# 2 Summary

## Resistance in bacteria of human clinical isolates

Since 2008, different trends have been observed in Gram-positive and Gram-negative bacteria. Methicillin-resistant *Staphylococcus aureus* (MRSA) rates have continued to decrease significantly in invasive isolates, mainly in the western part of Switzerland. This trend was also observed in several other European countries, including the neighboring countries Germany, France and Austria. In contrast, MRSA rates are increasing in wound and abscess samples from outpatients. Penicillin resistance in *Streptococcus pneumoniae* has also decreased over time. This effect is mainly due to a reduction in the prevalence of more resistant serotypes, due to the introduction of pneumococcal vaccines. Vancomycin resistance in enterococci is still very low, but increasing rates observed during the last months are worrisome.

In contrast, we have observed a steady increase in quinolone resistance and 3rd/4th 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. During the last two years, this trend seems to have stabilized in Switzerland, as well as in some other European countries. Fortunately, carbapenem resistance still is rare in *E. coli* and *K. pneumoniae*. While carbapenem resistance in *E. coli* is rare in most European countries as well, increasing carbapenem resistance is observed in Europe in *K. pneumoniae*; in 2016 resistance rates above 25 % have even been described in Italy, Greece and Romania. 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*, the increasing resistance rates for piperacillin-tazobactam and ceftazidime peaked in 2015 and have slightly decreased since then, while resistance rates for aminoglycosides are steadily increasing. No significant trends were observed in *Acinetobacter* spp. and in contrast to Europe, carbapenemase rates were stable.

## Antibiotic consumption in human medicine

In Swiss acute care hospitals, consumption of antibacterial agents for systemic use (ATC group J01) increased by 16 % to 62.2 DDDs (defined daily doses) per 100 bed-days between 2007 and 2017, whereas it was relatively stable when expressed in DDDs 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 group J01C), followed by the other beta-lactam antibacterials, including cephalosporins (ATC group J01D) and quinolones (ATC group J01M).

In outpatient care, the total consumption of antibacterial agents for systemic use (ATC group J01) was 10.7 DDDs per 1,000 inhabitants per day in 2017. The most commonly used class of antibiotics was the penicillins (ATC group J01C), followed by the macrolides, lincosamides and streptogramins (ATC group J01F), tetracyclines (ATC group J01A) and fluoroquinolones (ATC group J01MA). 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).

## Resistance in zoonotic bacteria

In poultry, the resistance rate to ciprofloxacin and tetracycline in *Campylobacter jejuni (C. jejuni)* has increased significantly in the last years. From 15 % in 2006, the resistance rate to ciprofloxacin rose to 51.4 % in 2016, and to 40 % for tetracycline. In contrast, resistance to erythromycin (2.9 %) was rarely found. According to the WHO, fluoroquinolones and macrolides are highest-priority critically important antimicrobials in human medicine, 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 years, up to 81.4 % in 2017. The resistance rates for tetracycline (62.1 %) and ciprofloxacin (50.3 %) did not change significantly between 2015 and 2017.

*Salmonella* spp. 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 constantly 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.

The enterococcal species *E. faecalis* and *E. faecium* isolated from broilers showed opposite trends in resistance rates. Whereas for *E. faecalis* resistance to ampicillin and tetracycline has increased since 2012, the resistance rates of *E. faecium* isolates decreased within the same period. A comparable effect was seen with enterococci isolates from veal calves. Vancomycin-resistant enterococci (VRE) have only occasionally been detected in the last years. No VRE have been detected in broilers in 2016, nor in fattening pigs and veal calves in 2017.

High resistance rates to ampicillin (14.2%–38.7%), sulfamethoxazole (46.9%–26.8%) and tetracycline (13.2%–41.2%) are found in commensal *E. coli* isolates from broilers, fattening pigs and veal calves. Additionally, high resistance to ciprofloxacin was found in isolates from broilers (37.9%). Resistance to these substances increased in isolates from broilers between 2006 and 2012, then clearly decreased until 2014, whereas no decrease could be detected in 2016, except for tetracycline. In isolates from calves, a decreasing trend for resistance was also observed from 2006 to 2013. However, resistances to tetracycline, sulfamethoxazole and ampicillin increased again until 2014, with a steady state in 2015 and 2017. In fattening pigs, the resistance rates in *E. coli* isolates showed a steady state or a slightly decreasing trend from 2013 to 2017 for the abovementioned antimicrobials.

ESBL/pAmpC-producing *E. coli* were detected in 52.4% of broiler flocks, in 17.6% of fattening pigs and in 33.2% of veal calves. The increase of the ESBL/pAmpC prevalence in broilers is ongoing, although on a lower level than in previous years (2014: 41.8%). In contrast, the ESBL prevalence of fattening pigs (2015: 25.7%) has decreased and remained on a high level for calves (2015: 37.6%).
No carbapenemase-producing *E. coli* were found in species of livestock.

In Switzerland, the occurrence of methicillin-resistant *S. aureus* (MRSA) in fattening pigs at slaughter has increased constantly since detection of MRSA became part of the monitoring. Starting at 2% in 2009 and increasing to 20.8% in 2013, the MRSA prevalence reached 44.0% in 2017. Moreover, the same trend but on a lower level is seen for MRSA carriage of veal calves. The actual prevalence in 2017 was 8.1%. The results reported for MRSA confirm that *spa* type t034 and *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). LA-MRSA can be transmitted between animals and humans. An analysis on MRSA carriage in Swiss inpatients detected two cases of LA-MRSA carriage (n=163) in Swiss patients.

## Resistance in indicator bacteria from meat

In 49.3% of chicken meat samples, ESBL/pAmpC-producing *E. coli* have been detected. The prevalence differs markedly between Swiss meat (41.9%) and meat produced abroad (64.9%). For both, the overall prevalence has decreased in the reporting time (2014: Swiss meat 65.5%; meat from abroad: 85.6%). Although a decreasing trend has been detected, the prevalence of these multidrug-resistant *E. coli* are still very high, which corresponds to the finding of a high prevalence of ESBL/pAmpC-producing *E. coli* in broilers.

In contrast, only one ESBL/pAmpC-producing *E. coli* was detected in pork (n=302) and two ESBL/pAmpC-producing *E. coli* have been found in beef samples (n=299). This difference might be related to the lower prevalence of ESBL/pAmpC-producing *E. coli* in Swiss pigs and calves and the distinct slaughtering processes of these animals. No carbapenemase-producing *E. coli* were found in fresh meat samples.

MRSA was only detected in considerable amounts in chicken meat produced abroad (2016: 9.3%). In 2016, no MRSA was detected in Swiss chicken meat samples (n=205). Moreover, no MRSA was found in Swiss beef (n=299) and only two MRSA cases were detected in Swiss pork (n=301). The latter is of special interest, as the strong increase of MRSA in fattening pigs (prevalence 44.0%) seemed not to increase the prevalence of MRSA in fresh meat thereof. The data confirmed that food is not regarded as a relevant source of MRSA transmission to humans.

## Resistance in bacteria from animal clinical isolates

Monitoring of antimicrobial resistance for relevant pathogens from diseased livestock and companion animals is important for veterinarians, as it allows them to make appropriate therapeutic antibiotic choices, which oftentimes cannot be based on an antibiogram prior to the first treatment. Moreover, these data fill another important gap regarding monitoring of antimicrobial resistance from the One-Health perspective.

Therefore, in 2015, the Federal Food Safety and Veterinary Office (FSVO) launched a pilot project for the monitoring of veterinary pathogens in Switzerland, together with the Swiss national reference laboratory for antibacterial resistance, the Center for Zoonoses, Animal Bacterial Diseases and Antimicrobial Resistance (ZOBA).

All strains were isolated from clinical submissions of diseased animals analyzed by the ZOBA. Samples from animals with antimicrobial treatment prior to sampling were excluded from this study. In contrast to the monitoring of isolates from healthy slaughter animals, minimal inhibitory concentration (MIC) data were interpreted according to clinical breakpoints. Exemplarily, for small-animal medicine, resistance data of *S. pseudintermedius*, isolated from wound infections of dogs, and *E. coli*, isolated from canine urogenital tract infections, are reported. *Staphylococcus aureus* from bovine mastitis samples and *Streptococcus equi* subspecies *zooepidemicus,* derived from purulent infections from horses, completed the data set.

The presence of high levels of resistance to important antimicrobials underlines the need for systematic monitoring of

antimicrobial resistance. Infections in animals caused by multidrug-resistant pathogens must be expected for veterinary pathogens. However, the use of critically important antimicrobials cannot be supported by the data presented, as first-line antibiotics with sufficient efficacy are available for the different clinical settings. In the future, this monitoring will be even more representative, as isolates from other Swiss laboratories will be included from 2019 onwards.

## Sales of antimicrobials in veterinary medicine

The sales volume of antimicrobials continued to decline in 2016 and 2017. Overall, 38 377 kg of antimicrobials were sold for veterinary medicine in 2016 and 32 328 kg in 2017. This amounts to a decline of 53 % (37 tons) 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. The quantity of antibiotics approved only for pets comprises 2,5 % of the total volume. The sales of the highest-priority critically important antibiotic classes for human medicine decreased in 2016 and 2017; the sales of macrolides have decreased by 25 % in 2016 and another 20 % in 2017. The sales of fluoroquinolones declined by 21 % in 2016 and by 25 % in 2017. The sales of cephalosporins (3rd/4th generation) decreased by about 23 % in 2016 as well as in 2017. The sales volume of colistin has declined approximately 79 % since 2008. Expressed in correlation to the biomass under exposure, the level is 0.4 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 mg/PCU or below for European countries in order to maintain its efficacy in the treatment of severe infections in humans.

## Analysis

For the first time in Switzerland, an analysis to compare human and veterinary data on antibiotic use, and an attempt to evaluate associations between use and resistance, was conducted in this report. The objective was to analyze the Swiss antibiotic consumption and resistance data in a similar fashion as the JIACRA report. However, due to a lack of data and time, only a preliminary analysis was conducted. With improved data, more significant analyses will be possible in the upcoming years, focussing on potential associations between use of antibiotics and resistance.

In order to understand the epidemiology of methicillin-resistant *S. aureus* (MRSA) and the risk for the transmission from animals to humans, a study into the molecular characteristics of this pathogen was undertaken. Molecular features of Swiss MRSA strains, isolated from livestock and meat thereof with MRSA isolates from healthy veterinarians and farmers as well as human isolates from Swiss hospitals were compared. With this analysis, useful information on the distribution of hospital-acquired (HA) MRSA, community-acquired (CA) MRSA and livestock-associated (LA) MRSA in human and veterinary settings can be provided, helping to obtain insights into transmission risks in Switzerland. Swiss fattening pigs have shown a strong increase in the prevalence of MRSA carriage over the last ten years. The prevalence of MRSA in Swiss pork, beef and chicken meat is very low. The detected MRSA belonged to the LA-MRSA type. A study with Swiss veterinarians and farmers revealed that the majority of MRSA from veterinarians and farmers belonged to the LA-MRSA type. This is in line with findings on MRSA isolated from livestock, which also belong to the LA-MRSA type. The vast majority of MRSA isolated from inpatients are HA- and CA-MRSA; however, in two patients a LA-MRSA was detected. Continuous monitoring is needed, including molecular typing of both human and animal MRSA isolates.