

SCIENTIFIC REPORT OF EFSA AND ECDC

EU Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2013¹

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ABSTRACT

The antimicrobial resistance data on zoonotic and indicator bacteria in 2013, submitted by 28 EU MSs, were jointly analysed by EFSA and ECDC. Resistance in zoonotic Salmonella and Campylobacter species from humans, animals and food, and resistance in indicator Escherichia coli and enterococci, as well as data on meticillin-resistant Staphylococcus aureus, in animals and food were addressed. 'Microbiological' resistance was assessed using epidemiological cut-off (ECOFF) values in animal and food isolates and, where possible, in human isolates. For human isolates interpreted based on clinical breakpoints, the 'clinically' resistant and 'intermediate' resistant categories were combined into a 'non-susceptible' group, resulting in close correspondence with the ECOFF-defined 'microbiological' resistance for most antimicrobials. In Salmonella from humans, high proportions of isolates were resistant to ampicillin, sulfonamides and tetracyclines, while proportions of isolates resistant to third-generation cephalosporins and clinically non-susceptible to fluoroquinolones generally remained low. In Salmonella and Escherichia coli isolates from fowl, pigs, cattle and meat thereof, resistance to ampicillin, tetracyclines and sulfonamides was commonly detected, while resistance to third-generation cephalosporins was generally uncommon. High to very high resistance to (fluoro)quinolones was observed in Salmonella from turkeys, fowl and broiler meat. In Campylobacter from humans, a high to very high proportion of isolates were resistant to ciprofloxacin and tetracyclines, while resistance to erythromycin was low to moderate. The resistance to fluoroquinolones in some MSs was extremely high; in such settings, the effective treatment option for human enteric Campylobacter infection may be significantly reduced. High to extremely high resistance to ciprofloxacin, nalidixic acid and tetracyclines was observed in *Campylobacter* isolates from fowl, broiler meat, pigs and cattle, whereas much lower levels were observed for erythromycin and gentamicin. Increasing trends in ciprofloxacin resistance were observed in *Campylobacter* from broilers and/or pigs in several MSs. Multi-resistance and co-resistance to critically important antimicrobials in both human and animal isolates were uncommon. A minority of isolates from animals belonging to a few Salmonella serovars (notably Kentucky and Infantis) had a high level of resistance to ciprofloxacin.

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KEY WORDS

antimicrobial resistance, zoonotic bacteria, indicator bacteria

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EUROPEAN UNION SUMMARY REPORT

Antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in the EU in 2013

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Summary

Clinical' resistance and 'microbiological' resistance: use of clinical breakpoints and epidemiological cut-off values

The development of resistance in bacteria is a major threat to public health. It is therefore important to detect any occurrence of resistance and increases in resistance levels as early as possible. In this report, acquired resistance in bacteria is denoted 'microbiological' resistance and harmonised epidemiological cut-off values are used to interpret the results of susceptibility testing in isolates from animals, food and, to the extent possible, humans. The majority of the results of susceptibility testing of clinical isolates from humans, however, were interpreted using clinical breakpoints to guide medical treatment of the patient. The breakpoints for 'clinical' resistance are, in many cases, less sensitive than the epidemiological cut-off value for a specific bacteria–drug combination. By combining the 'clinically' resistant and 'intermediate' resistant categories, however, close correspondence with the epidemiological cut-off value was achieved (see breakpoint Figures 1 and 32). One notable exception is ciprofloxacin for Salmonella, for which the clinical breakpoint from EUCAST in 2013 was substantially higher than the epidemiological cut-off value. For this combination, animal and food isolates interpreted with epidemiological cut-off values will be classified as ('microbiologically') resistant more often than human isolates classified as non-susceptible according to the clinical breakpoint. Caution is required in making comparisons between isolates from different sources unless it is clear that methods and criteria for interpretation correspond.

Zoonoses are infections that are transmissible between animals and humans. Infection can be acquired directly from animals, or through the ingestion of contaminated foodstuffs. The severity of these diseases in humans can vary from mild symptoms to life-threatening conditions. The zoonotic bacteria that are resistant to antimicrobials are of particular concern, as they might compromise the effective treatment of infections in humans. In order to follow the occurrence of antimicrobial resistance in zoonotic bacteria isolated from humans, animals and food in the European Union (EU), information from the EU Member States is collected and analysed.

In 2013, 28 Member States (MSs) reported data on antimicrobial resistance in zoonotic bacteria to the European Commission (EC) and the European Food Safety Authority (EFSA), and 21 MSs submitted data to the European Centre for Disease Prevention and Control (ECDC). In addition, three other European countries provided information. Assisted by their contractors – the Animal Health and Veterinary Laboratories Agency in the United Kingdom, the Technical University of Denmark and the National University of Ireland, Galway – the EFSA and the ECDC analysed the data, the results of which are published in this EU Summary Report on antimicrobial resistance. Information on resistance was reported regarding *Salmonella* and *Campylobacter* isolates from humans, food and animals, whereas data on indicator *Escherichia coli* and indicator enterococci isolates were related to only animals and food. Information was reported by some MSs on the occurrence of meticillin-resistant *Staphylococcus aureus* isolates was additionally reported by two countries.

The quantitative data on antimicrobial resistance in isolates from humans, food and animals were assessed using harmonised epidemiological cut-off values that detect 'microbiological' resistance, i.e. reduced susceptibility to the antimicrobials tested, as well as using clinical breakpoints where considered appropriate. The categorical (qualitative) data on antimicrobial resistance in isolates from humans interpreted by using clinical breakpoints were aligned with 'microbiological' resistance by combining 'clinically' resistant and 'intermediate' resistant isolates into a non-susceptible group. Direct comparisons between isolates from different sources should be made only when methods and interpretive criteria are comparable.

The reporting of antimicrobial resistance data at the isolate level by a significant number of MSs allowed the second analysis at the EU level of multi-resistance and co-resistance patterns to critically important antimicrobials in both human and animal isolates. Detailed analyses of multiple drug resistance (MDR) in certain *Salmonella* serovars, including analysis of high-level resistance to ciprofloxacin and pentavalent resistance, were possible for MSs reporting isolate-based data and included for the first time in the report. In addition, for certain bacterial species, antimicrobial resistance data could be analysed at the production-type level, such as broilers, laying hens and breeders of *Gallus gallus*, which allows the analysis of the data to be fine-tuned.



Salmonella

The Salmonella spp. data presented in this report comprise results for all reported non-typhoidal Salmonella serovars which have been amalgamated to represent the overall occurrence of antimicrobial resistance in Salmonella in humans and the various animal and food categories. The differences in the distribution and prevalence of particular serovars and phage types of Salmonella in different countries and in different animal species, and their associated patterns of resistance, may explain some of the differences in the levels of antimicrobial resistance observed, as well as in those of multi-resistance (reduced susceptibility to at least three of the 10 antimicrobial classes tested according to epidemiological cut-off values (ECOFFs). The spread of particularly resistant clones and the occurrence of resistance genes within these clones can be exacerbated by the use of antimicrobials in human and animal populations and the selective pressure this exerts. Other factors, such as foreign travel by humans, international food trade, animal movements, farming systems, animal husbandry and the pyramidal structure of some types of animal primary production, can also influence the spread of resistant clones.

In addition to the amalgamated data for *Salmonella* spp., resistance data for the most numerous *Salmonella* serovars in humans, *S*. Enteritidis, *S*. Typhimurium, monophasic *S*. Typhimurium and *S*. Infantis, were analysed separately. Data are also presented separately for serovars *S*. Derby and *S*. Kentucky owing to their high prevalence in pigs and turkeys, respectively, and the high level of resistance observed in both human and animal isolates, particularly in *S*. Kentucky.

In humans

In 2013, 21 MSs and two non-MSs provided information on antimicrobial resistance in *Salmonella* isolates from cases of salmonellosis in humans. Seven countries were able to provide data as measured values (quantitative data), which were collected for the first time.

The reported data represented 19.3 % of the confirmed salmonellosis cases reported in the EU/European Economic Area (EEA) in 2013. High proportions of human *Salmonella* isolates were resistant to ampicillin (36.1 %), sulfonamides (35.7 %) and tetracyclines (34.5 %). Multi-resistance was high (31.8 %) in the EU, with very high occurrence in some countries. Some of the investigated serovars exhibited very or extremely high multi-resistance, such as monophasic *S*. Typhimurium $\underline{1},4,[5],12$:i:- (83.8 %) and *S*. Kentucky (67.3 %). However, 44.2 % of all isolates tested were susceptible to the complete range of antimicrobial classes in the human data collection. The proportion of *Salmonella* isolates resistant to either of the clinically important antimicrobials ciprofloxacin and cefotaxime was on average relatively low (3.8 % non-susceptible to ciprofloxacin and 1.4 % 'microbiologically' resistant to cefotaxime). An extremely high proportion (81.8 %) of *S*. Kentucky was, however, non-susceptible to ciprofloxacin, which probably reflects the spread of a particularly resistant clone, as described earlier (Le Hello et al., 2011; Westrell et al., 2014). Co-resistance to ciprofloxacin and cefotaxime was overall very low in *Salmonella* spp. (0.2 %). Resistance to quinolones (ciprofloxacin and nalidixic acid) was generally higher in *S*. Enteritidis isolates than in *S*. Typhimurium isolates.

When assessed by geographical region of probable acquisition, a larger proportion of *Salmonella* spp. isolates exhibited resistance to ampicillin, sulfonamides and tetracyclines among infections acquired within the EU/EEA countries compared with other regions, while the highest levels of resistance to ciprofloxacin and gentamicin were observed in isolates from cases that had travelled in Africa.

In animals and food

In 2013, information on antimicrobial resistance in *Salmonella* isolates from animals and food was reported by 22 MSs and two non-MSs.

Among the *Salmonella* spp. isolates from meat, the highest levels of resistance to ciprofloxacin and nalidixic acid were noted in broilers and turkeys, where high to extremely high levels were recorded by most of the MSs included in the analysis. Ciprofloxacin resistance was reported in *Salmonella* spp. isolates from pig meat at low to moderate levels and was not detected among the relatively few isolates from meat from bovine animals. In most of the reporting MSs, 'microbiological' resistance to the third-generation cephalosporins (cefotaxime) in *Salmonella* spp. from meat was either not discerned or detected at low levels, with the notable exception of the isolates from broiler and turkey meat tested in the Netherlands, where high or very high resistance to cefotaxime was observed.

Resistance to tetracyclines, ampicillin and sulfonamides in *Salmonella* spp. typically ranged from moderate to extremely high in meat. Generally, the highest levels of resistance to tetracyclines, ampicillin and sulfonamides were found among isolates of *S*. Infantis from broiler meat and *S*. Typhimurium (including the monophasic variants) from pig meat, resulting in extremely high levels of multi-resistance (>70.0 %). Multi-resistance (reduced susceptibility to at least three of the 10 antimicrobial classes tested) was generally



moderate to very high in pig meat and low to very high in broiler meat. In *S*. Enteritidis from broiler meat, the majority of isolates were fully susceptible to the harmonised set of antimicrobials tested.

Low levels of 'microbiological' co-resistance to ciprofloxacin and cefotaxime in *Salmonella* spp. from meat from broilers and pigs were reported by five MSs. However, when the resistance to ciprofloxacin and cefotaxime was interpreted using clinical breakpoints, only isolates from Romanian broiler meat displayed 'clinical' resistance.

Among all serovars, isolates resistant to ciprofloxacin, but not nalidixic acid, were observed, probably indicating an increasing occurrence of plasmid-mediated quinolone resistance.

Among *Salmonella* spp. isolates from animals, most MSs reported moderate or high to extremely high resistance to tetracyclines and sulfonamides and similar or slightly lower levels of ampicillin resistance. Resistance levels were generally higher in isolates from pigs and turkeys than from broilers, laying hens, breeding hens and cattle.

Overall, high to extremely high levels of resistance to ciprofloxacin and nalidixic acid were observed in *Salmonella* spp. isolates from fattening turkeys and broilers compared with the low or moderate levels recorded in *Salmonella* spp. isolates from laying hens, pigs and cattle. Resistance to third-generation cephalosporins (cefotaxime) was generally at very low or low levels in *Salmonella* spp. isolates from *Gallus gallus*, turkeys, pigs and cattle in most reporting MSs. However, moderate to high levels of cefotaxime resistance were reported in *Salmonella* spp. from broilers in Croatia, Italy, the Netherlands and Romania.

'Clinical' resistance to ciprofloxacin and cefotaxime was absent from most *Salmonella* isolates from production animals, but was observed in 11 MSs, mainly in isolates from *Gallus gallus* and turkeys but also in a few pig isolates. 'Clinical' resistance to cefotaxime was found at low levels in *Salmonella* spp. isolates from *Gallus gallus*, turkeys and pigs in nine MSs.

Only France reported data for resistance to carbapenems in *Salmonella* in animals (poultry only), and carbapenem resistance was not observed. Colistin-resistant *Salmonella* isolates were found by several MSs originating from all animal species, but high-level colistin resistance (minim inhibitory concentration, MIC <16) was not reported.

Multi-resistance was generally high in *Salmonella* isolates from broilers (56 %), pigs (37.9 %) and turkeys (73.0 %), and low levels of 'microbiological' co-resistance to ciprofloxacin and cefotaxime occurred in *Salmonella* from broilers, laying hens and/or pigs (Belgium, Italy, Romania and Spain). 'Clinical' co-resistance to ciprofloxacin and cefotaxime was overall observed at the very low level of 0.3 % in broilers and not detected in pigs and turkeys.

Campylobacter

In humans

Overall, 14 MSs and two non-MSs provided information on antimicrobial resistance in isolates from campylobacteriosis cases in humans for 2013. Five countries were able to provide data as measured values (quantitative data), which were collected for the first time.

Data from antimicrobial susceptibility testing represented 15.0 % and 20.1 % of the human cases with *C. jejuni* and *C. coli*, respectively, reported in the EU/EEA in 2013.

Very high occurrence of resistance to the clinically important antimicrobial ciprofloxacin was reported in human *Campylobacter* isolates in the EU with more than half (54.6 %) of *C. jejuni* and two-thirds (66.6 %) of *C. coli* isolates being resistant. Large differences in occurrence were observed between countries (range 23.1–91.5 % for *C. jejuni*). The proportion of clinical isolates resistant to fluoroquinolones was extremely high in some MSs; in such settings, the effective treatment options for human enteric *Campylobacter* infection are significantly reduced. Given the high levels of resistance to fluoroquinolones in broilers, and the assessment that a large proportion of human campylobacteriosis infections comes from handling, preparation and consumption of broiler meat (EFSA BIOHAZ Panel, 2010a), this is a compelling example of how AMR in food and animals may impact on the availability of effective antimicrobial agents for the treatment of severe human *Campylobacter* infections. Nevertheless, co-resistance to critically important ciprofloxacin and erythromycin varied by country but was overall low (1.7 % in *C. jejuni* and 4.1 % in *C. coli*).

High levels of tetracycline resistance were also observed (33.5 % for *C. jejuni* and 58.1 % for *C. coli*). Resistance to the clinically important antimicrobial erythromycin was generally low (1.5 %) in *C. jejuni* but moderately high in *C. coli* (13.4 %).



When assessed by geographical region of probable acquisition, isolates acquired during travel in Asia were resistant to ciprofloxacin and erythromycin almost twice as often as isolates from infections acquired in the EU/EEA.

In animals and food

In 2013, 18 MSs and three non-MSs reported quantitative MIC data for *Campylobacter* isolates from food and animals. When considering all host species, the highest levels of resistance were seen for the (fluoro)quinolones (ciprofloxacin and nalidixic acid) and tetracyclines. Resistance to erythromycin and gentamicin was comparatively low among *Campylobacter* isolates from food and animals. Resistance was generally higher in *C. coli* than in *C. jejuni* from the same host species (*Gallus gallus*).

For *C. jejuni* isolates from *Gallus gallus*, resistance was high for ciprofloxacin (54.6 %), nalidixic acid (52.3 %) and tetracyclines (41.4 %), while the level of resistance to erythromycin was very low at 0.4 % and no resistance to gentamicin was recorded. A similar pattern was seen for *C. coli* isolates from *Gallus gallus*; however, levels of resistance were higher overall. Levels of resistance to ciprofloxacin, nalidixic acid and tetracyclines were high to extremely high at 68.8 %, 63.9 % and 70.4 %, respectively, while levels of resistance to erythromycin and gentamicin were moderate (13.7 %) and low (2.4 %), respectively.

Multi-resistance (reduced susceptibility to at least three antimicrobial classes according to ECOFFs) was very low, low or not detected in *C. jejuni* isolates from broilers, and co-resistance to the clinically important antimicrobials ciprofloxacin and erythromycin in the same isolates was either not detected or recorded at low levels (0.5 %) in the reporting MSs. The situation was different for *C. coli* from broilers, where multi-resistance as a percentage of all isolates received by the individual MSs ranged from 6.3 % to 64.7 % and co-resistance to ciprofloxacin and erythromycin ranged from 0 % to 42.6 % (overall co-resistance: 12.3 %).

Resistance to ciprofloxacin, erythromycin and nalidixic acid in *Gallus gallus* varied greatly among reporting MSs from 2007 to 2013 and statistically increasing trends in resistance to these antimicrobials were observed for several MSs, for both *C. jejuni* and *C. coli*.

For *C. jejuni* isolates from broiler meat, resistance, considering all reporting MSs, ranged from high to very high for ciprofloxacin (53.0 %), nalidixic acid (50.3 %) and tetracyclines (33.3 %), while levels of resistance to erythromycin and gentamicin were very low at 0.9 % and 0.1 %, respectively. A similar pattern was seen for *C. coli* isolates from broiler meat; however, levels of resistance were higher overall. Levels of resistance to ciprofloxacin and nalidixic acid were extremely high at 76.2 % and 72.6 %, respectively, very high for tetracyclines at 57.8 %, moderate for erythromycin at 10.9 % and very low for gentamicin at 0.3 %.

C. coli isolates from pigs were derived from fattening pigs. Resistance to ciprofloxacin, nalidixic acid and tetracyclines ranged from high to extremely high at 31.1 %, 30.7 % and 72.3 %, respectively. Resistance was high to erythromycin (20.7 %) and low to gentamicin (1.9 %). Resistance to ciprofloxacin, erythromicyn and/or nalidixic acid in *C. coli* from pigs showed a significantly decreasing trend in three reporting MSs from 2007 to 2013.

Multi-resistance (reduced susceptibility to at least three antimicrobial classes according to ECOFFs) varied greatly in *C. coli* isolates from pigs from the different MSs, ranging from 17.7 % to 88.0 %. Co-resistance to the clinically important antimicrobials, ciprofloxacin and erythromycin, was low to moderate for three reporting countries, ranging from 7.9 % to 12.8 %, but very high in one MS at 56.5 % (overall co-resistance: 19.5 %)

C. jejuni isolates from cattle were also considered. Overall, resistance was high for ciprofloxacin (35.8 %), nalidixic acid (36.1 %) and tetracyclines (29.7 %), while resistance to erythromycin and gentamicin was low or very low at 1.1 % and 0.9 %, respectively. No statistically significant trends in ciprofloxacin, erythromicyn and nalidixic acid resistance were observed in any of the reporting countries.

Multi-resistance (reduced susceptibility to at least three antimicrobial classes according to ECOFFs) ranged from 0 % to 7.9 % in *C. jejuni* isolates from cattle from the reporting MSs. Co-resistance to the clinically important antimicrobials, ciprofloxacin and erythromycin, was low or not detected in the reporting MSs (overall co-resistance: 1.1 %).

Indicator (commensal) Escherichia coli

Thirteen MSs and two non-MSs reported quantitative data on antimicrobial resistance in indicator *E. coli* isolates from animals and food in 2013. Most of the data were related to isolates from *Gallus gallus*, pigs and cattle; four MSs reported results for meat derived from each of those species.

Indicator *E. coli* from meat from *Gallus gallus*, pigs and cattle showed moderate to very high levels of 'microbiological' resistance to ampicillin, sulfonamides and tetracyclines, considering all reporting MSs.



Resistance was less than 5 % to gentamicin, less than 10 % to cefotaxime and less than 13 % to chloramphenicol at MS group level and for meat from all three animal species. The levels of resistance were high in meat from broilers considering all antimicrobials and all reporting MSs, and lower in meat from pigs and cattle.

Most data on *Gallus gallus* referred to broilers, although two MSs provided data on *E. coli* from laying hens. Resistance levels were in general higher among *E. coli* from broilers than from laying hens. Regarding broilers, the highest overall 'microbiological' resistance levels observed at the reporting MS group level were to ampicillin (58.6 %), ciprofloxacin (58.2 %), nalidixic acid (55.4 %), streptomycin (50.4 %), sulfonamides (48.6 %) and tetracyclines (45.6 %). Resistance to cefotaxime was 6.6 % in broilers. There was substantial variation in the level of resistance to these antimicrobials between reporting MSs. Countries mostly reported relatively stable resistance in *E. coli* isolates from *Gallus gallus* between 2007 and 2013. However, statistically significant trends in resistance to all of these antimicrobials have been identified: these trends have more commonly been increasing resistance than decreasing resistance.

Concerning indicator *E. coli* isolates from pigs, the highest overall 'microbiological' resistance levels in the reporting group of MSs were observed for tetracyclines (52.8 %), streptomycin (47.8 %), sulfonamides (42.1 %) and ampicillin (30.3 %). Resistance to ciprofloxacin and nalidixic acid was low at 6.1 % and 3.8 %, respectively. Overall, only 1.3 % of isolates were resistant to cefotaxime. There were large differences in the occurrence of resistance between MSs. There were more statistically significant trends than in isolates from *Gallus gallus*.

Multi-resistance levels (reduced susceptibility to at least three antimicrobial classes according to ECOFFs) were generally high in indicator *E. coli* isolates from broilers and pigs, and in a number of reporting countries. Co-resistance/reduced susceptibility to the clinically important antimicrobials, ciprofloxacin and cefotaxime, was also detected in very few isolates from these species.

In the reporting group of MSs, resistance levels in indicator *E. coli* isolates from cattle were generally lower than among isolates from *Gallus gallus* and pigs. The highest resistance levels observed were to tetracyclines (23.2 %), sulfonamides (20.2 %), streptomycin (17.6 %) and ampicillin (13.9 %). 'Microbiological' resistance to ciprofloxacin and nalidixic acid was low, around 5 %. Overall, only a few isolates (1.2 %) expressed resistance to cefotaxime. The occurrence of resistance was variable between MSs for most of the antimicrobials. As for *Salmonella*, MSs presented data at the production-type level for cattle. There have been statistically significant trends in resistance since 2007, mainly of a decreasing nature.

Strains of *E. coli* are not separated on phenotypic characteristics (e.g. serotype) in the current monitoring programme and a less detailed analysis is therefore possible than for Salmonella where isolates can be subdivided by serovar. The common core patterns of 'microbiological' resistance to ampicillin, streptomycin, sulfonamides, tetracyclines and trimethoprim (and combinations thereof) frequently observed in the monitoring of E. coli isolates are probably related to the presence of class 1 or class 2 integrons, which generally carry genes conferring resistance to these antimicrobials. A common core of 'microbiological' resistance to ampicillin, sulfonamides and tetracyclines, generally with 'microbiological' resistance to ciprofloxacin and frequently with such resistance to streptomycin and trimethoprim, was discernible in broilers. However, no single pattern or patterns of 'microbiological' resistance occurred at a high frequency in broilers. In fattening pigs, two MDR patterns were predominant ((1) ampicillin, streptomycin, sulfonamides, tetracyclines, trimethoprim; and (2) ampicillin, chloramphenicol, streptomycin, sulfonamides, tetracyclines and trimethoprim) and both accounted for more than 9.0% of the total number of E. coli isolates from fattening pigs for which isolate-based data were available. Ciprofloxacin resistance ('microbiological') frequently occurred as a component of MDR in E. coli from broilers and was observed in 72.0 % of MDR isolates (674 out of 936), whereas 'microbiological' resistance to ciprofloxacin occurred infrequently as a component of MDR in pigs and was present in 17.2 % (90 out of 524) of porcine MDR in E. coli isolates and 23.4 % (102 out of 435) of cattle MDR in *E. coli* isolates.

Indicator (commensal) Enterococcus

In 2013, nine MSs and two non-MSs reported antimicrobial resistance data regarding enterococcal isolates from animals or food. Most of the data concerned isolates from broilers (*Gallus gallus*), pigs and cattle, although three MSs reported results for isolates from meat derived from those species.

Overall, results at the EU level were not gained for meat, as relatively few MSs reported data on indicator enterococci in meat. Within each of the three included MSs, resistance to erythromycin, streptomycin and tetracyclines was generally lower in *E. faecalis* from pig meat than in isolates from broiler meat. Generally, the levels of resistance were lower in *E. faecuum* and/or *E. faecalis* from Danish meat than in isolates from Hungary, the Netherlands and Slovenia.

There was substantial variation in the resistance levels observed in the different MSs. The highest resistance levels among *Enterococcus faecium* (*E. faecium*) and *Enterococcus faecalis* (*E. faecalis*) isolates from broilers (*Gallus gallus*) were observed for tetracyclines (61.6 % and 87.0 %, respectively) and erythromycin (59.0 % and 60.6 %, respectively). The isolates from pigs expressed resistance to tetracyclines at a level of 45.6 % in *E. faecium* and 85.5 % in *E. faecalis*. Lower levels of resistance to tetracyclines were registered in cattle (30.8 % in *E. faecium* and 70.3 % in *E. faecalis*). Multi-resistance levels differed substantially between reporting MSs in *E. faecium* from pigs and *Gallus gallus*.

Resistance levels in *E. faecium* to the combination of antimicrobials quinupristin/dalfopristin have been analysed in this report for the various animal species and were found to be at very high to extremely high levels (73.7 % to 94.7 %). This has, however, to be considered in relation to the very low levels of resistance to vancomycin observed in all animal species (maximum 1.6 %).

Owing to cross-resistance between avoparcin and the human antimicrobial vancomycin, the use of avoparcin as an antimicrobial growth promoter was banned in the EU in 1997. In 2013, vancomycin resistance was found in only 0.1 % of *E. faecium* isolates from broilers, 0.6 % of *E. faecalis* isolates from broilers, 0.5 % of *E. faecalis* isolates from pigs, 1.4 % of *E. faecalis* isolates from cattle and 1.6 % of *E. faecium* isolates from cattle. Resistance to vancomycin was not detected in *E. faecalis* isolates from pigs.

Meticillin-resistant Staphylococcus aureus

A low number of MSs reported the results of monitoring food for meticillin-resistant *Staphylococcus aureus* (MRSA). MRSA was detected in meat from broilers, turkeys, pigs and bovine animals. The occurrence of MRSA in meat and products derived from animals may reflect colonisation of those animals with MRSA.

In relation to healthy food-producing animals, MRSA was detected in meat-producing broiler flocks, but not in breeding flocks in one MS. There was a large degree of variation between MSs in the occurrence of MRSA in pigs: 20.8 %–97.8 % of animals/herd slaughter batches were positive in slaughterhouse monitoring. Three MSs examined cattle for MRSA; the number of animals that were positive in sampling on farms for one MS was similar to when calves were sampled at the slaughterhouse. Molecular typing data were reported by one MS in relation to isolates from cattle; the majority of isolates were *spa*-type t011 belonging to MRSA clonal complex (CC) 398, the common livestock-associated type of MRSA occurring in Europe.

Several MSs reported results of clinical investigations which yielded MRSA in food-producing animals and companion animals. MRSA was detected in cats, dogs and horses, as well as in clinical diagnostic samples from food-producing animals.

Temporal trends in the occurrence of MRSA in animals could be assessed for one MS and one non-MS. Monitoring of sheep and goats on farms in 2011 and 2012 in one MS did not reveal the presence of MRSA in these animals in either year and there was no further monitoring in 2013. One MS monitored calves under one year of age on the farms in 2010, 2012 and 2013 and reported similar numbers of animals positive for MRSA in 2010 and 2012 (19.6 % and 19.2 %, respectively) and a slightly decreased number in 2013 (11.0 %). One non-MS reported data on the occurrence of MRSA in fattening pigs at slaughter through the monitoring of nasal swabs in consecutive years from 2009 to 2013. The numbers of animals positive for MRSA slowly increase over this period from 2.2 % in 2009 to 20.8 % in 2013. Molecular typing data were also available for these MRSA isolates, the majority of which belonged to *spa*-type t034, CC398, while much lower numbers of MRSA sequence type ST49 were reported.



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Legal basis

According to Directive 2003/99/EC on the monitoring of zoonoses and zoonotic agents, MSs (MSs) are obliged to monitor and report antimicrobial resistance in *Salmonella* and *Campylobacter* isolates obtained from healthy food-producing animals and from food. Commission Decision 2007/407/EC⁴ lays down detailed requirements on the harmonised monitoring and reporting of antimicrobial resistance of *Salmonella* isolates from various poultry populations and pigs. The monitoring and reporting of antimicrobial resistance in indicator organisms *E. coli* and enterococci is voluntary.

The data collection on human diseases from MSs is conducted in accordance with Decision 1082/2013/EU⁵ on serious cross-border threats to health, which in October 2013 replaced Decision 2119/98/EC on setting up a network for the epidemiological surveillance and control of communicable diseases in the European Union (EU). The case definitions to be followed when reporting data on infectious diseases, including antimicrobial resistance, to the European Centre for Disease Prevention and Control (ECDC) are described in Decision 2012/506/EU.⁶ ECDC has provided data on zoonotic infections in humans, as well as their analyses, for the Community Summary Reports since 2005. Since 2007, data on human cases have been reported from The European Surveillance System (TESSy), maintained by ECDC.

About EFSA

The European Food Safety Authority, located in Parma, Italy, and established and funded by the EU as an independent agency in 2002, provides objective scientific advice, in close collaboration with national authorities and in open consultation with its stakeholders, with a direct or indirect impact on food and feed safety, including animal health and welfare and plant protection. EFSA is also consulted on nutrition in relation to EU legislation. EFSA's risk assessments provide risk managers (the European Commission (EC), the European Parliament and the Council) with a sound scientific basis for defining policy-driven legislative or regulatory measures required to ensure a high level of consumer protection with regard to food and feed safety. EFSA communicates to the public in an open and transparent way on all matters within its remit. Collection and analysis of scientific data, identification of emerging risks and scientific support to the EC, particularly in the case of a food crisis, are also part of EFSA's mandate, as laid down in founding Regulation (EC) No 178/2002⁷ of 28 January 2002.

About ECDC

The European Centre for Disease Prevention and Control (ECDC), an EU agency based in Stockholm, Sweden, was established in 2005. The objective of ECDC is to strengthen Europe's defences against infectious diseases. According to Article 3 of founding Regulation (EC) No 851/2004⁸ of 21 April 2004, ECDC's mission is to identify, assess and communicate current and emerging threats to human health posed by infectious diseases. In order to achieve this goal, ECDC works in partnership with national public health bodies across Europe to strengthen and develop EU-wide disease surveillance and early warning systems. By working with experts throughout Europe, ECDC pools Europe's knowledge in health to develop authoritative scientific opinions about the risks posed by current and emerging infectious diseases.

Terms of reference

The EU system for the monitoring and collection of information on zoonoses is based on the Zoonoses Directive 2003/99/EC, which obliges EU MSs to collect relevant and, where applicable, comparable data on zoonoses, zoonotic agents, antimicrobial resistance and food-borne outbreaks. In addition, MSs are required to assess trends and sources of these agents, as well as outbreaks in their territory, submitting an annual report each year by the end of May to the EC covering the data collected. EFSA is assigned the tasks of examining these data and publishing the EU annual Summary Reports. In accordance with Article 9 of the Zoonoses Directive 2003/99/EC, EFSA shall examine the submitted national reports of the EU MSs and publish by the end of November a summary report on the trends and sources of zoonoses, zoonotic agents and antimicrobial resistance in the EU.

⁴ Commission Decision 2007/407/EC of 12 June 2007 on a harmonised monitoring of antimicrobial resistance in *Salmonella* in poultry and pigs. OJ L 153, 14.6.2007, p. 26–29.

⁵ Decision No 1082/2013/EU of the European Parliament and of the Council of 22 October 2013 on serious cross-border threats to health and repealing Decision No 2119/98/EC. OJ L 293, 5.11.2013, p. 1–15.

⁶ Commission Decision 2012/506/EU amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council. OJ L 262, 27.9.2012, p. 1–57.

 ⁷ Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the EFSA and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1–24.
⁸ Regulation (EC) No 851/2004 of the European Parliament and of the Council of 21 April 2004 establishing a European centre for



1. Introduction

The antimicrobial agents used in food-producing animals in Europe are frequently the same, or belong to the same classes, as those used in human medicine. Antimicrobial resistance is the main undesirable side effect of antimicrobial use in both humans and animals and results from the continuous positive selection of resistant bacterial clones, whether these are pathogenic, commensal or even environmental bacteria. This will modify the population structure of microbial communities, leading to accelerated evolutionary trends with unpredictable consequences for human health. The use of antimicrobials can differ in humans and food-producing animals, in terms of both the methods of administration and the quantities administered; there are important variations between and within food-producing animal species, as well as between countries.

Bacterial resistance to antimicrobials occurring in food-producing animals can spread to people not only via food-borne routes, but also by routes such as water or environmental contamination, as well as through direct animal contact. *Campylobacter, Salmonella* and some strains of *Escherichia coli* are examples of zoonotic bacteria which can infect people by the food-borne route. Infections with bacteria which are resistant to antimicrobials may result in treatment failures or necessitate the use of second-line antimicrobials for therapy. The commensal bacterial flora can also form a reservoir of resistance genes which may transfer between bacterial species, including transference to organisms capable of causing disease in both humans and animals (EFSA, 2008).

The monitoring of antimicrobial resistance in zoonotic and commensal bacteria in food-producing animals and food thereof is a prerequisite for understanding the development and diffusion of resistance, providing relevant risk assessment data, and evaluating targeted interventions. Resistance monitoring entails specific and continuous data collection, analysis and reporting that quantitatively follow temporal trends in the occurrence and distribution of resistance to antimicrobials, and should also allow the identification of emerging or specific patterns of resistance.

1.1. Antimicrobial resistance monitoring and reporting at the EU level

Based on Article 33 in Regulation (EC) 178/2002, EFSA is responsible for examining data on antimicrobial resistance collected from the Member States (MSs) in accordance with Directive 2003/99/EC and for preparing the EU (EU) Summary Report from the results. This EU Summary Report 2013 includes data related to the occurrence of antimicrobial resistance both in isolates from animals and foodstuffs and in isolates from human cases. The report is a joint collaboration between the EFSA (EFSA) and the European Centre for Disease Prevention and Control (ECDC) with the assistance of EFSA's contractors – the Animal Health and Veterinary Laboratories Agency (AHVLA) in the United Kingdom and the Technical University of Denmark – and of ECDC's contractor – The National University of Ireland, Galway. MSs, other reporting countries, the European Commission (EC) and the relevant EU Reference Laboratories (EU-RL) were consulted while preparing the report. The efforts made by MSs, the reporting non-MSs and the EC in the reporting of zoonoses data and in the preparation of this report are gratefully acknowledged.

The main issues when comparing antimicrobial resistance data originating from different countries are the use of different laboratory methods and different interpretive criteria of resistance. These issues have been addressed by the development of EFSA's guidelines for harmonised monitoring and reporting of resistance in food-producing animals and food thereof. The resistance monitoring performed under these guidelines utilises epidemiological cut-off (ECOFF) values which separate the naive, susceptible wild-type bacterial populations from isolates that have developed reduced susceptibility to a given antimicrobial agent (Kahlmeter et al., 2003). The ECOFFs may differ from breakpoints used for clinical purposes, which are defined against a background of clinically relevant data, including therapeutic indication, clinical response data, dosing schedules, pharmacokinetics and pharmacodynamics. In the EU Summary Reports on antimicrobial resistance from 2004 to 2012, ECOFFs were applied to minimum inhibitory concentration (MIC) data to define resistant *Salmonella, Campylobacter*, indicator *E. coli* and indicator enterococci isolates from animals and food. The use of harmonised methods and ECOFFs ensured the comparability of data over time at the country level and also facilitated the comparison of the occurrence of resistance between MSs. The same methods and principles have been applied in this 2013 Summary Report on antimicrobial resistance.

The antimicrobial susceptibility data reported to EFSA for 2013 for *Campylobacter*, *Salmonella*, indicator enterococci and indicator *E. coli* isolates from animals and food were analysed and all quantitative data were interpreted using ECOFFs. This report also includes results of phenotypic monitoring of resistance caused by extended-spectrum beta-lactamases (ESBLs) in *Salmonella* and indicator *E. coli*, conferring resistance to third-generation cephalosporins, as well as the third investigation at the EU level of the occurrence of complete susceptibility and multi-resistance in data reported at the isolate level. A list of the antimicrobials



included in this evaluation of multi-resistance can be found in Section 2, 'Materials and methods'. The majority of antimicrobial resistance data reported to EFSA by MSs comprised data collected in accordance with EFSA's monitoring guidelines; quantitative disc diffusion data constituted only a small percentage of the total data and were analysed in the report as qualitative data only. ECOFFs are now currently also available for the different disc diffusion methods for *Salmonella* for azithromycin, cefoxitin, ceftazidime, chloramphenicol, gentamicin, meropenem, tetracycline, tigecycline and trimethoprim. This is the result of the European Committee on Antimicrobial Susceptibility Testing (EUCAST)–ECDC project where laboratories from the Food and Water-borne Disease (FWD) network contributed data. These new ECOFFs were applied to the quantitative human data, where relevant.

The report also encompasses resistance in *Salmonella* and *Campylobacter* isolates from human cases of salmonellosis and campylobacteriosis, respectively. These data were reported by MSs to The European Surveillance System (TESSy) either as categorical/qualitative data or, for the first time possible, as quantitative data. The quantitative data were interpreted using EUCAST ECOFFs where available. The majority of human data were, however, quantitative and interpreted using clinical breakpoints (CBPs) to guide medical treatment of the patient. The breakpoints for 'clinical' resistance are, in many cases, less sensitive than the ECOFF for a specific bacteria–drug combination resulting in higher levels of 'microbiological' resistance than 'clinical' resistance. By combining the categories of 'clinically' resistant and intermediate resistant into a non-susceptible category, however, close correspondence with the ECOFF was achieved.

Universal adoption and understanding of the distinction between CBPs and ECOFFs would enable clinicians to choose the appropriate treatment based on information relevant to the individual patient, but would recognise that epidemiologists need to be aware of small changes in bacterial susceptibility, which may indicate emerging resistance and allow for appropriate control measures to be considered. ECOFFs, CBPs and related concepts regarding antimicrobial resistance/susceptibility are presented in detail hereafter.

1.2. Epidemiological cut-off values and clinical breakpoints

EUCAST has defined CBPs and ECOFFs. A microorganism is defined as 'clinically' resistant when the degree of resistance shown is associated with a high likelihood of therapeutic failure. The microorganism is categorised as resistant by applying the appropriate CBP in a defined phenotypic test system, and this breakpoint may alter with legitimate changes in circumstances (for example alterations in dosing regime, drug formulation, patient factors).

A microorganism is defined as wild type for a bacterial species when no acquired or mutational resistance mechanisms are present to the antimicrobial in question. A microorganism is categorised as wild type for a given bacterial species presenting a lower MIC to the antimicrobial in question than the appropriate ECOFF in a defined phenotypic test system. This cut-off value will not be altered by changing circumstances (such as alterations in frequency of antimicrobial administration). Wild-type microorganisms may or may not respond clinically to antimicrobial treatment. A microorganism is defined as non-wild type for a given bacterial species by the presence of an acquired or mutational resistance mechanism to the antimicrobial in question. A microorganism is categorised as non-wild type for a given bacterial species by applying the appropriate ECOFF value in a defined phenotypic test system; non-wild-type organisms are considered to show 'microbiological' resistance (as opposed to 'clinical' resistance). CBPs and ECOFFs may be the same, although it is often the case that the ECOFF is lower than the CBP.

Comparative advantages and disadvantages of the use of CBPs versus ECOFFs (see box hereafter) have been taken into account in the detailed specifications for harmonised monitoring schemes on antimicrobial resistance in animals and food devised by EFSA. These guidelines have been published (EFSA, 2007, 2008) and the terminology used is that devised by EUCAST (Kahlmeter et al., 2003). As far as possible, ECOFFs have been used in this report, as recommended in the guidelines, to determine non-wild-type organisms also termed 'microbiologically' resistant organisms, and to ensure that results from different MSs are comparable. Hereafter in this report, 'microbiologically' antimicrobial-resistant organisms are referred to as 'resistant' for brevity.



Clinical breakpoints (clinical resistance)

The clinician, or veterinarian, choosing an antimicrobial agent to treat humans or animals with a bacterial infection requires information that the antimicrobial selected is effective against the bacterial pathogen. Such information will be used, together with clinical details such as the site of infection, ability of the antimicrobial to reach the site of infection, formulations available and dosage regimes, when determining an appropriate therapeutic course of action. The in vitro susceptibility of the bacterial pathogen can be determined and clinical breakpoints (CBPs) used to ascertain whether the organism is likely to respond to treatment. CBPs will take into account the clinical behaviour of the drug following administration and assume that a clinical response will be obtained if the drug is given as recommended and there are no other adverse factors which affect the outcome. Conversely, if the CBP indicates resistance, then it is likely that treatment will be unsuccessful. Frequency of dosing is one factor that can affect the antimicrobial concentration achieved at the site of infection. Therefore, different dosing regimes can lead to the development of different CBPs, as occurs in some countries for certain antimicrobials where different therapeutic regimes are in place. Although the rationale for the selection of different CBPs may be clear, their use makes the interpretation of results from different countries.

Epidemiological cut-off values (microbiological resistance)

For a given bacterial species, the pattern of the minimum inhibitory concentration (MIC) distribution or the inhibition zone diameter (IZD) distribution (i.e. the frequency of occurrence of each given MIC or zone diameter plotted against the MIC value or zone diameter obtained) can enable the separation of the wild-type population of microorganisms from those populations which show a degree of acquired resistance. The wild-type susceptible population is assumed to have no acquired or mutational resistance and commonly shows a normal distribution.

When bacteria acquire resistance by a clearly defined and efficacious mechanism, such as the acquisition of a plasmid bearing a gene which produces an enzyme capable of destroying the antimicrobial, then the MIC or zone diameter distribution commonly shows two major sub-populations, one a fully susceptible normal distribution of isolates and the other a fully resistant population which has acquired the resistance mechanism. Resistance may be achieved by a series of small steps, such as changes in the permeability of the bacterial cell wall to the antimicrobial or other mechanisms which occur lying between the fully susceptible population and more resistant populations. The epidemiological cut-off (ECOFF) value indicates the MIC or zone diameter above which the pathogen has some detectable reduction in susceptibility. ECOFFs are derived by testing an adequate number of isolates to ensure that the wild-type population can be confidently identified for a given antimicrobial. The clinical breakpoint, which is set to determine the therapeutic effectiveness of the antimicrobial, may fail to detect emergent resistance. Conversely, the ECOFF detects any deviation in susceptibility from the wild-type population, although it may not be appropriate for determining the likelihood of success or failure for clinical treatment.

1.3. Developments in the harmonised monitoring of antimicrobial resistance

Revision of epidemiological cut-off values

The epidemiological cut-off value (ECOFF) for Escherichia coli versus ciprofloxacin has been revised by the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Wild-type isolates are now considered to have a ciprofloxacin minimum inhibitory concentration lower than or equal to 0.06 mg/L (which is a change from the original tentative ECOFF of 0.03 mg/L and which now corresponds to the ECOFF for Salmonella spp.).

The EUCAST ECOFFs which have been applied in this 2013 EU Summary Report to interpret the results obtained by MSs are the revised ones and are quoted in Commission Decision 2013/652/EU. Historical data were re-evaluated using the revised ECOFFs.



Together with its FWD network, ECDC has developed an EU protocol for harmonised monitoring of antimicrobial resistance in human *Salmonella* and *Campylobacter* isolates (ECDC, 2014b). This document is intended for the National Public Health Reference Laboratories to guide the susceptibility testing needed for EU surveillance and reporting to ECDC. Consultation was also sought from EFSA, EUCAST and the EU-RL for Antimicrobial Resistance to facilitate comparison of data between countries and with results from the antimicrobial resistance monitoring performed in isolates from animals and food products. The protocol is effective from 2014 and supports the implementation of the Commission Action Plan on antimicrobial resistance. One of the recommendations is that, for the purpose of the joint report with EFSA, human data should also be interpreted based on ECOFFs. As this requires quantitative data, ECDC introduced this possibility for reporting of the 2013 antimicrobial susceptibility testing (AST) data from human *Salmonella* and *Campylobacter* isolates. ECDC also set up at joint project with EUCAST to establish inhibition zone diameter ECOFFs for *Campylobacter jejuni, C. coli* and *Salmonella* spp. in 2014 (EUCAST, 2014). So far, new disc diffusion ECOFFs have been established for nine antimicrobials for *Salmonella* spp., while the project continues for *Campylobacter jejuni* and *C. coli*.

A new legislation on harmonised monitoring of antimicrobial resistance in animals and food

In 2013, based on the proposals issued by the European Food Safety Authority, the EC put forward and discussed with the MSs a new legislation on the harmonised monitoring of antimicrobial resistance in Salmonella, Campylobacter and indicator bacteria in food-producing animals and food. Commission Decision 2013/652/EU⁹ of 12 November 2013 establishes a list of combinations of bacterial species, food-producing animal populations and food products and sets up priorities for the monitoring of antimicrobial resistance from a public health perspective. Commission Implementing Decision 2013/652/EU entered into force in 2014, as did Commission Implementing Decision 2013/653/EU of 12 November 2013 as regards a Union financial aid towards a coordinated control plan for antimicrobial resistance monitoring in zoonotic agents in 2014.

Monitoring of antimicrobial resistance in Escherichia coli became mandatory, as it is for Salmonella and C. jejuni in the major food-producing animal populations and their derived meat. Sampling should be performed at the level of domestically produced animal populations, corresponding to different production types with the aim of collecting data that, in the future, could be combined with those on exposure to antimicrobials. Provisions have been taken where possible to exploit samples that would be collected under other existing control programmes.

Microdilution methods for testing are confirmed and this should be accompanied by the application of European Committee on Antimicrobial Susceptibility Testing epidemiological cut-off (ECOFF) values for the interpretation of 'microbiological' resistance. The harmonised panel of antimicrobials used for Salmonella, Campylobacter, E. coli and Enterococcus spp. is broadened with the inclusion of substances that either are important for human health or can provide clearer insight into the resistance mechanisms involved. The concentration ranges to be used ensure that both the ECOFF and the clinical breakpoint are included so that comparability of results with human data is made possible.

The specific monitoring of extended-spectrum beta-lactamase-, AmpC- and carbapenemase-producing Salmonella and indicator commensal E. coli is also foreseen. The collection and reporting of data are to be performed at the isolate level, in order to enable more in-depth analyses to be conducted, in particular on the occurrence of multi-resistance.

⁹ Commission Implementing Decision 2013/652/EU of 12 November 2013 on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria. OJ L 303, 14.11.2013, p. 26–39.



2. Materials and methods

2.1. Antimicrobial susceptibility data from humans available in 2013

MSs report results from AST to ECDC through TESSy. Interpreted categorical AST data (qualitative data) for 2013 were submitted via the case-based reporting system in connection with the annual data collection for the EU Summary Report of Trends and Sources of Zoonoses and Zoonotic Agents by the end of May 2014. For the first time, countries also had the possibility of reporting measured values (quantitative AST data) to ECDC via the isolate-based molecular surveillance. These data were actively collected in September and October 2014. As the data collected by EFSA are also quantitative, movement towards collection of quantitative data from human isolates has improved and will improve comparability of data between the two sectors, as the same interpretive criteria can be applied to both datasets.

For 2013, however, most human isolate data submitted was still categorical. Therefore, in the 2013 report, as an interim measure to improve alignment between the two sectors, the categories of 'clinically' intermediate and 'clinically' resistant were combined in a non-susceptible group. Alignment of the susceptible category with the 'wild type' category based on ECOFFs and of the non-susceptible category with the ECOFF-based 'non-wild type' category indicates that these categories now correspond closely for most antimicrobials agents included (see Figure 1 and Figure 32).

2.1.1. Salmonella data of human origin

Twenty-one MSs, Iceland and Norway provided data for 2013 on human *Salmonella* isolates. Seven countries (Austria, Denmark, Finland, Luxembourg, the Netherlands, Norway and Romania) reported isolate-based AST results as measured values (inhibition zone diameters or MICs) (Table 1). Sixteen countries reported case-based AST results interpreted as susceptible (S), intermediate (I) or resistant (R) according to the CBPs applied.

The antimicrobials included in the 2013 report (Table 1) followed the priority panel of antimicrobials from the EU protocol for harmonised monitoring of antimicrobial resistance in human *Salmonella* and *Campylobacter* isolates (ECDC, 2014b). As the panel was agreed during 2013 and published in 2014, in 2013 only a few countries had been able to start testing the agents that were new to the panel. Thus, limited data were available for meropenem and ceftazidime. Most countries also still tested the combination drug co-trimoxazole (sulfamethoxazole and trimethoprim) rather than testing the substances separately, partly because no EUCAST interpretive criterion exists for sulfamethoxazole for *Salmonella*.

Information on the methods and guidelines used for testing and interpretation in 2013 were provided by the public health reference laboratories. Ten MSs plus Iceland and Norway used disc diffusion methods, six other MSs used dilution methods and another four MSs used a combination of the two depending on the situation and the antimicrobial (Table 1). The method used in one MS was not reported. The number of countries exclusively using Clinical and Laboratory Standards Institute (CLSI) interpretive criteria declined from nine in 2012 to five in 2013 reflecting greater use of available EUCAST criteria. Thirteen countries (including the seven for which ECDC interpreted the data) used a combination of EUCAST and CLSI criteria, two countries used only EUCAST criteria and three countries used national interpretive criteria (Table 1). For information on the exact breakpoints applied by countries, see Table <u>MM1</u>. It should be noted that, in some countries, the public health reference laboratory performs susceptibility testing on only a fraction of the isolates reported. The remaining AST data arrives from isolates tested by hospitals or local laboratories, and the methods and interpretive criteria used by these are often not available to ECDC.

As resistance levels differ substantially between *Salmonella* serovars, data were presented separately for the three most common serovars – *S.* Enteritidis, *S.* Typhimurium and *S.* Infantis – in addition to *Salmonella* spp. Moreover, *S.* Typhimurium data were further divided between monophasic *S.* Typhimurium $\underline{1},4,[5],12$:i:- and other *S.* Typhimurium. Data were also presented for serovars *S.* Derby and *S.* Kentucky owing to their high prevalence in pigs and turkey, respectively, and the high level of resistance observed in both human and animal isolates, particularly of *S.* Kentucky. The proportion of resistant isolates are only shown when at least 20, or for less common serovars 10, isolates were tested in that MS.

In order to better assess the impact from food consumed within each reporting country on the antimicrobial resistance levels found in human *Salmonella* isolates, the analysis focused on domestically acquired cases. However, as several countries had not provided any information on travel (or non-travel) of their cases, cases with unknown travel status were also included in addition to domestically acquired cases. The proportion of travel-associated, domestic and unknown cases among the tested *Salmonella* isolates is presented in Table <u>MM2</u>. An analysis was also made on the most likely country of infection of each disease



case to compare resistance levels in human *Salmonella* infections acquired within the EU/European Economic Area (EEA) with those acquired when travelling in regions outside the EU/EEA.

Multi-drug resistance (MDR) of human Salmonella spp. to eight antimicrobial classes were analysed. Multidrug resistance of an isolate was defined as non-susceptibility to at least three different antimicrobial classes (Magiorakos et al., 2012). The antimicrobials included were ampicillin, cefotaxime, chloramphenicol, ciprofloxacin/nalidixic acid. gentamicin, sulfonamides/sulfamethoxazole, tetracyclines and trimethoprim/trimethoprim/sulfa (co-trimoxazole). Resistance to nalidixic acid and resistance to ciprofloxacin were addressed together, as they belong to the same class of antimicrobials: guinolones. In the event that an isolate was resistant or exhibited intermediate resistance to either of these antimicrobials, the isolate was classified as non-susceptible to the combined antimicrobial ciprofloxacin/nalidixic acid. Trimethoprim and cotrimoxazole were also addressed together, as most countries had only tested the combination. This approach was considered appropriate because some countries provided data on both trimethoprim alone and the combination co-trimoxazole and, based on those data, it appears that the proportion non-susceptible to trimethoprim alone and to the combination correspond closely. Co-resistance to ciprofloxacin and cefotaxime was also estimated, as these two antimicrobials are considered the most important for treatment of severe salmonellosis (ECDC et al., 2009).



Country	Ampicillin	Cefotaxime	Ceftazidime	Chloramphenicol	Ciprofloxacin	Gentamicin	Meropenem	Nalidixic acid	Sulfonamides	Tetracyclines	Trimethoprim	Trimethoprim-sulfa	Method used	Type of Data	Interpretive criteria
Austria	•	•		•	•	•		•	•	•	•		DD	Q	Interpreted by ECDC. EUCAST ECOFFs 2013 (or 2014 for newly defined ECOFFs) for all except EUCAST CB 2013 (Cip) and CLSI 2013 (Sul)
Belgium	٠	٠		٠	٠	٠		٠	٠	٠		٠	DD	SIR	EUCAST CB 2013 (Amp, Ctx, Chl, Gen, Sxt), CLSI CB 2013 (Cip, Nal, Sul, Tet)
Denmark	٠	٠		٠	٠	•		٠	٠	•	•		DL	Q	Interpreted by ECDC, as for Austria
Estonia	•	•		٠	٠	•		٠	•	•		٠	DD	SIR	WHO Collaborating Centre 2010, DTU Food (breakpoints based on CLSI)
Finland	٠	٠		٠	٠	٠		٠	٠	٠	•		DD	Q	Interpreted by ECDC, as for Austria
France	٠	٠	٠	٠	٠	٠	٠	٠	٠	٠	•	٠	DD/DL ^(a)	SIR	CA-SFM CB 2013
Germany	٠	٠			٠	٠		٠				٠	DL	SIR	No update provided. Earlier German DIN
Greece	٠			٠	٠			٠		٠		٠	DD	SIR	CLSI CB 2013 (M100-S23). For Cip, the Enterobacteriaceae breakpoint was applied
Hungary	٠	٠		٠	٠	٠		٠	٠	٠		٠	DD/DL	SIR	EUCAST CB 2013 except CLSI CB 2013 (Nal, Sul). Only Cip tested for invasive isolates
Iceland	٠			٠	٠							٠	DD	SIR	EUCAST 2013
Ireland	٠	٠		٠	٠	٠		٠	٠	٠		٠	DL	SIR	EUCAST CB 2013 except CLSI CB 2013 (Sul, Tet)
Italy	•	٠		•	٠	•		•	•	•		٠	DD	SIR	Changed from CLSI to EUCAST CB 2013 in Jul 2013 except CLSI CB 2009 (Nal, Sul, Tet, Tmp)
Latvia	٠	٠			٠							٠	NR	SIR	No update provided. Earlier CLSI
Lithuania	٠	٠		٠	٠	٠		٠	٠	٠		٠	DD	SIR	No update provided. Earlier CLSI
Luxembourg	٠	٠	٠	٠	٠	٠	٠	٠	٠	٠	•	٠	DD/DL	Q	Interpreted by ECDC, as for Austria
Malta	٠				٠		• ^(b)					٠	DL	SIR	Biomerieux Vitek II system; follows EUCAST CB 2010
Netherlands	٠	٠	•	٠	٠	٠		٠	٠	•	•		DL	Q	Interpreted by ECDC, as for Austria
Norway	٠			٠	٠			٠		•		٠	DD	Q	Interpreted by ECDC, as for Austria
Romania	•	•	•	•	•	٠		٠	•	•		٠	DD	Q	Interpreted by ECDC, as for Austria
Slovakia	•	•	•	•	٠		• ^(b)	•	٠	•		٠	DD/microDL	SIR	EUCAST CB 2013 except for CLSI CB 2013 (Nal, Sul, Tet)
Slovenia	•	٠		•	٠	•		٠	•	•	•	٠	DD	SIR	CLSI CB 2013 (M100-S23)
Spain	•	٠		•	•	٠		٠	•	•		٠	DD	SIR	EUCAST CB 2013 except for CLSI CB 2010 (Nal, Tet)
UK	٠	٠	٠	٠	٠	٠		٠		•		٠	DL ^(c)	SIR	No update provided. Earlier HPA methodology based on Frost (1994)

Table 1. Antimicrobials reported, methods used, type of data reported and interpretive criteria applied by MSs for human Salmonella AST data in 2013

AST: antimicrobial susceptibility testing; DD: Disc diffusion; DL: Dilution; Q: Quantitative data; SIR: Susceptible, Intermediate, Resistant (categorical data);

ECDC: European Centre for Disease Prevention and Control; ECOFF: epidemiological cut-off; EUCAST: European Committee on Antimicrobial Susceptibility Testing; CA-SFM: French Society for Microbiology; CLSI: Clinical and Laboratory Standards Institute; HPA: Health Protection Agency (UK); WHO: World Health Organization; MSs: Member States.

(a): gradient strip (b): All gentamicin results for Salmonella automatically reported as resistant and therefore excluded. (c): in agar breakpoint



2.1.2. Campylobacter data of human origin

Fourteen MSs, Iceland and Norway provided data for 2013 on human *Campylobacter jejuni and/or C. coli* isolates. Five countries (Austria, Denmark, Luxembourg, Norway and Romania) reported isolate-based AST results as measured values (inhibition zone diameters or MICs) (Table 2). Eleven countries reported case-based AST results interpreted as susceptible (S), intermediate (I) or resistant (R) according to the CBPs applied.

The antimicrobials included in the 2013 report (Table 2) followed the panel of antimicrobials from the EU protocol for harmonised monitoring of antimicrobial resistance in human *Salmonella* and *Campylobacter* isolates (ECDC, 2014b). The priority panel for *Campylobacter* includes ciprofloxacin, erythromycin and tetracyclines. Gentamicin and co-amoxiclav (amoxicillin and clavulanic acid) are from the list of optional antimicrobials where gentamicin is recommended for monitoring of invasive isolates.

Information on the methods and guidelines used for testing and interpretation in 2013 were provided by the public health reference laboratories. Five MSs used disc diffusion methods, six other MSs and Norway used dilution methods and another three MSs and Iceland used a combination of the two depending on the situation and the antimicrobial (Table 2). Six countries, compared with nine in 2012, were solely using interpretive criteria from EUCAST. Six other countries (including the five where ECDC interpreted the data) used a combination of EUCAST and French Society for Microbiology (CA-SFM) criteria (no EUCAST criteria exist for *Campylobacter* and co-amoxiclav or for gentamicin for disc diffusion) (Table 2). One country did not report which criteria had been applied to the data. For information on the exact breakpoints applied by country, see Table <u>MM3</u>. It should be noted that, in some countries, the public health reference laboratory performs antimicrobial susceptibility testing on only a fraction of the isolates. The remaining AST data arrives from isolates tested by hospitals or local laboratories, and the methods and interpretive criteria used by these are often not available to ECDC.

Resistance levels differ substantially between the two most important *Campylobacter* species, *C. jejuni* and *C. coli*, and data are therefore presented separately for these. The proportion of resistant isolates are only shown when at least 20 isolates were reported from that MS, with the exception of MDR analysis for *C. coli* where the limit was set to 10 isolates.

In order to better assess the impact from food consumed within each reporting country on the antimicrobial resistance levels found in human *Campylobacter* isolates, the analysis focused on domestically acquired cases. However, as several countries had not provided any information on travel (or non-travel) of their cases, cases with unknown travel status were included in the analysis. The proportion of travel-associated, domestic and unknown cases among the tested *Campylobacter* isolates is presented in Table <u>MM4</u>. An analysis was also made on the most likely country of infection of each disease case to compare resistance levels in human *C. jejuni* infections acquired within the EU/EEA with those acquired when travelling in regions outside the EU/EEA. There were not enough isolates tested for AST in *C. coli* isolates associated with travel outside of the EU/EEA for a meaningful analysis to be made.

Multi-drug resistance of a *C. jejuni* or *C. coli* isolate was defined as non-susceptibility to at least three different antimicrobial classes (Magiorakos et al., 2012). The antimicrobials included in the MDR analysis were ciprofloxacin, erythromycin, gentamicin and tetracyclines. Co-resistance to ciprofloxacin and erythromycin was also estimated, as these two antimicrobials are considered the most important for treatment of severe campylobacteriosis (ECDC et al., 2009).



Table 2. Antimicrobials reported, method used, type of data reported and interpretive criteria applied by MSs for human Campylobacter AST data in 2013

Country	Ciprofloxacin	Co-amoxiclav	Erythromycin	Gentamicin	Tetracyclines	Method used	Type of Data	Interpretive criteria
Austria	•		٠	٠	٠	DL	Q	Interpreted by ECDC. EUCAST ECOFFs 2013 for all except CA-SFM 2013 (Amc, Gen for disc diffusion)
Denmark	•		•	•	•	DL	Q	Interpreted by ECDC, as for Austria
Estonia	•	•	•	٠	•	DD	SIR	CA-SFM 2010
France	٠	٠	٠	٠	(a)	DD	SIR	EUCAST CB 2013 (Cip, Ery, Tet), CA-SFM CB 2013 (Amc, Gen)
Iceland	٠		٠		٠	DD/DL ^(b)	SIR	EUCAST CB 2013
Italy	٠		٠	٠	٠	DD	SIR	EUCAST CB 2013 (Cip, Ery, Tet), CLSI CB M45-A (Gen)
Lithuania	٠		٠			DD	SIR	No information
Luxembourg	٠	٠	٠	٠	٠	DD/DL ^(b)	Q	Interpreted by ECDC, as for Austria
Malta	٠		٠			DL ^(b)	SIR	EUCAST CB 2013 (Cip, Ery)
Netherlands	٠		٠		٠	DD/DL	SIR	Survey in 12 clinical labs in NL in 2009 (Ned Tijdschr Med Microbiol 2009;17:nr1)
Norway	٠		٠	٠	٠	DL ^(b)	Q	Interpreted by ECDC, as for Austria
Romania	•		٠	٠	٠	DD	Q	Interpreted by ECDC, as for Austria
Slovakia	٠	•	٠	٠	•	DL	SIR	CLSI CB
Slovenia	٠	•	•	٠	٠	DD/DL ^(b)	SIR	CA-SFM CB 2010 for disc diffusion, CLSI M45-A CB (Cip, Ery gradient strip)
Spain	٠		٠	٠	٠	DL ^(b)	SIR	EUCAST CB 2013 (Cip, Ery, Tet), CA-SFM CB 2013 (Amc, Gen)
United Kingdom	٠	٠	٠	٠	٠	DL ^(c)	SIR	EUCAST CB 2013

AST: antimicrobial susceptibility testing; DD: Disc diffusion; DL: Dilution; Q: Quantitative data; SIR, Susceptible, Intermediate, Resistant (categorical data); ECDC, European Centre for Disease Prevention and Control; ECOFF: epidemiological cut-off; EUCAST: European Committee on Antimicrobial Susceptibility Testing; CA-SFM: French Society for Microbiology; CLSI: Clinical and Laboratory Standards Institute; MSs: Member States.

(a): Tested but not reported. (b): gradient strip. (c): in agar breakpoint.



2.2. Antimicrobial susceptibility data from animals and food available in 2013

2.2.1. Data reported under Directive 2003/99/EC in 2013

For 2013, 28 MSs and three non-MSs reported data on antimicrobial resistance in tested *Salmonella* and *Campylobacter*, commensal *E. coli* or meticillin-resistant *Staphylococcus aureus* (MRSA) isolates from various food-producing animals and/or food categories, sampled through a number of different national schemes. Isolates may have been collected by different monitoring approaches, either by active monitoring of animals and foods or, in some cases, by passive monitoring based on diagnostic submission of samples from clinical cases of disease in animals, or from foods sampled as part of investigatory work. In the case of passive monitoring, the isolates tested often constituted a sub-sample of the total isolates available at the National Reference Laboratory (NRL). Clinical investigation data were not accounted for in this report.

Data on antimicrobial resistance in tested *Salmonella* and *Campylobacter* have been reported by the MSs on a mandatory basis under Directive 2003/99/EC and data on antimicrobial resistance in tested commensal *E. coli* and commensal enterococci or MRSA isolates have been reported on a voluntary basis. An overview of the MS and non-MS reporting antimicrobial resistance data to EFSA in 2013 is shown in Table 3.

Table 3. MSs and non-MSs reporting data in 2013 from animals and food

Bacteria	Number of MSs and non-MSs reporting quantitative or qualitative data
Salmonella	28 MSs+3 non-MSs
Campylobacter	21 MSs+3 non-MSs
Indicator Escherichia coli	16 MSs+2 non-MSs
Indicator enterococci	10 MSs+2 non-MSs
MRSA ^(a)	2 MSs+1 non-MS

MSs: Member States; MRSA: meticillin-resistant Staphylococcus aureus.

(a): In 2013, seven MSs and one non-MS reported data on the occurrence of MRSA.

Dilution and disc diffusion testing methods were used by reporting MSs for susceptibility testing, and both quantitative¹⁰ and qualitative¹¹ data were reported at the EU level. For the purpose of this report, only quantitative dilution has been considered. Quantitative disc diffusion data are presented in <u>Appendix A</u>.

The antimicrobials incorporated in this summary analysis were selected based on their relative public health importance and as representatives of different antimicrobial classes, taking into account EFSA's reports and recommendations on the harmonised monitoring and reporting of antimicrobial susceptibility data (EFSA 2007, 2008).

2.2.2. Analyses of antimicrobial resistance data

2.2.2.1. Overview tables of the resistance data reported

Quantitative MIC data, generated by dilution methods recommended by EFSA, have been reported and analysed together; quantitative inhibition zone diameter data, which constitute a very small fraction of the total data, have not been included in the analysis of quantitative data and have been described separately in <u>Appendix A</u>. Some MSs reported antimicrobial resistance data as both quantitative and qualitative data; in that case, only the quantitative data have been included. Data generated from the antimicrobial susceptibility testing and reported as quantitative/qualitative by MSs have been described in the **overview tables** in individual sections.

2.2.2.2. Minimum inhibitory concentration distributions, epidemiological cut-off values and the occurrence of resistance

For each combination of microorganism, antimicrobial and food or animal category tested, **MIC distributions** have been presented as frequency tables, giving the number of isolates tested that have a given MIC at each test dilution (mg/L) of the antimicrobial.

¹⁰ 'Quantitative data' derived from dilution methods consisted of the number of isolates having a specific MIC value (measured in mg/L) relative to the total number of isolates tested, for each antimicrobial agent and in each specific food/animal category. 'Quantitative data' derived from diffusion methods comprised the number of isolates having a specific inhibition zone diameter (measured in mm) relative to the total number of isolates tested, for each antimicrobial agent and in each food/animal category.

¹¹ 'Qualitative data' consisted of the number of isolates out of the total number of isolates that were resistant to each antimicrobial agent in each food/animal category; qualitative data can be generated either from MIC determination or from disc diffusion testing.



Quantitative MIC data for *Salmonella* were, wherever possible, **interpreted using recently revised ECOFFs** as listed in Decision 2013/652/EC and presented in Table 4. An isolate was defined as 'microbiologically' resistant (i.e. displaying a decreased susceptibility) to a selected antimicrobial when its MIC value was above the ECOFF. A more sensitive MIC breakpoint or ECOFF (i.e. a lower MIC breakpoint or ECOFF) might be expected to result in more isolates being defined as 'clinically' or 'microbiologically' resistant, respectively; the number of isolates affected in that way will of course depend on the distribution of MIC results. This report incorporates all of these changes in a comprehensive revision, which also reevaluated the historical data using the revised ECOFFs, as well as taking into account revised EU legislation in this area, which included the revised ECOFFs.

The occurrence of resistance to a number of antimicrobials was determined (giving the percentage of isolates 'microbiologically' resistant out of those tested) for *Salmonella*, *Campylobacter*, indicator *E. coli* and enterococcal isolates from fowl (*Gallus gallus*), turkeys, pigs and cattle, and meat from *Gallus gallus*, pigs and cattle and are presented and analysed in **tables on the occurrence of resistance** in this report. These are the animal and food categories most frequently reported by most MSs. In addition, data have been presented at the production-type level where possible. Data are included only if quantitative MIC data are provided by more than four MSs or if disc diffusion data are provided by more than two MSs for the bacterium–animal/food category combination. An exception to this rule has nevertheless been made on *Salmonella* serovars of public health importance (see below) and on MRSA. Data reported from fewer than 10 tested isolates per combination and per MS are not included. Data are reported in separate sections dedicated to each microorganism and in <u>Appendix A</u> for *Salmonella* data obtained from disc diffusion. In addition, the occurrence of resistance (i.e. resistance levels) in reporting MS groups was calculated as totals (the total number of resistant isolates out of the total number of tested isolates across reporting MSs), and not the weighted means.

2.2.2.3. Resistance in Salmonella serovars of public health importance

In this report, antimicrobial resistance in tested *Salmonella* isolates were aggregated to give a value for *Salmonella* spp. for each country and food/animal category. In addition, whenever sufficient data were transmitted by MSs for a particular food/animal category, the most prevalent *Salmonella* serovars – *S.* Enteritidis and *S.* Typhimurium – were also reported separately for that food/animal category. Additional tables have been included in this report to describe the occurrence of antimicrobial resistance among selected *Salmonella* serovars of public health importance or of high prevalence in animals (monophasic *S.* Typhimurium, *S.* Infantis, *S.* Derby and *S.* Kentucky). In order to present a complete overview of the animal populations and food categories in which specific *Salmonella* serovars of public health importance have been included.

2.2.2.4. Data description

Throughout the report, **level or occurrence of antimicrobial resistance** means the percentage of resistant isolates as a proportion of the isolates tested of that microorganism. **MSs reporting group** means the MSs that provided data and were included in the relevant table of antimicrobial resistance for that bacterium–food or animal category–antimicrobial combination.

Terms used to describe the levels or occurrence of antimicrobial resistance are 'rare: <0.1 %', 'very low: 0.1 % to 1.0 %', 'low: >1 % to 10.0 %', 'moderate: >10.0 % to 20.0 %', 'high: >20.0 % to 50.0 %', 'very high: >50.0 % to 70.0 %', 'extremely high: >70.0 %'. These terms are applied to all antimicrobials. However, the significance of a given level of resistance will depend on the particular antimicrobial and its importance in human and veterinary medicine.

2.2.2.5. Temporal trends in resistance

Where the minimum criteria were met for the inclusion of data in this report (i.e. more than 10 isolates tested by an MS and more than four MSs reporting results for that antimicrobial, microorganism, food or animal category), **temporal trend graphs** were generated showing the resistance to different antimicrobials from 2007 to 2013, by plotting the level of resistance for each year of sampling. Only countries which had reported for four or more years in the 2007 to 2013 period were included.

In order to assess the statistical significance of temporal trends, the proportions of resistance were modelled against time in a logistic regression. This analysis was carried out using the PROC LOGISTIC of SAS 9.2 for each country where there were five years or more of available data to use in the model. The PROC LOGISTIC function uses a logit transform to model the proportion of prevalence against year, and provides estimates for both intercepts and slope. Models where the likelihood ratio test suggested it to be meaningful and resulting in a p-value associated with slope of <0.05 were considered to be significant.



For ciprofloxacin, nalidixic acid, ampicillin and cefotaxime (*Salmonella*), ciprofloxacin, nalidixic acid and erythromycin (*Campylobacter*), ciprofloxacin, nalidixic acid, cefotaxime, ampicillin, streptomycin and tetracycline (indicator *E. coli*) and erythromycin, streptomycin and tetracycline (indicator enterococci), resistance trends over time were visually explored by *trellis* graphs, using the *lattice* package in the R software (R version 2.14.2 (29.02.2012)). Graphs were created for those countries for which resistance data were available for four or more years, for at least one of the two antimicrobials. MS-specific resistance levels trend graphs use a unique scale and countries are shown in alphabetical order.

2.2.2.6. Spatial analysis of resistance through maps

MS-specific antimicrobial resistance levels for selected bacterium–food or animal category combinations were plotted in maps for 2013, using ArcGIS 9.3. In the maps, resistance levels are presented with colours reflecting the continuous scale of resistance to the antimicrobial of interest among reporting MSs; thus, there might be some apparent discrepancies between the colours and resistance levels between maps. Percentages shown in this map refer to countries that reported quantitative MIC data for more than 10 isolates in 2013. When quantitative 2013 data were not available, the 2012 level of resistance was used instead and is referred to by a footnote in the map. The countries labelled as '<10 isolates' therefore include MIC data for fewer than 10 isolates.

Table 4. ECOFFs used to interpret MIC distributions (mg/L) for bacteria from animals and food – the given values define the 'microbiologically' resistant isolates

	Salmonella	E. coli	E. faecium	E. faecalis	C. jejuni	C. coli
Antimicrobial agent	mg/L	mg/L	mg/L	mg/L	mg/L	mg/L
Ampicillin	>8	>8	>4	>4		
Apramycin	>16	>16				
Avilamycin			>16	>8		
Cefotaxime	>0.5	>0.25				
Ceftazidime	>2	>0.5				
Ceftiofur	>2	>1				
Chloramphenicol	>16	>16	>32	>32	>16	>16
Ciprofloxacin	>0.064	>0.064	>4	>4	>0.5	>0.5
Erythromycin			>4	>4	>4	>8
Florfenicol	>16	>16				
Gentamicin	>2	>2	>32	>32	>2	>2
Linezolid			>4	>4		
Nalidixic acid	>16	>16			>16	>16
Neomycin	>4	>8				
Spectinomycin		>64				
Streptomycin	>32	>16	>128	>512	>4	>4
Sulfonamides	>256 ^(a)	>64				
Quinupristin/dalfopristin			>1			
Tetracyclines	>8	>8	>4	>4	>1	>2
Trimethoprim	>2	>2				
Vancomycin			>4	>4		

(a): Cut-off values were not defined by the European Committee on Antimicrobial Susceptibility Testing; instead, cut-off values defined by the EU Reference Laboratory on antimicrobial resistance (Technical University of Denmark) were used.

2.2.3. Analysis of multi-drug resistance and co-resistance data

As a consequence of the availability of antimicrobial resistance data at an isolate-based level in an important number of volunteer MSs, the analysis of multi-resistance and co-resistance data becomes a feasible and important exercise in the light of the public health relevance of the emergence of multi-resistant bacteria. The intention is to focus mainly on multi-/co-resistance patterns involving critically important antimicrobials according to the bacterial species, such as cephalosporins, fluoroquinolones and macrolides, and to summarise important information in the EU Summary Report. The occurrence of the isolates of a serotype/resistance pattern of interest is studied at the MS level and at the reporting MS group/EU level, as the overall picture for all MSs might show a more definite pattern of emergence and spread. In addition, the



analysis of data may reveal the existence of new or emerging patterns of multi-resistance, particularly in *Salmonella* serotypes.

2.2.3.1. Definitions

For the purpose of this analysis, a **multi-resistant isolate** is one defined as resistant to at least three different antimicrobial substances, belonging to any three antimicrobial families listed in the harmonised set of antimicrobials included in the EFSA recommendations (EFSA, 2007, 2008). Table <u>MM11</u> lists those recommended antimicrobials. Resistance to nalidixic acid and resistance to ciprofloxacin are addressed together: an isolate that is resistant to either of the two will be termed resistant to the combined antimicrobial ciprofloxacin/nalidixic acid, as the two substances belong to the same antimicrobial family. In contrast, a **fully susceptible isolate** is one defined as non-resistant to all of the antimicrobial substances included in the set of substances recommended for *Salmonella*, *Campylobacter* and indicator *E. coli*.

The term **co-resistance** has been defined as two or more resistance genes which are genetically linked, i.e. located adjacent or close to each other on a mobile genetic element (Chapman, 2003). For brevity, the term is used slightly more loosely in this report and indicates two or more phenotypic resistances to different classes of antimicrobials, exhibited by the same bacterial isolate.

2.2.3.2. Multi-resistance patterns

The frequency and percentage of isolates exhibiting various multi-resistance patterns considering the antimicrobials tested were determined for *Salmonella* (*Salmonella* spp., *S*. Enteritidis, *S*. Typhimurium and monophasic *S*. Typhimurium), *Campylobacter* species and indicator *E. coli* for each country and each animal population/food category. Isolates for which no susceptibility data were provided for some of the antimicrobial substances were disregarded. Data analysis was presented for a particular country only when the number of tested isolates was at least 10, except for monophasic *S*. Typhimurium.

2.2.3.3. 'Summary indicators' and 'diversity' of multi-resistance

To illustrate the relative proportions of multi-resistant isolates and the diversity of the resistance to multiple antimicrobials, graphical illustration was chosen. The percentages of isolates susceptible and resistant to one, two, three, etc., antimicrobials are shown using a composite bar graph displaying stacked bars, but only for certain combinations of bacterium–animal population or food category–MSs of particular interest.

The objective is first to give an overview of the situation on multi-resistance through summary indicators: (1) the proportion of fully susceptible isolates; (2) the proportion of multi-resistant isolates. The 'summary indicators' of multi-resistance can be calculated and reported yearly and, therefore, used to follow evolution of the multi-resistance situation across animal populations/food categories and MSs over time.

2.2.3.4. The co-resistance patterns of interest

Co-resistance to cefotaxime and ciprofloxacin was estimated in *Salmonella* and *E. coli* isolates, as these two antimicrobials are of particular interest in human medicine. Co-resistance was addressed using both ECOFFs and CBPs in isolates of these bacteria. In *C. jejuni* and *C. coli* isolates, co-resistance to ciprofloxacin and erythromycin was estimated, as these two antimicrobials are of particular interest in human medicine in the treatment of severe campylobacteriosis. The interpretive ECOFFs used to address co-resistance to ciprofloxacin and erythromycin were, for *C. jejuni*, Cip>0.5 mg/L and Ery>4 mg/L. These values may be considered as very similar to CBPs.

2.2.4. Resistance data in Salmonella from animals and food

Quantitative (MIC) results on antimicrobial resistance in *Salmonella* isolates from animals and food were reported by 22 MSs and two non-MSs (Norway and Switzerland) in 2013. One MS reported inhibition zone diameter data on antimicrobial resistance in animals and food for 2013 which are presented in <u>Appendix A</u>. For further information, see the summary tables in the <u>Overview</u> tables and the <u>submitted and validated MS</u> data published on the EFSA website. The information collected by these countries was collected in accordance with EFSA's recommendations (EFSA, 2007); these data are described in Section <u>3.1.2</u>. The countries that reported results for only low numbers of isolates (fewer than 10) have been excluded from the analysis. The analysis includes data from MSs that reported quantitative MIC susceptibility data from ≥10 isolates for *Salmonella* servars for each kind of meat or animal species.

In 2013, both dilution and disc diffusion methods were used to test the susceptibility of *Salmonella* isolates from animals and food by MSs. Tables <u>MM5</u> and <u>MM6</u> show the antimicrobials selected by the different countries for susceptibility testing. Quantitative dilution results allowed MIC distributions to be reported for *Salmonella* for ampicillin, apramycin, azithromycin, cefepime, cefotaxime, ceftazidime, ceftiofur, chloramphenicol, ciprofloxacin, colistin, florfenicol, gentamicin, kanamycin, meropenem, nalidixic acid,



neomycin, spectinomycin, streptomycin, sulfonamides, tetracyclines, tigecycline and trimethoprim. For further information on reported MIC distributions and the number of resistant isolates, refer to the <u>submitted and</u> <u>validated MS data</u> published on the EFSA website.

Data on *Salmonella* which were reported as disc diffusion data are presented in <u>Appendix A</u>. Although results may not be directly comparable between MSs, it is anticipated that, in most cases, procedures will not have changed markedly over time within a country, and therefore comparisons of the proportion of resistant isolates over time in that country may be possible.

2.2.5. Resistance data in Campylobacter from animals and food

In 2013, 18 MSs and three non-MSs (Iceland, Norway and Switzerland) reported quantitative data on antimicrobial resistance in *Campylobacter*. All *Campylobacter* results were reported as MIC values in accordance with EFSA's recommendations (EFSA, 2007). These data are described in Section <u>3.2.2</u>.

In 2013, all quantitative *Campylobacter* data were reported as MIC values, generated by dilution methods. Table <u>MM8</u> shows the antimicrobials selected by the different countries for susceptibility testing of *Campylobacter* isolates. In this report, antimicrobial resistance was reported separately for *C. jejuni* and *C. coli*.

MIC distributions were analysed for the following antimicrobials: ampicillin, chloramphenicol, ciprofloxacin, clarithromycin, erythromycin, gentamicin, imipenem, nalidixic acid, neomycin, streptomycin, tetracyclines and tulathromycin. For further information on reported MIC distributions and the number of resistant isolates, refer to the <u>submitted and validated MS data</u> published on the EFSA website.

In this section, resistance to ciprofloxacin, erythromycin, gentamicin, nalidixic acid and tetracyclines is described in detail. The occurrence of resistance is tabulated, a portrait of temporal evolution and spatial distribution of resistance is drawn and multi-resistance is analysed. These analyses were performed, and the corresponding results were presented, depending on if a minimum of four or more countries reported quantitative data for a given *Campylobacter* species and the origin of the sample (animal population and food category), and if data were related to at least 10 isolates per country, per origin of sample and per year. *C. jejuni* and *C. coli* are both addressed, as monitoring data on the prevalence of *Campylobacter* in broilers and broiler meat in some reporting countries can reveal that *C. coli* prevalence is either not negligible or of the same magnitude as that of *C. jejuni* (EFSA and ECDC, 2014a).

- Temporal trend graphs were generated, showing the percentage resistance to different antimicrobials among *Campylobacter* isolates, per sample origin, from 2007 to 2013, by year of sampling. Temporal trend graphs were included only for countries which had reported on four or more years in the 2007 to 2013 period.
- The spatial distributions of ciprofloxacin and erythromycin resistance rates in *C. jejuni* from *Gallus gallus* and *C. coli* from pigs are presented. For countries where resistance level figures for 2013 were not available, 2012 figures were used instead. For cattle, the number of reporting countries was lower than for other animal species monitored and, therefore, no spatial distribution maps were generated.
- Multi-resistance was analysed in the isolate-based dataset of *Campylobacter* isolates tested for the full harmonised set of five antimicrobials (ciprofloxacin, erythromycin, gentamicin, streptomycin and tetracyclines) belonging to different classes. 'Multi-resistance' was defined as non-susceptibility to at least three different antimicrobial classes. The proportions of isolates susceptible to all and resistant (non-susceptible) to any one of up to five antimicrobials are presented. Co-resistance to ciprofloxacin and erythromycin was also estimated, as these two antimicrobials are of particular interest in human medicine in the treatment of campylobacteriosis.

MIC distributions were analysed for the following antimicrobials: ampicillin, chloramphenicol, ciprofloxacin, clarithromycin, erythromycin, gentamicin, imipenem, nalidixic acid, neomycin, streptomycin, tetracyclines and tulathromycin. For further information on reported MIC distributions and the number of resistant isolates, refer to the <u>submitted and validated MS data</u> published on the EFSA website.

2.2.6. Resistance data in indicator Escherichia coli from animals and food

For indicator (commensal) *E. coli*, a total of 14 MSs and two non-MSs (Norway and Switzerland) reported quantitative dilution (MIC) results from animals or meat derived from those animals: these data are described in Section <u>3.3</u>. Some countries reported results for only low numbers of isolates (fewer than 10); these data have been excluded from the analysis.



Table <u>MM8</u> shows the antimicrobials selected by the different countries for susceptibility testing. In this report, susceptibility data from food and animal isolates are presented.

The proportions of resistant isolates to the antimicrobial agents ampicillin, cefotaxime, chloramphenicol, ciprofloxacin, gentamicin, nalidixic acid, streptomycin, sulfonamides and tetracyclines are described in detail later in this section. The tables of occurrence of resistance were generated, and MDR analysis was performed if more than four countries reported quantitative data per sampling origin. In addition, only data where 10 or more isolates were available per country, per sampling origin and per year are included in the report. In the graphs illustrating trends in the evolution of antimicrobial resistance over time, results for MIC data interpreted using ECOFFs are shown. Only a few MSs have reported data for the seven consecutive years from 2007 to 2013, as the monitoring of resistance in indicator *E. coli* is performed on a voluntary basis.

Where the minimum criteria for detailed analysis were met, multi-resistance was analysed in the isolatebased dataset on the indicator *E. coli* isolates tested for the full harmonised set of nine antimicrobials belonging to different classes. Multi-resistance is defined as non-susceptibility to at least three different antimicrobial classes. The proportions of isolates susceptible to all antimicrobial substances tested and resistant (non-susceptible) to any one of up to nine substances are presented. Co-resistance to cefotaxime and ciprofloxacin was estimated, as these two antimicrobials are of particular interest in human medicine. Co-resistance was addressed using both ECOFFs (Ctx>0.25 mg/L and Cip>0.064 mg/L) and clinical breakpoints (Ctx>2 mg/L and Cip>1 mg/L).

MIC distributions were analysed for the following antimicrobials: ampicillin, apramycin, cefazolin, cefotaxime, cefotaxime+clavulanic acid, cefepime, ceftazidime, ceftazidime+clavulanic acid, ceftiofur, cefpodoxime, cefoxitin, ceftriaxone, cephalothin, chloramphenicol, ciprofloxacin, colistin, florfenicol, gentamicin, imipenem, kanamycin, meropenem, nalidixic acid, neomycin, piperacillin, spectinomycin, streptomycin, sulfonamides, tetracyclines and trimethoprim. These antimicrobials were selected based on their public health relevance and as representatives of different antimicrobial classes. For further information on reported MIC distributions and the number of resistant isolates, refer to the <u>submitted and validated MS data</u> published on the EFSA website.

2.2.7. Resistance data in indicator enterococci from animals and food

For indicator enterococci (*E. faecalis* and *E. faecium*), in total 10 MSs and two non-MSs (Norway and Switzerland) reported quantitative MIC data; these are described in Section <u>3.4</u>. All countries reporting quantitative MIC data used the methods recommended by EFSA (EFSA, 2008).

In 2013, for enterococci, only susceptibility data from dilution methods are presented by MSs. Tables <u>MM9</u> and <u>MM10</u> show the antimicrobials selected by the different countries for susceptibility testing. Only susceptibility data from animal isolates are presented, as very few countries reported susceptibility data for enterococcal isolates from food.

MIC distributions were analysed for the following antimicrobials: tetracycline, chloramphenicol, ampicillin, erythromycin, streptomycin, vancomycin, quinupristin/dalfopristin and linezolid. For further information on reported MIC distributions and number of resistant isolates, refer to the <u>submitted and validated MS data</u> published on the EFSA website.

2.2.8. Resistance data to third-generation cephalosporins

In relation to third-generation cephalosporin resistance in indicator *E. coli* and *Salmonella* spp., EFSA's recommendations suggest the use of cefotaxime alone to detect important types of resistance (EFSA, 2007). Most MSs reported results for cefotaxime; some also reported results for ceftazidime; these data are described in Section <u>3.6</u>. Cefotaxime is likely to detect the presence of most cefotaximases (CTX-M enzymes), which currently appear to be the most prevalent type of ESBL enzymes in bacteria isolated from food-producing animals in the EU. The use of cefotaxime will also detect the presence of AmpC enzymes in *Salmonella* or *E. coli*. Some ESBLs are ceftazidimases rather than cefotaximases (particularly enzymes in the TEM and SHV families of ESBLs). Although testing both cefotaxime and ceftazidime is therefore optimal for the detection of all ESBLs and AmpC enzymes, EFSA's guidelines have recommended testing cefotaxime to detect all CTX-M enzymes mainly for reasons of affordability.

2.2.9. Data on meticillin-resistant *Staphylococcus aureus* (MRSA)

In 2013, Belgium and Slovenia reported data on susceptibility testing of MRSA isolates from breeding pigs and pig meat, respectively, and Switzerland reported data from cattle and fattening pigs. Details of the antimicrobials selected by Belgium and Switzerland are provided in Section <u>3.5</u>. For further information on



reported MIC distributions and the number of resistant isolates, refer to the <u>submitted and validated MS data</u> published on the EFSA website.

Data relating to MRSA prevalence were reported by seven MSs and one non-MS (Switzerland). The methods for collecting and testing samples for MRSA are not harmonised between MSs and, as a result, MSs may use differing procedures. Owing to the variety of methods employed by MSs, these are explained in detail within Section 3.5 to enable readers to better follow the procedures carried out by individual countries.

There is an important difference between the methods used to isolate *Salmonella*, *Campylobacter* and indicator *E. coli* and the method used to isolate MRSA. For the former group of organisms, there is no selective medium used to isolate organisms possessing a particular resistance from primary samples, whereas, for MRSA, antimicrobials are used to selectively isolate only those *Staphylococcus aureus* isolates which are resistant to meticillin. Some MSs may have sampled particular production types of animals (for example laying hens in *Gallus gallus* or veal calves in cattle), and this introduces another source of possible variation which may account for observed differences between MSs.



3. Assessment

3.1. Antimicrobial resistance in Salmonella

Twenty-one MSs, Iceland and Norway provided data for 2013 on human *Salmonella* isolates. Seven countries (Austria, Denmark, Finland, Luxembourg, the Netherlands, Norway and Romania) reported isolate-based AST results as measured values (inhibition zone diameters or MICs). Sixteen countries reported case-based AST results interpreted as susceptible (S), intermediate (I) or resistant (R) according to the CBPs applied (Table <u>OVER1</u>).

Twenty-two MSs and two non-MSs (Norway and Switzerland) reported quantitative MIC and inhibition zone diameter data on the antimicrobial resistance of *Salmonella* isolates recovered from animals and food in 2013 (Table <u>OVER1</u>).

3.1.1. Antimicrobial resistance in Salmonella isolates from humans

The majority of *Salmonella* infections result in mild, self-limiting, gastrointestinal illness and usually do not require antimicrobial treatment. In some patients the infection may be more serious and can be life-threatening. In cases of severe enteric disease or invasive infection, effective antimicrobials are essential for treatment. Fluoroquinolones are widely recommended for treating adults and third-generation cephalosporins are recommended for treating children. Infection with *Salmonella* strains resistant to these antimicrobials may be associated with treatment failure, which in turn can lead to poor outcomes for patients. Therefore, recommended treatment should take account of up-to-date information on local patterns of resistance.

Methods and interpretive criteria used for antibiotic susceptibility testing of *Salmonella* isolates from humans

The method of testing for antimicrobial susceptibility and the selection of the isolates to be tested varied between countries. The methods and interpretive criteria used for antimicrobial susceptibility testing of Salmonella are presented in Table 1.

Quantitative data were interpreted by the European Centre for Disease Control (ECDC) based on the European Committee on Antimicrobial Susceptibility Testing (EUCAST) epidemiological cut-off (ECOFF) values, where available. Where ECOFFs do not exist, EUCAST or Clinical and Laboratory Standards Institute (CLSI) clinical breakpoints were applied. For the qualitative SIR¹² data, intermediate and resistant results were combined into a non-susceptible category.

For the nine antimicrobials reported from both human and animal/food isolates, the commonly used interpretive criteria were aligned (Figure 1). For this purpose, susceptible isolates were aligned with wild-type isolates based on ECOFFS and non-susceptible isolates (intermediate and resistant) were aligned with non-wild-type isolates. Analysed in these terms there is now generally close concordance (±1 doubling dilution) across interpretive categories. A notable exception is the EUCAST clinical breakpoint for ciprofloxacin in effect for 2013, which is substantially higher than the ECOFF or CLSI clinical breakpoint. In 2014, EUCAST changed the breakpoint so that it is now aligned with the CLSI clinical breakpoint and the ECOFF.





CBP: clinical breakpoint; CLSI: Clinical and Laboratory Standards Institute; ECOFF: epidemiological cut-off; EUCAST: European Committee on Antimicrobial Susceptibility Testing; MIC: minimum inhibitory concentration.

CLSI (M100-S23 2013), EUCAST clinical breakpoints (2013), EUCAST ECOFFS (according to Decision 2013/652/EU).

*No EUCAST ECOFF exists for sulfonamides/sulfamethoxazole. EFSA therefore applies the clinical breakpoint from CLSI.

3.1.1.1. Antimicrobial resistance in *Salmonella* spp. in humans

In total, 16,232 *Salmonella* isolates were tested for resistance to one or more antimicrobials and reported by 21 MSs, Iceland and Norway. This represents 19.3 % of all (N=84,104) confirmed human salmonellosis cases reported in the EU/EEA in 2013. The number of antimicrobials tested per isolate varied by country, from three countries testing only three or four antimicrobials to 14 MSs that tested all nine antimicrobials. Testing of the combination trimethoprim–sulfamethoxazole (co-trimoxazole) remained more common than testing sulfonamides/sulfamethoxazole and trimethoprim separately. Only a few countries reported data on ceftazidime and meropenem in 2013 and this was for only limited numbers of isolates. These data are therefore not shown in the tables, but are briefly mentioned in the text.

In order to better assess the impact from food consumed within each reporting country on the antimicrobial resistance levels found in human *Salmonella* isolates, the analysis focused on domestically acquired cases.

Resistance levels in Salmonella spp. isolates from humans

Interpretation of data must take account of the wide variation in the numbers of *Salmonella* isolates reported by MSs. While this may in part be related to true differences in the incidence of salmonellosis, it is also likely to be greatly influenced by practices in the country related to the capture of isolates and/or data from primary clinical laboratories. In France, for example, AST is performed on all isolates of specific serovars of interest, while, for the most common serovars, a representative sample is tested. In Slovakia, non-invasive isolates are tested against only a few antimicrobials, while invasive isolates are tested against a larger panel.

The highest proportions of resistance in human *Salmonella* spp. isolates in 2013 were reported for ampicillin (36.1 %), sulfonamides/sulfamethoxazole (35.7 %) and tetracyclines (34.5 %) (Table 5). Resistance to the two clinically most important antimicrobials was reported in 3.8 % of isolates for ciprofloxacin and 1.4 % for cefotaxime. Six and three countries, respectively, reported some data on ceftazidime and meropenem in 2013 (not shown in Table 2). These antimicrobials are new in the panel advised to be reported for human *Salmonella* infections (ECDC, 2014b). Of these countries, only France, where isolates resistant to ampicillin were tested further, reported some resistance to these antimicrobials (2.9 % for ceftazidime and 0.2 % for meropenem, N=524).

Some data points in Table 2 merit comment. Ciprofloxacin and trimethoprim–sulfamethoxazole resistance data for Malta are outliers at 53.7 % and 85.4 %, respectively. Latvia reported a very low level of resistance to ampicillin (2.7 %). These data points have been confirmed with both MSs.



Country	Ampicillin		Cefotaxime		Chloramphenicol		Ciprofloxacin ^(b)		Gentamicin		Nalidixic acid		Sulfonam	ides ^(c)	Tetracy	/clines	Trimethoprim		Trimethoprim- sulfa	
	N	%R	Ν	%R	N	%R	N	%R	N	%R	N	%R	N	%R	N	%R	N	%R	N	%R
Austria ^(a)	1,035	13.8	1,035	0.8	1,035	3.8	1,035	1.1	1,035	1.4	1,035	18.3	1,035	17.1	1,035	17.5	1,03 5	2.2	_	-
Belgium	887	42.5	887	1.8	887	6.3	887	4.8	887	5.5	887	15.2	-	_	887	29.8	-	_	887	7.2
Denmark ^(a)	297	29.0	297	1.0	297	3.7	297	0.7	297	2.4	297	3.0	297	32.0	297	28.3	297	8.1	-	_
Estonia	149	18.8	150	2.0	146	9.6	149	6.0	144	1.4	143	8.4	142	19.0	142	19.7	_	_	150	6.0
Finland ^(a)	340	22.1	340	1.5	340	7.4	340	0.3	340	2.9	340	11.2	340	22.1	340	22.1	340	5.6	-	_
France	997	31.8	524	3.8	997	5.9	997	15.4	997	11.2	997	27.0	997	34.5	997	37.4	997	7.7	997	6.7
Germany	2,017	42.5	2,017	1.5	_	_	2,017	0.8	2,017	10.0	2,016	5.0	_	_	_	_	_	_	2,017	9.1
Greece	138	15.2	_	_	138	3.6	138	0.0	_	_	138	11.6	-	_	138	20.3	_	_	25	24.0
Hungary	675	53.6	675	0.7	675	11.0	675	2.1	675	0.9	675	18.8	675	51.6	675	52.4	-	-	675	5.8
Ireland	268	29.5	268	1.5	268	11.6	268	0.4	268	1.5	268	7.8	268	29.5	268	30.6	-	-	268	4.9
Italy	672	55.2	672	1.0	672	4.9	672	4.5	671	1.6	671	11.8	668	55.5	671	56.3	-	-	328	5.2
Latvia	37	2.7	2	NA	_	_	34	0.0	-	_	_	-	-	-	-	-	_	-	33	0
Lithuania	1,178	23.6	1,021	0.5	623	1.6	958	0.3	532	0.8	526	15.0	517	8.9	513	12.1	-	-	1,176	3.1
Luxembourg ^(a)	121	43.0	107	0.9	121	20.7	121	1.7	121	1.7	121	9.1	121	58.7	121	46.3	121	6.6	121	6.6
Malta	82	56.1	-	_		_	82	53.7	_	_	_	-	-	_	_	-	-	-	82	85.4
Netherlands ^(a)	455	61.1	3	NA	455	12.1	455	0.2	455	2.9	455	0.4	3	33.3	455	65.1	3	0	1	_
Romania ^(a)	221	30.8	221	0.5	221	2.3	221	7.2	221	3.6	221	21.7	221	52.5	221	24.9	_	-	221	11.3
Slovakia	648	12.3	285	4.2	10	NA	343	6.1	_	_	13	30.8	5	60	464	12.5	_	-	292	4.5
Slovenia	313	14.4	312	0.3	314	1.6	314	19.4	312	0.6	314	9.6	311	15.4	312	12.5	311	1.3	314	1.3
Spain	1,892	53.4	1,892	1.4	1,894	9.6	1,894	1.4	1,894	4.3	1,873	22.5	1,893	46.1	1,892	47.6	_	_	1,891	7.6
UK	617	20.9	578	0.9	598	4.2	646	2.9	613	3.4	613	13.5	-	_	575	24.3	69	10.1	644	22.2
EU total	13,039	36.1	11,286	1.4	9,691	6.8	12,543	3.8	11,479	4.8	11,603	14.4	7,493	35.7	10,003	34.5	3,173	5.1	10,121	8.3
Iceland	16	NA	-	_	16	NA	16	NA	-	_	_	-	-	_	-	-	_	-	16	NA
Norway ^(a)	368	17.9	-	_	368	5.4	368	0.8	-	-	368	7.6	-	_	368	18.5	_	-	368	3.8

Table 5. Antimicrobial resistance in Salmonella spp. (all non-typhoidal serovars) from humans per country in 2013

N: number of isolates tested; %R: percentage of resistant isolates (either interpreted as non-wild type by ECOFFs or clinically non-susceptible by combining resistant and intermediate categories); -: no data reported; NA: not applicable (if fewer than 20 isolates were tested, resistance was not calculated); I: intermediate; R: resistant.

(a): Provided measured values. Data interpreted by ECDC.

(b): Data for ciprofloxacin show the proportion of non-susceptible isolates (I+R) interpreted based on clinical breakpoints which differ by ≥3 dilutions from the EUCAST ciprofloxacin ECOFF.

(c): Combined data on the class sulfonamides and the substance sulfamethoxazole within this group.

Comparison of resistance levels in Salmonella spp. isolates acquired within the EU/EEA and in other geographical regions

Patterns of infection outside of Europe are likely to be associated with preferred travel destinations for residents of a given MS. Differences in testing methodology between MSs may influence the apparent pattern of regional variation in resistance. Furthermore, the numbers of isolates associated with travel to regions other than Africa and Asia are relatively small. It is therefore appropriate to be cautious in drawing conclusions. Resistance to ciprofloxacin and gentamicin was more frequent in isolates associated with travel to Africa, and resistance to cefotaxime was highest in isolates associated with travel to Asia (Table 6). Resistance to certain other agents such as ampicillin, sulfonamides and tetracyclines, however, was more frequent in isolates acquired in the EU than in isolates acquired in any other region.

Table 6. Antimicrobial resistance in Salmonella spp. (all non-typhoidal serovars) from humans acquired in the EU/EEA and other geographical regions in 2013

Region	Ampicillin		Cefotaxime		Chloramphenicol		Ciprofloxacin ^(a)		Gentamicin	
	N	%R	Ν	%R	Ν	%R	N	%R	Ν	%R
Europe (EU/EEA countries)	13,841	35.1	11,441	1.4	10,485	6.6	13,354	3.6	11,640	4.7
Europe (non- EU/EEA countries)	78	0	44	0	68	1.5	78	2.6	42	0
Africa	315	22.9	207	1.9	294	6.1	315	8.3	205	11.7
Asia	901	22.8	322	2.8	877	7.5	915	3.7	331	6.3
Northern and Central America	67	6.0	39	0	65	3.1	69	1.4	40	0
South America	26	23.1	11	NA	21	14.3	26	3.8	11	NA
Oceania	5	NA	2	NA	4	NA	5	NA	2	NA

Region	Nalidixic acid		Sulfonamides ^(b)		Tetracyclines		Trimethoprim		Trimethoprim-sulfa	
	N	%R	Ν	%R	N	%R	N	%R	Ν	%R
Europe (EU/EEA countries)	12,373	14.2	7,610	35.5	10,760	33.6	3,288	5.0	10,829	8.1
Europe (non- EU/EEA countries)	73	17.8	37	0	68	1.5	35	0	43	4.7
Africa	305	25.6	114	24.6	291	28.5	105	14.3	214	17.8
Asia	900	20.6	209	34.0	861	21.8	191	13.1	749	9.3
Northern and Central America	65	9.2	21	4.8	63	7.9	16	NA	53	5.7
South America	26	30.8	6	NA	21	23.8	3	NA	23	26.1
Oceania	4	NA	2	NA	4	NA	3	NA	3	NA

N: number of isolates tested; %R: percentage of resistant isolates (either non-wild type by ECOFFs or clinically non-susceptible by combining resistant and intermediate categories); NA: not applicable (if fewer than 20 isolates were tested, resistance was not calculated); EU: European Union; EEA: European Economic Area; I: intermediate; R: resistant.

(a): Data for ciprofloxacin show the proportion of non-susceptible isolates (I+R) interpreted based on CBPs which differ by ≥3 dilutions from the EUCAST ciprofloxacin ECOFF.

(b): Combined data on the class sulfonamides and the substance sulfamethoxazole within this group.

Multi-drug resistance among Salmonella spp. isolates from humans

Thirteen MSs tested at least twenty isolates for the eight antimicrobial classes included in the MDR analysis. On average, 44.2 % of *Salmonella* spp. isolates were susceptible to all eight antimicrobial classes, varying from 23.0 % in Hungary to 72.5 % in Estonia (Table <u>MDR1</u>). Few isolates (0.2 %) exhibited co-resistance to both ciprofloxacin and cefotaxime. Of these 10 isolates, six were *S*. Kentucky and the other four were *S*. Agona, *S*. Brandenburg, *S*. Give and monophasic *S*. Typhimurium <u>1</u>,4,[5],12:i:-. The highest proportion of co-resistance was observed in isolates from France at 1.1 % (Table <u>MDR1</u>).

Multi-drug resistance was high (31.8 %) at the EU level, with the highest levels reported from Italy (51.5 %). The proportions of isolates susceptible to all and resistant (or non-susceptible) to up to eight antimicrobial classes are presented by MS in Figure 2. The proportions differed substantially between countries. Isolates resistant to five antimicrobials were reported from all 13 MSs, and eight MSs (Austria, Denmark, France, Ireland, Lithuania, Romania, Slovenia and Spain) reported a few isolates resistant to seven or all eight antimicrobial classes. The serotypes of the isolates resistant to seven or eight antimicrobial classes included *S*. Infantis (five isolates), *S*. Agona (one), *S*. Corvallis (one), *S*. Give (one) and *S*. Kentucky (one).



Figure 2. Frequency distribution of Salmonella spp. isolates from humans completely susceptible or resistant to one to eight antimicrobial classes, 2013



N: number of isolates tested for susceptibility against the eight antimicrobial classes included in the multi-drug resistance analysis; Susceptible: proportion of isolates susceptible to all eight antimicrobial classes included in the multi-drug resistance analysis; res1–res8: proportion of isolates resistant (non-wild type or clinically non-susceptible with resistant and intermediate categories combined) to one to eight antimicrobial classes.

(a): Provided measured values. Data interpreted by ECDC.

3.1.1.2. Antimicrobial resistance in Salmonella Enteritidis in humans

As in previous years, S. Enteritidis was the most common *Salmonella* serovar identified in 2013, with 29,090 cases reported in the EU/EEA. AST data were reported for 17.3 % of these cases in 2013 by 20 MSs, Iceland and Norway.

Resistance levels in Salmonella Enteritidis isolates from humans

The highest proportions of resistance among *S*. Enteritidis isolates in 2013 were observed for nalidixic acid (19.5 %) and ampicillin (11.0 %). The highest country-specific proportions were observed in Spain for nalidixic acid (42.6 %) and in Lithuania for ampicillin (19.4 %) (Table 7). It is generally expected that there should be a correlation between the activity of nalidixic acid and ciprofloxacin against *Salmonella*. Spain, however, despite reporting the highest level of nalidixic acid resistance, reported a very low level of ciprofloxacin resistance (0.2 %) in *S*. Enteritidis. Slovenia was the MS reporting the highest level of ciprofloxacin resistance in *S*. Enteritidis (17.0 %), although nalidixic acid resistance was reported as less common (5.7 %).

As in previous years, resistance to cefotaxime was generally not detected or detected at low levels in *S*. Enteritidis (Table 7).


Table 7. Antimicrobial resistance in Salmonella Enteritidis from humans per country in 2013

Country	Total Salmonella tested	Amp	icillin	Cefota	axime	Chloram	phenicol	Ciproflox	acin ^(b)	Genta	micin	Nalio ac		Sulfona	mides ^(c)	Tetracy	yclines	Trimeth	noprim	Trimett su	noprim- Ifa
	N	Ν	%R	Ν	%R	Ν	%R	Ν	%R	Ν	%R	Ν	%R	N	%R	Ν	%R	Ν	%R	Ν	%R
Austria ^(a)	1,035	470	1.3	470	0.4	470	0.2	470	0	470	0	470	8.3	470	0.4	470	0.4	470	0.4	-	_
Belgium	887	266	6.4	266	0	266	0.8	266	0	266	0.8	266	11.3	-	_	266	2.6	-	_	266	0.4
Denmark ^(a)	297	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	-	_
Estonia	152	49	4.1	51	3.9	47	0	50	10.0	46	2.2	45	15.6	44	2.3	45	4.4	-	_	50	2.0
Finland ^(a)	340	46	4.3	46	0	46	0	46	0	46	0	46	21.7	46	2.2	46	2.2	46	0	_	_
France	997	72	2.8	3	NA	72	1.4	72	0	72	0	72	31.9	72	6.9	72	4.2	72	2.8	72	1.4
Germany	2,017	193	8.8	193	0	_	-	193	0	193	1.0	193	4.1	-	_	_	-	-	_	193	0
Greece	138	30	0	-	-	30	0	30	0	_	-	30	6.7	-	-	30	0	-	-	2	NA
Hungary	675	61	9.8	61	1.6	61	1.6	61	3.3	61	0	61	6.6	61	9.8	61	8.2	-	-	61	0
Ireland	268	42	9.5	42	0	42	0	42	0	42	0	42	28.6	42	4.8	42	7.1	-	_	42	0
Italy	672	63	4.8	63	0	63	0	63	6.3	62	0	63	22.2	61	1.6	63	0	-	_	28	0
Latvia	38	29	0	1	NA	-	-	28	0	-	-	-	-	-	-	-	_	-	_	27	0
Lithuania	1,188	952	19.4	824	0.4	494	0.2	778	0.1	414	0	408	15.9	406	0.2	402	5.0	_	-	950	0.9
Luxembourg ^(a)	121	29	3.4	25	0	29	0	29	0	29	0	29	10.3	29	37.9	29	3.4	29	3.4	29	3.4
Malta	82	15	NA	-	-	_	-	15	NA	Ι	_	-	_	-	-	-	-	-	-	15	NA
Romania ^(a)	221	129	10.1	129	0	129	0	129	3.1	129	0	129	17.1	129	39.5	129	1.6	-	_	129	1.6
Slovakia	662	460	4.6	194	2.1	4	NA	244	4.1	Ι	-	7	NA	-	_	329	1.8	-	_	192	4.2
Slovenia	314	141	9.9	141	0	141	0	141	17.0	141	0	141	5.7	141	4.3	141	2.1	141	0	141	0
Spain	1,894	585	17.3	585	0.2	585	0.3	585	0.2	585	0.5	584	42.6	585	2.9	585	2.1	-	-	585	0.3
UK	658	142	12.0	137	0	140	1.4	148	2.0	143	0.7	144	23.6	-	-	136	8.8	14	NA	150	10.7
EU total	12,656	3,775	11.0	3,232	0.4	2,620	0.4	3,391	1.8	2,700	0.3	2,731	19.5	2,087	5.0	2,847	2.8	773	0.8	2,932	1.8
Iceland	16	3	NA	_	_	3	NA	3	NA	_	-	-	-	-	_	_	_	-	-	3	NA
Norway ^(a)	368	85	4.7	-	-	85	0	85	0	Ι	-	85	12.9	-	_	85	0	-	-	85	0

N: number of isolates tested; % R: percentage of resistant isolates (either non-wild type by ECOFFs or clinically non-susceptible by combining resistant and intermediate categories); -: no data reported; NA: not applicable (if fewer than 20 isolates were tested, resistance was not calculated); EU: European Union; I: intermediate; R: resistant. (a): Provided measured values. Data interpreted by ECDC.

(b): Data for ciprofloxacin show the proportion of non-susceptible isolates (I+R) interpreted based on clinical breakpoints which differ by ≥3 dilutions from the EUCAST ciprofloxacin ECOFF.
(c): Combined data on the class sulfonamides and the substance sulfamethoxazole within this group.



Multi-drug resistance among Salmonella Enteritidis isolates from humans

Eleven MSs tested at least twenty isolates for the eight antimicrobial classes included in the MDR analysis. Multi-drug resistance is uncommon in this serovar (1.5 % at the EU level) and co-resistance to ciprofloxacin and cefotaxime was not reported among non-travel-related isolates (Table <u>MDR2</u>). Six countries reported isolates resistant to four classes and one country (Spain) reported two isolates resistant to five antimicrobial classes (Figure 3).

Figure 3. Frequency distribution of Salmonella Enteritidis isolates from humans completely susceptible or resistant to one to eight antimicrobial classes, 2013



N: number of isolates tested for susceptibility against the eight antimicrobial classes included in the multi-drug resistance analysis; Susceptible: proportion of isolates susceptible to all eight antimicrobial classes included in the multi-drug resistance analysis; res1–res8: proportion of isolates resistant (non-wild type or clinically non-susceptible with resistant and intermediate categories combined) to one to eight antimicrobial classes.

(a): Provided measured values. Data interpreted by ECDC.

3.1.1.3. Antimicrobial resistance in Salmonella Typhimurium in humans

As in previous years, *S*. Typhimurium was the second most common *Salmonella* serovar identified in 2013, with 14,852 cases reported in the EU/EEA (monophasic *S*. Typhimurium $\underline{1},4,[5],12:i:$ - excluded). AST data were reported for 22.6 % of these cases in 2013 by 21 MSs, Iceland and Norway.

Resistance levels in Salmonella Typhimurium isolates from humans

The highest proportion of resistance in S. Typhimurium was observed for ampicillin (60.7 %), sulfonamides (51.2 %) and tetracyclines (46.7 %) (Table 8). The proportions of resistance to these antimicrobials were high to extremely high in the reporting MSs. However, the proportion of isolates resistant to the two clinically most critical antimicrobials were on average 0.7 % for ciprofloxacin and 1.1 % for cefotaxime. The highest proportion of isolates resistant to ciprofloxacin was reported from Slovenia (13.2 %), which reported nalidixic acid resistance at less than half this level (5.3 %). The highest proportion of cefotaxime resistance was reported from Ireland (4.3 %) (Table 8).



	Total																				
Country	Salmonella tested	Ampi	cillin	Cefota	axime	Chloram	phenicol	Ciproflox	kacin ^(b)	Genta	micin	Nalio ac		Sulfor	lamides ^(c)	Tetracy	clines/	Trimet	hoprim	Trimeth su	oprim- Ifa
	N	N	%R	Ν	%R	N	%R	N	%R	N	%R	Ν	%R	N	%R	N	%R	N	%R	N	%R
Austria ^(a)	1,035	163	33.1	163	0	163	16.0	163	0	163	1.2	163	4.3	163	31.9	163	35.6	163	5.5	_	-
Belgium	887	278	65.5	278	2.5	278	12.2	278	0	278	1.1	278	8.3	-	_	278	32.4	-	_	278	9.0
Denmark ^(a)	297	119	27.7	119	0	119	5.0	119	0	119	0.8	119	0.8	119	29.4	119	18.5	119	8.4	-	-
Estonia	152	23	78.3	23	0	23	56.5	23	0	23	4.3	23	4.3	23	78.3	23	73.9	-	_	23	17.4
Finland ^(a)	340	92	26.1	92	1.1	92	17.4	92	0	92	0	92	3.3	92	27.2	92	25.0	92	2.2	-	-
France	997	83	53.0	82	2.4	83	39.8	83	0	83	0	83	9.6	83	60.2	83	63.9	83	8.4	83	7.2
Germany	2,017	833	80.7	833	1.1	-	-	833	0.1	833	13.3	832	3.6	-	-	-	-	-	_	833	14.6
Greece	138	24	33.3	_	-	24	8.3	24	0	Ι	-	24	12.5	-	-	24	45.8	-	_	5	NA
Hungary	675	276	60.5	276	0.7	276	25.4	276	0.4	276	0.7	276	4.0	276	57.6	276	56.9	-	_	276	10.1
Ireland	268	69	44.9	69	4.3	69	34.8	69	0	69	0	69	2.9	69	42.0	69	43.5	-	-	69	5.8
Italy	672	97	64.9	97	0	97	19.6	97	2.1	97	0	97	9.3	97	61.9	97	61.9	-	-	54	7.4
Latvia	38	3	33.3	1	NA	-	-	3	NA	-	-	_	-	-	-	-	-	-	-	1	NA
Lithuania	1,188	84	64.3	68	0	56	16.1	75	0	41	7.3	41	14.6	40	72.5	40	65.0	-	-	85	16.5
Luxembourg ^(a)	121	30	86.7	27	0	30	66.7	30	0	30	0	30	3.3	30	83.3	30	76.7	30	3.3	30	3.3
Malta	82	8	NA	_	-	-	-	8	NA	-	-	-	-	-	-	-	-	-	-	8	NA
Netherlands ^(a)	455	253	43.9	_	-	253	15.8	253	0.4	253	2.4	253	0.8	-	-	253	45.1	-	_	_	-
Romania ^(a)	221	51	78.4	51	0	51	7.8	51	0	51	0	51	3.9	51	60.8	51	49.0	-	-	51	17.6
Slovakia	662	87	35.6	33	3.0	2	NA	43	2.3	-	_	1	NA	3	NA	69	40.6	-	_	40	5.0
Slovenia	314	38	26.3	38	0	38	7.9	38	13.2	38	0	38	5.3	38	31.6	38	26.3	38	5.3	38	5.3
Spain	1,894	123	81.3	123	0.8	124	42.7	124	0	124	2.4	123	17.1	124	74.2	123	75.6	-	_	124	17.7
UK	658	138	51.4	125	1.6	133	10.5	150	4.0	139	3.6	135	5.9	-	_	124	58.1	24	16.7	148	49.3
EU total	13,111	2,872	60.7	2,498	1.1	1,911	20.2	2,832	0.7	2,709	5.1	2,728	5.1	1,208	51.2	1,952	46.7	549	6.4	2,146	15.2
Iceland	16	4	NA	-	-	4	NA	4	NA	-	-	_	-	-	-	-	-	-	-	4	NA
Norway ^(a)	368	98	48.0	_	-	98	13.3	98	0	-	-	98	4.1	-	-	98	49	-	_	98	5.1

Table 8. Antimicrobial resistance in Salmonella Typhimurium from humans per country in 2013

N: number of isolates tested; %R: percentage of resistant isolates (either non-wild type by ECOFFs or clinically non-susceptible by combining resistant and intermediate categories); -: no data reported; NA: not applicable (if fewer than 20 isolates were tested, resistance was not calculated); EU: European Union, I: intermediate; R: resistant.

Provided measured values. Data interpreted by ECDC. (a):

Data for ciprofloxacin show the proportion of non-susceptible isolates (I+R) interpreted based on clinical breakpoints which differ by \geq 3 dilutions from the EUCAST ciprofloxacin ECOFF. Combined data on the class sulfonamides and the substance sulfamethoxazole within this group. (b):

(c):



Multi-drug resistance among Salmonella *Typhimurium isolates from humans*

Thirteen MSs tested at least twenty isolates for the eight antimicrobial classes included in the MDR analysis. Multi-resistance is far more common in *S*. Typhimurium than in *S*. Enteritidis in the EU with more than half of isolates multi-resistant in seven of 13 MSs (Table <u>MDR3</u>, Figure 4). However, as with *S*. Enteritidis, co-resistance to ciprofloxacin and cefotaxime was not reported.

Figure 4. Frequency distribution of Salmonella Typhimurium isolates from humans completely susceptible or resistant to one to eight antimicrobial classes, 2013



N: number of isolates tested for susceptibility against the eight antimicrobial classes included in the multi-drug resistance analysis; Susceptible: proportion of isolates susceptible to all eight antimicrobial classes included in the multi-drug resistance analysis; res1–res8: proportion of isolates resistant (non-wild type or clinically non-susceptible with resistant and intermediate categories combined) to one to eight antimicrobial classes.

(a): Provided measured values. Data interpreted by ECDC.

3.1.1.4. Antimicrobial resistance in monophasic Salmonella Typhimurium 1,4,[5],12:i:- in humans

A separate code was introduced in TESSy in 2010 to enable reporting of monophasic *S*. Typhimurium <u>1</u>,4,[5],12:i:-. For the purpose of this report, this is treated as a separate serovar. Monophasic *S*. Typhimurium <u>1</u>,4,[5],12:i:- has become the third most common *Salmonella* serovar in Europe. In 2013, 6,313 cases were reported by the EU/EEA countries. AST data were reported for 26.8 % of these cases by 11 MSs.

Resistance levels in monophasic Salmonella Typhimurium 1,4,[5],12:i:- isolates from humans

Extremely high levels of resistance were observed for tetracyclines (89.4 %), ampicillin (87.4 %) and sulfonamides (86.5 %) in monophasic *S*. Typhimurium <u>1</u>,4,[5],12:i:- (Table 9). This resistance pattern, ASuT, is a well-known characteristic of monophasic *S*. Typhimurium <u>1</u>,4,[5],12:i:- and was observed at similar levels in all 11 reporting MSs. The pattern of resistance also typically includes resistance to streptomycin; however, as described in the materials and methods section, data on this antimicrobial are no longer included in this report.

The proportion of isolates resistant to the two clinically most important antimicrobials was 0.9 % for ciprofloxacin and 1.7 % for cefotaxime.



Country	Total Salmonella tested	Ampi	icillin	Cefota	axime	Chloramp	ohenicol	Ciprofl	oxacin ^(b)	Genta	micin	Nalio ac		Sulfona	mides ^(c)	Tetrac	yclines	Trimeth	oprim	Trimeth -sul	
	N	N	%R	N	%R	N	%R	Ν	%R	N	%R	Ν	%R	N	%R	N	%R	N	%R	N	%R
Austria ^(a)	1,035	59	94.9	59	3.4	59	1.7	59	0	59	0	59	0	59	94.9	59	83.1	59	3.4	_	-
Denmark ^(a)	297	56	83.9	56	1.8	56	3.6	56	1.8	56	1.8	56	0	56	83.9	56	89.3	56	5.4	_	-
Estonia	152	3	NA	3	NA	3	NA	2	NA	3	NA	3	NA	3	NA	3	NA	_	-	3	NA
France	997	64	87.5	64	1.6	64	3.1	64	0	64	0	64	3.1	64	87.5	64	89.1	64	6.3	64	6.3
Greece	138	19	NA	_	-	19	NA	19	NA	-	-	19	NA	-	-	19	NA	-	_	3	NA
Hungary	675	189	82.5	189	0.5	189	1.1	189	0	189	0	189	1.6	189	84.1	189	88.4	_	_	189	3.7
Ireland	268	45	91.1	45	2.2	45	11.1	45	2.2	45	8.9	45	6.7	45	93.3	45	91.1	-	_	45	6.7
Italy	672	306	83.7	306	0	306	2.0	306	3.6	306	1.6	305	9.8	305	83.0	306	83.7	_	_	153	3.3
Luxembourg ^(a)	121	25	76.0	22	4.5	25	8.0	25	0	25	4.0	25	0	25	72.0	25	88.0	25	8.0	25	8.0
Netherlands ^(a)	455	197	84.8	-	-	197	7.6	197	0	197	3.6	197	0	-	_	197	91.9	-	-	-	-
Spain	1,894	644	92.1	644	2.5	645	8.7	645	0.3	645	6.2	626	8.8	644	88.2	644	92.4	-	_	645	10.1
Total (MSs 11)	6,704	1,607	87.4	1,388	1.7	1,608	5.7	1,607	0.9	1,589	3.7	1,588	6.0	1,390	86.5	1,607	89.4	204	5.4	1,127	7.8

Table 9. Antimicrobial resistance in monophasic Salmonella Typhimurium 1,4,[5],12:i:- from humans per country in 2013

N: number of isolates tested; %R: percentage of resistant isolates (either non-wild type by ECOFFs or clinically non-susceptible by combining resistant and intermediate categories); -: no data reported; NA: not applicable (if fewer than 20 isolates were tested, resistance was not calculated); MSs: Member States; I: intermediate; R: resistant.

Provided measured values. Data interpreted by ECDC. (a):

Data for ciprofloxacin show the proportion of non-susceptible isolates (I+R) interpreted based on clinical breakpoints which differ by ≥3 dilutions from the EUCAST ciprofloxacin ECOFF. Combined data on the class sulfonamides and the substance sulfamethoxazole within this group. (b):

(c):



Multi-drug resistance among monophasic Salmonella *Typhimurium 1,4,[5],12:i:- isolates from humans*

Eight MSs tested at least twenty monophasic S. Typhimurium $\underline{1},4,[5],12:i$:- isolates for the eight antimicrobial classes included in the MDR analysis. Multi-drug resistance was extremely high in monophasic S. Typhimurium $\underline{1},4,[5],12:i$:- from all reporting MSs with an average of 83.8 % (Table <u>MDR4</u>, Figure 5). Only one country (Ireland), however, reported any isolates resistant to both ciprofloxacin and cefotaxime.

Figure 5. Frequency distribution of monophasic Salmonella *Typhimurium 1,4,[5],12:i:- isolates from humans completely susceptible or resistant to one to eight antimicrobial classes, 2013*



N: number of isolates tested for susceptibility against the eight antimicrobial classes included in the multi-drug resistance analysis; Susceptible: proportion of isolates susceptible to all eight antimicrobial classes included in the multi-drug resistance analysis; res1–res8: proportion of isolates resistant (non-wild type or clinically non-susceptible with resistant and intermediate categories combined) to one to eight antimicrobial classes.

(a): Provided measured values. Data interpreted by ECDC.

3.1.1.5. Antimicrobial resistance in Salmonella Infantis in humans

S. Infantis was the fourth most common serovar in 2013 with 2,226 cases reported by the EU/EEA countries. AST data were reported for 28.7 % of these cases by 20 MSs, Iceland and Norway.

Resistance levels in Salmonella Infantis isolates from humans

There was a wide variation in the proportion of *S*. Infantis isolates reported in relation to all *Salmonella* spp. by MSs (Table 10). It represented about 10.0 % of all human isolates reported from Germany in 2013 and approximately 5.0 % of isolates in Austria, Belgium, France, Romania and Iceland, but a lower proportion in other MSs.

The proportion of isolates resistant to the two clinically most important antimicrobials was on average 7.2 % for ciprofloxacin and 4.9 % for cefotaxime, which was markedly higher than for all *Salmonella* spp. (3.8 % and 1.4 %, respectively). Ciprofloxacin resistance was particularly commonly reported in Romania (54.5 %) and Slovenia (81.8 %). Italian isolates were frequently resistant to cefotaxime (40.0 %). Another striking feature of the data was the very high level of resistance to ampicillin in Romania (63.6 %) and to a lesser extent in Italy (46.7 %). It should be noted, however, that the numbers of isolates reported for all these observations were small.



Table 10. Antimicrobial resistance in Salmonella Infantis from humans per country in 2013

Country	Total Salmonella tested	Ampi	cillin	Cefot	axime	Chloram	phenicol	Ciprofl	oxacin ^(b)	Genta	micin		dixic cid	Sulfona	mides ^(c)	Tetracy	clines	Trimeth	oprim	Trimeth -sul	
	N	Ν	%R	Ν	%R	N	%R	N	%R	N	%R	Ν	%R	N	%R	N	%R	N	%R	N	%R
Austria ^(a)	1,035	62	6.5	62	3.2	62	9.7	62	4.8	62	3.2	62	66.1	62	64.5	62	62.9	62	4.8	_	_
Belgium	887	40	22.5	40	15.0	40	10.0	40	2.5	40	10.0	40	20	-	_	40	22.5	_	-	40	12.5
Denmark ^(a)	297	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	_	_
Estonia	152	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	_	-	5	NA
Finland ^(a)	340	12	8.3	12	0	12	0	12	0	12	8.3	12	33.3	12	16.7	12	16.7	12	16.7	_	-
France	997	62	1.6	-	-	62	3.2	62	0	62	0	62	8.1	62	9.7	62	8.1	62	1.6	62	0
Germany	2,017	216	13.4	216	2.3	_	-	216	1.4	216	12.5	216	6.0	-	-	-	-	_	-	216	6.5
Greece	138	1	NA	_	-	1	NA	1	NA	-	_	1	NA	-	_	1	NA	_	-	_	_
Hungary	675	9	NA	9	NA	9	NA	9	NA	9	NA	9	NA	9	NA	9	NA	_	-	9	NA
Ireland	268	10	0	10	0	10	10.0	10	0	10	0	10	10.0	10	10.0	10	10.0	-	-	10	10.0
Italy	672	15	46.7	15	40.0	15	6.7	15	13.3	15	0	15	46.7	15	53.3	15	53.3	-	-	7	NA
Latvia	38	1	NA		-	_	-	1	NA	١	-	-	-	-	-	-	-	_	-	1	NA
Lithuania	1,188	22	4.5	19	0	16	0	19	0	16	0	16	6.3	16	6.3	16	0	_	-	22	0
Luxembourg ^(a)	121	4	NA	3	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA
Malta	82	3	NA	-	-	_	-	3	NA	-	-	-	_	-	-	-	-	-	-	3	NA
Romania ^(a)	221	11	63.6	11	0	11	0	11	54.5	11	0	11	100	11	100	11	100	-	-	11	72.7
Slovakia	662	24	25.0	11	9.1	1	NA	13	38.5	-	-	1	NA	-	-	15	80.0	-	-	15	6.7
Slovenia	314	11	9.1	11	0	11	0	11	81.8	11	0	11	72.7	11	63.6	11	72.7	11	0	11	0
Spain	1,894	28	21.4	28	10.7	28	17.9	28	0	28	10.7	28	17.9	28	25.0	28	25.0	_	-	28	25.0
UK	658	17	5.9	17	0	18	0	19	26.3	18	5.6	18	50.0	-	-	17	58.8	3	NA	20	50.0
EU total	12,656	557	13.8	473	4.9	309	6.1	545	7.2	523	7.3	525	24.0	249	36.9	322	37.6	158	4.4	464	10.6
Iceland	16	1	NA	-	-	1	NA	1	NA	-	-	-	-	-	-	-	-	-	-	1	NA
Norway ^(a)	368	4	NA	Ι	-	4	NA	4	NA	1	-	4	NA	-	-	4	NA	-	_	4	NA

N: number of isolates tested; %R: percentage of resistant isolates (either non-wild type by ECOFFs or clinically non-susceptible by combining resistant and intermediate categories); -: no data reported; NA: not applicable (if fewer than 10 isolates were tested, resistance was not calculated) EU: European Union; I: intermediate; R: resistant.

Provided measured values. Data interpreted by ECDC. (a):

(b): Data for ciprofloxacin show the proportion of non-susceptible isolates (I+R) interpreted based on clinical breakpoints which differ by ≥3 dilutions from the EUCAST ciprofloxacin ECOFF.
(c): Combined data on the class sulfonamides and the substance sulfamethoxazole within this group.



3.1.1.6. Antimicrobial resistance in Salmonella Derby in humans

S. Derby was the fifth most common serovar in 2013 with 818 cases reported by the EU/EEA countries. AST data were reported for 30.6 % of these cases by 16 MSs.

Resistance levels in Salmonella Derby isolates from humans

S. Derby accounted for approximately 8.0 % of human isolates reported from France, which reflects targeted reporting of this serovar in France. Resistance to sulfonamides and tetracycline was relatively common in *S*. Derby (52.3 % and 46.6 %, respectively) (Table 11). Cefotaxime resistance was high at 5.4 % compared with 1.4 % for *Salmonella* spp. Overall, however, this is based on a small number of isolates.

3.1.1.7. Antimicrobial resistance in Salmonella Kentucky in humans

S. Kentucky was the eighth most common serovar in 2013 with 649 cases reported by the EU/EEA countries. AST data were reported for 54.8 % of these cases by 15 MSs and Norway.

Resistance levels in Salmonella Kentucky isolates from humans

S. Kentucky was more commonly reported in relation to all *Salmonella* spp. from France and Malta, and to a lesser extent from Belgium and Romania, compared with other countries. In France, all *S*. Kentucky isolates from human cases are submitted for AST. Very high to extremely high proportions of *S*. Kentucky isolates were resistant to ampicillin, ciprofloxacin, gentamicin, nalidixic acid, sulfonamides and tetracyclines (Table 12), consistent with dissemination of a multi-resistant clonal group or groups (Le Hello et al., 2011, Westrell et al., 2014). It is of interest to note that France reported an *S*. Kentucky isolate non-susceptible to imipenem. A full description of this isolate from a case with a travel history to northern Africa has been published (Le Hello et al., 2013a,b).

Multi-drug resistance among Salmonella Kentucky isolates from humans

Only two MSs tested at least 10 *S*. Kentucky isolates for the eight antimicrobial classes included in the MDR analysis. Multi-drug resistance was very high (67.3 %, N=220) in *S*. Kentucky isolates and 47.7 % of the isolates also exhibited penta-resistance. One isolate was reported as being resistant to all eight antimicrobial classes, and six isolates (2.7 %, N=220) were resistant to both ciprofloxacin and cefotaxime.



Table 11. Antimicrobial resistance in Salmonella Derby from humans per country in 2013

Country	Total <i>Salmonella</i> tested	Ampi	cillin	Cefot	axime	Chloramp	ohenicol	Ciprofic	oxacin ^(b)	Genta	micin	Nalio ac		Sulfonar	nides ^(c)	Tetracy	clines	Trimeth	oprim	Trimeth -sul	
	N	N	%R	N	%R	N	%R	N	%R	N	%R	N	%R	N	%R	N	%R	N	%R	N	%R
Austria ^(a)	1,035	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	_	-
Belgium	887	32	34.4	32	0	32	0	32	3.1	32	3.1	32	6.3	-	-	32	9.4	-	-	32	6.3
Denmark ^(a)	297	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	_	_
Estonia	152	10	0	10	0	10	0	10	0	10	0	10	0	10	0	10	0	-	_	10	0
Finland ^(a)	340	2	NA	2	NA	2	NA	2	NA	2	NA	2	NA	2	NA	2	NA	2	NA	_	_
France	997	81	9.9	1	NA	81	1.2	81	0	81	0	81	2.5	81	61.7	81	61.7	81	7.4	81	6.2
Germany	2,017	36	8.3	36	2.8	-	_	36	0	36	5.6	36	0	-	-	-	-	-	-	36	5.6
Greece	138	2	NA	-	-	2	NA	2	NA	_	_	2	NA	-	_	2	NA	-	-	_	_
Hungary	675	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	-	-	5	NA
Italy	672	20	20.0	20	0	20	0	20	5.0	20	0	20	5.0	19	52.6	20	55.0	-	-	10	10.0
Lithuania	1,188	8	NA	8	NA	7	NA	7	NA	7	NA	7	NA	7	NA	7	NA	-	-	8	NA
Malta	82	1	NA	-	Ι	_	-	1	NA	_	_	_	_	-	_	-	_	-	-	1	NA
Romania ^(a)	221	3	NA	3	NA	3	NA	3	NA	3	NA	3	NA	3	NA	3	NA	-	-	3	NA
Slovakia	662	11	45.5	4	NA	-	-	1	NA	-	_	-	-	-	-	4	NA	-	_	2	NA
Spain	1,894	13	23.1	13	7.7	13	0	13	0	13	7.7	13	15.4	13	69.2	13	92.3	-	_	13	15.4
UK	658	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	_	_	5	NA	-	-	5	NA
Total (MSs 16)	11,915	238	16.8	148	5.4	189	1.1	227	1.3	223	2.2	225	3.6	149	52.3	193	46.6	92	9.8	206	8.7

N: number of isolates tested; %R: percentage of resistant isolates (either non-wild type by ECOFFs or clinically non-susceptible by combining resistant and intermediate categories); -: no data reported; NA: not applicable (if fewer than 10 isolates were tested, resistance was not calculated); MSs: Member States; I: intermediate; R: resistant.

(a): Provided measured values. Data interpreted by ECDC.

(b): Data for ciprofloxacin show the proportion of non-susceptible isolates (I+R) interpreted based on clinical breakpoints which differ by \geq 3 dilutions from the EUCAST ciprofloxacin ECOFF. (c): Combined data on the class sulfonamides and the substance sulfamethoxazole within this group.



Table 12. Antimicrobial resistance in Salmonella Kentucky from humans per country in 2013

Country	Total Salmonella tested	Ampi	cillin	Cefot	axime	Chloram	phenicol	Ciproflo	xacin ^(b)	Gen	tamicin		idixic cid	Sulfona	amides ^(c)	Tetracy	clines	Trimeth	oprim	Trimeth su	
	Ν	Ν	%R	Ν	%R	N	%R	N	%R	Ν	% R	Ν	%R	N	%R	N	%R	N	%R	N	%R
Austria ^(a)	1,035	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	-	-
Belgium	887	43	74.4	43	2.3	43	9.3	43	88.4	43	72.1	43	88.4	-	_	43	88.4	-	-	43	9.3
Denmark ^(a)	297	2	NA	2	NA	2	NA	2	NA	2	NA	2	NA	2	NA	2	NA	2	NA	_	_
France	997	172	72.7	171	2.9	172	2.9	172	84.9	172	55.8	172	84.9	172	64.5	172	70.3	172	6.4	172	7.0
Germany	2,017	11	54.5	11	0	-	_	11	54.5	11	36.4	11	54.5	-	-	-	_	-	-	11	9.1
Hungary	675	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	-	-	4	NA
Ireland	268	3	NA	3	NA	3	NA	3	NA	3	NA	3	NA	3	NA	3	NA	_	Ι	3	NA
Italy	672	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	-	Ι	1	NA
Lithuania	1,188	2	NA	2	NA	2	NA	2	NA	2	NA	2	NA	2	NA	2	NA	-	-	2	NA
Luxembourg ^(a)	121	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA
Malta	82	11	45.5	_	_	-	_	11	45.5	-	_	-	-	-	_	-	-	_	-	11	90.9
Romania ^(a)	221	7	NA	7	NA	7	NA	7	NA	7	NA	7	NA	7	NA	7	NA	-	-	7	42.9
Slovenia	314	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA
Spain	1,894	23	60.9	23	4.3	23	0	23	91.3	23	56.5	23	91.3	23	52.2	23	56.5	-	-	23	0
UK	658	1	NA	1	NA	2	NA	2	NA	2	NA	2	NA	-	_	1	NA	1	NA	2	NA
Total (MSs 15)	11,326	290	70.3	278	2.5	269	4.1	291	81.8	280	59.3	280	83.6	224	64.7	268	72.8	182	6.0	281	10.7
Norway ^(a)	368	4	NA	_	-	4	NA	4	NA	_	_	4	NA	_	-	4	NA	-	-	4	NA

N: number of isolates tested; %R: percentage of resistant isolates (either non-wild type by ECOFFs or clinically non-susceptible by combining resistant and intermediate categories); -: no data reported; NA: not applicable (if fewer than 10 isolates were tested, resistance was not calculated); MSs: Member States; I: intermediate; R: resistant. (a): Provided measured values. Data interpreted by ECDC.

(b): Data for ciprofloxacin show the proportion of non-susceptible isolates (I+R) interpreted based on clinical breakpoints which differ by \geq 3 dilutions from the EUCAST ciprofloxacin ECOFF. (c): Combined data on the class sulfonamides and the substance sulfamethoxazole within this group.



3.1.2. Antimicrobial resistance in *Salmonella* isolates from animals and food

Antimicrobial resistance in *Salmonella* isolates from the following animal species was analysed: *Gallus gallus* (broilers, laying hens and breeders), turkeys, pigs and cattle, and from meat derived thereof. The *Salmonella* isolates from animals were mainly collected as part of national surveillance and control programmes carried out according to the EU legislation. Isolates were obtained either from faecal samples and environmental samples (boot swabs or dust) collected on farms or from caecal samples, lymph node samples and carcase swabs collected at the slaughterhouse. The United Kingdom reported survey data on pigs. Clinical investigations and suspect sampling were excluded from the analyses.

Salmonella spp. includes results for all Salmonella serovars as reported for different animal or food categories. As the potential for acquiring antimicrobial resistance markedly varies between serovars, the relative contribution of different serovars importantly influences the general level of resistance presented for *Salmonella* spp. Trends in the dissemination of specific clones or resistance traits should ideally be considered individually for the different serovars.

3.1.2.1. Antimicrobial resistance in Salmonella isolates from meat

In the reporting MSs, data on antimicrobial resistance in *Salmonella* isolates from meat was obtained from active monitoring carried out within the framework of either official sampling or hazard analysis and critical point control (HACCP) and own-check programmes at slaughterhouses (the Czech Republic, Denmark, Estonia, Ireland, Italy, Latvia and Romania) or cutting/processing plants and retail/catering outlets (the Czech Republic, Estonia, Italy, Latvia, Romania and Slovenia). Eight MSs reported investigations without indicating sampling stage. *Salmonella* isolates were mainly obtained from randomly collected carcase swabs or meat/neck skin samples.

Meat from broilers

Resistance levels in Salmonella spp. from broiler meat

In 2013, 10 MSs reported quantitative MIC data on *Salmonella* spp. isolates from broiler meat (Table 13). The reported levels of resistance to nalidixic acid, sulfonamides and tetracyclines ranged from high to extremely high (28.0 %–100 %) in *Salmonella* spp. from broiler meat in most of the reporting MSs, while lower levels were recorded in Ireland and Belgium. Resistance to ampicillin was generally low to moderate in most reporting MSs (3.8 %–16.9 %), although high to very high levels (24.1 %–59.9 %) were observed in three MSs. Overall resistance to gentamicin (2.5 %) and chloramphenicol (2.1 %) remained low. High to extremely high levels of 'microbiological' resistance to ciprofloxacin were reported by most MSs (26.8 %–100 %, low levels reported by Ireland). 'Microbiological' resistance to cefotaxime was recorded at low levels generally, although, in the Netherlands, 53.3 % of the *Salmonella* spp. isolates from broiler meat tested were resistant to cefotaxime (primarily in *S*. Heidelberg).

Five MSs reported isolate-based data addressed in the MDR analysis (N=580). From 8.1 % to 70.8 % of the *Salmonella* spp. isolates were multi-resistant, whereas the proportion of fully susceptible isolates varied from 10.5 % to 81.1 % (Figure 6). 'Microbiological' co-resistance to ciprofloxacin and cefotaxime was generally low in *Salmonella* spp. isolates from broiler meat, but was observed in four of the five MSs, ranging up to 11.4 % in the isolates tested in Germany (Table <u>MDR5</u>). 'Clinical' resistance to both ciprofloxacin and cefotaxime was rare, and only detected in one *S*. Kentucky isolate in Romania (Table <u>MDR5</u>).

Resistance levels in certain Salmonella serovars from broiler meat

Among the isolates for which serovar information was provided (N=764), the most common serovars detected in broiler meat (Table <u>SER1</u>) were *S*. Infantis (11 MSs, 44.6 %) and *S*. Enteritidis (nine MSs, 15.2 %). Resistance and MDR levels in *S*. Enteritidis were generally lower than those recorded in *S*. Infantis and *Salmonella* spp.

In **S. Enteritidis** isolates from broiler meat (four MSs, N=138), resistance to chloramphenicol and gentamicin was not detected, resistance to ampicillin and sulfonamides was observed at low to moderate levels in two MSs, and only one MS reported tetracycline resistance at moderate levels (18.2 %). The highest levels of resistance were to ciprofloxacin and nalidixic acid, varying from 6.5 % to 69.1 %, whereas cefotaxime resistance was not detected (Table <u>SA1</u>). The majority of the *S*. Enteritidis isolates, in three of the four MSs, was fully sensitive to all nine antimicrobials included in the MDR analysis (72.0 %–89.1 %), compared with 30.9 % of isolates from Romania, which was also the only MSs reporting multi-resistant isolates (16.4 %) (Table <u>MDRP12</u>).

Extremely high resistance to sulfonamides, tetracyclines and nalidixic acid was observed in **S. Infantis** isolates from broiler meat (N=391) in seven of the eight reporting MSs (Table <u>SA1</u>). While ciprofloxacin



resistance was generally extremely high in the *S*. Infantis isolates tested, with the exception of Belgium, cefotaxime resistance was typically not detected, except in six (N=30) isolates in Poland. It is of note that 70.0 % of the *S*. Infantis isolates originated from Hungary and Romania, but levels of resistance are comparable to most other reporting MSs. In contrast to *S*. Enteritis, a very high proportion of isolates were multi-resistant (81.3 %–100 %) and a generally high level of MDR was observed among only the 10 isolates from Belgium (30.0 %) (Table MDR6).

Meat from turkeys

Resistance levels in Salmonella spp. from turkey meat

In 2013, six MSs reported quantitative MIC data in *Salmonella* spp. isolates from turkey meat (Table 13). Most levels of resistance were comparable to those observed in broiler meat, although gentamicin resistance was moderate (overall, 14.6 %). The proportion of multi-resistant *Salmonella* spp. isolates varied from none of the isolates tested in Romania to extremely high levels (70.0 %–81.8 %) in those isolates tested in the Czech Republic, Germany and Italy (Figure 7). Co-resistance to ciprofloxacin and cefotaxime was not detected among the multi-resistant isolates (four MSs, N=94) (Table <u>MDR7</u>).

Meat from pigs

Resistance levels in Salmonella spp. from pig meat

In 2013, 12 MSs reported quantitative MIC data for *Salmonella* spp. isolates from pig meat (Table 14). The reported levels of resistance to ampicillin, sulfonamides and tetracyclines ranged from moderate to extremely high (12.5 %–81.8 %). The overall resistance to chloramphenicol (7.2 %) and gentamicin (1.3 %) was low, and gentamicin resistance was not detected in six MSs. Overall, the 'microbiological' resistance to ciprofloxacin (3.9 %), nalidixic acid (3.0 %) and cefotaxime (0.9 %) was low or very low and, in five of the 12 reporting MSs, all *Salmonella* spp. isolates tested were fully susceptible to these 3 antimicrobial agents.

The MDR levels in *Salmonella* spp. in pig meat (nine MSs, N=725) ranged from high to very high in most reporting MSs (25.8 %–68.8 %), except in isolates from Latvia (12.5 %), where most (87.5 %) of them were fully susceptible to the nine antimicrobials considered in the MDR analysis. Among the other MSs, the level of fully susceptible isolates was moderate to very high (Figure 8). 'Microbiological' co-resistance to ciprofloxacin and cefotaxime was detected in five multi-resistant *Salmonella* spp. isolates from pig meat in three of the nine MSs, ranging up to 3.2 % (Table MDR8).

Resistance levels in certain Salmonella serovars from pig meat

In 2013, S. Derby and S. Typhimurium (including the monophasic variants) were the most frequently reported serovars in pigs and pig meat (Tables <u>SER1</u> and <u>SER6</u>). Resistance levels to ampicillin, sulfonamides and tetracyclines were generally higher in *S*. Typhimurium (including the monophasic variants) than in *S*. Derby; therefore, the relative distribution between these serovars often dominated the overall *Salmonella* spp. resistance levels (Table <u>SA2</u>).

Most MSs reported high to extremely high resistance to ampicillin, sulfonamides and tetracyclines in **S. Typhimurium** from pig meat (seven MSs, N=215), moderate to high levels of resistance to chloramphenicol and low or no resistance to gentamicin (Table <u>SA2</u>). 'Microbiological' resistance to ciprofloxacin was generally absent or low (<4 % in two MSs). Cefotaxime resistance was not detected in *S.* Typhimurium, whereas the overall resistance was 0.6 % in 2012. The isolates from Romania (N=24) differed from this pattern with low to moderate resistance to sulfonamides and tetracyclines, no chloramphenicol resistance and moderate resistance to ciprofloxacin. Multi-resistance was generally higher in *S.* Typhimurium than in *Salmonella* spp. and 50.0 % to 90.0 % of the isolates (six MSs, N=202) were multi-resistant, except from the Romanian isolates which had only 16.7 % MDR (Table <u>MDR9</u>).

In **S. Derby** (seven MSs, N=215), the levels of resistance to sulfonamides and tetracyclines varied from none to 53.8 %, with the highest levels of resistance in the isolates from Italy and Romania (Table <u>SA2</u>). Resistance to ampicillin varied from none to 10.7 %, and no or low resistance to gentamicin and nalidixic acid occurred. In contrast with *S*. Typhimurium, low levels of resistance to chloramphenicol were observed in *S*. Derby. For the *S*. Derby isolates from pig meat, only Italy (2.2 %) reported resistance to ciprofloxacin and only Germany (7.1 %) observed cefotaxime resistance. The available data were not adequate for evaluating the level of MDR in *S*. Derby from meat from pigs, but MDR patterns was done (Table <u>MDRP28</u>).

Meat from bovine animals

Resistance levels in Salmonella spp. from bovine meat

In 2013, five MSs reported quantitative MIC data on *Salmonella* spp. isolates from meat from bovine animals (Table 14). Overall, the 'microbiological' resistance to ampicillin, sulfonamides and tetracyclines ranged from



moderate to high levels and varied substantially between the reporting MSs (8.3 %–90.9 %). Resistance to cefotaxime, ciprofloxacin, nalidixic acid and gentamicin was not reported in the reporting MSs in 2013, although, in 2012, a few *Salmonella* isolates resistant to one or more of the four antimicrobial substances were detected in Italy, the Netherlands and Spain. In the four MSs (N=54) where the MDR rate could be analysed, most of the isolates were fully susceptible to the antimicrobials addressed, and only 9.1 % to 30.0 % of the *Salmonella* spp. isolates were multi-resistant (Figure 9). No multi-resistant isolates were detected as co-resistant to ciprofloxacin and cefotaxime (Table MDR10).



Table 13. Occurrence of resistance to selected antimicrobials in <u>Salmonella spp.</u> isolates from <u>meat from broilers</u> and <u>meat from turkeys</u> in 2013, using harmonised ECOFFs

0	Amp	icillin	Cefot	axime	Chloram	phenicol	Ciprof	loxacin	Genta	micin	Nalidia	kic acid	Sulfor	namides	Tetrac	yclines
Country	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Meat from broiler	's						-	•			-	•		•		
Belgium	112	24.1	112	2.7	112	3.6	112	26.8	112	0	112	26.8	112	28.6	112	8.9
Czech Republic	80	3.8	80	0	80	0	80	46.3	80	0	80	45.0	80	36.3	80	36.3
Germany	132	28.8	132	12.9	132	6.1	132	47.7	132	4.5	132	44.7	132	40.2	132	28.0
Hungary	155	16.1	155	0	155	0	155	100	155	6.5	155	100	155	78.7	155	86.5
Ireland	37	10.8	37	2.7	37	0	37	8.1	37	0	37	8.1	37	10.8	37	5.4
Netherlands	137	59.9	137	53.3	137	4.4	137	78.8	137	3.6	137	76.6	136	76.5	137	67.9
Poland	83	16.9	93	7.5	83	1.2	84	65.5	80	0	83	57.8	81	51.9	79	57.0
Romania	219	13.7	219	0.5	219	0.9	219	87.2	219	1.8	219	84.0	219	69.4	219	71.7
Slovakia	15	13.3	15	0	15	0	15	73.3	15	0	15	73.3	15	53.3	15	53.3
Slovenia	25	4.0	25	0	25	0	25	96.0	25	0	25	96.0	25	84.0	25	80.0
Total (MSs 10)	995	22.7	1,005	10.1	995	2.1	996	68.0	992	2.5	995	65.8	992	57.2	991	54.0
Meat from turkeys	5				•		•				•					
Czech Republic	10	80.0	10	0	10	0	10	90.0	10	40.0	10	90.0	10	50.0	10	70.0
Germany	31	41.9	31	0	31	6.5	31	64.5	31	9.7	31	51.6	31	54.8	31	74.2
Hungary	59	47.5	59	0	59	0	59	98.3	59	27.1	59	100	59	52.5	59	54.2
Italy	11	45.5	11	0	11	0	11	45.5	11	9.1	11	36.4	11	54.5	11	81.8
Netherlands	39	30.8	39	23.1	39	12.8	39	89.7	39	10.3	39	84.6	39	20.5	39	53.8
Romania	42	7.1	42	0	42	0	42	33.3	42	0	42	11.9	42	0	42	16.7
Total (MSs 6)	192	35.9	192	4.7	192	3.6	192	73.4	192	14.6	192	65.6	192	34.9	192	51.6

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates.



Table 14. Occurrence of resistance to selected antimicrobials in <u>Salmonella spp.</u> isolates from <u>meat from pigs</u> and <u>meat from bovine animals</u> in 2013, using harmonised ECOFFs

0	Am	picillin	Cefo	taxime	Chloran	nphenicol	Cipro	floxacin	Gent	amicin	Nalidi	xic acid	Sulfo	namides	Tetrac	cyclines
Country	N	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res
Meat from pigs																
Belgium	139	40.3	139	0	139	5.0	139	2.9	139	0.7	139	2.2	139	40.3	139	36.0
Czech Republic	36	27.8	36	0	36	13.9	36	0	36	0	36	2.8	36	36.1	36	33.3
Denmark	148	29.7	148	0	148	2.7	148	0	148	0.7	148	0	148	37.8	148	43.9
Estonia	18	33.3	18	0	18	0	18	0	18	0	18	0	18	38.9	18	38.9
Germany	116	52.6	116	2.6	116	12.9	116	3.4	116	1.7	116	1.7	116	54.3	116	51.7
Hungary	24	66.7	24	0	24	25.0	24	8.3	24	0	24	8.3	24	70.8	24	79.2
Ireland	32	62.5	32	0	32	31.3	32	0	32	3.1	32	0	32	78.1	32	75.0
Italy	127	30.7	127	0.8	127	3.9	127	3.1	127	3.1	127	2.4	127	40.9	127	52.0
Latvia	16	12.5	16	0	16	0	16	0	16	0	16	0	16	12.5	16	12.5
Netherlands	15	46.7	15	0	15	6.7	15	6.7	15	0	15	6.7	15	80.0	15	60.0
Portugal	11	63.6	11	0	12	25.0	11	0	11	0	11	0	11	81.8	11	81.8
Romania	93	43.0	93	3.2	93	0	93	16.1	93	1.1	93	11.8	93	17.2	93	35.5
Total (MSs 12)	775	39.7	775	0.9	776	7.2	775	3.9	775	1.3	775	3.0	775	42.3	775	45.9
Meat from bovine	animals															
Czech Republic	21	14.3	21	0	21	4.8	21	0	21	0	21	0	21	19.0	21	14.3
Denmark	11	9.1	11	0	11	0	11	0	11	0	11	0	11	9.1	11	9.1
Germany	12	16.7	12	0	12	0	12	0	12	0	12	0	12	25.0	12	8.3
Italy	10	30.0	10	0	10	20.0	10	0	10	0	10	0	10	30.0	10	20.0
Portugal	11	27.3	11	0	11	27.3	11	0	11	0	11	0	11	81.8	11	90.9
Total (MSs 5)	65	18.5	65	0	65	9.2	65	0	65	0	65	0	65	30.8	65	26.2

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates.



Figure 6. Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials in Salmonella spp. from <u>broiler meat</u> in MSs reporting isolate-based data, 2013



Figure 8. Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials in Salmonella spp. from <u>turkey meat</u> in MSs reporting isolate-based data, 2013



N: total number of isolates tested for susceptibility against the whole common antimicrobial set for *Salmonella*; sus: susceptible to all antimicrobial substances of the EFSA common set for *Salmonella*; res1–res9: resistance to one to nine antimicrobial substances of the common set for *Salmonella*.

Figure 7. Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials in Salmonella spp. from <u>pig</u> <u>meat</u> in MSs reporting isolate-based data, 2013



Figure 9. Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials in Salmonella spp. from bovine meat in MSs reporting isolate-based data, 2013





3.1.2.2. Antimicrobial resistance in Salmonella spp. isolates from domestic fowl (Gallus gallus)

In 2013, 17 MSs reported quantitative MIC data on *Salmonella* spp. isolates from *Gallus gallus*, and reporting generally included information on production type (flocks of broilers, laying hens or breeders (Tables <u>SA3</u> and <u>SA4</u>). As 26.0 % of the *Salmonella* spp. isolates from domestic fowl (primarily from broilers) included in the analysis originated from Romania, where the resistance levels observed were frequently among the highest reported, the resistance rates presented at the reporting MS group level are highly impacted by the occurrence of resistance recorded in Romania.

Resistance levels in Salmonella spp. in Gallus gallus

When including all production types of domestic fowl (N=4,636), the overall resistance to nalidixic acid, sulfonamides and tetracyclines was observed at high levels in the *Salmonella* spp. isolates tested, although with substantial variations between MSs from none to 67.1 % (Table <u>SA3</u>). Overall, resistance to ampicillin was moderate, varying from none to 30.1 %, and resistance to all four antimicrobials was reported by all MSs except Ireland (N=14). Resistance to gentamicin and chloramphenicol was either not detected or low in most MSs. However, among the relatively large proportion of isolates from Romania, moderate levels of resistance to gentamicin (18.4 %) and chloramphenicol (19.0 %) were reported, thus importantly influencing the overall resistance levels. High levels of 'microbiological' resistance to ciprofloxacin were observed, ranging from none to 72.5 % in isolates from Romania. Resistance to cefotaxime was absent or low in *Salmonella* spp. from most MSs, except in the Netherlands (14.8 %) and Romania (10.1 %) (Figure 30).

Resistance levels in Salmonella spp. in broilers

In 2013, 16 MSs reported quantitative MIC data on *Salmonella* spp. isolates from broilers (Table <u>SA4</u>). Most MSs recorded high to extremely high resistance to nalidixic acid, sulfonamides and tetracyclines (overall 49.2 %, 49.5 and 42.5 %, respectively) and moderate to high resistance to ampicillin (overall 23.8 %) (Figure 30). Resistance to chloramphenicol and gentamicin overall was low, although resistance levels varied markedly, from none to 26.9 %, between MSs. In most MSs, resistance to ciprofloxacin was high to extremely high, although low levels (<10.0 %) were recorded in Denmark, France, Ireland and the United Kingdom. Resistance to cefotaxime was not registered among the *Salmonella* spp. isolates tested in nine MSs and was reported at moderate to high levels in four MSs (Croatia, Italy, Netherlands and Romania). Overall, the cefotaxime resistance was low.

Eleven MSs submitted isolate-based data included in the MDR analysis (N=2,084). Situations varied markedly between MSs, as none to 72.7 % of the *Salmonella* spp. isolates were multi-resistant, and 8.1 % to 100 % of them were fully susceptible to the nine antimicrobials considered (Figure 16). In Hungary and Romania, the rates of MDR and full susceptibility (to the nine antimicrobials addressed) were about 70.0 % and 10.0 %, respectively (Table <u>MDR11</u>).

Resistance levels in Salmonella spp. from laying hens

In 2013, 13 MSs reported quantitative MIC data on *Salmonella* spp. isolates from laying hens (Table <u>SA4</u>). With the exception of Romania, most MSs registered low to moderate levels of resistance to ampicillin, nalidixic acid, sulfonamides and tetracyclines. Resistance to chloramphenicol and gentamicin was generally low. Resistance to ciprofloxacin was generally low to moderate, although high resistance was recorded in Italy, Romania and Spain. Resistance to cefotaxime was generally low, and was absent among the *Salmonella* spp. isolates from nine of the 13 MSs (absent in isolates from both broilers and laying hens in five MSs). However, 10.3 % of the *Salmonella* spp. isolates from laying hens in the Netherlands were resistant to cefotaxime. Compared with isolates from broilers, generally, similar or lower levels of resistance were reported in *Salmonella* from laying hens.

Most (71.0 %) of the *Salmonella* spp. isolates included in the MDR analysis (nine MSs, N=749) were fully susceptible to the nine antimicrobials considered (Figure 17), and between none and 35.9 % of the *Salmonella* spp. isolates were multi-resistant (high level only in isolates from Romania) (Table <u>MDR12</u>).



Resistance levels in Salmonella spp. from breeding flocks of Gallus gallus

In 2013, four MSs reported quantitative MIC data on *Salmonella* spp. isolates from breeding flocks. Levels of resistance were generally similar to what was reported by the MSs for broilers and laying hens (Table <u>SA4</u>). Romania reported higher levels of resistance to ciprofloxacin (40.0 %) than to nalidixic acid (26.7 %), indicating a possible vertical spread of plasmid-mediated quinolone resistance in the Romanian poultry production. Generally, high levels of complete susceptibility were observed in *Salmonella* spp. isolates from breeding flocks (Figure 18). Only France and Greece reported data for resistance to carbapenems in *Salmonella* in animals (poultry only). Carbapenem resistance was observed in one *S*. Livingstone isolate from a breeding flock for the broiler production line in Greece (samples analysed by diffusion methods only).

Resistance levels in certain Salmonella serovars from Gallus gallus

Among serotyped isolates submitted (N=4,201), the most commonly reported serovars in domestic fowl (*Gallus gallus*) were *S*. Infantis (25.1 %) and *S*. Enteritidis (17.9 %), followed by *S*. Typhimurium (5.1 %). *S*. Kentucky was observed in 3.9 % of the isolates (Table <u>SER4</u>).

Among **S.** Enteritidis isolates (13 MSs, Table 15), resistance to ampicillin, sulfonamides and tetracyclines was generally not detected or recorded at low or moderate levels (overall 3.7 %–5.0 %), and resistance to chloramphenicol and gentamicin was not recorded in isolates from most MSs. Overall, resistance to nalidixic acid was moderate in *S*. Enteritidis (21.9 %), ranging from none to 47.8 %. 'Microbiological' resistance to cefotaxime was only rarely reported in *S*. Enteritidis, whereas ciprofloxacin resistance varied markedly between MSs from none to more than 45.0 % in three MSs (Poland, Romania and Spain). Most of the *S*. Enteritidis isolates (83.2 %) were fully sensitive to all nine antimicrobials included in the MDR analysis for broilers (three MSs, N=202) (Figure 19) and laying hens (seven MSs, N=170) (Figure 20). However, only 50.0 % and 40.9 % of the *S*. Enteritidis from Romanian broilers and layers, respectively, were fully susceptible, whereas 33.3 % and 18.2 %, respectively, were multi-resistant. A low occurrence of multi-resistant *S*. Enteritidis was also reported from broilers in Belgium and laying hens in Hungary and Italy (Tables <u>MDR14</u> and <u>MDR15</u>).

In **S. Infantis** isolates (13 MSs, Table 16), resistance to sulfonamides and tetracyclines was mostly high to extremely high (overall 75.0 % and 72.0 %, respectively), whereas resistance to ampicillin overall was moderate (11.3 %), but varied considerably from none to very high. Generally, the isolates displayed low to moderate resistance to chloramphenicol (overall 12.2 %), and only three MSs observed resistance to gentamicin (overall 5.3 %). Five MSs recorded resistance to cefotaxime varying from 1.4 % to 44.4 % (from Italy) resulting in an overall low occurrence (6.5 %), whereas extremely high levels of resistance to ciprofloxacin were found in *S.* Infantis from most MSs, except Spain (5.0 %). It is notable that isolates from Romania represented 50.0 % of the *S.* Infantis isolates. Most (>80 %) of the *S.* Infantis isolates from broilers (seven MSs, N=757) and 64.3 % of *S.* Infantis from laying hens (three MSs, N=28) included in the MDR analysis were multi-resistant (Tables MDRP32 and MDRP33).

In **S. Kentucky** isolates (three MSs, Table 16), high to extremely high levels of resistance to nalidixic acid and tetracyclines were reported, whereas resistance to ampicillin, gentamicin and sulfonamides varied markedly between MSs from none to 98.0 %. Resistance to chloramphenicol was generally low (none to 4.0 %). Almost all *S.* Kentucky isolates were resistant to ciprofloxacin (90.0 %–100 %), as well as at clinical levels among isolates from Romania and Spain, but none were among the isolates from Italy. Two of the three MSs reported low to moderate levels of resistance to cefotaxime; very few isolates from Italy and Romania displayed 'clinical' resistant to cefotaxime. Note that isolates from Romania represent 64.0 % of the *S.* Kentucky isolates. In *S.* Kentucky isolates from broilers (four MSs, N=104) and laying hens (three MSs, N=50), 98.1 % and 58.0 % of the isolates included in the MDR analysis were multi-resistant, respectively (Tables <u>MDRP26</u> and <u>MDRP27</u>).

Resistance levels to ampicillin, sulfonamides and tetracyclines (overall 32.9 %–37.6 %) in **S. Typhimurium** isolates (Table <u>SA5</u>) were found to mainly be high to extremely high. Chloramphenicol resistance varied from none to 38.5 % (overall 8.8 %), whereas no resistance to gentamicin was reported. Resistance to cefotaxime was absent, whereas ciprofloxacin resistance varied markedly between MSs from none to 71.4 % (Romania). In broilers, 51.0 % (six MSs, N=50) of the *S*. Typhimurium isolates and 37.5 % of the isolates from laying hens (four MSs, N=32) were multi-resistant (Tables <u>MDRP16</u> and <u>MDRP17</u>).



Temporal trends in resistance among Salmonella spp. from Gallus gallus

Fourteen MSs provided resistance data on five years or more to be included in the statistical analysis. Over the seven years of data, levels of resistance to ampicillin remained mostly constant for most of the reporting MSs, although slight but statistically significant increases occurred in four MSs, while statistically decreasing trends were observed in three other MSs. Statistically significant increasing trends in resistance to ciprofloxacin and/or nalidixic acid were registered in five MSs, whereas statistically significant decreasing trends were observed in three MSs. Within each MS, similar levels of resistance to ciprofloxacin and nalidixic acid were observed from 2007 to 2013. Resistance to cefotaxime is generally very low; however, a statistically significant increasing trend was observed in two MSs, whereas the trend in five MSs was decreasing (Figure 10).

As antimicrobial resistance is associated with particular serovars or clones within serovars, fluctuations in the occurrence of resistance in *Salmonella* spp. isolates within a country may be the result of changes in the proportions of different *Salmonella* serovars which contribute to the total numbers of *Salmonella* spp. isolates.

In *S. Enteritidis*, resistance to ampicillin remained relatively constant from 2007 to 2013 within each MS (Figure 11). A statistically significant increasing trend of resistance to ciprofloxacin and/or nalidixic acid in *S.* Enteritidis was observed in two MSs, whereas statistically significant decreasing trends were observed in five MSs. Resistance to ciprofloxacin and nalidixic acid was comparable within MSs from 2007 to 2013.

Spatial trends in resistance among Salmonella spp. from Gallus gallus

The levels of resistance to ciprofloxacin in *Salmonella* spp. from broilers were extremely high (>70 %) in some MSs from eastern and southern Europe (Croatia, Hungary, Romania and Slovenia), and high to very high in most other MSs. Low levels of ciprofloxacin resistance (<10.0 %) were reported by only a few MSs from northern and western Europe (Denmark, France, Ireland and the United Kingdom) (Figure 12). In these four MSs, as well as in several eastern and southern European MSs (Austria, the Czech Republic, Hungary, Poland, Slovakia and Slovenia), low to moderate levels of resistance to ampicillin were reported, whereas higher levels were reported from other MSs across Europe, not including the northern European MSs (Figure 13).



	Am	picillin	Cefo	taxime	Chloran	nphenicol	Cipro	floxacin	Gent	tamicin	Nalidi	ixic acid	Sulfor	namides	Tetrac	cyclines
Country	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res
All Gallus gallus																
Austria	17	0	17	0	17	0	17	0	17	0	17	0	17	0	17	5.9
Belgium	55	7.3	55	1.8	55	0	55	0	55	0	55	0	55	7.3	55	3.6
Croatia	25	8.0	25	4.0	25	0	25	4.0	25	0	25	4.0	25	16.0	25	0
Czech Republic	158	3.2	158	0	158	0	158	2.5	158	0	158	1.9	158	0	158	0
France	10	0	10	0	10	0	10	0	10	0	10	0	10	0	10	0
Germany	62	0	62	0	62	0	62	1.6	62	0	62	1.6	62	0	62	0
Hungary	23	4.3	23	0	23	0	23	4.3	23	0	23	4.3	23	8.7	23	4.3
Italy	17	11.8	17	0	17	0	17	5.9	17	5.9	17	0	17	5.9	17	5.9
Netherlands	36	8.3	36	0	36	0	36	25.0	36	0	36	25.0	36	2.8	36	2.8
Poland	218	3.2	218	0	218	0	218	47.2	218	0	218	44.0	218	3.2	218	0
Romania	80	15.0	80	1.3	80	0	80	46.3	80	3.8	80	47.5	80	22.5	80	26.3
Slovakia	12	0	12	0	12	0	12	8.3	12	0	12	8.3	12	0	12	0
Spain	23	4.3	23	0	23	0	23	47.8	23	0	23	47.8	23	0	23	0
Total (MSs 13)	736	5.0	736	0.4	736	0	736	23.0	736	0.5	736	21.9	736	5.0	736	3.7
Broilers																
Belgium	21	9.5	21	4.8	21	0	21	0	21	0	21	0	21	14.3	21	4.8
Czech Republic	145	3.4	145	0	145	0	145	2.8	145	0	145	2.1	145	0	145	0
Romania	36	13.9	36	2.8	36	0	36	44.4	36	2.8	36	47.2	36	27.8	36	36.1
Slovakia	10	0	10	0	10	0	10	10.0	10	0	10	10.0	10	0	10	0
Total (MSs 4)	212	5.7	212	0.9	212	0	212	9.9	212	0.5	212	9.9	212	6.1	212	6.6
Laying hens	-				-		-									
Austria	15	0	15	0	15	0	15	0	15	0	15	0	15	0	15	6.7
Belgium	21	4.8	21	0	21	0	21	0	21	0	21	0	21	0	21	0
Croatia	20	0	20	0	20	0	20	5.0	20	0	20	5.0	20	10.0	20	0
Germany	31	0	31	0	31	0	31	0	31	0	31	0	31	0	31	0
Hungary	20	5.0	20	0	20	0	20	5.0	20	0	20	5.0	20	10.0	20	5.0
Italy	16	12.5	16	0	16	0	16	6.3	16	6.3	16	0	16	6.3	16	6.3
Romania	44	15.9	44	0	44	0	44	47.7	44	4.5	44	47.7	44	18.2	44	18.2
Spain	23	4.3	23	0	23	0	23	47.8	23	0	23	47.8	23	0	23	0
Total (MSs 8)	190	6.3	190	0	190	0	190	18.4	190	1.6	190	17.9	190	6.8	190	5.8

Table 15. Occurrence of resistance to selected antimicrobials in Salmonella Enteritidis isolates from Gallus gallus in 2013, using harmonised ECOFFs

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates.



Table 16. Occurrence of resistance to selected antimicrobials in Salmonella Infantis and Kentucky isolates from Gallus gallus in 2013, using harmonised ECOFFs

O a sure trans	Amp	icillin	Cefot	axime	Chloram	phenicol	Cipro	iloxacin	Genta	micin	Nalidix	ic acid	Sulfon	amides	Tetrac	yclines
Country	Ν	% Res	N	% Res	N	% Res	Ν	% Res	Ν	% Res	Ν	% Res	N	% Res	N	% Res
Salmonella Infantia	S															
Austria	37	0	37	0	37	0	37	91.9	37	0	37	91.9	37	91.9	37	91.9
Belgium	25	0	25	0	25	4.0	25	32.0	25	0	25	28.0	25	28.0	25	28.0
Croatia	18	33.3	18	11.1	18	11.1	18	94.4	18	0	18	100	18	11.1	18	22.2
Czech Republic	47	34.0	47	0	47	0	47	89.4	47	0	47	89.4	47	89.4	47	89.4
Germany	12	0	12	0	12	0	12	50.0	12	0	12	50.0	12	58.3	12	50.0
Hungary	154	7.8	154	0	154	3.2	154	99.4	154	0	154	99.4	154	85.1	154	82.5
Italy	27	55.6	27	44.4	27	7.4	27	66.7	27	3.7	27	66.7	27	70.4	27	70.4
Netherlands	34	2.9	34	0	34	8.8	34	67.6	34	0	34	67.6	34	55.9	34	52.9
Poland	64	0	70	1.4	70	0	70	32.9	70	7.1	70	32.9	40	0	70	32.9
Romania	526	11.4	526	9.9	526	21.7	526	91.3	526	9.3	526	90.3	526	82.3	526	77.0
Slovakia	34	5.9	34	0	34	0	34	91.2	34	0	34	91.2	34	91.2	34	91.2
Slovenia	38	10.5	38	0	38	0	38	92.1	38	0	38	86.8	38	89.5	38	89.5
Spain	20	5.0	20	5.0	20	0	20	5.0	20	0	20	5.0	20	0	20	0
Total (MSs 13)	1,036	11.3	1,042	6.5	1,042	12.2	1,042	83.6	1,042	5.3	1,042	82.9	1,012	75.0	1,042	72.0
Salmonella Kentud	:ky															
Italy	45	55.6	45	6.7	45	2.2	45	95.6	45	0	45	95.6	45	4.4	45	48.9
Romania	99	98.0	99	13.1	99	4.0	99	100	99	91.9	99	99.0	99	88.9	99	94.9
Spain	10	20.0	10	0	10	0	10	90.0	10	80.0	10	90.0	10	50.0	10	40.0
Total (MSs 3)	154	80.5	154	10.4	154	3.2	154	98.1	154	64.3	154	97.4	154	61.7	154	77.9

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates.



Figure 10. Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested <u>Salmonella spp.</u> isolates from <u>Gallus gallus</u> in reporting MSs, 2007–2013, quantitative data



A statistically significant decreasing trend for five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for all antimicrobials in the Netherlands (\downarrow); for cefotaxime, ciprofloxacin and nalidixic acid in Spain (\downarrow); for ampicillin in Italy (\downarrow) and Poland (\downarrow); for ciprofloxacin in Portugal (\downarrow); for cefotaxime in France (\downarrow), Germany (\downarrow) and Italy (\downarrow). A statistically significant increasing trend was observed for both ciprofloxacin and nalidixic acid in Austria (\uparrow), the Czech Republic (\uparrow), Germany (\uparrow), Poland (\uparrow) and Slovakia (\uparrow); for cefotaxime in Portugal (\downarrow); and for ampicillin in the Czech Republic (\uparrow), Germany (\uparrow), Germany (\uparrow), Slovakia (\uparrow) and Spain (\uparrow).

Figure 11. Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested <u>Salmonella Enteritidis</u> isolates from <u>Gallus gallus</u> in reporting MSs, 2007–2013, quantitative data



A statistically significant decreasing trend for five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed in the Czech Republic (\downarrow), France (\downarrow), Germany (\downarrow), the Netherlands (\downarrow) and Spain (\downarrow) for both ciprofloxacin and nalidixic acid; in Italy (\downarrow) for ciprofloxacin; and in Spain (\downarrow) for cefotaxime. A statistically significant increasing trend was observed in Poland (\uparrow) and Portugal (\uparrow) for both ciprofloxacin and nalidixic acid, and in Portugal (\uparrow) for cefotaxime.



Figure 12. Spatial distribution of <u>ciprofloxacin</u> resistance among Salmonella spp. from <u>broilers</u> in countries reporting MIC data in 2013^(a)



Percentages shown on this map refer to countries which reported quantitative MIC data for more than 10 isolates in 2013. When quantitative 2013 data were not available, 2012 data have been used instead. The countries labelled as '<10 isolates' include MIC data for fewer than 10 isolates.

(a): For Poland and Portugal, 2012 data were used.

Figure 13. Spatial distribution of <u>ampicillin</u> resistance among Salmonella spp. from <u>broilers</u> in countries reporting MIC data in 2013^(a)



Percentages shown on this map refer to countries which reported quantitative MIC data for more than 10 isolates in 2013. When quantitative 2013 data were not available, 2012 data have been used instead. The countries labelled as '<10 isolates' include those reporting MIC data for fewer than 10 isolates. (a): For Poland and Portugal, 2012 data were used.



3.1.2.3. Antimicrobial resistance in *Salmonella* spp. isolates from turkeys

Resistance in Salmonella spp. from turkeys

In 2013, nine MSs reported quantitative MIC data on *Salmonella* spp. isolates from turkeys (Figure 30). In the five MSs specifying production type, almost all isolates derived from fattening turkeys.

Most MSs reported high to extremely high levels of resistance to ampicillin, nalidixic acid, sulfonamides and tetracyclines, except for moderate levels of resistance to ampicillin in isolates from Austria and Germany, and resistance to nalidixic acid in isolates from Italy and the United Kingdom. Overall resistance levels to these four antimicrobials ranged between 41.1 % and 64.1 % (Table 17).

Contrasting levels of resistance to chloramphenicol and gentamicin were observed. As in 2012, chloramphenicol resistance was either not recorded or observed at low levels in most MSs. Only Poland and Spain reported moderate to very high resistance to chloramphenicol (16.1 % and 51.6 %, respectively). Moderate to high resistance levels to gentamicin were reported by four MSs, while the remaining MSs observed low levels or absence of resistance.

'Microbiological' resistance to ciprofloxacin was high to extremely high in *Salmonella* spp. isolates from most reporting MSs, and 'clinical' resistance was observed in a number of isolates from several MSs. Cefotaxime resistance was recorded at low levels in France and Poland only, and, overall, was registered at a very low level (0.5 %).

High to extremely high levels of resistance to ampicillin, ciprofloxacin, gentamicin, nalidixic acid, sulfonamides and tetracyclines were found in the **S. Kentucky** isolates included in the analysis (three MSs, Table 17). In contrast, resistance to cefotaxime and chloramphenicol was absent.

The level of MDR varied considerably between the seven MSs that submitted isolate-based data for the MDR analysis (N=637) (Figure 21). All *Salmonella* spp. isolates from Spain were multi-resistant, in contrast to 16.7 % of isolates from Austria. In addition, the proportion of fully susceptible isolates varied from none to 53.3 % in the *Salmonella* spp. from German turkey flocks (Table MDRP16).

Temporal trends in resistance among Salmonella from turkeys

Resistance to ampicillin in *Salmonella* spp. from turkeys varied markedly between MSs from 2007 to 2013 (eight MSs, Figure 14), but only the three MSs that reported data from five years or more were included in the statistical analysis. Statistically significant increasing trends in resistance to ciprofloxacin and to ampicillin were observed in one MS each. Furthermore, statistically significant decreasing trends were observed for ciprofloxacin and ampicillin in one and two MSs, respectively, but to nalidixic acid in all three MSs. Most of the reporting MSs observed a similarity in their trends in resistance to ciprofloxacin and nalidixic acid, except in Spain, where only resistance to nalidixic acid has been decreasing. In Germany, Poland and Spain, higher levels of resistance to ciprofloxacin than to nalidixic acid were observed, probably reflecting the spread of plasmid-mediated genes leading to fluoroquinolone resistance. Plasmid-mediated ciprofloxacin resistance *qnr* genes have been demonstrated in isolates from meat originating from Germany and Poland (Cavaco et al., 2009). Resistance to cefotaxime has remained at a stable low level. Statistical significant trends were not observed in any MS.

Spatial trends in resistance among Salmonella spp. from turkeys

The spatial distribution of ampicillin and nalidixic acid resistance in *Salmonella* spp. isolated from turkeys in 2013 show great variation across the EU (data not shown). Except for the United Kingdom, high to extremely high levels of ciprofloxacin resistance were observed across Europe (Figure 15), the highest occurrence being observed in Spain and in some eastern European MSs (the Czech Republic, Hungary and Poland).



Table 17. Occurrence of resistance to selected antimicrobials in <u>Salmonella spp</u>. and Salmonella <u>Kentucky</u> isolates from <u>turkeys</u> in 2013, using harmonised ECOFFs

Country	Amp	picillin	Cefo	taxime	Chloram	phenicol	Cipro	floxacin	Gen	tamicin	Nalidix	kic acid	Sulfor	namides	Tetra	cyclines
Country	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res	Ν	% Res
Salmonella spp.																
Austria	36	11.1	36	0	36	0	36	38.9	36	0	36	38.9	36	16.7	36	44.4
Czech Republic	31	54.8	31	0	31	0	31	80.6	31	29.0	31	77.4	31	32.3	31	45.2
France	156	29.5	156	1.3	156	3.8	156	39.1	156	3.2	156	39.1	156	31.4	156	30.8
Germany	45	11.1	45	0	45	4.4	45	37.8	45	2.2	45	31.1	45	31.1	45	28.9
Hungary	150	46.7	150	0	150	1.3	150	85.3	150	15.3	150	84.0	150	46.0	150	68.7
Italy	50	64.0	50	0	50	2.0	50	24.0	50	38.0	50	16.0	50	54.0	50	92.0
Poland	62	67.7	63	3.2	62	16.1	62	64.5	62	25.8	46	65.2	46	43.5	62	59.7
Spain	155	97.4	155	0	155	51.6	155	96.1	155	1.3	155	28.4	155	83.2	155	99.4
United Kingdom	170	25.9	170	0	170	0	170	14.1	170	0	170	14.1	170	70.0	170	68.8
Total (MSs 9)	855	48.1	856	0.5	855	11.8	855	55.0	855	8.8	839	41.1	839	52.8	855	64.1
Salmonella Kentucky	,															
Czech Republic	12	100	12	0	12	0	12	100	12	75.0	12	100	12	75.0	12	75.0
Hungary	25	100	25	0	25	0	25	100	25	88.0	25	100	25	88.0	25	88.0
Poland	10	90.0	10	0	10	0	10	90.0	10	90.0	10	90.0	10	90.0	10	90.0
Total (MSs 3)	47	97.9	47	0	47	0	47	97.9	47	85.1	47	97.9	47	85.1	47	85.1

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates.



Figure 14. Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested <u>Salmonella spp.</u> isolates from <u>turkeys</u> in reporting MSs, 2007–2013, quantitative data



A statistically significant decreasing trend was observed for both ciprofloxacin and nalidixic acid in Italy (\downarrow); for nalidixic acid in Germany (\downarrow) and Spain (\downarrow); and for ampicillin in Germany (\downarrow) and Poland (\downarrow). A statistically significant increasing trend over five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for ampicillin in Italy (\uparrow) and for ciprofloxacin in Spain (\uparrow).

Figure 15. Spatial distribution of <u>ciprofloxacin</u> resistance among <u>Salmonella spp.</u> from <u>turkeys</u> in countries reporting MIC data in 2013^(a)



Percentages shown on this map refer to countries which reported quantitative MIC data for more than 10 isolates in 2013. When quantitative 2013 data were not available, 2012 data have been used instead. The countries labelled as '<10 isolates' include those reporting MIC data for fewer than 10 isolates.

(a): For Ireland, 2012 data were used.



Figure 16. Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials in Salmonella spp. from broilers in MSs reporting isolate-based data, 2013



Figure 17. Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials in Salmonella spp. from laying hens in MSs reporting isolate-based data, 2013



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Figure 18. Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials in Salmonella spp. from breeding hens in MSs reporting isolate-based data, 2013



Figure 19. Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials in Salmonella Enteritidis from broilers in MSs reporting isolate-based data, 2013



Figure 20. Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials in Salmonella Enteritidis from laying hens in MSs reporting isolate-based data, 2013





Figure 21. Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials in Salmonella spp. from turkeys in MSs reporting isolate-based data, 2013



Figure 22. Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials in Salmonella spp. from fattening pigs in MSs reporting isolate-based data, 2013



Figure 23. Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials in Salmonella spp. from cattle in MSs reporting isolate-based data, 2013



N: total number of isolates tested for susceptibility against the whole common antimicrobial set for *Salmonella*; sus: susceptible to all antimicrobial substances of the EFSA common set for *Salmonella*; res1–res9: resistance to one to nine antimicrobial substances of the common set for *Salmonella*.



3.1.2.4. Antimicrobial resistance in *Salmonella* spp. isolates from pigs

In 2013, 11 MSs reported quantitative MIC data for *Salmonella* spp. isolates from pigs (Table <u>SA7</u>). Six MSs reported most of their isolates as originating from fattening pigs, and approximately half of these originated from Denmark and all isolates from breeding pigs originated from Belgium. Thus, the overall resistance levels in *Salmonella* from pigs are highly influenced by the two MSs reporting the majority of isolates.

Resistance levels in Salmonella spp. from pigs

As in previous years, most MSs (N=1,426) reported high to extremely high levels of resistance to ampicillin, sulfonamides and tetracyclines, and overall levels ranged from 51.7 % to 55.8 %. Resistance to chloramphenicol overall was moderate (14.0 %), but varied between MSs from none to 41.4 %, the latter being in isolates from Ireland, where all resistant isolates were *S*. Typhimurium or monophasic variants. Gentamicin resistance was typically low in the reporting MSs ranging from 0 % to 16.3 % (Figure 30).

Overall, low levels of resistance to ciprofloxacin and nalidixic acid were reported (6.3 % and 3.2 %, respectively); however, one MS reported high resistance levels. Resistance to cefotaxime was generally not detected or reported at low levels in *Salmonella* spp. from pigs, with only four MSs reporting cefotaxime resistance ranging from 1.4 % to 4.5 %. A few cefotaxime-resistant isolates from breeding pigs were also observed (Belgium) (Table <u>SA7</u>).

High to extremely high levels of MDR (27.2 %–81.8 %) were reported by the five MSs providing isolatebased *Salmonella* spp. data from fattening pigs (Figure 22) or breeding pigs for the MDR analysis (N=616). Among the *Salmonella* spp. isolates from Belgian breeding pigs, approximately half of the isolates were multi-resistant, whereas one-third of the isolates were fully susceptible to nine of the antimicrobials included. Among the other MSs, the proportion of fully susceptible *Salmonella* spp. isolates varied from 9.1 % to 48.5 % (Tables <u>MDR17</u>, <u>MDRP9</u> and <u>MDRP10</u>).

Resistance levels in certain Salmonella serovars from pigs

Among the isolates with serovar information (N=1,288), the most commonly reported serovars in pigs were *S*. Typhimurium (34.3 %), *S*. Derby (23.7 %) and monophasic *S*. Typhimurium (18.5 %, Table <u>SER6</u>). Generally, *S*. Derby displays less resistance than *S*. Typhimurium, including the monophasic variants, so the relative distribution between these serovars often dominates the overall *Salmonella* spp. resistance levels.

In **S. Typhimurium** (seven MSs, Table 18), most, and in some cases all, isolates were resistant to ampicillin, sulfonamides and/or tetracyclines (overall 72.4 %–76.6 %). Overall resistance to chloramfenicol was moderate (27.6 %) and overall low levels of resistance to gentamicin (4.1 %) and nalidixic acid (2.9 %) were reported; however, the occurrences varied substantially between MSs. Resistance to ciprofloxacin and cefotaxime was low overall, and was absent in two and five MSs, respectively. However, resistance to ciprofloxacin occurred at levels ranging up to 21.4 % (Ireland). High to very high levels of MDR were observed in the *S*. Typhimurium isolates from Danish fattening pigs (30.8 %) and from Belgian breeding pigs (65.3 %, Tables MDRP18).

In addition, in the **monophasic S. Typhimurium** variants (six MSs, Table 19), resistance levels to ampicillin, sulfonamides and/or tetracyclines were extremely high, and generally comparable to generic *S.* Typhimurium isolates. However, cefotaxime resistance was absent among the included monophasic *S.* Typhimurium isolates. Most of the monophasic *S.* Typhimurium isolates from fattening pigs from Denmark and Spain were multi-resistant (>90 %, Table <u>MDRP24</u>).

In **S. Derby** (seven MSs, N=289), the overall levels of resistance to ampicillin, sulfonamides and/or tetracyclines were generally much lower than in the *S.* Typhimurium isolates (12.5 %–28.7 %); however, some MSs reported very high levels of resistance to sulfonamides and/or tetracyclines. In contrast to 2012, resistance to nalidixic acid was not reported in *S.* Derby, and ciprofloxacin resistance was reported by Belgium only (1.4 %). Cefotaxime resistance were recorded in a few *S.* Derby isolates (n=4) (Table <u>SA8</u>).



0	Am	picillin	Cefo	taxime	Chloran	nphenicol	Cipro	floxacin	Gent	tamicin	Nalidi	xic acid	Sulfor	namides	Tetra	cyclines
Country	N	% Res	N	% Res	N	% Res	N	% Res	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res
All pigs						•				•						
Belgium	75	78.7	75	2.7	75	28.0	75	6.7	75	2.7	75	0	75	68.0	75	58.7
Croatia	15	80.0	15	0	22	9.1	15	6.7	15	0	15	0	15	86.7	15	66.7
Denmark	26	26.9	26	0	26	7.7	26	0	26	0	26	0	26	38.5	26	38.5
Germany	223	82.5	223	1.3	223	27.8	223	8.1	223	4.0	223	3.6	223	83.9	223	82.1
Ireland	14	78.6	14	0	14	64.3	14	21.4	14	0	14	21.4	14	85.7	14	71.4
Netherlands	26	57.7	26	0	26	11.5	26	3.8	26	0	26	3.8	26	50.0	26	53.8
United Kingdom	31	83.9	31	0	31	51.6	31	0	31	19.4	31	0	31	87.1	31	83.9
Total (MSs 7)	410	76.6	410	1.2	417	27.6	410	6.8	410	4.1	410	2.9	410	76.3	410	72.4
Fattening pigs																
Croatia	15	80.0	15	0	22	9.1	15	6.7	15	0	15	0	15	86.7	15	66.7
Denmark	26	26.9	26	0	26	7.7	26	0	26	0	26	0	26	38.5	26	38.5
Total (MSs 2)	41	46.3	41	0	48	8.3	41	2.4	41	0	41	0	41	56.1	41	48.8
Breeding pigs	•															
Belgium	75	78.7	75	2.7	75	28.0	75	6.7	75	2.7	75	0	75	68.0	75	58.7

Table 18. Occurrence of resistance to selected antimicrobials in Salmonella Typhimurium isolates from pigs in 2013, using harmonised ECOFFs

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates.

Table 19. Occurrence of resistance to selected antimicrobials in <u>monophasic Salmonella Typhimurium</u> isolates from <u>pigs</u> in 2013, using harmonised ECOFFs

Country	Ampicillin		Cefotaxime		Chloramphenicol		Ciprofloxacin		Gentamicin		Nalidixic acid		Sulfonamides		Tetracyclines	
	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	Ν	% Res	N	% Res
Belgium	73	87.7	73	0	73	9.6	73	9.6	73	2.7	73	6.8	73	91.8	73	82.2
Denmark	37	91.9	37	0	37	0	37	0	37	2.7	37	0	37	94.6	37	94.6
Italy	23	100	23	0	23	30.4	23	13.0	23	17.4	23	4.3	23	100	23	95.7
Netherlands	25	80.0	25	0	25	8.0	25	4.0	25	0	25	4.0	25	80.0	25	92.0
Spain	21	90.5	21	0	21	0	21	4.8	21	9.5	21	0	21	90.5	21	100
United Kingdom	50	76.0	50	0	50	24.0	50	4.0	50	20.0	50	0	50	88.0	50	94.0
Total (MSs 6)	229	86.5	229	0	229	12.2	229	6.1	229	8.3	229	3.1	229	90.8	229	90.8

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates.



Temporal trends in resistance among Salmonella spp. from pigs

Resistance to ampicillin varies markedly in *Salmonella* spp. from pigs between MSs from 2007 to 2013 (seven MSs provided data from five years or more, Figure 24), and statistically significant increasing trends were observed in five MSs. Statistically significant increasing trends in resistance to both ciprofloxacin and nalidixic acid occurred in two MSs: in *Salmonella* spp. from pigs from Germany, and in Ireland there were increasing differences in resistance to ciprofloxacin and nalidixic acid from 2007 to 2013, even though the levels of resistance varied for both compounds during this period. This indicates a spread of plasmid-mediated quinolone resistance in *Salmonella* in pigs within the EU, as is the case for turkeys in Spain. Resistance to cefotaxime is generally low, and a statistically significant decreasing trend was observed in Estonia.

Figure 24. Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested <u>Salmonella spp.</u> isolates from <u>pigs</u> in reporting MSs, 2007–2013, quantitative data



A statistically significant increasing trend over five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed in Germany (\uparrow) and Ireland (\uparrow) for both ciprofloxacin and nalidixic acid, and for ampicillin in Ireland (\uparrow), Italy (\uparrow), the Netherlands (\uparrow) and Spain (\uparrow). A statistically significant decreasing trend was observed for both ciprofloxacin and nalidixic acid in Estonia (\downarrow), nalidixic acid only in the Netherlands (\downarrow) and for cefotaxime in Estonia (\downarrow).

Danish data are not comparable between years: data from 2006 to 2010 contained only S. Typhimurium isolates, while all the isolates were reported in 2011–2013.

Spatial trends in resistance among Salmonella spp. from pigs

Large differences in ciprofloxacin and ampicillin resistance rates were observed between MSs in 2013 (2012 data from Hungary and Poland). The levels of resistance to ciprofloxacin in *Salmonella* spp. from pigs were highest in some of the eastern European MSs (Hungary, Poland and Romania), and, across Europe, low to moderate levels were observed. Ciprofloxacin resistance was absent in the two northern European MSs reported data (Figure 25). Tetracycline is the most commonly used antimicrobial agent in pigs, which is reflected in the very high to extremely high levels of tetracycline resistance reported by most MSs (Figure 26). High to extremely high levels of resistance to ampicillin were reported by MSs, but no clear spatial distributions were observed for *Salmonella* spp. in pigs (data not shown).



Figure 25. Spatial distribution of <u>ciprofloxacin</u> resistance among Salmonella spp. from pigs in countries reporting MIC data in 2013^(a)



Percentages shown on this map refer to countries which reported quantitative MIC data for more than 10 isolates in 2013. When quantitative 2013 data were not available, 2012 data have been used instead. The countries labelled as '<10 isolates' include those reporting MIC data for fewer than 10 isolates. (a) For Hungary and Poland, 2012 data were used.

Figure 26. Spatial distribution of <u>tetracycline</u> resistance among Salmonella spp. from pigs in countries reporting MIC data in 2013^(a)



Percentages shown on this map refer to countries which reported quantitative MIC data for more than 10 isolates in 2013. When quantitative 2013 data were not available, 2012 data have been used instead. The countries labelled as '<10 isolates' include those reporting MIC data for fewer than 10 isolates. (a): For Hungary and Poland, 2012 data were used.



3.1.2.5. Antimicrobial resistance in *Salmonella* spp. isolates from cattle

In this report, calves, dairy cattle, beef cows and heifers are included under the term 'cattle'. In 2013, four MSs reported quantitative MIC data for *Salmonella* spp. isolates from cattle (Table <u>SA9</u>).

Resistance levels in Salmonella spp. from cattle

High levels of resistance to ampicillin, sulfonamides and tetracyclines were reported, ranging from 24.6 % to 52.0 % (Table <u>SA9</u>). Overall, the levels of resistance to nalidixic acid, chloramphenicol and gentamicin were low, but varied from none to 30.8 %. In contrast to previous years, all MSs reported gentamicin-resistant isolates (not just Germany and Italy as has previously been reported). Resistance to ciprofloxacin overall was low, but occurred at high levels in the isolates from Belgium (30.8 %). Cefotaxime resistance was absent, whereas one resistant isolate was reported in 2012 (Figure 30).

Three MSs provided isolate-based *Salmonella* data from the MDR analysis (N=125), where 27.9 % to 52.0 % of the isolates were multi-resistant and 25.6 % to 62.3 % of the isolates were fully susceptible to the nine antimicrobials included in the analysis (Table <u>MDR18</u>, Figure 23).

Generally, resistance levels among the isolates specified as *S*. Typhimurium (three MSs, Table <u>SA10</u>) resembled the general levels for *Salmonella* spp. in cattle.

Temporal trends in resistance among Salmonella spp. from cattle

Resistance to ampicillin in *Salmonella* spp. from cattle was generally high in 2013, and only in Germany did a statistically significant decreasing trend occur from 2007 to 2013 (five MSs reported data from five or more years, Figure 27). A statistically significant increasing trend was observed for ampicillin in the Netherlands. No apparent temporal trends were observed among the MSs reporting quantitative data on resistance to nalidixic acid in *Salmonella* spp. from cattle. Differences in resistance to ciprofloxacin and nalidixic acid from 2007 to 2013 occurred in three MSs; however, these differences are due to one or two more isolates being resistant to ciprofloxacin than the number of isolates resistant to nalidixic acid.

Figure 27. Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested <u>Salmonella spp.</u> isolates from <u>cattle</u> in reporting MSs, 2007–2013, quantitative data



A statistically significant decreasing trend for five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for resistance to ampicillin in Germany (\downarrow). A statistically significant increasing trend was observed for ampicillin in the Netherlands (\uparrow).

Spatial trends in resistance among Salmonella spp. from cattle

Resistance to ciprofloxacin continues to be absent in *Salmonella* from cattle in the northern European MSs reporting (2012 data from Finland and Sweden), and low or moderate levels are observed in the other reporting MSs. As in 2012, a high level of ciprofloxacin resistance occurred in *Salmonella* from Belgian cattle (Figure 28). Moderate to very high levels of resistance to ampicillin were reported by the MSs; however, no clear spatial distributions were observed for *Salmonella* spp. in cattle (Figure 29).



Figure 28. Spatial distribution of <u>ampicillin</u> resistance among Salmonella spp. from cattle in countries reporting MIC data in 2013^(a)



Percentages shown on this map refer to countries which reported quantitative MIC data for more than 10 isolates in 2013. When quantitative 2013 data were not available, 2012 data have been used instead. The countries labelled as '<10 isolates' include those reporting MIC data for fewer than 10 isolates.

(a): For Finland and Sweden, 2012 data were used.

Figure 29. Spatial distribution of <u>ciprofloxacin</u> resistance among Salmonella spp. from cattle in countries reporting MIC data in 2013^(a)



Percentages shown on this map refer to countries which reported quantitative MIC data for more than 10 isolates in 2013. When quantitative 2013 data were not available, 2012 data have been used instead. The countries labelled as '<10 isolates' include those reporting MIC data for less than 10 isolates.

(a): For Finland and Sweden, 2012 data were used.

3.1.2.6. Comparison of 'clinical' and 'microbiological' resistance to ciprofloxacin

Fluoroquinolones and third-generation cephalosporins, including the class representatives ciprofloxacin and cefotaxime, are internationally recognised as critically important in human medicine (Collignon et al., 2009) and often constitute the first-line treatment for invasive salmonellosis, although fluoroquinolones are not recommended for children (Chen et al., 2013). Fluoroquinolones and, to a lesser extent, third-generation cephalosporins are used for treatments in animals, and the high levels of ciprofloxacin resistance observed among *Salmonella* spp. in some animal species are of concern.

In *Salmonella* spp. from *Gallus gallus*, an overall high level of 'microbiological' resistance to ciprofloxacin (42.0 %) was reported, and four MSs (Croatia, Hungary, Romania and Slovenia) recorded very high to extremely high levels. Low levels of ciprofloxacin resistance were reported in Denmark, France and the United Kingdom, and ciprofloxacin resistance was not detected in isolates from Ireland (N=14). Applying the EUCAST CBPs, 'clinical' resistance was found in seven out of 17 MSs, contributing to an overall low level of 'clinical' resistance to ciprofloxacin (6.4 %). This is despite a high occurrence of 'clinical' resistance in isolates from Romania, representing 26.0 % of all isolates (Table 20). The 'microbiological' resistance to cefotaxime in *Salmonella* spp. from *Gallus gallus* was generally low (overall 5.4 %), and most MSs reported no to very low levels of resistance to cefotaxime. Only Romania and the Netherlands reported moderate 'microbiological' resistance to cefotaxime. Cefotaxime resistance at 'clinical' levels was found in only seven out of 17 MSs, and overall a low 'clinical' resistance (3.2 %) was observed. However, the majority of 'microbiological' cefotaxime-resistant isolates from the Netherlands were also 'clinically' resistant (14.8 % vs. 14.4 %) (Table 21).

In **turkeys**, very high levels of 'microbiological' resistance to ciprofloxacin were observed in *Salmonella* spp. (nine MSs, overall 55.0 %), with very high to extremely high occurrences in isolates from the Czech Republic, Hungary, Poland and Spain. 'Clinical' resistance was overall 10-fold lower; however, moderate to high levels were reported from the Czech Republic, Hungary and Poland (nine MSs, Table 20). Low levels of 'microbiological' resistance and 'clinical' resistance to cefotaxime were observed in *Salmonella* spp. and were reported in only France (1.3 % vs. 1.3 %) and Poland (3.2 % vs. 1.6 %) (Table 21).

In *Salmonella* spp. from **pigs**, an overall low level of 'microbiological' resistance to ciprofloxacin was observed (11 MSs, 6.3 %). Only one MS (Romania) reported a high level of antimicrobial resistance at 45.5 % (N=11). When applying the EUCAST CBPs, resistance was detected at very low levels in Belgium and Germany only, and overall 'clinical' resistance to ciprofloxacin in *Salmonella* spp. from pigs was overall very low (0.1 %) (Table 20). An overall low level of 'microbiological' and 'clinical' resistance to cefotaxime was observed in *Salmonella* spp. from pigs (1.2 % vs. 1.1 %). Only four MSs (Belgium, Germany, Italy and Spain) reported 'microbiological' resistance, but in low levels. In three MSs, all cefotaxime-resistant isolates were 'clinically' resistant, and only in Spain was cefotaxime resistance in *Salmonella* spp. from pigs below 'clinical' levels (11 MSs, Table 21).

The level of 'microbiological' resistance to ciprofloxacin in *Salmonella* spp. from **cattle** varied from low to very high (Belgium 30.8 %) among the four reporting MSs. None of these MSs was found to have any resistant isolates when using the EUCAST breakpoints (Table 20). None of the four MSs reported either 'microbiological' or 'clinical' resistance to cefotaxime among *Salmonella* spp. from cattle (Table 21).

The term 'microbiological' resistance is used when resistance is interpreted using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) epidemiological cut-off values, whereas the term 'clinical' resistance is noted when resistance is analysed using the EUCAST clinical breakpoints.

Quinolone and fluoroquinolone resistance in the Enterobacteriaceae is mostly attributed to point mutations in the quinolone resistance-determining regions (QRDR) of the gyrase (gyrA and gyrB) and topoisomerase IV (parC and parD) genes. Other resistance mechanisms include efflux pump mechanisms; qepA, enzymatic modifications; aac(6')lb-cr and qnr genes; and qnrA, qnrB, qnrD and qnrS genes (Cavaco et al., 2009).

The presence of two single point mutations in the QRDR will confer 'clinical' resistance to ciprofloxacin (minimum inhibitory concentration (MIC)>1 mg/L) as well as to nalidixic acid (MIC>16mg/L). In contrast, isolates harbouring only one single point mutation in the QRDR will be 'clinical' resistant to nalidixic acid, whereas the susceptibility to ciprofloxacin is reduced to only a 'microbiological' resistance level.

Any other harboured (fluoro)quinolone resistance mechanisms such as the qnr genes will confer only 'microbiological' resistance to ciprofloxacin, but the isolate will be susceptible to nalidixic acid.


Table 20. Occurrence of resistance to ciprofloxacin among Salmonella spp. from Gallus gallus, turkeys, pigs and cattle in 2013, using harmonised ECOFFs and EUCAST CBPs

		Gallus gallus			Turkeys			Pigs			Cattle	
Country	N	Epidemiological % Res	Clinical % Res	N	Epidemiological % Res	Clinical % Res	N	Epidemiological % Res	Clinical % Res	N	Epidemiological % Res	Clinical % Res
Austria	175	27.4	0	36	38.9	0	-	-	-	-	-	-
Belgium	426	27.5	1.6	-	_	_	318	6.6	0.3	39	30.8	0
Croatia	91	57.1	3.3	-	_	_	41	4.9	0	-	-	_
Czech Republic	288	22.2	6.9	31	80.6	38.7	_	_	_	_	-	_
Denmark	30	3.3	0	-	_	_	206	0	0	-	-	_
Estonia	_	_	_	_	_	_	31	0	0	_	-	_
France	257	3.9	0	156	39.1	0	_	_	_	_	-	_
Germany	232	26.7	0	45	37.8	0	321	10.3	0.3	61	1.6	0
Hungary	252	67.5	3.6	150	85.3	18.0	_	_	_	_	-	_
Ireland	14	0	0	_	_	_	29	10.3	0	_	-	_
Italy	344	27.0	0	50	24.0	0	89	10.1	0	25	12.0	0
Netherlands	508	41.7	0	_	_	_	162	2.5	0	102	2.0	0
Poland	357	42.6	0.3	62	64.5	14.5	_	_	_	_	-	_
Romania	1,187	72.5	21.0	_	_	_	11	45.5	0	_	_	_
Slovakia	68	50.0	0	_	_	_	_	_	_	_	_	_
Slovenia	57	61.4	0	_	_	_	_	_	_	_	_	_
Spain	137	24.8	7.3	155	96.1	1.3	69	13.0	0	_	_	_
United Kingdom	226	3.1	0	170	14.1	0	147	2.0	0	-	_	_
Total (MSs 18)	4,649	42.0	6.4	855	55.0	5.8	1,424	6.3	0.1	227	7.9	0

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported. For ciprofloxacin, the harmonised ECOFF was MIC \geq 0.064 µg/mL and the CBP was MIC \geq 4 µg/mL.



Table 21. Occurrence of resistance to cefotaxime among Salmonella spp. from Gallus gallus, turkeys, pigs and cattle in 2013, using harmonised ECOFFs and EUCAST CBPs

		Gallus gallus			Turkeys			Pigs			Cattle	
Country	N	Epidemiological % Res	Clinical % Res	N	Epidemiological % Res	Clinical % Res	N	Epidemiological % Res	Clinical % Res	N	Epidemiological % Res	Clinical % Res
Austria	175	0	0	36	0	0	_	_	_	-	_	_
Belgium	426	4.0	4.0	-	_	_	318	1.6	1.6	39	0	0
Croatia	91	8.8	0	-	-	_	41	0	0	-	_	-
Czech Republic	288	1.0	1.0	31	0	0	-	-	-	-	-	-
Denmark	30	0	0	-	-	_	206	0	0	-	_	-
Estonia	-	_	_	-	_	_	31	0	0	-	_	_
France	257	0.8	0.4	156	1.3	1.3	_	_	_	-	_	_
Germany	232	0.4	0	45	0	0	321	2.2	2.2	61	0	0
Hungary	252	0	0	150	0	0	_	_	_	-	_	_
Ireland	14	0	0	-	-	-	29	0	0	-	-	-
Italy	344	6.7	6.7	50	0	0	89	4.5	4.5	25	0	0
Netherlands	508	14.8	14.4	-	_	_	162	0	0	102	0	0
Poland	357	0.3	0	63	3.2	1.6	_	_	_	-	_	_
Romania	1,187	10.1	2.4	-	_	_	11	0	0	-	_	_
Slovakia	68	0	0	-	_	_	_	_	_	-	_	_
Slovenia	58	0	0	-	_	_	_	_	_	-	_	_
Spain	137	0.7	0.7	155	0	0	69	1.4	0	-	_	_
United Kingdom	226	0	0	170	0	0	147	0	0	-	_	_
Total (MSs 18)	4,650	5.4	3.2	856	0.5	0.4	1,424	1.2	1.1	227	0	0

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; –: no data reported. For cefotaxime, the harmonised ECOFF was MIC \geq 0.5 µg/mL and the CBP was MIC \geq 4 µg/mL.



3.1.2.7. Analysis of high-level ciprofloxacin resistance

High-level resistance to ciprofloxacin, defined as resistance to MIC values \geq 4 mg/L, in *Salmonella* of animal and food origin is shown in Tables <u>HLR1</u> to <u>HLR8</u>.

Most of the *Salmonella* isolates that displayed high-level resistance to ciprofloxacin originated from domestic fowl (*Gallus gallus*) and turkey meat. No isolates from pigs or cattle displayed high-level resistance, and only a few *S*. Brandenburg isolates from pig meat in Romania exhibited such high-level resistance. Among the 20 MSs reporting ciprofloxacin-resistant *Salmonella* isolates, 10 MSs provided isolate-based MIC data to be used in the analysis of high-level ciprofloxacin resistance.

Most of the *Salmonella* spp. isolates from broilers included in the analysis originated from Romania, where 10.4 % of the isolates showed high-level resistance (mainly S. Kentucky) (Table <u>HLR4</u>). Among the other nine MSs included in the analysis of broiler isolates, high-level resistance was reported by the Czech Republic (1.7 %, N=236), Hungary (1.6 %, N=183) and Spain (23.1 %, N=26). Reflecting the generally lower levels of resistance in *Salmonella* from laying hens, high-level ciprofloxacin resistance was observed in only two of the seven included MSs: Romania (3.9 %, N=103) and Spain (3.6 %, N=111). In addition, from Romania, isolates from broiler meat (4.1 %, N=219) and breeding hens (10.0 %, N=30) displayed high-level ciprofloxacin resistance.

In turkeys, high-level ciprofloxacin resistance was observed in the Czech Republic (38.7 %, N=31), Hungary (17.3 %, N=150) and Spain (1.3 %, N=155), but not in Austria (N=36), and was observed in turkey meat from the Czech Republic (50.0 %, N=10) and Germany (3.2 %, N=31) (Table <u>HLR6</u>). In 2012, high-level ciprofloxacin resistance of *Salmonella* from domestic fowl, turkeys and meat thereof were reported by the same MSs as in 2013, whereas a single *S*. Kentucky isolate from broiler meat was reported by Ireland in 2012.

In poultry, a variety of serovars displayed high-level ciprofloxacin resistance and these isolates were frequently also resistant to other antimicrobials. High-level resistance to ciprofloxacin was most often observed in the **S**. Kentucky isolates in *Gallus gallus* and turkeys and meat thereof from the Czech Republic, Hungary, Romania and Spain. Almost all of the S. Kentucky isolates with high-level ciprofloxacin resistance (n=157) were multi-resistant (98.7 %), and most isolates (79.1 %) were also resistant to gentamicin, ampicillin, nalidixic acid, sulfonamides, tetracyclines and often also streptomycin (Gen-(Str)-Cip-Amp-Nal-Sul-Tet). Resistance to several, or even all, other antimicrobials included in the MDR analysis were also observed. Only Romania reported isolates with high-level ciprofloxacin resistance and resistance to cefotaxime (n=14).

S. Infantis also displayed high-level resistance to ciprofloxacin (n=12), and was encountered in breeding hens, broilers and broiler meat mainly from Romania but also in broilers from Hungary. All isolates were multi-resistant and, besides the high-level ciprofloxacin resistance, most *S*. Infantis isolates (91.7 %) were also resistant to nalidixic acid, sulfonamides, tetracyclines and, in most cases, streptomycin ((Str)-Cip-Nal-Sul-Tet). From Romania, a few isolates of other serovars showed high-level ciprofloxacin resistance. **S.** Enteritidis was reported in broiler meat and laying hens, whereas the serovars *S*. Liverpool, *S*. Bredeney, *S*. Tennessee and *S*. Agona were reported from broilers.

3.1.2.8. Multi-drug resistance in certain Salmonella serovars

The data relating to *Salmonella* spp. from an MS typically cover a variety of different serovars, each of which may have a different propensity to exhibit antimicrobial resistance. Differences in the occurrence of serovars among MSs may account for much of the pronounced variation in the recorded MDR parameters for *Salmonella* spp. For example, *S.* Enteritidis in general exhibited much lower MDR than *S.* Typhimurium; however, there were marked differences between MSs in the occurrence of MDR for each of these serovars.

Salmonella spp.

Overall, nine MSs provided data for analysis of MDR, and the patterns of antimicrobial resistance exhibited by all reported *Salmonella* isolates revealed numerous combinations of resistance to the nine different antimicrobial agents included in the analysis. The reported MS occurrences of specific MDR profiles in meat and animals are presented in the <u>MDRP</u> tables.

Detailed analysis of the specific patterns of resistance detected is most useful when performed at the serovar level. However, the overall data from all *Salmonella* spp. have also been examined to determine the pattern most common in highly prevalent sources per country. In broilers (n=1,168) (Table <u>MDRP5</u>) and broiler meat (n=301) (Table <u>MDRP1</u>), the most common pattern was a combination of ciprofloxacin/nalidixic acid, sulfamethoxazole and tetracycline, followed by the addition of streptomycin, both accounting for 24.3 % of the broiler isolates and 39.2 % of the broiler meat isolates included in the analysis. These resistant profiles



were predominately reported by Austria (97.4 %, broilers), the Czech Republic (59.8 %, broilers and meat from broilers), Hungary (77.9 %, only broilers) and Romania (20.9 %, broilers and meat from broilers). The same combination of antimicrobial resistance patterns as that found in turkeys was not reported for other poultry sources (Table MDRP8). In turkeys (n=472), the most common patterns seem to be more related to single MSs such as the most common pattern: streptomycin, sulfamethoxazole and tetracycline being reported by the United Kingdom (59.5 %). This common pattern was also sporadically reported by nine other MSs (Belgium, the Czech Republic, Denmark, Estonia, Germany, Ireland, Italy, Latvia and Romania). The second and third most common patterns were mainly reported by Spain: ampicillin, chloramphenicol, ciprofloxacin/nalidixic acid, streptomycin, sulfamethoxazole, tetracycline and trimethoprim (38.1 %) and the same MDR pattern but without chloramphenicol and streptomycin (29.0 %). In pig meat (n=284), the most common resistance pattern was ampicillin, streptomycin, sulfamethoxazole and tetracycline (36.3 %), followed by the addition of trimethoprim (13.4 %) (Table MDRP2).

Salmonella Enteritidis

Information on MDR was sparsely available for *S*. Enteritidis isolates and only reported from broilers (n=13, Belgium, Romania) (Table MDRP13), meat thereof (n=9, Romania) (Table MDRP12) and laying hens (n=10, Hungary, Italy, and Romania) (Table MDRP14). A few isolates from laying hens were reported to show penta- and hexavalent resistance mainly to combinations of ampicillin, ciprofloxacin, gentamicin, sulfamethoxazole, tetracycline and trimethoprim. MDR has never been and is still not common in *S*. Enteritidis isolates. Most of the *S*. Enteritidis isolates from broilers (83.7 %), broiler meat (60.1 %) and laying hens (76.1 %) tested were reported fully susceptible to the nine antimicrobials addressed in the analysis (comprising 10 MSs). A potentially invasive clone of *S*. Enteritidis carrying virulence genes as well as MDR (Amp-Chl-Str-Sul-Tet-Tmp) has been reported from the African continent and from related cases in the United Kingdom (Rodriquez et al., 2012). None of the *Salmonella* isolates included in the MDR analysis displayed this pattern.

Salmonella Typhimurium

MDR S. Typhimurium isolates were reported in pig meat (n=125) (Table MDRP15), breeding pigs (n=49) (Table MDRP19), broilers (n=25) (Table MDRP16), cattle (n=25) (Table MDRP20), fattening pigs (n=19) (Table MDRP18) and laying hens (n=12) (Table MDRP17). A wide range of different MDR patterns were reported in all sources. The most frequent MDR pattern was resistance to ampicillin, streptomycin, sulfamethoxazole and tetracycline in most sources. In previous years, the pattern associated with phage type DT104 conferring resistance to ampicillin, chloramphenicol, streptomycin, sulfonamides and tetracycline; this 'ACSSuT' pattern has been reported to be the most common MDR pattern in all types of animals except in broilers, where it was the second most commonly observed pattern. It is noteworthy that, in 2013, the ACSSuT pattern was only observed as the second most common profile in pig meat (19.2 %) and breeding pigs (18.4 %), whereas this MDR pattern was either absent or much less common in the other animal sources. However, penta-, hexa- and heptavalent resistance were reported in cattle, fattening pigs, breeding pigs, pig meat and broilers, which were all suspected of being associated with DT104 because of the acquisition of resistance to ciprofloxacin and/or trimethoprim and the absence of resistance to chloramphenicol. Resistance to cefotaxime was reported with only one isolate from fattening pigs but was absent in all other sources. Ciprofloxacin resistance was usually uncommon in S. Typhimurium MDR isolates, although it was most frequent in pig meat and broilers.

Monophasic Salmonella Typhimurium

The MDR patterns for monophasic *S*. Typhimurium isolates were reported from fattening pigs (n=54) (Table MDRP24), cattle (n=12) (Table MDRP25), broilers (n=23) (Table MDRP22), laying hens (n=9) (Table MDRP23) and pig meat (n=49) (Table_MDRP21). The most frequent pattern of resistance observed was resistance to ampicillin, streptomycin, sulfamethoxazole and tetracycline ranging from 66.7 % in cattle to 88.9 % in laying hens. MDR monophasic *S*. Typhimurium seems to be mostly reported by Italy and Spain in most of the sources, whereas it is mostly reported in fattening pigs and pig meat from Denmark. In previous years, MDR monophasic *S*. Typhimurium has also been reported in turkeys from Germany.

Salmonella Kentucky

The patterns of MDR for *S*. Kentucky isolates were reported from broilers (n=102) (Table <u>MDRP26</u>) and laying hens (n=29) (Table <u>MDRP27</u>). About 62.8 % of the isolates from broilers had the core pattern of hexavalent resistance to ampicillin, ciprofloxacin, gentamicin, streptomycin, sulfamethoxazole and tetracycline reported by the Czech Republic, Hungary and Romania. However, this core hexavalent resistance pattern was observed in only a few isolates in laying hens, for which the most common MDR pattern reported was resistance to ampicillin, ciprofloxacin and tetracycline.



Salmonella Infantis

MDR patterns for *S*. Infantis were available from broiler meat (n=172) (Table MDRP31), broilers (n=641) (Table MDRP32), laying hens (n=18) (Table MDRP33) and turkeys (n=47) (Table MDRP34), where most of the isolates originated from Romania (62.8 %) and Hungary (18.7 %). Like *S*. Typhimurium, *S*. Infantis displayed a wide range of different MDR patterns; however, almost all MDR patterns (>90 %) included resistance to ciprofloxacin and/or nalidixic acid, as well as resistance to sulfonamides and tetracyclines. Resistance to ciprofloxacin/nalidixic acid, streptomycin, sulfonamides and tetracyclines was the most common pattern in *S*. Infantis from broiler meat (63.2 %), broilers (40.7 %), laying hens (53.5 %) and turkeys (95.6 %). This core MDR pattern (Cip-Str-Sul-Tet) is commonly associated with *S*. Infantis definitive phage type 213. In Italy, however, the most common MDR pattern in *S*. Infantis from broilers was Amp-Cip/Nal-Ctx-Sul-Tet-Tmp (58.8 %, n=17), followed by this pattern in combination with streptomycin (11.8 %). All other multi-resistant *S*. Infantis isolates having resistance to cefotaxime originated from Romanian broilers (11.9 %, n=413), where the core MDR pattern was supplemented with resistance to cefotaxime as well as to ampicillin, chloramphenicol, gentamicin and/or trimethoprim.

Pentavalent resistance

Pentavalent resistance to ampicillin, chloramphenicol, streptomycin, sulfonamides and tetracycline (also called ACSSuT resistance) was observed in several different serovars. From broilers (n=47), ACSSuT resistance was mainly reported in *S*. Infantis (n=14), *S*. Paratyphi B (n=8) and *S*. Agona (n=7). In 2013, ACSSuT-resistant *S*. Infantis isolates were observed only in broilers; however, in 2012, ACSSuT resistance was reported from broiler meat, pig meat, broilers and laying hens. In fattening pigs and pig meat, ACSSuT resistance (n=11 and n=38, respectively) was mainly observed in *S*. Typhimurium (n=4 and n=32, respectively). ACSSuT-resistant *S*. Rissen is common in pig production systems in Asia, and was reported in fattening pigs in 2013 (n=3) and in cattle in 2012 (n=1). In Europe, the numbers of human infections with *S*. Rissen is usually low, and these cases have been associated with travel mainly to Thailand or outbreaks as a result of imported food products (Henriksen et al., 2008). To determine if the observed *S*. Rissen isolates belong to the clones originating from Asia, genotypic analysis is required (Pornsukarom et al., 2015, Table PENT1).

3.1.2.9. Overview of the findings on antimicrobial resistance in Salmonella, 2013

Figure 30 and Figure 31 illustrate the resistance levels for the groups of MSs reporting quantitative MIC data in 2013. These data were not all derived from the same group of MSs, which needs to be considered when interpreting these figures. Resistance levels to ampicillin, chloramphenicol, sulfonamides and tetracyclines in *S*. Typhimurium from *Gallus gallus* were higher than in *S*. Enteritidis from *Gallus gallus*. However, resistance to ciprofloxacin and nalidixic acid was higher in *S*. Enteritidis than in *S*. Typhimurium. In terms of all *Salmonella* spp., resistance levels in isolates from broiler meat were higher than those in isolates from *Gallus gallus*.





Figure 31. Occurrence of resistance to selected antimicrobials in <u>Salmonella spp.</u> from broilers of Gallus gallus and broiler meat, <u>Salmonella Enteritidis</u> and <u>Salmonella Typhimurium</u> from broilers of Gallus gallus at reporting MS group level in 2013





3.1.3. Discussion

Although there has been a significant decline in human salmonellosis cases from 2007 to 2013, salmonellosis continues to be the second most commonly reported zoonotic disease in humans in the EU, exceeded only by campylobacteriosis. The decline in incidence seems to mainly be attributed to the reduction in the prevalence of *Salmonella* in flocks of laying hens but also in broilers and turkeys, probably as a result of the national control and monitoring programmes implemented by the MSs in the corresponding production sectors (EFSA and ECDC, 2014a).

In 2013, information on antimicrobial resistance in *Salmonella* isolates from human cases was reported by 21 MSs and two non-MSs. The number of isolates for which susceptibility data were available corresponded to about one-fifth of the total salmonellosis cases reported within the EU in 2013. Resistance in human *Salmonella* isolates was high to ampicillin, sulfonamides and tetracyclines and moderate for nalidixic acid (as in 2012). These antimicrobials or other agents of the same class are used commonly for the treatment of infection in animals and humans (although not usually for the treatment of salmonellosis in humans). For ampicillin, sulfonamide and tetracycline, the resistance observed was largely due to the high to extremely high resistance levels observed among *S*. Typhimurium and particularly monophasic *S*. Typhimurium isolates. This pattern of resistance to all three of these agents (ASuT) is commonly observed among monophasic *S*. Typhimurium definitive phage type 193/120 strains (EFSA BIOHAZ Panel, 2010b).

Although less common in terms of number of cases, human *S*. Kentucky isolates exhibited very high to extremely high resistance levels to ampicillin, ciprofloxacin, gentamicin, nalidixic acid, sulfonamides and tetracycline, which is consistent with dissemination of a multi-resistant clonal group (Le Hello et al., 2011; Westrell et al., 2014). Resistance to nalidixic acid (and the associated raised MIC to ciprofloxacin) was also more commonly associated with *S*. Infantis and *S*. Entertidis. Resistance to ciprofloxacin and cefotaxime/ceftriaxone, which are currently favoured for empirical therapy of serious/invasive salmonellosis, remains less common. However, the interpretation of inter-country variation in resistance to ciprofloxacin is particularly challenging because of differences in the susceptibility breakpoints applied. Until recently (including 2013), there was a large difference between some CBPs for ciprofloxacin resistance and the EUCAST ECOFF.

In 2013, like in 2012, 13 MSs reported results for all antimicrobials included in the MDR analysis. Among these isolates, less than half were susceptible to the complete range of antimicrobial classes reported for humans. About 30.0 % of human Salmonella spp. isolates exhibited MDR, meaning that they were nonsusceptible to at least three different antimicrobial classes. Three MSs recorded MDR levels at or close to 50.0 %. MDR was particularly associated with monophasic S. Typhimurium and S. Kentucky, with more than 80.0 % and almost 70.0 %, respectively, of these isolates being multi-drug resistant. Co-resistance to the critically important therapeutic antimicrobials ciprofloxacin and cefotaxime was reported from five countries and represented just 0.2 % of all isolates reported. Although co-resistance to these agents remains low at this point, MSs are encouraged to consider monitoring for resistance to reserve agents, such as meropenem, that may need to be considered for treatment of extremely drug-resistant isolates. This is especially the case because some human isolates were resistant to a large number or all of the antimicrobial classes routinely reported in 2013 and France reported one isolate non-susceptible to carbapenems. In the absence of routine monitoring, resistance to reserve agents may grow and remain undetected. Resistance to reserve agents that are not used in food-producing animals may be related to cross-resistance to agents used in foodproducing animals for some agents, or to antimicrobial use in humans or exposure to sources of Salmonella other than those associated with food-producing animals.

In order to assess the importance of **travel-associated infections**, antimicrobial resistance was also analysed based on the most likely country of infection and aggregated by geographical region. Overall, human *Salmonella* spp. isolates acquired within the EU/EEA countries exhibited greater resistance to ampicillin, sulfonamides and tetracyclines than isolates from any other region, while the highest levels of resistance to ciprofloxacin were associated with Africa and the highest levels of resistance to cefotaxime were associated with Asia. In many cases, however, the number of isolates associated with particular regions is modest.

In terms of **data quality and comparability**, major improvements in harmonisation of human data between countries and with data from animals and food were made in this report. For the first time, countries could report measured values (quantitative AST data as opposed to interpreted categories) to ECDC and seven countries were able to submit *Salmonella* data in this way. These data were interpreted with EUCAST ECOFFs, where available. With respect to categorical data, the categories of intermediate and resistant were combined into a non-susceptible group. Alignment of interpretive criteria for the antimicrobial agents under consideration suggests that, with this approach, the ECOFF-based category of 'wild type' corresponds closely to the susceptible category, and the ECOFF-based category of 'non-wild type' corresponds closely to



the non-susceptible (i.e. intermediate or resistant) category. Thus, this approach further improves the comparability of human and non-human data. In addition, in 2013, data from four out of five countries were interpreted with EUCAST criteria, while only one in three were interpreted in this way in 2012.

For future reports, it is hoped that more countries will report measured values data. More harmonisation is also needed when it comes to the selection of isolates to test and report at the EU level, as, in many countries, the selection and the antimicrobials tested for a particular selection of isolates is not random and represents different fractions of all the identified isolates in a country. In 2013, there continued to be some aspects of the reported human data that were problematic to interpret. For some countries, the reported percentage of isolates resistant to ciprofloxacin was substantially higher than the reported percentage resistant to nalidixic acid. This finding is not readily explained in the context of the common mechanisms of resistance to quinolones and fluoroquinolones and, although plasmid-mediated resistance could confer this pattern, the differences in breakpoints applied complicate the analysis. There are also some reports of levels of resistance that represent extreme deviation from that observed in other MSs. It is uncertain to what degree these outlier values represent methodological variation as distinct from actual biological differences.

In the ECDC external quality assurance scheme for *Salmonella*, it was concluded that the use of different, sometimes non-standardised, interpretive criteria could contribute to unexpected results (ECDC, 2012). Therefore, in the EU protocol for harmonised monitoring of antimicrobial resistance in human *Salmonella* and *Campylobacter* isolates, ECDC is promoting the use of EUCAST methods and breakpoints in all laboratories submitting AST results to TESSy (ECDC, 2014b). The EU protocol recommends testing with nalidixic acid to enhance detection of low-level fluoroquinolone resistance in laboratories using disc diffusion. Since the protocol was published, however, EUCAST has issued a recommendation to test for pefloxacin susceptibility instead of nalidixic acid in order to also detect resistance due to plasmid-mediated *qnr* genes (EUCAST, 2014). The EU protocol may therefore have to be updated on this point.

In *Salmonella* isolates from animals and meat, harmonised quantitative MIC data were reported by 22 MSs and two non-MSs in 2013. Fifteen MSs provided isolate-based data enabling analysis of MDR patterns, high-level of resistance to ciprofloxacin and co-resistance to ciprofloxacin and cefotaxime, agents critically important for treating human salmonellosis. Where possible, the levels of resistance are presented by serovar for the different animal production types; the division of *Gallus gallus* into broilers and laying hens is particularly relevant. The sub-division of resistance data allows for more accurate analysis, but is possible only where MSs include information on serovars and production type. In 2013, the large number of MSs providing data on isolates from *Gallus gallus* by production type allowed for more accurate analysis. However, more information is required at the production level for other animal species, particularly cattle, to improve these sections of the report in future years.

Antimicrobials such as **ampicillin**, **sulfonamides** and **tetracyclines** have been widely used for many years in veterinary medicine to treat infections in production animals. Generally, moderate to high levels of resistance to these antimicrobials are reported by MSs from producing animals and meat products thereof. The highest levels of resistance to ampicillin, sulfonamides and tetracyclines, as well as to chloramphenicol, were recorded in *Salmonella* isolates from pigs, followed by isolates from turkeys and cattle. Considering all reporting MSs, isolates from *Gallus gallus* displayed the lowest levels of resistance to these antimicrobials, even though moderate to high levels were reported in broilers by some individual MSs. Levels of resistance were generally higher in *Salmonella* spp. and *S*. Enteritidis from broiler flocks than from laying hen flocks, particularly in the case of resistance to tetracyclines and sulfonamides. This may reflect that laying hens are usually less frequently treated with antimicrobials than broilers. In many MSs, only a limited number of antimicrobial compounds are authorised for the treatment of laying hens and the relatively higher levels of ciprofloxacin resistance reflect that this is one of the compounds available.

The occurrence of resistance to **fluoroquinolones** (ciprofloxacin) was in general particularly related to certain animal species and sources – turkeys, broilers, and meat thereof – combined with a clearly defined geographical distribution, including the following countries: Austria, Belgium, the Czech Republic, Germany, Hungary, Italy, Romania and, to a certain degree, Spain. In the reported data, it is clear that *S*. Kentucky and *S*. Infantis were mainly responsible for the occurrence of fluoroquinolone resistance in the mentioned sources, which is highly indicative of clonal expansion (*S*. Kentucky ST198-X1) in the production of the food animals, especially poultry (Le Hello et al., 2011, 2013b; Westrell et al., 2014).

Resistance to third-generation **cephalosporins**, such as cefotaxime, was detected in *Salmonella* isolates from domestic fowl (*Gallus gallus*), turkeys, pigs, cattle and the meat from broilers, turkeys and pigs. Overall, low or very low levels of resistance to cefotaxime were observed, but levels varied among the reporting MSs. Notably, high levels of cefotaxime resistance were reported in isolates from broilers and/or broiler meat from Croatia, Italy, the Netherlands and Romania. The occurrence of cefotaxime resistance was highest in



S. Infantis, but several MSs also reported a low level of resistance in *S.* Enteritidis from *Gallus gallus* (Belgium, Croatia and Romania) and in *S.* Typhimurium from pigs (Belgium and Germany).

Third-generation cephalosporins and fluoroquinolones are critically important for the treatment of human salmonellosis. Co-resistance to cefotaxime and ciprofloxacin differed between MSs and was not detected in isolates from the majority of MSs reporting isolate-based data. In the MSs where it was detected, co-resistance to these antimicrobials in *Salmonella* spp. occurred at a moderate level in broilers and meat thereof, especially from Italy and Romania, and was associated with *S*. Kentucky. In addition, it was reported at very low levels in isolates from laying hens, pig meat, fattening pigs and breeding pigs.

As in previous years, the reported levels of ciprofloxacin and nalidixic acid resistance in isolates from the different types of meat or animal species between MSs were generally very similar; however, isolates with resistance to ciprofloxacin, but susceptible to nalidixic acid, were reported more frequently in 2013, probably indicating the increasing occurrence of plasmid-mediated *qnr* genes leading to fluoroquinolone resistance. This was observed among all animal species, but especially in *Salmonella* isolates from turkeys and pigs, and it occurred in several serovars.

MDR, defined as resistance to three or more of nine antimicrobial classes, was generally high in Salmonella spp. from broilers, pigs and cattle; the proportion of multi-resistant isolates was higher in southern and eastern European countries than in isolates from northern European countries. Most of the multi-resistant isolates originated from Romania. In laying hens, however, MDR levels were generally low to moderate, especially in *S*. Entertidis. Generally, the resistance levels varied among serovars that may exhibit particular MDR patterns, so the relative contribution of different serovars in different production types and between MSs should be kept in mind when comparing the situation between the reporting countries.

The analysis of MDR resistance patterns also highlighted multi-resistant strains of *Salmonella* occurring in several MSs. High-level ciprofloxacin resistance (MIC >4) was observed in a number of multi-resistant *S*. Kentucky isolates from broilers, laying hens and turkeys and in a few isolates of *S*. Infantis and other serovars. No isolates from pigs or cattle displayed high-level ciprofloxacin resistance and there was only a single multi-resistant *S*. Brandenburg isolate reported from pig meat (Romania). The MSs reporting high levels of ciprofloxacin-resistant *S*. Kentucky and *S*. Infantis isolates in 2013 also reported similar findings in 2012 (the Czech Republic, Hungary, Romania and Spain); however, only 10 MSs provided isolate data suitable for the analysis of high-level ciprofloxacin resistance.

From 2014, MSs will collect *Salmonella* isolates for susceptibility testing according to the new harmonised monitoring plan (Decision 2013/652/EU). In line with this decision, the antimicrobial agents included in the test panels will change; most importantly, testing of resistance to streptomycin is not required, which will have a strong impact on how MDR patterns may be interpreted.

Within a given MS, any attempt to relate antimicrobial resistance in human *Salmonella* isolates to antimicrobial resistance in isolates from food and food-producing animals in that MS is complicated, because much of the food consumed in an MS may have originated in other MSs or in third countries. *Salmonella* infections can also be associated with foreign travel, other types of animal contact (such as pet reptiles) or the environment. Some human infections can also occur through spread between affected human patients. To improve investigation of these relationships, isolates from cases notified as having been acquired during travel outside of the reporting country were excluded from the analysis, except with respect to the analysis of resistance in different geographical regions. The comparison would further improve if a distinction could be made between food isolates from domestically produced animals and those from other countries, although this is not currently possible.

3.2. Antimicrobial resistance in *Campylobacter*

Campylobacter causes a large number of human cases of gastroenteritis and has been the most frequently reported cause of human food-borne zoonoses in the EU since 2004 (EFSA and ECDC, 2014a). Patients may experience mild to severe illness. Symptoms may include (bloody) diarrhoea, abdominal pain, fever, headache and nausea. The mean duration of illness is reported as two to five days but can be up to 10 days. The majority of campylobacteriosis enteric infections are self-limiting; however, infection can be associated with serious complications. Campylobacteriosis is an important trigger for autoimmune inflammatory conditions of the central nervous system, heart and joints, which can result in prolonged and debilitating illness (e.g. Guillain–Barré syndrome, acute transverse myelitis and reactive arthritis). Blood stream infection with *Campylobacter* spp. is very rare, except for infections with *C. fetus*.

Antimicrobial treatment is usually not needed, but effective treatment may shorten the duration of illness. Resistance to antimicrobials in *Campylobacter* is of concern because of the large number of human infections and the fact that some cases require treatment. Treatment of enteric infections in humans may



involve administration of macrolides, such as erythromycin or fluoroquinolones (e.g. ciprofloxacin), as the first- and second-choice drugs (ECDC et al., 2009). With ciprofloxacin, resistance may develop rapidly.

Fourteen MSs, Iceland and Norway provided data for 2013 on human *Campylobacter* isolates. Five countries (Austria, Denmark, Luxembourg, Norway and Romania) reported isolate-based AST results as measured values (inhibition zone diameters or MICs). Eleven countries reported case-based AST results interpreted as susceptible (S), intermediate (I) or resistant (R) according to the CBPs applied. Only data on *C. jejuni* and *C. coli* are presented in the report for comparison with AST data from animals and food.

In 2013, 18 MSs and three non-MSs (Iceland, Norway and Switzerland) reported quantitative dilution data on antimicrobial resistance in *Campylobacter* isolates from animals and food. AST was carried out for *C. jejuni* and *C. coli* only; all other *Campylobacter* species were excluded from the monitoring programme of antimicrobial resistance in *Campylobacter* (Table <u>OVER4</u>).

3.2.1. Antimicrobial resistance in *Campylobacter* isolates from humans

C. jejuni and *C. coli* accounted for 99.6 % of all human campylobacteriosis cases with species information reported to ECDC in 2013. Resistance levels differ substantially between these two species and data are therefore presented separately. Results are presented for the three first-priority antimicrobials currently included in the harmonised panel of antimicrobials to be tested for human *Campylobacter* isolates (ciprofloxacin, erythromycin and tetracycline) and for two optional agents (co-amoxiclav and gentamicin) (ECDC, 2014b). The MDR analysis included the three priority antimicrobials and gentamicin, as the latter will be included in the priority panel, when ECOFF values are available for disc diffusion in addition to dilution. The number of antimicrobials tested per isolate varied by country: two countries tested only two antimicrobials, 13 countries tested the three priority antimicrobials and five countries tested all five antimicrobials.

Interpretation of data must take account of the wide variation in the numbers of *Campylobacter* isolates reported by MSs. While this may in part be related to true differences in the incidence of campylobacteriosis, it is also likely to be greatly influenced by practices in the country related to capture of isolates and/or data from primary clinical laboratories.

Methods and interpretive criteria used for antimicrobial susceptibility testing of *Campylobacter* isolates from humans

The method of testing for antimicrobial susceptibility and the selection of the isolates to be tested varied between countries. The methods and interpretive criteria used for antimicrobial susceptibility testing of Campylobacter are presented in Table <u>MM3</u>.

Quantitative data were interpreted by the ECDC(ECDC) with reference to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) epidemiological cut-off (ECOFF) values, where available. Where ECOFFs do not exist, clinical breakpoints from the French Society for Microbiology (CA-SFM) were applied. For the qualitative SIR data, the intermediate and resistant results were combined into a 'nonsusceptible' category.

For the four antimicrobials reported for both human and animal/food isolates, the commonly used interpretive criteria were aligned (Figure 32). For this purpose, 'susceptible' isolates were aligned with wild-type isolates based on ECOFFS, and 'non-susceptible' isolates ('intermediate' and 'resistant') were aligned with non-wild-type isolates. This resulted in close concordance (±1 doubling dilution) across interpretive categories, except for the clinical breakpoints from the Clinical and Laboratory Standards Institute (CLSI) and CA-SFM for tetracyclines, which are two doubling dilutions higher than the EUCAST ECOFF for C. jejuni.



Figure 32. Comparison of CBPs and ECOFFs used to interpret MIC data reported for Campylobacter spp. from humans, animals or food



CBP: clinical breakpoint; CLSI: Clinical and Laboratory Standards Institute; ECOFF: epidemiological cut-off; EUCAST: European Committee on Antimicrobial Susceptibility Testing; MIC: minimum inhibitory concentration. CLSI (M45-A2), EUCAST clinical breakpoints (2013), CA-SFM (2013), EUCAST ECOFFS (according to Decision 2013/652/EU).

3.2.1.1. Resistance levels in *Campylobacter jejuni* isolates from human cases

As in previous years, *C. jejuni* was the most common *Campylobacter* species identified in 2013, with 84,585 cases reported in the EU/EEA. AST data were reported for 15.0 % of these cases in 2013 by 14 MSs, Iceland and Norway.

More than half (54.6 %) of human *C. jejuni* isolates in the EU were resistant to ciprofloxacin in 2013 (Table 22). The lowest proportions of resistant isolates were reported by Norway (20.8 %) and Denmark (23.1 %) and the highest were reported by Lithuania (88.2 %) and Spain (91.5 %). The level of resistance to erythromycin was relatively low, on average 1.5 %, but was variable between countries. The highest proportion of erythromycin-resistant isolates was reported by Malta (18.1 %). This is substantially higher than the level of resistance reported by any other country, although Romania (9.1 %) and Italy (7.3 %) also reported levels higher than other countries. Another noteworthy observation is that, in addition to the very high level of resistance to ciprofloxacin, Spain also reported an extremely high proportion of isolates resistant to tetracyclines (80.1 %).

Comparison of resistance in Campylobacter jejuni isolates acquired within the EU/EEA and in other geographical regions

Patterns of infection outside Europe are likely to be associated with preferred travel destinations for residents of a given MS. Differences in testing methodology between MSs may also influence the apparent pattern of regional variation in resistance.

Only a limited number of isolates from cases associated with travel outside the EU/EEA were tested and/or reported, and only regions where at least 20 isolates had been tested are shown in Table 23. Resistance to ciprofloxacin and tetracyclines was noticeably more frequent in isolates acquired in Asia than the overall levels of resistance within the EU/EEA, with almost two-fold higher levels of ciprofloxacin resistance (Table 23); this is similar to 2012. However, individual MSs reporting the highest level of resistance in domestically acquired cases or cases with unknown travel history (Table 22) reported higher levels of resistance than those associated with Asia for both agents.



0	Ciprofl	oxacin	Co-am	oxiclav	Erythro	omycin	Genta	amicin	Tetrac	yclines
Country	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Austria ^(a)	303	63.0	_	_	303	0	303	0	303	21.5
Denmark ^(a)	65	23.1	-	_	65	1.5	65	0.0	65	20.0
Estonia	293	57.7	154	8.4	270	0.7	153	0.7	248	21.4
France	3,816	49.7	3,524	0.9	3,822	0.5	3,822	0.5	_	_
Italy	235	67.2	-	-	233	7.3	117	4.3	208	57.2
Lithuania	178	88.2	_	_	222	0.5	_	_	_	_
Luxembourg ^(a)	566	59.4	566	5.7	566	1.2	566	0.4	566	43.8
Malta	138	69.6	-	-	138	18.1	-	_	-	-
Netherlands	2,811	56.9	_	_	2,392	1.9	_	_	1,414	36.4
Romania ^(a)	44	77.3	_	_	44	9.1	44	0	44	56.8
Slovakia	992	39.9	116	4.3	1,205	0.7	7	NA	1,184	19.8
Slovenia	877	64.1	688	14.0	877	0.6	877	0.5	877	27.7
Spain	281	91.5	-	-	281	3.9	281	2.1	281	80.1
United Kingdom	1,110	46.9	11	NA	851	2.5	6	NA	32	34.4
Total (MSs 14)	11,709	54.6	5,059	3.5	11,269	1.5	6,241	0.6	5,222	33.5
Iceland	6	NA	_	_	6	NA	_	_	1	NA
Norway ^(a)	106	20.8	_	_	106	0	106	0.9	106	14.2

Table 22. Antimicrobial resistance in Campylobacter jejuni from humans per country in 2013

N: number of isolates tested; % Res: percentage of resistant isolates (either non-wild type by ECOFFs or clinically non-susceptible by combining resistant and intermediate categories); -: no data reported; NA: not applicable (if fewer than 20 isolates were tested resistance was not calculated); MSs: Member States.

(a): Provided measured values. Data interpreted by ECDC.

Table 23. Antimicrobial resistance in Campylobacter jejuni by reported geographical region of infection, 2013

Region	Ciproflo	oxacin	Co-amo	oxiclav	Erythr	omycin	Genta	micin	Tetrac	cyclines
Region	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Europe (EU/EEA countries)	11,948	54.4	5,062	3.5	11,508	1.5	6,463	0.6	5,451	33.6
Africa	24	54.2	2	NA	23	0.0	20	0.0	24	29.2
Asia	102	90.2	2	NA	102	2.9	96	1.0	99	55.6

N: number of isolates tested; % Res: percentage of resistant isolates (either non-wild type by ECOFFs or clinically non-susceptible by combining resistant and intermediate categories); NA: not applicable (if fewer than 20 isolates were tested resistance was not calculated).



Multi-drug resistance among Campylobacter jejuni *isolates from human cases*

Eight MSs and Norway tested at least twenty isolates of *C. jejuni* for the four antimicrobial classes included in the MDR analysis. It is important to note that, for this year, the MDR analysis focused on a limited range of antimicrobials relevant to human health. Therefore, direct comparison with previous years is not valid. Overall, 30.2 % of human *C. jejuni* isolates in the eight reporting MSs were susceptible to all four antimicrobial classes. As in 2012, particularly low levels of susceptibility were reported from Spain (5.0 %) (Table MDR19). MDR was, on average, low in the eight MSs (1.5 %). There was, however, a large variation in the level of MDR between countries ranging from 0 % in Austria, Denmark and Norway to 10.6 % in Italy. A low proportion (1.7 %) of isolates exhibited resistance to both ciprofloxacin and erythromycin in the eight MSs. The proportions of *C. jejuni* isolates susceptible to all or resistant (non-susceptible) to up to four antimicrobial classes by MSs are presented in Figure 33. Four isolates resistant to all four antimicrobial classes were reported from Italy.

Figure 33. Frequency distribution of Campylobacter jejuni isolates from humans completely susceptible or resistant to one to four antimicrobial classes, 2013



N: number of isolates tested for susceptibility against the four antimicrobial classes included in the multi-drug resistance analysis; MSs: Member State; Susceptible: number of isolates susceptible to all four antimicrobial classes included in the multi-drug resistance analysis; res1–res4: number of isolates resistant to one to four antimicrobial classes. (a): Provided measured values. Data interpreted by ECDC.

3.2.1.2. Resistance levels in *Campylobacter coli* isolates from human cases

C. coli was the second most common *Campylobacter* species identified in 2013, with 7,465 cases reported in the EU/EEA. AST data were reported for 20.1 % of these cases in 2013 by 13 MSs and Norway.

Very high proportions of resistance were observed for ciprofloxacin (66.7 %) and tetracyclines (58.1 %) among *C. coli* isolates (Table 24). Proportions of erythromycin and gentamicin resistance were also markedly higher in *C. coli* than in *C. jejuni* (13.4 % vs. 1.5 % and 11.1 % vs. 0.6 %, respectively). The highest levels of resistance to all three priority agents were reported from Spain. Italy and Malta also reported high levels of resistance to erythromycin (31.8 % and 25.0 %, respectively). The number of isolates reported in the case of these three countries was low (N=22–53).

Comparison of resistance in Campylobacter coli isolates acquired within the EU/EEA and in other geographical regions

There were not enough AST data on *C. coli* isolates associated with travel outside the EU/EEA for a meaningful analysis.



0	Ciprof	loxacin	Co-am	oxiclav	Erythr	omycin	Gent	amicin	Tetrac	yclines
Country	N	% Res	N	% Res	N	% Res	Ν	% Res	Ν	% Res
Austria ^(a)	34	61.8	-	_	34	0.0	34	0.0	34	35.3
Estonia	9	NA	8	NA	9	NA	8	NA	8	NA
France	678	71.7	632	0.9	679	14.3	679	14.3	_	_
Italy	24	79.2	_	_	22	31.8	15	NA	24	75.0
Lithuania	12	NA	-	-	15	NA	-	_	-	-
Luxembourg ^(a)	90	68.9	90	32.2	90	13.3	90	1.1	90	74.4
Malta	44	68.2	-	-	44	25.0	_	_	_	-
Netherlands	236	59.7	_	-	184	14.1	_	_	133	55.6
Romania ^(a)	5	NA	_	_	5	NA	5	NA	5	NA
Slovakia	25	36.0	15	NA	40	2.5	1	NA	40	40.0
Slovenia	73	58.9	42	16.7	73	1.4	73	0.0	73	41.1
Spain	53	94.3	_	_	53	34.0	53	15.1	53	96.2
United Kingdom	132	47.0	2	NA	102	7.8	2	NA	8	NA
Total (MSs 13)	1,415	66.6	789	6.2	1,350	13.4	960	11.1	468	58.1
Norway ^(a)	3	NA	-	-	3	NA	3	NA	3	NA

Table 24. Antimicrobial resistance in Campylobacter coli from humans per country in 2013

N: number of isolates tested; % Res: percentage of resistant isolates (either non-wild type by ECOFFs or clinically non-susceptible by combining resistant and intermediate categories); -: no data reported; NA: not applicable (if fewer than 20 isolates were tested resistance was not calculated); MSs: MSs.

(a): Provided measured values. Data interpreted by ECDC.

Multi-drug resistance among Campylobacter coli isolates from human cases

Five MSs tested at least ten isolates for the four antimicrobial classes included in the MDR analysis. Overall, 15.7 % of the human *C. coli* isolates were susceptible to all four antimicrobial classes, with a particularly low proportion of susceptible isolates reported in Spain (1.9 %, N=53) (Table MDR20). On average, the level of MDR was moderate (12.6 %) but ranged from 0 % to 36.4 % between countries. The overall level of corresistance to ciprofloxacin and erythromycin was 4.1 %. The proportions of *C. coli* isolates susceptible to all or resistant (non-susceptible) to up to four antimicrobial classes by MSs are presented in Figure 34. Two MSs (Spain and Luxembourg) together reported seven isolates resistant to all four antimicrobial classes.

Figure 34. Frequency distribution of Campylobacter coli isolates from humans completely susceptible or resistant to one to four antimicrobial classes, 2013



N: number of isolates tested for susceptibility against the four antimicrobial classes included in the multi-drug resistance analysis; MSs: Member State; Susceptible: total number of isolates susceptible to all four antimicrobial classes included in the multi-drug resistance analysis; res1–res4: total number of isolates resistant to one to four antimicrobial classes. (a): Provided measured values. Data interpreted by ECDC.



3.2.2. Antimicrobial resistance in *Campylobacter* isolates from animals and food

The countries reporting Campylobacter resistance from various animal and food sampling origins in 2013 are presented in Table <u>OVER4</u>. Antimicrobials selected by the different MSs, and non-MSs, for susceptibility testing of *C. jejuni* and *C. coli* are shown in Table <u>MM7</u>.

The revision of EUCAST ECOFFs for Campylobacter

There have been some recent minor revisions to the epidemiological cut-off (ECOFF) value provided by the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Thus, the EUCAST ciprofloxacin ECOFF for C. coli is currently 'susceptible' (i.e. wild-type) ≤ 0.5 mg/L, a decline of one log value from the previous ECOFF value of 'resistant' (i.e. non-wild-type) >1 mg/L. Similarly, the ECOFF values for C. coli and erythromycin, C. coli and nalidixic acid and C. jejuni and both ciprofloxacin and tetracyclines have declined by one dilution step. Conversely, the ECOFF has increased by one log dilution for C. jejuni versus gentamicin and streptomycin. Although deviation from wild-type susceptibility is a fixed microbiological characteristic, as greater numbers of bacterial isolates are tested, the wild-type distribution may become better defined and minor changes in the ECOFF might therefore be expected. The breakpoints used in this report to discriminate between 'microbiologically resistant' and wild-type bacteria are those included in the latest revision of the EUCAST ECOFFs and in the new EU legislation (Decision 2013/652). The historical data have been re-interpreted in this report using the revised EUCAST ECOFFs.

3.2.2.1. Antimicrobial resistance in Campylobacter isolates from meat

Representative sampling and monitoring

In the reporting MSs, data on antimicrobial resistance in *Campylobacter* isolates from meat from *Gallus gallus* derived from active monitoring/surveillance programmes or surveys (Sweden) were based mainly on the random collection of broiler meat samples obtained at slaughterhouses, cutting plants or retail outlets. Data on antimicrobial resistance in *Campylobacter* isolates from meat from turkeys were submitted by Poland and Hungary. No information on the sampling context was provided by these two MSs.

Resistance levels among C. jejuni and C. coli isolates from meat from broilers

For 2013, eight MSs provided quantitative antimicrobial resistance data on *C. jejuni* and *C. coli* isolates from broiler meat (Table 25 and Table 26). Although resistance is typically higher among *C. coli* than *C. jejuni* isolates, common features in the levels of resistance to ciprofloxacin, erythromycin, gentamicin, nalidixic acid and tetracyclines can be observed in the two *Campylobacter* species monitored. For the commonly used antimicrobials, resistance to tetracyclines and nalidixic acid generally ranged from high to extremely high levels, whereas resistance to gentamicin varied less among reporting MSs and was either undetected or recorded at low levels. For clinically important antimicrobials, resistance to ciprofloxacin was high to extremely high in reporting MSs and, as expected, closely paralleled the results obtained for nalidixic acid, whereas resistance to erythromycin was much lower considering all reporting MSs. The recorded levels of resistance to erythromycin considering *C. jejuni* and *C. coli* were contrasting, with higher resistance generally observed in *C. coli*. In contrast to the other reporting MSs, Portugal recorded an extremely high resistance level to erythromycin in *C. coli* at 72.7 %, although a low number of isolates was tested. Germany and the Netherlands reported moderate resistance to erythromycin in *C. coli* at resistance to erythromyc

Multi-resistance among C. jejuni and C. coli isolates from meat from broilers

The isolate-based resistance data on 10 or more isolates of *C. jejuni* and *C. coli* were not available from broiler meat; the corresponding MDR analysis is not presented in this report.



Table 25. Occurrence of resistance to selected antimicrobials in Campylobacter jejuni from meat in 2013, using harmonised ECOFFs

Country	Ciprot	floxacin	Erythr	omycin	Gent	amicin	Nalidi	xic acid	Tetrac	cyclines
Country	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res
Meat from broi	lers (Gal	lus gallus)								
Austria	144	71.5	144	0	144	0	144	68.8	144	29.9
Belgium	216	38.9	216	1.9	216	0.5	216	39.8	216	37.0
Denmark	70	20.0	70	0	70	0	70	20.0	70	10.0
Germany	266	61.3	266	0.4	266	0	266	52.3	266	36.8
Hungary	24	75.0	24	0	24	0	24	79.2	24	54.2
Netherlands	54	57.4	54	3.7	54	0	54	61.1	54	53.7
Poland	46	47.8	141	0.7	143	0	53	49.1	53	13.2
Sweden	12	50.0	12	0	12	0	12	50.0	12	16.7
Total (MSs 8)	832	53.0	927	0.9	929	0.1	839	50.3	839	33.3
Meat from turk	ey									
Hungary	10	80.0	10	0	10	0	10	70.0	10	50.0

 Table 26. Occurrence of resistance to selected antimicrobials in Campylobacter coli from meat in MSs reporting MIC data in 2013, using harmonised ECOFFs

0	Cipro	floxacin	Erythr	omycin	Gent	amicin	Nalidi	xic acid	Tetra	cyclines
Country	Ν	% Res	Ν	% Res	N	% Res	N	% Res	Ν	% Res
Meat from broil	ers (<i>Gall</i> u	us gallus)								
Austria	99	69.7	99	3.0	99	0	99	68.7	99	53.5
Belgium	60	65.0	60	10.0	60	0	60	65.0	60	73.3
Denmark	22	36.4	22	0	22	0	22	36.4	22	36.4
Germany	103	87.4	103	14.6	103	0	103	84.5	103	74.8
Hungary	56	85.7	56	3.6	56	3.6	56	83.9	56	57.1
Netherlands	72	81.9	72	16.7	72	0	72	80.6	72	80.6
Poland	55	72.7	_	_	172	0	15	0	70	2.9
Portugal	11	100	11	72.7	11	0	11	100	11	100
Total (MSs 8)	478	76.2	423	10.9	595	0.3	438	72.6	493	57.8
Meat from turke	∌y								•	
Hungary	11	72.7	11	9.1	11	0	11	54.5	11	45.5
Poland	_	_	10	0	12	0	-	_	-	_
Total (MSs 2)	11	72.7	21	4.8	23	0	11	54.5	11	45.5
Meat from pig										
Belgium	53	50.9	53	17.0	53	0	53	52.8	53	86.8
Poland	19	57.9	17	0	18	0	18	55.6	-	_
Total (MSs 2)	72	52.8	70	12.9	71	0	71	53.5	53	86.8

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.



3.2.2.2. Antimicrobial resistance in *Campylobacter* isolates from broilers of *Gallus gallus*

Representative sampling and monitoring

In this section, data on antimicrobial resistance in *Campylobacter* isolates from fowl (*Gallus gallus*) are completely derived from broilers. The vast majority of samples was collected from healthy broilers at the slaughterhouse. Entire caeca or caecal contents were collected in Austria, the Czech Republic, Finland, Germany, Slovenia and Spain, cloacal swabs were collected in Denmark and Switzerland, and faeces were collected before slaughter in Iceland. For most of the MSs specifying details of the sampling strategy, sampling was randomised throughout the year, with the exception of Finland, where sampling was more intense over the high-risk period of the summer months. In accordance with EFSA's recommendations (EFSA, 2007), only one representative sample of caecal content per flock/batch, derived from either a unique carcase or a number of carcases, was gathered to avoid clustering. Typically, given the relatively high prevalence of *Campylobacter* in broilers, representative subsets of *C. jejuni* and *C. coli* isolates recovered from caecal samples, each representing one flock, were randomly selected at the laboratory for susceptibility testing.

Resistance levels among C. jejuni and C. coli isolates from broilers

For 2013, 11 MSs and three non-MSs reported quantitative MIC data on *C. jejuni* isolates from broilers (Table 27), while quantitative data on *C. coli* isolates were submitted by eight MSs and one non-MS (Table 28). Generally, in both *C. jejuni* and *C. coli*, resistance to gentamicin and erythromycin was either undetected or recorded at low to moderate levels, while the observed resistance to tetracyclines and (fluoro)quinolones (ciprofloxacin and nalidixic acid) was high to extremely high among reporting countries. A striking exception to this was the low resistance to all antimicrobials tested in *C. jejuni* isolates recorded in the Nordic countries (Iceland, Finland and Norway). Resistance in *C. coli* was typically either similar or greater than that observed in *C. jejuni* in those MSs reporting results for both *Campylobacter* species. Considering *C. jejuni* and *C. coli*, levels of resistance to ciprofloxacin and nalidixic acid were similar for the two species, as expected. Generally, resistance in *C. coli* and *C. jejuni* from broiler meat and broilers was reported at similar levels in the MSs reporting data on both animal and meat origins.

Temporal trends in resistance among C. jejuni and C. coli isolates from broilers

The observed temporal trends in antimicrobial resistance in *C. jejuni* isolates from *Gallus gallus* from 2007 to 2013 (Figure 35) show that resistance to ciprofloxacin and nalidixic acid varied greatly among reporting MSs over this period. Statistically significant increasing trends in resistance to both ciprofloxacin and nalidixic acid were observed in Austria, Denmark, France, Spain and Switzerland for five or more years. Resistance to erythromycin remained absent or low from 2007 to 2013, and statistically significant decreasing trends in erythromycin resistance were detected in Germany, Hungary and the Netherlands over the reporting period. With regards to gentamicin, resistance remained generally at levels lower than 10.0 % with slight fluctuations for all reporting countries from 2007 to 2013 (data not shown).

Figure 36 presents observed trends in antimicrobial resistance in *C. coli* from *Gallus gallus*. In 2013, as was the case in previous years, a high degree of variation was observed in levels of resistance to ciprofloxacin and nalidixic acid among reporting MSs. For ciprofloxacin and nalidixic acid, statistically significant increasing trends for the last five or more years were observed in Austria, Spain and Switzerland (Figure 36). For erythromycin, resistance was generally lower over the reporting period than for the other antimicrobials presented. Resistance to erythromycin increased significantly over the seven years presented in Spain and decreased in Hungary. For gentamicin, the resistance levels reported over the period were lower than 10.0 % with the exception of Spain (data not shown).

Spatial distribution of resistance among C. jejuni isolates from broilers

The spatial distributions of ciprofloxacin and erythromycin resistance in *C. jejuni* from *Gallus gallus* (Figure 37 and Figure 38) show that, for both antimicrobials, overall resistance was lower among the reporting Nordic countries than in the rest of the European reporting countries.



Table 27. Occurrence of resistance to selected antimicrobials in Campylobacter jejuni from broilers of Gallus gallus in countries reporting MIC data in 2013, using harmonised ECOFFs

Country	Cipro	floxacin	Erythr	omycin	Gent	amicin	Nalidi	xic acid	Tetrac	cyclines
Country	Ν	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Austria	122	73.0	122	0	122	0	122	70.5	122	24.6
Czech Republic	36	86.1	36	0	36	0	36	88.9	36	27.8
Denmark	54	25.9	54	1.9	54	0	54	25.9	54	20.4
Finland	76	0	76	0	76	0	76	9.2	76	0
France	65	53.8	65	0	65	0	65	55.4	65	69.2
Germany	40	47.5	40	0	40	0	40	42.5	40	32.5
Hungary	56	85.7	56	0	56	0	-	-	56	50.0
Netherlands	167	49.1	167	0	167	0	167	49.7	167	49.1
Slovenia	32	75.0	32	0	32	0	32	68.8	32	34.4
Spain	72	90.3	72	2.8	72	0	72	87.5	72	88.9
United Kingdom	61	31.1	61	0	61	0	61	31.1	61	47.5
Total (MSs 11)	781	54.5	781	0.4	781	0	725	52.3	781	41.4
Iceland	16	0	16	0	16	0	16	0	16	6.3
Norway	96	5.2	96	0	96	0	96	5.2	96	3.1
Switzerland	157	41.4	157	1.3	157	0	157	41.4	157	21.0

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.

 Table 28. Occurrence of resistance to selected antimicrobials in Campylobacter coli from broilers of Gallus gallus in countries reporting MIC data in 2013, using harmonised ECOFFs

Country	Cipro	loxacin	Erythr	omycin	Gent	amicin	Nalidi	xic acid	Tetrac	cyclines
Country	Ν	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Austria	31	48.4	31	3.2	31	0	31	48.4	31	83.9
Czech Republic	19	89.5	19	0	19	0	19	78.9	19	47.4
France	71	64.8	71	8.5	71	0	71	64.8	71	93.0
Germany	16	81.3	16	0	16	0	16	81.3	16	68.8
Hungary	51	92.2	51	0	51	0	-	-	51	52.9
Netherlands	83	48.2	83	16.9	83	0	83	48.2	83	45.8
Spain	68	94.1	68	42.6	68	13.2	68	91.2	68	98.5
United Kingdom	33	42.4	33	3.0	33	0	33	42.4	33	54.5
Total (MSs 8)	372	68.8	372	13.7	372	2.4	321	63.9	372	70.4
Switzerland	11	54.5	11	9.1	11	0	11	54.5	11	27.3

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.

Comparison of resistance in broilers and meat from broilers

Considering individual MSs, the levels of ciprofloxacin and tetracycline resistance in *C. coli* and *C. jejuni* isolates from meat from broilers tended to parallel the values obtained for isolates from broilers, usually at slightly lower levels. Generally, resistance levels to antimicrobials were higher in *C. coli* than in *C. jejuni* both for broilers and for meat from broilers.





Figure 35. Trends in ciprofloxacin, erythromycin and nalidixic acid resistance in <u>Campylobacter jejuni</u> from <u>Gallus gallus</u> in reporting MSs and non-MSs, 2007–2013, quantitative data



MSs: Member States.

A statistically significant increasing trend over five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for both ciprofloxacin and nalidixic acid in Austria (\uparrow), Denmark (\uparrow), France (\uparrow), Spain (\uparrow) and Switzerland (\uparrow); and for nalidixic acid in the Czech Republic (\uparrow), Finland (\uparrow) and Hungary (\uparrow). A statistically significant decreasing trend over five or more years for erythromycin was observed in Germany (\downarrow), Hungary (\downarrow) and the Netherlands (\downarrow).

Figure 36. Trends in ciprofloxacin, erythromycin and nalidixic acid resistance in <u>Campylobacter coli</u> from <u>Gallus gallus</u> in reporting MSs and one non-MS, 2007–2013, quantitative data



MSs: Member States.

A statistically significant trend over five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for both ciprofloxacin and nalidixic acid in Austria (\uparrow), Spain (\uparrow), Switzerland (\uparrow) and the Netherlands (\downarrow). A statistically significant trend over five or more years for erythromycin was observed in Spain (\uparrow) and Hungary (\downarrow).



Figure 37. Spatial distribution of ciprofloxacin resistance among Figure 38. Spatial distribution of erythromycin resistance among Campylobacter jejuni from broilers of Gallus gallus in countries reporting MIC data in 2013^(a)

Campylobacter jejuni from broilers of Gallus gallus in countries reporting MIC data in 2013^(a)



MSs: Member States.

Percentages shown on these maps refer to countries that reported quantitative MIC data for more than 10 isolates in 2013. When quantitative 2013 data were not available, 2012 data have been used instead.

(a): For Romania and Sweden, 2012 data were used.



Multi-drug resistance among Campylobacter jejuni and Campylobacter coli isolates from broilers

The 2013 isolate-based data on resistance in *C. jejuni* and *C. coli* isolates from broilers, reported by nine MSs and two non-MSs, and seven MSs and one non-MS, respectively, were analysed for MDR. A large variation in the levels of complete susceptibility to the common set of antimicrobials for *Campylobacter* (five antimicrobials) was observed among the reporting countries. Complete susceptibility was generally found in more than 10.0 % of the *C. jejuni* isolates tested in the reporting MSs, and reached up to 100 % in Finland and 90.6 % in Norway, while in the Czech Republic, Hungary and Spain, the proportion of fully susceptible isolates was much lower (under 15.0 %). In *C. coli*, complete susceptibility was generally lower than that observed in *C. jejuni*.

MDR was not recorded or was detected at levels lower than 5.0 % in *C. jejuni* isolates in most reporting countries, while in Hungary and Spain 10.7 % and 6.9 % of isolates exhibited MDR, respectively (Table MDR21). In *C. coli*, the occurrence of MDR was greater than that reported in *C. jejuni* isolates (Table MDR22). The frequency distributions of the numbers of antibiotics to which individual isolates were resistant (Figure 39 and Figure 40) showed variation between different reporting countries. Most of the reporting countries detected resistance to a maximum of three antimicrobial classes in *C. jejuni* (Figure 39), whereas multi-resistant *C. coli* isolates generally displayed resistance to three to five different classes of antimicrobials (Figure 40).

The co-resistance¹³ important for public health, i.e. resistance to both ciprofloxacin and erythromycin, was undetected in *C. jejuni* from most (nine out of 11) reporting MSs; two countries reported such co-resistance at a low level of less than 3.0 % of *C. jejuni* isolates, resulting in an overall co-resistance in *C. jejuni* of 0.5 %. In *C. coli* isolates, co-resistance to ciprofloxacin and erythromycin was detected in five out of eight reporting countries, with Spain reporting the highest occurrence in 42.6 % of isolates; resulting in an overall co-resistance in *C. coli* of 12.3 %.

Patterns of multi-drug resistance in Campylobacter jejuni and Campylobacter coli isolates from broilers

Considering *C. jejuni*, isolate-based data were available from nine contributing MSs and two non-MSs, which in total reported details of 835 isolates. The isolates reported by the Czech Republic (N=36), Finland (N=76), Germany (N=40), the United Kingdom (N=61) and Norway (N=96) are not addressed in this Table MDRP38, as they were not multi-resistant. Considering *C. coli*, analysis of the patterns of resistance to erythromycin, ciprofloxacin, tetracyclines, streptomycin and gentamicin was possible for 300 *C. coli* isolates from seven contributing MSs and one non-MS, which provided isolate-based data.

Among the 835 *C. jejuni* isolates from broilers from the reporting group of MSs submitting isolate-based data, 2.0 % (n=17) exhibited MDR (Table <u>MDRP38</u>). The most common pattern of MDR was resistance to ciprofloxacin, tetracyclines and streptomycin, occurring in 14 out of 17 resistant isolates (and constituting the core resistance pattern in a further two isolates, which also showed erythromycin resistance) reported by submitting MSs. The situation differed in *C. coli* (Table <u>MDRP37</u>), where 25.3 % of all isolates for which isolate-based data were available (N=300) exhibited MDR and 2.7 % of these *C. coli* isolates showed MDR to all of the antimicrobials in the test panel.

The proportion of isolates of *C. jejuni* from broilers showing MDR and the diversity of MDR within that multiresistant population were lower than in *C. coli* from broilers. The proportion of *C. coli* isolates from broilers showing resistance to all antimicrobials in the panel (2.7 %) was lower than that in *C. coli* isolates from pigs which showed an identical pattern of resistance (3.4 %).

The most common MDR pattern detected in *C. coli* isolates from broilers was resistance to ciprofloxacin, tetracyclines and streptomycin occurring in 12.7 % of all *C. coli* isolates. This pattern of resistance, together with additional erythromycin resistance, occurred in 4.7 % of isolates, while a further 5.0 % of isolates demonstrated resistance to ciprofloxacin, erythromycin and tetracyclines. These three patterns accounted for more than 80.0 % of the multi-resistant isolates detected. Gentamicin resistance, as a component of MDR patterns, was observed only in Spain. Spain contributed isolates with a greater range of different resistance patterns than other MSs, although this may have merely reflected the small isolate sample size from other MSs.

¹³ The term co-resistance has been defined as two or more resistance genes which are genetically linked, i.e. located adjacent or close to each other on a mobile genetic element (Chapman, 2003). For brevity, the term is used slightly more loosely in this report and indicates two or more phenotypic resistances to different classes of antimicrobials, exhibited by the same bacterial isolate.



Figure 39. Frequency distribution of Campylobacter jejuni isolates Figure 40. Frequency distribution of Campylobacter coli isolates completely susceptible and resistant to one to five antimicrobials in broilers in MSs and non-MSs reporting isolate-based data, 2013

completely susceptible and resistant to one to five antimicrobials, in broilers in MSs and one non-MS reporting isolate-based data, 2013





MSs: Member States.

N: total number of isolates tested for susceptibility against the whole common antimicrobial set for Campylobacter; sus: susceptible to all antimicrobial substances of the EFSA common set for Campylobacter; res1-res5: resistance to one to five antimicrobial substances of the common set for Campylobacter.



3.2.2.3. Antimicrobial resistance in Campylobacter isolates from pigs

Representative sampling and monitoring

In the reporting MSs, antimicrobial resistance monitoring in *Campylobacter* isolates from pigs was based primarily on active monitoring plans involving random sampling of healthy pig carcases at the slaughterhouse. Hungary did not report the sampling context. The sampling plan was typically stratified per slaughterhouse, by allocating the number of samples collected per slaughterhouse in proportion with the annual throughput of each slaughterhouse. An approximately equal distribution of the collected samples over the year enabled the different seasons to be covered. Only one representative faecal sample per epidemiological unit (batch/farm), either derived from a unique carcase or pooled from a number of carcases, was gathered to account for clustering, in accordance with EFSA's recommendations (EFSA, 2007).

In the reporting MSs, antimicrobial resistance monitoring in *Campylobacter* spp. in pigs primarily focused on *C. coli*, as this is the more prevalent.¹⁴ *Campylobacter* species in pigs. In some reporting countries, representative subsets of *C. coli* isolates recovered from faecal samples were randomly selected at the laboratory for susceptibility testing, whereas, in others, all *C. coli* isolates were tested for susceptibility.

Resistance levels among Campylobacter coli isolates from pigs

For 2013, quantitative data were provided by six MSs and one non-MS (Switzerland) on *C. coli* isolates from pigs (Table 29). As seen in previous years, the range of resistance to the antimicrobials studied varied greatly between the reporting countries in 2013. However, in general, the levels of resistance to tetracyclines observed were high to extremely high, while those to nalidixic acid, ciprofloxacin and erythromycin were moderate to high. Exceptions to this general pattern of resistance to these substances were observed for isolates from Finland, which reported the lowest occurrence of resistance (at low to moderate levels), and Spain, which recorded the highest resistance, at levels classed as extremely high. Another exception to this general pattern of resistance to ciprofloxacin, erythromycin and nalidixic acid. In contrast, gentamicin resistance was either undetected or reported at a low level. Only Spain recorded a moderate resistance to gentamicin.

Table 29. Occurrence of resistance to selected antimicrobials in <u>Campylobacter coli</u> from <u>pigs</u> in countries reporting MIC data in 2013, using harmonised ECOFFs

Country	Cipro	floxacin	Eryth	omycin	Gent	amicin	Nalidi	xic acid	Tetrac	cyclines
Country	Ν	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Finland	131	18.3	131	2.3	131	0	131	19.1	131	0
France	94	47.9	94	28.7	94	0	94	47.9	94	90.4
Hungary	60	51.7	60	15.0	60	1.7	_	_	60	93.3
Netherlands	214	6.1	214	7.0	214	0.5	214	8.4	214	85.0
Spain	108	93.5	108	58.3	108	11.1	108	93.5	108	98.1
United Kingdom	141	13.5	141	27.0	141	0	141	15.6	141	79.4
Total (MSs 6)	748	31.1	748	20.7	748	1.9	688	30.7	748	72.3
Switzerland	226	38.1	226	12.4	226	0.4	226	38.5	226	29.2

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.

¹⁴ Because of the very low *C. jejuni* prevalence in pigs, the number of samples required to be collected to achieve a sufficient number of *C. jejuni* isolates would have been too large to be cost effective.



Temporal trends in resistance among Campylobacter coli isolates from pigs

Five MSs and one non-MS provided resistance data on five years or more to be included in the statistical analysis. The trends in antimicrobial resistance observed in *C. coli* from pigs from 2007 to 2013 (Figure 41) show that, for most of the antimicrobials considered, levels of resistance have remained relatively stable. For ciprofloxacin, a statistically significant decreasing trend was seen for Hungary, while France and the Netherlands reported significantly decreasing levels of resistance to erythromycin over the reporting period.





A statistically significant decreasing trend over five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for ciprofloxacin in Hungary (\downarrow), and for erythromycin in France (\downarrow) and the Netherlands (\downarrow).

Spatial distribution of resistance among Campylobacter coli isolates from pigs

The spatial distributions of ciprofloxacin and erythromycin resistance in *C. coli* isolates from pigs (Figure 43 and Figure 44) show that the highest levels of resistance to these substances were reported by southern European countries, while northern European countries reported lower levels.

Multi-resistance among Campylobacter coli isolates from pigs

For 2013, three MSs and one non-MS reported isolate-based data on resistance in *C. coli* isolates from pigs. Isolates exhibiting complete susceptibility accounted for around or less than 1.0 % of isolates in France, Hungary and Spain, while, in Switzerland, they accounted for 13.3 % (Table <u>MDR23</u>). Conversely, MDR was moderate in Switzerland (17.7 %) and was high in Hungary (41.7 %), France (50.0 %) and Spain (88.0 %). The frequency distributions (Figure 42) showed an important diversity between the reporting countries. All countries reported isolates displaying resistance to up to four or five different classes of antimicrobials. In addition, a high proportion of isolates showing co-resistance to ciprofloxacin and erythromycin was observed in isolates from Spain, and overall the co-resistance was at 19.5 %.



Figure 42. Frequency distribution of <u>Campylobacter coli</u> isolates completely susceptible and resistant to one to five antimicrobials, in <u>fattening pigs</u> in MSs and one non-MS reporting isolate-based data, 2013



N: total number of isolates tested for susceptibility against the whole common antimicrobial set for *Campylobacter*; sus: susceptible to all antimicrobial substances of the EFSA common set for *Campylobacter*; res1–res5: resistance to one to five antimicrobial substances of the common set for *Campylobacter*.

Patterns of multi-drug resistance in Campylobacter coli isolates from fattening pigs

Isolate-based data were available for 488 *C. coli* isolates from fattening pigs, provided by three reporting MSs and one non-MS, and of these 207 (42.4 %) exhibited MDR (Table <u>MDRP37</u>). The most common MDR pattern observed in fattening pigs was resistance to ciprofloxacin, tetracyclines and streptomycin, occurring in 18.9 % of the total number of isolates for which isolate-based data were available. The next most common pattern of MDR was resistance to the above-mentioned antimicrobials, together with resistance to erythromycin. Taken together, these patterns of resistance accounted for more than 70.0 % of the total multi-resistant *C. coli* isolates from pigs. The range of MDR patterns observed in *C. coli* from pigs was greater than that observed in broilers and, unlike in broilers, gentamicin resistance, as part of the MDR pattern, was observed in three of four reporting MSs, albeit in single isolates in two contributing MSs. Most (>85.0 %) multi-resistant *C. coli* isolates from pigs were resistant to gentamicin were also resistant to streptomycin. Resistance to ciprofloxacin and tetracyclines was observed in more than 90.0 % of the multi-resistant *C. coli* isolates from pigs.





Figure 43. Spatial distribution of <u>ciprofloxacin</u> resistance among <u>Campylobacter coli</u> from <u>pigs</u> in countries reporting MIC data in 2013^(a)

Figure 44. Spatial distribution of <u>erythromycin</u> resistance among <u>Campylobacter coli</u> from <u>pigs</u> in countries reporting MIC data in 2013^(a)



MSs: Member States.

Percentages shown on these maps refer to countries that reported quantitative MIC data for more than 10 isolates in 2013. When quantitative 2013 data were not available, 2012 data have been used instead.

(a): For Denmark, 2012 data were used.

3.2.2.4. Antimicrobial resistance in *Campylobacter* isolates from cattle (bovine animals)

Representative sampling and monitoring

In 2013, antimicrobial resistance data in *C. jejuni* isolates from cattle were derived from samples collected at the slaughterhouse (Croatia, Denmark and Sweden). Two MSs (Germany and Spain) did not report information about the sampling stage. Different production types and ages of cattle, including calves and meat-production animals, have been tested; Denmark reported an unspecified type of cattle tested. Sampling programmes were randomised over the year and stratified by the number of slaughtered animals by slaughterhouse across the MSs. The sampling was evenly distributed throughout the year or a significant part of the year to account for a possible seasonal effect. Only one caecal/faecal sample per bovine animal carcase was collected. In the reporting MSs, antimicrobial resistance monitoring in *Campylobacter* spp. in cattle focused on *C. jejuni*, as this is the more prevalent *Campylobacter* species in cattle. In some reporting countries, representative subsets of *Campylobacter* isolates recovered from animal samples were randomly selected at the laboratory for susceptibility testing, while, in others, all isolates were tested for susceptibility.

Resistance levels among Campylobacter jejuni isolates from cattle

For 2013, five MSs provided quantitative data on *C. jejuni* isolates from cattle (Table 30). *C. jejuni* isolates tested were derived from calves of less than one year of age (Croatia, Sweden), meat-production animals (Germany and Spain) and cattle of production type unspecified (Denmark). Like in 2012, the range of resistance to the antimicrobials studied varied greatly between the reporting countries in 2013. The levels of resistance to ciprofloxacin, nalidixic acid and tetracyclines were generally high, while resistance to erythromycin and gentamicin was either not detected or recorded at low to very low levels.

Table 30. Occurrence of resistance to selected antimicrobials inCampylobacter jejunifrom cattle incountries reporting MIC data in 2013, using harmonised ECOFFs

Country	Cipro	iloxacin	Erythr	omycin	Gent	amicin	Nalidi	xic acid	Tetrac	cyclines
Country	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Croatia	62	35.5	_	_	62	0	62	37.1	62	22.6
Denmark	86	20.9	86	0	86	0	86	22.1	86	3.5
Germany	66	39.4	66	0	66	0	66	36.4	66	36.4
Spain	101	62.4	101	4.0	101	2.0	101	61.4	101	77.2
Sweden	109	21.1	109	0	109	1.8	109	22.9	109	6.4
Total (MSs 5)	424	35.8	362	1.1	424	0.9	424	36.1	424	29.7

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.

Temporal trends in resistance among Campylobacter jejuni isolates from cattle

Three MSs provided resistance data on five years or more to be included in the statistical analysis. The temporal trends in resistance in *C. jejuni* from cattle show that, as seen in *C. coli* in pigs, the levels of resistance in *C. jejuni* in cattle remained relatively stable from 2007 to 2013for individual MSs (Figure 45). In general, resistance to ciprofloxacin, nalidixic acid and tetracyclines was higher than resistance to erythromycin and gentamicin for the reporting MSs. When considering trends in ciprofloxacin, nalidixic acid and erythromycin resistance, no significant changes were observed over the reporting period.

Multi-drug resistance among Campylobacter jejuni isolates from cattle

In 2013, four MSs reported isolate-based data on resistance in *C. jejuni* isolates from differing cattle populations (Table <u>MDR24</u>). Differences in the cattle populations monitored probably explain at least some of the variability observed in the summary indicators of MDR among reporting countries. Denmark and Sweden recorded high levels of complete susceptibility and did not observe any multi-resistant *C. jejuni* isolates. Other reporting countries (Germany, Spain) detected isolates displaying reduced susceptibility to three or five different classes of antimicrobials (Figure 46). In addition, four isolates exhibited co-resistance to both ciprofloxacin and erythromycin, resulting in an overall co-resistance rate of 1.1 %.

Figure 45. Trends in ciprofloxacin, erythromycin and nalidixic acid resistance in <u>Campylobacter jejuni</u> from <u>cattle</u> in reporting MSs, 2007–2013, quantitative data



No statistically significant trends over five or more years were observed in the reporting countries.





N: total number of isolates tested for susceptibility against the whole common antimicrobial set for *Campylobacter*; sus: susceptible to all antimicrobial substances of the EFSA common set for *Campylobacter*; res1–res5: resistance to one to five antimicrobial substances of the common set for *Campylobacter*.

Patterns of multi-drug resistance in Campylobacter jejuni isolates from cattle

Isolate-based data were available for 362 *C. jejuni* isolates submitted by four reporting countries. Denmark and Sweden reported isolate-based data but did not detect MDR in the *C. jejuni* isolates from cattle tested. In the remaining reporting countries (Germany and Spain), the most common pattern of MDR was resistance to ciprofloxacin, tetracyclines and streptomycin, occurring in 44.0 % of multi-resistant isolates (Table MDRP38) and this formed the core resistance pattern in most (eight out of nine) multi-resistant isolates. Gentamicin resistance was detected in multi-resistant isolates of *C. jejuni* from cattle in Spain.

3.2.2.5. Overview of the findings on antimicrobial resistance in *Campylobacter*, 2013

The resistance at the reporting MS group level and the variability in the occurrence of resistance among reporting countries are shown in Figure 47 based on the quantitative data submitted in 2013 for the various animal species and meat derived from those animal species. These data may derive from different MS groups, which should be considered when interpreting the figure. As was the case in previous years, *C. coli* isolates tended to be more resistant than *C. jejuni* isolates. Direct comparisons of the levels of resistance in *Campylobacter* from *Gallus gallus* and in broiler meat may not be entirely appropriate using data combined from several countries to provide a summary figure, because different MSs have reported different proportions of isolates tested from meat and live fowl. The levels of resistance sometimes differ between different MSs and the relative contribution of individual MSs can affect the summary group level figures.



Figure 47. Occurrence of resistance to selected antimicrobials in <u>Campylobacter jejuni</u> and <u>Campylobacter coli</u> from fowl, pigs and cattle at reporting MS group level in 2013

MSs: Member States.

3.2.3. Discussion

For 2013, information on antimicrobial resistance in *Campylobacter* isolates from human cases of campylobacteriosis was collated from 14 MSs and two non-MSs (Iceland and Norway). The data submitted by these countries represented isolates from 15.0 % of the human campylobacteriosis cases reported within the EU/EEA in 2013.

There was some variation with regard to the number of antimicrobials tested among the reporting countries. **Erythromycin** and **ciprofloxacin** were the antimicrobials for which the greatest numbers of AST data of human *Campylobacter* spp. were reported. The proportion of human *C. jejuni* isolates resistant to erythromycin was overall low, but moderately high in *C. coli*, although the number of tested isolates for this bacterial species was small. Very high resistance levels to ciprofloxacin were reported in human *Campylobacter* isolates. This is of direct public health significance. The level of acquired resistance to fluoroquinolones in *C. jejuni* and *C. coli* in some MSs is so high that this agent can no longer be considered appropriate for routine empirical treatment of human *Campylobacter* infection. Given the corresponding data on isolates of food or animal origin, with particularly high levels of resistance to fluoroquinolones in broilers, and the understanding that a large proportion of human campylobacteriosis infections comes from handling, preparation and consumption of broiler meat or can be attributed to the chicken reservoir as a whole (EFSA BIOHAZ Panel, 2010a), this is a compelling example of the direct impact of acquired antimicrobial resistance in food and animals on the availability of effective antimicrobial agents for the treatment of a human infection.



Human antimicrobial susceptibility data were available for all antimicrobials included in the **MDR** analysis from eight MSs and Norway for *C. jejuni* and from five MSs for *C. coli*. Overall, only one in three human *C. jejuni* isolates and one in six human *C. coli* isolates were fully susceptible to all antimicrobials. Just 1.5 % of *C. jejuni* and 12.6 % of *C. coli* exhibited MDR, meaning that they were clinically non-susceptible to at least three of the four different antimicrobial classes. It is important to emphasise that the 2013 data on MDR are not comparable to those reported in 2012 because of a change in the data analysis approach to focus on a limited range of antimicrobial agents of direct relevance to human health. The 2012 data considered resistance to a wider range of classes of antimicrobial agents and, therefore, the proportion of isolates multi-resistant to three or more agents was higher (EFSA and ECDC, 2014b). 'Clinical' co-resistance to the critically important antimicrobials ciprofloxacin and erythromycin was low in *C. jejuni* (1.7 %) and comparable to that observed in 2012 data. For *C. coli*, 4.1 % were co-resistant to the two primary agents used for treatment.

In order to assess the importance of **travel-associated infections**, antimicrobial resistance was also analysed based on the most likely country of infection reported. Human isolates acquired in Asia had the highest frequency of resistance to the antimicrobials tested, with the proportion of isolates resistant to ciprofloxacin being almost twice the proportion of isolates acquired within the EU/EEA. It is important to note, however, that the proportions of resistant isolates in some MSs are equal to or exceed those that appear to be associated with travel to Asia.

In terms of **data quality and comparability**, major improvements in harmonising data between countries and across sectors were made in this report. For the first time, countries could report measured values (quantitative AST data as opposed to interpreted categories) to ECDC and five countries were able to submit *Campylobacter* data in this way. These data were interpreted based on EUCAST ECOFF values, where available. With respect to categorical data, the categories of 'intermediate' and 'resistant' were combined in a 'non-susceptible' group. Alignment of interpretive criteria for the antimicrobial agents under consideration suggests that, with this approach, the ECOFF-based category of 'wild type' corresponds closely to the 'susceptible' category and the ECOFF-based category of 'non-wild type' corresponds closely to the 'nonsusceptible' category. Thus, this approach further improves the comparability of human and non-human data. For countries submitting categorical data, all but three had shifted to EUCAST criteria in 2013, which was a significant improvement compared with 2012.

For future reports, EFSA and ECDC hope that more countries will report measured values data. More harmonisation is also needed when it comes to the selection of isolates to test and report at the EU level, as, in many countries, the selection and the antimicrobials tested for a particular selection are not random and represent different fractions of all isolates identified in a country.

Like in 2012, isolates from cases notified as having been acquired while travelling abroad were excluded from any analysis other than the analysis of resistance in different geographical regions. The rationale for this is to facilitate assessment of the relationship between antimicrobial resistance in *Campylobacter* isolates from food and food-producing animals in an MS with antimicrobial resistance in human isolates of *Campylobacter* spp. in that MS. As imported or traded food, however, can constitute a large proportion of the food available in some countries, the relationship between resistance in food and food-producing animals and in the human population is complex.

The data relating to the susceptibility of *Campylobacter* of food and animal origin reported by MSs were, in general, well harmonised with almost all MSs adopting the EFSA guidelines and recommendations. The numbers of countries reporting qualitative data in 2013 increased compared with 2012 for *C. jejuni* and *C. coli* in broilers and for *C. coli* in pigs, although declined slightly for *C. jejuni* in cattle. Commission Implementing Decision 2013/652/EU sets out the requirements for monitoring resistance in *C. jejuni* in broilers and fattening turkeys in 2014 and should lead to comprehensive monitoring in these species; monitoring of *C. coli* in pigs and broilers is optional in 2014. Overall, levels of antimicrobial resistance in *Campylobacter* isolates from animals and food were similar to those observed in 2012. Considering all reporting MSs, ciprofloxacin resistance in *C. jejuni* from *Gallus gallus* and cattle was 54.5 % and 35.8 %, respectively, while in *C. coli* from *Gallus gallus* and pigs, it was 68.8 % and 31.1 %, respectively.

Among *Campylobacter* isolates from *Gallus gallus* and broiler meat, very high to extremely high levels of resistance to one or more antimicrobials were reported by a number of MSs, with the exception of some Nordic countries, as well as central and eastern European countries, particularly when using ECOFFs as interpretive criteria of reduced susceptibility or 'microbiological' resistance. For example, extremely high resistance rates to **ciprofloxacin** were detected, whether using ECOFFs or CBPs. The resistance rates observed in some reporting countries do not always seem to correlate well with the degree of usage of fluoroquinolones (SVARM, 2014). Over 2009–2011, the highest levels of resistance to quinolones and fluoroquinolones were in general detected in *Campylobacter* isolates from *Gallus gallus* or (in 2012) from

broiler meat. The position was similar in 2013, where resistance levels, considering all MSs, to ciprofloxacin in both *C. jejuni* and *C. coli* were higher in broilers and broiler meat than in *C. coli* from pigs or *C. jejuni* from cattle. In those MSs which reported resistance in *Campylobacter* isolates from both broiler meat and broilers, levels of resistance were mostly similar. The resistance exhibited by *C. jejuni* and *C. coli* isolates to ciprofloxacin and tetracyclines varied very widely between MSs; in the case of *C. jejuni* and erythromycin, resistance levels were generally low or non-existent, while, for *C. coli*, there was again a wide variation in levels or resistance at the MS level, irrespective of the source of the isolates.

This high level of ciprofloxacin resistance in Campylobacter from broiler meat is of particular concern, as the EFSA Panel on Biological Hazards (BIOHAZ), in its scientific opinion on the quantification of the risk of campylobacteriosis posed to humans by broiler meat, estimated that the handling, preparation and consumption of broiler meat may account for 20.0 % to 30.0 % of human campylobacteriosis cases, while 50.0 % to 80.0 % of cases may be attributed to the chicken (broiler) reservoir as a whole (EFSA BIOHAZ Panel, 2010a). In 2013, ciprofloxacin resistance in C. coli isolates from humans was 66.9 % for all contributing MSs (range: 36.0 %-94.3 %) and 31.1 % in pigs (range: 6.1 %-93.5 %). However, the picture is clearly complex in relation to the sources of human infections because these may be related to consumption of pig or poultry meat (as well as other sources). International trade also means that consumers may be exposed to meat produced in a number of different countries. Similar considerations apply when comparing resistance levels in humans and animals for other resistances. However, resistance to gentamicin in C. coli from humans, meat from broilers, broilers and pigs does show similarities at the MS level. While gentamicin resistance was reported in C. coli from Gallus gallus (13.2 %) and pigs (11.1 %) from Spain but was not reported in broilers (Austria, France), meat from broilers (Austria) or pigs (France), C. coli from human infections showed 15.1 %, 0 % and 14.3 % gentamicin resistance in Spain, Austria and France, respectively. However, Campylobacter strains from the broiler reservoir may also reach humans via routes other than food (e.g. the environment or by direct contact).

From 2007 to 2013, statistically significant increasing trends in ciprofloxacin and nalidixic acid resistance in *C. jejuni* from broilers were observed over five or more years in five reporting countries; this was also observed in *C. coli* from broilers in one reporting country. Considering *C. coli* from pigs, a statistically significant decreasing trend in ciprofloxacin resistance was observed in one MS.

Regarding resistance to erythromycin – a representative of the macrolides (commonly used in the treatment of human campylobacteriosis) - in all reporting MSs, erythromycin resistance in C. jejuni from Gallus gallus and cattle was 0.4 % and 1.1 %, respectively, while, in C. coli from Gallus gallus and pigs, resistance was 13.7 % and 20.7 %, respectively. This situation in which low to moderately high levels of resistance were registered is similar to that observed over the 2009 to 2012 period. In countries which reported results for C. coli from both pigs and Gallus gallus and C. jejuni from Gallus gallus, resistance to erythromycin has usually been highest in C. coli isolates from pigs and lower in the isolates from other sources, for each country, from 2009 to 2012. Similar results have also been observed in other studies in which macrolideresistant isolates of C. coli from food-producing animals have mainly been of porcine origin (Gibreel and Taylor, 2006). Erythromycin resistance showed increasing trends in C. coli from pigs in three countries and broilers in one country, while erythromycin resistance showed a decreasing trend in C. jejuni from broilers in two countries. The range of dilutions over which erythromycin is currently tested is limited and so an analysis of resistance at much higher levels was not possible from the current data. Particular resistance mutations have been associated with high-level erythromycin resistance and further evaluation of the resistance detected to erythromycin could include such an evaluation. This might be particularly relevant where resistance is already high, as a possible indication of ongoing high selective pressure.

Two MSs provided data on **MDR** for *C. coli* and *C. jejuni* from both humans and animals. Although a lack of harmonisation¹⁵ may preclude detailed direct comparison of the MDR figures in isolates from animals and humans, some trends are evident. The MSs with the higher proportion of MDR in broilers (in both *Campylobacter* spp.) also reported a high proportion of MDR in isolates from humans. Considering these two MSs, parallel trends are also evident for certain other resistance characteristics (for example gentamicin and erythromycin resistance, co-resistance to ciprofloxacin and erythromycin). In the MSs that provided the most comprehensive data among the reporting MSs, it is interesting that the figures for co-resistance to erythromycin and ciprofloxacin for *C. coli* isolates from humans are intermediate between those for broilers and pigs.

Campylobacter can develop resistance to several of the different antimicrobials in the common test panel by different mechanisms. Thus, resistance to ciprofloxacin and erythromycin in *Campylobacter* is usually the result of mutation with or without the additional action of efflux pumps (Piddock et al., 2003; Ge et al., 2005;

¹⁵ The antimicrobial substances included in the analysis of MDR in isolates from humans and animals and the interpretive thresholds of resistance, either CBPs or ECOFFs, have not yet been fully harmonised between both sectors.



Luangtongkum et al., 2009). However, the efflux pump CmeABC acting alone has been shown to confer a degree of resistance to erythromycin, ciprofloxacin and tetracyclines (Ge et al., 2005). Tetracycline resistance, which can therefore be related to CmeABC, was commonly shown in a United Kingdom study to be related to the presence of the tetracycline resistance gene *tet*(O) (Piddock et al., 2008), which encodes a protein promoting the release of tetracycline from its binding site (Connell et al., 2003). The existence of different resistance mechanisms conferring either resistance against the different individual compounds or resistance against combinations of compounds complicates the process of trying to infer the genotype from the phenotype and account for the multiple resistance patterns detected. Isolates of both *C. coli* and *C. jejuni,* from animals and humans,¹⁶ showed resistance to erythromycin, ciprofloxacin and tetracyclines, raising the possibility that CmeABC may have been responsible for or contributed to the observed pattern of resistance.

Gentamicin resistance in *Campylobacter* was uncommon in animal isolates, but where it did occur in multiple-resistant isolates of *C. coli* and *C. jejuni*, streptomycin resistance was usually also observed, with only one *C. coli* isolate from pigs proving the exception to this observation. Recently a cluster of aminoglycoside-modifying enzymes has been reported in *C. coli* from broiler chickens in China (Qin et al., 2012). The occurrence of isolates of *C. coli* and *C. jejuni*, resistant to both gentamicin and streptomycin, suggests that resistance genes to each of these aminoglycosides have been acquired by these multiple-resistant isolates. However, the results indicate that streptomycin and gentamicin resistance can occur independently of each other in at least some *C. coli* and *C. jejuni* isolates. The genomic island described by Qin et al. (2012) contained a truncated tetracycline resistance genes.

Streptomycin and tetracycline resistance were also very commonly associated with each other in multipledrug-resistant strains of both *C. coli* and *C. jejuni* in animals. Conjugative plasmids have been described in *C. jejuni*, which can carry clusters of aminoglycoside resistance genes (Nirdnoy et al., 2005), and *tet*(O) conferring tetracycline resistance either can be carried on a plasmid or may be chromosomally located (Piddock et al., 2008).

The molecular basis for the observed patterns of MDR was not reported for the isolates, but molecular investigation and characterisation of selected isolates, representative of particular patterns of importance or interest, would assist greatly in determining significance and assessing the potential for further dissemination through, for example, co-selection or the occurrence of conjugative plasmids.

3.3. Antimicrobial resistance in indicator Escherichia coli

Commensal indicator organisms, rather than pathogenic types of *E. coli*, such as enterotoxigenic *E. coli* (ETEC) or verotoxigenic *E. coli* (VTEC), are the target of the monitoring of indicator *E. coli*. Commensal *E. coli* is commonly chosen as an indicator of antimicrobial resistance in Gram-negative bacterium, as it is commonly present in animal faeces, is relevant to human medicine and can often acquire conjugative plasmids, which are resistance determinants transferred between enteric bacteria. Commensal *E. coli*, present in the intestines of farm animals, have a reservoir of resistance genes that can spread horizontally to zoonotic and other bacteria present in the food chain. The monitoring of antimicrobial resistance in indicator *E. coli*, isolated from either randomly selected healthy animals or carcases and meat derived thereof, and chosen to be representative of the general population, provides valuable data on the resistance occurring in that population. Determining the occurrence of resistance to antimicrobials in indicator *E. coli* provides data useful for investigating the relationship with the selective pressure exerted by the use of antimicrobials on the intestinal population of bacteria in food-producing animals. Indicator *E. coli* are also useful as representatives of the *Enterobacteriaceae* to monitor the emergence and changes in the proportion of bacteria possessing ESBLs.

In total, 13 MSs and two non-MSs (Norway and Switzerland) reported quantitative MIC data in commensal (indicator) *E. coli* isolates from animals in 2013 (Table <u>OVER5</u>). Four of these countries and Slovenia provided MIC data on isolates collected from food. Antimicrobial susceptibility data were interpreted using ECOFFs laid down in Decision 2013/652/EC to determine organisms exhibiting reduced susceptibility, i.e. showing 'microbiological' resistance (as opposed to 'clinical' resistance).¹⁷ For further information on antimicrobials tested by the reporting countries and the reported MIC distributions for *E. coli* in 2013, please refer to Table <u>MM8</u> and to the <u>submitted and validated MS data</u> published on the EFSA website, respectively.

¹⁶ Of the human *Campylobacter* isolates in 2013, 42 *C. jejuni* and 48 *C. coli* isolates were resistant to all these three substances (data not shown in the section).

¹⁷ Of particular note is that 'microbiological' resistance to ciprofloxacin was addressed using ECOFF Cip >0.064 mg/L in this report (see Section 3.3.5 'Discussion', for further details).



3.3.1. Antimicrobial resistance in indicator *Escherichia coli* isolates from meat

For 2013, four MSs and one non-MS (Norway) reported quantitative MIC data on *E. coli* isolates from meat from bovine animals, broilers (*Gallus gallus*) and pigs. As too few MSs reported isolate-based data on more than 10 isolates of indicator *E. coli* in food, tables and graphs on MDR are not presented in this report. Resistance to selected antimicrobials in indicator *E. coli* isolates from different kinds of meat is presented in Table 31.

Representative sampling and monitoring

The antimicrobial resistance data on indicator *E. coli* isolates from the four kinds of meat, reported by Denmark, Germany, Hungary, Slovenia and Norway, are mostly derived from active and representative monitoring programmes. Only one MS did not report details on either the sampling stages or the sampling design of meat samples. In Denmark, *E. coli* isolates originated from meat sampled at wholesale and retail outlets, collected randomly in all regions of the country and spread evenly throughout the year, in the framework of three centrally coordinated sampling plans corresponding to each kind of meat. In Slovenia, *E. coli* isolates originated from pig meat collected randomly in slaughterhouses.

Resistance levels in meat from broilers, meat from pigs and meat from bovine animals

Considering data on antimicrobial resistance from the reporting MSs, resistance levels to ampicillin, sulfonamides and tetracyclines were high in meat from broilers (at 56.6 %, 45.0 % and 37.2 %, respectively) and in meat from pigs (at 30.7 %, 29.7 % and 32.6 %, respectively), while slightly lower, and moderate, in meat from bovine animals (at 17.1 %, 14.6 % and 19.5 %, respectively). Resistance to these antimicrobials in meat from broilers was highly variable between the reporting MSs, ranging from 24.1 % to 73.9 % for ampicillin, from 18.1 % to 54.1 % for sulfonamides and from 11.2 % to 58.7 % for tetracyclines.

Conversely, resistance to chloramphenicol at the reporting MS group level was moderate at 12.8 %, ranging from 0 % to 17.0 % in meat from broilers, and was low in meat from pigs (8.0 %) and meat from bovine animals (7.3 %). Overall, gentamicin resistance was not detected in meat from bovine animals and was found at low levels in meat from pigs (1.4 %) and in meat from broilers (4.9 %).

Resistance to ciprofloxacin and nalidixic acid among reporting MSs was markedly high, at 41.8 % and 39.5 %, respectively, in meat from broilers compared with the low to very low levels recorded in meat from pigs and bovine animals. The overall level of resistance to cefotaxime across the reporting MSs was 9.1 % in meat from broilers and lower in meat from pigs and bovine animals at 3.6 % and 1.2 %, respectively.

Comparison of resistance among Escherichia coli isolates from meat and animals

Four MSs reported on antimicrobial resistance in meat, but they generally reported comparable resistance levels between meat and the corresponding source animal species. In Denmark, the resistance reported in isolates from broiler meat and pig meat is roughly similar to that recorded in isolates from broilers and pigs. Similarly, resistance in isolates from meat from cattle recorded in Denmark and Germany was roughly comparable to that reported in bovine animals in the same MSs (Table 31 and Table 36). Germany reported on isolates from meat-production animals and Denmark reported on isolates from an unspecified cattle type. Hungary, which reported data on meat and bovine animals (calves less than one year of age) recorded important differences; for instance, resistance to ampicillin in cattle meat was 43.5 % and in calves under one year of age was 2.0 %.

3.3.2. Antimicrobial resistance in indicator Escherichia coli isolates from animals

3.3.2.1. Antimicrobial resistance in indicator *Escherichia coli* isolates from domestic fowl (*Gallus gallus*)

In 2013, 10 MSs and one non-MS provided quantitative MIC data in indicator *E. coli* isolates from broilers, among which Poland also provided comparable data on laying hens (Table 32). Norway reported *E. coli* data on laying hens only. Where available, resistance data on broilers and laying hens are presented separately.

Representative sampling and monitoring

The majority of MSs collected indicator *E. coli* isolates as part of their national monitoring programmes of antimicrobial resistance. In all reporting countries except Norway, monitoring programmes were based on random sampling of carcases of healthy broilers at the slaughterhouse. Isolates were recovered from caecal contents in Austria, Croatia and France, from faeces in Spain and from cloacal swabs in Denmark and Switzerland. In Norway, indicator *E. coli* was isolated from faeces sampled from laying hen flocks on the farm.



Resistance levels among Escherichia coli isolates from Gallus gallus

Generally, the occurrence of resistance in *E. coli* isolates from **broilers** varied markedly between reporting countries. Resistance to ampicillin, streptomycin, sulfonamides and tetracyclines was high to very or extremely high in most reporting countries, with the exception of Denmark, which recorded low to moderate resistance to streptomycin and tetracyclines. Resistance to chloramphenicol ranged from low to high, with only Denmark reporting no resistance. The gentamicin resistance was reported at very low to low levels, with the exceptions of Germany and Spain, recording moderate and high resistance (11.1 % and 30.6 %, respectively).

Resistance to ciprofloxacin and nalidixic acid was generally high to very or extremely high among the reporting countries, with the exception of Denmark, which recorded low resistance to these substances. A side-by-side comparison of resistance to ciprofloxacin and nalidixic acid in each reporting country shows that similar levels of resistance to both antimicrobials were typically recorded. Resistance to cefotaxime was generally low in most reporting countries, although two MSs reported moderate levels of resistance.

Resistance levels in *E. coli* isolates from **laying hens** tested in Poland were half (or even lower than half) those reported in broilers, with the exception of sulfonamides. In Norway, the resistance was typically low for all antimicrobials tested.



Table 31. Occurrence of resistance to selected antimicrobials in indicator Escherichia coli from <u>meat</u> in countries reporting MIC data in 2013, using harmonised ECOFFs

Country	Amp	oicillin	Cefo	taxime	Chloram	phenicol	Cipro	floxacin	Gent	amicin	Nalidi	xic acid	Strept	omycin	Sulfor	amides	Tetrac	yclines
Country	Ν	% Res	N	% Res	N	% Res	N	% Res	Ν	% Res	Ν	% Res	N	% Res	N	% Res	N	% Res
Meat from bro	ilers (G	allus gall	us)	•								•						
Denmark	116	24.1	116	1.7	116	0	116	5.2	116	0	116	5.2	116	9.5	116	18.1	116	11.2
Germany	440	62.0	440	8.6	440	17.0	440	45.2	440	5.9	440	43.2	440	51.1	440	54.1	440	42.0
Hungary	46	73.9	46	8.7	46	10.9	46	80.4	46	8.7	46	76.1	46	23.9	46	43.5	46	58.7
Slovenia	54	66.7	54	29.6	54	7.4	54	59.3	54	3.7	54	51.9	54	18.5	54	29.6	54	35.2
Total (MSs 4)	656	56.6	656	9.1	656	12.8	656	41.8	656	4.9	656	39.5	656	39.2	656	45.0	656	37.2
Meat from turk	(eys																	
Norway	154	23.4	154	0	154	2.6	154	1.3	154	0.6	154	1.3	_	_	154	5.2	154	17.5
Meat from pige	S										-				-			
Denmark	93	26.9	93	1.1	93	6.5	93	1.1	93	0	93	1.1	93	44.1	93	34.4	93	34.4
Hungary	12	50.0	12	0	12	16.7	12	25.0	12	0	12	8.3	12	25.0	12	25.0	12	50.0
Slovenia	35	34.3	35	11.4	33	9.1	35	14.3	35	5.7	33	6.1	33	15.2	33	18.2	33	21.2
Total (MSs 3)	140	30.7	140	3.6	138	8.0	140	6.4	140	1.4	138	2.9	138	35.5	138	29.7	138	32.6
Meat from bov	ine aniı	nals																
Denmark	24	4.2	24	0	24	4.2	24	0	24	0	24	0	24	4.2	24	4.2	24	4.2
Germany	35	8.6	35	2.9	35	2.9	35	2.9	35	0	35	2.9	35	17.1	35	14.3	35	20.0
Hungary	23	43.5	23	0	23	17.4	23	0	23	0	23	0	23	26.1	23	26.1	23	34.8
Total (MSs 3)	82	17.1	82	1.2	82	7.3	82	1.2	82	0	82	1.2	82	15.9	82	14.6	82	19.5

MSs; Member States N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.



Table 32. Occurrence of resistance to selected antimicrobials in indicator Escherichia coli from <u>Gallus gallus</u> in countries reporting MIC data in 2013, using harmonised ECOFFs

Country	Ampicillin		Cefotaxime		Chloramphenicol		Ciprofloxacin		Gentamicin		Nalidixic acid		Streptomycin		Sulfonamides		Tetracyclines	
	N	% Res	N	% Res	Ν	% Res	N	% Res	N	% Res	Ν	% Res	N	% Res	Ν	% Res	N	% Res
All Gallus gallus																		
Austria	146	38.4	146	2.1	146	5.5	146	65.1	146	2.1	146	62.3	146	34.9	146	38.4	146	22.6
Belgium	234	84.6	234	10.3	234	32.5	234	74.8	234	5.1	234	70.5	234	73.9	234	69.7	234	60.3
Croatia	150	63.3	150	18.0	150	14.7	150	88.7	150	4.0	150	85.3	150	53.3	150	61.3	150	56.0
Denmark	125	25.6	125	0.8	125	0	125	6.4	125	0	125	3.2	125	8.0	125	26.4	125	15.2
France	193	57.5	193	6.2	193	6.7	193	42.5	193	1.0	193	42.0	193	36.8	193	49.2	193	65.8
Germany	599	58.1	599	5.0	599	18.7	599	47.7	599	8.3	599	45.7	599	54.4	599	52.3	599	35.2
Hungary	152	44.1	152	6.6	152	9.9	152	68.4	152	2.0	152	63.2	152	23.7	152	33.6	152	37.5
Netherlands	494	42.5	494	2.6	494	10.1	494	42.1	494	4.7	494	41.5	494	45.1	494	37.9	494	35.8
Poland	343	59.2	343	5.2	343	16.0	319	62.7	343	5.0	343	53.4	343	33.5	245	21.2	343	46.1
Spain	170	70.0	170	15.9	170	15.3	170	83.5	170	30.6	170	81.2	170	62.9	170	50.6	170	64.1
Total (MSs 10)	2,606	55.2	2,606	6.3	2,606	14.5	2,582	55.5	2,606	6.4	2,606	52.4	2,606	45.7	2,508	45.0	2,606	42.8
Norway	186	9.1	186	0	186	0.5	186	0.5	186	2.2	186	0.5	-	_	186	11.3	186	7.0
Switzerland	189	25.4	189	0.5	189	1.1	189	35.4	189	0.5	189	34.4	189	15.3	189	27.0	189	23.8
Broilers																		
Austria	146	38.4	146	2.1	146	5.5	146	65.1	146	2.1	146	62.3	146	34.9	146	38.4	146	22.6
Belgium	232	85.3	232	10.3	232	32.8	232	75.4	232	5.2	232	71.1	232	74.6	232	70.3	232	60.8
Croatia	150	63.3	150	18.0	150	14.7	150	88.7	150	4.0	150	85.3	150	53.3	150	61.3	150	56.0
Denmark	125	25.6	125	0.8	125	0	125	6.4	125	0	125	3.2	125	8.0	125	26.4	125	15.2
France	193	57.5	193	6.2	193	6.7	193	42.5	193	1.0	193	42.0	193	36.8	193	49.2	193	65.8
Germany	434	69.8	434	5.1	434	25.3	434	53.5	434	11.1	434	51.4	434	70.0	434	67.3	434	41.7
Hungary	152	44.1	152	6.6	152	9.9	152	68.4	152	2.0	152	63.2	152	23.7	152	33.6	152	37.5
Netherlands	494	42.5	494	2.6	494	10.1	494	42.1	494	4.7	494	41.5	494	45.1	494	37.9	494	35.8
Poland	172	80.8	172	5.8	172	23.3	148	85.8	172	7.6	172	73.3	172	50.6	74	0	172	61.6
Spain	170	70.0	170	15.9	170	15.3	170	83.5	170	30.6	170	81.2	170	62.9	170	50.6	170	64.1
Total (MSs 10)	2,268	58.6	2,268	6.6	2,268	15.9	2,244	58.2	2,268	7.1	2,268	55.4	2,268	50.4	2,170	48.6	2,268	45.6
Switzerland	189	25.4	189	0.5	189	1.1	189	35.4	189	0.5	189	34.4	189	15.3	189	27.0	189	23.8
Laying hens																		
Poland	171	37.4	171	4.7	171	8.8	171	42.7	171	2.3	171	33.3	171	16.4	171	30.4	171	30.4
Norway	186	9.1	186	0	186	0.5	186	0.5	186	2.2	186	0.5	_	_	186	11.3	186	7.0

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.


Temporal trends in resistance among indicator Escherichia coli isolates from broilers of Gallus gallus

Temporal trends in resistance to selected antimicrobials in indicator *E. coli* isolates from broilers of *Gallus gallus* over the seven-year study period of 2007 to 2013 are displayed on Figure 48 and Figure 49. Four MSs provided resistance data on five years or more to be included in the statistical analysis. Marked discrepancies in resistance levels between reporting MSs was observed for many of the antimicrobials. Spain and the Netherlands tended to report the highest levels of resistance to most antimicrobials over the period, although Austria, Spain and the Netherlands recorded the highest resistance to quinolones between 2010 and 2013, and France, Spain and the Netherlands registered the highest resistance to tetracyclines from 2007 to 2013. Conversely, Denmark generally recorded the lowest resistance levels reported.

The resistance to ciprofloxacin reported over the study period was high to very high for all reporting countries, with the exception of Denmark for the whole period. A close similarity in resistance levels to ciprofloxacin and nalidixic acid was observed in most MSs (Figure 49). There was less variation between countries in the resistance to cefotaxime which, in most countries, was at a moderate or low level. However, although resistance levels in 2012 tended to generally be similar to those observed in 2011, there were a few exceptions; for example, in Poland (data not shown) and Switzerland, resistance to ampicillin and cefotaxime in broiler flocks increased from 2011 to 2012 and decreased in 2013. Such inter-annual evolutions need to be confirmed by longer term trends.

Although resistance to many of the antimicrobials were broadly stable or had shown only gradual increases or decreases over the study period, statistically significant trends in resistance to some of the antimicrobials over five or more years were discerned. France and Switzerland recorded significant increases in resistance to ampicillin, cefotaxime, ciprofloxacin and nalidixic acid, while, contrastingly, the Netherlands reported significant declines in resistance to ampicillin, cefotaxime, ciprofloxacin, nalidixic acid, streptomycin and tetracyclines and over the last four years.

Spatial distribution of resistance among indicator Escherichia coli from broilers of Gallus gallus

The spatial distributions of nalidixic acid and tetracycline resistance in *E. coli* from *Gallus gallus* are shown in Figure 50 and Figure 51. The Nordic countries reported the lowest levels of resistance to both antimicrobials. The highest resistance to tetracyclines tended to be reported by the most western countries, while the spatial pattern for nalidixic acid was less clear.



Figure 48. Trends in ampicillin, streptomycin and tetracyclines resistance in indicator Escherichia coli from broilers of Gallus gallus in reporting MSs and one non-MS, 2007–2013, quantitative data

2010 2012 2011 2009 2013 Austria Denmark France 80 60 40 % Resistant isolates 20 Netherlands Spain Switzerland 80 0 60 40 20 2003 2008 2009 2010 2011 2013 2010 2013 2002 2008 2009 2011 2012 AMP TET +++

Figure 49. Trends in cefotaxime, ciprofloxacin and nalidixic acid resistance in indicator Escherichia coli from broilers of Gallus gallus in reporting MSs and one non-MS, 2007–2013, quantitative data





Statistically significant increasing trends over five or more years, as tested by a logistic regression model ($p \leq 05$), were observed for cefotaxime, ciprofloxacin and nalidixic acid in France (\uparrow) and Switzerland (1). Statistically significant decreasing trends over five or more years were observed for cefotaxime, ciprofloxacin and nalidixic acid in the Netherlands (\downarrow) .



Figure 50. Spatial distribution of <u>nalidixic acid</u> resistance among indicator Escherichia coli from <u>broilers</u> of Gallus gallus in countries reporting MIC data in 2013



MSs: Member States.

Percentages shown on this map refer to countries that reported quantitative MIC data for more than 10 isolates in 2013.

Figure 51. Spatial distribution of <u>tetracycline</u> resistance among indicator Escherichia coli from <u>broilers</u> of Gallus gallus in countries reporting MIC data in 2013



MSs: Member States.

Percentages shown on this map refer to countries that reported quantitative MIC data for more than 10 isolates in 2013.



Multiple resistance among indicator Escherichia coli isolates from broilers

For 2013, seven MSs and one non-MS provided isolate-based data regarding resistance in indicator *E. coli* in broilers. Among the reporting countries, marked variations were observed in the percentages of completely susceptible isolates, which varied from 3.4 % in Belgium to 57.6 % in Denmark. Although all reporting countries recorded multi-resistant isolates, the proportion differed substantially between them, reaching up to 83.6 % in Belgium (Table MDR25). The frequency distributions (Figure 52) showed that isolates resistant to as many as five antimicrobials were reported from all reporting countries, and three MSs reported a few isolates resistant to nine substances. Co-resistance to cefotaxime and ciprofloxacin was either undetected or detected at low to very low levels in the MSs, when CBPs were applied (Table MDR25).





N: total number of isolates tested for susceptibility against the whole common antimicrobial set for *E. coli*; sus: susceptible to all antimicrobial substances of the EFSA common set for *E. coli*; res1–res9: resistance to one to nine antimicrobial substances of the common set for *E. coli*.

Multi-/co-resistance patterns among indicator Escherichia coli *isolates from broilers*

As expected, most isolates resistant to ciprofloxacin were also resistant to nalidixic acid when using ECOFFs as interpretive thresholds of resistance. One isolate from Austria and one isolate from Belgium were resistant to ceftazidime but not to cefotaxime; hence, they appear in Table 33, but not in Table CO2. Considering the resistance patterns of isolates co-resistant to ciprofloxacin and cefotaxime (71 isolates), a number of isolates (28 out of 71 or 39.0 %) were also resistant to sulfonamides, streptomycin and tetracyclines, with or without additional resistances. Trimethoprim resistance was also commonly observed in isolates co-resistant to ciprofloxacin and cefotaxime (71 isolates). A variety of resistance patterns (23) was observed in co-resistant isolates, each pattern occurring at a low frequency (less than 0.6 % of the total number of isolates). The most common pattern of co-resistance was resistance to ciprofloxacin, cefotaxime and ampicillin, occurring in 0.6 % of the total number of isolates and detected in five reporting countries. Analysing the occurrence of higher levels of resistance to ciprofloxacin in *E. coli* reveals marked differences between MSs (Table CO2); high-level ciprofloxacin resistance. A wide variety of resistance patterns was observed in high-level ciprofloxacin resistance was most frequently observed in countries with a high proportion of isolates showing 'microbiological' resistance. A wide variety of resistance patterns was observed in high-level ciprofloxacin resistant isolates, each pattern occurring at a low frequency (less than 0.6 % of resistance patterns).

R

R

R

R

R

R

R

R

R

Esch	erichia	a coli fi	rom <u>b</u>	<u>roilers</u> i	n MSs a	and one no	n-MS re	porting	solate	e-base	d data, I	2013		
Co-ı	resistai	nce pati	tern	Gro	oup of re countri (N=1,64	es	Austria (N=146)	Belgium (N=232)	Denmark (N=125)	France (N=193)	Germany (N=434)	Hungary (N=152)	Spain (N=170)	Switzerland (N=189)
cip	Ctx	Caz	Nal	n	%	Group %	n	n	n	n	n	n	n	n

90

0

3

0

0

1

94

141

21

2

0

0

1

165

4

0

0

0

0

0

4

73

6

6

0

0

0

85

213

9

11

0

2

0

235

88

0

0

8

0

0

96

114

23

3

1

0

0

141

63

1

0

0

0

0

64

Table 33. <u>Co-resistance</u> to fluoroquinolones and third-generation cephalosporins in indicator Escherichia coli from <u>broilers</u> in MSs and one non-MS reporting isolate-based data, 2013

Caz: ceftazidime; Cip: ciprofloxacin; Ctx: cefotaxime; N: total number of isolates tested for susceptibility against the whole common antimicrobial set for *E. coli* and multi-resistant; n: number of multi-/co-resistant isolates; Nal: nalidixic acid; R: minimum inhibitory concentration above EUCAST ECOFFs.

3.3.2.2. Antimicrobial resistance in indicator Escherichia coli isolates from pigs

Representative sampling and monitoring

R

R

R

R

R

R

R

R

Total

786

60

25

9

2

2

884

88.91

6.79

2.83

1.02

0.23

0.23

100

47.9

3.7

1.5

0.5

0.1

0.1

53.9

In 2013, 10 MSs and one non-MS (Switzerland) provided quantitative antimicrobial resistance data on indicator *E. coli* in pigs which were included in the following analysis (Table 34). These data were not split by production type, as isolates originated from either fattening pigs (seven MSs and one non-MS) or breeding animals (one MS) or the production type was not specified (two MSs). The majority of MSs collected isolates as part of their national monitoring programme of antimicrobial resistance, mostly based on random sampling of healthy slaughter pig carcases at the slaughterhouse. A two-stage stratified sampling design, with slaughterhouses as primary sampling units and carcases as secondary units, with proportional allocation of the number of samples to the annual throughput of the slaughterhouse, was typically applied in the reporting countries. The sample collection was approximately evenly distributed over the year. Only one representative faecal sample per epidemiological unit (batch), either derived from a unique carcase or pooled from a number of carcases, was gathered to account for clustering. Belgium, Hungary and Poland did not report detailed information on sampling stage, sample type or sampling context.

Resistance levels among indicator Escherichia coli isolates from pigs

In 2013, resistance to ampicillin in *E. coli* isolates from pigs was generally high among reporting MSs, ranging from 9.5 % to 76.5 %, while resistance to streptomycin, sulfonamides and tetracyclines was high to very high in all reporting countries, ranging from 18.4 % to 77.6 %, 13.7 % to 75.9 % and 23.5 % to 89.4 %, respectively. Conversely, resistance to chloramphenicol was low to moderate in most reporting countries, with the notable exception of Spain, Belgium and the United Kingdom, which reported high resistance, while gentamicin resistance was generally recorded at low to very low levels. Resistance to ciprofloxacin and nalidixic acid was low among almost all reporting countries, ranging between 0 % and 9.2 %, with the exception of Spain reporting a moderate level of resistance for nalidixic acid and a high level of resistance for ciprofloxacin. The resistance to cefotaxime was either not detected or reported at low levels in all reporting countries.

Temporal trends in resistance among indicator Escherichia coli isolates from pigs

Figure 53 and Figure 54 display the trends in resistance to selected antimicrobials in indicator *E. coli* from pigs from 2007 to 2013. Six MSs and one non-MS provided resistance data on five years or more to be included in the statistical analysis. There was variation in the resistance levels in different MSs, particularly for tetracyclines (Figure 53). However, the differences between MSs were often not as marked as was observed for isolates from *Gallus gallus*. Cefotaxime resistance has been below 5.0 % in all MSs since 2007, and at a lower level than in *Gallus gallus* (Figure 54). Resistance to both ciprofloxacin and nalidixic acid has also generally been at a low level since 2007 (Figure 54).

For many of the antimicrobials, the resistance levels were relatively stable with only minor fluctuations or gradual changes. There were fewer statistically significant trends than observed among isolates from *Gallus gallus*. Denmark reported significant increases in resistance to ampicillin and streptomycin, Spain

reported significant increases in resistance to ciprofloxacin and streptomycin, and Switzerland reported significant increases in resistance to cefotaxime. In contrast, the Netherlands reported significant declines in resistance to ampicillin, ciprofloxacin, nalidixic acid and tetracyclines, and France reported significant declines in resistance to streptomycin and tetracyclines.

Spatial distribution of resistance among indicator Escherichia coli isolates from pigs

The spatial distribution of nalidixic acid and tetracycline resistance in indicator *E. coli* from pigs is shown in Figure 55 and Figure 56, respectively. For nalidixic acid, most countries reported low levels of resistance so the spatial pattern was less clear. Figure 56 illustrates the variability in levels of tetracyclines resistance in *E. coli* across the EU and the absence of a clear spatial distribution.



Table 34. Occurrence of resistance to selected antimicrobials in indicator Escherichia coli from <u>pigs</u> in countries reporting MIC data in 2013, using harmonised ECOFFs

Country	Amp	oicillin	Cefo	otaxime	Chloram	phenicol	Cipro	floxacin	Gen	tamicin	Nalid	lixic acid	Strep	otomycin	Sulfo	namides	Tetra	cyclines
Country	Ν	% Res	N	% Res	N	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	N	% Res
Austria	150	17.3	150	1.3	150	5.3	150	4.0	150	2.0	150	2.0	150	56.7	150	28.7	150	52.7
Belgium	204	45.1	204	1.0	204	26.5	204	5.4	204	2.0	204	3.4	204	55.9	204	54.4	204	52.0
Denmark	146	29.5	146	0	146	5.5	146	1.4	146	2.1	146	1.4	146	41.8	146	37.0	146	34.9
Finland	315	9.5	315	0.6	315	1.0	315	1.9	315	1.0	315	1.3	315	18.4	315	13.7	315	23.5
France	196	26.0	196	0.5	196	18.9	196	4.6	196	2.0	196	3.6	196	53.1	196	53.6	196	64.3
Hungary	152	41.4	152	2.6	152	17.8	152	9.2	152	2.0	152	5.9	152	52.6	152	40.8	152	64.5
Netherlands	289	23.5	289	1.7	289	10.4	289	0	289	0.7	289	0	289	50.2	289	43.3	289	52.6
Poland	175	24.6	175	4.6	175	9.7	175	8.0	175	1.1	175	4.6	175	44.6	175	39.4	175	50.9
Spain	170	76.5	170	0.6	170	40.6	170	32.9	170	4.1	170	19.4	170	77.6	170	75.9	170	89.4
United Kingdom	157	29.9	157	0.6	157	21.7	157	1.3	157	2.5	157	1.3	157	49.0	157	51.6	157	66.9
Total (MSs 10)	1,954	30.3	1,954	1.3	1,954	14.7	1,954	6.1	1,954	1.8	1,954	3.8	1,954	47.8	1,954	42.1	1,954	52.8
Switzerland	183	18.0	183	1.1	183	6.6	183	4.9	183	2.2	183	4.4	183	47.0	183	38.8	183	33.9

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates.





Figure 53. Trends in <u>ampicillin</u>, <u>streptomycin</u> and <u>tetracyclines</u> resistance in indicator Escherichia coli from <u>pigs</u> in reporting MSs and one non-MS, 2007–2013, quantitative data

2010 2012 2013 2011 2008 2009 Austria Denmark Estonia 80 60 40 20 0 Netherlands Poland France % Resistant isolates 80 60 40 0 20 Λ Switzerland Spain 80 Δ Δ 60 40 + 20 0 2010 2011 2012 2013 2007 2008 2009 AMP TET +++

Statistically significant increasing or decreasing trends over five or more years, as tested by a logistic regression model ($p \le 05$), were observed in Denmark (\uparrow) for ampicillin and streptomycin; in France (\downarrow) for streptomycin and tetracyclines; in the Netherlands (\downarrow) for ampicillin and tetracyclines; and in Spain (\uparrow) for streptomycin.

Figure 54. Trends in <u>cefotaxime</u>, <u>ciprofloxacin</u> and <u>nalidixic acid</u> resistance in indicator Escherichia coli from <u>pigs</u> in reporting MSs and one non-MS, 2007–2013, quantitative data



Statistically significant increasing or decreasing trends over five or more years, as tested by a logistic regression model ($p \le 05$), were observed in the Netherlands (\downarrow) for ciprofloxacin and nalidixic acid; in Spain (\uparrow) for ciprofloxacin; in Poland (\downarrow) for nalidixic acid; and in Switzerland (\uparrow) for cefotaxime.



Figure 55. Spatial distribution of <u>nalidixic acid</u> resistance among indicator Escherichia coli from <u>pigs</u> in countries reporting MIC data in 2013



MSs: Member States.

Percentages shown on this map refer to countries that reported quantitative MIC data for more than 10 isolates in 2013.

Figure 56. Spatial distribution of <u>tetracycline</u> resistance among indicator Escherichia coli from <u>pigs</u> in countries reporting MIC data in 2013



MSs: Member States.

Percentages shown on this map refer to countries that reported quantitative MIC data for more than 10 isolates in 2013.



Multiple resistance among indicator Escherichia coli isolates from fattening pigs

Six MSs and one non-MS tested the harmonised set of nine antimicrobials for *E. coli* and reported isolatebased data. Around 30.0 %–40.0 % of the isolates tested were susceptible to the panel tested in three reporting countries, while the proportion was lower than 25.0 % in Hungary, France and Spain. In Finland, the majority of isolates (66.0 %) were fully susceptible. Levels of MDR (i.e. reduced susceptibility to three or more antimicrobial classes) ranged from moderate to extremely high in reporting countries (Table <u>MDR26</u>). The frequency distributions (Figure 57) showed that all reporting countries detected MDR to as many as six or seven antimicrobial classes. Very few isolates exhibited co-resistance to cefotaxime and ciprofloxacin using either ECOFFs or CBPs as interpretive criteria (Table <u>MDR26</u>).

Figure 57. Frequency distribution of Escherichia coli isolates completely susceptible and resistant to one to nine antimicrobials in <u>fattening pigs</u> in MSs and one non-MS reporting isolate-based data, 2013



N: total number of isolates tested for susceptibility against the whole common antimicrobial set for *E. coli*; sus: susceptible to all antimicrobial substances of the EFSA common set for *E. coli*; res1–res9: resistance to one to nine antimicrobial substances of the common set for *E. coli*.

Multi-/co-resistance patterns among indicator Escherichia coli isolates from fattening pigs

Indicator *E. coli* isolates resistant to cefotaxime and ciprofloxacin were observed in Spain and France, and streptomycin and tetracycline resistance was often present in the isolates tested (Table 35 and Table <u>MDRP41</u>). These additional resistances (together with trimethoprim resistance in some cases) were noted in *E. coli* isolates showing high-level ciprofloxacin resistance (Table <u>CO3</u>).

Table 35. Co-resistance to fluoroquinolones and third-generation cephalosporins in indicator Escherichia coli from <u>fattening pigs</u> in MSs and one non-MS reporting isolate-based data, 2013

Co	o-resista	nce patte	ərn	Group of reporting countries (N=1,312) n % Group %				Denmark (N=146)	Finland (N=315)	France (N=196)	Hungary (N=152)	Spain (N=170)	Switzerland (N=183)
ctx	Caz	Cip	Nal	n	%	Group %	n	n	n	n	n	n	n
R			R	60	88.24	4.6	3	2	4	6	9	28	8
	R	R		6	8.82	0.5	2	0	2	0	0	0	2
R	R	R	R	2	2.94	0.2	0	0	0	1	0	1	0
	Total				100	5.2	5	2	6	7	9	29	10

Caz: ceftazidime; Cip: ciprofloxacin; Ctx: cefotaxime; N: total number of isolates tested for susceptibility against the whole common antimicrobial set for *E. coli* and multi-resistant; n: number of multi-/co-resistant isolates; Nal: nalidixic acid; R: minimum inhibitory concentration above EUCAST ECOFFs.

3.3.2.3. Antimicrobial resistance in indicator *Escherichia coli* isolates from cattle (bovine animals)

Representative sampling and monitoring

In 2013, quantitative MIC data on indicator *E. coli* in cattle were provided by nine MSs and one non-MS (Switzerland) (Table 36). Different production types and ages of cattle, including calves, young cattle, meatproduction animals, adult cattle and dairy cows, were investigated; Denmark and Poland did not specify the type of cattle tested. The overall results for cattle presented in Table 36 include all isolates of *E. coli* that were collected from this animal species by MSs which tested more than 10 isolates from cattle in total. Results are also presented for the specific production levels of cattle from which these *E. coli* isolates originated.

Among the reporting MSs, antimicrobial resistance monitoring in indicator *E. coli* isolates from cattle was chiefly based on monitoring plans of healthy bovine animals randomly selected at the slaughterhouse (Austria, Denmark, Spain, Sweden and Switzerland). Indicator *E. coli* isolates were recovered from caecal contents in Austria and Sweden, from recto-anal swabs in Switzerland and from faeces in Denmark by sampling healthy cattle at slaughter. Belgium, Hungary and Poland did not report information on the sample type, sampling context and sampling stage.

Resistance levels among Escherichia coli isolates from cattle

The occurrence of resistance to ciprofloxacin, gentamicin and nalidixic acid was less common, with overall proportions at the reporting MS group level of 5.1 %, 2.0 % and 5.0 %, respectively. Four countries reported no resistance to cefotaxime, with the highest resistance levels being 5.7 % and 3.7 %, recorded by Poland and Belgium among unspecified production type and calves (under one year of age), respectively.

In indicator *E. coli* isolates from calves of less than one year of age, tested in Austria, Belgium, the Netherlands and Switzerland, resistance to ampicillin, streptomycin, sulfonamides and tetracyclines was generally high, while resistance to chloramphenicol and gentamicin was generally recorded at low to moderate and low levels, respectively. The occurrence of resistance to (fluoro)quinolones and third-generation cephalosporins was less common, as ciprofloxacin and nalidixic acid resistance was reported at low to moderate levels, while resistance to cefotaxime was low to very low. The resistance recorded by Hungary and that recorded by Sweden were generally at a lower level.

Austria which also submitted data concerning young cattle (aged one to two years) and adult cattle (over two years) reported lower resistance levels in these age groups than in calves of less than one year of age. The Netherlands reported much lower resistance among dairy cows, at around 1.0 %, than among veal calves.

Temporal trends in resistance among indicator Escherichia coli isolates from cattle

Figure 59 and Figure 60 display the trends in resistance to selected antimicrobials in *E. coli* from cattle. Five MSs and one non-MS provided resistance data on five years or more to be included in the statistical analysis. It should be noted that the figures presented for each country combine the results for all cattle production types and/or ages submitted each year. As in the other livestock species, the resistance levels varied substantially between MSs for several of the antimicrobials, including ampicillin, streptomycin and tetracyclines. Austria and Denmark reported the lowest levels of resistance for many of the antimicrobials.

Considering the previous years of reporting, the resistance levels reported by Denmark in 2012 and 2013 were broadly comparable. In Austria, since 2012, a new sampling strategy has been applied with one sampling plan for all age groups, with only one sampling plan for all cattle in the years before 2012; therefore, statistical trends were not calculated. Switzerland reported decreases in resistance to most antimicrobials between 2010 and 2012, which is most probably because the study population in 2010 was veal calves less than six months old whereas in 2011 older cattle (>12 months) were sampled. In 2013, calves of one year of age were tested; therefore, an increase of resistance was observed. Germany tested calves in 2009, 2010 and 2012 and beef cattle in 2011 and 2013. In Germany, resistance rates were much lower in 2011 and 2013 than in 2010 and 2012. However, in 2010 and 2012, veal calves were tested, while, in 2011 and 2013, young beef animals were tested, which usually differ in management and antimicrobial exposure.

Some countries, such as Austria, Denmark and the Netherlands, have shown relatively stable resistance levels or only minor fluctuations or trends since 2007, whereas other countries, such as Germany and Switzerland, have shown more substantial fluctuations in resistance levels that are, at least partially, due to the sampling of different cattle production types in different years. There have been numerous statistically significant trends in resistance levels since 2007; for example, the Netherlands showed significant declines in resistance to six of the antimicrobials. Significant increasing trends were observed in Denmark (ampicillin,



streptomycin and tetracyclines) and Switzerland (ampicillin, ciprofloxacin, nalidixic acid, streptomycin and tetracyclines).

Spatial distribution of resistance among indicator Escherichia coli isolates from cattle

The spatial distributions of nalidixic acid and tetracycline resistance among *E. coli* from cattle are shown in Figure 61 and Figure 62. With respect to nalidixic acid, the majority of countries reported low levels of resistance and no spatial pattern was evident. Nevertheless, there was still some evidence that the lowest resistance to tetracyclines occurred in northern European countries and the highest occurred in the southern and western European countries.

Multiple resistance among indicator Escherichia coli isolates from cattle

Seven MSs and one non-MS tested the complete harmonised set of antimicrobials for *E. coli* and reported isolate-based data. More than 70.0 % of the isolates tested were susceptible to the panel of nine antimicrobials tested in five reporting countries and the proportion was greater than 39.0 % in all reporting countries. In Sweden, 95.4 % of isolates were fully susceptible. Multiple resistance levels (i.e. reduced susceptibility to three or more antimicrobial classes) was lower than 50.0 % in all reporting countries and lower than 10.0 % in four reporting countries (Table MDR27). The frequency distributions (Figure 58) demonstrate the relatively high proportion of full susceptibility in several countries. Very few isolates from only one MS exhibited co-resistance to cefotaxime and ciprofloxacin using either ECOFFs or CBPs as interpretive criteria (Table MDR27). These co-resistant isolates displayed different resistance patterns, with no single pattern dominating. Although 'microbiological' resistance was infrequent in cattle (Table HLR12), occurring in 96 out of 1,660 isolates (5.8 %), 2.1 % or nearly half of the total number of isolates showed high-level ciprofloxacin resistance.

Figure 58. Frequency distribution of Escherichia coli isolates completely susceptible and resistant to one to nine antimicrobials in <u>cattle</u> in MSs and one non-MS reporting isolate-based data, 2013



N: total number of isolates tested for susceptibility against the whole common antimicrobial set for *E. coli*; sus: susceptible to all antimicrobial substances of the EFSA common set for *E. coli*; res1–res9: resistance to one to nine antimicrobial substances of the common set for *E. coli*.



	Ampi	cillin	Cefo	taxime	Chloramp	ohenicol	Ciprot	iloxacin	Gent	amicin	Nalidi	xic acid	Strept	tomycin	Sulfor	namides	Tetrac	cyclines
Country	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	N	% Res	N	% Res
All cattle																		
Austria	310	6.1	310	0.3	310	3.2	310	1.9	310	0.3	310	1.9	310	12.9	310	13.5	310	16.8
Belgium	406	41.6	406	3.7	406	25.4	406	18.0	406	7.4	406	18.2	406	42.1	406	51.2	406	49.0
Denmark	103	3.9	103	0	103	1.9	103	0	103	0	103	0	103	7.8	103	7.8	103	11.7
Germany	526	7.2	526	0.8	526	2.9	526	1.5	526	1.3	526	1.5	526	9.1	526	8.7	526	10.8
Hungary	51	2.0	51	0	51	2.0	51	3.9	51	2.0	51	3.9	51	9.8	51	21.6	51	9.8
Netherlands	588	13.8	588	0.2	588	7.3	588	4.6	588	0.9	588	4.8	588	16.3	588	17.7	588	27.2
Poland	172	4.7	176	5.7	172	2.9	172	2.9	172	0.6	172	1.7	172	8.7	172	14.0	172	8.1
Spain	170	16.5	170	0	170	13.5	170	2.9	170	3.5	170	2.9	170	33.5	170	37.1	170	47.6
Sweden	197	1.0	197	0	197	0	197	1.0	197	0	197	0.5	197	1.5	197	1.5	197	2.5
Total (MSs 9)	2,523	13.9	2,527	1.2	2,523	8.0	2,523	5.1	2,523	2.0	2,523	5.0	2,523	17.6	2,523	20.2	2,523	23.2
Switzerland	176	27.3	176	0	176	9.7	176	7.4	176	3.4	176	7.4	176	40.9	176	46.0	176	38.1
Calves (under 1	year)																	
Austria	151	10.6	151	0.7	151	4.6	151	2.6	151	0.7	151	2.6	151	21.2	151	22.5	151	25.8
Belgium	406	41.6	406	3.7	406	25.4	406	18.0	406	7.4	406	18.2	406	42.1	406	51.2	406	49.0
Hungary	51	2.0	51	0	51	2.0	51	3.9	51	2.0	51	3.9	51	9.8	51	21.6	51	9.8
Netherlands	317	24.9	317	0.3	317	13.6	317	8.5	317	1.6	317	8.8	317	29.3	317	31.9	317	48.3
Sweden	197	1.0	197	0	197	0	197	1.0	197	0	197	0.5	197	1.5	197	1.5	197	2.5
Total (MSs 5)	1,122	23.8	1,122	1.5	1,122	13.7	1,122	9.6	1,122	3.3	1,122	9.7	1,122	27.1	1,122	31.8	1,122	35.7
Switzerland	176	27.3	176	0	176	9.7	176	7.4	176	3.4	176	7.4	176	40.9	176	46.0	176	38.1
Young cattle (1-2	2 years)						1		-		1		1		1		1	
Austria	73	1.4	73	0	73	1.4	73	0	73	0	73	0	73	5.5	73	4.1	73	6.8
Adult cattle (over	r 2 years						1		-		1		1		1		1	
Austria	86	2.3	86	0	86	2.3	86	2.3	86	3.4	86	2.3	86	40.9	86	5.8	86	38.1
Meat-production	animals	•													-			
Germany	526	7.2	526	0.8	526	2.9	526	1.5	526	1.3	526	1.5	526	9.1	526	8.7	526	10.8
Spain	170	16.5	170	0	170	13.5	170	2.9	170	3.5	170	2.9	170	33.5	170	37.1	170	47.6
Total (MS 2)	696	9.5	696	0.6	696	5.5	696	1.9	696	1.9	696	1.9	696	15.1	696	15.7	696	19.8
Dairy cows	1						1				1		1		T			
Netherlands	271	0.7	271	0	271	0	271	0	271	0	271	0	271	4.7	271	1.1	271	9.3

Table 36. Occurrence of resistance to selected antimicrobials in indicator Escherichia coli from <u>cattle</u> in countries reporting MIC data in 2013, using harmonised ECOFFs

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates.





Figure 59. Trends in a<u>mpicillin</u>, <u>streptomycin</u> and <u>tetracyclines</u> resistance in indicator Escherichia coli from <u>cattle</u> in reporting MSs and one non-MS, 2007–2013, quantitative data



Figure 60. Trends in <u>cefotaxime</u>, <u>ciprofloxacin</u> and <u>nalidixic acid</u> resistance in indicator Escherichia coli from <u>cattle</u> in reporting MSs and one non-MS, 2007–2013, quantitative data



Statistically significant decreasing or increasing trends over five or more years, as tested by a logistic regression model ($p \le 0.05$), were observed for ampicillin, streptomycin and tetracyclines in Austria (\uparrow), Estonia (\downarrow), Germany (\downarrow) and the Netherlands (\downarrow). Austria, Germany and Switzerland data are not comparable between years, as different animal populations were analysed over the years. In Switzerland, in 2006, 2008, 2009, 2011 and 2012, young cattle (12–24 months) were tested, and in 2006, 2010 and 2013, calves (<6 months) were tested. Germany tested calves in 2009, 2010 and 2012 and beef cattle in 2011 and 2013.

Statistically significant decreasing or increasing trends over five or more years, as tested by a logistic regression model ($p \le 0.05$), were observed in Germany (\downarrow) and the Netherlands (\downarrow) for cefotaxime, ciprofloxacin and nalidixic acid. Austria, Germany and Switzerland data are not comparable between years, as different animal populations were analysed over the years. In Switzerland, in 2006, 2008, 2009, 2011 and 2012, young cattle (12–24 months) were tested, and in 2006, 2010 and 2013, calves (<6 months) were tested. Germany tested calves in 2009, 2010 and 2012 and beef cattle in 2011 and 2013.



Figure 61. Spatial distribution of <u>nalidixic acid</u> resistance among indicator Escherichia coli from <u>cattle</u> in countries reporting MIC data in 2013^(a)



MSs: Member States

Percentages shown on this map refer to countries that reported quantitative MIC data for more than 10 isolates in 2013. When quantitative 2013 data were not available, 2012 data were used instead.

(a): For Finland, 2012 data were used.

Figure 62. Spatial distribution of <u>tetracycline</u> resistance among indicator Escherichia coli from <u>cattle</u> in countries reporting MIC data in 2013^(a)



MSs: Member States.

Percentages shown on this map refer to countries that reported quantitative MIC data for more than 10 isolates in 2013. When quantitative 2013 data were not available, 2012 data were used instead.

(a): For Finland, 2012 data were used.



3.3.3. Multiple drug resistance patterns in indicator *Escherichia coli* isolates

The MDR patterns in indicator *E. coli* from broilers, fattening pigs and cattle, in MSs reporting isolate-based data, are shown in Tables MDRP39 - MDRP41.

3.3.3.1. Multiple drug resistance in Escherichia coli isolates from broilers

A large number of different MDR patterns in indicator *E. coli* isolates from broilers were evident (135 different patterns displayed by 936 isolates), reflecting the diverse nature of the *E. coli* strains tested (Table MDRP39). Resistance to ampicillin, ciprofloxacin, streptomycin, sulfonamides, tetracyclines and trimethoprim was observed in 5.6 % of all *E. coli* isolates from broilers and was the predominant MDR pattern. This differed from the previous year, when no single pattern occurred at a frequency greater than 3.0 % among the MDR patterns obtained from broilers, although a common core of resistance to ampicillin, sulfonamides and tetracyclines, generally with resistance to ciprofloxacin and frequently with resistance to streptomycin and trimethoprim, was discernible. Patterns which occurred at a higher frequency (>1 %) did not include resistance to cefotaxime; cefotaxime resistance occurred as a component of infrequent MDR patterns. Ciprofloxacin resistance frequently occurred as a component of MDR in *E. coli* from broilers and was a component of 91 of the 135 MDR patterns detected (67.4 %) and was observed in 72.0 % of MDR isolates (674 out of 936).

3.3.3.2. Multiple drug resistance in *Escherichia coli* isolates from fattening pigs

The overall range of different MDR patterns observed in indicator *E. coli* isolates from pigs in MSs reporting isolate-based data were similar to that seen in broilers, with a large number of different resistance patterns evident (73 different patterns displayed by 524 isolates), again reflecting the diverse nature of the *E. coli* strains which have been tested (Table MDRP40). Particular MDR patterns were predominant in fattening pigs, with one pattern occurring at a frequency of 13.7 % amongst the MDR patterns obtained. Three other multi-resistance patterns each accounted for approximately 9.0 % of the total multi-resistance isolates. In pigs, *E. coli* with four MDR patterns (including a common core pattern of resistance to streptomycin, sulfonamides and tetracyclines) therefore accounted for approximately 40.0 % of the total number of multi-resistant *E. coli* isolates for which isolate-based data were available. Resistance to streptomycin, sulfonamides and tetracyclines also occurred as a recurring core pattern in isolates showing additional resistances. Considering those resistance patterns occurring at a higher frequency in pigs, these did not generally include resistance to cefotaxime; however, cefotaxime resistance did occur as a component of infrequent resistance patterns. Ciprofloxacin resistance occurred less frequently than in broilers as a component of MDR in pigs, occurring in 29 of the 73 (39.7 %) resistance patterns observed and was present in 17.0 % of porcine MDR *E. coli* isolates (90 out of 524).

3.3.3.3. Multiple drug resistance in Escherichia coli isolates from cattle

Considering the different resistance patterns in indicator *E. coli* isolates from cattle, there were 65 different MDR patterns displayed by 435 MDR isolates, reflecting the diverse nature of the *E. coli* strains which have been tested (Table MDRP41). Resistance to streptomycin, sulfonamides and tetracyclines was observed in 16.3 % of all *E. coli* isolates from cattle and was the predominant multi-resistance pattern. Resistance patterns which occurred at a higher frequency (>1 %) did not include resistance to cefotaxime; cefotaxime resistance occurred as a component of infrequent resistance patterns. Ciprofloxacin resistance occurred as a component of MDR in 27 of the 65 multi-resistance patterns detected (41.5 %) and was observed in 23.4 % of MDR isolates (102 out of 435).



3.3.4. Overview of findings on antimicrobial resistance in indicator *Escherichia coli*, 2013

Figure 63 displays the resistance levels among *E. coli* isolates in the reporting MS group, based on quantitative data submitted in 2013. These data were not all derived from the same group of MSs, which needs to be considered when interpreting these figures.

The levels of resistance were broadly similar for meat from broilers, pigs and bovine animals for all reporting MSs for these antimicrobials. The situation was different for ciprofloxacin and nalidixic acid, where resistance was high in meat from broilers, considering all reporting MSs, at 41.8 % and 39.5 %, respectively, but low in meat from pigs and meat from bovine animals at less than 7.0 %.

The resistance levels observed in *E. coli* isolates from cattle were lower than in *E. coli* isolates from either *Gallus gallus* or pigs, most notably for ampicillin, streptomycin, sulfonamides and tetracyclines (Figure 63). The variations at the reporting MS group level between years could be attributable to different MSs contributing data and different production types of the livestock being sampled.

As in previous years, isolates from pigs had the highest levels of resistance to streptomycin and tetracyclines, while isolates from *Gallus gallus* had the highest resistance to ampicillin, ciprofloxacin, nalidixic acid and sulfonamides. Resistance to chloramphenicol and gentamicin was relatively low in all types of livestock, with the highest resistance level occurring in *Gallus gallus*. Chloramphenicol has not been used for food-production animals in the EU for several years; thus, the resistance observed must indicate either persistence of resistance genes or co-selection resulting from the use of related compounds (such as florfenicol). The lowest levels of resistance observed were usually to cefotaxime; the highest level of resistance to this antimicrobial occurred in isolates from *Gallus gallus*, which was also the case in previous years.





MSs: Member States.



3.3.5. Discussion

Studying the antimicrobial resistance of indicator commensal *E. coli* from animals and food provides information on the reservoir of resistance genes occurring in those bacteria that could be transferred to bacteria that are pathogenic for humans and/or animals. The occurrence of resistance to antimicrobials in indicator *E. coli* is likely to depend on a number of factors including the selective pressure exerted by use of antimicrobials in various food-producing animal populations; clonal spread of resistant organisms; dissemination of particular genetic elements, such as resistance plasmids; and the effects of co-selection in multi-resistant organisms.

A total of 13 MSs and two non-MSs provided quantitative MIC data in 2013 on at least one of the livestock species. Reported antimicrobial resistance data in *E. coli* isolates from food-producing animals and food, derived mainly from active and representative monitoring programmes, were chiefly based on randomised sampling performed at slaughterhouses. At the reporting MS group level, a high level of 'microbiological' resistance was observed to several antimicrobials among food-producing animals, with some countries reporting a very or extremely high occurrence of such resistance. As resistance levels tend to vary substantially between countries, the variation in resistance in *Gallus gallus*, pigs and cattle observed between 2009 and 2013, at the overall MS group level, may partly result from different MSs contributing to data as well as different production types of livestock being sampled.

In 2013, four MSs reported on antimicrobial resistance in meat and, in general, comparable resistance levels were generally higher among *E. coli* isolates from *Gallus gallus* and pigs than isolates from cattle. This was the third year that resistance data were reported separately for different production types of *Gallus gallus* and cattle. However, only two countries provided data on laying hens, and one of these MSs also provided data on broilers. Although there is limited information available for 2011–2013 on which to draw firm conclusions, 'microbiological' resistance levels were generally higher among broilers than in laying hens. Similarly, in 2013, only two MSs reported more than one production type or age group of cattle. The Netherlands reported much higher 'microbiological' resistance levels among younger animals and a similar trend to higher resistance in young animals was also observed in Austria.

Generally, similar 'microbiological' resistance levels were identified for **streptomycin**, **sulfonamides and tetracyclines**, both in individual MSs and at the MS group level. These compounds are commonly used therapeutically in animals and have been for many years; resistance to all three compounds often features as a component of MDR patterns. At the MS group level, resistance to gentamicin was highest in *Gallus gallus* (6.4 %) and lowest in pigs (1.8 %). Gentamicin is an interesting antimicrobial because there are differences in the degree of usage in different MSs of this and other antimicrobials to which cross-resistance may occur (for example apramycin).

'Microbiological' resistance to fluoroquinolones (ciprofloxacin) – a class of antimicrobials critically important in human medicine - was at much higher levels in E. coli isolates from meat from broilers than from meat from other species. Similarly, the occurrence of resistance to nalidixic acid and ciprofloxacin was higher in E. coli from broilers than in isolates from pigs or cattle. As resistance to fluoroquinolones commonly includes a mutational component, this suggests either that E. coli isolates from broilers are exposed to greater selective pressure from the overall use of fluoroquinolones or that the use of fluoroquinolones at a particular part of the production pyramid (which selects for mutational resistance) causes resistance which is subsequently disseminated to flocks lower in the pyramid by the spread and transfer of resistant bacterial clones. Although the occurrence of high-level fluoroquinolone resistance is likely to be influenced by the degree of fluoroquinolone usage, it is also likely to be influenced by the degree to which terminal hygiene and disinfection procedures allow strains that have developed some resistance to persist and colonise the subsequent group of animals. The occurrence of resistance to nalidixic acid was usually similar to that for ciprofloxacin, suggesting that mutation was responsible for resistance. However, in some MSs, the occurrence of resistance to ciprofloxacin was slightly higher than that obtained for nalidixic acid, particularly in pigs. In these cases, mechanisms such as transferable fluoroquinolone resistance conferred by qnr genes may have been responsible for resistance; as such, plasmid-mediated mechanisms can result in this phenotypic pattern of resistance.

Revision of epidemiological cut-off values for ciprofloxacin for Escherichia coli

The epidemiological cut-off value (ECOFF) for Escherichia coli versus ciprofloxacin has been recently revised by the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Wild-type isolates are now considered to have a ciprofloxacin minimum inhibitory concentration lower than 0.064 mg/L, an increase from the previous ECOFF of lower than 0.03 mg/L. The proportion of isolates showing 'microbiological' resistance according to this breakpoint will alter when the new breakpoint is adopted and in fact will be reduced. This report incorporates all of these changes in a comprehensive revision, which also re-evaluated the historical data using the revised ECOFFs, as well as taking into account revised EU legislation in this area, which includes revised ECOFFs.

'Microbiological' resistance to third-generation cephalosporins (**cefotaxime**) – another class categorised as critically important in human medicine – was infrequently detected in 2013 in *E. coli* from pigs and cattle, where levels were <6 % in all reporting MSs. A number of reporting MSs recorded high to moderate levels in *E. coli* from *Gallus gallus*, and resistance was typically higher in isolates from *Gallus gallus* than in pigs or cattle. Monitoring using selective media for cefotaxime resistance can detect cefotaxime-resistant *E. coli* present as a minor component of the total bacterial flora in the test sample, which might only occasionally be detected by random sampling from non-selective culture plates, and this will be performed from 2015, in accordance with Decision 2013/652/EU.

Although the levels of multi-resistance¹⁸ in most reporting countries were relatively high in indicator *E. coli* isolates from both broilers (18.4 % to 83.6 %) and pigs (14.6 % to 88.2 %), they were lower in isolates from cattle (1.5 % to 48.8 %); as expected, the numbers of fully susceptible isolates showed the inverse pattern. In general, the Nordic countries showed higher levels of full susceptibility than other MSs; thus, in broilers, Denmark was the only reporting MS with >50 % full susceptibility, whilst, in pigs, Finland was the only reporting MS with >50 % full susceptibility. Considering clinical resistance, co-resistance to cefotaxime and ciprofloxacin was detected at very low or low levels in broilers in three MSs and in single MSs in pigs and cattle in 2013. These *E. coli* isolates were randomly chosen from non-selective culture plates and they may have limited direct relevance to human medicine; they are reported because they provide an indication of the extent to which this combination of resistance is occurring in the *E. coli* flora of animals in the different reporting countries.

This year, the **MDR patterns** shown by indicator *E. coli* from broilers and pigs from MSs reporting isolatebased data have again been included in this report. Resistance to ampicillin, ciprofloxacin, streptomycin, sulfonamides, tetracyclines and trimethoprim was observed in 5.6 % of all *E. coli* isolates from broilers and was the predominant multi-resistance pattern. Particular MDR patterns were predominant in fattening pigs, with one pattern occurring at a frequency of 13.7 % amongst the MDR patterns obtained. Three other multiresistance patterns each accounted for approximately 9.0 % of the total multi-resistance isolates. The occurrence of these particular patterns might reflect spread of particular clones of bacteria which exhibit that pattern of resistance or dissemination of plasmids carrying those resistances and possibly being transmitted between different strains of *E. coli*. The findings indicate some differences between pigs and broilers in relation to the occurrence of multi-drug-resistant *E. coli* and also reveal for broilers slight differences from the previous year, when no single MDR pattern was predominant.

In broilers, but not in pigs, ciprofloxacin resistance was particularly noted in MDR patterns, and resistance to this compound can be mediated through chromosomal mutations or through transferable mechanisms of resistance. Ciprofloxacin resistance was observed in 72.0 % of MDR *E. coli* isolates from broilers (674 out of 936), whereas ciprofloxacin resistance occurred infrequently as a component of MDR in pigs and was present in 17.0 % (90 out of 524) of porcine MDR *E. coli* isolates. Considering the resistance patterns occurring at a higher frequency in broilers, pigs and cattle, these did not generally include resistance to cefotaxime; however, cefotaxime resistance did occur as a component of infrequent resistance patterns.

The most common pattern of multiple resistance in *E. coli* isolates from broilers that were co-resistant to ciprofloxacin and cefotaxime was resistance to ciprofloxacin, cefotaxime and ampicillin. This occurred in 0.6 % of the total number of *E. coli* isolates from broilers and was detected in five reporting countries. A relatively simple pattern of MDR was therefore shown by these isolates and it follows that only a limited number of antimicrobials or antimicrobial classes is likely to be responsible for selection of isolates with this resistance pattern; clonal spread of this MDR strain is a further possibility which could be investigated through strain typing of these *E. coli* isolates. Co-resistance to ciprofloxacin and cefotaxime was uncommon

¹⁸ Proportions of isolates showing reduced susceptibility to at least three antimicrobial classes according to epidemiological cut-off values.



in pigs and cattle; co-resistance to cefotaxime and nalidixic acid was more frequently detected in pigs (without ciprofloxacin resistance).

A variety of resistance patterns was observed in high-level ciprofloxacin-resistant *E. coli* isolates from broilers and pigs, with each pattern occurring at a low frequency. The position was different for cattle in one MS, where certain resistance patterns were associated with high-level ciprofloxacin resistance in a number of isolates. This may suggest that, in pigs and broilers, there is random mutation occurring in diverse strains of *E. coli*, which are accumulating mutations and acquiring resistance, whereas, in cattle in some MSs, it is possible that clonal spread of particular MDR strains with high-level ciprofloxacin resistance is occurring.

A recent study in Spain examined the integrons carried by E. coli isolates recovered from healthy broilers and pigs (Marchant et al., 2013). Integrons can be associated with particular antimicrobial resistance genes and, in the Spanish study, both class 1 and class 2 integrons were detected in pigs and chickens. Class 1 integrons classically carry the resistance gene *sul1*; additionally, both types of integrons in the Spanish study often carried genes associated with streptomycin and trimethoprim resistance, while resistance genes conferring chloramphenicol and gentamicin resistance were detected in the variable region of class 1 integrons only. The widespread occurrence of integrons and their associated antimicrobial resistance genes in E. coli from animals is likely to account for some of the resistance patterns (or associations between resistances) which are evident in the MDR tables and probably explains why sulfonamide, streptomycin and trimethoprim resistance are common components of MDR patterns. The Spanish study also reported that the presence of integrons was associated with resistance to amoxicillin (equivalent to ampicillin for resistance purposes) and tetracyclines. The common core patterns of resistance to ampicillin, streptomycin, sulfonamides, tetracyclines and trimethoprim (and combinations thereof) frequently observed in the monitoring of E. coli isolates are probably therefore related to the presence of integrons. The predominant multi-resistance pattern in E. coli from cattle was resistance to streptomycin, sulfonamides and tetracyclines, observed in 16.3 % of all isolates, and this is probably related to the occurrence of integrons.

Full resistance to all of the antimicrobials in the test panel was noted for only a single *E. coli* isolate from pigs in 2012, but, in 2013, was observed not in pigs, but rather both in broilers (0.2 % of all isolates) and cattle (0.2 % of all isolates). All cattle isolates (four in total) originated from one MS, whereas the three isolates from broilers all originated from different MSs. Further typing data of these isolates would determine whether clonal spread or plasmid dissemination of these highly resistant organisms was important; the number of isolates fully resistant to all antimicrobials in the test panel may be a useful headline figure against which developments may be monitored in future.

3.4. Antimicrobial resistance in indicator *Enterococcus*

The *Enterococcus* species *E. faecium* and *E. faecalis* are suitable as indicators of antimicrobial resistance in Gram-positive bacteria, as both species are commonly isolated from animal faeces. These species of *Enterococcus* are also important in human medicine, especially vancomycin-resistant *E. faecium* strains that may be resistant to most or all antimicrobials effective for treatment of vancomycin-susceptible enterococci infections (Arias et al., 2010). Furthermore, the occurrence of *E. faecium* and *E. faecalis* in the intestinal tract of animals or on food, even if not directly significant for humans, may constitute a reservoir of resistance genes which may be transferred either to pathogenic bacteria or to other commensal bacteria. Determining the occurrence of resistance to antimicrobial agents in commensal enterococci also provides data useful for investigating the selective pressure exerted by the use of antimicrobials on the intestinal population of bacteria in food-producing animals.

The EFSA monitoring guidelines (EFSA, 2008) recommend that monitoring may be carried out at the farm or slaughterhouse levels and that a representative part of the animal population in the MSs should be included in the sampling frame. Samples should be collected randomly either from selected holdings or flocks or from carcases randomly selected within the slaughterhouse. Samples collected and subsequently tested in accordance with the EFSA recommendations should therefore be representative of the general population and comparable between MSs. Harmonised monitoring of *E. faecium* and *E. faecalis* from food and animals is to be implemented on a voluntary basis in the MSs in 2014 (Decision 2013/652/EU).

Levels of antimicrobial resistance in *E. faecalis* and *E. faecium* were analysed in broilers, pigs (fattening pigs and breeding animals) and cattle (calves and young cattle) and meat derived from these animal species. Quantitative MIC data from 2013 were submitted by nine MSs and two non-MSs (Table <u>OVER6</u>). Mainly data from 2013 will be included in the analysis; however, comparisons will be made with the quantitative MIC data from 2012 submitted by eight MSs and one non-MS.

3.4.1. Antimicrobial resistance in *Enterococcus faecalis* and *Enterococcus faecium* isolates from meat

In 2013, four MSs (Denmark, Hungary, the Netherlands and Slovenia) reported quantitative MIC data on enterococci isolates from meat (Table 37 and Table 38). Isolates originated from national surveys and monitoring programmes where meat samples were collected at retail outlets during 2013 in Denmark and Slovenia. Hungary and the Netherlands did not indicate sampling details.

From **broiler meat**, the levels of resistance to tetracyclines reported ranged from high to extremely high in the *E. faecalis* isolates (four MSs, 46.8 %–80.0 %), whereas resistance to erythromycin and streptomycin varied from none to very high levels (51.6 %) between MSs. In *E. faecium* from broiler meat (three MSs) resistance to tetracyclines, streptomycin and erythromycin varied from none to 100 %, and resistance to quinupristin/dalfopristin was very high (54.5 %–73.3 %). Resistance to ampicillin, chloramphenicol and gentamicin was either absent or reported at low levels in both *Enterococcus* species (<10.0 %). Among the *E. faecium* (three MSs) and *E. faecalis* (four MSs) isolates collected from broiler meat in 2012 similar levels of resistance were observed. Resistance to linezolid was only reported in two *E. faecium* isolates by the Netherlands (2013 and 2012) and a single *E. faecalis* isolate from Sweden (2012). Resistance to vancomycin (cross-resistance to the growth promoter avoparcin) was absent in most of the isolates, and only Hungary (n=2, 2012 and 2013) and the Netherlands (n=1, 2012) reported a few vancomycin-resistant *E. faecalis* isolates.

Resistance to tetracyclines ranged from moderate to high in *E. faecalis* from **pig meat** (three MSs, 11.3 %– 50.0 %), and resistance to erythromycin and streptomycin varied from low to high levels (4.0 %–21.2 %). As in the isolates from broilers, resistance to ampicillin, chloramphenicol and gentamicin was either absent or observed at low levels (<10.0 %). In 2013, the analysis included *E. faecium* from Danish pig meat only, where resistance to quinupristin/dalfopristin only was observed, although at an extremely high level (72.7 %). High and very high levels of resistance to quinupristin/dalfopristin were also observed in *E. faecium* from pig meat collected in 2012 (Denmark and the Netherlands), where high levels of resistance to erythromycin were also observed in the isolates from the Netherlands. None of the *Enterococcus* isolates from pig meat were resistant to vancomycin or linezolid in either 2012 (three MSs) or 2013.

Relatively few *Enterococcus* isolates from **bovine meat** were included in the analysis. Only three MSs reported resistance in enterococci species from bovine meat collected in 2012 and 2013. Generally the isolates from bovine meat displayed resistance patterns within the range of the *Enterococcus* isolates from meat from broilers and pigs. In 2013, linezolid resistance was observed in only one isolate from the Netherlands (*E. faecium*) and, in 2012, two isolates, also from the Netherlands, were resistant to vancomycin (*E. faecalis*).

3.4.2. Antimicrobial resistance in indicator *Enterococcus faecalis and Enterococcus faecium* isolates from animals

In 2013, seven MSs and two non-MSs reported quantitative MIC susceptibility data on enterococci isolates from animals (Table 39 and Table 40). The analysis included isolates mainly collected as part of national monitoring programmes obtained from faeces (Spain and Finland), cloacal swabs (Switzerland) or caecum samples (Croatia, Denmark and Sweden) sampled at the slaughterhouses. Norway collected faecal samples at the farms. Belgium and the Netherlands did not indicate sampling details.



Country	Amp	picillin	Chloram	phenicol	Erythromycin		Gentamicin		Lin	ezolid		upristin/ opristin	Strep	tomycin	Tetra	cyclines	Vanc	omycin
	N	% Res	Ν	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Meat from broil	ers (Ga	llus gallus	s)															
Denmark	66	1.5	66	0	66	7.6	66	0	66	0	66	54.5	66	3.0	66	9.1	66	0
Netherlands	75	13.3	75	0	75	44.0	75	2.7	75	1.3	75	73.3	75	25.3	75	40.0	75	0
Slovenia	16	6.3	16	0	16	0	16	0	16	0	16	62.5	16	100	16	50.0	16	0
Total (MSs 3)	157	7.6	157	0	157	24.2	157	1.3	157	0.6	157	64.3	157	23.6	157	28.0	157	0
Meat from pig																		
Denmark	22	0	22	0	22	0	22	0	22	0	22	72.7	22	0	22	0	22	0
Meat from bovi	ne anim	als																
Denmark	12	0	12	0	12	0	12	0	12	0	12	41.7	12	0	12	8.3	12	0
Netherlands	10	0	10	10.0	_	_	10	10.0	10	10.0	10	60.0	10	10.0	10	10.0	10	0
Total (MSs 2)	22	0	22	4.5	12	0	22	4.5	22	4.5	22	50.0	22	4.5	22	9.1	22	0

Table 37. Occurrence of resistance to selected antimicrobials in indicator Enterococcus faecium isolates from meat in MSs reporting MIC data in 2013, using harmonised ECOFFs

MS: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.



Country	Amp	icillin	Chloran	nphenicol	Erythr	omycin	Gent	amicin	Line	zolid	Strept	omycin	Tetrac	cyclines	Vanc	omycin
Country	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	Ν	% Res	N	% Res	N	% Res
Meat from broilers	s (Gallus g	gallus)												•		
Denmark	62	0	62	1.6	62	22.6	62	0	62	0	62	9.7	62	46.8	62	0
Hungary	35	0	35	0	35	40.0	35	8.6	35	0	35	25.7	35	80.0	35	5.7
Netherlands	221	0.5	221	0.5	221	51.6	221	2.3	221	0	221	37.1	221	75.1	221	0
Slovenia	77	0	77	0	77	0	77	0	77	0	77	10.4	77	51.9	77	0
Total (MSs 4)	395	0.3	395	0.5	395	35.9	395	2.0	395	0	395	26.6	395	66.6	395	0.5
Meat from pigs																
Denmark	150	0	150	3.3	150	5.3	150	2.7	150	0	150	4.0	150	11.3	150	0
Netherlands	15	0	15	0	15	6.7	15	6.7	15	0	15	13.3	15	26.7	15	0
Slovenia	52	0	52	0	52	21.2	52	0	52	0	52	17.3	52	50.0	52	0
Total (MSs 3)	217	0	217	2.3	217	9.2	217	2.3	217	0	217	7.8	217	21.7	217	0
Meat from bovine	animals															
Denmark	24	0	24	8.3	24	12.5	24	0	24	0	24	12.5	24	29.2	24	0
Hungary	21	0	21	0	21.0	0	21	0	21	0	21	9.5	21	57.1	21	0
Total (MSs 2)	45	0	45	4.4	45	6.7	45	0	45	0	45	11.1	45	42.2	45	0

Table 38. Occurrence of resistance to selected antimicrobials in indicator Enterococcus faecalis isolates from meat in MSs reporting MIC data in 2013, using harmonised ECOFFs

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates.



Mainly isolates from broilers are included in the analysis for 2013, and only Norway reported data from laying hens (Table 39 and Table 40).

In 2013, resistance to tetracyclines ranged from very high to extremely high in *E. faecalis* (five MSs) and *E. faecium* (four MSs) from broilers (53.7 %–88.9 %), except in *E. faecalis* isolates from Denmark (37.7 %). Most MSs reported slightly lower levels of resistance to erythromycin (20.2 %–78.7 %) and streptomycin (0.9 %–50.0 %) in both species of enterococci. In *E. faecium* very high to extremely high resistance to quinupristin/dalfopristin (65.2 %–86.3 %) and moderate to high levels of ampicillin resistance (18.8 %– 32.9 %) were reported in 2013 from broilers.

Generally, levels of resistance in enterococci were comparable between MSs reporting in 2013 and 2012. However, Denmark and Sweden reported on *E. faecium* only in 2012, observing very low to low resistance to ampicillin and streptomycin, and low to moderate resistance to erythromycin and tetracyclines (Table EN3).

Resistance to chloramphenicol and gentamicin was either absent or reported at low levels in both *Enterococcus* species (<10.0 %). Resistance to linezolid was observed in only very few *E. faecium* isolates from broilers by Croatia (2.9 %, 2013) and France (1.0 %, 2012) and in *E. faecalis* isolates from *Gallus gallus* by Belgium (2.7 %, 2012) (Table <u>EN4</u>). Resistance to vancomycin was absent in most of the isolates from broilers, and was reported in *E. faecalis* only by Croatia (4.9 %, 2013) and in *E. faecium* only by Belgium (1.4 % in 2013) and France (1.0 % in 2012).

In 2013, resistance in *Enterococcus* isolates from laying hens was reported by Norway only, and generally at lower levels than in broiler isolates from the other reporting countries. In 2012, Sweden reported similar or lower levels of resistance in both species of *Enterococcus* from laying hens than from broilers, except for a higher occurrence of tetracycline resistance in *E. faecalis* from laying hens.

Temporal trends in resistance among enterococci from Gallus gallus

From 2007 to 2013, five MSs and one non-MS provided resistance data on five years or more to be included in the statistical analysis for *E. faecium* (Figure 64) and three MSs and one non-MS provided resistance data on five years or more for *E. faecalis* (Figure 65). This was particularly noticeable for erythromycin and tetracycline resistance in *E. faecium*, where Denmark and Switzerland often reported the lowest resistance levels compared with the other countries included. For *E. faecalis*, more comparable levels between MSs have been observed during the period.

Most of the observed statistically significant trends in *E. faecium* showed decreasing levels of resistance to ampicillin (two MSs and one non-MS), erythromycin (two MSs), streptomycin (three MSs), tetracyclines (one MS) and vancomycin (three MSs) (data not shown). Statistically significant increasing trends were observed only in resistance to ampicillin and erythromycin (one MS for each).

In *E. faecalis* from the Netherlands, statistically significant decreases in resistance to ampicillin, erythromycin, streptomycin and tetracyclines occurred from 2007 to 2013. Resistance to tetracyclines was also statistically significantly reduced in *E. faecalis* from two MSs. Statistically significant increasing trends were observed in only one non-MS for erythromycin and only one MS for tetracyclines.

Spatial trends in resistance among enterococci from Gallus gallus

Relatively few countries have reported on enterococci from cattle, and spatial analysis of resistance patterns was not possible.

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Table 39. Occurrence of resistance to selected antimicrobials in indicator Enterococcus faecium isolates from animals in countries reporting MIC data in 2013, using harmonised ECOFFs

Country	Amj	bicillin	Chloram	phenicol	Eryth	romycin	Gent	tamicin	Lin	ezolid		pristin/ pristin	Strep	tomycin	Tetra	cyclines	Van	comycin
	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res	Ν	% Res
Broilers flocks																		
Belgium	73	32.9	73	0	73	68.5	73	1.4	73	0	73	86.3	73	49.3	73	63.0	73	1.4
Croatia	69	18.8	69	1.4	69	46.4	69	2.9	69	2.9	69	65.2	-	_	69	71.0	69	0
Netherlands	423	21.5	423	0	423	47.3	423	1.7	423	0	423	72.3	423	29.8	423	53.7	423	0
Spain	-	-	104	0	104	69.2	-	-	104	0	104	76.0	-	_	104	86.5	104	0
Total (MSs 4)	565	22.7	669	0.1	669	52.9	565	1.8	669	0.3	669	73.7	496	32.7	669	61.6	669	0.1
Switzerland	58	5.2	58	0	58	27.6	-	-	58	0	58	62.1	58	3.4	58	31.0	58	0
Laying hens flo	ocks																	
Norway	103	1.0	103	0	103	29.1	103	0	103	0	Ι	-	-	—	103	7.8	103	0
Fattening pigs																		
Finland	41	0	41	0	41	36.6	41	0	41	0	-	-	41	2.4	41	9.8	41	0
Spain	-	-	76	0	76	71.1	-	-	76	2.6	76	94.7	-	-	76	78.9	76	0
Total (MSs 2)	41	0	117	0	117	59.0	41	0	117	1.7	76	94.7	41	2.4	117	54.7	117	0
Breeding pigs																		
Belgium	65	9.2	65	0	65	21.5	65	1.5	65	1.5	65	86.2	65	15.4	65	29.2	65	1.5
Bovine animals	, calves	s (under 1	year)															
Sweden	42	0	42	0	42	9.5	42	2.4	42	0	-	-	42	0	42	2.4	42	0
Switzerland	68	0	68	0	68	11.8	_	-	68	0	68	88.2	68	2.9	68	10.3	68	0
Bovine animals	, young	cattle (1-	-2 years)		-													
Belgium	125	11.2	125	1.6	125	38.4	125	3.2	125	2.4	125	88.0	125	27.2	125	36.0	125	2.4
Bovine animals																		
Spain MSs: Mombor Stat	_	_	14	0	14	42.9	_	_	14	0	14	64.3	-	_	14	71.4	14	0

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.



Table 40. Occurrence of resistance to selected antimicrobials in indicator Enterococcus faecalis isolates from animals in countries reporting MIC data in 2013, using harmonised ECOFFs

0 and the second	Amp	bicillin	Chloran	nphenicol	Eryth	romycin	Gen	tamicin	Lin	ezolid	Strept	omycin	Tetra	cyclines	Vanco	omycin
Country	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	Ν	% Res	N	% Res
Broilers flocks														•		
Belgium	68	0	68	4.4	68	70.6	68	0	68	0	68	50.0	68	88.2	68	0
Croatia	81	0	81	4.9	81	45.7	81	3.7	81	0	_	-	81	88.9	81	4.9
Denmark	114	0	114	0.9	114	20.2	114	0	114	0	114	0.9	114	37.7	114	0
Netherlands	342	0	266	1.1	266	68.8	266	2.3	291	0	266	42.5	266	80.5	266	0
Spain	_	_	164	0	164	78.7	_	-	164	0	164	47.0	164	84.1	164	0
Total (MSs 5)	605	0	693	1.6	693	60.6	529	1.7	718	0	612	36.8	693	76.0	693	0.6
Switzerland	155	0	155	0.6	155	16.8	_	_	155	0	155	3.2	155	38.1	155	0
Laying hens flocks	5												-			
Norway	89	1.1	89	0	89	10.1	89	0	89	0	_	-	89	31.5	89	0
Fattening pigs																
Denmark	109	0	109	17.4	109	45.0	109	15.6	109	0	109	33.9	109	90.8	109	0
Finland	53	0	53	1.9	53	34.0	53	1.9	53	0	53	7.5	53	71.7	53	0
Spain	-	_	46	0	46	76.1	-	-	46	0	46	63.0	46	95.7	46	0
Total (MSs 3)	162	0	208	9.6	208	49.0	162	11.1	208	0	208	33.7	208	87.0	208	0
Breeding pigs																
Belgium	12	0	12	25.0	12	33.3	12	0	12	0	12	25.0	12	58.3	12	0
Bovine animals, ca	alves (un	der 1 year)													
Sweden	11	0	11	0	11	0	11	0	11	0	11	0	11	0	11	0
Switzerland	108	0	108	27.8	108	42.6	_	_	108	0	108	48.1	108	77.8	108	0.9
Bovine animals, yo	oung cat	tle (1–2 yea	ars)													
Belgium	63	0	63	58.7	63	76.2	63	9.5	63	0	63	68.3	63	82.5	63	1.6

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.



Figure 64. Trends in ampicillin, erythromycin, streptomycin and tetracycline resistance in tested <u>Enterococcus faecium</u> isolates from Gallus gallus in reporting countries, 2007–2013, quantitative data



Figure 65. Trends in ampicillin, erythromycin, streptomycin and tetracycline resistance in tested <u>Enterococcus faecalis</u> isolates from Gallus gallus in reporting countries, 2007–2013, quantitative data



A statistically significant decreasing trend over five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for ampicillin in Denmark (\downarrow), the Netherlands (\downarrow) and Switzerland (\downarrow); for erythromycin in Austria (\downarrow) and Denmark (\downarrow); for streptomycin in Denmark (\downarrow), France (\downarrow) and the Netherlands (\downarrow); and for tetracycline in the Netherlands (\downarrow). A statistically significant increasing trend was observed for ampicillin in France (\uparrow) and for erythromycin in the Netherlands (\uparrow).

A statistically significant decreasing trend over five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for ampicillin in the Netherlands (\downarrow); for erythromycin in the Netherlands (\downarrow); for streptomycin in the Netherlands (\downarrow) and Switzerland (\downarrow); and for tetracycline in Austria (\downarrow), the Netherlands (\downarrow) and Switzerland (\downarrow). A statistically significant increasing trend was observed for erythromycin in Switzerland (\uparrow) and for tetracycline in Denmark (\uparrow).



3.4.2.2. Antimicrobial resistance in indicator *Enterococcus faecalis* and *Enterococcus faecium* isolates from pigs

Only four MSs reported quantitative MIC susceptibility data for enterococci from pigs in 2013. Denmark, Finland and Spain submitted data from fattening pigs, and Belgium included data from breeding animals (Table 39 and Table 40).

In 2013, the highest resistance levels among *E. faecalis* isolates from pigs were recorded for tetracyclines (four MSs, 58.3 %–95.7 %), followed by resistance to erythromycin (33.3 %–76.1 %) and streptomycin (7.5 %–63.0 %). The highest levels for all three agents were reported from Spain. Moderate to high resistance to chloramphenicol was observed in *E. faecalis* from Danish (17.4 %) and Belgian (25.0 %) pigs, in contrast to the low occurrence (<5 %) observed in *E. faecalis* from Danish and Belgian broilers. In *E. faecium* from pigs (three MSs in 2013 and five MSs in 2012), resistance to tetracyclines and erythromycin varied from 9.8 % to 84.4 %, with the highest levels reported by Spain and the Netherlands (2012) and the lowest levels reported by Finland and Switzerland (2012) (Table EN3). Very high to extremely high levels of resistance to quinupristin/dalfopristin (68.1 %–94.7 %) were reported in pigs in 2013 and 2012. Chloramphenicol resistance was reported in *E. faecium* from pigs only in 2012 by France (1.1 %) and Belgium (1.7 %). In previous years, resistance to chloramphenicol has also generally been lower in *E. faecium* than in *E. faecalis*.

In 2013, resistance to ampicillin and gentamicin was either absent or reported at low levels in both *Enterococcus* species (<10.0 %), except for a moderate level of resistance to gentamicin in *E. faecalis* from Danish fattening pigs (15.6 %, 2013) and breeding animals from Belgium (18.2 %, 2012) (Table <u>EN4</u>). In 2012, however, moderate to very high levels of resistance to ampicillin was reported in *E. faecium* from pigs by Belgium, Denmark, France and the Netherlands.

Linezolid resistance was reported in very few *E. faecium* isolates from slaughter pigs by Spain (2.6 % in 2013) and from breeding pigs by Belgium (1.5 % in 2013, 3.3 % in 2012). Vancomycin resistance was reported for *E. faecium* only by Belgium (1.5 % in 2013, 4.1 % in 2012) and France (1.1 % in 2012).

Temporal trends in resistance among indicator enterococci from pigs

Four MSs for *E. faecium* and three MSs and one non-MS for *E. faecalis* provided resistance data on five years or more to be included in the statistical analysis. In addition, in the enterococci species from pigs, substantial variation between countries in the reported levels of resistance was observed from 2007 to 2013, particularly resistance to ampicillin, erythromycin and streptomycin in *E. faecium*. Tetracycline is one of the most commonly used antimicrobial agents in pigs and, except for *E. faecalis* in Denmark, no statistically significant trends were observed in tetracycline resistance in either *Enterococcus* species for the included MSs.

In *E. faecium* isolates from pigs (Figure 66), statistically significant decreasing resistance to erythromycin (four countries), streptomycin (two MSs) and vancomycin (two MSs, data not shown) was observed. From two MSs, a statistically significant increasing trend was observed in resistance to ampicillin from 2007 to 2013.

A statistically significant decrease in resistance to streptomycin was observed in *E. faecalis* from one MS (Figure 67). A statistically significant increasing trend for tetracyclines was observed in one MS.

Spatial trends in resistance among enterococci from pigs

As very few MSs have reported data on resistance in enterococci from pigs, the spatial patterns are very fragmented. Among the MSs providing data (Austria, Belgium, Denmark, Finland, France, the Netherlands, Spain and Switzerland), Spain reported the highest levels of resistance to tetracyclines and erythromycin, whereas the lowest levels of resistance were reported by Belgium and Finland. Only Belgium reported resistance to vancomycin at a low level in *E. faecium* from pigs during 2012 and 2013; however, previously, Denmark and the Netherlands both reported very low resistance levels.





Figure 66. Trends in ampicillin, erythromycin, streptomycin and tetracycline resistance in tested <u>Enterococcus faecium</u> isolates from pigs in reporting MSs, 2007–2013, quantitative data



A statistically significant decreasing trend over five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for erythromycin in Denmark (\downarrow), France (\downarrow), the Netherlands (\downarrow) and Switzerland (\downarrow); and for streptomycin in France (\downarrow) and the Netherlands (\downarrow). A statistically significant increasing trend was observed for ampicillin in Denmark (\uparrow) and France (\uparrow).

Figure 67. Trends in ampicillin, erythromycin, streptomycin and tetracycline resistance in tested <u>Enterococcus faecalis</u> *isolates from pigs in reporting MSs, 2007–2013, quantitative data*



A statistically significant decreasing trend over five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for streptomycin in the Netherlands (\downarrow). A statistically significant increasing trend was observed for tetracycline in Denmark (\uparrow).

3.4.2.3. Antimicrobial resistance in *Enterococcus faecalis* and *Enterococcus faecium* isolates from cattle

Only three MSs and one non-MS reported quantitative MIC susceptibility data for enterococci from cattle in 2013 (Table 39 and Table 40), and three additional MSs reported data in 2012 only (Table EN3 and EN4).

In 2013, Sweden reported data from calves (under one year of age), where all of the 11 *E. faecalis* isolates were susceptible to the eight antimicrobial agents included in the analysis, and only low resistance to erythromycin, gentamicin and tetracyclines was reported in the *E. faecium* isolates.

Belgium reported very high to extremely high levels of resistance to tetracyclines, streptomycin, erythromycin and chloramphenicol in *E. faecalis* from young cattle (58.7 %–82.5 %), whereas low resistance to gentamicin and vancomycin was observed. Generally, the resistance levels in *E. faecalis* from young cattle from Belgium were higher than observed in *E. faecalis* from Belgian pigs and broilers.

In *E. faecium* from Belgium and Spain, resistance to erythromycin, tetracyclines and quinupristin/dalfopristin was high or extremely high (35.7 %–88.1 %), whereas resistance to chloramphenicol was low or absent.

Linezolid resistance was reported in very few *E. faecium* isolates from cattle by Belgium (0.6 % in 2012, 2.4 % in 2013) and the Netherlands (1.7 %, 2012). Linezolid was also observed in a single *E. faecalis* isolate from Belgian cattle (1.2 %, 2012). Vancomycin resistance was reported by Belgium in both *E. faecalis* (2.4 % in 2013, 1.3 % in 2012) and *E. faecalis* (1.6 % in 2013, 1.2 % in 2012), as well as by Switzerland in *E. faecalis* (0.9 %, 2013).

Temporal trends in resistance among indicator enterococci from cattle

Only three MSs and one non-MS reported susceptibility data from enterococci from cattle for five or more years from 2007 to 2013 (Figure 68 and Figure 69). In one MS, statistically significant decreasing resistance to erythromycin, streptomycin and tetracyclines was observed in both *Enterococcus* species. In contrast, statistically significant increasing resistance to erythromycin, streptomycin and tetracyclines observed in both *Enterococcus* species. In contrast, statistically significant increasing resistance to erythromycin, streptomycin and tetracyclines occurred in *E. faecalis* isolates from Austria. In *E. faecium* from cattle in one MS, the increase in erythromycin resistance and decrease in vancomycin resistance was statistically significant (data not shown).

Spatial trends in resistance among enterococci from cattle

Relatively few countries have reported on enterococci from cattle, and therefore spatial analysis of resistance patterns was not possible.





Figure 68. Trends in ampicillin, erythromycin, streptomycin and tetracycline resistance in tested <u>Enterococcus faecium</u> isolates from cattle in reporting MSs, 2007–2013, quantitative data



Figure 69. Trends in ampicillin, erythromycin, streptomycin and tetracycline resistance in tested <u>Enterococcus faecalis</u> isolates from cattle in reporting MSs, 2007–2013, quantitative data



A statistically significant decreasing trend over five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for erythromycin, streptomycin and tetracyclines in the Netherlands (\downarrow). A statistically significant increasing trend was observed for erythromycin in Austria (\uparrow). Switzerland data are not comparable between years, as different animal populations were analysed over the years. In the years 2006, 2008, 2009, 2011 and 2012, young cattle (12–24 months) were tested and, in 2006, 2010 and 2013, calves (<6 months) were tested.

A statistically significant decreasing trend over five or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for erythromycin, streptomycin and tetracyclines in the Netherlands (\downarrow). A statistically significant increasing trend was observed for erythromycin, streptomycin and tetracyclines in Austria (\uparrow). Switzerland data are not comparable between years, as different animal populations were analysed over the years. In the years 2006, 2008, 2009, 2011 and 2012, young cattle (12–24 months) were tested and, in 2006, 2010 and 2013, calves (<6 months) were tested.



3.4.3. High-level gentamicin resistance

Only four MSs provided isolate-based data for the analysis of high-level resistance to gentamicin, defined as resistance to MIC values >128 mg/L, in *Enterococcus* species from animals. Denmark was the only MS providing data from meat (Tables <u>HLR13</u> and <u>HLR14</u>). The *Enterococcus* isolates that displayed high-level gentamicin resistance were *E. faecalis* originating from fattening pigs and meat thereof (data from Denmark and Finland: n=21, N=312) and cattle (Belgium: n=6, N=63). In *E. faecuum*, high-level gentamicin resistance was reported in cattle (Belgium: n=4, N=126), broilers (Belgium: n=1, N=73) and breeding pigs (Belgium: n=1, N=65).

Among these isolates, the most common MDR pattern in *E. faecalis* isolates was Gen-Str-Chl-Ery-Tet observed in pigs and meat thereof (n=13) and in cattle (n=4). The MDR pattern Gen-Str-Ery-Tet was also observed in cattle (n=2) and pigs (n=6). A similar pattern was observed in a single *E. faecium* isolate each from cattle and broilers, although also including quinupristin/dalfopristin resistance (Gen-Str-Ery-Qd-Tet). Importantly, the co-occurrence of high-level resistance to gentamicin and ampicillin resistance was reported in three *E. faecium* isolates from Belgian cattle (Gen-Str-Ery-Amp-Qd-Tet). Resistance to ampicillin as well as high-level gentamicin resistance is frequently observed in *E. faecium* belonging to the clonal complex CC17 that has spread among hospitals globally; however, these isolates are usually also resistant to quinolones (Top et al., 2008).

Among human infections, high-level aminoglycoside resistance in *E. faecalis* occurs frequently, with the majority of the countries reporting percentages of resistant isolates between 25.0 % and 50.0 % (ECDC, 2013). Optimal therapy for severe human enterococcal infections requires a synergistic combination of cell wall active agents such as beta-lactams and an aminoglycoside, often ampicillin and gentamicin (or vancomycin). Therefore, the occurrence of isolates with high-level resistance to gentamicin in combination with ampicillin resistance limits the options for treatment considerably (Arias et al., 2010).

3.4.4. Further analysis of multiple drug resistance among enterococci

The proportion of multi-resistant isolates and the frequency of MDR patterns could be assessed for only five MSs reporting quantitative MIC susceptibility data for *E. faecalis* and/or *E. faecium* from *Gallus gallus* (mainly broilers), cattle and/or pigs in 2012 and 2013. The detailed tables are presented in Tables <u>MDRP42</u> to <u>MDRP46</u>.

In *E. faecium*, multi-resistant isolates were defined as isolates with reduced susceptibility to at least three of the nine antimicrobial classes: ampicillin, chloramphenicol, erythromycin, gentamicin, linezolid, quinupristin/dalfopristin, streptomycin, tetracyclines and vancomycin, whereas quinupristin/dalfopristin was excluded from the evaluation of MDR patterns for *E. faecium*.

The frequency of multi-resistant isolates varied considerably between MSs, and relatively few *Enterococcus* isolates were resistant to several antimicrobials of critical importance to human treatment (ampicillin, gentamicin, linezolid and vancomycin).

In 2013, among the *E. faecium* isolates from Belgian broilers (N=73), 65.8 % were multi-resistant, of which 57.5 % were co-resistant to erythromycin, quinupristin/dalfopristin and tetracyclines. The most common MDR pattern was resistance to Amp-Ery-Qd-Str-Tet, followed by Ery-Qd-Str-Tet and Ery-Qd-Tet (21.9 %, 16.4 % and 13.7 % of all isolates, respectively). Denmark also reported four multi-resistant *E. faecium* isolates from broilers (N=107, 2012) which were all resistant to erythromycin and quinupristin/dalfopristin, displaying MDR patterns less frequently observed than among the Belgian isolates. In addition, in cattle, most of the multi-resistant *E. faecium* isolates from Belgium (31.7 %, N=126) had the common MDR patterns Ery-Qd-Str-Tet and Amp-Ery-Qd-Str-Tet (32.5 % and 22.5 % of all isolates, respectively).

Overall, resistance to vancomycin and/or linezolid was observed among eight of the multi-resistant *E. faecium* isolates from animals in 2013 and 2012, displaying several MDR patterns: Ery-(Qd)-Str-Tet-Van, Ery-Qd-Van-(Lzd), Ery-(Chl-Qd)-Lzd-Str-Tet and Amp-Chl-Ery-Lzd-Qd-Str-Tet-Van. The isolates originated from pigs (n=5), cattle (n=2) and broilers (n=1). Only five of the multi-resistant *E. faecium* isolates from cattle (three isolates in 2013) and pigs (two isolates in 2012) were resistant to both ampicillin and gentamicin (Amp-Ery-Gen-Qd-Str-Tet).

As described, *E. faecalis* is considered intrinsically resistant to quinupristin/dalfopristin, and co-resistance to erythromycin and tetracyclines was observed in all multi-resistant isolates from broilers (n=36 in 2013, n=14 in 2012) and pigs (n=39 in 2013, n=59 in 2012) and >90 % of the multi-resistant isolates from cattle (n=45 in 2013, n=72 in 2012). The majority of multi-resistant *E. faecalis* isolates from broilers originated from Belgium; however, Austria, Denmark and Sweden also reported some multi-resistant isolates. From fattening pigs, the

multi-resistant isolates originated mainly from Denmark and Austria, and only two multi-resistant isolates were included from Finland. All multi-resistant *E. faecalis* isolates from cattle originated from Belgium. In 2013 and 2012, resistance to erythromycin, streptomycin and tetracycline (Ery-Str-Tet) was commonly observed in multi-resistant *E. faecalis* from broilers (17.6 % and 4.4 % of all isolates, respectively), fattening pigs (7.4 % and 7.5 %, respectively) and cattle (7.9 % and 5.0 %, respectively). This MDR pattern, including resistance to chloramphenicol (Chl-Ery-Str-Tet), was often observed in multi-resistant isolates from cattle (38.1 % and 9.7 %, respectively), but also in the isolates from broilers (1.6 % and 2.7 %, respectively) and fattening pigs (4.3 % and 8.5 %, respectively). In fattening pigs, additional resistance to gentamicin was also common (Chl-Ery-Gen-Str-Tet, 6.2 % and 3.3 %, respectively). Two of the multi-resistant *E. faecalis* isolates from Belgian cattle (2013 and 2012) were resistant to vancomycin (Ery-Str-Tet-Van and Chl-Ery-Str-Tet-Van, respectively) and one isolate from 2012 was resistant to linezolid (Ery-Str-Tet-Lzd).

3.4.5. Overview of the findings on antimicrobial resistance in indicator *Enterococcus*, 2013

Figure 70 shows the resistance levels in the group of MSs reporting quantitative MIC data on *E. faecalis* and *E. faecium* in 2013 for domestic fowl (*Gallus gallus*), pigs and cattle. It should be borne in mind that the data are derived from very few MSs, and the MSs vary regarding the different animals species included.

Generally, the highest levels of resistance in the indicator enterococci from domestic animals were to tetracyclines and erythromycin, followed by streptomycin. In *E. faecium*, very high to extremely high levels of resistance to quinupristin/dalfopristin was also reported by several MSs. Considering the low number of reporting MSs in 2013, general resistance to tetracyclines and erythromycin was higher in *E. faecalis* than in *E. faecium* isolates from broilers, pigs and cattle. Between 2010 and 2012, more MSs submitted susceptibility data on indicator enterococci, and here isolates from cattle showed that erythromycin resistance was lower in *E. faecalis* than in *E. faecium*.

Resistance to both chloramphenicol and gentamicin was generally low in 2013, although moderate to high levels of resistance to chloramphenicol were reported in *E. faecalis* from pigs and cattle. There was very low resistance to linezolid and vancomycin in both species of *Enterococcus*.

Figure 70. Occurrence of resistance to selected antimicrobials in indicator Enterococcus faecium and Enterococcus faecalis from Gallus gallus, pigs and cattle at the reporting MS group level in 2013



MSs: Member States.



3.4.6. Discussion

Antimicrobial resistance in commensal *Enterococcus* isolates from animals and food is used as an indicator of the reservoir of resistance genes in the Gram-positive flora; genes which could be transferred to bacteria that are pathogenic for humans and/or animals. As with indicator *E. coli*, *Enterococcus* isolates can also be used to investigate the relationship between antimicrobial resistance levels and the extent of usage of antimicrobials in food-producing animal species. Both enterococcal species can cause human disease; however, *E. faecium* isolates from human clinical outbreaks often belong to different clonal complexes than *E. faecium* from food and animals, whereas the same multi-locus sequence typing (MLST) types can be detected in *E. faecalis* isolates from food, animals and patients with clinical infections (Hammerum, 2012).

E. faecalis is considered intrinsically (i.e. naturally) resistant to streptogramin A and streptogramin B (quinupristin/dalfopristin), and susceptible *in vitro* to ampicillin (Arias et al., 2010). Low-level intrinsic resistance to aminoglycosides (streptomycin and gentamicin) is an inherent property of enterococci (Murray, 1990), accounting for the higher ECOFFs evident for these bacteria than for the other bacteria monitored in this report.

In 2013, nine MSs and two non-MSs provided quantitative data on antimicrobial resistance in *Enterococcus* from different populations of food-producing animals and meat derived thereof. Owing to the limited number of MSs included in the analysis, trends in resistance at the MS group or community levels could not be assessed.

Only four MSs were included in the analysis of resistance in enterococci from meat, and generally the levels of resistance were lower in *E. faecium* and/or *E. faecalis* isolates from Danish meat than in isolates from Hungary, the Netherlands and Slovenia. Even though the number of included MSs is very low, the previously observed general trend with higher resistance levels in enterococci from broiler meat than in isolates from meat from pigs and cattle could also be observed in the data from both 2013 and 2012.

'Microbiological' resistance to erythromycin, streptomycin and tetracyclines in domestic animals was usually at a very high level in both species of *Enterococcus*, with resistance in some MSs reaching extremely high levels. There was often substantial variation in the levels of resistance observed in the reporting MSs, which may reflect variation in veterinary antimicrobial usage patterns or in the production types of livestock that were sampled. Resistance occurred more commonly in isolates from *Gallus gallus* and pigs than in isolates from cattle, although the observed differences should be treated with caution, as very few MSs reported data. Resistance levels were similar in *E. faecalis* and/or *E. faecium* isolates from broiler meat and broilers within the Netherlands, Denmark and Sweden (2012) that reported data from both sources. Only Denmark and the Netherlands (2012) reported data from pig meat and fattening pigs, where resistance was relatively lower in *E. faecalis* and/or *E. faecium* from pig meat than that observed in isolates from pigs at the slaughterhouse.

Plasmid-associated co-resistance between glycopeptide antimicrobials, such as vancomycin, and macrolide antimicrobials, such as erythromycin, has previously been described in *E. faecium* (Hegstad et al., 2010). As macrolides are used therapeutically in animal husbandry, the possibility of co-resistance with vancomycin resistance may exist, owing to the possible co-localisation of their genetic determinants on the same plasmids. This could in theory result in maintenance of genes conferring vancomycin resistance among enterococci from animals, even though the use of glycopeptides (avoparcin) as growth promoters has been discontinued in the EU for more than a decade (Hammerum, 2012).

In 2013, four *E. faecium* isolates (three from cattle and one from broilers) and a single *E. faecalis* isolate (from cattle) were found to be resistant to vancomycin. These isolates originated from Belgium and were also resistant to erythromycin. It cannot be excluded that the occurrence of the five vancomycin-resistant isolates is linked with co-resistance towards erythromycin by the therapeutic use of macrolides in production animals. However, as erythromycin resistance is very common in both *E. faecalis* and *E. faecium* isolates from Belgium, this cannot be determined based on phenotypic data only, but would require further genotypic analysis.

In general, a high occurrence of MDR to erythromycin, quinupristin/dalfopristin and tetracyclines was observed among *E. faecium* from all animal species. In *E. faecium*, one of the genes conferring resistance to quinupristin/dalfopristin also confers cross-resistance to erythromycin (Hegstad et al., 2010). This could explain the very high resistance to quinupristin/dalfopristin which was observed, as erythromycin may be used for therapeutic treatment of sick animals.

E. faecalis is intrinsically resistant to quinupristin/dalfopristin. All isolates were thus assumed to be resistant and susceptibility data for this compound were not reported. Almost all *E. faecalis* isolates were observed to be resistant to erythromycin and tetracyclines, and were assumed to be resistant to quinupristin/dalfopristin,



indicating a general trend in both *E. faecalis* and *E. faecium* isolates to exhibit high occurrence of coresistance to these three antimicrobial classes.

Interestingly, in 2012, resistance to linezolid was observed in a few *E. faecium* and *E. faecalis* isolates from broiler meat, broilers, pigs and cattle, whereas none of the isolates tested for linezolid resistance in 2011 was resistant. In 2013, linezolid-resistant *E. faecium* isolates were also observed in low numbers in broiler meat, bovine meat, pigs and cattle. This relatively new drug has been used with some success to treat serious infections in humans caused by Gram-positive bacteria resistant to several other antimicrobials, such as vancomycin-resistant *E. faecium*. However, this use is usually only prescribed after first-line therapy has failed or if there is a risk of causing serious allergic reactions (Arias et al., 2010).

Resistance to linezolid has previously been shown to be conferred by expression of the *cfr* resistance gene and by mutations in the binding site of the 23S rRNA molecule (Scheetz et al., 2008). The *cfr* gene also confers cross-resistance to chloramphenicol. Among the five multi-resistant isolates displaying linezolid resistance, two *E. faecium* isolates and one *E. faecalis* isolate were not resistant to chloramphenicol, suggesting ribosomal mutations as the explanation for the resistance phenotype or presence of a yet uncharacterised resistance mechanism for linezolid. The two isolates (*E. faecium* and *E. faecalis*) resistant to both linezolid and chloramphenicol could in principle be explained by the presence of the *cfr* gene or by a combination of a chromosomal mutation in the 23S rRNA and presence of another gene conferring resistance towards chloramphenicol. As only phenotypic data are presented, further conclusions regarding a genotypic explanation would require genetic characterisation.

Also of clinical relevance is the occurrence of co-resistance to ampicillin and gentamicin, vancomycin and/or quinupristin/dalfopristin, as combinations of these antimicrobials (as well as daptomycin and tigecycline) are recommended for the treatment of multi-resistant enterococcal infections. Only one of the enterococcus isolates (*E. faecium* from cattle, 2012) was resistant to ampicillin, vancomycin and gentamicin, as well as to five other antimicrobials including linezolid and quinupristin/dalfopristin.

3.5. Meticillin-resistant *Staphylococcus aureus*

Meticillin-resistant Staphylococcus aureus (MRSA)

MRSA has been recognised as an important cause of healthcare-associated infections in humans for decades. Strains of MRSA have emerged which are particularly associated with community-associated infections in humans. Moreover, in recent years, MRSA has also been detected in several animal species, notably including pigs and companion animals, as well as some other farm animal species. Hospital-associated MRSA and community-associated MRSA are those strains predominantly affecting humans, and thse generally do not involve food-producing animals; however, livestock-associated MRSA may also be harboured by humans, especially where there is occupational contact with affected livestock. Livestock-associated MRSA may cause illness in humans, although transmissibility between humans has been shown to be very limited, even in healthcare facilities.

Antimicrobial susceptibility in European invasive Staphylococcus aureus isolates is reported by the MSs to the European Antimicrobial Resistance Surveillance Network (EARS-Net). Molecular typing data are not reported and thus, where there may be possible links to the animal reservoir, these cannot be detected easily with current monitoring procedures, at least at the European level. The European Union/European Economic Area population-weighted mean MRSA percentage was 18.0 % in 2013. Although a significantly decreasing trend was observed from 2010 to 2013, the decrease was less pronounced than in the previous four-year period. MRSA remains a human public health priority, as the percentage of MRSA remains above 25.0 % in 7 out of 30 countries, mainly in eastern and southern Europe (ECDC, 2014a).

The EFSA's assessment of the public health significance of MRSA in animals and food (EFSA, 2009c) and the Joint Scientific Report of ECDC, EFSA and the European Medicines Agency (EMEA) on MRSA in livestock, companion animals and food (EFSA, 2009a) provide more background information and recommendations on MRSA. A principal recommendation is that monitoring of food-producing animals, in particular intensively reared animals, is carried out periodically in conjunction with systematic surveillance of MRSA in humans, so that trends in the diffusion and evolution of zoonotically acquired MRSA in humans can be identified. In particular, isolates, representative of various animal and food origins, should be analysed for lineage determination, antimicrobial susceptibility and virulence-associated traits. These issues were reviewed in the recent EFSA Scientific Report proposing technical specifications to improve the



harmonisation of the monitoring and reporting of the prevalence, genetic diversity and multi-resistance profile of MRSA in food-producing animals and food thereof (EFSA, 2012b).

3.5.1. Meticillin-resistant Staphylococcus aureus in food and animals

Livestock-associated MRSA isolates are the principal focus of this section, which summarises the MRSA prevalence and resistance results in various food and food-producing animal species/populations reported by MSs to EFSA in 2013. This section also includes prevalence data reported on companion animals. Six MSs submitted data on MRSA prevalence in food and animals in their national zoonoses reports for 2013 (Table <u>OVER7</u>). The methods for the isolation of MRSA from food and animals to date have not been harmonised at the EU level and, therefore, the methods used by individual reporting MSs may differ in sensitivity. In addition, data on antimicrobial resistance of MRSA isolates from food-producing animals were reported by only three countries in 2013; two of these countries also reported molecular typing data.

3.5.1.1. Meticillin-resistant Staphylococcus aureus in food

In 2013, three MSs (Germany, Slovenia and Spain) reported information on the occurrence of MRSA in various categories of food (Table 41). Germany investigated a wide range of meat from broilers and bovine animals for MRSA. Slovenia investigated 102 samples of meat from pigs, among which 18 samples tested positive for MRSA. Spain examined a range of food products for MRSA and positive isolates were obtained from meat preparations from turkeys (three isolates: 3.9 %), fresh meat from pigs (five isolates: 8.3 %) and meat products from pigs (six isolates: 8.5 %). The corresponding *spa*-typing data were not available from reporting MSs, as positive isolates were reported of unspecified *spa*-type. Generally, meat from several different sources proved positive for MRSA, including meat from poultry, pigs and cattle, at various levels of prevalence.

Food species/ country	Description	Sample unit	Number of units tested	Number (%) positive for MRSA
Meat from broiler	s (Gallus gallus)			
Cormony	Carcase, at slaughterhouse, monitoring	Slaughter batch	341	167 (49.0)
Germany -	Fresh, at retail, monitoring	Single	443	107 (24.2)
Spain	Meat preparation	Single	25	0
Meat from turkeys	S			
Cracia	Meat preparation	Single	77	3 (3.9)
Spain -	Meat products	Single	6	0
Meat from pigs				
Slovenia	Fresh, at slaughterhouse, monitoring	Single	102	18 (17.6)
Cracia	Fresh	Single	60	5 (8.3)
Spain -	Meat products	Single	71	6 (8.5)
Meat from bovine	animals			
0	Carcase, at slaughterhouse, monitoring	Single	323	16 (5.0)
Germany -	Meat, at retail, monitoring	Single	421	23 (5.5)
Spain	Minced meat	Single	8	0
Cow's milk				
Spain	Raw milk intended for direct human consumption	Single	5	0

Table 41. Meticillin-resistant Staphylococcus aureus in food, 2013

MRSA: meticillin-resistant Staphylococcus aureus.

3.5.1.2. Meticillin-resistant Staphylococcus aureus in animals

Monitoring meticillin-resistant Staphylococcus aureus in food-producing animals

For 2013, Belgium, Germany, Hungary, the Netherlands and Switzerland reported information on the prevalence of MRSA in food-producing animals and/or their environment within a monitoring, surveillance or unspecified sampling context (Table 42).

The MRSA prevalence in fattening pigs in Switzerland was high at 20.8 %, while an extremely high MRSA prevalence was recorded in the Netherlands in slaughter pigs (97.8 %). Germany reported a high prevalence (39.4 %) in broilers at the slaughterhouse, while, considering the same animal population sampled on the


farm by means of environmental dust sampling, the prevalence of positive flock was 1.3 %. An animal prevalence of 86.1 % was also recorded in *Gallus gallus* in Hungary. Germany reported a low prevalence (8.2 %) in meat-production bovine animals sampled at the slaughterhouse, while, considering the same animal population sampled by the Netherlands, the prevalence was 71.9 %.

A number of different *spa*-types were reported (Table 42). The majority of isolates from pigs in Switzerland were *spa*-type t034, with lower numbers of t011; both of these *spa*-types are associated with MRSA CC398 and accounted for 100 % of the MRSA isolates from fattening pigs in Switzerland. The same *spa*-types were recovered from cattle in Switzerland, with the addition of t1255 (associated with CC398) and a single isolate of t032 (a *spa*-type linked to hospital-associated MRSA). Belgium provided *spa*-type data for MRSA isolates from pigs at the slaughterhouse and *spa*-type t011 was predominant (83.0 %) and is associated with sequence type ST398. The other *spa*-types reported from Belgian pigs were present in much lower numbers and of these, t034, t1344, t1456, t1451, t2370, t2922 and t4872 were all detected in the baseline survey of breeding pigs (EFSA, 2009b) and are associated with CC398. *Spa*-types t1580, t1985, t2123, t3423 and t6228 are also all associated with MLST sequence type ST239, and this MRSA sequence type is considered to be a hospital-associated strain of MRSA. t037 ST239 was also recovered from Belgian poultry in 2011 (Butaye and Nemeghaire, 2012). *Spa*-type t337 is associated with sequence type ST9 (t1430).

Spa-type t044 is associated with MRSA sequence type ST80. This sequence type and associated *spa*-type is observed in a widely disseminated European clone of community-associated MRSA (Larsen et al., 2008). However, *spa*-type t044 has also been associated with sequence type ST9 in a report of a pig with pneumonia (Lulitanond et al., 2013).



Table 42. Meticillin-resistant Staphylococcus aureus in food-producing animals (excluding clinical investigations), 2013

Animal species/ country	Production type/description	Sample unit	Number of units tested	Number (%) positive for MRSA
Gallus gallus			••••••	
	Breeding flocks for broiler production line, adult, at farm, dust, monitoring	Flock	156	0
Germany	Broilers, before slaughter, at farm, dust, monitoring	Flock	157	2 (1.3)
	Broilers, at slaughterhouse, skin swabs, monitoring	Animal	213	84 (39.4)
Hungary		Animal	79	68 (86.1)
Turkeys				
Hungary		Animal	148	101 (68.2)
Pigs				
Belgium ^(a)	At slaughterhouse, nasal swabs, monitoring	Slaughter batch	327	216 (66.1)
Netherlands	Fattening pigs, at slaughterhouse, nasal swabs, monitoring	Herd	93	91 (97.8)
Switzerland ^(b)	Fattening pigs, at slaughterhouse, nasal swabs, monitoring	Animal	351	73 (20.8)
Cattle (bovine ani	mals)			
Cormony	Meat production animals, at farm, dust, monitoring	Herd	328	36 (11.0)
Germany	Meat production animals, at slaughterhouse, nasal swabs, monitoring	Animal	319	26 (8.2)
Netherlands	Meat production animals, at slaughterhouse, nasal swabs, monitoring	Herd	96	69 (71.9)
Switzerland ^(c)	Meat production animals, at slaughterhouse, nasal swabs, monitoring	Animal	253	10 (4.0)

MRSA: meticillin-resistant Staphylococcus aureus.

(a): Isolates belonged to the *spa*-types t011 (176 isolates), t034 (6), t044 (2), t1456 (3), t1580 (3), t1985 (2), t3423 (2), t1344 (1), t1451 (2), t2123 (1), t2370 (1), t2922 (1), t3171 (1), t337 (1), t3854 (1), t4150 (1), t4432 (1), t4872 (1), t5051 (1), t5452 (1), t6228 (1), t8100 (1) and one was not typed. For six isolates, the *spa*-type was not provided.

(b): Isolates belonged to the *spa*-types t034 (63 isolates) and t011 (10).

(c): Isolates belonged to the *spa*-types t011 (5 isolates), t034 (3), t032 (1) and t1255 (1).

Clinical investigations for meticillin-resistant Staphylococcus aureus in food-producing animals

Clinical investigations typically differ from monitoring data in food-producing animals or meat in that selective culture methods may not be used, the number of units tested may be low and the sample may involve a biased sample population. Although these data are not prevalence data and cannot be extrapolated at the population/group level, the results were nevertheless presented in this report, as it is considered important to report the range of animal species/populations which can be affected. In 2013, two MSs (the Netherlands and Slovakia) reported information on results of clinical investigations for MRSA in different kinds of food-producing animals, which tested, most frequently, positive (Table 43).



Table 43. Meticillin-resistant Staphylococcus aureus in food-producing animals, clinical investigations, 2013

Animal species/ country	Production type/description	Sample unit	Number of units tested	Number (%) positive for MRSA
Gallus gallus (for	vi)			
Slovakia	Laying hens, at farm, organ/tissue	Flock	2	1 (50)
Pigeons				
Slovakia	Meat production flocks, at farm, organ/tissue	Flock	17	1 (5.9)
Pigs				
Netherlands	_	Animal	2	1 (50)
Slovakia	At farm, organ/tissue	Animal	22	5 (22.7)
Cattle (bovine an	imals)			
Netherlands	_	Animal	8	0
Slovakia	Calves (under 1 year), at farm, organ/tissue	Animal	4	1 (25.0)
SIOVAKIA	Dairy cows, at farm, milk	Animal	2,052	296 (14.4)
Goats				
Slovakia	Animals over 1 year, at farm, milk	Animal	63	11 (17.5)
Sheep				
Netherlands	_	Animal	1	0
Clavakia	Animals under 1 year (lambs), at farm, organ/tissue	Animal	14	4 (28.6)
Slovakia	Milk ewes, at farm, milk	Animal	36	9 (25.0)
Rabbits				
Slovakia	At farm	Animal	6	6 (100)

MRSA: meticillin-resistant *Staphylococcus* aureus; –: no details reported.

Clinical investigations for meticillin-resistant Staphylococcus aureus in companion animals

Two MSs reported data on MRSA in companion animals in 2013. MRSA was confirmed in 24 horses (N=55), 15 dogs (N=67) and 1 cat (N=41) in the Netherlands and in 2 dogs (N=13) and 18 cats (N=87) in Slovakia. The corresponding *spa*-typing data were not available (Table <u>MRSA1</u>).

Temporal trends in the occurrence of meticillin-resistant Staphylococcus aureus

Although methodological differences may occur between reporting countries, where repeat studies were performed in countries, the same methods were usually employed.

Germany reported annual results on the occurrence of MRSA in calves, at the herd/farm level, in 2010, 2012 and 2013 and, in all years, similar moderate levels of prevalence were registered (Table <u>MRSA2</u>). Differences in the sample type in 2013 compared with those in 2010 and 2012 may mean that a direct comparison between 2013 and the figures for previous years is not appropriate. No data on the genotypes of the strains of MRSA isolated were reported to EFSA.

Switzerland reported results on the yearly prevalence of MRSA in fattening pigs from 2009 to 2013. Prevalence in 2013 was similar to that recorded in 2012, but had significantly increased compared with the previous years, when it was low: 2.2 % in 2009, after which the prevalence increased three-fold to 5.9 % in 2010 and 5.6 % in 2011, and reached 18.1 % in 2012 and 20.8 % in 2013. The marked increase is primarily the result of the diffusion within the Swiss population of fattening pigs of clones of *spa*-types t034 and t011, both belonging to the clonal complex CC398.

3.5.1.3. Susceptibility testing of meticillin-resistant Staphylococcus aureus isolates

In 2013, data on the susceptibility of MRSA and *S. aureus* isolates were reported only by Belgium and Switzerland in animals and by Slovenia in food. All countries used a broth dilution method and applied EUCAST ECOFFs to determine the susceptibility of isolates to cefoxitin, chloramphenicol, ciprofloxacin, clindamycin, erythromycin, fusidic acid, gentamicin, kanamycin, linezolid, mupirocin, quinupristin/dalfopristin, sulfamethoxazole, tetracyclines, tiamulin and vancomycin. All MRSA strains isolated were resistant to penicillin, and only one isolate from pigs recovered by Belgium was not resistant to cefoxitin (data not shown).



In relation to the observed susceptibility of MRSA isolates, there are certain general considerations which apply. Thus, tetracycline resistance was common in the MRSA isolates and, where *spa*-typing data were available, most isolates belonged to *spa*-types associated with CC398. This was expected, as livestock-associated MRSA isolates belonging to sequence type ST398 are usually tetracycline resistant (Crombé et al., 2013). Vancomycin is one of the antimicrobials of last resort for treating *S. aureus* infections in humans and resistance to this antimicrobial is currently extremely rare. None of the isolates from cattle and pigs or meat from pigs, tested for susceptibility, was resistant to vancomycin.

Considering the susceptibility of MRSA isolates from cattle reported by Switzerland, five isolates belonged to *spa*-type t011, three to *spa*-type t034 and one to *spa*-type t1255 (all associated with CC398). The remaining isolate tested in 2013 from cattle was *spa*-type t032, a hospital-associated MRSA *spa*-type. For these MRSA isolates (N=10) from meat-production cattle in Switzerland tested in 2013, resistance was not detected to chloramphenicol, fusidic acid, linezolid, mupirocin, rifampicin, sulfamethoxazole or vancomycin (Table <u>MRSA3</u>). Most isolates were resistant to tetracyclines (as expected for CC398). The occurrence of resistance in cattle tended to parallel that detected in MRSA isolates from fattening pigs in Switzerland.

Among MRSA isolates (N=73) from pigs in Switzerland, no resistance was detected to chloramphenicol, linezolid or vancomycin (Table <u>MRSA3</u>). Resistance was reported at extremely high levels to tetracycline (100 %), clindamycin and erythromycin (86.3 % and 82.2 %, respectively), tiamulin (86.3 %) and quinupristin/dalfopristin (86.3 %), and at low levels for gentamicin and kanamycin (8.2 %), ciprofloxacin (5.5 %), sulfamethoxazole (2.7 %) and mupirocin (2.7 %). Slovenia reported that 100 % of isolates from pig meat were resistant to fusidic acid, kanamycin and streptomycin, with 76.5 % resistant to tetracyclines.

3.5.1.4. Multiple-resistance patterns in meticillin-resistant Staphylococcus aureus isolates

Switzerland reported the susceptibility patterns for eight isolates from cattle and 69 isolates from fattening pigs (Table <u>MDRP47</u>) all isolates were resistant to tetracyclines (a feature of CC398) from both species. In multi-drug-resistant MRSA isolates from Switzerland, tiamulin resistance was invariably associated with clindamycin, quinupristin/dalfopristin, trimethoprim and tetracycline resistance, while gentamicin and kanamycin always occurred together.

The majority of MRSA isolates (39 out of 69) from fattening pigs in Switzerland (Table <u>MDRP47</u>) shared the same core resistance pattern of resistance to beta-lactams, tetracyclines, macrolides, lincosamides, trimethoprim, pleuromutilins, streptomycin and quinupristin/dalfopristin. Twenty-one additional isolates were resistant to all these antimicrobials, except for streptomycin. Gentamicin and kanamycin resistance consistently occurred together when they were present in MRSA isolates from Switzerland from both cattle and fattening pigs.

A diverse range of MDR patterns in MRSA from breeding pigs was recorded in Belgium (Table MDRP49). The predominant type, occurring in 15.7 % of all MRSA isolates from breeding pigs, was resistance to tetracyclines, trimethoprim and ciprofloxacin, with this pattern plus additional erythromycin and clindamycin resistance occurring in 6.7 % of all MRSA isolates tested. Considering the most common *spa*-type, t011, resistance to different antimicrobials within this *spa*-type was variable, with resistance or susceptibility detected to most of the antimicrobials tested, with the exception of vancomycin (to which all MRSA isolates were susceptible) and linezolid, where a single t011 resistant isolate was detected. The other exceptions to this generalisation were tetracyclines, where all *spa*-type t011 isolates were resistant, and trimethoprim, where most isolates were resistant.

Resistance to fusidic acid, kanamycin, streptomycin and tetracyclines with susceptibility to gentamicin was not observed amongst the isolates tested from Switzerland or Belgium. Belgium did not report MDR data for the two *spa*-type t044 isolates recovered from breeding pigs. This susceptibility pattern/*spa*-type combination is commonly seen in the most frequent European strain of community-associated MRSA (Larsen et al., 2008).

Resistance to mupirocin in conjunction with resistance to 14 other antimicrobials tested (all except linezolid and vancomycin) was observed in 3.3 % of MRSA isolates from breeding pigs in Belgium. Overall, mupirocin resistance was seen in 10.0 % of MRSA isolates from breeding pigs in Belgium.

Molecular typing data relating to the genetic mechanisms of resistance were not submitted by reporting countries. Genes conferring multiple antibiotic resistance have been detected in MRSA sequence type ST398 isolates and can occur on mobile genetic elements, accounting for the diverse and variable resistance patterns observed. Resistance to ciprofloxacin and fusidic acid can, however, also arise by mutation and might therefore be observed independently of other resistance genes or in association with particular clones, following clonal expansion. Particular patterns of resistance can be associated with certain resistance genes. Thus, the *vga* genes confer resistance to pleuromutilins, streptogramin A and



lincosamides (Hauschild et al., 2012) and the cfr gene confers resistance to pleuromutilins, streptogramin A, lincosamides, phenicols and oxazolidinones (Kehrenberg et al., 2009). Considering the panel of antimicrobials tested, these genes will therefore confer resistance either to tiamulin, quinupristin/dalfopristin and clindamycin (vga) or to these antimicrobials plus chloramphenicol and linezolid (cfr). The latter pattern was observed in a single MRSA isolate of spa-type t011 from breeding pigs in Belgium, while the former pattern was more common. Out of 210 MRSA isolates from Belgium, 68 were multi-drug resistant, including resistance to tiamulin. Of these tiamulin multi-drug-resistant isolates, 55 were resistant to tiamulin. clindamycin and guinupristin/dalfopristin, 13 were resistant to tiamulin and clindamycin and one was tiamulin resistant but susceptible to clindamycin and guinupristin/dalfopristin. All tiamulin-resistant MRSA isolates from fattening pigs in Switzerland were also resistant to clindamycin and guinupristin/dalfopristin. Out of 69 isolates from Swiss fattening pigs, 60 were resistant to both erythromycin and clindamycin and three were resistant to clindamycin only, and all erythromycin- or clindamycin-resistant isolates were also tiamulinresistant. Out of 210 MRSA isolates from Belgian breeding pigs, 116 were resistant to both clindamycin and erythromycin, 22 were resistant to clindamycin but not erythromycin and four were resistant to erythromycin but not clindamycin. Most of these differences may be accounted for by the presence of vga genes – as vga(A) and vga(C) confer resistance to the lincosamide clindamycin, quinupristin/dalfopristin and tiamulin but not to the macrolide erythromycin (Kadlec et al., 2010) - and either inducible or constitutively expressed erm genes, which, respectively, confer resistance to erythromycin or to both erythromycin and clindamycin (Livermore et al., 2001). Erm genes were frequently detected in bovine MRSA CC398 isolates in a recent Belgian study (Vandendriessche et al., 2013).

Considering resistance to the aminoglycosides, all isolates from fattening pigs in Switzerland resistant to gentamicin were also resistant to kanamycin, as were the two gentamicin-resistant isolates recovered from cattle. There were 83 out of 210 isolates from breeding pigs in Belgium that were multi-drug resistant, including resistance to both kanamycin and gentamicin, 13 isolates were multi-drug resistant and resistant to gentamicin but not kanamycin, and six isolates were resistant to kanamycin but not gentamicin. Aminoglycoside-modifying enzymes have been described as conferring resistance to one or both compounds; thus, APH(2') and AAC(6') confer resistance to both gentamicin and kanamycin, and ANT (4')(4')I, APH(3') and APH(3')III confer resistance to kanamycin but not gentamicin. The gene *apmA* produces an enzyme reported to confer decreased susceptibility to gentamicin and apramycin in staphylococci (Wendlandt et al., 2013).

3.5.2. Discussion

Although food is not currently considered to be a relevant source of MRSA infection or colonisation of humans (EFSA, 2009c), the monitoring of MRSA in various food products performed in several MSs consistently indicates that MRSA can be detected, quite frequently, in different types of food. Such foods included poultry, pork and beef in 2013. However, it is of note that the laboratory techniques used to detect MRSA employ selective bacterial culture and, therefore, low levels of contamination can be detected. In each case, molecular typing would be very useful in investigating the strains of MRSA involved, which might assist in interpreting the findings and unravelling the epidemiology.

Considering the three broad epidemiological classes of MRSA (livestock-associated MRSA, healthcareassociated MRSA and community-associated MRSA), *spa*-typing data confirms that *spa*-types associated with CC398 were most frequent and therefore livestock-associated MRSA remained the type of MRSA most frequently detected in food-producing animals in 2013. *Spa*-types associated with healthcare-associated MRSA were much less frequent. Additionally, *spa*-type t044 was reported in breeding pigs by one MS and MRSA belonging to this *spa*-type comprises the common type of community-associated MRSA observed in Europe. Further investigation of these isolates is required to confirm if they are community-associated MRSA, but the possibility is raised that all three types of MRSA have been detected in livestock in Europe and this is discussed further below. Where *spa*-typing data are not available, the susceptibility of isolates may give some indication of the type of MRSA likely to have been detected, because livestock-associated MRSA belonging to CC398 are usually resistant to tetracycline (Crombé et al., 2013), although this is of course not a definitive characteristic because tetracycline resistance also occurs in other strains of MRSA. Livestock-associated MRSA is considered a poor coloniser of humans and occurs uncommonly in persons without contact with livestock (Graveland et al., 2010).

Belgium and Switzerland reported *spa*-type data for MRSA isolates from food-producing animals. Isolates from Switzerland (cattle and fattening pigs) and most isolates from Belgium (breeding pigs) belonged to *spa*-types associated with livestock-associated MRSA clonal complex 398. Belgium also reported the detection of *spa*-type t4150 (associated with sequence type ST239) and last year reported t037 and t388 (also associated with sequence type ST239); this is of interest, as these are generally considered to be hospital-associated strains of MRSA. t037 sequence type ST239 was also recovered from Belgian poultry in 2011



(Butaye and Nemeghaire, 2012). The EU baseline survey of breeding pigs (EFSA, 2009b) reported the occurrence of *spa*-type t008 in breeding pigs, associated with sequence type ST8, which in turn belongs to clonal complex 8 (a clonal complex to which sequence type ST239 also belongs). The occurrence of MRSA *spa*-types associated with sequence types ST8 and ST239 in different food-producing animals, occurring over several different years, indicates that this may be a further strain of MRSA able to colonise different animal species and reinforces the value of such ongoing surveillance, because these are types usually considered as healthcare-associated MRSA.

Spa-type t337 is associated with sequence type ST9 and was detected in breeding pigs in Belgium. The baseline survey of breeding pigs (EFSA, 2009b) detected t1430, which is also associated with sequence type ST9. MRSA sequence type ST9/CC9 has been reported as the predominant sequence type in pigs in China (Cui et al., 2009) and has been identified in meticillin-susceptible *Staphylococcus aureus* from pigs and cattle in Denmark (Hasman et al., 2009). However, the phenomenon of heterogeneity amongst *spa*-types, which was observed in the EFSA survey of breeding pigs (EFSA, 2009b), means that isolates assigned to CC398 can have *spa*-types usually associated with other sequence types of MRSA by MLST. Both typing systems are therefore complementary in some circumstances.

Finally, Belgium also reported two isolates of *spa*-type t044 from fattening pigs. *Spa*-type t044 is usually associated with a widely distributed European community-associated MRSA clone which is generally positive for the Panton–Valentine leukocidin and which often shows characteristic MDR patterns, commonly of resistance to fusidic acid, tetracyclines, streptomycin and kanamycin, but susceptibility to gentamicin (Larsen et al., 2008). However, more typing data are required for these isolates to fully characterise them, because they did not show the characteristic MDR pattern of the community-associated MRSA t044 clone. *Spa*-type t044 has also been reported from a pig with pneumonia from Thailand and in this case was associated with MRSA sequence type ST9. Interestingly, Slovenia reported 100 % of isolates from pig meat resistant to fusidic acid, kanamycin and streptomycin, with 76.5 % resistant to tetracyclines; *spa*-typing data were not available for these isolates. As stated above, this pattern of resistance (with most isolates susceptible to gentamicin) is that commonly reported for community-associated MRSA belonging to *spa*-type t044, which in many European countries is the most common type of community-associated MRSA occurring in humans in Europe. Further characterisation is necessary to allow a definitive conclusion, but the results raise the possibility that community-associated MRSA may have also been detected in food and livestock in 2013.

Where data are available in classes of animals tested both on the farm and at slaughter, comparison of the proportion of MRSA-positive animals generally reveals a higher prevalence when animals are tested at slaughter than when animals are tested on farms. This may reflect either cross-colonisation of animals during transport to abattoirs (or while awaiting slaughter in temporary lairage pens at the slaughterhouse) or acquisition of the organism from various sources encountered during transport and lairage (pens, human contact, vehicles, etc.). It is therefore of note that the high prevalence of MRSA in pigs (99.0 % in 2012, 97.8 % in 2013) and in cattle (79.0 % in 2012, 71.9 % in 2013) in the Netherlands was assessed at slaughter. A similar finding is also illustrated in the case of broilers in Germany, where on-farm monitoring detected that 1.3 % of farms were positive, whereas 39.4 % of birds at slaughter were positive. The occurrence of resistance in cattle tended to parallel that detected in MRSA isolates from fattening pigs in Switzerland, although the number of isolates tested from cattle was lower. This, and the common *spa*-types detected in these animals, suggests a possible epidemiological link between them, for example common sources or transfer between animals on mixed livestock farms.

The MDR patterns reported for MRSA indicated that only a single isolate from breeding pigs in Belgium had a resistance phenotype consistent with carrying of the *cfr* gene, conferring resistance to a range of antimicrobials. Tiamulin resistance with resistance to quinupristin/dalfopristin and lincosamides was relatively common, suggesting widespread occurrence of *vga* genes. Mupirocin resistance was noted in some isolates and these frequently showed resistance to a range of other antimicrobials. The occurrence of mupirocin resistance may have potential importance where decolonisation of human carriers of MRSA is advised. All MRSA isolates tested were susceptible to vancomycin, a critically important antimicrobial for the treatment of infections in humans.

3.6. Third-generation cephalosporin resistance in *Escherichia coli* and *Salmonella*

Resistance to third-generation cephalosporins: the importance of extended-spectrum beta-lactamases and AmpC enzymes

Extended-spectrum beta-lactamases (ESBLs) are considered to be an important emerging issue in Gram-negative bacteria of public health significance. Bacteria which possess ESBL resistance are usually resistant to third-generation cephalosporins, which are critically important antibiotic drugs for the treatment of systemic or invasive Gram-negative bacterial infections in humans. These drugs play a critical role in the treatment of certain invasive Salmonella infections, particularly in children, in whom the use of fluoroquinolones may not be favoured because of certain potential adverse effects. A low level of resistance in Salmonella may therefore still constitute an important finding. Commensal bacteria, such as indicator Escherichia coli, may contribute to the dissemination of ESBL resistance because such resistance is usually transferable.

Salmonella and E. coli may become resistant to third-generation cephalosporins by several different mechanisms. Among these different mechanisms, the most common is the acquisition of beta-lactamase enzymes on plasmids (small covalently closed circles of DNA which can be transferred between bacteria during bacterial conjugation). There are several different types of beta-lactamase which can confer resistance to third-generation cephalosporins. These are conveniently sub-divided into four classes, designated A to D: ESBL enzymes of the TEM, SHV and cefotaximase families belong to class A, while class C includes the AmpC beta-lactamases.

Wild-type Salmonella isolates never possess a beta-lactamase of any class. For beta-lactamases to occur in Salmonella, acquisition must generally have occurred by conjugation, usually with other Enterobacteriaceae through transfer of plasmids. Although all four different types of beta-lactamase classes have been described in Salmonella globally, within the EU (EU), the most important types of beta-lactamase resistance acquired by Salmonella are primarily ESBL resistance and, secondly, AmpC resistance. E. coli can acquire beta-lactamases from other bacteria in a similar fashion to Salmonella but, as it also possesses an endogenous AmpC beta-lactamase, in some circumstances this can be activated, conferring resistance to third-generation cephalosporins.

The position has been further complicated in recent years by the emergence of resistance to carbapenems in human medicine. Carbapenems are used for the treatment of highly resistant infections in humans, including, for example, the treatment of infections with Gram-negative bacteria which possess ESBL enzymes. These compounds are not used in food-producing animals anywhere within the EU. Resistance to carbapenems in Gram-negative bacteria is usually related to the acquisition of carbapenemase enzymes and a number of different types are recognised. Although carbapenem antimicrobials are not used in food-producing animals in the EU, resistance has occasionally been detected in bacteria carried by animals (Woodford et al., 2013), and dissemination from humans to animals directly or through environmental routes is suspected. In view of the great importance of the carbapenem compounds, they have been added to the panels of antimicrobials recommended for testing by MSs to improve surveillance for resistance (EFSA, 2012a).

The EFSA guidelines for monitoring resistance in indicator *E. coli* (EFSA, 2008) state that cefotaxime is a good substrate for what are currently the most common and important ESBLs in humans in Europe, the cefotaximase (CTX-M) enzymes, which can therefore be used as an indicator for ESBL resistance. ECOFFs for *Salmonella* and *E. coli* for the antimicrobial cefotaxime facilitate detection of CTX-M ESBLs, but resistance to cefotaxime may, of course, be conferred by mechanisms of resistance other than ESBLs, such as certain other types of beta-lactamases, including AmpC beta-lactamases. In this section, the occurrence of resistance to ceftofur, and because this compound is not considered optimal for the detection of ESBL enzymes, results for ceftiofur are not included in this section. Furthermore, because this report covers only phenotypic monitoring, it is not possible to determine the class or exact type of beta-lactamase enzyme which is responsible for conferring the resistance detected to third-generation cephalosporins.

The monitoring reported here and performed in accordance with EFSA's guidelines (EFSA, 2008) does not utilise selective primary isolation media containing cephalosporins so the results generally relate to organisms chosen effectively at random from primary culture media. In certain types of monitoring, selective media containing cephalosporins may be used to investigate the presence or absence of cephalosporin-resistant organisms in a particular sample (within the limit of detection) and, in that case, a different type of result would be obtained from such monitoring, which has a greater sensitivity. Ideally, the establishment of



optimum phenotypic testing systems for sensitive, specific and rapid detection of ESBLs would be a very important component of antimicrobial resistance monitoring programmes. Recommendations for such monitoring recently developed by EFSA (EFSA, 2012a) notably put forward further testing of isolates which are resistant to third-generation cephalosporins, including testing to establish whether isolates have an ESBL- or AmpC-producing phenotype.

3.6.1. Third-generation cephalosporin resistance in *Salmonella* isolates from food and animals

3.6.1.1. Third-generation cephalosporin resistance in Salmonella isolates from food

In most reporting MSs, resistance was either not detected or reported at low levels in the four kinds of meat (Table <u>ESBL1</u>). Resistance to cefotaxime was typically equal or similar to that observed to ceftazidime at the MSs level. Considering all MSs, the apparent difference in resistance to each compound in meat from broilers largely reflects differences in the number of sensitive isolates contributing to the denominator.

Resistance to cefotaxime or ceftazidime was not detected in *S*. Enteritidis from meat from broilers (Table <u>ESBL2</u>) or in *S*. Typhimurium isolates and monophasic *S*. Typhimurium isolates from meat from pigs (Table <u>ESBL3</u>). Exceptions to this are resistance to cefotaxime and ceftazidime in *Salmonella* spp. isolates from broiler meat recorded at levels greater than 10.0 % in Germany and around 50.0 % in the Netherlands and meat from turkey at levels greater than 20.0 % in the Netherlands (Table <u>ESBL1</u>).

3.6.1.2. Third-generation cephalosporin resistance in Salmonella isolates from animals

Resistance levels in Gallus gallus (fowl)

A low level of resistance to cefotaxime and to ceftazidime of 5.4 % was reported in *Salmonella* spp. isolates from all reporting MSs, reflecting either no or very low to low resistance recorded in nearly all reporting countries (Table <u>ESBL4</u>). Only the Netherlands and Romania recorded much higher levels of resistance above 10.0 % to both antimicrobials.

Considering differing populations of *Gallus gallus* separately, levels of resistance to third-generation cephalosporins in *Salmonella* spp. isolates from broiler, laying hen and breeding flocks and were generally either not detected or recorded at low levels (Table <u>ESBL4</u>). The levels of resistance in broilers were generally slightly higher than those reported when all *Gallus gallus* isolates were considered, as most reporting MSs detected resistance, while, in laying hen and breeding flocks, resistance was generally not recorded. In *Salmonella* spp. from laying hens and breeding flocks, only three (Italy, the Netherlands and Romania) and three MSs (Czech Republic, Italy and Romania) detected low level resistance to third-generation cephalosporins out of the 12 and four reporting MSs, respectively. In broilers, four MSs reported levels of resistance to third-generation cephalosporins greater than 10.0 %.

The resistance to cefotaxime and ceftazidime in *S*. Enteritidis isolates from *Gallus gallus*, broilers and laying hens was generally not detected in reporting MSs (Table <u>ESBL5</u>). Resistance to both cefotaxime and ceftazidime was reported at low levels in Belgium and Romania and only to cefotaxime in Croatia. Among the reporting MSs on broilers, Belgium and Romania observed resistance to cefotaxime at a low level below 5.0 %. Considering isolates from laying hens, resistance to ceftazidime or to cefotaxime was not detected by any of the MSs.

Resistance to third-generation cephalosporins in *S*. Typhimurium isolates from *Gallus gallus* (Table <u>ESBL6</u>) was reported by eight MSs. None of the reporting countries detected resistance to cefotaxime or to ceftazidime.

Resistance levels in turkeys

Resistance to both cefotaxime and ceftazidime was reported by France at low proportions, whereas Spain reported very low resistance to cefotaxime only (Table <u>ESBL7</u>).

Resistance levels in pigs

Most reporting MSs did not detect any resistance, making the overall level of resistance at the MS group level in pigs low at 1.2 % for cefotaxime and 1.9 % for ceftazidime (Table <u>ESBL8</u>). Three MSs detected both cefotaxime and ceftazidime resistance in *Salmonella* spp. isolates from pigs. In fattening pigs, cefotaxime and ceftazidime resistance was observed only by Spain (1.4 %), while, in breeding pigs, Belgium recorded cefotaxime and ceftazidime resistance at the same levels of 1.6 %.

Among MSs reporting results on the third-generation cephalosporins in *S*. Typhimurium from pigs, Belgium and Germany were the only countries to report cefotaxime and ceftazidime resistance in *S*. Typhimurium, at the same levels, for both substances, of 2.7 % and 1.3 %, respectively (Table <u>ESBL9</u>). The overall levels of



resistance for all reporting MSs were, therefore, at low levels of 1.2 % for cefotaxime and 1.7 % for ceftazidime.

Resistance to third-generation cephalosporins in monophasic *S*. Typhimurium isolates from pigs was not detected by any of the MSs (Table <u>ESBL10</u>).

Resistance levels in cattle

Among the four MSs reporting data on resistance to cefotaxime and three ceftazidime in *Salmonella* spp. from cattle (Table <u>ESBL11</u>), none of the MSs detected resistance. None of the *S*. Typhimurium isolates tested exhibited any resistance to these compounds amongst the three and two, respectively, reporting MSs (Table <u>ESBL11</u>).

Salmonella serovars from animals demonstrating resistance to third-generation cephalosporins

Third-generation cephalosporin resistance was identified in a range of *Salmonella* serovars in 2013. Reporting MSs do not necessarily list all of the *Salmonella* serovars identified, and so the list of affected serovars is likely to be incomplete. In 2013, the following third-generation cephalosporin-resistant serovars were identified from one or more sources (pigs, *Gallus gallus*, turkey and/or cattle) and from one or more MSs: S. Agona, S. Derby, S. Infantis and S. Typhimurium.

Reporting of specific data on extended-spectrum beta-lactamases in Salmonella

In 2012, EFSA published a report (EFSA, 2012a) providing detailed recommendations and discussions relating to how future surveillance for third-generation cephalosporin, ESBL, AmpC and carbapenem resistance monitoring could be enhanced. Two MSs (Czech Republic and Italy) reported data on the identity of the ESBL detected in *Salmonella* isolates from pigs. Two isolates (of serovars *S*. Derby and monophasic *S*. Choleraesuis) were reported, producing CTX-M-1 and CTX-M, respectively. CTX-M-1 is an ESBL enzyme which has been previously recognised in pigs in several MSs. One *S*. Typhimurium isolate produced the enzyme OXA-1, which confers resistance to the action of clavulanic acid, a beta-lactamase enzyme inhibitor, by breaking down the clavulanate compound.

3.6.2. Third-generation cephalosporin resistance in indicator *Escherichia coli* isolates from food and animals

3.6.2.1. Third-generation cephalosporin resistance in indicator Escherichia coli isolates from food

Two MSs (Denmark and Hungary) reported results for resistance to cefotaxime in *E. coli* isolates from meat from broilers, meat from pigs and meat from bovine animals in 2013. Germany reported data from meat from broilers and meat from bovine animals and Slovenia reported data from meat from broilers and meat from pigs. Germany tested ceftazidime and recorded similar resistance levels to those obtained for cefotaxime. Overall, resistance to third-generation cephalosporins was either not detected or reported at low levels ranging between 1.1 % and 8.7 %. Slovenia reported moderate level of resistance in meat from pigs and high resistance in meat from broilers (Table ESBL12).

3.6.2.2. Third-generation cephalosporin resistance in indicator *Escherichia coli* isolates from animals

Resistance levels in Gallus gallus (fowl)

Data on resistance in indicator *E. coli* isolates from *Gallus gallus* were reported by 10 reporting MSs, as well as Norway and Switzerland, distinguishing, where possible, between broilers and laying hens (Table <u>ESBL13</u>). All reporting countries tested resistance to cefotaxime and five reporting MSs also tested isolates for ceftazidime resistance. The levels of resistance reported were generally low, although Belgium, Croatia and Spain reported moderate levels of resistance in *Gallus gallus*. In the case of Poland, where resistance to cefotaxime was reported in isolates from both broilers and laying hens, the levels of resistance, when considering isolates from broiler flocks, were approximately at the same levels as reported from laying hens.

Resistance levels in pigs

Overall, the levels of resistance in reporting countries were low and Denmark detected no resistance in indicator *E. coli* from pigs (Table <u>ESBL14</u>).

Resistance levels in cattle

The overall occurrence of resistance to cefotaxime and to ceftazidime in indicator *E. coli* isolates from cattle was 1.2 % (Table <u>ESBL15</u>). Denmark, Hungary, Spain, Sweden and Switzerland did not detect cefotaxime resistance in indicator *E. coli* from cattle in 2013, and in the remaining MSs a low or very low level (0.2 %– 5.7 %) of resistance to both antimicrobials was detected.



Indicator commensal *E. coli* in healthy animals may constitute a reservoir of resistance genes which can be transferred to zoonotic organisms, such as *Salmonella*, and this process may be particularly enhanced in some circumstances, for example under selection pressure resulting from antimicrobial usage. Once *Salmonella* isolates have acquired plasmids carrying genes conferring resistance to third-generation cephalosporins (either ESBL or AmpC resistance genes), the dissemination of such resistant *Salmonella* clones will also play a major part in influencing the occurrence of third-generation cephalosporin resistance.

Considering the prevalence of resistance to cefotaxime and resistance in MSs to Salmonella spp. and *E. coli* in all species for which relevant data are available, in all reporting MSs where resistance was detected in 2013, the prevalence of resistance is higher in *E. coli* than it is in Salmonella spp. with the exception of Belgium and isolates from pigs and Netherlands isolates for *Gallus gallus*. Table 44 summarises the data and illustrates some interesting observations relating to the occurrence of cefotaxime resistance in *Salmonella* spp. and *E. coli* in MSs.

Where resistance is detected in *Salmonella* spp. in an MS, it is also invariably present in *E. coli* in that reporting MS and usually occurs at a higher level (with only two exceptions). Some MSs do not report cefotaxime resistance in *Salmonella* spp. or in *E. coli* for some food-producing animals. The degree of resistance observed in *Salmonella* spp. and *E. coli* may be correlated in those MSs which have a high level of resistance in *Salmonella* spp. and have a high level of resistance in *Salmonella* spp. and have a high level of resistance in *Salmonella* spp. and have a high level of resistance in *Salmonella* spp. and have a high level of resistance in *Salmonella* spp. and have a high level of resistance in *Salmonella* spp. and have a high level of resistance in *Salmonella* spp. It tends to appear not always hold true and would not be expected to hold where clonal dissemination of particular strains of *Salmonella* were responsible for the observed prevalence of resistance in *Salmonella* spp. It tends to appear that, in most MSs, commensal *E. coli* is the primary reservoir of beta-lactamase resistance, which is less frequently observed in *Salmonella* spp.

All MSs detected resistance to cefotaxime in broilers except Austria, Denmark and Hungary; the prevalence ranged from 0.3 % to 14.8 %. Where MSs reported data for both pigs and broilers, the levels observed in pigs were consistently lower. In cattle, some MSs reported that cefotaxime resistance was intermediate, lying between that observed in pigs and broilers (Belgium and the Netherlands). However, it is of note that differences in the types of cattle sampled may make direct comparisons between MSs inappropriate.

3.6.4. Discussion

etsa

In 2013, as in the previous years, resistance to third-generation cephalosporins was generally detected at low levels in *Salmonella* and indicator *E. coli* isolates recovered from major food-producing animals and meat thereof. In most MSs, the prevalence of resistance to cefotaxime in both *Salmonella* spp. and *E. coli* was equal to that observed for ceftazidime. Although resistance assessed using ECOFFs tends to usually detect resistance to both compounds, this is not always the case and differences in resistance to each compound may be observed, reflecting whether the ESBL enzyme conferring resistance is primarily a cefotaximase or a ceftazidimase. ESBLs belonging to the CTX-M family (primarily, although not entirely, cefotaximases) are currently the most important types of ESBL in both animals and humans in the majority of MSs. However, EFSA has recommended that both cefotaxime and ceftazidime are included in future harmonised mandatory monitoring to ensure optimal detection of all ESBLs (EFSA, 2012a), as surveillance procedures should anticipate possible changes in the status of different ESBL enzymes.

Resistance to cefotaxime in *Salmonella* spp. isolates recovered from meat from broilers was reported at low or moderate levels in most reporting MSs. In most MSs, the observed levels of resistance in meat from broilers and *Gallus gallus* (or broilers) showed many similarities; however, in a number of MSs, differences in the levels of cefotaxime resistance in meat and the species from which the meat was produced were observed. For example, in Germany and Ireland, resistance to cefotaxime or ceftazidime was not detected in *Salmonella* spp. from broilers, while resistance to the same compounds was reported at low and moderate levels in meat from broilers. Conversely, in Romania, the cefotaxime resistance was recorded at very low levels in *Salmonella* spp. isolates from broiler meat and at moderate levels in isolates from broilers. The reasons underlying the absence of a clear correlation between the prevalence of resistance observed in livestock and that in meat derived from those animals within an MS may be related to the lack of direct comparability between the target populations used for the monitoring in retail meat and in broilers. The retail meat monitored may notably include not only domestic poultry meat, but also imported meat from other countries.

Considering all MSs, resistance to cefotaxime in *Salmonella* spp. recovered from meat from turkeys, pigs and cattle was 4.9 %, 0.9 % and 0 %, respectively, all of which are lower than the figure of 10.3 % reported for meat from broilers. Two factors contribute to this observed difference: (1) the proportion of reporting MSs



which did not report resistance to cefotaxime in meat from pigs and cattle was higher than that for meat from broilers, and (2) in MSs which did report resistance, the levels of resistance reported for *Salmonella* spp. from meat broilers were higher than for meat from pigs and cattle.

The results have been presented by animal production type (where available and relevant). Differences in the occurrence of resistance may be related to husbandry methods, age or stage of production, the degree of antimicrobial usage or the influence the structure of the particular livestock industry may have on clonal spread of resistant organisms. The prevalence of resistance to cefotaxime in *Salmonella* spp. was higher in broilers than in laying hens (when resistance was detected) for all MSs. Laying hens tend to be infrequently treated with antimicrobials, especially once in lay. *S.* Enteritidis from broilers and layers were susceptible to cefotaxime, in laying hens, suggesting that a ceftazidimase enzyme may have been present. *Salmonella* spp. resistant to cefotaxime was most frequently observed in broilers and the proportion of MSs observing any degree of resistance was higher than that for other animal species (turkeys, pigs and cattle).

Breeding animals may play a role in the clonal dissemination of resistance in particular serovars of *Salmonella* when animals colonised at breeding units are moved to fattening farms. A proportion of the reporting MSs observed cefotaxime resistance in *Salmonella* spp. isolates from breeding flocks of *Gallus gallus* and from breeding pigs. None of the MSs reported third-generation cephalosporin resistance in *Salmonella* spp. isolates from cattle.

Some *Salmonella* serovars have particular public health significance because they either are common causes of human salmonellosis or have acquired resistance to a large number of different antimicrobial compounds (or even exhibit both of these traits). Resistance to third-generation cephalosporins was detected in a number of serovars of particular public health importance, including *S*. Typhimurium and *S*. Infantis.

Although thorough cooking and appropriate food hygiene procedures kill any bacteria present on food and prevents cross-contamination of foods with resistant or susceptible bacteria, it is highly desirable that the level of resistance in zoonotic organisms is very low or zero, especially in relation to important antimicrobials for human treatment. Among the strains of *E. coli* occurring in animals, some may be able to cause infections in humans (many will be largely harmless animal commensals) and some, although they are primarily commensals of animals, may be able to transiently or permanently colonise the human intestine. During transient colonisation or passage through the human intestine, *E. coli* may be able to exchange their resistance plasmids with the commensal *E. coli* flora of humans. Therefore, it is also desirable that resistance to important antimicrobials for human treatment is also very low or zero in animal strains of *E. coli*, which might otherwise form a reservoir of resistance genes.



Table 44. Resistance (%) to cefotaxime in Salmonella spp. and indicator E. coli isolates in MSs in 2013 testing both bacterial species in Gallus gallus, pigs or cattle

		Gallus	gallus			Pig	S	Cattle				
Country	Salmon	<i>ella</i> spp.	E. coli		Salmonella spp.		E. coli		Salmonella spp.		E. coli	
	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Austria	175	0	146	2.1	-	-	-	-	-	-	-	-
Belgium	426	4.0	234	10.3	318	1.6	204	1.0	39	0	406	3.7
Croatia	91	8.8	150	18.0								
Denmark	30	0	125	0.8	206	0	146	0	_	_	_	_
France	257	0.8	193	6.2								
Germany	232	0.4	599	5.0	_	_	_	_	61	0	526	0.8
Hungary	252	0	152	6.6	_	_	_	_	_	_	_	_
Netherlands	508	14.8	494	2.6	162	0	289	1.7	102	0	588	0.2
Poland	357	0.3	343	5.2	10	0	190	2.6	-	_	_	_
Spain	137	0.7	170	15.9	69	1.4	170	0.6	-	_	-	_
United Kingdom	-	_	-	_	147	0	157	0.6	-	_	-	_

MSs: Member State; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.



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List of abbreviations

Abbreviation	Definition
%	percentage of resistant isolates per category of susceptibility or multiple resistance
% f	percentage frequency of isolates tested
% Res	percentage of resistant isolates
-	no data reported
AHVLA	Animal Health and Veterinary Laboratories Agency
AMR	antimicrobial resistance
AST	antimicrobial susceptibility testing
BIOHAZ	EFSA Panel on Biological Hazards
CA-SFM	French Society for Microbiology
CC	clonal complex
CLSI	Clinical and Laboratory Standards Institute
CBP	clinical breakpoints
CTX-M	cefotaximase
DIN	Deutsches Institut für Normung
DNA	deoxyribonucleic acid
EARS-Net	European Antimicrobial Resistance Surveillance Network
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
ECOFF	epidemiological cut-off value
EEA	European Economic Area
EFSA	European Food Safety Authority
ESBL	extended spectrum beta-lactamase
ETEC	enterotoxigenic <i>E. coli</i>
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
EU-RL	EU Reference Laboratory
FWD	food- and waterborne diseases and zoonoses
HACCP	hazard analysis and critical control point
HPA	Health Protection Agency (UK)
1	intermediate
IZD	inhibition zone diameter
MDR	multiple drug resistance
MIC	minimum inhibitory concentration
MLST	multi-locus sequence typing
MRSA	meticillin-resistant Staphylococcus aureus
MSA	meticillin-susceptible Staphylococcus aureus
MS	Member State
NA	not applicable
NCP	National Control Programme
NRL	National Reference Laboratory
R	resistant
res1–res9	resistance to one antimicrobial substance/resistance to nine antimicrobial substances of the common set for Salmonella
S	susceptible
spp.	species
ST	sequence type
TESSy	The European Surveillance System
VTEC	vero(cyto)toxigenic <i>E. coli</i>



Antimicrobial substances

Abbreviation	Antimicrobials
Amc	amoxicillin/clavulanate
Amp	ampicillin
Caz	ceftazidime
Chl	chloramphenicol
Сір	ciprofloxacin
Ctx	cefotaxime
Ery	erythromycin
Gen	gentamicin
Nal	nalidixic acid
Sul	sulfonamides
Str	streptomycin
Sxt	sulfamethoxazole
Tet	tetracycline
Tmp	trimethoprim

MSs of the EU and other reporting countries in 2013

Member State	Country abbreviations
Austria	AT
Belgium	BE
Bulgaria	BG
Croatia	HR
Cyprus	CY
Czech Republic	CZ*
Denmark	DK
Estonia	EE
Finland	FI
France	FR
Germany	DE
Greece	GR
Hungary	HU
Ireland	IE
Italy	IT
Latvia	LV
Lithuania	LT
Luxembourg	LU
Malta	MT
Netherlands	NL*
Poland	PL
Portugal	PT
Romania	RO
Slovakia	SK
Slovenia	SI
Spain	ES
Sweden	SE
United Kingdom	UK*

* In text, referred to as the Czech Republic, the Netherlands and the United Kingdom



Non-MSs reporting, 2014

Country	Country abbreviations
Iceland	IS
Norway	NO
Switzerland	СН

Definitions

Term	Definition and o	description					
'Antimicrobial-resistant isolate'	In the case of quantitative data, an isolate was defined as 'resistant' to a select antimicrobial when its minimum inhibitory concentration (MIC) value (in mg/L) was above the cut-off value or the disc diffusion diameter (in mm) was below th cut-off value. The cut-off values, used to interpret MIC distributions (mg/L) for bacteria from animals and food, are shown in Table 4 In the case of qualitative data, an isolate was regarded as resistant when the						
		it as resistant using its own cut-off value or break point					
'Level of antimicrobial resistance'	The percentage	e of resistant isolates among the tested isolates					
'Reporting MS group'	· · · ·	provided data and were included in the relevant table for istance data for the bacteria–food/animal category–antimicrobial					
Terms used to describe the	Rare:	< 0.1 %					
antimicrobial resistance levels	Very low:	0.1 % to 1.0 %					
	Low:	>1.0 % to 10.0 %					
	Moderate:	>10.0 % to 20.0 %					
	High:	>20.0 % to 50.0 %					
	Very high:	>50.0 % to 70.0 %					
	Extremely high:	>70.0 %					

List of institutions contributing to antimicrobial resistance monitoring in animals and food

Member State	Institution
Austria	 Federal Ministry for Health, Vienna Austrian Agency for Health and Food Safety (AGES), Vienna and Linz
Belgium	 Veterinary and Agrochemical Research Centre (CODA-CERVA), Uccle Institute of Public Health, Brussels Federal Agency for the Safety of the Food Chain, Brussels
Bulgaria	 National Diagnostic and Research Veterinary Institute, Sofia Bulgarian Food Safety Agency, Sofia
Croatia	Croatian Veterinary Institute, Zagreb
Cyprus	 Veterinary Services, Nicosia Ministry of Agriculture, Nicosia
Czech Republic	 State Veterinary Institute, Prague and Olomouc State Veterinary Administration of the Czech Republic, Prague
Denmark	 National Food Institute, Technical University of Denmark, Lyngby Danish Veterinary and Food Administration, Glostrup
Estonia	 Estonian Veterinary and Food Laboratory, Tartu Veterinary and Food Board, Tallinn
Finland	EVIRA, Finnish Food Safety Authority, Helsinki
France	 ANSES, French Agency for Food, Environmental Occupational Health and Safety: Fougères Laboratory, Maisons-Alfort Laboratory, Ploufragan/Plouzané Laboratory Ministère de l'agriculture, de l'alimentation, de la pêche, de la ruralité et de l'aménagement du territoire, Direction Générale de l'Alimentation, Paris
Germany	Federal Institute for Risk Assessment (BfR), Berlin
Greece	Veterinary Laboratory, ChalkisMinistry of Rural Development and Food, Athens
Hungary	 Central Agricultural Office, Veterinary Diagnostical Directorate, Budapest Ministry of Rural Agriculture, Budapest
Ireland	 Central Veterinary Research Laboratory, Celbridge Food Safety Authority of Ireland, Dublin
Italy	 Istituto Zooprofilattico Sperimentale delle Regioni Lazio e Toscana, Rome Ministry of Health, Rome
Latvia	 Institute of Food Safety, Animal Health and Environment 'BIOR', Animal Disease Diagnostic Laboratory, Riga Food and Veterinary Service of Latvia, Riga
Lithuania	 National Food and Veterinary Risk Assessment Institute, Vilnius State Food and Veterinary Service, Vilnius
Luxembourg	Laboratoire de Médecine Vétérinaire, Luxembourg
Malta	Ministry for Resources and Rural Affairs, Santa Venera

Table continued overleaf.

List of institutions contributing to antimicrobial resistance monitoring in animals and food (continued)

Member State	Institution
Netherlands	 Central Veterinary Institute, part of Wageningen UR (CVI), Lelystad National Institute of Public Health and the Environment (RIVM), Bilthoven Ministry of Agriculture, Nature and Food Quality, Den Haag Animal Health Service, Deventer
Poland	 National Veterinary Research Institute, Pulawy General Veterinary Inspectorate, Warsaw
Portugal	 Laboratório Nacional de Investigação Veterinária, Lisbon Direcção Geral de Veterinária, Lisbon
Romania	 Institute for Diagnostic and Animal Heath, Bucharest Institute for Hygiene and Veterinary Public Heath, Bucharest National Sanitary Veterinary and Food Safety Authority, Bucharest
Slovakia	 State Veterinary and Food Institute, Dolny Kubin and Bratislava State Veterinary and Food Administration of the Slovak Republic, Bratislava
Slovenia	 National Veterinary Institute, Veterinary Faculty, Ljubljana Ministry for Agriculture and Environment, Veterinary Administration, Ljubljana
Spain	 Laboratorio Central de Sanidad Animal de Santa Fe, Granada Laboratorio Central de Veterinaria de Algete, Madrid VISAVET Health Surveillance Center, Complutense University, Madrid Ministerio de Agricultura, Alimentación y Medio Ambiente, Madrid Agencia Española de Seguridad Alimentaria y Nutrición, Madrid
Sweden	 National Veterinary Institute (SVA), Department of Animal Health and Antimicrobial Strategies, Uppsala National Food Administration, Uppsala
United Kingdom	Animal Health and Veterinary Laboratories Agency (AHVLA), Addlestone, Surrey (and offices nationwide)

Other reporting country	Institution
Iceland	 Institute for Experimental Pathology, Keldur Icelandic Food and Veterinary Authority, Selfoss
Norway	Norwegian Veterinary Institute, Oslo
Switzerland	 ZOBA–Centre for Zoonoses, Bacterial Animal Diseases and Antimicrobial Resistance– Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Bern Federal Food Safety and Veterinary Office, Bern



Appendix A: Antimicrobial resistance in *Salmonella* – qualitative data

In 2013, Greece and Spain reported on antimicrobial resistance in *Salmonella* from animals as quantitative disc diffusion data, which have been analysed as qualitative data and presented in this section. These disc diffusion data have been analysed using the breakpoints for resistance specified by the reporting MS and in accordance with the method used.

In the case of data reported exclusively as qualitative data, when information on the thresholds used to interpret the resistance was also available, it has been possible to pool the data submitted by MSs and present them in this section. It should, however, be noted that countries may not have used the same threshold values or qualitative methods, and so direct comparisons between the proportions of resistant isolates in MSs reporting only qualitative data should be interpreted with caution. For this reason, tables do not show the summary figure for the reporting MS group and the spatial distributions of the levels of resistance for *Salmonella* based on qualitative data are not shown here; this is in accordance with previous reports. Furthermore, for those countries that reported quantitative data on antimicrobial resistance, as presented in Section <u>3.2</u>, corresponding qualitative data have been excluded from the overview Table <u>OVER8</u>) and the analyses presented in this section.

Resistance to the following antimicrobial agents are described in detail below: ampicillin, chloramphenicol, ciprofloxacin, gentamicin, nalidixic acid, sulfonamides and tetracyclines.

Antimicrobial resistance in *Salmonella* isolates from meat (qualitative data)

Resistance levels among Salmonella spp. isolates

Six MSs reported qualitative data on resistance among *Salmonella* spp. from meat from broilers in 2013 and only one MS reported qualitative data on resistance among *Salmonella* spp. from meat from pigs. The results are presented in Table 45.

Antimicrobial resistance in Salmonella isolates from animals (qualitative data)

Resistance levels among Salmonella

Five MSs and one non-MS reported qualitative data for isolates of *Salmonella* from *Gallus gallus*. The results are presented in Table 46.

Croatia and Iceland were the only countries to report qualitative data for isolates of *Salmonella* spp. from pigs. The results are presented in Table 46.

Discussion

Very few countries reported qualitative data for *Salmonella* in 2013. Furthermore, it is difficult to compare accurately the data collected using disc diffusion techniques with those derived from dilution methods and collected quantitatively as MIC data. Therefore, as in previous years, a detailed analysis and interpretation of the results has not been undertaken.

Greece used CLSI disc diffusion methods to test the *Salmonella* isolates recovered from *Gallus gallus* and interpreted the results using CLSI breakpoints. The results will not be directly comparable to the results obtained by MSs performing broth microdilution MIC determinations and applying EUCAST ECOFFs to interpret those results and have therefore been presented separately.



Country	Amp	oicillin	Cefotaxime		Chloramphenicol		Ciprof	Ciprofloxacin		amicin	Nalidixic acid		Sulfonamides		Tetracyclines	
Country	Ν	% Res	N	% Res	Ν	% Res	N	N % Res	N	% Res	N	% Res	N	% Res	N	% Res
Meat from broil	ers															
Lithuania	20	25.0	_	_	20	0	20	0	20	0	20	0	20	25.0	20	0
Netherlands	129	63.6	129	56.6	129	4.7	129	82.9	129	3.9	129	80.6	129	80.6	129	71.3
Poland	88	17.0	71	16.9	88	2.3	88	63.6	88	2.3	88	55.7	88	51.1	88	48.9
Slovakia	15	13.3	15	0	15	0	15	73.3	15	0	15	73.3	15	53.3	15	53.3
Slovenia	26	7.7	_	_	26	0	26	96.2	26	0	26	96.2	_	_	26	80.8
Spain	13	15.4	_	_	_	_	12	0	14	0	13	15.4	_	_	_	_
Total (6 MSs)	291	37.1	215	39.5	278	2.9	290	68.6	292	2.4	291	65.6	252	64.3	278	59.0
Meat from pigs																
Spain	24	79.2	0	0	22	22.7	18	5.6	24	4.2	24	8.3	20	80.0	22	90.9

Table 45. Occurrence of resistance to selected antimicrobials in Salmonella spp. isolates from meat in MSs reporting qualitative data in 2013

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.



Country	Ampicillin		Cefotaxime		Chloramphenicol		Ciprofloxacin		Gentamicin		Nalidixic acid		Sulfonamides		Tetracyclines	
Country	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Gallus gallus																
Croatia	91	17.6	-	_	91	3.3	91	57.1	91	1.1	91	58.2	91	14.3	91	11.0
Cyprus	50	28.0	-	_	50	8.0	50	44.0	50	14.0	50	40.0	50	44.0	50	40.0
Malta	22	63.6	-	-	22	0	22	72.7	22	36.4	22	45.5	-	-	22	40.9
Poland	365	15.3	365	0.3	365	2.5	365	33.2	365	1.6	365	29.3	360	14.4	360	11.7
Slovakia	68	10.3	68	0	68	0	68	50.0	68	0	68	50.0	68	45.6	68	51.5
Total (5 MSs)	596	18.0	433	0.2	596	2.7	596	41.1	596	3.7	596	37.6	569	20.7	591	19.6
Iceland	18	0	-	_	18	0	18	0	-	_	_	_	18	0	_	_
Pigs																
Croatia	41	41.5	0	0	41	14.6	41	4.9	41	0	41	0	41	63.4	41	34.1
Iceland	11	27.3	0	0	11	0	11	0	_	_	_	_	11	27.3	_	_

Table 46. Occurrence of resistance to selected antimicrobials in Salmonella spp. isolates from animals in MSs reporting qualitative data in 2013

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates; -: no data reported.



Appendix B: List of usable data

Submitted and validated MS data, containing information on reported MIC distributions and data on the number of resistant isolates, are available on the EFSA website.

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Table	Campylobacter tables					
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MM7	Antimicrobials selected for susceptibility testing of <i>Campylobacter</i> isolates from animals and food by MSs and non-MSs reporting quantitative data as MIC distributions, in 2013
MM8	Antimicrobials selected for susceptibility testing of <i>Escherichia coli</i> isolates from animals and food by MSs and non-MSs reporting quantitative data as MIC distributions, in 2013
MM9	Antimicrobials selected for susceptibility testing of isolates of <i>Enterococcus faecium isolates</i> , by MSs and non-MSs reporting quantitative data as MIC distributions, in 2013
MM10	Antimicrobials selected for susceptibility testing of isolates of <i>Enterococcus faecalis isolates</i> , by MSs and non-MSs reporting quantitative data as MIC distributions, in 2013
MM11	Harmonised set of antimicrobials listed in the EFSA recommendations

SA	Salmonella - food and animals-additional tables
SA1	Occurrence of resistance to selected antimicrobials in Salmonella main serovars isolates from meat from broilers in 2013, using harmonised epidemiological cut-off values
SA2	Occurrence of resistance to selected antimicrobials in Salmonella main serovars isolates from meat from pigs in 2013, using harmonised epidemiological cut-off values
SA3	Occurrence of resistance to selected antimicrobials in <i>Salmonella</i> spp. isolates from <i>Gallus gallus</i> in 2013, using harmonised epidemiological cut-off values
SA4	Occurrence of resistance to selected antimicrobials in Salmonella spp. isolates from Gallus gallus categories in 2013, using harmonised epidemiological cut-off values



SA	Salmonella - food and animals-additional tables
SA5	Occurrence of resistance to selected antimicrobials in Salmonella Typhimurium isolates from Gallus gallus categories in 2013, using harmonised epidemiological cut-off values
SA6	Occurrence of resistance to selected antimicrobials in Salmonella isolates from turkeys categories in 2013, using harmonised epidemiological cut-off values
SA7	Occurrence of resistance to selected antimicrobials in Salmonella spp. isolates from pigs categories in 2013, using harmonised epidemiological cut-off values
SA8	Occurrence of resistance to selected antimicrobials in Salmonella Derby isolates from pigs in 2013, using harmonised epidemiological cut-off values
SA9	Occurrence of resistance to selected antimicrobials in Salmonella spp. isolates from cattle in 2013, using harmonised epidemiological cut-off values
SA10	Occurrence of resistance to selected antimicrobials in <i>Salmonella</i> Typhimurium isolates from cattle in 2013, using harmonised epidemiological cut-off values

SER	Salmonella serovars
SER1	Frequency distribution of Salmonella serovars in meat from broilers (Gallus gallus), in 2013
SER2	Frequency distribution of Salmonella serovars in meat from turkey, in 2013
SER3	Frequency distribution of Salmonella serovars in meat from pigs, in 2013
SER4	Frequency distribution of Salmonella serovars in meat from bovine animals, in 2013
SER5	Frequency distribution of Salmonella serovars in Gallus gallus (fowl), in 2013
SER6	Frequency distribution of Salmonella serovars in broilers of Gallus gallus (fowl), in 2013
SER7	Frequency distribution of Salmonella serovars in laying hens of Gallus gallus (fowl), in 2013
SER8	Frequency distribution of Salmonella serovars in turkey, in 2013
SER9	Frequency distribution of Salmonella serovars in pigs, in 2013
SER10	Frequency distribution of Salmonella serovars in bovine animals, in 2013

PENT	Salmonella pentavalent resistance
PENT1	Salmonella serovars detected with pentavalent resistance amongst those for which isolate-based data is available

EN	Enterococcus additional tables 2012 data
EN1	Occurrence of resistance to selected antimicrobials in <i>Enterococcus faecium</i> from meat in 2012, using harmonised epidemiological cut-off values
EN2	Occurrence of resistance to selected antimicrobials in <i>Enterococcus faecalis</i> from meat in 2012, using harmonised epidemiological cut-off values
EN3	Occurrence of resistance to selected antimicrobials in <i>Enterococcus faecium</i> from animals in countries reporting MIC data in 2012, using harmonised epidemiological cut-off values
EN4	Occurrence of resistance to selected antimicrobials in <i>Enterococcus faecalis</i> from animals in countries reporting MIC data in 2012, using harmonised epidemiological cut-off values

MRSA	Staphylococcus aureus meticillin resistant additional tables
MRSA1	MRSA in companion animals, clinical investigations, 2013
MRSA2	Temporal occurrence of MRSA in animals
MRSA3	Occurrence of resistance to selected antimicrobials in MRSA from food and animals in countries reporting MIC data in 2013, using harmonised epidemiological cut-off values



ESBL	Third-generation cephalosporin resistance in Salmonella and Escherichia coli -additional tables
ESBL1	Occurrence of resistance to cefotaxime and ceftazidime in Salmonella spp. isolates from meat in 2013
ESBL2	Occurrence of resistance to cefotaxime and ceftazidime in <i>Salmonella</i> Enteritidis isolates from meat from broilers in 2013
ESBL3	Occurrence of resistance to cefotaxime and ceftazidime in Salmonella serovars isolates from meat from pigs in 2013
ESBL4	Occurrence of resistance to cefotaxime and ceftazidime in Salmonella spp. isolates from Gallus gallus categories in 2013
ESBL5	Occurrence of resistance to cefotaxime and ceftazidime in Salmonella Enteritidis isolates from Gallus gallus categories in 2013
ESBL6	Occurrence of resistance to cefotaxime and ceftazidime in Salmonella Typhimurium isolates from Gallus gallus in 2013
ESBL7	Occurrence of resistance to cefotaxime and ceftazidime in Salmonella spp. isolates from turkey categories in 2013
ESBL8	Occurrence of resistance to cefotaxime and ceftazidime in Salmonella spp. isolates from pigs categories in 2013
ESBL9	Occurrence of resistance to cefotaxime and ceftazidime in Salmonella Typhimurium isolates from pigs categories in 2013
ESBL10	Occurrence of resistance to cefotaxime and ceftazidime in main Salmonella serovars isolates from pigs in 2013
ESBL11	Occurrence of resistance to cefotaxime and ceftazidime in main Salmonella serovars isolates from cattle in 2013
ESBL12	Occurrence of resistance to cefotaxime and ceftazidime in E. coli isolates from meat in 2013
ESBL13	Occurrence of resistance to cefotaxime and ceftazidime in <i>E. coli</i> isolates from <i>Gallus gallus</i> categories in 2013
ESBL14	Occurrence of resistance to cefotaxime and ceftazidime in E. coli isolates from pigs in 2013
ESBL15	Occurrence of resistance to cefotaxime and ceftazidime in E. coli isolates from cattle categories in 2013

СО	Co-resistance to cefotaxime and ciprofloxacin
CO1	<u>Co-resistance to cefotaxime and ciprofloxacin in Salmonella serovars from broilers in countries reporting</u> isolate-based data, 2013
CO2	Co-resistance to cefotaxime and ciprofloxacin in <i>Escherichia coli</i> from broilers in countries reporting isolate- based data, 2013
CO3	Co-resistance to cefotaxime and ciprofloxacin in <i>Escherichia coli</i> from fattening pigs in countries reporting isolate-based data, 2013
CO4	<u>Co-resistance to cefotaxime and ciprofloxacin in <i>Escherichia coli</i> from cattle in countries reporting isolate- based data, 2013</u>

MDR	Complete susceptibility, multiple resistance and co-resistance tables
MDR1	Complete susceptibility, multi-resistance and co-resistance (non-susceptibility) to ciprofloxacin and cefotaxime in Salmonella spp. from humans by MSs, 2013
MDR2	Complete susceptibility, multi-resistance and co-resistance (non-susceptibility) to ciprofloxacin and cefotaxime in <i>Salmonella</i> Enteritidis from humans by MSs, 2013
MDR3	Complete susceptibility, multi-resistance and co-resistance (non-susceptibility) to ciprofloxacin and cefotaxime in <i>Salmonella</i> Typhimurium from humans by MSs, 2013
MDR4	<u>Complete susceptibility, multi-resistance and co-resistance (non-susceptibility) to ciprofloxacin and cefotaxime in monophasic Salmonella Typhimurium 1,4,[5],12:i:- from humans by MSs, 2013</u>
MDR5	Complete susceptibility, multi-resistance and index of diversity in Salmonella spp. from meat from broilers in MSs reporting isolate-based data, 2013
MDR6	<u>Complete susceptibility, multi-resistance and index of diversity in Salmonella Infantis from meat from</u> broilers in MSs reporting isolate-based data, 2013
MDR7	Complete susceptibility, multi-resistance and index of diversity in Salmonella spp. from meat from turkeys in MSs reporting isolate-based data, 2013
MDR8	Complete susceptibility, multi-resistance and index of diversity in Salmonella spp. from meat from pigs in MSs reporting isolate-based data, 2013
MDR9	Complete susceptibility, multi-resistance and index of diversity in Salmonella Typhimurium from meat from pigs in MSs reporting isolate-based data, 2013
MDR10	Complete susceptibility, multi-resistance and index of diversity in <i>Salmonella</i> spp. from meat from bovine animals in MSs reporting isolate-based data, 2013



MDR	Complete susceptibility, multiple resistance and co-resistance tables
MDR11	Complete susceptibility, multi-resistance and index of diversity in Salmonella spp. from broilers in MSs
	reporting isolate-based data, 2013
MDR12	Complete susceptibility, multi-resistance and index of diversity in Salmonella spp. from laying hens in MSs
	reporting isolate-based data, 2013
MDR13	Complete susceptibility, multi-resistance and index of diversity in Salmonella spp. from breeding hens in
	MSs reporting isolate-based data, 2013
MDR14	Complete susceptibility, multi-resistance and index of diversity in Salmonella Enteriditis from broilers in
	MSs reporting isolate-based data, 2013
MDR15	Complete susceptibility, multi-resistance and index of diversity in Salmonella Enteriditis from laying hens in
	MSs reporting isolate-based data, 2013
MDR16	Complete susceptibility, multi-resistance and index of diversity in Salmonella spp. from turkeys in MSs
	reporting isolate-based data, 2013
MDR17	Complete susceptibility, multi-resistance and index of diversity in Salmonella spp. from fattening pigs in
	MSs reporting isolate-based data, 2013
MDR18	Complete susceptibility, multi-resistance and index of diversity in Salmonella spp. from cattle in MSs
MBITTO	reporting isolate-based data, 2013
MDR19	Complete susceptibility, multi-resistance and co-resistance (non-susceptibility) to ciprofloxacin and
mercio	erythromycin in Campylobacter jejuni from humans, 2013
MDR20	Complete susceptibility, multi-resistance and co-resistance (non-susceptibility) to ciprofloxacin and
11121 (20	erythromycin in Campylobacter coli from humans, 2013
MDR21	Complete susceptibility, multi-resistance and index of diversity in Campylobacter jejuni from broilers in MSs
merter	reporting isolate-based data, 2013
MDR22	Complete susceptibility, multi-resistance and index of diversity in Campylobacter coli from broilers in MSs
MDI	reporting isolate-based data, 2013
MDR23	Complete susceptibility, multi-resistance and index of diversity in Campylobacter coli from fattening pigs in
MDI (20	MSs reporting isolate-based data, 2013
MDR24	Complete susceptibility, multi-resistance and index of diversity in Campylobacter jejuni from cattle in MSs
MDI(24	reporting isolate-based data, 2013
MDR25	Complete susceptibility, multi-resistance and index of diversity in Escherichia coli from broilers in MSs
MDR23	reporting isolate-based data, 2013
MDR26	Complete susceptibility, multi-resistance and index of diversity in Escherichia coli from fattening pigs in
WDR20	MSs reporting isolate-based data, 2013
MDR27	Complete susceptibility, multi-resistance and index of diversity in Escherichia coli from cattle in MSs
	reporting isolate-based data, 2013

MDRP	Multi-drug resistance patterns tables
MDRP1	Multi-resistance patterns of interest in Salmonella spp. from meat from broilers in MSs reporting isolate- based data, 2013
MDRP2	Multi-resistance patterns of interest in Salmonella spp. from meat from pigs in MSs reporting isolate-based data, 2013
MDRP3	Multi-resistance patterns of interest in Salmonella spp. from meat from turkeys in MSs reporting isolate- based data, 2013
MDRP4	Multi-resistance patterns of interest in Salmonella spp. from meat from bovine animals in MSs reporting isolate-based data, 2013
MDRP5	Multi-resistance patterns of interest in Salmonella spp. from broilers in MSs reporting isolate-based data, 2013
MDRP6	Multi-resistance patterns of interest in Salmonella spp. from laying hens in MSs reporting isolate-based data, 2013
MDRP7	<u>Multi-resistance patterns of interest in Salmonella spp. from breeding hens in MSs reporting isolate-based</u> data, 2013
MDRP8	Multi-resistance patterns of interest in Salmonella spp. from turkeys in MSs reporting isolate-based data, 2013
MDRP9	Multi-resistance patterns of interest in Salmonella spp. from fattening pigs in MSs reporting isolate-based data, 2013
MDRP10	Multi-resistance patterns of interest in Salmonella spp. from breeding pigs in MSs reporting isolate-based data, 2013
MDRP11	Multi-resistance patterns of interest in Salmonella spp. from cattle in MSs reporting isolate-based data, 2013
MDRP12	Multi-resistance patterns of interest in Salmonella Enteritidis from meat from broilers in MSs reporting isolate-based data, 2013
MDRP13	Multi-resistance patterns of interest in Salmonella Enteritidis from broilers in MSs reporting isolate-based data, 2013



MDRP	Multi-drug resistance patterns tables
MDRP14	Multi-resistance patterns of interest in Salmonella Enteritidis from from laying hens in MSs reporting isolate-based data, 2013
MDRP15	Multi-resistance patterns of interest in Salmonella Typhimurium from meat from pig in MSs reporting isolate-based data, 2013
MDRP16	Multi-resistance patterns of interest in Salmonella Typhimurium from broilers in MSs reporting isolate- based data, 2013
MDRP17	Multi-resistance patterns of interest in Salmonella Typhimurium from laying hens in MSs reporting isolate- based data, 2013
MDRP18	Multi-resistance patterns of interest in Salmonella Typhimurium from fattening pigs in MSs reporting isolate-based data, 2013
MDRP19	Multi-resistance patterns of interest in Salmonella Typhimurium from breeding pigs in MSs reporting isolate-based data, 2013
MDRP20	Multi-resistance patterns of interest in Salmonella Typhimurium from cattle in MSs reporting isolate-based data, 2013
MDRP21	Multi-resistance patterns of interest in monophasic Salmonella Typhimurium from meat from pig in MSs reporting isolate-based data, 2013
MDRP22	Multi-resistance patterns of interest in monophasic Salmonella Typhimurium from broilers in MSs reporting isolate-based data, 2013
MDRP23	Multi-resistance patterns of interest in monophasic Salmonella Typhimurium from laying hens in MSs reporting isolate-based data, 2013
MDRP24	Multi-resistance patterns of interest in monophasic Salmonella Typhimurium from fattening pigs in MSs reporting isolate-based data, 2013
MDRP25	Multi-resistance patterns of interest in monophasic Salmonella Typhimurium from cattle in MSs reporting isolate-based data, 2013
MDRP26	Multi-resistance patterns of interest in Salmonella Kentucky from broilers in MSs reporting isolate-based data, 2013
MDRP27	Multi-resistance patterns of interest in Salmonella Kentucky from laying hens in MSs reporting isolate- based data, 2013
MDRP28	Multi-resistance patterns of interest in Salmonella Derby from meat from pig in MSs reporting isolate-based data, 2013
MDRP29	Multi-resistance patterns of interest in Salmonella Derby from turkeys in MSs reporting isolate-based data, 2013
MDRP30	Multi-resistance patterns of interest in Salmonella Derby from fattening pigs in MSs reporting isolate-based data, 2013
MDRP31	Multi-resistance patterns of interest in Salmonella Infantis from meat from broilers in MSs reporting isolate- based data, 2013
MDRP32	Multi-resistance patterns of interest in Salmonella Infantis from broilers in MSs reporting isolate-based data, 2013
MDRP33	Multi-resistance patterns of interest in Salmonella Infantis from laying hens in MSs reporting isolate-based data, 2013
MDRP34	Multi-resistance patterns of interest in Salmonella Infantis from turkeys in MSs reporting isolate-based data, 2013
MDRP35	Multi-resistance patterns of interest in Campylobacter coli from broilers in MSs reporting isolate-based data, 2013
MDRP36	Multi-resistance patterns of interest in Campylobacter jejuni from broilers in MSs reporting isolate-based data, 2013
MDRP37	Multi-resistance patterns of interest in Campylobacter coli from fattening pigs in MSs reporting isolate- based data, 2013
MDRP38	Multi-resistance patterns of interest in Campylobacter jejuni from cattle in MSs reporting isolate-based data, 2013
MDRP39	Multi-resistance patterns of interest in <i>Escherichia coli</i> from broilers in MSs reporting isolate-based data, 2013
MDRP40	Multi-resistance patterns of interest in <i>Escherichia coli</i> from fattening pigs in MSs reporting isolate-based data, 2013
MDRP41	Multi-resistance patterns of interest in <i>Escherichia coli</i> from cattle in MSs reporting isolate-based data, 2013
MDRP42	Multi-resistance patterns of interest in <i>Enterococcus faecium</i> from broilers in MSs reporting isolate-based data, 2013
MDRP43	Multi-resistance patterns of interest in <i>Enterococcus faecalis</i> from broilers in MSs reporting isolate-based data, 2013
MDRP44	Multi-resistance patterns of interest in Enterococcus faecalis from fattening pigs in MSs reporting isolate- based data, 2013



MDRP	Multi-drug resistance patterns tables
MDRP45	Multi-resistance patterns of interest in <i>Enterococcus</i> faecalis from cattle in MSs reporting isolate-based data, 2013
MDRP46	Multi-resistance patterns of interest in <i>Enterococcus</i> faecium from cattle in MSs reporting isolate-based data, 2013
MDRP47	Multi-resistance patterns of interest in <i>Staphylococcus aureus</i> meticillin resistant from fattening pigs in Switzerland reporting isolate-based data, 2013
MDRP48	Multi-resistance patterns of interest in <i>Staphylococcus aureus</i> meticillin resistant from breeding pigs in Belgium reporting isolate-based data, 2013
MDRP49	Multi-resistance patterns of interest in Staphylococcus aureus meticillin resistant from cattle in Switzerland reporting isolate-based data, 2013

HLR	High-level resistance tables
HLR1	Ciprofloxacin resistance assessed at differing thresholds in Salmonella serovars from broiler meat in MSs reporting isolate-based data, 2013
HLR2	Ciprofloxacin resistance assessed at differing thresholds in Salmonella serovars from turkey meat in MSs reporting isolate-based data, 2013
HLR3	Ciprofloxacin resistance assessed at differing thresholds in Salmonella serovars from pig meat in MSs reporting isolate-based data, 2013
HLR4	High-level ciprofloxacin resistance in Salmonella serovars from broilers in MSs reporting isolate-based data, 2013
HLR5	Ciprofloxacin resistance assessed at differing thresholds in Salmonella serovars from laying hens in MSs reporting isolate-based data, 2013
HLR6	Ciprofloxacin resistance assessed at differing thresholds in Salmonella serovars from breeding hens in MSs reporting isolate-based data, 2013
HLR7	Ciprofloxacin resistance assessed at differing thresholds in Salmonella serovars from turkeys in MSs reporting isolate-based data, 2013
HLR8	Ciprofloxacin resistance assessed at differing thresholds in Salmonella serovars from fattening pigs in MSs reporting isolate-based data, 2013
HLR9	Ciprofloxacin resistance assessed at differing thresholds in Salmonella serovars from cattle in MSs reporting isolate-based data, 2013
HLR10	Ciprofloxacin resistance assessed at differing thresholds in <i>Escherichia coli</i> from broilers in MSs reporting isolate-based data, 2013
HLR11	Ciprofloxacin resistance assessed at differing thresholds in <i>Escherichia coli</i> from fattening pigs in MSs reporting isolate-based data, 2013
HLR12	Ciprofloxacin resistance assessed at differing thresholds in <i>Escherichia coli</i> from cattle in MSs reporting isolate-based data, 2013
HLR13	High-level gentamicin resistance in indicator <i>Enterococcus faecium</i> in MSs reporting isolate-based data, 2013
HLR14	High-level gentamicin resistance in indicator <i>Enterococcus faecalis</i> in MSs reporting isolate-based data, 2013