30	59													
Vancomycin								44	42	3										

Table II.22: Distribution (n) of MICs (mg/L) in *Enterococcus faecium* from broilers in 2014.

Minimal Inhibitory Concentration (MIC) / broiler / *Enterococcus faecium* / Number of isolates (N=80)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin									70	6	3			1						
Chloramphenicol									3	15	53	8	1							
Ciprofloxacin							5	24	24	24	3									
Erythromycin							22	21	11	4	2	2	18							
Gentamicin															80					
Linezolid							1	11	45	23										
Quinupristin / Dalfopristin							4	16	24	30	1	3	2							
Tetracycline								53	2	1	1	4	1	18						
Vancomycin								76	1	3										

Table II.23: Distribution (n) of MICs (mg/L) in *Enterococcus faecalis* from veal calves in 2015.

Minimal Inhibitory Concentration (MIC) / veal calves / *Enterococcus faecalis* / Number of isolates (N=56)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin								32	22	2										
Chloramphenicol									2		40	3	1	10						
Ciprofloxacin							7	34	15											
Daptomycin					2		3	28	20	3										
Erythromycin							33		2	1						20				
Gentamicin										20		29				1		1	5	
Linezolid								5	43	8										
Quinupristin / Dalfopristin								1	1	18	17	11	5	2	1					
Teicoplanin						56														
Tetracycline							18		3	1	1			18	12	3				
Tigecycline				18	34	4														
Vancomycin							34		22											

Table II.24: Distribution (n) of MICs (mg/L) in *Enterococcus faecium* from veal calves in 2015.

Minimal Inhibitory Concentration (MIC) / veal calves / *Enterococcus faecium* / Number of isolates (N=151)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin						6		34	94	16	1									
Chloramphenicol									42		104	4	1							
Ciprofloxacin							2	114	22	10	3									
Daptomycin					2		2	23	29	89	6									
Erythromycin							5		3	95	32	3				13				
Gentamicin										34		109	8							
Linezolid						1		1	41	108										
Quinupristin / Dalfopristin								9	5	132	5									
Teicoplanin						149		2												
Tetracycline							132		1	2		2	2	2	9	1				
Tigecycline				50	100	1														
Vancomycin							149		1	1										

Table II.25: Distribution (n) of MICs (mg/L) in *Enterococcus faecalis* from fattening pigs in 2015.

Minimal Inhibitory Concentration (MIC) / fattening pigs / *Enterococcus faecalis* / Number of isolates (N=28)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin								9	17	2										
Chloramphenicol											16	7		4	1					
Ciprofloxacin							1	13	14											
Daptomycin								3	15	10										
Erythromycin							6		5	5						12				
Gentamicin										3		22	1						2	
Linezolid								2	20	6										
Quinupristin / Dalfopristin										2	2	18	4	2						
Teicoplanin						28														
Tetracycline							5		2				1	10	10					
Tigecycline				10	18															
Vancomycin							9		12	7										

Table II.26: Distribution (n) of MICs (mg/L) in *Enterococcus faecium* from fattening pigs in 2015.

Minimal Inhibitory Concentration (MIC) / fattening pigs / *Enterococcus faecium* / Number of isolates (N=53)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin						1		13	28	3	6	2								
Chloramphenicol									4		43	2		4						
Ciprofloxacin							2	25	13	10	2	1								
Daptomycin								2	10	32	9									
Erythromycin							3		10	29	4					7				
Gentamicin										28		23	1						1	
Linezolid									12	41										
Quinupristin / Dalfopristin						1		5	2	31	7	7								
Teicoplanin						49		2			1				1					
Tetracycline							33		2				1	4	12	1				
Tigecycline				16	37															
Vancomycin							44		7						1	1				

Table II.27: Distribution (n) of MICs (mg/L) in *Escherichia coli* from broilers in 2014.

Minimal Inhibitory Concentration (MIC) / broiler / *Escherichia coli* / Number of isolates (N=200)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin								37	65	51	2				45					
Azithromycin									16	119	60	4		1						
Cefotaxime						194	1			1	4									
Ceftazidime							194	3	1		1	1								
Chloramphenicol											193	1				6				
Ciprofloxacin		122	9	5	19	25	7			1	6	6								
Colistin								200												
Gentamicin							140	56	2	2										
Meropenem			197	3																
Nalidixic acid										131	1	1	10	8	26	23				
Sulfamethoxazole											49	53	43	5					50	
Tetracycline									153	2			2	24	19					
Tigecycline						187	13													
Trimethoprim						134	37	5						24						

Table II.28: Distribution (n) of MICs (mg/L) in *Escherichia coli* from fattening pigs, EUVSEC, in 2015.

Minimal Inhibitory Concentration (MIC) / fattening pigs / *Escherichia coli* / Number of isolates (N=182)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin							11		72	65	3				31					
Azithromycin								13		91	75	3								
Cefotaxime					178	3	1													
Ceftazidime	178						3	1												
Chloramphenicol										161	3	3	10	4		1				
Ciprofloxacin	159	3	13	1		2	3					1								
Colistin							179	3												
Gentamicin						109	3	61	6	1				2						
Meropenem		179	3																	
Nalidixic acid									172	3	1			2	1	3				
Sulfamethoxazole										24		38	27	17	1			1	74	
Tetracycline								118	2	7	1	3		25	26					
Tigecycline					163	3	16													
Trimethoprim					82	1	52	7						40						

Table II.29: Distribution (n) of MICs (mg/L) in *Escherichia coli* from fattening pigs, EUVSEC2, in 2015.

Minimal Inhibitory Concentration (MIC) / fattening pigs / *Escherichia coli* / Number of isolates (N=4)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefepime			1	3																
Cefotaxime					1	3														
Cefotaxime / clavulanic acid			1	3																
Cefoxitin										3	1									
Ceftazidime					1	3														
Ceftazidime / clavulanic acid				1	3															
Ertapenem	1	3																		
Imipenem				1	2	1														
Meropenem		1	3																	
Temocillin										4										

Table II.30: Distribution (n) of MICs (mg/L) in *Escherichia coli* from veal calves, EUVSEC, in 2015.

Minimal Inhibitory Concentration (MIC) / veal calves / *Escherichia coli* / Number of isolates (N=190)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin							4		56	55	5	1			69					
Azithromycin								7		78	95	9	1							
Cefotaxime					183		3				4									
Ceftazidime						183		3	1	1	1	1								
Chloramphenicol										163		5	5	5	3	9				
Ciprofloxacin	153		23	1	3	6	1					3								
Colistin							189						1							
Gentamicin						106		69	4	1	1	3	2	4						
Meropenem		188		1							1									
Nalidixic acid									177		1			1	6	5				
Sulfamethoxazole										23		46	30	12	4			1	74	
Tetracycline								110		2	1		1	24	52					
Tigecycline					175		15													
Trimethoprim					86		62	12						30						

Table II.31: Distribution (n) of MICs (mg/L) in Escherichia coli from veal calves, EUVSEC2, in 2015.

Minimal Inhibitory Concentration (MIC) / veal calves / *Escherichia coli* / Number of isolates (N=7)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefepime			2		1	1				1	2									
Cefotaxime					3		1					1	1	1						
Cefotaxime / clavulanic acid			6		1															
Cefoxitin									2	3	2									
Ceftazidime					2		1	1	1	1	1									
Ceftazidime / clavulanic acid				6		1														
Ertapenem	6		1																	
Imipenem				6		1														
Meropenem		7																		
Temocillin										5	2									

Table II.32: Distribution (n) of MICs (mg/L) in suspected ESBL/pAmpC-producing *Escherichia coli* from broilers, EUVSEC, in 2014.

Minimal Inhibitory Concentration (MIC) / broiler / *Escherichia coli* / Number of isolates (N=124)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin														2	122					
Azithromycin									2	73	48	1								
Cefotaxime							4	7	10	13	90									
Ceftazidime							12	26	15	13	29	29								
Chloramphenicol											101		2		2	19				
Ciprofloxacin		61	7	1	6	12	10	4	2		11	10								
Colistin								123	1											
Gentamicin							70	50	4											
Meropenem			122	1	1															
Nalidixic acid										68	5	2	1	4	12	32				
Sulfamethoxazole											13	19	11	4					77	
Tetracycline									57	1			2	43	21					
Tigecycline						103	20	1												
Trimethoprim						74	9	3						38						

Table II.33: Distribution (n) of MICs (mg/L) in suspected ESBL/pAmpC-producing *Escherichia coli* from broilers, EUVSEC2, in 2014.

Minimal Inhibitory Concentration (MIC) / broiler / Escherichia coli / Number of isolates (N=124)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefepime				4	14	39	14	5	3	23	16	3	2	1						
Cefotaxime							6	9	4	18	32	25	17	9	4					
Cefotaxime / clavulanic acid				62	6	3			3	19	26	4			1					
Cefoxitin									10	45	14	2	15	20	18					
Ceftazidime							11	24	17	14	33	20	4		1					
Ceftazidime / clavulanic acid					53	13	3	2	5	22	21	4		1						
Ertapenem		68	19	15	20	1		1												
Imipenem					55	63	6													
Meropenem			119	4	1															
Temocillin									12	50	54	8								

Table II.34: Distribution (n) of MICs (mg/L) in suspected ESBL/pAmpC-producing *Escherichia coli* from chicken meat, EUVSEC, in 2014.

Minimal Inhibitory Concentration (MIC) / chicken meat / *Escherichia coli* / Number of isolates (N=232)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin													2	16	214					
Azithromycin									15	130	84		1	1	1					
Cefotaxime						1	11	22	26	51	121									
Ceftazidime							13	50	37	40	58	34								
Chloramphenicol											214	2	4	1	1	10				
Ciprofloxacin		104	15		16	44	17	5		4	11	16								
Colistin								226	2	1	3									
Gentamicin							164	50	8		1	1	3	5						
Meropenem			228	4																
Nalidixic acid										122	12	3	9	16	27	43				
Sulfamethoxazole											18	40	42	8	1	123				
Tetracycline									131	2		2	8	39	50					
Tigecycline						197	35													
Trimethoprim						144	21	8						59						

Table II.35: Distribution (n) of MICs (mg/L) in suspected ESBL/pAmpC-producing *Escherichia coli* from chicken meat, EUVSEC2, in 2014.

Minimal Inhibitory Concentration (MIC) / chicken meat / *Escherichia coli* / Number of isolates (N=232)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefepime				13	62	56	20	7	10	45	16	2		1						
Cefotaxime						1	18	21	16	46	54	47	26	2	1					
Cefotaxime / clavulanic acid				107	6	1	2	10	21	45	35	5								
Cefoxitin									17	65	27	12	56	34	21					
Ceftazidime							15	41	44	34	61	30	5	2						
Ceftazidime / clavulanic acid					92	21	3	4	21	49	37	5								
Ertapenem		125	69	19	16	3														
Imipenem					131	95	6													
Meropenem			227	4	1															
Temocillin									16	100	106	10								

Table II.36: Distribution (n) of MICs (mg/L) in suspected ESBL/pAmpC-producing *Escherichia coli* from fattening pigs, EUVSEC, in 2015.

Minimal Inhibitory Concentration (MIC) / fattening pigs / *Escherichia coli* / Number of isolates (N=77)																			
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin									1	1			1		74					
Azithromycin								1		34	33	3	2	4						
Cefotaxime					4		1	7	11	8	46									
Ceftazidime						10		17	11	17	15	7								
Chloramphenicol										63	2	1	2	1	5	3				
Ciprofloxacin	39	2	8	1	1	9	3		1	1	4	8								
Colistin							75	2												
Gentamicin						29	1	27	6		4		4	6						
Meropenem		75	2																	
Nalidixic acid									49	2	7	1		2	2	14				
Sulfamethoxazole										3		4	11	5				4	50	
Tetracycline								29	1			1		12	34					
Tigecycline					63	2	12													
Trimethoprim					20	1	24	2						30						

Table II.37: Distribution (n) of MICs (mg/L) in suspected ESBL/pAmpC-producing *Escherichia coli* from fattening pigs, EUVSEC2, in 2015.

Minimal Inhibitory Concentration (MIC) / fattening pigs / *Escherichia coli* / Number of isolates (N=77)																			
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefepime			12		8	10	1	1	3	20	16	5	1							
Cefotaxime					4		2	12	6	5	3	14	11	14	6					
Cefotaxime / clavulanic acid			49	1	5	1	5	10	4	2										
Cefoxitin									6	32	19	3	10	3	4					
Ceftazidime					4		4	18	11	20	9	9	1	1						
Ceftazidime / clavulanic acid				36	1	17	3		12	3	4	1								
Ertapenem	60	1	15	1																
Imipenem				46	2	28	1													
Meropenem		74	2	1																
Temocillin								1	5	33	35	2	1							

Table II.38: Distribution (n) of MICs (mg/L) in suspected ESBL/pAmpC-producing *Escherichia coli* from pork meat, EUVSEC, in 2015.

Minimal Inhibitory Concentration (MIC) / pork meat / *Escherichia coli* / Number of isolates (N=2)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin															2					
Azithromycin											1	1								
Cefotaxime											2									
Ceftazidime									2											
Chloramphenicol										2										
Ciprofloxacin	1		1																	
Colistin							2													
Gentamicin						1		1												
Meropenem		2																		
Nalidixic acid									2											
Sulfamethoxazole																			2	
Tetracycline								2												
Tigecycline					2															
Trimethoprim														2						

Table II.39: Distribution (n) of MICs (mg/L) in suspected ESBL/pAmpC-producing *Escherichia coli* from pork meat, EUVSEC2, in 2015.

Minimal Inhibitory Concentration (MIC) / pork meat / *Escherichia coli* / Number of isolates (N=2)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefepime												2								
Cefotaxime														2						
Cefotaxime / clavulanic acid			2																	
Cefoxitin										2										
Ceftazidime									1	1										
Ceftazidime / clavulanic acid						2														
Ertapenem	2																			
Imipenem				2																
Meropenem		2																		
Temocillin										2										

Table II.40: Distribution (n) of MICs (mg/L) in suspected ESBL/pAmpC-producing *Escherichia coli* from veal calves, EUVSEC, in 2015.

Minimal Inhibitory Concentration (MIC) / veal calves / *Escherichia coli* / Number of isolates (N=112)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin														7	105					
Azithromycin								3		35	60	6	2	6						
Cefotaxime								16	18	6	72									
Ceftazidime						6		12	33	27	27	7								
Chloramphenicol										71		3		4	11	23				
Ciprofloxacin	43		8		5	19	6	2			12	17								
Colistin							111		1											
Gentamicin						33		32	4		4	5	9	25						
Meropenem		108	1	3																
Nalidixic acid									56		17			2	6	31				
Sulfamethoxazole										5		5	6	1				1	94	
Tetracycline								17		2				23	70					
Tigecycline					89	1	20	2												
Trimethoprim					17		31	1	1					62						

Table II.41: Distribution (n) of MICs (mg/L) in suspected ESBL/pAmpC-producing *Escherichia coli* from veal calves, EUVSEC2, in 2015.

Minimal Inhibitory Concentration (MIC) / veal calves / *Escherichia coli* / Number of isolates (N=112)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefepime			16		17	5	2	5	6	24	22	11	2	2						
Cefotaxime							2	22	8	6	10	10	22	22	10					
Cefotaxime / clavulanic acid			62		12	2	11	16	8		1									
Cefoxitin									4	39	31	9	20	8	1					
Ceftazidime					1		4	14	29	32	25	6	1							
Ceftazidime / clavulanic acid				50		24	1	10	13	9	4	1								
Ertapenem	79	1	25	4	1	2														
Imipenem				70	1	39	2													
Meropenem		108	1	3																
Temocillin									4	56	47	4	1							

Table II.42: Distribution (n) of MICs (mg/L) in suspected ESBL/pAmpC-producing *Escherichia coli* from beef meat, EUVSEC, in 2015.

Minimal Inhibitory Concentration (MIC) / beef meat / *Escherichia coli* / Number of isolates (N=1)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Ampicillin									1											
Azithromycin										1										
Cefotaxime					1															
Ceftazidime						1														
Chloramphenicol										1										
Ciprofloxacin	1																			
Colistin							1													
Gentamicin						1														
Meropenem		1																		
Nalidixic acid									1											
Sulfamethoxazole														1						
Tetracycline								1												
Tigecycline					1															
Trimethoprim					1															

Table II.43: Distribution (n) of MICs (mg/L) in suspected ESBL/pAmpC-producing *Escherichia coli* from beef meat, EU-VSEC2, in 2015

Minimal Inhibitory Concentration (MIC) / beef meat / *Escherichia coli* / Number of isolates (N=1)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefepime			1																	
Cefotaxime					1															
Cefotaxime / clavulanic acid					1															
Cefoxitin										1										
Ceftazidime					1															
Ceftazidime / clavulanic acid				1																
Ertapenem	1																			
Imipenem				1																
Meropenem		1																		
Temocillin										1										

Table II.44: Distribution (n) of MICs (mg/L) in MRSA from fattening pigs in 2014.

Minimal Inhibitory Concentration (MIC) / fattening pigs / MRSA / Number of isolates (N=79)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefoxitin											7	72								
Chloramphenicol										2	76	1								
Ciprofloxacin						46	26		3		3	1								
Clindamycin					15	1	2		1	1	59									
Erythromycin						1	17	1				60								
Fusidic acid							79													
Gentamicin								73	1			1	4							
Kanamycin										69	3	2			5					
Linezolid								3	74	2										
Mupirocin							78	1												
Oxacillin										8	50	21								
Penicillin										79										
Rifampicin		77	1					1												
Streptomycin										1	31			47						
Sulfamethoxazole														75	1	2	1			
Tetracycline													79							
Tiamulin							8	9			62									
Trimethoprim									20					59						
Vancomycin								78	1											

Table II.45: Distribution (n) of MICs (mg/L) in MRSA from fattening pigs in 2015.

Minimal Inhibitory Concentration (MIC) / fattening pigs / MRSA / Number of isolates (N=77)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefoxitin											17	52	8							
Chloramphenicol									2			73	2							
Ciprofloxacin					27		39	2	3	1	1	4								
Clindamycin				20		1	1			1	54									
Erythromycin					5		18					54								
Fusidic acid						75			1		1									
Gentamicin							71		2		1	1	2							
Kanamycin									71		2			1	3					
Linezolid							6		65	4		2								
Mupirocin						72		4								1				
Penicillin										77										
Quinupristin / Dalfopristin						18		6	19	24	10									
Rifampicin	74			1			1	1												
Streptomycin									17		16	2	2	40						
Sulfamethoxazole													71		2			4		
Tetracycline						1							76							
Tiamulin						18		5			54									
Trimethoprim								22				1		54						
Vancomycin							74		2				1							

Table II.46: Distribution (n) of MICs (mg/L) in MRSA from pork meat in 2015.

Minimal Inhibitory Concentration (MIC) / pork meat / MRSA / Number of isolates (N=2)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefoxitin												2								
Chloramphenicol											2									
Ciprofloxacin							1		1											
Clindamycin											2									
Erythromycin												2								
Fusidic acid						1		1												
Gentamicin							2													
Kanamycin									2											
Linezolid									2											
Mupirocin						2														
Penicillin										2										
Quinupristin / Dalfopristin										2										
Rifampicin	2																			
Streptomycin														2						
Sulfamethoxazole													2							
Tetracycline													2							
Tiamulin											2									
Trimethoprim														2						
Vancomycin							2													

Table II.47: Distribution (n) of MICs (mg/L) in MRSA from veal calves in 2015.

Minimal Inhibitory Concentration (MIC) / veal calves / MRSA / Number of isolates (N=19)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefoxitin											3	12	4							
Chloramphenicol											18			1						
Ciprofloxacin					11		4	1			1	2								
Clindamycin				5							14									
Erythromycin					2		3					14								
Fusidic acid						18					1									
Gentamicin							16						3							
Kanamycin									16						3					
Linezolid							7		11			1								
Mupirocin						17		1								1				
Penicillin									1	18										
Quinupristin / Dalfopristin						5		8	1	2	3									
Rifampicin	18							1												
Streptomycin									7		3	1		8						
Sulfamethoxazole													19							
Tetracycline													19							
Tiamulin						11		2			6									
Trimethoprim								12						7						
Vancomycin							18						1							

Table II.48: Distribution (n) of MICs (mg/L) in MRSA from chicken meat in 2014.

Minimal Inhibitory Concentration (MIC) / chicken meat / MRSA / Number of isolates (N=22)																				
	0.01	0.02	0.03	0.06	0.13	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1,024	2,048	4,096
Cefoxitin											2	20								
Chloramphenicol											20	2								
Ciprofloxacin						13	4				1					4				
Clindamycin					3		1				18									
Erythromycin						2	4					16								
Fusidic acid							22													
Gentamicin								22												
Kanamycin										20	2									
Linezolid								1	21											
Mupirocin							19	3												
Oxacillin										5	9	8								
Penicillin										22										
Rifampicin		22																		
Streptomycin										3	15			4						
Sulfamethoxazole														19		3				
Tetracycline							3						19							
Tiamulin							1	3			18									
Trimethoprim									2		3			17						
Vancomycin								22												

Annexe III

Tables of multi-resistance patterns in bacterial isolates from animals in 2014

Annexe III: Tables of multi-resistance patterns in bacterial isolates from animals in 2014

Table III.1: Multi-resistance patterns of *Salmonella* spp. from poultry in 2014.

Number of resistances	Number of isolates	Serovar	Ampicillin	Azithromycin	Cefotaxime	Ceftazidime	Chloramphenicol	Ciprofloxacin	Colistin	Gentamicin	Meropenem	Nalidixic acid	Sulfamethoxazole	Tetracycline	Tigecycline	Trimethoprim
4 ABM	1	*S. typhimurium*														
3 ABM	2	Monophasic *S. typhimurium*														

ABM: antimicrobial

Table III.2: Multi-resistance patterns of *Salmonella* spp. from poultry in 2014.

Number of resistances	Number of isolates	Serovar	Ampicillin	Azithromycin	Cefotaxime	Ceftazidime	Chloramphenicol	Ciprofloxacin	Colistin	Gentamicin	Meropenem	Nalidixic acid	Sulfamethoxazole	Tetracycline	Tigecycline	Trimethoprim
4 ABM	3	*S. typhimurium*														
3 ABM	9	Monophasic *S. typhimurium*														

ABM: antimicrobial

Table III.3: Multi-resistance patterns of *Campylobacter jejuni* from broilers in 2014.

Number of resistances	Number of isolates	Chloramphenicol	Ciprofloxacin	Erythromycin	Gentamicin	Nalidixic acid	Streptomycin	Tetracycline
6 ABM	1							
4 ABM	1							
	2							
3 ABM	30							
	1							
2 ABM	39							

ABM: antimicrobial

Table III.4: Multi-resistance patterns of *Campylobacter coli* from broilers in 2014.

Number of resistances	Number of isolates	Chloramphenicol	Ciprofloxacin	Erythromycin	Gentamicin	Nalidixic acid	Streptomycin	Tetracycline
5 ABM	1							
4 ABM	1							
	1							
3 ABM	1							
	1							
2 ABM	1							
	1							

Table III.5: Multi-resistance patterns of *Enterococcus faecalis* from broilers in 2014.

Number of resistances	Number of isolates	Ampicillin	Chloramphenicol	Ciprofloxacin	Daptomycin	Erythromycin	Gentamicin	Linezolid	Teicoplanin	Tetracycline	Tigecycline	Vancomycin
4 ABM	1											
3 ABM	9											
	1											
2 ABM	19											
	18											
	1											
	1											
	1											

Table III.6: Multi-resistance patterns of *Enterococcus faecium* from broilers in 2014.

Number of resistances	Number of isolates	Ampicillin	Chloramphenicol	Ciprofloxacin	Daptomycin	Erythromycin	Gentamicin	Linezolid	Quinupristin/dalfopristin	Teicoplanin	Tetracycline	Tigecycline
4 ABM	1											
	1											
3 ABM	4											
	2											
2 ABM	15											
	13											
	1											

Table III.7: Multi-resistance patterns of *Escherichia coli* from broilers in 2014.

Number of resistances	Number of isolates	Ampicillin	Azithromycin	Cefotaxime	Ceftazidime	Chloramphenicol	Ciprofloxacin	Colistin	Gentamicin	Meropenem	Nalidixic acid	Sulfamethoxazole	Tetracycline	Tigecycline	Trimethoprim
7 ABM	1	R				R	R				R	R	R		R
	1	R		R			R				R	R	R		R
6 ABM	3	R					R				R	R	R		R
	1	R		R	R		R				R		R		
	1	R				R	R				R	R			R
5 ABM	4					R	R				R	R	R		
	1	R	R									R	R		R
	1	R		R	R							R	R		
	1	R		R	R							R			R
	1	R					R				R	R			R
	1	R					R				R	R	R		
	1						R				R	R	R		R
4 ABM	7	R										R	R		R
	5						R				R	R	R		
	2	R					R				R		R		
	1						R		R		R	R			
	1				R		R				R		R		
3 ABM	4						R				R		R		
	3	R					R				R				
	3	R										R			R
	3											R	R		R
	2	R		R	R										
	2						R				R	R			
	1						R		R		R				
2 ABM	30						R				R				
	5	R										R			
	3	R											R		
	2											R	R		
	1										R		R		
	1										R				R

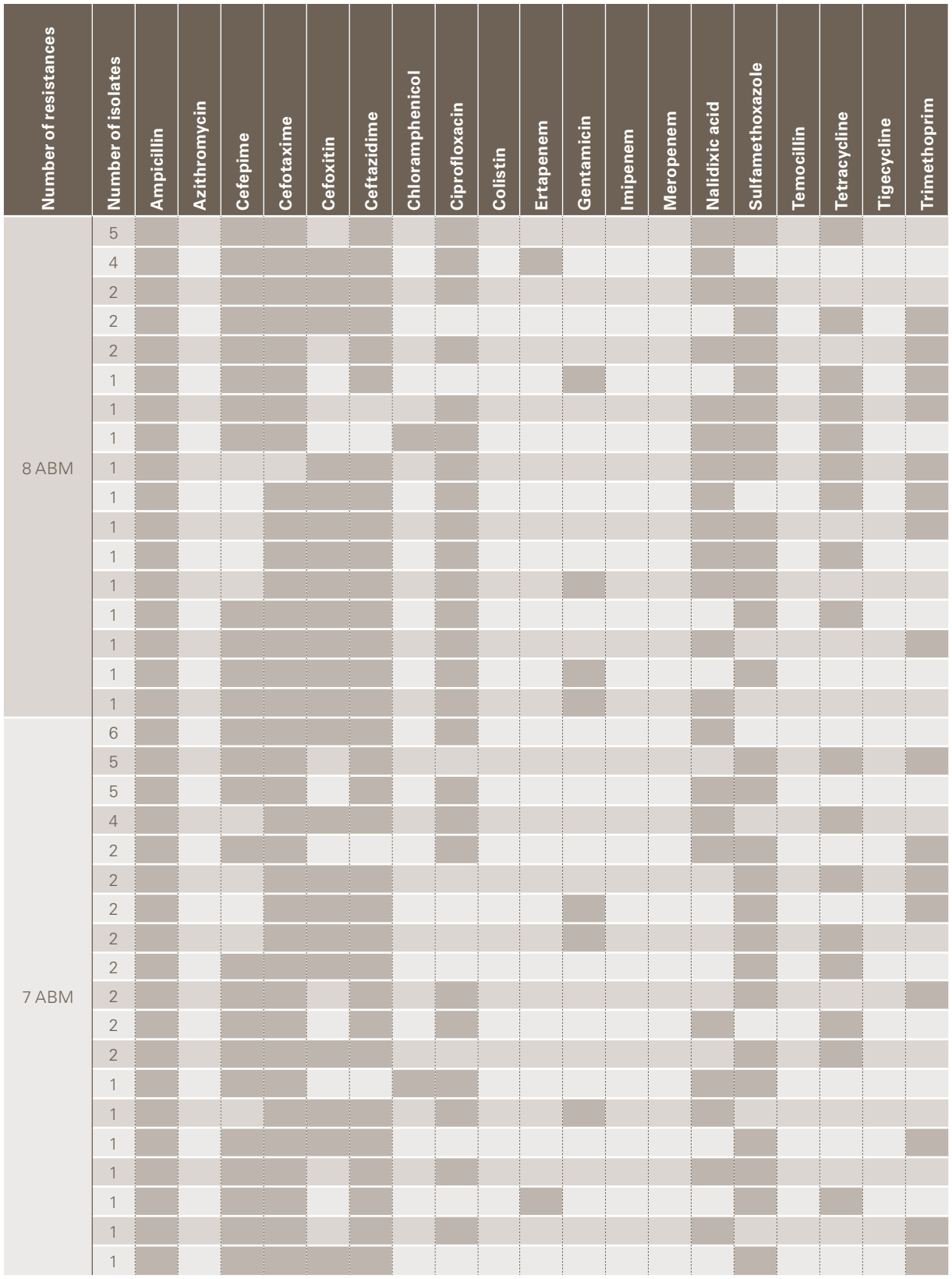
Table III.8: Multi-resistance patterns of suspected ESBL/AmpC-producing *Escherichia coli* from broilers in 2014.

Number of resistances	Number of isolates	Ampicillin	Azithromycin	Cefepime	Cefotaxime	Cefoxitin	Ceftazidime	Chloramphenicol	Ciprofloxacin	Colistin	Ertapenem	Gentamicin	Imipenem	Meropenem	Nalidixic acid	Sulfamethoxazole	Temocillin	Tetracycline	Tigecycline	Trimethoprim
11 ABM	9																			
10 ABM	4																			
9 ABM	5																			
	4																			
	3																			
	1																			
	1																			
8 ABM	3																			
	2																			
	2																			
	2																			
	2																			
	1																			
	1																			
	1																			
	1																			
	1																			
	1																			
7 ABM	7																			
	4																			
	2																			
	1																			
	1																			
	1																			
	1																			
	1																			
	1																			
	1																			
	1																			
6 ABM	7																			
	6																			
	5																			
	3																			
	2																			
	1																			
	1																			
	1																			
	1																			
	1																			

Number of resistances	Number of isolates	Ampicillin	Azithromycin	Cefepime	Cefotaxime	Cefoxitin	Ceftazidime	Chloramphenicol	Ciprofloxacin	Colistin	Ertapenem	Gentamicin	Imipenem	Meropenem	Nalidixic acid	Sulfamethoxazole	Temocillin	Tetracycline	Tigecycline	Trimethoprim
5 ABM	7																			
	2																			
	2																			
	1																			
	1																			
	1																			
	1																			
4 ABM	7																			
	2																			
	1																			
	1																			
	1																			
	1																			
3 ABM	3																			

Table III.9: Multi-resistance patterns of suspected ESBL/pAmpC-producing *Escherichia coli* from broiler meat in 2014.

Number of resistances	Number of isolates	Ampicillin	Azithromycin	Cefepime	Cefotaxime	Cefoxitin	Ceftazidime	Chloramphenicol	Ciprofloxacin	Colistin	Ertapenem	Gentamicin	Imipenem	Meropenem	Nalidixic acid	Sulfamethoxazole	Temocillin	Tetracycline	Tigecycline	Trimethoprim
12 ABM	1																			
11 ABM	6																			
10 ABM	2																			
9 ABM	2																			
	1																			
	1																			
	1																			
	1																			
	1																			
	1																			
	1																			
	1																			
	5																			
	4																			
	3																			
	1																			
	1																			
	1																			
	1																			
	1																			
	1																			


Number of resistances
Number of isolates
Ampicillin
Azithromycin
Cefepime
Cefotaxime
Cefoxitin
Ceftazidime
Chloramphenicol
Ciprofloxacin
Colistin
Ertapenem
Gentamicin
Imipenem
Meropenem
Nalidixic acid
Sulfamethoxazole
Temocillin
Tetracycline
Tigecycline
Trimethoprim
8 ABM
7 ABM

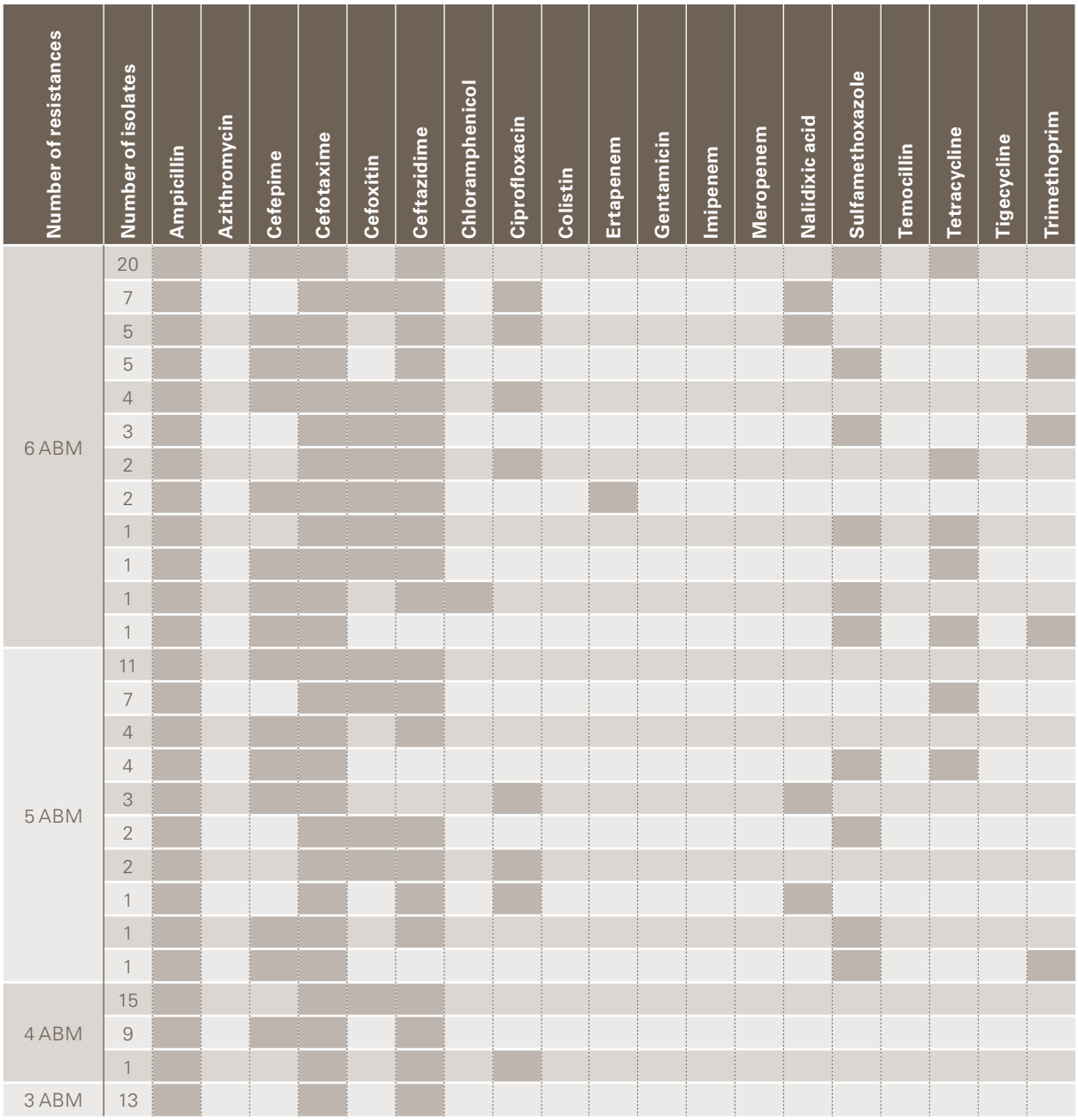

Number of resistances
Number of isolates
Ampicillin
Azithromycin
Cefepime
Cefotaxime
Cefoxitin
Ceftazidime
Chloramphenicol
Ciprofloxacin
Colistin
Ertapenem
Gentamicin
Imipenem
Meropenem
Nalidixic acid
Sulfamethoxazole
Temocillin
Tetracycline
Tigecycline
Trimethoprim
6 ABM
20
7
5
5
4
3
2
2
1
1
1
1
5 ABM
11
7
4
4
3
2
2
1
1
1
4 ABM
15
9
1
3 ABM
13

Table III.10: Multi-resistance patterns of MRSA from fattening pigs in 2014.

Number of resistances	Number of isolates	spa Type	Cefoxitin	Ciprofloxacin	Clindamycin	Erythromycin	Fusidic acid	Gentamicin	Kanamycin	Mupirocin	Oxacillin	Penicillin	Rifampin	Sulfamethoxazole	Streptomycin	Tetracycline	Tiamulin	Trimethoprim
11 ABM	4	3 x t034																
		1 x t2741																
10 ABM	3	3 x t034																
	2	2 x t034																
	1	t034																
	1	t034																
9 ABM	28	27 x t034																
		1 x t011																
	1	t 034																
8 ABM	16	16 x t034																
	2	2 x t034																
	1	1 x t011																
7 ABM	3	3 x t011																
	1	1 x t011																
6 ABM	1	t034																
	1	t208																
5 ABM	7	7 x t011																
4 ABM	7	6 x t011																
		1 x t034																

Table III.11: Multi-resistance patterns of MRSA from broiler meat.

Number of resistances	Number of isolates	spa Type	Cefoxitin	Ciprofloxacin	Clindamycin	Erythromycin	Fusidic acid	Gentamicin	Kanamycin	Mupirocin	Oxacillin	Penicillin	Rifampin	Sulfamethoxazole	Streptomycin	Tetracycline	Tiamulin	Trimethoprim
10 ABM	1	t034																
9 ABM	2	2 x t034																
	1	t034																
	1	t034																
8 ABM	10	8 x t034																
		1 x t571																
		1 x t899																
7 ABM	1	t011																
	1	t011																
	1	t034																
6 ABM	1	t011																
5 ABM	3	3 x t032																

Annexe IV

anresis.ch participants and steering committee

Annexe IV: anresis.ch participants and steering committee

Table IV.1: Hospital pharmacies (or other units) involved in the data collection

Hospital pharmacies (or other units)
Aarau, Kantonsspital Aarau, Spitalapotheke
Baar, Zuger Kantonsspital, Spitalapotheke
Baden, Kantonsspital Baden, Spitalapotheke
Basel, St. Claraspital, Spitalapotheke
Basel, Universitätsspital Basel, Spital-Pharmazie
Bellinzona, Ospedale regionale di Bellinzona e Valli, Servizio di farmacia ospedaliera EOFARM
Bern, Hirslanden Klinik Beau-Site, Apotheke
Bern, Inselspital, Institut für Spitalpharmazie
Bern, Spitalnetz, Spitalpharmazie
Biel, Spitalzentrum, Apotheke
Liestal, Kantonsspital Baselland, Spitalapotheke
Chur, Kantonsspital Graubünden, Institut für Spitalpharmazie
Fribourg, HFR Hôpital cantonal, Pharmacie
Genève, Hôpitaux Universitaires de Genève (HUG), Pharmacie
La Chaux-de-Fonds, Hôpital neuchâtelois, Service de Pharmacie
Langenthal, SRO Oberaargau, Spitalapotheke
Lausanne, Centre Hospitalier Universitaire Vaudois (CHUV)
Liestal, Kantonsspital Baselland, Spitalapotheke
Lugano, Clinica Luganese, farmacia
Luzern, Hirslanden Klinik St. Anna, Spitalapotheke
Luzern, Luzerner Kantonsspital, Zentrum für Spitalpharmazie
Morges, Pharmacie Interhospitalière de la Côte (PIC)
Moutier, Hôpitaux Jura/Jura bernois, Pharmacie interjurassienne
Rebstein, Spitalregion RWS, Spital Grabs, Spitalapotheke
Schaffhausen, Spitäler Schaffhausen, Spitalapotheke
Schlieren, Spital Limmattal, Spitalapotheke
Sion, Hôpital du Valais, Institut Central (ICHV), Service de pharmacie
Solothurn, Solothurner Spitäler, Spitalapotheke
St. Gallen, Kantonsspital St. Gallen, Spitalapotheke
Thun, Spital STS, Spitalapotheke
Unterseen, Spitäler fmi, Spitalapotheke
Vevey, Pharmacie des Hôpitaux de l'Est Lémanique (PHEL)
Winterthur, Kantonsspital Winterthur, Spitalapotheke
Yverdon, Pharmacie des Hôpitaux du Nord Vaudois et de la Broye (PHNVB)
Zürich, Klinik Hirslanden, Apotheke
Zürich, Stadtspital Triemli, Spitalapotheke
Zürich, Stadtspital Waid, Apotheke
Zürich, Universitätsklinik Balgrist, Apotheke
Zürich, Universitätsspital Zürich, Spitalhygiene

Table IV.2: Laboratories participating in anresis.ch

Laboratories	data included
Aarau, Zentrum für Labormedizin, Kantonsspital Aarau	since 2006
Baar, Polytest Labor Zug AG	2004–2006
Baden, Kantonsspital Baden, Zentrallabor, Bereich Mikrobiologie	since 2004
Basel, Labor Universitäts-Kinderspital beider Basel UKBB	2004–2010
Basel, Universitätsspital Basel, Klinische Mikrobiologie	since 2008
Basel, Viollier AG	since 2004
Bellinzona, Dipartimento di medicina di laboratorio EOLAB, Servizio di microbiologia	since 2004
Bern, Institut für Infektionskrankheiten	since 2004
Bern, Labormedizinisches Zentrum Dr. Risch	since 2007
Chur, Kantonsspital Graubünden, Zentrallabor	since 2004
Frauenfeld / Münsterlingen, Kantonsspitäler, Spital Thurgau AG, Institut für Labormedizin	since 2007
Fribourg, Laboratoire HFR – Hôpital cantonal, microbiologie	since 2004
Genève, Hôpitaux Universitaires de Genève (HUG), Laboratoire de Bactériologie	since 2004
Genf, Unilabs S.A.	since 2007
La Chaux-de-Fonds, ADMED Microbiologie	since 2008
Lausanne, Université de Lausanne, Institut de Microbiologie	since 2006
Luzern, Kantonsspital Luzern, Zentrum für Labormedizin	since 2004
Luzern, Labor Dr. Güntert AG	2005–2012
Schaffhausen, Spitäler Schaffhausen, Zentrallabor	since 2004
Sitten, Institut Central des Hôpitaux Valaisans (ICHV), Zentralinstitut	since 2004
St. Gallen, Zentrum für Labormedizin	since 2009
Zürich, Universität Zürich, Institut für Medizinische Mikrobiologie	since 2005
Zürich, Universitäts-Kinderspital Zürich, Infektionslabor	since 2004

[1] Since 2011 data included in Basel, Universitätsspital Basel, Klinische Mikrobiologie

Table IV.3: anresis.ch steering committee members in 2015

Homa Attar Cohen	Swiss Federal Office of Public Health (FOPH)
Raymond Auckenthaler	Synlab SUISSE
Abdessalam Cherkaoui	HUG, Laboratoire de Bactériologie, Genève
Olivier Dubuis	Viollier AG, Basel
Adrian Egli	Klinische Mikrobiologie, Universitätsspital Basel
Valeria Gaia	Dipartimento di medicina di laboratorio EOLAB, Servizio di microbiologia, Bellinzona
Daniel Koch	Swiss Federal Office of Public Health (FOPH)
Andreas Kronenberg	Institut für Infektionskrankheiten, Universität Bern
Stephen Leib	Institut für Infektionskrankheiten, Universität Bern
Stephane Luyet	Schweizerische Konferenz der kantonalen Gesundheitsdirektorinnen und -direktoren GDK
Jonas Marschall	Spitalhygiene, Departement Infektiologie, Universitätsspital Bern
Patrice Nordmann	Molecular and Medical Microbiology, Dept Medicine, Université de Fribourg
Vincent Perreten	Institut für Veterinär-Bakteriologie, Universität Bern
Jean-Claude Piffaretti	Interlifescience, Massagno
Guy Prod'hom	CHUV, Institut de microbiologie, Lausanne
Jacques Schrenzel	HUG, Laboratoire de Bactériologie, Genève
Andreas Widmer	Abteilung für Spitalhygiene, Universität Basel
Giorgio Zanetti	CHUV, Service de médecine préventive hospitalière, Lausanne
Reinhard Zbinden	Universität Zürich, Institut für medizinische Mikrobiologie, Zürich

Index

Figures, tables and textboxes

Figures

Tables

Textboxes