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.