SCIENTIFIC REPORT



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The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2014

European Food Safety Authority European Centre for Disease Prevention and Control

Abstract

The data on antimicrobial resistance in zoonotic and indicator bacteria in 2014, submitted by 28 EU Member States (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 as well as meticillin-resistant Staphylococcus aureus in animals and food was assessed. 'Microbiological' resistance was assessed using epidemiological cut-off (ECOFF) values; for some countries, quantitative data on human isolates were interpreted in a way which corresponds closely to the ECOFF-defined 'microbiological' resistance. In Salmonella from humans, high proportions of isolates were resistant to ampicillin, sulfonamides and tetracyclines, whereas resistance to thirdgeneration cephalosporins and to fluoroquinolones remained generally low, although it was markedly higher in some serovars commonly associated with broilers and turkeys. In Salmonella and Escherichia coli isolates from broilers, fattening turkeys and meat thereof, resistance to ampicillin, (fluoro)quinolones, tetracyclines and sulfonamides was frequently detected, whereas resistance to third-generation cephalosporins was uncommon. For the first time, presumptive extended spectrum beta-lactamase (ESBL)-/AmpC-/carbapenemase production in Salmonella and Escherichia coli was monitored in poultry. The occurrence of ESBL-/AmpC-producers was low, and carbapenemaseproducers were not detected. Resistance to colistin was observed at low levels in Salmonella and Escherichia coli from poultry and meat thereof. In Campylobacter from humans, a high to very high proportion of isolates were resistant to ciprofloxacin and tetracyclines, whereas resistance to erythromycin was low to moderate. Resistance to fluoroquinolones in some MSs was extremely high; in such settings, the effective treatment options for human enteric Campylobacter infection may be significantly reduced. High resistance to ciprofloxacin and tetracyclines was observed in Campylobacter isolates from broilers and broiler meat, whereas much lower levels were recorded for erythromycin. Co-resistance to critically important antimicrobials in both human and animal isolates was generally uncommon, but very high to extremely high MDR levels were observed in some Salmonella serovars. A minority of Salmonella isolates from animals belonging to a few serovars (notably Kentucky and Infantis) exhibited high-level resistance to ciprofloxacin.

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Summary

Highlights

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

For 2014, 28 MSs reported data on AMR in zoonotic bacteria to 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. The enhanced monitoring of AMR in bacteria from food and food-producing animals set out in the Commission Implementing Decision 2013/652/EU was successfully implemented in reporting MSs and non-MSs in the EU during 2014. In accordance with the legislation, the 2014 AMR data on food and food-producing animals specifically targeted different poultry populations and meat derived thereof. EFSA and ECDC performed the analyses of the data, the results of which are published in this EU Summary Report on AMR. Data on resistance were reported regarding *Salmonella* and *Campylobacter* isolates from humans, poultry and meat thereof, whereas data on indicator *Escherichia coli* isolates were related only to poultry and meat derived thereof. Some MSs also reported data on the occurrence of meticillin-resistant *Staphylococcus aureus* (MRSA) in animals and food; the antimicrobial susceptibility of MRSA isolates was additionally reported by two countries.

The quantitative data on AMR in isolates from humans, poultry and meat thereof were assessed using harmonised epidemiological cut-off values that define 'microbiological' resistance, i.e. reduced susceptibility to the antimicrobials tested, as well as using clinical breakpoints (CBPs), where considered appropriate. The categorical (qualitative) data on AMR in isolates from humans interpreted by using CBPs were aligned with 'microbiological' resistance by combining 'clinically resistant' and 'intermediate resistant' isolates into a non-susceptible group. Isolates from different sources should only be directly compared when methods and interpretive criteria are comparable.

For the first time, all MSs reported AMR data on poultry and meat thereof at the isolate level. This enabled analysis of multi-drug resistance (MDR) and co-resistance patterns to critically important antimicrobials in both human and animal isolates at the EU level but also at country level. In addition, for all bacterial species, AMR data could be analysed at the production-type level, such as broilers and laying hens of *Gallus gallus* and fattening turkeys, which allows the analysis of the data to be fine-tuned. More specifically, reporting data at isolate level allowed characterisation of important patterns of resistance, enabling *Salmonella* serovars to be linked to particular resistance patterns and to identify high-level resistance to fluoroquinolones and important resistance phenotypes in both *Salmonella* and indicator *E. coli*. The information published in this report provides an overview of resistance in most MSs with detailed consideration of certain important aspects.

Highlights of this report include the continued monitoring of the spread of certain highly resistant *Salmonella* serovars. Two serovars in particular, *S.* Infantis and *S.* Kentucky, contribute significantly to the overall numbers of multidrug-resistant *Salmonella* in Europe. Both serovars display high-level resistance to ciprofloxacin, which is an important public health concern because ciprofloxacin is a common first-line treatment for invasive salmonellosis in humans.

The introduction of Commission implementing Decision 2013/652/EU with revised panels of antimicrobials to be tested has been timely, preceding recent reports of emergence of transferable colistin and erythromycin resistance in Asia (Liu et al., 2015; Wang et al., 2015). The continually evolving threat from emerging resistance underlines the need to review the data collected, interpret the findings and assess trends. This report has attempted to highlight some of the most important findings in 2014, but space constraints mean that it is necessarily selective.



Horizon Scanning – transferable resistance to colistin and erythromycin.

- Some types of resistance, e.g. to colistin and erythromycin, have been considered as not being subject to transfer between different strains of bacteria. They were believed to be only inherited from a bacterial cell to its daughter cells by cell division. This assumption applied to resistance which was mutational, frequently located on the bacterial chromosome or affected the bacterial ribosome (bacterial protein machinery). Recently, however, interbacterial transfer has been described in Asia for colistin resistance in Enterobacteriaceae and erythromycin resistance in *Campylobacter* (Liu et al., 2015; Wang et al., 2015).
- These are important developments because chromosomal resistances which are not transferable can only spread by clonal expansion of bacterial strains, whereas transferable resistance, such as plasmid-mediated resistance, can spread rapidly between different bacterial strains leading to widespread dissemination.
- Erythromycin resistance in *Campylobacter* and colistin resistance in Enterobacteriaceae are both of public health significance, but occur at low, very low or undetected levels in many MSs.

The inclusion within the harmonised monitoring scheme of a supplementary panel of antimicrobials, to be tested when certain resistances to an initial panel of antimicrobials are detected, enabled detailed screening of resistance to three carbapenem compounds. No resistance to meropenem was detected and this is a crucial finding, because carbapenems are critically important in human medicine. Only nine *E. coli* isolates from broilers and one from fattening turkeys isolated in 6 MSs showed resistance to ertapenem, and all these isolates presented a putative extended spectrum beta-lactamase (ESBL) or AmpC phenotype. These isolates are being further investigated.

The supplementary testing also allowed, for the first time, detailed characterisation of the beta-lactam resistance phenotypes occurring in *Salmonella* and indicator *E. coli*. It enabled further phenotypic characterisation of third-generation cephalosporin and carbapenem resistance in *Salmonella* and indicator *E. coli*, by inferring presumptive profiles of ESBL-/AmpC-/carbapenemase-producers. The occurrence of ESBL-/AmpC-producers in *Salmonella* and indicator *E. coli* from poultry was assessed as being at low levels. It also showed that *S*. Infantis in Italy and *S*. Heidelberg in the Netherlands have probably each acquired a different mechanism of third-generation cephalosporin resistance (an ESBL enzyme in *S*. Infantis and an AmpC enzyme in *S*. Heidelberg) and have subsequently spread within each MS.

Main findings regarding *Salmonella*

The *Salmonella* spp. data presented in this report comprise all reported non-typhoidal *Salmonella* serovars and represent the overall occurrence of AMR in *Salmonella* in humans and various poultry populations and food categories. Differences in the prevalence of particular serovars and phage types of *Salmonella* in different countries and poultry populations, and their associated patterns of resistance, may explain some of the differences in the levels of AMR and MDR (reduced susceptibility to at least three of the nine 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 its selective pressure. 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, may also influence the spread of resistant clones.

In addition to the aggregated data for *Salmonella* spp., resistance data for the most common *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 turkeys and the high level of resistance observed in both human and animal isolates, particularly in *S.* Kentucky. In poultry populations and poultry meat, resistance profiles of isolates belonging to these serovars were considered also when less than 10



isolates were recovered from a given animal/food category in a country to account for the low prevalence of certain serovars and for the sake of completeness.

In humans

In 2014, 21 MSs and Norway reported data on AMR in *Salmonella* isolates from human cases of salmonellosis. Twelve countries provided data as measured values (quantitative data), five more than the previous year when this type of data collection was implemented. The reported data from the 22 countries represented 16.0% of the confirmed salmonellosis cases reported in the EU/European Economic Area (EEA) in 2014.

High proportions of human *Salmonella* isolates were resistant to tetracyclines (30.3%), sulfonamides (28.6%) and ampicillin (28.2%). MDR was high overall (26.0%) in the EU, with very high prevalence in some countries. Some of the investigated serovars exhibited very high to extremely high MDR, such as *S*. Kentucky (74.6%), monophasic *S*. Typhimurium 1,4,[5],12:i:- (69.4%) and *S*. Infantis (61.9%). However, more than half (54.8%) of all isolates from humans were susceptible to the complete range of antimicrobial classes tested. The proportions of *Salmonella* isolates resistant to the clinically important antimicrobials ciprofloxacin and cefotaxime was overall relatively low (8.8% resistant to ciprofloxacin and 1.1% to cefotaxime). The higher ciprofloxacin resistance in 2014 compared to 2013 is most likely due to a combination of the lowered European Committee on Antimicrobial Susceptibility Testing (EUCAST, www.eucast.org) CBP for ciprofloxacin in 2014 – now directly comparable with the ECOFF – and the implementation by a few countries of a better marker (pefloxacin) than ciprofloxacin for screening with disk diffusion of low-level fluoroquinolone resistance in *Salmonella*.

An extremely high proportion (84.0%) of *S*. Kentucky was resistant to ciprofloxacin, which is consistent with the dissemination of the ciprofloxacin-resistant *S*. Kentucky ST198 strain in Europe and elsewhere since 2010 (Le Hello et al., 2013). Resistance to third-generation cephalosporins was more common in *S*. Infantis and *S*. Kentucky with particularly high levels observed in Italy, most likely due to the circulation of a multiresistant and ESBL-producing (cefotaximase (CTX-M) type) clone of *S*. Infantis.

'Clinical' and 'microbiological' co-resistance to ciprofloxacin and cefotaxime was overall very low in *Salmonella* spp. (0.5% and 0.6%, respectively).

Resistance to colistin was commonly detected in *S*. Enteritidis (67.5%, two MSs) which could be due to intrinsic resistance in this serovar (see text box 'Resistance to colistin'). As the CBP is at the same concentration as the ECOFF applied in the analysis, the observed colistin resistance is of concern since this last-resort drug might no longer be effective for treating severe human infections with the most common *Salmonella* serovar.

In poultry populations and meat derived thereof

In 2014, information on AMR in *Salmonella* isolates from poultry populations and meat derived thereof was reported by 24 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 broiler meat, where high to extremely high levels were recorded by most of the MSs included in the analysis (overall, 42.6% and 39.7%, respectively). In *Salmonella* spp. isolates from turkey meat, ciprofloxacin resistance varied between low and extremely high levels among the 3 reporting MSs (overall, 24.3%). Conversely, 'microbiological' resistance to the third-generation cephalosporins (cefotaxime and ceftazidime) in *Salmonella* spp. from poultry meat was either not discerned or detected at low levels in most of the reporting MSs.

Resistance to tetracycline, ampicillin and sulfamethoxazole in *Salmonella* spp. isolates from poultry meat generally ranged from moderate to extremely high. The highest levels of resistance to these substances were typically observed among *S*. Infantis isolates from broiler meat, resulting in extremely high levels of MDR (> 70.0%). MDR (reduced susceptibility to at least three of the nine antimicrobial classes tested) was overall low in laying hens, high in broiler meat, turkey meat and broilers, and very high in turkeys. In *S*. Enteritidis from broiler meat, broilers and laying hens, the majority of isolates were fully susceptible to the harmonised set of antimicrobials tested.



Generally, low to very low levels of 'microbiological' co-resistance to ciprofloxacin and cefotaxime in *Salmonella* spp. from broiler flocks (1.8%) and laying hen flocks (0.12%) were reported. When the resistance to ciprofloxacin and cefotaxime was interpreted using CBPs, only one *S*. Kentucky isolate from broilers in Spain displayed 'clinical' resistance.

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

Among *Salmonella* spp. isolates from poultry populations, 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 fattening turkeys than from broilers and laying hens.

Overall, high levels of resistance to ciprofloxacin and nalidixic acid were observed in *Salmonella* spp. isolates from fattening turkeys and broilers compared with the moderate levels recorded in *Salmonella* spp. isolates from laying hens. Resistance to third-generation cephalosporins (cefotaxime and ceftazidime) was generally at very low or low levels in *Salmonella* spp. isolates from broilers and laying hens in most reporting MSs, with the striking exception of the high levels of cefotaxime and ceftazidime resistance reported in *Salmonella* spp. from broilers in Italy. No resistance to third-generation cephalosporins was detected in fattening turkeys.

'Clinical' resistance to cefotaxime was found at low to high levels in *Salmonella* spp. isolates from broilers and laying hens in 10 MSs. The supplementary testing performed in 2014 allowed further phenotypic characterisation of those *Salmonella* isolates which were resistant to third-generation cephalosporins.

Table 1:	Summary of phen Salmonella from p	<i>,</i> ,	of third generatior	cephalosporin resistance in
		Presumptive	Procumptivo	Procumptivo

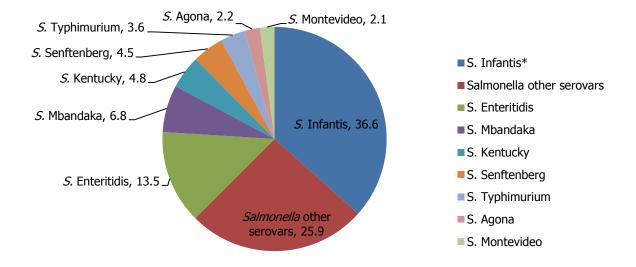
	Presumptive ESBL phenotype n (% R)	Presumptive AmpC phenotype n (% R)	Presumptive ESBL + AmpC phenotype n (% R)
Meat from broilers (N=672)	0 (0%)	1 (0.1%)	2 (0.3%)
Broilers (N=2,293)	30 (1.3%)	18 (0.8%)	4 (0.2%)
Laying hens (N=872)	0 (0%)	3 (0.3%)	0 (0%)

N: number of the isolates tested; n: number of the isolates resistant; % R: percentage of resistant isolates; ESBL: extended spectrum beta-lactamase.

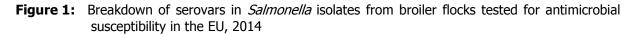
Most *Salmonella* spp. isolates from broilers with an ESBL phenotype were *S*. Infantis (18/30, 60%) with *S*. Paratyphi B L(+) tartrate positive (*S*. Paratyphi B var. Java) comprising a further 6/30 (20%). Considering those isolates with an AmpC phenotype, 9/18 (50%) were *S*. Heidelberg, whereas single isolates of *S*. Infantis and *S*. Paratyphi B var. Java had an AmpC phenotype. *Salmonella* spp. from broilers with an AmpC and an ESBL phenotype included three isolates of *S*. Infantis and a single isolate of *S*. Enteritidis. Three *Salmonella* isolates from laying hens with an AmpC phenotype belonged to serovars *S*. Enteritidis, *S*. Anatum and *S*. Glostrup.

Resistance to carbapenems in *Salmonella* in poultry and meat thereof was not observed in any of the reporting countries.

Broilers and fattening turkeys were the main focus of the monitoring in 2014 in accordance with Decision 2013/652/EU. The detailed reporting of results at serovar level clearly demonstrates the major contribution of a few serovars to the observed prevalence of resistance in *Salmonella*. In broilers, eight serovars (Infantis, Enteritidis, Mbandaka, Kentucky, Senftenberg, Typhimurium, Agona and Montevideo) accounted for 74.1% of *Salmonella* spp. (Figure 1) and in laying hens eight serovars (Enteritidis, Typhimurium, Infantis, Kentucky, Montevideo, Mbandaka, Senftenberg and Livingstone) accounted for 62.3% of *Salmonella* spp. In fattening turkeys, eight serovars (Derby, Kentucky, Newport, Hadar, Infantis, Saintpaul, Bredeney and Stanley) accounted for 68.1% of *Salmonella* spp. Patterns of resistance associated with these serovars, may therefore be expected to have a marked influence on the overall resistance levels in *Salmonella* from these types of poultry (Figure 2).



* One third of the *S.* Infantis isolates were reported by Romania.



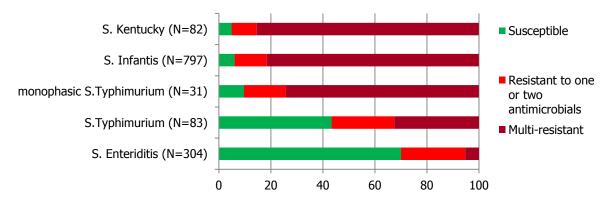


Figure 2: Proportions of isolates fully susceptible, resistant to one to two classes of substances and multiresistant in the most commonly recovered *Salmonella* serovars in broiler flocks in the EU, 2014

S. Infantis is a dominant serovar in broilers, accounting for 35.9% of all *Salmonella* isolates examined from broilers (762/2,122), and commonly showing resistance. The proportion of all isolates showing MDR in broilers was also greatly influenced by the occurrence of multiresistant *S*. Infantis, this serovar accounting for approximately 31% of the multiresistant isolates in broilers. Particular MDR patterns were associated with *S*. Infantis and because this serovar was prevalent in many countries, these patterns greatly influenced the overall resistance figures. Underlining the significance of resistance in *S*. Infantis, resistance to third-generation cephalosporins in isolates from broilers in Italy (with a presumptive ESBL phenotype) and high-level resistance to ciprofloxacin were both detected in this serovar. High-level ciprofloxacin resistance was otherwise detected mainly in *S*. Kentucky, a further significant serovar in poultry in Europe in 2014.

In contrast, *S*. Enteritidis was less commonly multiresistant than *S*. Infantis, although one isolate was identified with an ESBL and AmpC phenotype. Higher levels of resistance to colistin were observed for *S*. Enteritidis than for other *Salmonella* serovars. This has been reported previously (Agersø et al., 2012) and is considered to reflect probable intrinsic differences in susceptibility for certain serovars of *Salmonella* (so-called 'group D' *Salmonella* according to the Kauffman-White Scheme, Grimont and Weill, 2013).



High-level resistance to ciprofloxacin was most often observed in *S*. Kentucky isolates from *Gallus gallus* in Cyprus, Hungary, Italy, Romania and Spain, and from turkeys in the Czech Republic, Hungary, Italy, Poland and Spain and in broiler meat from Hungary and Spain. Most of the *S*. Kentucky isolates with high-level ciprofloxacin resistance (n=161) were multiresistant (73.3%). *S*. Kentucky with high-level ciprofloxacin resistance is likely to belong to the multilocus sequence type ST198 clone, which has shown epidemic spread in North Africa and the Middle East (Le Hello, 2013a).

Colistin-resistant *Salmonella* isolates were found by several MSs originating from broilers, laying hens and fattening turkeys. Further information is provided in the text box below.

Microbiological resistance to tigecycline was reported in 9.3% of all *Salmonella* spp. from broilers, 0.6% of isolates from laying hens and 8% from turkeys. There was a marked association of tigecycline microbiological resistance with *S*. Infantis in poultry and most microbiologically resistant strains had minimum inhibitory concentrations (MICs) just above the ECOFF at 2 or 4 mg/l. Resistance to tigecycline in *Salmonella* is thought to be mediated by increased activity of efflux pumps, through modifications to the expression of efflux pump regulatory genes and this may explain the distribution of MICs which was obtained. Determining the susceptibility of tigecycline is not entirely straightforward as the method can be affected by oxidation of the reagents and the tigecycline results are being further investigated by the European Union Reference Laboratory for AMR (EURL-AR, www.crl-ar.eu).

Main findings regarding *Campylobacter*

In humans

In 2014, 13 MSs and Norway reported data on AMR in *Campylobacter* isolates from human cases of campylobacteriosis. Eight countries provided data as measured values (quantitative data), three more than the previous year when this type of data collection was implemented. The reported data from the 14 countries represented 12.3% and 17.4% of the confirmed human cases with *Campylobacter jejuni* and *Campylobacter coli*, respectively, reported in the EU/EEA in 2014.

The proportion of human *C. jejuni* isolates resistant to erythromycin was overall low, but moderately high in *C. coli* and high (> 20.0–50.0%) to very high (> 50.0–70.0%) in *C. coli* in a few reporting countries. Very high to extremely high resistance levels to ciprofloxacin were reported in human *Campylobacter* isolates from all reporting MSs (although lower in Norway). Five of 13 MSs reported ciprofloxacin resistance in > 80% of isolates and one country in 97.7%; in such settings, 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 the availability of effective antimicrobial agents for treating severe human *Campylobacter* infections. High levels of tetracycline resistance were also observed (46.4% for *C. jejuni* and 53.8% for *C. coli*).

Co-resistance to the critically important antimicrobials ciprofloxacin and erythromycin varied by country but was overall low (0.3%) in *C. jejuni* and moderate in *C. coli* (13.6%). In the case of *C. coli*, two MSs reported co-resistance in 44.8–57.6% of isolates. Multidrug resistance, i.e. microbiological resistance to at least three of the four different antimicrobial classes, was low (0.4%) in *C. jejuni* but markedly higher (13.6%) in *C. coli*.

In poultry populations and meat derived thereof

For 2014, 26 MSs and two non-MSs reported data on *Campylobacter* isolates from broilers, fattening turkeys and meat derived thereof. When considering both poultry populations, the highest levels of resistance were observed for (fluoro)quinolones (ciprofloxacin and nalidixic acid) and tetracyclines. Resistance to erythromycin and gentamicin was comparatively low in *Campylobacter* isolates from poultry and derived meat. Resistance was generally higher in *C. coli* than in *C. jejuni* from the same poultry populations.

In *C.* jejuni isolates from broilers, overall resistance was very high for ciprofloxacin (69.8%), nalidixic acid (65.1%) and tetracycline (54.4%), whereas overall resistance to erythromycin and to gentamicin



was respectively low (5.9%) and very low (0.9%). A similar pattern of resistance to these substances occurred in *C. coli* from broilers, although at overall higher levels than those observed in *C. jejuni*, at 74.3%, 69.5% and 59.6%, for ciprofloxacin, nalidixic acid and tetracycline and at 14.5% and 2.6% for erythromycin and gentamicin, respectively.

Multidrug resistance (reduced susceptibility to at least three antimicrobial classes according to ECOFFs) was overall low (4.6%) in *C. jejuni* from broilers. Co-resistance to the criticially important antimicrobials ciprofloxacin and erythromycin was either not detected or recorded up to high levels (overall, at 4.8%). The situation was different for *C. coli* from broilers, where MDR as a percentage of all isolates received by the individual MSs ranged from 2.8% to 33.3% (overall MDR at 13.6%) in the reporting MSs.

Over the 2008–2014 period, resistance to ciprofloxacin, erythromycin and nalidixic acid in broilers varied greatly among reporting MSs and statistically significant increasing trends in resistance to these antimicrobials were observed for several MSs, for both *C. jejuni* and *C. coli*.

In *C. jejuni* isolates from broiler meat, resistance, considering all reporting MSs, ranged from high to very high for ciprofloxacin (65.7%), nalidixic acid (61.8%) and tetracyclines (36.3%), whereaslevels of resistance to erythromycin and gentamicin were low at 1.6% and very low 0.3%, respectively. A similar pattern was observed 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 85.8% and 85.1%, respectively, very high for tetracycline at 73.9%, moderate for erythromycin at 17.2% and not detected for gentamicin.

Despite the fact that imported food can contribute to cases of *Campylobacter* infection, there were striking parallels in the observed occurrence of resistance to ciprofloxacin, erythromycin, gentamicin and tetracyclines in *C. jejuni* isolates from broiler meat, broilers and humans in Austria and in *C. coli* isolates from broiler meat and humans in Portugal, with similar levels of resistance to each antimicrobial seen in isolates originating from these different sources within each country. Austria and Portugal were the only MSs who reported results for *Campylobacter* isolates from meat and from human cases of infection. Interestingly, Austria also reported results for *C. jejuni* from meat from turkeys and fattening turkeys; isolates from turkeys also closely paralleled the results obtained for isolates from human cases, whereas ciprofloxacin resistance was rather higher in isolates from turkey meat.

Erythromycin resistance in *Campylobacter* spp.

Macrolides are important compounds for the treatment of human *Campylobacter* infections. In broilers, 5.9% of *C. jejuni* isolates from 25 MSs and 14.5% of *C. coli* from 8 MSs, were microbiologically resistant to erythromycin. In turkeys, 2.5% of *C. jejuni* from 10 MSs and 43.3% of *C. coli* from three MSs were erythromycin resistant. The occurrence of resistance to erythromycin in *Campylobacter* spp. varied markedly between individual MSs.

Resistance to macrolides in *Campylobacter* spp. has generally been the result of mutations in ribosomal RNA or ribosomal proteins and these mutations are thought to have incurred fitness costs, accounting for the low occurrence of erythromycin resistance in many countries (Wang et al., 2014). Ribosomal mutations can confer high-level erythromycin resistance (Gibreel and Taylor, 2006). Transferable resistance to erythromycin was first described in *Campylobacter* isolates from food-producing animals (including pigs, chickens and ducks) from China in 2014 (Qin et al., 2014, Wang et al., 2014) and frequently resulted in high level resistance to erythromycin, with MICs recorded at > 512 mg/L. Resistance is conferred by the rRNA methylase gene *erm*(B), which can be associated with either chromosomal multidrug resistance islands or transferable plasmids.

The recent emergence of transferable macrolide resistance in *Campylobacter* may provide a means whereby macrolide resistance can spread rapidly in *Campylobacter*. The situation may be compared to tetracycline resistance, which is frequently plasmid mediated in *Campylobacter*, and is frequently detected in many EU MSs at high levels.



Erythromycin resistance in *Campylobacter* spp. (continued)

Although transferable erythromycin resistance conferred by *erm*(B) generally results in high-level resistance to erythromycin, mutational resistance can also result in high-level resistance to erythromycin, but may equally result in lower MICs (above the ECOFF), dependent on the particular mutations which have occurred. The distribution of erythromycin MICs can be used to identify the numbers of isolates which have higher levels of resistance to erythromycin. These isolates may have transferable or mutational erythromycin resistance and fluctuations in the number detected will provide an early indication of changes in the occurrence of high-level macrolide resistance in *Campylobacter*. Genetic investigation of isolates will be necessary for definitive characterisation of the resistance mechanisms which are present.

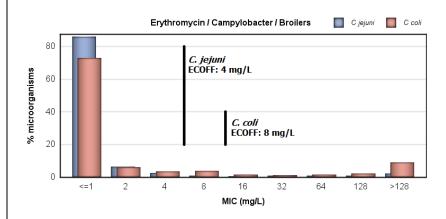
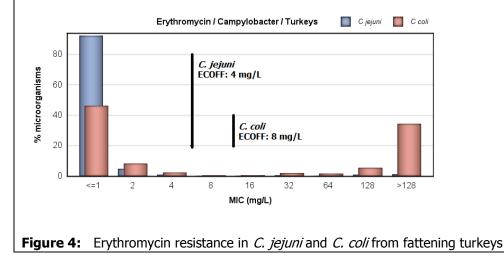


Figure 3: Erythromycin resistance in *C. jejuni* and *C. coli* from broilers



Main findings regarding indicator commensal *Escherichia coli*

Twenty-seven MSs and two non-MSs reported quantitative data on AMR in indicator *E. coli* isolates from poultry populations and meat derived thereof in 2014. Most of the data were related to isolates from broilers and fattening turkeys; two MSs reported results for meat derived from these species.

Regarding broilers, the highest overall 'microbiological' resistance levels observed at the reporting MS group level were to ciprofloxacin (65.7%), nalidixic acid (62.6%), ampicillin (58.7%), sulfamethoxazole (53.1%) and tetracycline (50.1%). Resistance to cefotaxime was 5.1% and was similar to the resistance to ceftazidime (5.0%) 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 2008 and 2014. 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.



MDR levels (reduced susceptibility to at least three antimicrobial classes according to ECOFFs) were generally very high in indicator *E. coli* isolates from broilers (overall 54.6%), with extremely high level in a number of reporting countries. Co-resistance/reduced susceptibility to the clinically important antimicrobials, ciprofloxacin and cefotaxime, was also detected in 4.0% of isolates from broilers. When the resistance to ciprofloxacin and cefotaxime was interpreted using 'CBPs', only 1.9% isolates from broilers displayed 'clinical' resistance.

In the reporting group of MSs, resistance levels in indicator *E. coli* isolates from fattening turkeys were generally lower than among isolates from broilers. The highest resistance levels observed were to tetracyclines (70.9%), ampicillin (69.0%), sulfamethoxazole (51.1%), ciprofloxacin (50.3%) and nalidixic acid (43.5%). The occurrence of resistance was variable between MSs for most of the antimicrobials. Overall, only a few isolates (2.3%) expressed resistance to cefotaxime and 2.2% to ceftazidime.

MDR (reduced susceptibility to at least three of the eleven antimicrobial classes tested) was overall very high in fattening turkeys (59.3%). Generally low levels of 'microbiological' co-resistance to ciprofloxacin and cefotaxime in *E. coli* from fattening turkeys were reported and when the resistance to ciprofloxacin and cefotaxime was interpreted using clinical breakpoints, only few isolates displayed 'clinical' resistance (overall at 0.8%).

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 sub-divided by serovar. A common core of 'microbiological' resistance to ampicillin, ciprofloxacin/nalidixic acid, sulfamethoxazole, tetracycline and trimethoprim was observed in 41.2% of all *E .coli* isolates from broilers. In fattening turkeys, one MDR pattern was predominant (ampicillin, chloramphenicol, ciprofloxacin/nalidixic acid, tetracycline, sulfamethoxazole and trimethoprim) and accounted for more than 20.0% of the MDR patterns in *E. coli* isolates from fattening turkeys and 12.5% *E. coli* isolates data available. In contrast to the situation in *Salmonella*, tigecycline resistance was infrequently detected in *E. coli*.

Colistin-resistant indicator *E. coli* isolates were found by several MSs originating from broilers and fattening turkeys. Further information is provided in the text box below.

Monitoring was enhanced in 2014 to allow further characterisation of third-generation cephalosporin and carbapenem resistance in indicator *E. coli*. The presumptive ESBL phenotype alone was more frequently detected than the AmpC phenotype in indicator *E. coli* from both broiler and fattening turkeys, although at low levels, in less than 5% of isolates in each animal population. An AmpC together with an ESBL phenotype was detected in 0.5% of isolates from broilers, but was not detected in isolates from fattening turkeys. Indicator *E. coli* is considered to represent a reservoir of ESBL and AmpC resistance, which may be transferred to other organisms such as *Salmonella*. The proportions of indicator *E. coli* showing such ESBL and AmpC phenotypic resistance were higher than those observed in *Salmonella* (Table 2: below), but more detailed investigations, including comparison of resistance genes and plasmids, would be required to confirm the inferred phenotype and investigate whether there was any direct relationship between the resistance detected in the populations of *E. coli* and *Salmonella* included in the monitoring.

Table 2:	Summary of phenotypic characterisation of third generation cephalosporin resistance in
	<i>E. coli</i> from poultry in 2014

	Presumptive ESBL phenotype n (% R)	Presumptive AmpC phenotype n (% R)	Presumptive ESBL + AmpC phenotype n (% R)
Broilers (N=4,179)	152 (3.6%)	73 (1.7%)	20 (0.5%)
Turkeys (N=1,457)	30 (2.1%)	6 (0.4%)	0 (0%)

N: number of the isolates tested; n: number of the isolates resistant; % R: percentage of resistant isolates; ESBL: extended spectrum beta-lactamase.

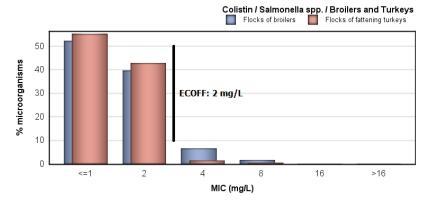


Main findings regarding colistin resistance in Salmonella and E. coli

A specific gene, *mcr-1*, has recently been identified in *E. coli* in China (Liu et al., 2015) which confers resistance to colistin and is located on a plasmid (a mobile genetic element able to transfer between different bacteria). The *mcr-1* gene encodes a phosphoethanolamine transferase, which adds a phosphoethanolamine moiety to the lipid A of the lipopolysaccharide component of the bacterial cell wall. Previously, resistance to colistin was only described as related to chromosomal alterations, which also affected lipid A and reduced the binding of colistin to the cell wall, but these chromosomal alterations were not transferable.

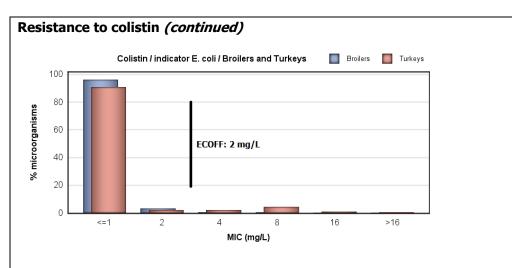
This is a major development because prior to this discovery, all known resistance mechanisms to colistin were not transferable between different bacteria and could only be inherited from a mother bacterial cell by its own daughter cells on cell division. The research to identify the resistance gene was stimulated by an observed rise in resistance to colistin in food-producing animals and food in China; the monitoring of resistance to colistin in food-producing animals and food in Europe assumes a much greater prominence with the detection of transferable resistance in Asia. As this report was being prepared, the Technical University of Denmark announced that they had screened the whole genome sequences of approximately 3,000 Gram-negative bacteria (*E. coli* and *Salmonella*) for the *mcr-1* gene. The gene was found in one patient, who suffered from a blood infection in 2015 and in five food samples that have been imported from 2012 to 2014 (Hasman et al., 2015). Other MSs have started similar scanning of available strain collections to check for the presence of the gene in question. Further reports on the detection of this gene have been recently made by Belgium (Malhotra-Kumar et al., 2016), France (Webb et al., 2015; Haenni et al., 2016), Germany (Falgenhauer et al., 2016), Italy (Battisti, 2016 ProMed), the Netherlands (Wageningen, 2015; Arcilla, 2016), Switzerland (Poirel et al., 2016) and the United Kingdom (Woodmansey et al., 2015).

2014 was the first year of mandatory EU monitoring for colistin resistance in Salmonella and E. coli from animals and the results will provide a baseline in poultry against which changes can be measured. Colistin resistance can be conferred by the transferable mcr-1 gene, or related to a number of other different mechanisms (Olaitan et al., 2014). In addition, some serovars of Salmonella, namely those which possess the O4 somatic antigen, appear to show a degree of intrinsic resistance to colistin (Agersø et al., 2012). The level of colistin resistance in *E, coli* conferred by mcr-1 was generally 4–8 mg/L (Liu et al., 2015) only slightly above the ECOFF for *E. coli* of > 2mg/L. The MIC distributions for *E. coli* and *Salmonella* in broilers and turkeys are shown in Figure 5 and Figure 6. Some MSs encountered technical difficulties in accurately determining colistin susceptibility. The reported occurrence of colistin resistance is unlikely to equate directly to the occurrence of mcr-1 gene, because a number of different resistance mechanisms can confer colistin resistance (Olaitan et al., 2014). A number of colistin-resistant isolates from the EU monitoring programme are undergoing testing either at the EURL-AR or at the MS level for the presence of *mcr-1* gene. Thus, more detailed data on colistin resistance may be available at the MS level later in 2016, dependent on the outcome of these further investigations.











The MIC distributions reveal the presence of *Salmonella* and *E. coli* isolates with colistin MICs > 2 mg/L; however, as mentioned above, it has been previously recognised that certain *Salmonella* serovars belonging to group D in the Kauffmann–White typing scheme (which possess O4 somatic antigens) are intrinsically resistant to colistin at higher levels than other non-Group D serovars (Agersø et al., 2012). Group D *Salmonella* serovars include *S*. Enteritidis which is highly represented among the *Salmonella* isolates tested in broilers, accounting for 13.5% of isolates. Colistin resistance was observed in 8.3% of all *Salmonella* isolates from broilers and 10.5% from laying hens; 72% of these colistin-resistant *Salmonella* isolates from broilers and 80% from laying hens were *S*. Enteritidis. A large proportion of the resistance to colistin detected in *Salmonella* in *Gallus gallus* therefore appears to be related to the previously described higher level of intrinsic resistance of *S*. Enteritidis. According to some of the reports mentioned above, for other serovars such as *S*. Paratyphi B var. Java, *S*. Schwarzengrund, *S*. Typhimurium and or monofasic variants, the presence of *mcr-1* could play a role.

For the first time in 2014, colistin resistance was monitored in indicator *E. coli* in poultry, and 0.9% of *E. coli* from broilers and 7.4% of *E. coli* from turkeys were resistant to colistin in the reporting MSs.

Main findings regarding meticillin-resistant Staphylococcus aureus

A low number of MSs reported the monitoring of meticillin-resistant *Staphylococcus aureus* (MRSA) in food. MRSA was detected in meat from broilers, turkeys and pigs in three countries, with the highest prevalence detected in turkey meat and the lowest in broiler meat. 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 laying hens and breeding flocks in one MS. There was a large degree of variation between MSs in the occurrence of MRSA in pigs, as 0.1–26.5% of animals/herd/slaughter batches tested positive. Molecular typing data were reported by two countries in relation to isolates from pigs; the majority of isolates were *spa*-type t034 with lower numbers of t011; both of these *spa*-types belonging to MRSA clonal complex (CC) 398, the common livestock-associated type of MRSA occurring in Europe. Two MSs examined dairy cows for MRSA; the proportion of animals which tested positive equalled 9.7% in one MS and 16.9% in the other MS.

Several MSs reported results of clinical investigations which yielded MRSA in food-producing animals, including Hungary which reported detection in rabbits (as did the Netherlands) and a pheasant in addition to chickens, sheep and cattle. Considering companion animals, MRSA was detected in cats, dogs and horses in some MSs.

Temporal trends in the occurrence of MRSA in animals could be only assessed in Switzerland, which reported on the occurrence of MRSA in fattening pigs at slaughter – obtained by testing nasal swabs – in consecutive years from 2009 to 2014. The numbers of animals positive for MRSA slowly increased over this period, from 2.2% in 2009 to 26.5% in 2014. The majority of these MRSA isolates belonged to *spa*-type t034, CC398, whereas much lower numbers of MRSA sequence type ST49 were also



reported. The 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.

Monitoring for MRSA in food and animals is performed on a voluntary basis and consequently a relatively low number of MSs/non-MSs (four) reported the results of MRSA monitoring of either food and/or food-producing animals. MRSA detection methods can be very susceptible and consequently detect low levels of the organism; food is not currently regarded as a source of livestock-associated MRSA infection for humans. Three isolates of a healthcare-associated MRSA (*spa*-type t032) recovered from broiler meat at retail may have originated from human sources, as this *spa*-type is not well-recognised in animals, but is common in humans in some countries.

The voluntary monitoring performed reflects the priorities of MSs and although monitoring is not coordinated across MSs, LA-MRSA is evidently widespread geographically and in diverse mammalian and avian host species. It is unclear whether the broad range of species in which colonisation has been detected reflects diffusion in those different species and long-term colonisation, or transient crosscolonisation between species on mixed farms, from species in which colonisation occurs readily, such as pigs.



Table of contents

	bstract1									
Summa	ary3									
List of	ist of tables16									
List of	st of figures									
Legal b	asis21									
1.	Introduction									
1.1.	Monitoring and reporting of antimicrobial resistance at the EU level									
1.2.	Further harmonised monitoring of antimicrobial resistance									
1.2.1.	New legislation on antimicrobial resistance monitoring in animals and food23									
1.2.2.	Developments in the harmonised monitoring of antimicrobial resistance in humans23									
1.3.	The 2014 EU Summary Report on AMR									
2.	Materials and methods									
2.1.	Antimicrobial susceptibility data from humans available in 201425									
2.1.1.	Salmonella data of human origin									
2.1.2.	Campylobacter data of human origin									
2.2.	Antimicrobial susceptibility data from animals and food in 2014									
2.2.1.	Data reported under Directive 2003/99/EC and Decision 2013/652/EU									
2.2.2.	Data validation									
2.2.3.	Analyses of antimicrobial resistance data									
2.2.4.	Analysis of multidrug resistance and co-resistance data									
2.2.5.	Identification of presumptive phenotypes of ESBL-, AmpC- and/or									
	carbapenemase-producers									
2.2.6.	Data on meticillin-resistant <i>Staphylococcus aureus</i> (MRSA)									
3.	Assessment									
3.1.	Antimicrobial resistance in <i>Salmonella</i>									
3.1.1.	Antimicrobial resistance in <i>Salmonella</i> isolates from humans									
3.1.2.	Antimicrobial resistance in <i>Salmonella</i> isolates from animals and food60									
3.1.3.	Discussion									
3.2.	Antimicrobial resistance in <i>Campylobacter</i>									
3.2.1.	Antimicrobial resistance in <i>Campylobacter</i> isolates from humans									
3.2.2.	Antimicrobial resistance in <i>Campylobacter</i> isolates from animals and food									
3.2.3.	Discussion									
3.3.	Antimicrobial resistance in indicator <i>Escherichia coli</i>									
3.3.1.	Antimicrobial resistance in indicator <i>Escherichia coli</i> isolates from animals									
3.3.2.	Multiple drug resistance patterns in indicator <i>Escherichia coli</i> isolates									
3.3.3.	Discussion									
3.4.	Meticillin-resistant <i>Staphylococcus aureus</i>									
3.4.1.	Meticillin-resistant <i>Staphylococcus aureus</i> in food and animals									
3.4.2.	Discussion									
3.5.	Third-generation cephalosporin and carbapenem resistance in <i>Escherichia coli</i> and									
5.5.	Salmonella									
3.5.1.	Third-generation cephalosporin and carbapenem resistance in <i>Salmonella</i> isolates from food									
515111	and animals (routine monitoring)									
3.5.2.	Third-generation cephalosporin and carbapenem resistance in indicator <i>Escherichia coli</i>									
5.5.2.	isolates from food and animals (routine monitoring)									
3.5.3.	Specific monitoring of ESBL-/AmpC-/carbapenemase-producing <i>E. coli</i>									
3.5.4.	Comparison of cefotaxime resistance in <i>Salmonella</i> spp. and indicator <i>Escherichia coli</i>									
Ј.Ј. Т.	isolates from animals									
3.5.5.	Discussion									
	2.5. Discussion									
	List of abbreviations									
	dix: List of usable data									
Thhere										



List of tables

Table 1:	Summary of phenotypic characterisation of third generation cephalosporin resistance in
Table I.	Salmonella from poultry in 2014
Table 2:	Summary of phenotypic characterisation of third generation cephalosporin resistance in
	<i>E. coli</i> from poultry in 2014
Table 3:	Antimicrobials reported, methods used, type of data reported and interpretive criteria
	applied by MSs for human <i>Salmonella</i> AST data in 201427
Table 4:	Antimicrobials reported, method used, type of data reported and interpretive criteria
	applied by MSs for human <i>Campylobacter</i> AST data in 201428
Table 5:	Panel of antimicrobial substances included in AMR monitoring, EUCAST ECOFFs and
	concentration ranges tested in <i>Salmonella</i> spp. and indicator commensal <i>E. coli</i> (first
	panel)
Table 6:	Panel of antimicrobial substances included in AMR monitoring, EUCAST ECOFFs and
Tabla 7.	concentration ranges tested in <i>C. jejuni</i> and <i>C. coli</i>
Table 7:	Panel of antimicrobial substances, EUCAST ECOFFs and concentration ranges used for
	testing only <i>Salmonella</i> spp. and indicator commensal <i>E. coli</i> isolates resistant to cefotaxime, ceftazidime or meropenem (second panel)
Table 8:	Antimicrobial resistance in <i>Salmonella</i> spp. (all non-typhoidal serovars) from humans per
Table 0.	country in 2014
Table 9:	Antimicrobial resistance in <i>Salmonella</i> Enteritidis from humans per country in 201445
	Antimicrobial resistance in <i>Salmonella</i> Infantis from humans per country in 2014
	Antimicrobial resistance in <i>Salmonella</i> Kentucky from humans per country in 201455
Table 12:	Antimicrobial resistance in <i>Salmonella</i> Derby from humans per country in 201457
Table 13:	Occurrence of resistance to selected antimicrobials in <i>Salmonella</i> spp. isolates from meat
	from broilers and meat from fattening turkeys in 201463
Table 14:	Occurrence of resistance to selected antimicrobials in <i>Salmonella</i> spp. isolates from
	broilers in 2014, using harmonised ECOFFs
Table 15:	Occurrence of resistance to selected antimicrobials in <i>Salmonella</i> Enteritidis isolates from
Table 1C.	broilers in 2014
Table 10:	broilers in 2014, using harmonised ECOFFs
Table 17	Occurrence of resistance to selected antimicrobials in <i>Salmonella</i> spp. isolates from laying
	hens in 2014, using harmonised ECOFFs
Table 18:	Occurrence of resistance to selected antimicrobials in <i>Salmonella</i> Enteritidis isolates from
	laying hens in 2014
Table 19:	Occurrence of resistance to selected antimicrobials in <i>Salmonella</i> Infantis isolates from
	laying hens in 2014, using harmonised ECOFFs93
Table 20:	Occurrence of resistance to selected antimicrobials in Salmonella spp.,
	Salmonella Kentucky and Salmonella Derby isolates from turkeys in 201496
Table 21:	Occurrence of resistance to cefotaxime among <i>Salmonella</i> spp. from broilers, laying hens
Table 22.	and fattening turkeys in 2014, using harmonised ECOFFs and EUCAST CBPs
	Antimicrobial resistance in <i>Campylobacter jejuni</i> from humans per country in 2014112 Antimicrobial resistance in Campylobacter <i>coli</i> from humans per country in 2014114
	Occurrence of resistance to selected antimicrobials in <i>Campylobacter coli</i> and
	<i>Campylobacter jejuni</i> from meat in 2014, using harmonised ECOFFs
Table 25:	Occurrence of resistance to selected antimicrobials in <i>Campylobacter</i> from broilers in
	2014, using harmonised ECOFFs
Table 26:	Occurrence of resistance to selected antimicrobials in <i>Campylobacter</i> from fattening
	turkeys in 2014, using harmonised ECOFFs
Table 27:	Occurrence of resistance to selected antimicrobials in indicator Escherichia coli from
	broilers in MSs reporting data in 2014134
Table 28:	Co-resistance to (fluoro)quinolones and third-generation cephalosporins in indicator
	Escherichia coli from broilers in MSs, 2014
Table 29:	PCU-broilers, in 27 MSs, 2014144



Table 30:	Resistance in indicator <i>E. coli</i> from broilers assessed by the percentage of resistant isolates (Total) and 'summary indicator' (weighted mean of the proportions of resistant
Table 31:	isolates in the reporting MSs) in the EU, 27 MSs, 2014
Table 32:	Co-resistance to fluoroquinolones and third-generation cephalosporins in indicator <i>Escherichia coli</i> from fattening turkeys in MSs, 2014
	Meticillin-resistant <i>Staphylococcus aureus</i> in food, 2014155
Table 34:	Meticillin-resistant <i>Staphylococcus aureus</i> in food-producing animals (excluding clinical investigations), 2014
Table 35:	Meticillin-resistant <i>Staphylococcus aureus</i> in food-producing animals, clinical
	investigations, 2014
Table 36:	2014
	Temporal occurrence of meticillin-resistant <i>Staphylococcus aureus</i> in animals159
Table 38:	Occurrence of resistance (%) to selected antimicrobials in MRSA from food and animals, 2014
Table 39:	Occurrence of resistance to beta-lactam compounds in <i>Salmonella</i> spp. isolates from
	broilers, laying hens and meat from broilers collected within the routine monitoring and
Table 40.	subjected to supplementary testing (panel 2) in 2014
	broilers, laying hens and meat from broilers collected within the routine monitoring and
	subjected to supplementary testing (panel 2) in 2014 ^(a)
Table 41:	Occurrence of resistance to beta-lactam and carbapenem compounds in indicator <i>E. coli</i> isolates from broiler flocks collected within the routine monitoring and subjected to
	supplementary testing (panel 2) in 2014
Table 42:	Presumptive ESBL and AmpC phenotypes identified in indicator <i>E. coli</i> isolates from broiler
	flocks collected within the routine monitoring and subjected to supplementary testing (panel 2) in 2014
Table 43:	Occurrence of resistance to beta-lactam and carbapenem compounds in indicator <i>E. coli</i>
	isolates from fattening turkeys collected within the routine monitoring and subjected to
Table 44:	supplementary testing (panel 2) in 2014
	fattening turkeys collected within the routine monitoring and subjected to supplementary
Table 45.	testing (panel 2) in 2014
	collected within the specific carbapenemase-producing microorganisms monitoring in Italy
	in 2014
Table 46:	Prevalence of ESBL-/AmpC-producing <i>E. coli</i> from broilers and fattening turkeys within the specific ESBL-/AmpC-producing <i>E. coli</i> monitoring in Italy in 2014
Table 47:	Prevalence of ESBL-/AmpC-producing <i>Salmonella</i> from broilers and fattening turkeys
Table 40.	within national specific ESBL-/AmpC-producing <i>Salmonella</i> monitoring in Italy in 2014175
Table 48:	Occurrence of resistance to selected antimicrobials in <i>Escherichia coli</i> from broilers and fattening turkeys in reporting countries collected within thespecific ESBL-/Ampc-
	/carbapenemase-producing monitoring (Panel 1), in 2014
Table 49:	Occurrence of resistance to selected antimicrobials in <i>Escherichia coli</i> from broilers and
	fattening turkeys in reporting countries collected within the specific ESBL-/Ampc-/carbapenemase-producing monitoring (Panel 1), in 2014
Table 50:	Presumptive ESBL and AmpC phenotypes identified in <i>E. coli</i> isolates from meat from
	broilers, broilers and fattening turkeys collected within the specific ESBL-/Ampc-
	/carbapenemase-producing monitoring and subjected to supplementary testing or molecular typing confirmation in 2014 ^(a)
Table 51:	Resistance (%) to cefotaxime and ceftazidime in <i>Salmonella</i> spp. and indicator <i>E. coli</i>
	isolates in MSs in 2014 testing both bacterial species in broilers or fattening turkeys 180



List of figures

Figure 1:	Breakdown of serovars in <i>Salmonella</i> isolates from broiler flocks tested for antimicrobial
	susceptibility in the EU, 20147
Figure 2:	Proportions of isolates fully susceptible, resistant to one to two classes of substances and
	multiresistant in the most commonly recovered <i>Salmonella</i> serovars in broiler flocks in
	the EU, 20147
Figure 3:	Erythromycin resistance in <i>C. jejuni</i> and <i>C. coli</i> from broilers10
Figure 4:	Erythromycin resistance in <i>C. jejuni</i> and <i>C. coli</i> from fattening turkeys10
Figure 5:	Colistin resistance in <i>Salmonella</i> 12
Figure 6:	Colistin resistance in indicator <i>E. coli</i>
Figure 7:	Comparison of CBPs for non-susceptibility (intermediate and resistant categories
	combined) and ECOFFs used to interpret MIC data reported for <i>Salmonella</i> spp. from
	humans, animals or food
Figure 8:	Frequency distribution of <i>Salmonella</i> spp. isolates from humans completely susceptible or
-	resistant to one to eight antimicrobial classes in 201441
Figure 9:	Frequency distribution of <i>Salmonella</i> Enteritidis isolates from humans completely
-	susceptible or resistant to one to nine antimicrobial classes in 201444
Figure 10:	Spatial distribution of ciprofloxacin resistance among <i>S.</i> Enteritidis from human cases in
-	reporting countries in 2014
Figure 11:	Spatial distribution of nalidixic acid resistance among <i>S</i> . Enteritidis from human cases in
-	reporting countries in 2014
Figure 12:	Spatial distribution of cefotaxime resistance among <i>S</i> . Enteritidis from human cases in
-	reporting countries in 2014
Figure 13:	Frequency distribution of <i>Salmonella</i> Infantis isolates from humans completely
-	susceptible or resistant to one to nine antimicrobial classes in 2014
Figure 14:	Spatial distribution of ciprofloxacin resistance among <i>S.</i> Infantis from human cases in
-	reporting countries in 2014
Figure 15:	Spatial distribution of nalidixic acid resistance among <i>S</i> . Infantis from human cases in
-	reporting countries in 2014
Figure 16:	Spatial distribution of cefotaxime resistance among <i>S</i> . Infantis from human cases in
	reporting countries in 201453
Figure 17:	Frequency distribution of Salmonella Kentucky isolates from humans completely
	susceptible or resistant to one to nine antimicrobial classes in 201454
Figure 18:	Frequency distribution of <i>Salmonella</i> Typhimurium isolates from humans completely
	susceptible or resistant to one to nine antimicrobial classes in 201459
Figure 19:	Frequency distribution of monophasic <i>Salmonella</i> Typhimurium 1,4,[5],12:i:- isolates
	from humans completely susceptible or resistant to one to eight antimicrobial classes in
	2014
Figure 20:	Frequency distribution of completely susceptible isolates and resistant isolates to one to
	nine antimicrobial classes in <i>Salmonella</i> spp. from broiler meat in MSs in 201461
Figure 21:	Frequency distribution of completely susceptible isolates and resistant isolates to one to
	nine antimicrobial classes in <i>Salmonella</i> spp. from fattening turkey meat in MSs in 201462
Figure 22:	Frequency distribution of completely susceptible isolates and resistant isolates to one to
	nine antimicrobials classes in <i>Salmonella</i> spp. from broilers in MSs in 201464
Figure 23:	Spatial distribution of ciprofloxacin resistance among <i>Salmonella</i> spp. from broilers in
-	countries reporting MIC data in 201465
Figure 24:	Spatial distribution of nalidixic acid resistance among <i>Salmonella</i> spp. from broilers in
	countries reporting MIC data in 2014
Figure 25:	Spatial distribution of cefotaxime resistance among <i>Salmonella</i> spp. from broilers in
F !	countries reporting MIC data in 2014
Figure 26:	Frequency distribution of completely susceptible isolates and resistant isolates to one to
-	nine antimicrobials classes in <i>Salmonella</i> Infantis from broilers in MSs in 2014
Figure 27:	Spatial distribution of ciprofloxacin resistance among <i>Salmonella</i> Infantis from broilers in
F !	countries reporting MIC data in 2014
rigure 28:	Spatial distribution of nalidixic acid resistance among <i>Salmonella</i> Infantis from broilers in
	countries reporting MIC data in 201470



Figure 29:	Spatial distribution of cefotaxime resistance among Salmonella Infantis from broilers in
.	countries reporting MIC data in 2014
	countries reporting MIC data in 201471 Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> Enteritidis from broilers in MSs in 201472
Figure 31:	Spatial distribution of ciprofloxacin resistance among <i>Salmonella</i> Enteritidis from broilers in countries reporting MIC data in 2014
-	Spatial distribution of nalidixic acid resistance among <i>Salmonella</i> Enteritidis from broilers in countries reporting MIC data in 2014
Figure 33:	Spatial distribution of cefotaxime resistance among <i>Salmonella</i> Enteritidis from broilers in countries reporting MIC data in 201474
Figure 34:	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> Kentuky from broilers in MSs in 201475
Figure 35:	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> spp. from laying hens in MSs in 2014
Figure 36:	Spatial distribution of ciprofloxacin resistance among <i>Salmonella</i> spp. from laying hens in
Figure 37:	countries reporting MIC data in 2014
Figure 38:	Spatial distribution of cefotaxime resistance among <i>Salmonella</i> spp. from laying hens in countries reporting MIC data in 2014
Figure 39:	Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested <i>Salmonella</i> spp. isolates from <i>Gallus gallus</i> in reporting MSs, 2008–2014, quantitative data
Figure 40:	Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested <i>Salmonella</i> Enteritidis isolates from <i>Gallus gallus</i> in reporting MSs, 2008–2014, quantitative data
-	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> Enteritidis from laying hens in MSs in 201487
-	Spatial distribution of ciprofloxacin resistance among <i>Salmonella</i> Enteritidis from laying hens in countries reporting MIC data in 2014
Figure 43:	Spatial distribution of nalidixic acid resistance among <i>Salmonella</i> Enteritidis from laying hens in countries reporting MIC data in 2014
Figure 44:	Spatial distribution of cefotaxime resistance among <i>Salmonella</i> Enteritidis from laying hens in countries reporting MIC data in 2014
Figure 45:	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> Infantis from laying hens in MSs in 201490
Figure 46:	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> Kentucky from laying hens in MSs in 201490
Figure 47:	Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested <i>Salmonella</i> spp. isolates from turkeys in reporting MSs, 2008–2014, quantitative data98
Figure 48:	Spatial distribution of ciprofloxacin resistance among <i>Salmonella</i> spp. from fattening turkeys in 2014
Figure 49:	Spatial distribution of nalidixic acid resistance among <i>Salmonella</i> spp. from fattening turkeys in 2014
Figure 50:	Spatial distribution of cefotaxime resistance among <i>Salmonella</i> spp. from fattening turkeys in 2014
Figure 51:	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> spp. from fattening turkeys in 2014100
	Tigecycline resistance in <i>Salmonella</i> spp
-	<i>Campylobacter</i> spp. from humans, animals or food
rigure 54:	Frequency distribution of <i>Campylobacter jejuni</i> isolates from humans completely susceptible or resistant to one to four antimicrobial classes in 2014
Figure 55:	Spatial distribution of ciprofloxacin resistance among <i>Campylobacter jejuni</i> from human
-	cases in reporting countries in 2014
Figure 56:	Spatial distribution of erythromycin resistance among <i>Campylobacter jejuni</i> from human cases in reporting countries in 2014



Figure 57:	Frequency distribution of <i>Campylobacter coli</i> isolates from humans completely susceptible or resistant to one to four antimicrobial classes in 2014
	Trends in ciprofloxacin, erythromycin and nalidixic acid resistance in <i>Campylobacter jejuni</i> from broilers in MSs, 2008–2014
	from broilers in MSs, 2008–2014
-	Spatial distribution of ciprofloxacin resistance among <i>Campylobacter jejuni</i> from broilers of <i>Gallus gallus</i> in reporting countries in 2014
	Spatial distribution of erythromycin resistance among <i>Campylobacter jejuni</i> from broilers of <i>Gallus gallus</i> in reporting countries in 2014
-	Frequency distribution of <i>Campylobacter jejuni</i> isolates completely susceptible and resistant to one to four antimicrobials, in broilers in MSs, 2014
-	Frequency distribution of <i>Campylobacter coli</i> isolates completely susceptible and resistant to one to four antimicrobials, in broilers in MSs, 2014
	Spatial distribution of ciprofloxacin resistance among <i>Campylobacter jejuni</i> from fattening turkeys in reporting countries in 2014
-	Spatial distribution of erythromycin resistance among <i>Campylobacter jejuni</i> from fattening turkeys in reporting countries in 2014
	resistant to one to four antimicrobials, in fattening turkeys in MSs, 2014
	Trends in ampicillin and tetracyclines resistance in indicator <i>Escherichia coli</i> from broilers in reporting countries, 2008–2014
	Trends in cefotaxime, ciprofloxacin and nalidixic acid resistance in indicator <i>Escherichia coli</i> from broilers in reporting countries, 2008–2014
-	Spatial distribution of ciprofloxacin resistance among indicator <i>Escherichia coli</i> from broilers in reporting countries, in 2014
-	Spatial distribution of nalidixic acid resistance among indicator <i>Escherichia coli</i> from broilers in reporting countries, in 2014
	Spatial distribution of cefotaxime resistance among indicator <i>Escherichia coli</i> from broilers in reporting countries, in 2014
-	one to twelve antimicrobials in broilers in reporting countries, 2014
	fattening turkeys in reporting countries, in 2014
-	fattening turkeys in reporting countries, in 2014
-	fattening turkeys in reporting countries, in 2014
	one to 12 antimicrobials in fattening turkeys in MSs, 2014



Legal basis

According to Directive 2003/99/EC on the monitoring of zoonoses and zoonotic agents, Member States (MSs) are obliged to monitor and report antimicrobial resistance (AMR) in *Salmonella* and *Campylobacter* isolates obtained from healthy food-producing animals and from food. Commission Implementing Decision 2013/652/EU of 12 November 2013¹ sets up priorities for the monitoring of AMR from a public health perspective, establishes a list of combinations of bacterial species, food-producing animal populations and foodstuffs and lays down detailed requirements on the harmonised monitoring and reporting of AMR.

The data collection on human diseases from MSs is conducted in accordance with Decision 1082/2013/EU² 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 AMR, to the European Centre for Disease Prevention and Control (ECDC) are described in Decision 2012/506/EU³. 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 (EFSA), 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 178/2002⁴ 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 851/2004⁵ 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

¹ 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 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.

³ 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.

⁴ 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.

⁵ Regulation (EC) No 851/2004 of the European Parliament and of the Council of 21 April 2004 establishing a European centre for disease prevention and control. OJ L 142, 30.4.2004, p. 1–11.



data on zoonoses, zoonotic agents, AMR 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 AMR in the EU.

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 (AMR) 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 and animal health. Both the route of administration and the administered quantities of antimicrobials may differ between humans and food-producing animals; moreover, there are important variations between and within food-producing animal populations, 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 other 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 be transferred between bacterial species, including organisms capable of causing disease in both humans and animals (EFSA, 2008).

The monitoring of AMR 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 and enables to follow temporal trends in the occurrence and distribution of resistance to antimicrobials. Resistance monitoring should also allow for the identification of emerging or specific patterns of resistance.

1.1. Monitoring and reporting of antimicrobial resistance at the EU level

Based on Article 33 in Regulation (EC) 178/2002, EFSA is responsible for examining data on AMR collected from the Member States (MSs) in accordance with Directive 2003/99/EC and for preparing the European Union (EU) Summary Report from the results. This EU Summary Report 2014 includes data related to the occurrence of AMR both in isolates from animals and foodstuffs and in isolates from human cases. The report is a joint collaboration between the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC) with the assistance of EFSA's contractor – the Animal and Plant Health Agency (APHA) in the United Kingdom. MSs, other reporting countries, the European Commission (EC) and the relevant EU Reference Laboratory (EURL-AR) were consulted, while preparing the report. The efforts made by MSs, the reporting non-MSs and the EC in the reporting of data on AMR and in the preparation of this report are gratefully acknowledged.

1.2. Further harmonised monitoring of antimicrobial resistance

The main issues when comparing AMR 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 ECDC's protocol for harmonised monitoring and reporting of resistance in humans and recent legislation on harmonised monitoring in food-producing animals and food thereof.



1.2.1. New legislation on antimicrobial resistance monitoring in animals and food

Commission Decision 2013/652/EU of 12 November 2013⁶ establishes a list of combinations of bacterial species, food-producing animal populations and food products and sets up priorities for the monitoring of AMR from a public health perspective. Monitoring of AMR in E. coli became mandatory, as it is for Salmonella and Campylobacter jejuni in the major food-producing animal populations broilers, laying hens, fattening turkeys, fattening pigs, calves -- and their derived meat. The specific monitoring of extended-spectrum beta-lactamase (ESBL)-, 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 MDR. Representative sampling should be performed according to general provisions of the legislation and to detailed technical specifications issued by EFSA. Monitoring of AMR in food-producing animals 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. Commission Implementing Decision 2013/652/EU entered into force in 2014, as did Commission Implementing Decision 2013/653/EU of 12 November 2013 concerning financial aid towards a coordinated control plan for AMR monitoring in zoonotic agents in MSs in 2014.

Microdilution methods for testing should be used and result should be interpreted by the application of EUCAST epidemiological cut-off (ECOFF) values⁷ 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 CBPare included so that comparability of results with human data is made possible. Within the animal and food monitoring programmes, the new legislation has specified those types of animals which should be monitored in particular years. Ensuring that all MSs test the same species in a given year has simplified the presentation and increased the comparability of the results, because each annual report will now focus primarily on the target species for a given year.

A particular feature of the revised monitoring protocol for *Salmonella* and *E. coli* is the use of a supplementary panel of antimicrobials for testing isolates which show resistance to third-generation cephalosporins or carbapenems in the first panel. The reporting of isolate-based data, which was introduced several years ago, has facilitated the introduction of this change, which allows in depth phenotypic characterisation of certain mechanisms of resistance, for example, third-generation cephalosporin resistance and carbapenem resistance can be further characterised. It seems likely that this principle can be further developed and refined in time.

External quality assurance is provided by the EURL-AR, which distribute panels of well-characterised organisms to all MSs for susceptibility testing. MSs must test and obtain the correct results in such tests to ensure proficiency. The EURL-AR also provides a source of reference for MSs in cases where there are issues or problems with the susceptibility test methodology.

1.2.2. Developments in the harmonised monitoring of antimicrobial resistance in humans

Together with its Food- and Waterborne Diseases and Zoonoses (FWD) network, ECDC has developed an EU protocol for harmonised monitoring of AMR in human *Salmonella* and *Campylobacter* isolates (ECDC, 2014). This document is intended for the National Public Health Reference Laboratories to

⁶ 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.

⁷ The epidemiological cut-off (ECOFF) values 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. The use of harmonised methods and ECOFFs ensures the comparability of data over time at the country level and also facilitated the comparison of resistance between MSs.



guide the susceptibility testing required for EU surveillance and reporting to ECDC. Consultation was also sought from EFSA, EUCAST and the EURL-AR to facilitate comparison of data between countries and with results from the AMR monitoring performed in isolates from animals and from food products. The protocol is effective from 2014 and supports the implementation of the Commission Action Plan on AMR. 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 quantitative antimicrobial susceptibility testing (AST) data reporting in last year's data collection and encourages countries to use it. As the EU protocol is not a legal document but a recommendation and joint agreement, it is up to each National Public Health Reference Laboratory whether to adapt to the protocol, in 2014, whereas the optional antimicrobials were tested by fewer laboratories. The proposed testing algorithm for screening and confirmation of extended spectrum beta-lactamase (ESBL)-producing *Salmonella* spp., including detection of pAmpC, however, does not seem to have been implemented or at least not reported to ECDC as planned.

Since the majority of laboratories use disk diffusion for AST, ECDC set up a joint project with EUCAST to establish inhibition zone diameter ECOFFs for *C. jejuni, C. coli* and *Salmonella* spp. New disk diffusion ECOFFs were established for nine antimicrobials for *Salmonella* spp. in 2014 (Matuschek et al., 2015), whereas the project is still ongoing for *C. jejuni* and *C. coli*.

External quality assurance to support laboratories in implementing the recommended test methods and antimicrobials and obtaining high-quality AST results is provided by Statens Serum Institute in Denmark through a contract with ECDC.

1.3. The 2014 EU summary report on AMR

The majority of the data reported to EFSA by MSs comprises data collected in accordance with Commission implementing Decision 2013/652/EU. The antimicrobial susceptibility data reported to EFSA for 2014 for *Campylobacter, Salmonella*, 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 to third-generation cephalosporins caused by ESBLs and AmpC beta-lactamases in *Salmonella* and indicator *E. coli*, as well as the investigation at the EU level of the occurrence of complete susceptibility and MDR in data reported at the isolate level. A list of the antimicrobials included in this evaluation of MDR can be found in Section 2, 'Materials and methods'.

The report also includes 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) at ECDC either as quantitative or categorical/qualitative data. The quantitative data were interpreted using EUCAST ECOFFs, where available. The qualitative data had been interpreted using 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 bacterium–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.

CBPs enable clinicians to choose the appropriate treatment based on information relevant to the individual patient. ECOFFs 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.



2. Materials and methods

2.1. Antimicrobial susceptibility data from humans available in 2014

More than half of the reporting countries submitted isolate-based measured values (quantitative AST data) to ECDC for 2014, which is a substantial increase from 30% of the countries reporting measured values in the previous year when isolate-based reporting was introduced. The remaining countries submitted interpreted categorical (qualitative) AST data via the case-based reporting. As the data collected by EFSA are also quantitative, moving towards quantitative data from human isolates improves comparability between the two sectors, as the same interpretive criteria can be applied to the two data sets.

As in the 2013 report, the categories of 'clinically' intermediate and 'clinically' resistant in the interpreted data 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 provides better comparability and more straightforward interpretation of the data for most antimicrobial agents included (Figure 7, human section in *Salmonella* chapter).

2.1.1. *Salmonella* data of human origin

Twenty-one MSs and Norway provided data for 2014 on human *Salmonella* isolates. Twelve countries (Austria, Denmark, Estonia, Finland, Greece, Ireland, Italy, Luxembourg, the Netherlands, Norway, Portugal and Romania) reported isolate-based AST results as measured values (inhibition zone diameters or minimum inhibitory concentrations (MICs)) which was five countries more than for 2013. Ten countries reported case-based AST results interpreted as susceptible (S), intermediate (I) or resistant (R) according to the CBPs applied (Table 3).

In 2013, the national public health laboratories within the FWD network agreed on a panel of priority antimicrobials and optional antimicrobials to test for and report to ECDC (ECDC, 2014). Two antimicrobials — ceftazidime and meropenem — were new in the priority panel compared to earlier recommendations. Whereas only a few laboratories had started to test for susceptibility to these substances in 2013, the majority of laboratories were able to report on them for 2014.

Due to the problems in detecting low-level fluoroquinolone resistance in *Salmonella* spp. using disk diffusion, nalidixic acid has been used as a marker for fluoroquinolone resistance. This is also recommended in the EU protocol for harmonised monitoring of AMR in human *Salmonella* and *Campylobacter* isolates (ECDC, 2014). After the discovery that plasmid-mediated fluoroquinolone resistance is often not detected using nalidixic acid, EUCAST studied alternative disks and concluded that pefloxacin was an excellent surrogate marker (except for isolates having the *aac*(\mathcal{C})-*Ib-cr* gene as the only resistance determinant) (Skov et al, 2015). Since 2014, EUCAST recommend this agent for screening of low-level fluoroquinolone resistance in *Salmonella* with disk diffusion (EUCAST, 2014). A few of the countries using disk diffusion therefore replaced the ciprofloxacin and nalidixic acid testing with pefloxacin during 2014.

Some of the optional antimicrobials – azithromycin, colistin and tigecycline – are included in the report, where available, to enable comparison with the data reported from food and animals. Most countries also reported the combination drug co-trimoxazole (sulfamethoxazole and trimethoprim) in addition to or instead of testing the substances separately, partly because this combination is used for clinical treatment and partly because no EUCAST interpretive criterion exists for sulfamethoxazole for *Salmonella*.

Information on the methods and guidelines used for testing and interpretation in 2014 were provided by the public health reference laboratories. Twelve MSs plus Norway used disk diffusion methods (DDs), five MSs used dilution methods (DLs) and another four MSs used a combination of the two, mostly disk diffusion and gradient strip, depending on the situation and the antimicrobial (Table 3). Almost all countries' data were interpreted applying EUCAST criteria in 2014, where available. For two countries, no update on the criteria had been provided in the last years. For countries reporting quantitative measured values, all isolates had been tested at a central laboratory.

As resistance levels differ substantially between *Salmonella* serovars, results are presented separately for selected serovars of importance, particularly those found in poultry due to the focus of the 2014



report. The serovars presented in the report are *S*. Enteritidis, *S*. Infantis, *S*. Kentucky, *S*. Derby, *S*. Typhimurium and monophasic *S*. Typhimurium. Additional serovars among the ten most common in human cases in 2014 or serovars of particular interest due to recent outbreaks etc. are available in appendices (*S*. Bovismorbificans, *S*. Bredeney, *S*. Chester, *S*. Hadar, *S*. Indiana, *S*. Mbandaka, *S*. Muenchen, *S*. Newport, *S*. Paratyphi B var. L+ tartrate+ (var. Java), *S*. Rissen, *S*. Senftenberg, *S*. Stanley and *S*. Virchow). The proportion of resistant isolates are only shown when at least 20 isolates of *Salmonella* spp. or at least 10 isolates of separate serovars were tested in that MS.

In order to better assess the impact from food consumed within each reporting country on the AMR 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 proportions of travel-associated, domestic and unknown cases among the tested *Salmonella* isolates are presented in Table <u>SALMTRAVHUM</u>.

Multidrug resistance (MDR) of human Salmonella spp. to nine antimicrobial classes was analysed. For the 2014 report, ECDC and EFSA agreed to include the same antimicrobial classes in the MDR analysis for better comparison between the two sectors. For the human data analysis, this meant including also carbapenems which had not been possible in 2013 when too few countries reported on this class. Multidrug resistance of an isolate was defined as resistance or non-susceptibility to at least three different antimicrobial classes (Magiorakos et al., 2012). The antimicrobials included were ampicillin, cefotaxime/ceftazidime, chloramphenicol, ciprofloxacin/pefloxacin/nalidixic acid, gentamicin, meropenem, sulfonamides/sulfamethoxazole, tetracyclines and trimethoprim/sulfamethoxazole (cotrimoxazole). Resistance to nalidixic acid, ciprofloxacin and pefloxacin were addressed together, as they belong to the same class of antimicrobials: quinolones. Isolates that were resistant or nonsusceptible to any of these antimicrobials were classified as resistant or non-susceptible to the class of quinolones. The same method was applied to the two third generation cephalosporins cefotaxime and ceftazidime. Trimethoprim and co-trimoxazole were also addressed together since a few countries had only tested for susceptibility to the combination. This approach was considered appropriate because among the eight countries that provided data on both trimethoprim alone and the combination cotrimoxazole, the proportion of resistant or non-susceptibles corresponded closely between the two. Co-resistance to ciprofloxacin and cefotaxime was also analysed as these two antimicrobials are considered the most important for treatment of severe salmonellosis (ECDC et al., 2009). Both 'microbiological' co-resistance (using EUCAST ECOFFs) and 'clinical' co-resistance (using EUCAST CBPs) were determined.

For the first time, the proportions of human isolates resistant to ciprofloxacin, nalidixic acid and cefotaxime were also presented in maps to provide an overview of the spatial distribution of resistance. Data were only shown for countries reporting at least 10 isolates.

2.1.2. *Campylobacter* data of human origin

Thirteen MSs and Norway provided data for 2014 on human *Campylobacter* isolates. Eight countries (Austria, Estonia, Italy, Luxembourg, Norway, Portugal, Romania and Slovenia) reported isolate-based AST results as measured values (inhibition zone diameters or MICs (Table 4) which was three countries more than for 2013. Six 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 2014 report followed the panel of antimicrobials from the EU protocol for harmonised monitoring of AMR in human *Salmonella* and *Campylobacter* isolates (ECDC, 2014). 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 2014 were provided by the public health reference laboratories. Seven MSs used DDs, three MSs and Norway used DLs (microbroth dilution or gradient strip) and another three MSs used a combination of the two depending on the situation and the antimicrobial (Table 4). Almost all countries' data were interpreted applying EUCAST criteria in 2014, where available. Four countries did not provide an update on the criteria applied. For countries reporting quantitative measured values, all isolates had been tested at a central laboratory.



Country	Ampicillin	Azithromycin	Cefotaxime	Ceftazidime	Chloramphenicol	Ciprofloxacin/ pefloxacin	Colistin	Gentamicin	Meropenem	Nalidixic acid	Sulfonamides	Tetracyclines	Tigecycline	Trimethoprim	Trimethoprim- sulfa	Method used	Quantitative (Q) or categorical (SIR)	Interpretive criteria
Austria	•		•	•	•	•		•	•	•	•	•	•	•		DD	Q	Interpreted by ECDC. EUCAST ECOFFs 2014 for all except CLSI CBP 2014 for SUL
Belgium	•		•		•	•		•		•	•	•			•	DD	SIR	No update. In 2013, EUCAST CBP 2013 (AMP, CTX, CHL, GEN, SXT), CLSI CBP 2013 (CIP, NAL, SUL, TET)
Denmark	•	•	•	•	•	•	•	•	•	•	•	•	•	•		DL	Q	Interpreted by ECDC, as for Austria. EFSA criteria for AZM MIC
Estonia	•		•	•	•	•		•	•	•	•	•		•		DD	Q	Interpreted by ECDC, as for Austria
Finland	•		•		•	•		•		•	•	•		•		DD	Q	Interpreted by ECDC, as for Austria
France	•			•	•	•		•	•	•	•	٠		•	•	DD/DL ^(a)	SIR	CA-SFM CBP 2013
Greece	•		•	•	•	•			•	•		•				DD	Q	Interpreted by ECDC, as for Austria
Hungary	•		•		•	•		•		•		•		•	•	DD/DL ^(a)	SIR	EUCAST CBP 2014 except CLSI CBP 2014 for NAL, SUL and TCY
Ireland	•	•	•	•	•	•		•	•	•	•	•	٠	•		DL	Q	Interpreted by ECDC, as for Austria. EFSA criteria for AZM MIC
Italy	•		•	•	•	•		•	•	•	•	•		•	•	DD	Q	Interpreted by ECDC, as for Austria
Latvia	•					•									•	DD	SIR	CLSI and EUCAST CBP
Lithuania	•		•	•	•	•		•	•	•		•		•	•	DD	SIR	No update provided. Earlier CLSI
Luxembourg	•		•	•	•	•		•	•		•	•		•	•	DD/DL ^(a)	Q	Interpreted by ECDC, as for Austria
Malta	•					•		• ^(b)							•	DL	SIR	Biomerieux Vitek II system; follows EUCAST CBP 2014
Netherlands	•	•	•	•	•	•	•	•	•	•	•	•	•	•		DL	Q	Interpreted by ECDC, as for Austria. EFSA criteria for AZM MIC
Norway	•		•	•	•	•		•	•	•		•			•	DD	Q	Interpreted by ECDC, as for Austria
Portugal	•		•		•	•		•		•		•			•	DD	Q	Interpreted by ECDC, as for Austria
Romania	•		•	•	•	•		•	•	•	•	٠		•	•	DD	Q	Interpreted by ECDC, as for Austria
Slovakia	•		•	•	•	•		• ^(b)	•	•	•	•			•	DD/DL	SIR	No update provided. In 2013, EUCAST CBP 2013 except CLSI CBP 2013 for NAL, SUL and TCY
Slovenia	•		•	•	•	•		•	•		•	٠		٠	•	DD/DL ^(a)	SIR	EUCAST CBP 2014 except CLSI CBP 2014 for SUL and TET.
Spain	•		•		•	•		•		•		٠			•	DD	SIR	EUCAST CBP 2014 except CLSI CBP 2010 for NAL and TET
United Kingdom	•		•	•	•	•		٠	•	•	•	٠		•	•	DL ^(c)	SIR	No update provided. Earlier HPA methodology based on Frost 1994

Table 3:	Antimicrobials reported, methods used, type of data reported	and interpretive criteria applied by MSs for human <i>Salmonella</i> AST data in 2014

MSs: Member States; AST: antimicrobial susceptibility testing; DD: disk diffusion; DL: dilution; Q: quantitative data; SIR: susceptible, intermediate, resistant (categorical data); ECDC: European Centre for Disease Prevention and Control; EUCAST: European Committee on Antimicrobial Susceptibility Testing; ECOFF: epidemiological cut-off; CLSI: Clinical and Laboratory Standards Institute; CBP: clinical breakpoint; SUL: sulfonamides; AMP: ampicillin; CTX: cefotaxime; CHL: chloramphenicol; GEN: gentamicin; SXT: sulfamethoxazole; CIP: ciprofloxacin; NAL: nalidixic acid; TET: tetracycline; AZM: azithromycin; TCY: tigecycline; CA-SFM: French Society for Microbiology; HPA: Health Protection Agency (UK).

(a): Gradient strip.

(b): All gentamicin results for *Salmonella* automatically reported as resistant and therefore excluded.

(c): In agar breakpoint.



Resistance levels differ quite substantially between the two most important Campylobacter species, C. jejuni and C. coli, and data are therefore presented by species. The proportion of resistant isolates is only shown when at least 10 isolates were reported from a MS.

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 proportions of travel-associated, domestic and unknown cases among the tested *Campylobacter* isolates are presented in Table <u>CAMPTRAVHUM</u>.

Multidrug resistance of a *C. jejuni* or *C. coli* isolate was defined as resistance or non-susceptibility to at least three different antimicrobial classes (Magiorakos et al., 2012). For the 2014 report, the antimicrobials in the MDR analysis were harmonised between EFSA and ECDC and included ciprofloxacin, erythromycin, gentamicin and tetracyclines. Co-resistance to ciprofloxacin and erythromycin was also analysed, as these two antimicrobials are considered the most important for treatment of severe campylobacteriosis (ECDC, EFSA, EMEA and SCENIHR 2009). Both 'microbiological' co-resistance (using EUCAST ECOFFs) and 'clinical' co-resistance (using EUCAST CBPs) were determined.

For the first time, the proportion of human isolates resistant to erythromycin and ciprofloxacin were also presented in maps to provide an overview of the spatial distribution of resistance. Data were only shown for countries reporting at least 10 isolates.

Country	Ciprofloxacin	Co-amoxiclav	Erythromycin	Gentamicin	Tetracyclines	Method used	Type of data	Interpretive criteria
Austria	•		•	•	•	DL	Q	Interpreted by ECDC. EUCAST ECOFF (CIP, ERY, GEN MIC, TET), CA-SFM CBP 2014 (AMC, GEN DD)
Estonia	•		•		•	DD	Q	Interpreted by ECDC, as for Austria
France	•	•	•	•	•	DD	SIR	In 2013, EUCAST CBP 2013 (CIP, ERY, TET), CA-SFM CBP 2013 (AMC, GEN)
Italy	•		•		•	DD	Q	Interpreted by ECDC, as for Austria
Lithuania	•		•		•	DD	SIR	No information
Luxembourg	•	•	•		•	DD/DL ^(a)	Q	Interpreted by ECDC, as for Austria
Malta	•		•			DL/DL ^(a) /DD	SIR	EUCAST CBP 2014 (CIP, ERY)
Netherlands	•		•		•	DD/DL	SIR	Survey in 12 clinical labs in NL in 2009 (Ned Tijdschr Med Microbiol 2009;17:nr1)
Norway	•		•	•	•	DL ^(a)	Q	Interpreted by ECDC, as for Austria
Portugal	•		•	•	•	DD	Q	Interpreted by ECDC, as for Austria
Romania	•		•	•	•	DD	Q	Interpreted by ECDC, as for Austria
Slovakia	•	•	•	•	•	DL	SIR	In 2013, CLSI CBP
Slovenia	•		•		•	DD	Q	Interpreted by ECDC, as for Austria
Spain	•		•	•	•	DL ^(a)	SIR	EUCAST CBP 2014 (CIP, ERY, TET), CA-SFM CBP 2014 (AMC, GEN)

Table 4: Antimicrobials reported, method used, type of data reported and interpretive criteria applied by MSs for human *Campylobacter* AST data in 2014

MSs: Member States; AST: antimicrobial susceptibility testing; DD: disk diffusion; DL: dilution; Q: quantitative data; SIR: susceptible, intermediate, resistant (categorical data); ECDC: European Centre for Disease Prevention and Control; EUCAST: European Committee on Antimicrobial Susceptibility Testing; ECOFF: epidemiological cut-off; CIP: ciprofloxacin; ERY: erythromycin; GEN: gentamicin; MIC: minimum inhibitory concentration; TET: tetracycline; CA-SFM: French Society for Microbiology; CBP: clinical breakpoint; AMC: amoxicillin/clavulanate; TCY: tigecycline. (a): Gradient strip.



2.2. Antimicrobial susceptibility data from animals and food in 2014

2.2.1. Data reported under Directive 2003/99/EC and Decision 2013/652/EU

For 2014, 28 MSs and three non-MSs reported data on AMR in tested *Salmonella* and *Campylobacter*, commensal *E. coli* isolates from various poultry populations and/or related meat derived thereof, sampled through harmonised national schemes. Data on AMR in tested *Salmonella*, *C. jejuni* and commensal *E. coli* were obtained and reported by the MSs in accordance with Decision 2013/652/EU. Micro-broth dilution testing methods were used for susceptibility testing, and quantitative⁸ isolate-based data were reported to EFSA and considered for the purpose of this report. Resistance was interpreted using EUCAST ECOFF values (see following text box for further information). The antimicrobials incorporated in this summary analysis were selected based on their public health relevance and as representatives of different antimicrobial classes. Data on meticillin-resistant *Staphylococcus aureus* (MRSA) and on specific monitoring of *E. coli* ESBL-/AmpC-/carbapenemase-producers were reported on a voluntary basis.

Harmonised representative sampling and monitoring

Representative sampling should be performed according to general provisions of the legislation and to detailed technical specifications issued by EFSA (EFSA, 2014).

Salmonella

In 2014, representative *Salmonella* isolates for monitoring AMR were collected by MSs from populations of laying hens, broilers and fattening turkeys sampled within the framework of the *Salmonella* National Control Programmes (NCPs), established in accordance with Article 5(1) of Regulation (EC) No 2160/2003, as well as from carcases of both broilers and fattening turkeys sample for testing and verification of compliance, in accordance with point 2.1.5 of Chapter 2 of Annex 1 to Regulation (EC) No 2073/2005. Not more than one isolate per *Salmonella* serovar from the same epidemiological unit (flock of birds) per year should be included in the AMR monitoring. In most MSs, the isolates tested for antimicrobial susceptibility constituted a representative subsample of the total *Salmonella* isolates available at the National Reference Laboratory (NRL) and/or other laboratories involved, obtained in a way that ensured geographical representativeness and even distribution over the year. Conversely, in the case of low prevalence, all the Salmonella isolates available should be tested for susceptibility.

⁸ '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 specific food/animal category.



Epidemiological cut-off values (ECOFFs) and clinical breakpoints (CBPs)

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 regimen, 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 cutoff 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. EUCAST has defined CBPs and ECOFFs.

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 CBPs used to ascertain whether the organism is likely to respond to treatment. CBPs will take into account the distribution of the drug in the tissues of the body 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 regimens 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 in reports of this type problematic, as the results are not directly comparable between those different countries.

Epidemiological cut-off values (microbiological resistance)

For a given bacterial species, the pattern of the MIC distribution (i.e. the frequency of occurrence of each given MIC plotted against the MIC value) can enable the separation of the wild-type population of microorganisms from those populations which show a degree of acquired resistance. The wildtype 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 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 confer a degree of resistance. In this case, there may be populations of organisms 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.



Campylobacter and indicator E. coli⁹

MSs collected *Campylobacter* and indicator *E. coli* isolates as part of their national monitoring programme of AMR according to the provisions of the Decision 2013/652/EU, based on random sampling of carcases of healthy slaughter broilers/fattening turkeys 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 applied in the reporting countries. Only one representative caecal sample (single or pooled) per epidemiological unit (batch of carcases deriving from the same flock), was gathered to account for clustering. Isolates were recovered from caecal contents samples (single or pooled), in accordance with EFSA's recommendations (EFSA, 2013). The sample collection was approximately evenly distributed over the year 2014.

MRSA

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.

Harmonised antimicrobial susceptibility testing

Routine monitoring antimicrobial susceptibility

MSs tested antimicrobials and interpreted the results using the epidemiological cut-off values and concentration ranges shown in Table 5 and Table 6 to determine the susceptibility of *Salmonella* spp., *C. coli, C. jejuni,* indicator commensal *E. coli.* All *E. coli* isolates, randomly selected isolates of *Salmonella* spp. and *E. coli* that, after testing with the first panel of antimicrobials in accordance with Table 6, are found to be resistant to cefotaxime, ceftazidime or meropenem, were further tested with a second panel of antimicrobial substances as shown in Table 7. This panel notably includes cefoxitin, cefepime and clavulanate in combination with cefotaxime and ceftazidime for the detection of presumptive ESBL- and AmpC-producer, as well as imipenem, meropenem and ertapenem to phenotypically verify presumptive carbapenemase producers.

Specific monitoring of ESBL-/AmpC-/carbapenemase-producing E. coli and *specific monitoring of carbapenemase-producing microorganims*

Both specific monitoring programms were voluntary. For the specific monitoring of ESBL-/AmpC-/carbapenemase-producing *E. coli*, the method started with a non-selective pre-enrichment step, followed by inoculation on McConkey agar containing a third-generation cephalosporin in a selective concentration, in accordance with the most recent version of the detailed protocol for standardisation of the EURL-AR.¹⁰ Using this protocol, also carbapenemase-producing isolates could be recovered. For the specific monitoring of carbapenemase-producing microorganisms, isolation required the use of non-selective pre-enrichment and subsequent selective plating on carbapenem-containing media, in accordance with the most recent version of the detailed protocol of the EURL-AR.

The microbial species was identified using an appropriate method. If available, one presumptive ESBL-/AmpC-/carbapenemase-producing *E. coli* isolate obtained from each positive caecal sample and meat sample was tested for resistance to the first panel of antimicrobials (Table 5) and then submitted for extended susceptibility testing if they are resistant to cefotaxime, ceftazidime or meropenem, based on the interpretative criteria (epidemiological cut-off values).

All presumptive ESBL-/AmpC-/carbapenemase-producing *E. coli* isolates, identified through selective plating were further tested with the second panel of antimicrobials (Table 7) to phenotypically verify presumptive ESBL-/AmpC-/carbapenemase-producers.

⁹ The same sampling design was used to collect indicator *E. coli* isolates, whether dedicated to the routine monitoring of AMR or the specific monitoring of ESBL-/AmpC-/carbapenemase-producing *E. coli*.

¹⁰ Available online: www.crl-ar.eu



Table 5: Panel of antimicrobial substances included in AMR monitoring, EUCAST ECOFFs and concentration ranges tested in *Salmonella* spp. and indicator commensal *E. coli* (first panel)

Antimicrobial	Salmonella EUCAST ECOFF ^(a)	<i>E. coli</i> EUCAST ECOFF ^(a)	Concentration range, mg/L (no of wells)
Ampicillin	> 8	> 8	1–64 (7)
Cefotaxime	> 0.5	> 0.25	0.25-4 (5)
Ceftazidime	> 2	> 0.5	0.5–8 (5)
Meropenem	> 0.125	> 0.125	0.03–16 (10)
Nalidixic acid	> 16	> 16	4–128 (6)
Ciprofloxacin	> 0.064	> 0.064	0.015-8 (10)
Tetracycline	> 8	> 8	2–64 (6)
Colistin	> 2	> 2	1–16 (5)
Gentamicin	> 2	> 2	0.5–32 (7)
Trimethoprim	> 2	> 2	0.25–32 (8)
Sulfamethoxazole	NA ^(b)	> 64	8-1,024 (8)
Chloramphenicol	> 16	> 16	8-128 (5)
Azithromycin	NA ^(c)	NA ^(c)	2–64 (6)
Tigecycline	> 1	> 1	0.25-8 (6)

AMR: antimicrobial resistance; EUCAST: European Committee on Antimicrobial Susceptibility Testing; ECOFFs: epidemiological cut-off values; NA: not available.

(a): EUCAST epidemiological cut-off values.

(b): > 256 mg/L was used.

(c): > 16 mg/L was used.

Table 6: Panel of antimicrobial substances included in AMR monitoring, EUCAST ECOFFs and concentration ranges tested in *C. jejuni* and *C. coli*

Antimicrobial	<i>C. jejuni</i> EUCAST ECOFF ^(a)	<i>C. coli</i> EUCAST ECOFF ^(a)	Concentration range, mg/L (no of wells)
Erythromycin	> 4	> 8	1-128 (8)
Ciprofloxacin	> 0.5	> 0.5	0.12–16 (8)
Tetracycline	> 1	> 2	0.5–64 (8)
Gentamicin	> 2	> 2	0.12–16 (8)
Nalidixic acid	> 16	> 16	1-64 (7)
Streptomycin ^(b)	> 4	> 4	0.25–16 (7)

AMR: antimicrobial resistance; EUCAST: European Committee on Antimicrobial Susceptibility Testing; ECOFFs: epidemiological cut-off values; NA: not available.

(a): EUCAST epidemiological cut-off values.

(b): On a voluntary basis.

Table 7: Panel of antimicrobial substances, EUCAST ECOFFs and concentration ranges used for testing only *Salmonella* spp. and indicator commensal *E. coli* isolates resistant to cefotaxime, ceftazidime or meropenem (second panel)

Antimicrobial	<i>Salmonella</i> EUCAST ECOFF ^(a)	<i>E. coli</i> EUCAST ECOFF ^(a)	Concentration range, mg/L (no of wells)
Cefoxitin	> 8	> 8	0.5–64 (8)
Cefepime	NA ^(b)	> 0.125	0.06-32 (10)
Cefotaxime + clavulanic acid	NA	NA	0.06-64 (11)
Ceftazidime + clavulanic acid	NA	NA	0.125-128 (11)
Meropenem	> 0.125	> 0.125	0.03-16 (10)
Temocillin	NA ^(c)	NA ^(c)	0.5-64 (8)
Imipenem	> 1	> 0.5	0.12–16 (8)
Ertapenem	> 0.06	> 0.06	0.015–2 (8)
Cefotaxime	> 0.5	> 0.25	0.25–64 (9)
Ceftazidime	> 2	> 0.5	0.25-128 (10)

EUCAST: European Committee on Antimicrobial Susceptibility Testing; ECOFFs: epidemiological cut-off values; NA: not available.

(a): EUCAST epidemiological cut-off values.

(b): For cefepime the cut-off value used in the analysis for Salmonella was > 0.125 mg/L.

(c): For temocillin the cut-off value used in the analysis was > 32 mg/L.



2.2.2. Data validation

Validation against business rules

The reported data were first checked for usability against a series of 'business rules' which were automatically applied in the EFSA data collection system once a file was transmitted. This automatic data validation process refers to the first validation of incoming data. Quality checks are related to a specific business only. The positive result of the automatic validation process places the file in a valid state and makes it available for further steps of validation performed by EFSA.

Scientific data validation

The scientific validation of the data collected by the MSs/non-MSs and submitted to EFSA consisted on the revision of data and comparison between data reported for the same antimicrobials when tested by different panels. Special attention was given to new antimicrobials included for the first time in the panels (i.e. carbapenems, azithromycin, tigecycline, colistin, cefepime) and to possible discrepancies between results for antimicrobials present in both panels (i.e. cefotaxime, ceftazidime, meropenem).

If carbapenem resistance was reported and/or there was a discrepancy between MIC values reported for the antimicrobials present in both panels (impacting the categorisation of the isolate as resistant or susceptible), the MSs/non-MSs were requested by EFSA to re-test species identification and susceptibility values, performing the tests with both panels in parallel for the same isolate.

The EURL-AR had reported technical issues when testing azithromycin (some MSs had reported problems in the EURL workshop held in April 2015) and tigecycline (the company producing the plates reported problems with some batches of medium/material sold). Countries with outstanding prevalence for these antimicrobials were contacted by the EURL-AR/EFSA so that they can report whether they faced related problems but they did not report any. Regarding susceptibility testing to colistin, technical issues were also reported; the EURL-AR, EFSA and concerned MSs closely liaised together to address them.

2.2.3. Analyses of antimicrobial resistance data

Data are reported in separate sections dedicated to each microorganism. Clinical investigation data were not accounted for in this report.

Overview tables of the resistance data reported

Data generated from the antimicrobial susceptibility testing and reported as quantitative at the isolate level by MSs have been described in the overview tables published on the EFSA website.

Minimum inhibitory concentration distributions

For each combination of microorganism, antimicrobial and food category/animal population were tested, MIC distributions were tabulated in frequency tables, giving the number of isolates tested that have a given MIC at each test dilution (mg/L) of the antimicrobial. Isolate-based dilution results allowed MIC distributions reported:

- for Salmonella for ampicillin, azithromycin, cefepime, cefotaxime, cefotaxime and clavulanic acid, ceftazidime, ceftazidime and clavulanic acid, cefoxitin, chloramphenicol, ciprofloxacin, colistin, ertapenem, gentamicin, imipenem, meropenem, nalidixic acid, sulfamethoxazole, temocillin, tetracycline, tigecycline and trimethoprim.
- for *Campylobacter* for, ciprofloxacin, erythromycin, gentamicin, nalidixic acid, streptomycin and tetracycline.
- for indicator *E. coli* for ampicillin, azithromycin, cefepime, cefotaxime, cefotaxime and clavulanic acid, ceftazidime, ceftazidime and clavulanic acid, cefoxitin, chloramphenicol, ciprofloxacin, colistin, ertapenem, gentamicin, imipenem, meropenem, nalidixic acid, sulfamethoxazole, temocillin, tetracycline, tigecycline and trimethoprim.
- for MRSA for cefoxitin, chloramphenicol, ciprofloxacin, clindamycin, erythromycin, fusidic acid, gentamicin, kanamycin, linezolid, mupirocin, penicillin, quinupristin/dalfopristin, rifampicin, streptomycin, sulfamethoxazole, tetracycline, tiamulin, trimethoprim and vancomycin



Epidemiological cut-off values and the occurrence of resistance

ECOFFs, as listed in Decision 2013/652/EC, have been used in this report to interpret the isolatebased reported MIC data and determine non-wild-type organisms also termed 'microbiologically' resistant organisms (i.e. displaying a decreased susceptibility), 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. This report also incorporates re-evaluation of the historical data accounting for the revised EU legislation, which included the revised ECOFFs.

The occurrence of resistance¹¹ to a number of antimicrobials was determined for *Salmonella*, *Campylobacter*, indicator *E. coli* isolates from broilers and laying hens of *Gallus gallus*, fattening turkeys, and meat from broilers and fattening turkeys, and are tabulated at the production-type level in this report. Data are included only if quantitative MIC data are provided by more than four MSs for the bacterium–animal population/food category combination. An exception to this rule may have been made on *Salmonella* serovars of public health importance (see below), MRSA and ESBLs-/AmpC-/carbapenemase-producers. Data reported from fewer than 10 tested isolates per combination and per MS are not included, with the exception of the analysis in certain *Salmonella* serovars of importance. 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.

Resistance in Salmonella serovars of public health importance

In this report, AMR in tested *Salmonella* isolates were aggregated to give a value for *Salmonella* spp. for each country and food/animal category. In addition, the most prevalent *Salmonella* serovars were also reported separately for particular food/animal category. Additional tables have been included in this report to describe the occurrence of AMR 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 recovered, data derived from fewer than four reporting countries have been included.

Data description

Throughout the report, *level or occurrence of AMR* 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%'. Although these terms are applied to all antimicrobials, the significance of a given level of resistance depends on the particular antimicrobial and its importance in human and veterinary medicine.

Temporal trends in resistance

Where the minimum criteria¹² for data inclusion in this report were met, temporal trend graphs were generated showing the resistance to different antimicrobials from 2008 to 2014, by plotting the level of resistance for each year of sampling. Graphs were created for those countries for which resistance data were available for four or more years in the 2008–2014 period 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. For ciprofloxacin, nalidixic acid, ampicillin and cefotaxime (*Salmonella*), ciprofloxacin, nalidixic acid and erythromycin (*Campylobacter*), ciprofloxacin, nalidixic acid, cefotaxime, ampicillin, ciprofloxacin, nalidixic acid and tetracycline (indicator *E. coli*), resistance trends

¹¹ Giving the percentage of isolates 'microbiologically' resistant out of those tested.

¹² More than 10 isolates tested by a MS and more than four MSs reporting results for that antimicrobial, microorganism, food or animal category.



over time were visually explored by trellis graphs, using the lattice package in the R software (R version 2.14.2 (29/2/2012)).

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 5 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.

Spatial analysis of resistance through maps

MS-specific AMR levels for selected bacterium–food category/animal population combinations were plotted in maps for 2014, 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 2014. The countries labelled in *Salmonella* maps as '< 10 isolates' therefore include MIC data for fewer than 10 isolates.

2.2.4. Analysis of multidrug resistance and co-resistance data

As a consequence of the availability of AMR data at the isolate level in the MSs, the analysis of MDR and co-resistance data becomes an important exercise in the light of the public health relevance of the emergence of multiresistant 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 MDR, particularly in *Salmonella* serotypes.

Definitions

For the purpose of this analysis, **a multiresistant 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 Decision 2013/652/EU. Table 5: and Table 6: list those recommended antimicrobials. Resistance to nalidixic acid and resistance to ciprofloxacin, as well as the resistance to cefotaxime and to ceftazidime are respectively addressed together.

In contrast, **a fully susceptible isolate** is one defined as non-resistant to all of the antimicrobial substances included in the harmonised set of substances 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.

MDR patterns

The frequency and percentage of isolates exhibiting various MDR 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 all *Salmonella* serovars.



Summary indicators' and 'diversity' of MDR

The objective is first to give an overview of the situation on MDR through summary indicators: (1) the proportion of fully susceptible isolates; (2) the proportion of multiresistant isolates. To illustrate the relative proportions of multiresistant isolates and the diversity of the resistance to multiple antimicrobials, graphical illustration was chosen. The percentage 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 co-resistance patterns of interest

In *Salmonella* and *E. coli* isolates, co-resistance to cefotaxime (CTX) and ciprofloxacin (CIP) 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 CBPs (CTX > 2 mg/L and CIP > 1 mg/L) for *E. coli*. In *C. jejuni* and *C. coli* isolates, co-resistance to ciprofloxacin and erythromycin (ERY) 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 and, for *C. coli*, CIP > 0.5 mg/L and ERY >8 mg/L. These values may be considered as very similar to CBPs.

2.2.5. Identification of presumptive phenotypes of ESBL-, AmpC- and/or carbapenemase-producers

The categorisation of isolates resistant to third-generation cephalosporins and/or carbapenems in presumptive ESBL-,AmpC- or carbapenemase-producers (referred in this report as ESBL/AmpC/carbapenemase phenotype) was carried out based on the EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance (EUCAST, 2013). In these expert guidelines, and based on other EUCAST and CLSI guidelines to detect ESBL/AmpC producers, a screening breakpoint of > 1 mg/L is recommended for cefotaxime and ceftazidime. This screening breakpoint is higher than the ECOFFs applied for antimicrobial susceptibility of both antimicrobials for *E. coli*, and to cefotaxime for *Salmonella*. For this report, a first condition for classifying isolates as putative ESBL/AmpC producers related to their MIC for either cefotaxime or ceftazidime, was to apply this screening breakpoint of MICs greater 1 mg/L. Only isolates which presented MIC values accomplishing with this requisite (as expected for most of the ESBL/AmpC producers) were further considered.

The confirmation of the ESBL phenotype was performed using synergy test for cefotaxime and ceftazidime, in combination with clavulanic acid. An 8-fold reduction in the MIC for the cephalosporin combined with clavulanic acid compared with that obtained for the cephalosporin alone was interpreted as a positive synergy test. In all other cases, the synergy test was considered negative. For the present report, isolates with MICs > 1 mg/L for cefotaxime and/or ceftazidime and a synergy test positive for any of these antimicrobials were classified as ESBL-phenotype.

Regarding the AmpC phenotype, the combination MIC > 8 mg/L (ECOFF) for cefoxitin together with MICs > 1 mg/L for cefotaxime and/or ceftazidime was used as phenotypic criteria to investigate the presence of AmpC production in *E. coli*. It should be also underlined that there are a few AmpC enzymes that do not confer resistance to cefoxitin (i.e. ACC-1), and that there are other mechanisms (porin loss, presence of carbapenemases, a few ESBLs like cefotaximase (CTX-M)-5) that could generate similar MIC values for the different antimicrobials (EFSA, 2012a; EUCAST, 2013). Phenotypic AmpC confirmation tests (i.e. cloxacillin synergy) were not required for the present monitoring. For the present report, isolates with MICs > 1 mg/L for cefotaxime and/or ceftazidime and cefoxitin MIC > 8 mg/L, together with negative synergy test for both cefotaxime and ceftazidime/clavulanic acid, were considered as putative AmpC producers and classified in the AmpC phenotype category. No distinction between acquired AmpC and natural AmpC was done.

In some isolates, several mechanisms can be present at the same time, making it very difficult to differentiate the phenotypes. Also the high-level expression of AmpC β -lactamases can mask the presence of ESBLs. AmpC can also be present in isolates with positive ESBL tests (clavulanic acid



synergy). In this case, the cefepime/clavulanic acid synergy test should be used to overturn/confirm the presence of ESBLs in these isolates (EUCAST, 2013), but unfortunately, the combination cefepime/clavulanic acid was not included among the substances tested for the monitoring. The inclusion of resistance to cefepime with a MIC value \geq 4 mg/L, as an additional criteria proposed elsewhere (EFSA, 2012), could be useful to ascertain the presence of an ESBLproducer.

For the present report, isolates with MICs > 1 mg/L for cefotaxime and/or ceftazidime, positive synergy tests for any of these antimicrobials/clavulanic acid and cefoxitin MIC > 8 mg/L, were considered as putative ESBL- and AmpC-producers and were classified under the ESBL/AmpC-phenotype category.

For the classification of isolates into the putative carbapenem producers (CPs), a meropenem screening cut-off of > 0.12 mg/L (which coincides with the harmonised ECOFF) was chosen. It is known that other mechanisms (i.e. hyperproduction or combination of ESBLs and/or AmpC and porin loss) can also affect to the MIC values generated for the different carbapenems, especially for ertapenem. The confirmation of the carbapenems susceptibility testing data reported, but needs further phenotypic or molecular testing. Those MS which reported data suggesting the presence of putative CPs were recommended to validate the results by performing further confirmatory testing, and the EURL-AR offered to apply whole genome sequencing of the isolates. For the present report, isolates with MIC > 0.12 mg/L for meropenem would be considered as putative CP and were classified under the CP-phenotype. Isolates with a MIC > 0.12 for ertapenem and/or MIC > 1 mg/L for imipenem (EUCAST screening cut-offs, one dilution step higher than the currently defined ECOFFs) but no resistance to meropenem (MIC < 12 mg/L) were classified under the category 'other phenotype'.

Finally, isolates with MICs $\leq 1 \text{ mg/L}$ for cefotaxime and ceftazidime would be considered as not ESBLand/or AmpC producers. This implied that some isolates considered microbiologically resistant (MICs over the ECOFFS) would not be further classified, as probably other mechanisms or technical issues in the MIC testing (i.e. MIC value close to the ECOFF) would be responsible for the MIC values obtained. For the present report, cefotaxime- and ceftazidime-resistant isolates with MICs $\leq 1 \text{ mg/L}$ for both antimicrobials were considered as putative non ESBL/AmpC-producers and were classified under the category 'other phenotype'.

We are aware that without a further molecular characterisation of the isolates, it will not be possible to know exactly which resistance mechanisms are present. For epidemiological purposes and based on the EUCAST guidelines, the classification of 'putative' producers for the different mechanism conferring resistance to third-generation cephalosporins and/or carbapenems was considered.

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

In 2014, Belgium reported data on susceptibility testing of MRSA isolates *Gallus gallus* (fowl) breeding flocks for broiler production line and laying hens, and Switzerland reported data from meat from broilers 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 submitted and validated MS data published on the EFSA website.

Data relating to MRSA prevalence were reported by eight MSs and three non-MSs (Iceland, Norway and 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 <u>3.5</u> 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 dairy cows 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*

Human infections with Salmonella

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 as the bacteria may spread from the intestines to the blood stream and then to other body sites, which can be life-threatening. Acute *Salmonella* infections may sometimes also result in long-term sequelae affecting the joints (reactive arthritis). 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.

For 2014, 21 MSs and Norway provided data on AMR in human *Salmonella* isolates. Twelve countries (Austria, Denmark, Estonia, Finland, Greece, Ireland, Italy, Luxembourg, the Netherlands, Norway, Portugal and Romania) reported isolate-based AST results as measured values (inhibition zone diameters or MICs) which was five countries more than for 2013. Ten countries reported case-based AST results interpreted as susceptible (S), intermediate (I) or resistant (R) according to the CBPs applied (Table <u>SALMOVERVIEW</u>). Twenty-seven MSs and two non-MSs (Iceland and Norway) reported quantitative MIC data on the AMR of *Salmonella* isolates recovered from animals and food in 2014 (Table <u>SALMOVERVIEW</u>).

3.1.1. Antimicrobial resistance in *Salmonella* isolates from humans

When referring to 'Salmonella spp.', this includes results for all Salmonella serovars from human cases with AST results reported. The resistance levels for Salmonella spp. are greatly influenced by the serovars included, with some serovars exhibiting greater resistance to certain antimicrobials or expressing multidrug resistance to a higher degree than other serovars. Results are therefore presented separately for selected serovars of importance, particularly those commonly prevalent in poultry, given the focus of the 2014 report. The serovars presented in this report are *S*. Enteritidis, *S*. Infantis, *S*. Kentucky, *S*. Derby, *S*. Typhimurium and monophasic *S*. Typhimurium. Additional serovars among the ten most common in human cases in 2014 or serovars of particular interest due to recent outbreaks are available in appendices (*S*. Bovismorbificans, *S*. Bredeney, *S*. Chester, *S*. Hadar, *S*. Indiana, *S*. Mbandaka, *S*. Muenchen, *S*. Newport, *S*. Paratyphi B var. L+ tartrate+ (var. Java), *S*. Rissen, *S*. Senftenberg, *S*. Stanley and *S*. Virchow).

In total, 14,412 *Salmonella* isolates of 247 different serovars and serogroups were tested for resistance to one or more antimicrobials and reported by 21 MSs and Norway. This represents 16.0% of all 89,873 confirmed human salmonellosis cases reported in the EU/EEA in 2014. The number of antimicrobials tested per isolate varied by country, from two countries testing only three antimicrobials to thirteen countries testing all ten antimicrobials in the priority panel, but with three of these countries testing the combination drug trimethoprim–sulfamethoxazole (co-trimoxazole) instead of the substances separately. Since the implementation of the agreed panel in 2014 (ECDC, 2014), the number of countries in 2014. Three to four countries also tested the optional antimicrobials azithromycin, colistin and/or tigecycline. Colistin could only be tested by the few laboratories using dilution methods since its chemical properties render it impossible to be tested in agar plates.

To better assess the impact of food consumed within each reporting country on the AMR levels found in human *Salmonella* isolates, the analysis focused on domestically acquired cases.



Methods and interpretive criteria used for antimicrobial 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 3, Material and methods chapter.

Quantitative data were interpreted by ECDC based on the EUCAST ECOFF values, where available, in the same way as for the animal and food data. Where ECOFFs do not exist, EUCAST or Clinical and Laboratory Standards Institute (CLSI) CBPs were applied. For the qualitative SIR¹³ data, intermediate and resistant results were combined into a non-susceptible category.

For 11 antimicrobials, for which results were reported both as quantitative and interpreted data, the commonly used interpretive criteria were aligned (Figure 7). 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. When analysed in this way, there is generally close concordance (± 1 dilution) across categories, also for ciprofloxacin after the CBPs for *Salmonella* was lowered in 2014. A notable exception is the EUCAST CBPs for meropenem, which is substantially higher (+ 4 dilutions) than the ECOFF.

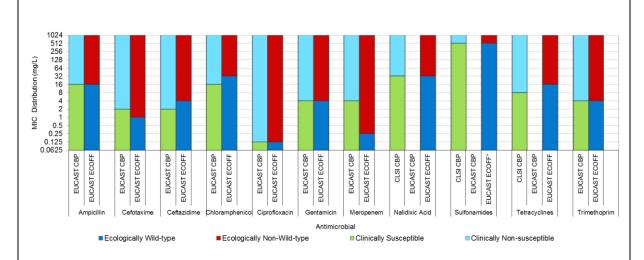


Figure 7: Comparison of CBPs for non-susceptibility (intermediate and resistant categories combined) and ECOFFs used to interpret MIC data reported for *Salmonella* spp. from humans, animals or food

¹³ SIR stands for susceptible, intermediate, resistant.



Antimicrobial resistance in *Salmonella* spp. in humans

Interpretation of monitoring results must take into account the wide variation in the sampling and testing strategies for *Salmonella* between MSs. While the number of reported isolates 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, whereas, for the most common serovars, a representative sample is tested. In Slovakia, non-invasive isolates are tested against only a few antimicrobials, whereas invasive isolates are tested against a larger panel.

The overall resistance levels for *Salmonella* spp. are also greatly influenced by the serovars included, with some serovars being more resistant to certain antimicrobials or expressing multidrug resistance to a higher degree than other serovars. The serovar distribution within the *Salmonella* spp. varies by country depending on their frequency among human cases and/or specific sampling strategies for further typing and AST at the national public health reference laboratories.

Resistance levels in Salmonella spp. isolates from humans

The highest proportions of resistance in human *Salmonella* spp. isolates in 2014 were reported for tetracyclines (30.3%), sulfonamides/sulfamethoxazole (28.6%) and ampicillin (28.2%) (Table 8). These proportions were significantly lower than in 2013 (34.5%, 35.7% and 36.1%, respectively) which could be an effect of the countries that reported data for each year and the number of isolates tested by each country (e.g. Germany did not report in 2014 but accounted for a large proportion of isolates in 2013). In the case of ampicillin, 12 countries reported lower levels in 2014 compared to 2013, whereas six reported a higher proportion.

Resistance to the two clinically most important antimicrobial classes was reported in 8.8% of isolates for ciprofloxacin and in 1.1% and 1.2% for cefotaxime and ceftazidime, respectively. Ciprofloxacin resistance more than doubled compared to 2013 (when it was 3.8%) which most likely reflects the lowering of the CBP for *Salmonella* and ciprofloxacin in 2014 and the introduction of pefloxacin for screening of low-level fluoroquinolones with disk diffusion. The relatively high resistance to cefotaxime and ceftazidime in Italy (both at 10.8%) is most likely due to the circulation of a multiresistant clone of *S*. Infantis in 2014 (Ida Luzzi, Istituto Superiore di Sanità, personal communication, August 2015). No isolates were reported resistant to meropenem in 2014 (data not shown in Table 8). Resistance to colistin was detected in both countries reporting this antimicrobial, in 5.9% and 21.5% of isolates, respectively.

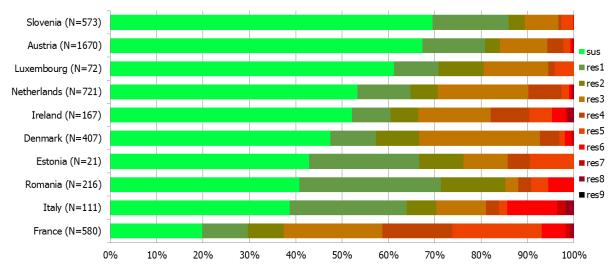
The resistance data for ciprofloxacin and trimethoprim–sulfamethoxazole for Malta are outliers at 50.0% and 80.3%, respectively. These data have been confirmed with the laboratory.



Multidrug resistance in Salmonella spp. isolates from humans

Ten MSs tested at least ten isolates for the nine antimicrobial classes included in the MDR analysis (meropenem new in the list for 2014). On average, 54.8% of *Salmonella* spp. isolates were susceptible to all nine antimicrobial classes, varying from 19.8% in France to 69.5% in Slovenia (Table <u>COMSALMHUM</u>). Few isolates exhibited 'microbiological' (0.6%) or 'clinical' (0.5%) coresistance to both ciprofloxacin and cefotaxime. Of the 21 isolates exhibiting clinical co-resistance, six were *S*. Typhimurium, five *S*. Infantis, four *S*. Schwarzengrund, three *S*. Stanley and the remaining three *S*. Kentucky, monophasic *S*. Typhimurium 1,4,[5],12:i:- and *S*. Uganda. The highest proportion of clinical co-resistance was observed in isolates from Ireland (3.6%), followed by Italy (1.8%) and Luxembourg (1.4%).

Multidrug resistance was high (26.0%) at the EU level, with the highest levels reported from France (62.6%). Of note, France only uses extended antibiograms with ceftazidime, cefotaxime and all betalactams for isolates resistant to ampicillin (Simon Le Hello, Institut Pasteur Paris, personal communication, November 2014). The proportions of isolates susceptible to all and resistant (or nonsusceptible) to up to nine antimicrobial classes are presented by MS in Figure 8. The proportions differed substantially between countries. Isolates resistant to five antimicrobials were reported from all ten MSs; six MSs (Austria, Denmark, France, Ireland, Italy and the Netherlands) reported a few isolates resistant to seven or eight antimicrobial classes included *S*. Typhimurium (seven isolates), monophasic *S*. Typhimurium (five), *S*. Schwarzengrund (four), *S*. Infantis (three), *S*. Kentucky (three), *S*. Brandenburg (two), *S*. Agona (two) and *S*. Corvallis (one). No isolates were reported resistant to all nine classes.



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

Figure 8: Frequency distribution of *Salmonella* spp. isolates from humans completely susceptible or resistant to one to eight antimicrobial classes in 2014



Country	Amp	icillin	Azithı	romycin	Cefot	axime	Cefta	zidime	Chloram	phenicol	Ciproflo	xacin ^(b)	Co	listin
	N	% Res	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res	Ν	% Res
Austria ^(a)	1,670	14.6	-	-	1,670	1.0	1,670	1.0	1,670	2.9	1,576	19.0	-	_
Belgium	871	39.8	_	_	871	1.1	_	_	871	7.5	871	2.6	_	_
Denmark ^(a)	407	39.8	407	1.7	407	1.0	407	0.5	407	3.9	407	5.7	407	5.9 ^(c)
Estonia ^(a)	21	38.1	_	_	21	0	21	0	21	9.5	21	14.3	_	_
Finland ^(a)	308	20.8	_	_	308	2.3	_	_	308	5.5	308	1.9	_	_
France	1,255	29.1	_	_	-	-	581	2.6	1254	9.3	1,255	12.7	_	_
Greece ^(a)	9	NA	_	_	9	NA	9	NA	9	NA	9	NA	_	_
Hungary	1,024	25.2	-	-	1,024	0.5	_	-	1,024	5.9	295	0.3	-	_
Ireland ^(a)	167	36.5	171	1.2	171	4.1	171	2.9	169	13.6	171	14.0	_	_
Italy ^(a)	111	30.6	_	_	111	10.8	111	10.8	111	8.1	111	4.5	_	_
Latvia	26	23.1	-	-	-	_	_	-	_	_	25	8.0	-	_
Lithuania	1,122	26.6	_	-	992	0.3	592	0.2	591	2.2	892	13.5	-	_
Luxembourg ^(a)	72	16.7	_	_	110	0.9	110	1.8	110	4.5	110	7.3	_	_
Malta	132	53.0	-	-	-	_	_	-	_	_	132	50.0	-	_
Netherlands ^(a)	721	32.2	721	0.6	721	0.8	721	0.3	721	4.7	721	9.2	721	21.5
Portugal ^(a)	140	55.0	-	-	140	0.7	-	-	140	12.1	140	0	-	_
Romania ^(a)	216	21.3	-	-	216	0	216	0	216	8.3	216	9.7	-	_
Slovakia	672	12.1	-	-	324	1.5	13	NA	13	30.8	427	1.2	-	_
Slovenia	591	11.8	_	_	591	0.2	580	0.7	591	3.0	589	8.8	_	_
Spain	1,715	46.2	_	_	1,714	1.3	-	-	1,714	7.8	1,714	1.2	_	_
United Kingdom	513	18.1	_	_	500	1.0	1	NA	517	4.6	540	5.0	_	_
Total (MS 21)	11,763	28.2	1,299	1.0	9,900	1.1	5,203	1.2	10,457	6.0	10,530	8.8	1,128	15.9
Norway ^(a)	342	28.4	_	_	342	0.9	342	0.3	141	10.6	342	3.2	-	_

Table 8: Antimicrobial resistance in *Salmonella* spp. (all non-typhoidal serovars) from humans per country in 2014

Country	Genta	micin	Nalidi	xic acid	Sulfameth	oxazole ^(d)	Tetracy	cline	Tigec	ycline	Trimet	hoprim	Co-trim	oxazole
-	N	% Res	Ν	% Res	N	% Res	N	% Res	N	% Res	Ν	% Res	Ν	% Res
Austria ^(a)	1,670	1.8	1,670	19.0	1,670	16.4	1,670	17.3	1670	1.2	1,670	3.5	_	_
Belgium	871	2.5	869	15.0	_	_	871	33.2	_	_	_	_	857	18.3
Denmark ^(a)	407	1.7	407	5.2	407	41.0	407	43.0	407	3.4	407	5.4	_	_
Estonia ^(a)	21	9.5	21	14.3	21	38.1	21	19.0	_	_	21	9.5	_	_
Finland ^(a)	308	2.9	308	10.7	308	23.7	308	19.5	_	_	308	3.6	_	_
France	1,255	8.8	1,256	30.0	1,255	38.5	1,256	40.0	_	_	1,254	14.4	532	17.5
Greece ^(a)	_	_	9	NA	_	_	9	NA	_	_	_	_	_	_
Hungary	1,024	0.4	295	37.3	_	_	1,024	34.4	_	_	1,024	3.4	1,012	3.3
Ireland ^(a)	171	5.3	170	10.6	171	39.8	168	32.7	171	2.3	169	12.4	_	_
Italy ^(a)	111	4.5	111	27.9	111	45.0	111	36.9	-	-	111	18.0	111	18.0
Latvia	_	_	_	_	_	_	_	-	_	_	_	_	25	8.0
Lithuania	506	1.4	456	20.0	_	_	483	16.4	_	_	485	3.7	1058	4.6
Luxembourg ^(a)	110	1.8	_	_	110	37.3	110	37.3	_	_	110	4.5	110	4.5
Malta	_	_	_	_	_	_	_	_	_	_	_	_	132	80.3
Netherlands ^(a)	721	1.5	721	7.4	721	34.1	721	33.8	721	3.1	721	9.4	_	_
Portugal ^(a)	140	2.9	140	10.0	_	_	139	54.0	_	_	_	_	139	5.0
Romania ^(a)	216	0.9	216	20.4	216	34.7	216	13.4	_	_	216	30.6	216	18.5
Slovakia	_	_	1	NA	1	NA	448	12.3	_	_	_	_	302	3.0
Slovenia	591	0.5	_	_	585	25.8	591	10.7	_	_	591	1.0	591	0.7
Spain	1,709	2.3	1,715	26.8	_	_	1,715	46.9	_	_	_	_	1,713	5.8
United Kingdom	521	2.9	517	16.6	510	21.0	499	21.0	_	_	536	7.8	37	10.8
Total (MS 21)	10,352	2.7	8,882	20.1	6,086	28.6	10,767	30.3	2,969	2.0	7,623	7.3	6,835	9.2
Norway ^(a)	342	3.8	141	12.8	_	_	141	53.9	_	_	_	_	342	3.8

Note: All *Salmonella* isolates tested were susceptible to meropenem.

N: number of isolates tested; % Res: percentage of microbiologically 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, the percentage of resistance was not calculated; MS: Member State.

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

(b): Ciprofloxacin has in several countries been replaced by pefloxacin for screening of fluoroquinolone resistance with disk diffusion, as recommended by EUCAST.

(c): Preliminary data to be confirmed.

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



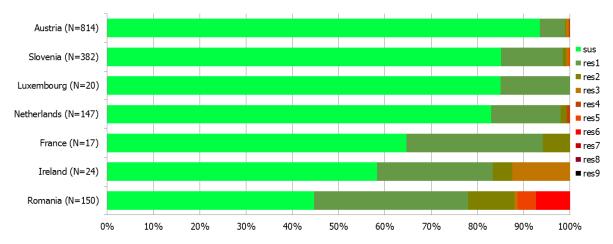
Antimicrobial resistance in *Salmonella* Enteritidis in humans

Resistance levels in S. Enteritidis isolates from humans

As in previous years, S. Enteritidis was the most common Salmonella serovar identified in 2014, with 33,965 cases reported in the EU/EEA. The highest proportion of resistance among human S. Enteritidis isolates was observed for nalidixic acid (24.5%) with the highest country-specific proportions observed in Spain (62.0%) and Portugal (47.6%) (21 MSs, Table 9). Ciprofloxacin resistance was observed in 6.0% of isolates, with Malta and Ireland reporting the highest level of ciprofloxacin resistance (58.8% and 29.2%, respectively), although the number of isolates tested were low. It is generally expected that there should be a correlation between the activity of nalidixic acid and ciprofloxacin against Salmonella. Some countries reported moderate to very high resistance levels in nalidixic acid, including Spain and Portugal, but reported much lower levels of ciprofloxacin resistance. Some of these differences could be due to the poor detection of low-level fluoroguinolone resistance with ciprofloxacin when using disk diffusion, and this is why EUCAST, since 2014, recommends testing of pefloxacin instead. Resistance to cefotaxime or ceftazidime was generally not detected or detected at low levels in S. Enteritidis. Only two countries reported data on colistin and among these, the resistance was very high, 67.5%. The very high resistance could be due to inherent resistance to colistin being common among certain Salmonella serovars, e.g. S. Dublin and S. Enteritidis, which share the same somatic antigens (0:1,9,12) (Agersø et al, 2012) whereas the ECOFF is not serovar-specific.

Multidrug resistance in S. Enteritidis isolates from humans

Most (84.7%) of the *S*. Enteritidis isolates from humans were susceptible to all nine antimicrobial classes included in the MDR analysis (7 MSs, N=1,554) (Figure 9, Table <u>COMENTERHUM</u>). MDR was detected in 2.1% of isolates (country average 3.8%) with the highest proportions reported in isolates from Ireland (12.5%) and Romania (12.0%), although the number of isolates tested in Ireland was low. No co-resistance to ciprofloxacin and cefotaxime was detected in any MS.



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

Figure 9: Frequency distribution of *Salmonella* Enteritidis isolates from humans completely susceptible or resistant to one to nine antimicrobial classes in 2014

Country	Am	bicillin	Azithro	omycin	Cefo	taxime	Cefta	zidime	Chloran	nphenicol	Ciprof	oxacin ^(b)	Coli	stin
-	N	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ň	% Res	Ν	% Res
Austria ^(a)	814	1.5	_	_	814	0.2	814	0.2	814	0.2	783	4.6	_	_
Belgium	236	6.8	_	_	236	1.3	_	_	236	1.3	236	0.8	_	_
Denmark ^(a)	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA
Estonia ^(a)	6	NA	_	_	6	NA	6	NA	6	NA	6	NA	_	_
Finland ^(a)	49	8.2	_	_	49	0	_	_	49	2.0	49	2.0	_	_
France	130	0.8	_	_	_	_	17	0	130	0	130	0.8	_	_
Greece ^(a)	2	NA	_	-	2	NA	2	NA	2	NA	2	NA	_	_
Hungary	386	1.6	_	_	386	0	_	_	386	0.5	12	0	_	_
Ireland ^(a)	24	20.8	24	0	24	0	24	0	24	0	24	29.2	_	_
Italy ^(a)	2	NA	_	-	2	NA	2	NA	2	NA	2	NA	_	_
Latvia	16	0	_	_	_	_	_	_	_	_	15	0	_	_
Lithuania	883	20.2	_	-	786	0.4	453	0	450	0.9	699	13.9	_	_
Luxembourg ^(a)	20	0	_	_	25	0	25	0	25	4.0	25	8.0	_	_
Malta	34	29.4	_	_	_	_	_	_	_	_	34	58.8	_	_
Netherlands ^(a)	147	4.8	147	0.7	147	0	147	0	147	0	147	14.3	147	68.0
Portugal ^(a)	21	4.8	_	-	21	0	_	_	21	0	21	0	_	-
Romania ^(a)	150	14.7	_	_	150	0	150	0	150	10.7	150	8.7	_	_
Slovakia	508	4.7	_	_	249	1.2	8	NA	3	NA	320	0.9	_	_
Slovenia	389	0.8	_	-	389	0	384	0.5	389	0	389	2.3	_	_
Spain	542	3.7	_	_	542	0.4	_	_	542	0.7	542	0.2	_	_
United Kingdom	159	5.0	_	_	158	0	1	NA	159	0.6	162	3.7	_	_
Total (MS 21)	4,522	7.0	175	0.6	3,990	0.3	2037	0.2	3539	1.0	3,752	6.0	151	67.5
Norway ^(a)	74	4.1	_	_	74	0	74	0	16	0	74	2.7	_	_

Table 9: Antimicrobial resistance in Salmonella Enteritidis from humans per country in 2014



Country	Gent	tamicin	Nalidi	xic acid	Sulfamet	hoxazole ^(c)	Tetra	acycline	Tige	ecycline	Trime	thoprim	Co-trin	noxazole
	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	N	% Res	Ν	% Res	N	% Res
Austria ^(a)	814	0.1	814	5.2	814	0.2	814	0.7	814	0.1	814	0.4	_	_
Belgium	236	0.4	234	18.8	_	_	236	1.7	_	_	_	_	231	0.9
Denmark ^(a)	4	NA	4	NA	4	NA	4	NA	4	NA	4	NA	_	_
Estonia ^(a)	6	NA	6	NA	6	NA	6	NA	_	_	6	NA	_	_
Finland ^(a)	49	0	49	30.6	49	2.0	49	4.1	_	_	49	2	_	_
France	130	0	130	22.3	130	4.6	130	3.8	_	_	130	0	16	0
Greece ^(a)	_	_	2	NA	_	_	2	NA	-	_	_	_	_	_
Hungary	386	0	12	0	_	_	386	0.8	_	_	386	0.3	375	0.3
Ireland ^(a)	24	0	24	29.2	24	8.3	24	4.2	24	4.2	24	8.3	-	-
Italy ^(a)	2	NA	2	NA	2	NA	2	NA	-	-	2	NA	2	NA
Latvia	_	_	_	_	_	_	_	_	_	_	_	_	15	0
Lithuania	374	0.5	337	20.5	_	_	361	5.8	_	_	359	0.6	840	1.9
Luxembourg ^(a)	25	0	_	_	25	12.0	25	8.0	_	_	25	0	25	0
Malta	_	_	_	_	_	_	_	_	_	_	_	_	34	64.7
Netherlands ^(a)	147	0	147	13.6	147	0.7	147	0.7	147	0.7	147	0	-	-
Portugal ^(a)	21	0	21	47.6	_	_	21	0	_	_	_	_	21	0
Romania ^(a)	150	0	150	22.0	150	34.7	150	11.3	_	_	150	26.0	150	16.7
Slovakia	_	_	1	NA	_	_	349	3.7	_	_	-	-	213	1.4
Slovenia	389	0	_	_	386	12.7	389	1.0	_	_	389	0.3	389	0.3
Spain	542	0.4	542	62.0	_	_	542	2.0	_	_	_	_	542	0.4
United Kingdom	159	0.6	158	21.5	158	2.5	157	2.5	_	_	162	1.2	5	NA
Total (MS 21)	3,458	0.2	2,633	24.5	1,895	6.4	3,794	2.5	989	0.3	2,647	1.9	2,858	2.5
Norway ^(a)	74	0	16	12.5	_	_	16	0	_	_	_	_	74	0

Note: All Salmonella isolates tested were susceptible to meropenem.

N: number of isolates tested; % Res: percentage of microbiologically 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 10 isolates were tested, the percentage of resistance was not calculated; MS: Member State.

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

(b): Ciprofloxacin has in several countries been replaced by pefloxacin for screening of fluoroquinolone resistance with disk diffusion, as recommended by EUCAST.

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



Spatial distribution of resistance among S. Enteritidis *isolates from human cases*

Ciprofloxacin resistance in *S.* Enteritidis isolates from human cases (Figure 10) did not show a clear spatial pattern. Malta and Ireland reported the highest levels of resistance, followed by the Netherlands and Lithuania. As expected, resistance levels to nalidixic acid were generally higher than those to ciprofloxacin, but they were significantly higher in some countries and the highest in Spain and Portugal (Figure 11) whereas those countries reported very low proportions or no resistance levels were generally low and did not show a spatial pattern, although only few countries reported data for at least 10 isolates (Figure 12).

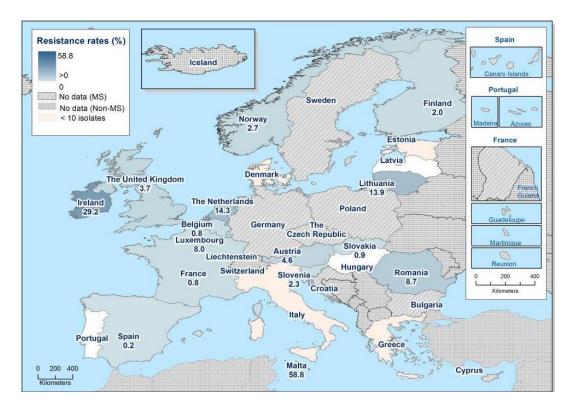


Figure 10: Spatial distribution of ciprofloxacin resistance among *S*. Enteritidis from human cases in reporting countries in 2014





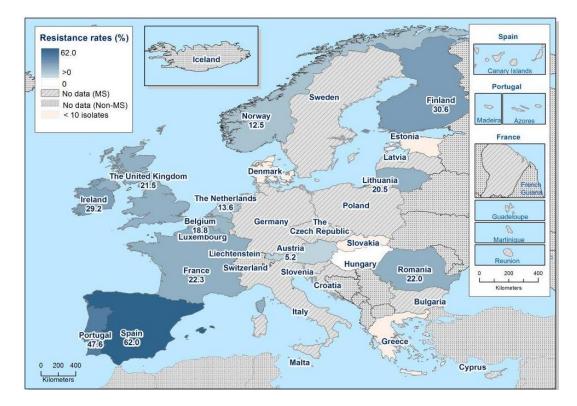


Figure 11: Spatial distribution of nalidixic acid resistance among *S.* Enteritidis from human cases in reporting countries in 2014

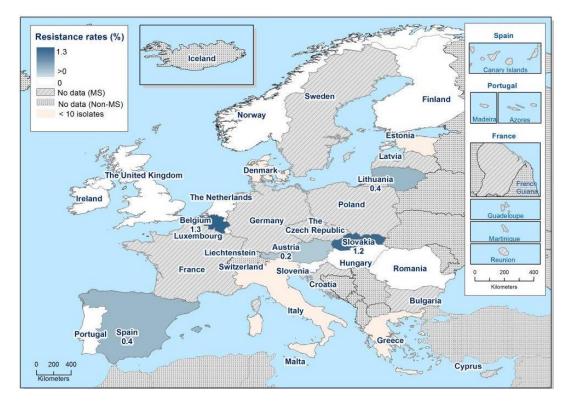


Figure 12: Spatial distribution of cefotaxime resistance among *S.* Enteritidis from human cases in reporting countries in 2014



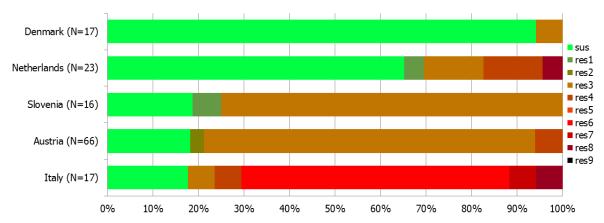
Antimicrobial resistance in Salmonella Infantis in humans

Resistance levels in S. Infantis isolates from humans

S. Infantis was the fourth most common serovar in 2014 with 1,846 cases reported by the EU/EEA countries. The highest resistance levels were observed for tetracylines (48.3%), nalidixic acid (44.0%) and sulfonamides (42.0%) (20 MSs, Figure 13) but levels varied markedly between countries. The proportion of isolates resistant to the two clinically most important antimicrobials was on average 16.4% for ciprofloxacin and 5.4% for cefotaxime, which was markedly higher than for all *Salmonella* spp. (8.8% and 1.1%, respectively). Ciprofloxacin resistance levels were particularly high in Slovenia (81.3%) and Austria (75.0%), and cefotaxime and ceftazidime in Italy (64.7% and 64.7%, respectively), although the number of isolates tested in Slovenia and Italy was low. In 2014 and continuing in 2015, Italy had circulation of a multiresistant and ESBL-producing (CTX-M type) clone of *S*. Infantis (Ida Luzzi, Istituto Superiore di Sanità, personal communication, August 2015).

Multidrug resistance in S. Infantis isolates from humans

MDR was detected in 61.9% (5 MSs, N=139) of human *S*. Infantis cases (country average 54.5%) (Figure 13, Table <u>COMINFANHUM</u>). 'Microbiological' as well as 'clinical' co-resistance to ciprofloxacin and cefotaxime were reported in 2.2% of isolates with a high proportion reported from Italy (11.8%, N=17).



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

Figure 13: Frequency distribution of *Salmonella* Infantis isolates from humans completely susceptible or resistant to one to nine antimicrobial classes in 2014

Country	Am	picillin	Azithro	omycin	Cefot	axime	Ceftaz	idime	Chloram	ohenicol	Ciproflo	xacin ^(b)	Colis	stin
-	Ν	% Res	Ν	% Res	Ν	% Res	N	% Res	N	% Res	N	% Res	Ν	% Res
Austria ^(a)	66	4.5	_	_	66	1.5	66	1.5	66	0	64	75.0	_	_
Belgium	51	13.7	_	_	51	9.8	_	_	51	9.8	51	0	_	_
Denmark ^(a)	17	0	17	0	17	0	17	0	17	0	17	0	17	0 ^(c)
Estonia ^(a)	2	NA	_	_	2	NA	2	NA	2	NA	2	NA	_	_
Finland ^(a)	9	NA	_	_	9	NA	_	_	9	NA	9	NA	_	_
France	120	2.5	_	_	-	-	2	NA	120	3.3	120	0.8	_	_
Greece ^(a)	1	NA	_	_	1	NA	1	NA	1	NA	1	NA	_	_
Hungary	190	6.3	_	_	190	1.1	_	_	190	2.6	100	1	_	_
Ireland ^(a)	6	NA	6	0	6	NA	6	NA	6	NA	6	NA	_	_
Italy ^(a)	17	70.6	_	_	17	64.7	17	64.7	17	17.6	17	11.8	_	_
Lithuania	13	7.7	_	_	11	0	11	0	11	0	13	0	_	_
Luxembourg ^(a)	1	NA	_	_	2	NA	2	NA	2	NA	2	NA	_	_
Malta	10	30.0	_	_	_	_	_	_	_	_	10	60	_	_
Netherlands ^(a)	23	13.0	23	0	23	4.3	23	4.3	23	8.7	23	21.7	23	0
Portugal ^(a)	1	NA	_	_	1	NA	-	-	1	NA	1	NA	_	_
Romania ^(a)	6	NA	_	_	6	NA	6	NA	6	NA	6	NA	_	_
Slovakia	35	22.9	_	_	13	7.7	_	_	2	NA	23	8.7	_	_
Slovenia	16	0	_	_	16	0	16	0	16	0	16	81.3	_	_
Spain	31	12.9	-	_	31	6.5	_	_	31	9.7	31	0	_	_
United Kingdom	16	37.5	_	_	16	6.3	_	_	18	16.7	18	11.1	_	_
Total (MS 20)	631	10.3	46	0	478	5.4	169	8.9	589	4.4	530	16.4	40	0
Norway ^(a)	2	NA	-	_	2	NA	2	NA	_	_	2	NA	_	_

Table 10: Antimicrobial resistance in Salmonella Infantis from humans per country in 2014

Country	Genta	amicin	Nalidi	xic acid	Sulfametho	xazole ^(d)	Tetra	cycline	Tigec	cline	Trimet	hoprim	Co-trin	noxazole
-	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res
Austria ^(a)	66	0	66	75.8	66	80.3	66	77.3	66	21.2	66	9.1	_	_
Belgium	51	9.8	51	25.5	_	_	51	41.2	_	_	_	_	50	34.0
Denmark ^(a)	17	0	17	0	17	5.9	17	5.9	17	0	17	5.9	-	_
Estonia ^(a)	2	NA	2	NA	2	NA	2	NA	_	_	2	NA	_	_
Finland ^(a)	9	NA	9	NA	9	NA	9	NA	_	_	9	NA	_	_
France	120	0	120	14.2	120	15.8	120	15.0	_	_	119	4.2	1	NA
Greece ^(a)	-	-	1	NA	_	_	1	NA	_	_	_	_	_	_
Hungary	190	0	100	84.0	_	_	190	71.1	_	_	190	1.6	190	1.6
Ireland ^(a)	6	NA	6	NA	6	NA	6	66.7	6	NA	6	NA	-	_
Italy ^(a)	17	5.9	17	82.4	17	82.4	17	82.4	_	_	17	76.5	17	76.5
Lithuania	11	0	9	NA	_	_	11	9.1	_	_	11	9.1	13	15.4
Luxembourg ^(a)	2	NA	_	_	2	NA	2	NA	_	_	2	NA	2	NA
Malta	_	_	_	_	_	-	-	_	_	_	-	_	10	70.0
Netherlands ^(a)	23	4.3	23	21.7	23	30.4	23	21.7	23	4.3	23	26.1	_	_
Portugal ^(a)	1	NA	1	NA	_	_	1	NA	_	_	_	_	1	NA
Romania ^(a)	6	NA	6	NA	6	NA	6	NA	_	_	6	NA	6	NA
Slovakia	_	_	_	_	_	_	21	38.1	_	_	_	_	21	4.8
Slovenia	16	0	_	-	16	75.0	16	75.0	-	-	16	0	16	0
Spain	31	6.5	31	22.6	_	-	31	19.4	_	_	-	_	31	9.7
United Kingdom	18	0	18	61.1	16	50.0	16	62.5	_	-	18	27.8	2	NA
Total (MS 20)	586	1.7	477	44.0	300	42.0	606	48.3	112	13.4	502	10.2	360	14.4
Norway ^(a)	2	NA	_	-	_	_	-	_	_	-	-	_	2	NA

Note: All *Salmonella* isolates tested were susceptible to meropenem.

N: number of isolates tested; % Res: percentage of microbiologically 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 10 isolates were tested, the percentage of resistance was not calculated; MS: Member State.

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

(b): Ciprofloxacin has in several countries been replaced by pefloxacin for screening of fluoroquinolone resistance with disk diffusion, as recommended by EUCAST.

(c): Preliminary data to be confirmed.

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



Spatial distribution of resistance among S. Infantis isolates from human cases

Ciprofloxacin resistance in *S.* Infantis isolates from human cases (Figure 14) was the highest in two countries in Central Europe, Austria and Slovenia, and in Malta. A similar pattern was observed for nalidixic acid resistance (Figure 15), now also including Hungary, Italy and the United Kingdom. The large discrepancy between nalidixic acid and ciprofloxacin resistance levels could be due to methodological issues, see discussion. Extremely high cefotaxime resistance levels were observed in *S.* Infantis in Italy whereas other countries reported relatively low resistance levels (Figure 16).

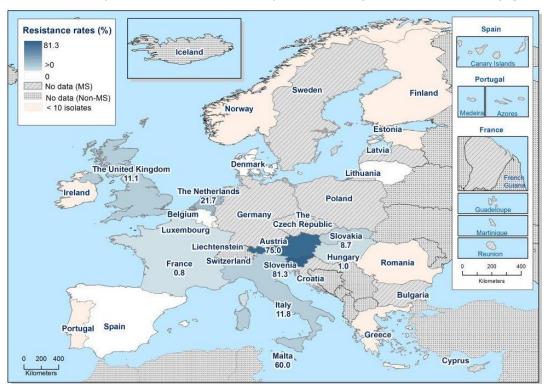


Figure 14: Spatial distribution of ciprofloxacin resistance among *S.* Infantis from human cases in reporting countries in 2014



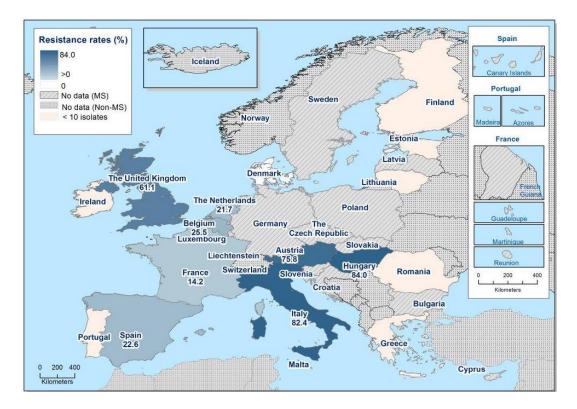


Figure 15: Spatial distribution of nalidixic acid resistance among *S.* Infantis from human cases in reporting countries in 2014

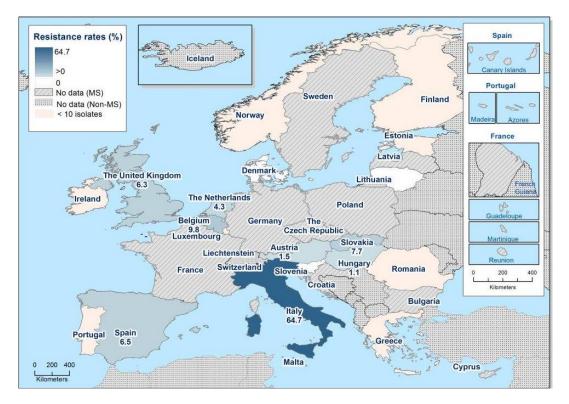


Figure 16: Spatial distribution of cefotaxime resistance among *S.* Infantis from human cases in reporting countries in 2014



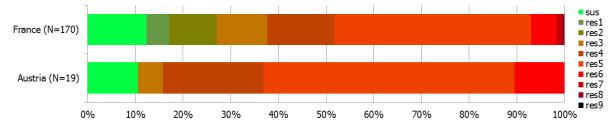
Antimicrobial resistance in Salmonella Kentucky in humans

Resistance levels in S. Kentucky isolates from humans

S. Kentucky was the eighth most common serovar in 2014 with 606 cases reported by the EU/EEA countries. France accounted for 66% of the *S*. Kentucky isolates with AST data (all human *S*. Kentucky isolates in France 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. This is consistent with the dissemination of the ciprofloxacin-resistant *S*. Kentucky ST198 strain in Europe, and elsewhere, since 2010 (Le Hello et al., 2013a). Cefotaxime and ceftazidime resistance levels were also higher (7.4% and 2.9%, respectively) than in other serovars.

Multidrug resistance in S. Kentucky isolates from humans

Multidrug resistance was very high (74.6%, N=189) (Table 11, Table <u>COMKENTHUM</u>) in the two MSs that reported data on at least 10 isolates, 49.7% of the isolates exhibited penta-resistance and three isolates were resistant to seven or eight antimicrobial classes. One isolates from Austria expressed 'microbiological' and 'clinical' co-resistance to ciprofloxacin and cefotaxime, and three isolates from France to ciprofloxacin and ceftazidime (cefotaxime was not tested).



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

Figure 17: Frequency distribution of *Salmonella* Kentucky isolates from humans completely susceptible or resistant to one to nine antimicrobial classes in 2014

Antimicrobial resistance in *Salmonella* Derby in humans

S. Derby was the seventh most common serovar in 2014 with 755 cases reported by the EU/EEA countries. Resistance to sulfonamides and tetracycline was relatively common in *S*. Derby (45.5% and 40.8%, respectively) (16 MSs, Table 12). The levels were influenced by the very high resistance levels reported in France, however, as France accounted for 40% of tested isolates, most likely reflecting the targeted testing of this serovar.

The proportion of isolates resistant to the two clinically most important antimicrobials was on average 1.7% for ciprofloxacin and 1.0% for cefotaxime. Multi-drug resistance was low (4.3%) in the two MSs that reported data on at least 10 isolates and no isolates were co-resistant to ciprofloxacin and cefotaxime (Table <u>COMDERBYHUM</u>).

Country	Am	picillin	Azithr	omycin	Cefota	ixime	Ceftaz	zidime	Chloramp	henicol	Ciproflox	kacin ^(b)	Со	listin
	N	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res
Austria ^(a)	19	78.9	_	_	19	5.3	19	5.3	19	5.3	19	89.5	_	_
Belgium	17	82.4	_	_	17	0	_	_	17	11.8	17	94.1	_	_
Denmark ^(a)	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA
Finland ^(a)	5	NA	_	_	5	NA	_	_	5	NA	5	NA	_	_
France	170	70.0	_	_	-	-	170	2.4	171	7.6	171	82.5	_	_
Ireland ^(a)	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	_	_
Italy ^(a)	1	NA	_	_	1	NA	1	NA	1	NA	1	NA	_	-
Lithuania	2	NA	_	_	2	NA	2	NA	2	NA	2	NA	_	_
Malta	5	NA	_	_	-	-	_	_	_	_	5	NA	_	_
Netherlands ^(a)	3	NA	3	NA	3	NA	3	NA	3	NA	3	NA	3	NA
Portugal ^(a)	1	NA	_	_	1	NA	_	_	1	NA	1	NA	_	_
Romania ^(a)	1	NA	_	_	1	NA	1	NA	1	NA	1	NA	_	_
Slovakia	1	NA	_	_	_	_	_	_	_	_	_	_	_	_
Slovenia	2	NA	_	_	2	NA	2	NA	2	NA	2	NA	_	_
Spain	16	68.8	_	_	16	12.5	_	_	15	13.3	15	80.0	_	_
United Kingdom	8	NA	_	_	8	NA	_	_	8	NA	8	NA	_	-
Total (MSs 16)	257	71.2	9	NA	81	7.4	204	2.9	251	8.0	256	84.0	8	NA
Norway ^(a)	5	NA	_	_	5	NA	5	NA	_	_	5	NA	_	_

Table 11: Antimicrobial resistance in Salmonella Kentucky from humans per country in 2014

Country	Genta	micin	Nalidix	ic acid	Sulfamet	noxazole ^(c)	Tetrac	cline	Tigec	ycline	Trimet	hoprim	Co-trim	oxazole
-	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res
Austria ^(a)	19	63.2	19	89.5	19	89.5	19	89.5	19	5.3	19	5.3	-	_
Belgium	17	58.8	17	100	_	_	17	94.1	_	_	_	_	17	11.8
Denmark ^(a)	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	-	_
Finland ^(a)	5	NA	5	NA	5	NA	5	NA	_	_	5	NA	_	_
France	171	50.9	171	85.4	171	64.3	171	74.9	_	_	171	8.8	171	8.2
Ireland ^(a)	1	NA	1	NA	1	NA	1	NA	1	NA	1	NA	-	-
Italy ^(a)	1	NA	1	NA	1	NA	1	NA	_	_	1	NA	1	NA
Lithuania	2	NA	2	NA	_	_	2	NA	_	_	2	NA	2	NA
Malta	_	_	_	-	_	_	_	_	_	_	_	-	5	NA
Netherlands ^(a)	3	NA	3	NA	3	NA	3	NA	3	NA	3	NA	_	_
Portugal ^(a)	1	NA	1	NA	-	-	1	NA	_	_	_	_	1	NA
Romania ^(a)	1	NA	1	NA	1	NA	1	NA	_	_	1	NA	1	NA
Slovakia	_	_	_	-	_	_	1	NA	_	_	_	-	-	_
Slovenia	2	NA	_	-	2	NA	2	NA	_	_	2	NA	2	NA
Spain	14	50.0	16	87.5	_	_	16	43.8	_	_	_	_	15	0
United Kingdom	8	NA	8	NA	8	NA	8	NA	_	_	8	NA	_	_
Total (MSs 16)	250	53.6	250	86.8	216	68.5	253	75.1	28	3.6	218	9.2	215	10.2
Norway ^(a)	5	NA	_	_	_	-	_	-	_	_	_	_	5	NA

All Salmonella isolates tested were susceptible to meropenem

N: number of isolates tested; % Res: percentage of microbiologically 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 10 isolates were tested, the percentage of resistance was not calculated; MS: Member State.

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

(b): Ciprofloxacin has in several countries been replaced by pefloxacin for screening of fluoroquinolone resistance with disk diffusion, as recommended by EUCAST.

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

Country	Amp	bicillin	Azithro	mycin	Cefot	axime	Ceftaz	idime	Chloram	ohenicol	Ciproflo	xacin ^(b)	Со	listin
	N	% Res	Ν	% Res	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res
Austria ^(a)	10	0	-	_	10	0	10	0	10	10.0	9	NA	-	_
Belgium	32	12.5	_	_	32	0	_	_	32	3.1	32	0	_	_
Denmark ^(a)	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA
France	71	2.8	_	_	_	_	4	NA	71	4.2	71	0	_	_
Italy ^(a)	1	NA	_	_	1	NA	1	NA	1	NA	1	NA	_	_
Latvia	1	NA	_	_	_	_	_	_	_	_	1	NA	_	_
Lithuania	10	0	_	_	10	0	9	NA	10	0	10	10	_	_
Luxembourg ^(a)	1	NA	_	_	2	NA	2	NA	2	NA	2	NA	_	_
Malta	1	NA	_	_	_	-	_	-	_	_	1	NA	_	_
Netherlands ^(a)	14	14.3	14	0	14	7.1	14	7.1	14	0	14	0	14	14.3
Portugal ^(a)	2	NA	_	_	2	NA	_	_	2	NA	2	NA	_	_
Romania ^(a)	2	NA	_	_	2	NA	2	NA	2	NA	2	NA	_	_
Slovakia	2	NA	_	_	2	NA	_	_	_	_	_	_	_	_
Slovenia	3	NA	_	_	3	NA	3	NA	3	NA	2	NA	_	_
Spain	18	5.6	_	_	18	0	_	_	18	0	18	0	_	_
United Kingdom	4	NA	_	_	4	NA	_	_	4	NA	4	NA	_	_
Total (MSs 16)	177	5.6	19	0	105	1.0	50	2.0	174	3.4	174	1.7	19	10.5

Table 12: Antimicrobial resistance in Salmonella Derby from humans per country in 2014

Country	Genta	micin	Nalidix	kic acid	Sulfamet	hoxazole ^(c)	Tetrac	ycline	Tigec	ycline	Trime	ethoprim	Co-trim	oxazole
	N	% Res	Ν	% Res	N	% Res	Ν	% Res	N	% Res	Ν	% Res	N	% Res
Austria ^(a)	10	0	10	20.0	10	20.0	10	10.0	10	0	10	0	-	_
Belgium	32	0	32	0	_	-	32	21.9	_	_	-	_	30	26.7
Denmark ^(a)	5	NA	5	NA	5	NA	5	NA	5	NA	5	NA	-	_
France	71	0	71	0	71	60.6	71	63.4	_	_	70	4.3	2	NA
Italy ^(a)	1	NA	1	NA	1	NA	1	NA	_	_	1	NA	1	NA
Latvia	_	_	_	_	_	-	_	_	_	_	-	_	1	NA
Lithuania	10	0	9	NA	_	_	10	0	_	_	9	NA	7	NA
Luxembourg ^(a)	2	NA	_	_	2	NA	2	NA	_	_	2	NA	2	NA
Malta	_	_	_	_	_	_	_	_	_	_	-	_	1	NA
Netherlands ^(a)	14	0	14	0	14	21.4	14	14.3	14	0	14	21.4	_	_
Portugal ^(a)	2	NA	2	NA	_	_	2	NA	_	_	-	-	2	NA
Romania ^(a)	2	NA	2	NA	2	NA	2	NA	_	_	2	NA	2	NA
Slovakia	_	_	_	_	_	_	_	_	_	_	-	_	1	NA
Slovenia	3	NA	_	_	3	NA	3	NA	_	_	3	NA	3	NA
Spain	18	0	18	5.6	_	_	18	50.0	_	_	-	_	18	11.1
United Kingdom	4	NA	4	NA	4	NA	4	NA	_	_	4	NA	-	_
Total (MSs 16)	174	0	168	1.8	112	45.5	174	40.8	29	0	120	5.8	70	17.1

All Salmonella isolates tested were susceptible to meropenem

N: number of isolates tested; % Res: percentage of microbiologically 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 10 isolates were tested, the percentage of resistance was not calculated; MS: Member State.

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

(b): Ciprofloxacin has in several countries been replaced by pefloxacin for screening of fluoroquinolone resistance with disk diffusion, as recommended by EUCAST.

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



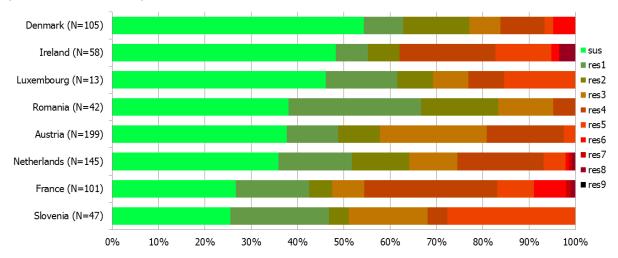
Antimicrobial resistance in *Salmonella* Typhimurium in humans

Resistance levels in S. Typhimurium isolates from humans

As in previous years, *S*. Typhimurium was the second most common *Salmonella* serovar identified in 2014, with 14,284 cases reported in the EU/EEA (monophasic S. Typhimurium 1,4,[5],12:i:-excluded). The highest proportion of resistance in *S*. Typhimurium was observed for ampicillin (52.8%), sulfonamides (46.2%) and tetracyclines (43.5%) (21 MSs, Table <u>TYPHIHUMD</u>). The proportions of resistance to these antimicrobials were high to extremely high in all reporting MSs, except in Finland and Romania where moderate resistance to both ampicillin and tetracyclines, and moderate resistance to tetracyclines were observed, respectively. The proportions of isolates resistant to the two clinically most critical antimicrobials were on average 4.3% for ciprofloxacin and 1.2% for cefotaxime. The highest proportion of isolates resistant to ciprofloxacin was reported from Slovenia (32.7%), whereas the highest proportion of cefotaxime resistance was reported from Ireland (8.5%).

Multidrug resistance in S. Typhimurium isolates from humans

In humans, 32.5% (8 MSs, N=710) of the *S*. Typhimurium isolates were multiresistant (Figure 18). 'Microbiological' and 'clinical' co-resistance to ciprofloxacin and cefotaxime were reported in 1.3% and 0.8% of isolates with the highest proportions reported from Ireland (8.6% for both types, N=58) (Table <u>COMTYPHIHUM</u>).



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

Figure 18: Frequency distribution of *Salmonella* Typhimurium isolates from humans completely susceptible or resistant to one to nine antimicrobial classes in 2014

Antimicrobial resistance in monophasic Salmonella Typhimurium in humans

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

For the purpose of this report, monophasic *S*. Typhimurium 1,4,[5],12:i:- is treated as a separate serovar, and as such, it is currently the third most common serovar in Europe. In 2014, 5,851 cases were reported by the EU/EEA countries. Extremely high levels of resistance were observed for tetracyclines (85.3%), ampicillin (83.8%) and sulfonamides (75.8%) in monophasic S. Typhimurium 1,4,[5],12:i:- (10 MSs, Table <u>MONTYPHIHUMD</u>). The resistance pattern, ASuT¹⁴, is a well-known characteristic of monophasic S. Typhimurium 1,4,[5],12:i:- and was observed at similar levels in all reporting MSs with the exception of Italy which reported lower levels to all three antimicrobials and Luxembourg which did so for ampicillin. The proportion of isolates resistant to the two clinically most

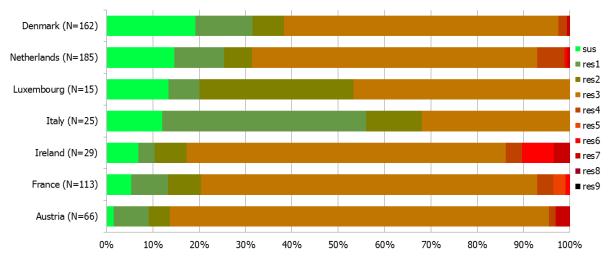
¹⁴ This pattern of MDR (resistance to ampicillin, sulfonamide and tetracycline) typically also includes resistance to streptomycin; however, as described in the Materials and methods section, data on this antimicrobial are no longer included in this report.



important antimicrobials was 1.1% for ciprofloxacin and 0.8% for cefotaxime, with the highest levels of ciprofloxacin resistance in Ireland (9.4%) and of cefotaxime resistance in Austria (1.5%) and Spain (1.3%).

Multidrug resistance in monophasic S. *Typhimurium 1,4,[5],12:i:- isolates from humans*

In humans, 69.4% (7 MSs, N=595) of the monophasic *S*. Typhimurium isolates were multiresistant (Figure 19). 'Microbiological' and 'clinical' co-resistance to ciprofloxacin and cefotaxime were only reported in one isolate from Denmark, resulting in 0.2% co-resistance among the seven reporting MSs (Table <u>COMMONTYPHIHUM</u>).



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

Figure 19: Frequency distribution of monophasic *Salmonella* Typhimurium 1,4,[5],12:i:- isolates from humans completely susceptible or resistant to one to eight antimicrobial classes in 2014

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

Based on the legislative requirements, the active AMR resistance in *Salmonella* isolates from broilers and laying hens of *Gallus gallus*, fattening turkeys and from meat derived thereof was mandatory in 2014. *Salmonella* isolates from *Gallus gallus* and turkeys were primarily obtained from faecal samples and/or environmental samples (boot swabs or dust) collected on farms, as part of *Salmonella* National Control Programmes (NCPs) carried out according to the EU legislation. Clinical investigations and follow-up sampling of flocks tested positive for *Salmonella* were excluded from the analyses. *Salmonella* isolates from meat were obtained from randomly collected neck skin samples collected within the framework of either official sampling or hazard analysis and critical point control (HACCP) and own-check programmes at slaughterhouses.

Salmonella spp. includes results for all *Salmonella* serovars reported for different animal populations or food categories. As the potential for acquiring AMR markedly varies between serovars, the relative contribution of different serovars may significantly influence 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 and results are presented for selected serovars of importance.

Antimicrobial resistance in *Salmonella* in meat from broilers

Resistance levels in Salmonella spp. isolates from broiler meat

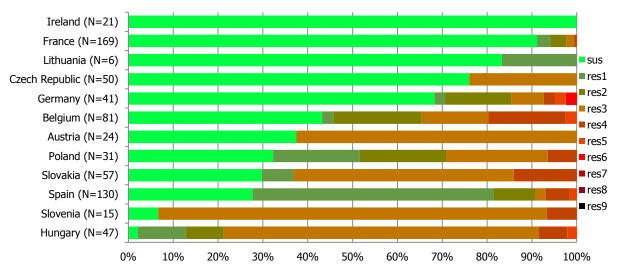
In 2014, 11 MSs reported data on more than 10 isolates of *Salmonella* spp. from broiler meat according to the provisions of Decision 2013/652/EU (Table 13). The reported levels of resistance to



ciprofloxacin, nalidixic acid, sulfamethoxazole and tetracycline ranged from low to extremely high (1.2-97.9%) in *Salmonella* spp. from broiler meat in most of the reporting MSs, whereas no resistance was recorded in Ireland. Resistance to ampicillin was generally low to moderate in most reporting MSs (4.3-14.0%), although high levels were also observed in two MSs and three MSs did not register any resistance. Overall resistance to gentamicin (0.7%) and chloramphenicol (2.2%) remained at low levels. Resistance was not detected or low levels of resistance to azithromycin, colistin and tigecycline were reported by most MSs (0-27.7%). 'Microbiological' resistance to cefotaxime and ceftazidime was recorded by only two MSs at very low or low levels.

Multidrug resistance in Salmonella spp. isolates from broiler meat

Thirteen MSs reported data on at least 10 isolates, which were addressed in the MDR analysis (N=597). From 0% to 93.3% of the *Salmonella* spp. isolates were multiresistant, whereas the proportion of fully susceptible isolates varied from 2.1% to 100% (Figure 20). 'Microbiological' and 'clinical' co-resistance to ciprofloxacin and cefotaxime was not observed in any MSs (Table <u>COMPSALMBRMEAT</u>).



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

Resistance levels in certain Salmonella serovars from broiler meat

Among the isolates for which serovar information was provided (N=1,082), the most common serovars detected in broiler meat (Table <u>SERBRMEAT</u>) were *S*. Infantis (16 MSs, 36.8%), *S*. Indiana (five MSs, 10.6%) and *S*. Enteritidis (11 MSs, 9.8%). Resistance and MDR levels in *S*. Enteritidis were generally lower than those recorded in *S*. Infantis and *Salmonella* spp. Overall high level of resistance (31.6%) to colistin was registered in *S*. Enteritidis, whereas no resistance was recorded in *S*. Infantis.

In *S.* Enteritidis isolates from broiler meat (six MSs, N=76), resistance to chloramphenicol, gentamicin, tetracycline and tigecycline was not detected; overall resistance to ampicillin, cefotaxime, sulfamethoxazole and trimethoprim was observed at low levels, whereas ceftazidime resistance was not detected. The highest level of resistance was to colistin (31.6%), followed by the resistance to ciprofloxacin and nalidixic acid (22.4% for both of antimicrobials) (Table ENTERBRMEATD). 64.0% of *S.* Enteritidis isolates were susceptible to all 11 antimicrobials included in the MDR analysis (33.3–100%) (Table COMENTERBRMEAT).

Overall extremely high resistance to sulfamethoxazole, tetracycline, ciprofloxacin and nalidixic acid was observed in *S.* Infantis isolates from broiler meat (N=147) (Table <u>INFANBRMEATD</u>). Azithromycin, colistin, cefotaxime and ceftazidime resistance was not detected. It is of note that 55.0% of the *S.* Infantis isolates originated from Hungary and Slovakia, but levels of resistance are

Figure 20: Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobial classes in *Salmonella* spp. from broiler meat in MSs in 2014



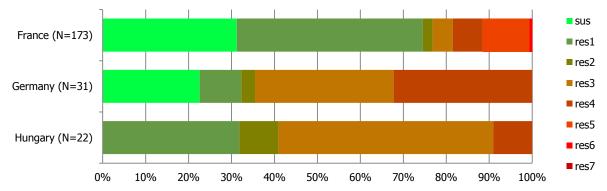
comparable to most other reporting MSs. In contrast to *S*. Enteritis, a very high proportion of isolates (83.1%) were multiresistant (79.5–100%) (Table <u>COMINFANBRMEAT</u>).

Out of 69 isolates of *S.* Indiana tested, only two isolates were found resistant: one only to ciprofloxacin and one to colistin and tetracycline (Table <u>INDIANABRMEATD</u>).

Antimicrobial resistance in Salmonella in meat from turkeys

Resistance levels in Salmonella *spp. isolates from turkey meat*

In 2014, three MSs reported more than 10 quantitative MIC data in *Salmonella* spp. isolates from turkey meat (Table 13). Levels of resistance were generally higher than those observed in broiler meat. The proportion of multiresistant *Salmonella* spp. isolates varied from none of the isolates tested in the Czech Republic and Poland, even if less than 10 isolates were tested, to extremely high levels (74.2–90.9%) in those isolates tested in Germany and Hungary (Figure 21). Co-resistance to ciprofloxacin and cefotaxime was not detected among the multiresistant isolates (five MSs, N=239) (Table <u>COMSALMTURKMEAT</u>).



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

Figure 21: Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobial classes in *Salmonella* spp. from fattening turkey meat in MSs in 2014



Country	Amp	picillin	Azithro	omycin	Cefc	taxime	Ceftaz	zidime	Chloram	phenicol	Ciprof	loxacin	Coli	stin ^(a)
-	N	% Res	Ν	% Res	N	% Res	N	% Res	Ν	% Res	N	% Res	N	% Res
Meat from broilers														
Austria	24	0	24	0	24	0	24	0	24	0	24	62.5	24	0
Belgium	81	23.5	81	6.2	81	3.7	81	2.5	81	4.9	81	43.2	81	3.7
Czech Republic	50	0	50	0	50	0	50	0	50	0	50	24	50	14.0
France	169	5.9	169	1.2	169	0	169	0	169	0.6	169	1.2	169	2.4
Germany	41	12.2	41	2.4	41	0	41	0	41	4.9	41	29.3	41	7.3
Hungary	47	4.3	47	0	47	0	47	0	47	0	47	97.9	47	0
Ireland	28	0	27	0	27	0	28	0	25	0	29	0	27	0
Poland	31	29.0	31	0	31	0	31	0	31	0	31	64.5	31	0
Slovakia	57	14.0	57	0	57	0	57	0	57	0	57	70.2	57	3.5
Slovenia	15	6.7	15	0	15	0	15	0	15	0	15	93.3	15	0
Spain	130	6.9	130	5.4	130	0.8	130	0.8	130	6.2	130	70	130	13.8
Total (MSs 11)	673	9.4	672	2.2	672	0.6	673	0.4	670	2.2	674	42.6	672	5.5
Meat from fattenin	a turkevs													
France	173	24.3	173	0	173	0	173	0	173	10.4	173	6.9	173	38.7
Germany	31	64.5	31	6.5	31	0	31	0	31	0	31	74.2	31	0
Hungary	22	27.3	22	0	22	0	22	0	22	0	22	90.9	22	0
Total (MSs 3)	226	30.1	226	0.9	226	0	226	0	226	8	226	24.3	226	29.6
Country	Ge	ntamicin	Na	lidixic acid		Sulfameth	ovazole	т	etracycline		Tigecycline		Trimeth	onrim
country ,	N	% Res	N	% Re		N	% Res	N	% R	es N		Res	N	% Res
Meat from broilers		1												
Austria	24	0	24	62.5		24	62.5	24	62.5		24	8.3	24	0
Belgium	81	0	81	42.0		81	39.5	81	0		-	_	81	53.1
Czech Republic	50	0	50	24.0		50	24.0	50	24.0	[50	0	50	0
France	169	0	169	0		169	4.7	169	3.6	16	59	0	169	1.8
Germany	41	0	41	29.3		41	9.8	41	7.3		11	0	41	26.8
Hungary	47	4.3	47	97.9		47	85.1	47	78.7	4	17	27.7	47	4.3
							0	28	0		28	0	28	0
Ireland	26	0	27	0		29	0	20					31	0
Ireland Poland		0	27	0 41.9		31	29.0	31	29.0	3	31	0	J I	
	26 31 57	-					29.0		-		31 57	0	57	0
Poland	31 57	0	31	41.9 70.2		31	29.0 63.2	31	29.0 63.2	Ę	57	0		0
Poland Slovakia	31	0	31 57	41.9		31 57	29.0	31 57	29.0	Ę	57 15	-	57	•
Poland Slovakia Slovenia	31 57 15	0 0 0	31 57 15	41.9 70.2 93.3		31 57 15	29.0 63.2 93.3	31 57 15	29.0 63.2 93.3	13 13	57 15 30	0 13.3 3.8	57 15	0
Poland Slovakia Slovenia Spain Total (MSs 11)	31 57 15 130 671	0 0 0 2.3	31 57 15 130	41.9 70.2 93.3 62.3		31 57 15 130	29.0 63.2 93.3 9.2	31 57 15 130	29.0 63.2 93.3 8.5	13 13	57 15 30	0 13.3 3.8	57 15 130	0 4.6
Poland Slovakia Slovenia Spain	31 57 15 130 671 ng turkeys	0 0 2.3 0.7	31 57 15 130 672	41.9 70.2 93.3 62.3		31 57 15 130	29.0 63.2 93.3 9.2 27.0	31 57 15 130 673	29.0 63.2 93.3 8.5 21.2	13 13 59	57 15 30 92	0 13.3 3.8 3.7	57 15 130 673	0 4.6 9.7
Poland Slovakia Slovenia Spain Total (MSs 11) Meat from fattenin France	31 57 15 130 671 ng turkeys 173	0 0 2.3 0.7	31 57 15 130 672 173	41.9 70.2 93.3 62.3 39.7 6.4		31 57 15 130 574 173	29.0 63.2 93.3 9.2 27.0 22.5	31 57 15 130 673 173	29.0 63.2 93.3 8.5 21.2 65.9	13 13 59	57 15 30 92 73	0 13.3 3.8	57 15 130 673 173	0 4.6 9.7 17.3
Poland Slovakia Slovenia Spain Total (MSs 11) Meat from fattenin	31 57 15 130 671 ng turkeys	0 0 2.3 0.7	31 57 15 130 672	41.9 70.2 93.3 62.3 39.7		31 57 15 130 574	29.0 63.2 93.3 9.2 27.0	31 57 15 130 673	29.0 63.2 93.3 8.5 21.2	13 13 59 17	57 15 30 92	0 13.3 3.8 3.7 1.7	57 15 130 673	0 4.6 9.7

Table 13: Occurrence of resistance to selected antimicrobials in S	Salmonella spp. isolates from meat from broilers a	nd meat from fattening turkeys in 2014
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All *Salmonella* isolates tested were susceptible to meropenem. N: number of isolates tested; % Res: percentage of microbiologically resistant isolates; –: no information available; MSs: Member States. (a): A number of colistin-resistant isolates are undergoing testing for the presence of *mcr-1* gene. The reported occurrence of colistin resistance is unlikely to equate to the occurrence of *mcr-1*.



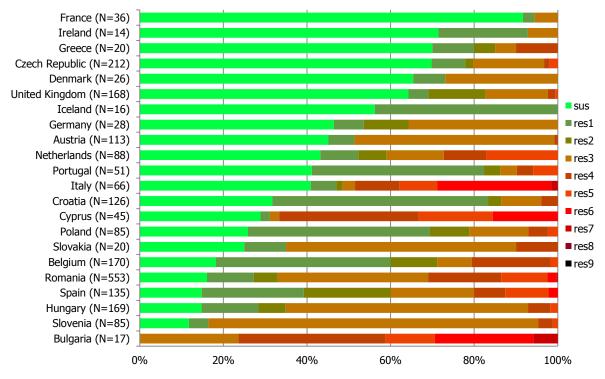
Antimicrobial resistance in Salmonella spp. in flocks from broilers

Resistance levels in Salmonella spp. isolates from broiler flocks

In 2014, 22 MSs reported on *Salmonella* spp. in broiler flocks (Table 14). Most MSs recorded high to extremely high resistance to ciprofloxacin, nalidixic acid, sulfamethoxazole and tetracycline, for which overall resistance equalled 53.5%, 48.7%, 45.1% and 40.4%, respectively. Overall resistance to ampicillin was moderate at 19.1%. Resistance to azithromycin, chloramphenicol and gentamicin was overall low, although resistance levels varied markedly from none to 35.3% between MSs. Resistance to cefotaxime and ceftazidime was generally either not detected (in 12 MSs) or reported at very low to low levels (MSs), except in the Netherlands and Italy, where moderate to high levels were respectively registered. Ireland and Malta detected isolates resistant to ceftazidime but not to cefotaxime. Colistin resistance levels observed were among the highest reported, accounted for nearly one quarter of the *Salmonella* spp. isolates from broiler flocks included in the analysis (Table 14), the resistance rates presented at the reporting MS group level are highly impacted by the occurrence of resistance recorded in Romania.

Multidrug resistance in Salmonella spp. isolates from broiler flocks

Twenty-two MSs submitted isolate-based data included in the MDR analysis (N=2,243). Situations varied markedly between MSs, as from 5.6% to 100% of the *Salmonella* spp. isolates were multiresistant, and none to 91.7% of them were fully susceptible to the nine antimicrobial classes considered (Figure 22) (Table <u>COMSALMBR</u>). 'Microbiological' co-resistance to ciprofloxacin and cefotaxime was generally low in *Salmonella* spp. isolates from broilers (1.8%) and it was observed in six of the 22 MSs, ranging up to 27.3% in the isolates tested in Italy (Table <u>COMSALMBR</u>). 'Clinical' resistance to both ciprofloxacin and cefotaxime was rare, and only detected in one *S.* Kentucky isolate in Spain (Table <u>COMSALMBR</u>).



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

Figure 22: Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in *Salmonella* spp. from broilers in MSs in 2014



Spatial trends in resistance among Salmonella spp. from broiler flocks

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 23). The levels of resistance to nalidixic acid in *Salmonella* spp. from broilers were extremely high (> 70%) in some MSs from eastern and southern Europe (Bulgaria, Hungary, Romania, Slovakia and Slovenia), and high to very high in most other MSs (Figure 24). High level of resistance to cefotaxime was reported in one MS (Figure 25).

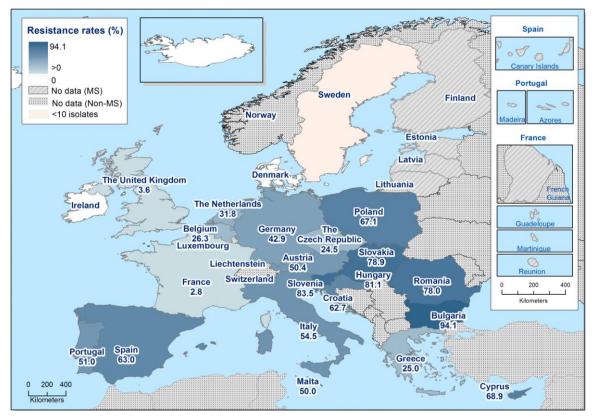


Figure 23: Spatial distribution of ciprofloxacin resistance among *Salmonella* spp. from broilers in countries reporting MIC data in 2014



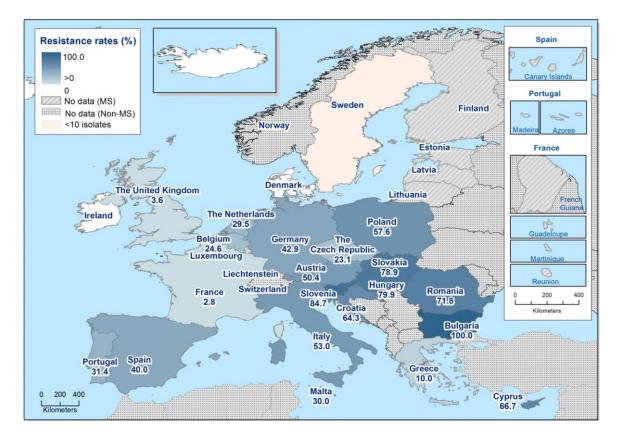


Figure 24: Spatial distribution of nalidixic acid resistance among *Salmonella* spp. from broilers in countries reporting MIC data in 2014

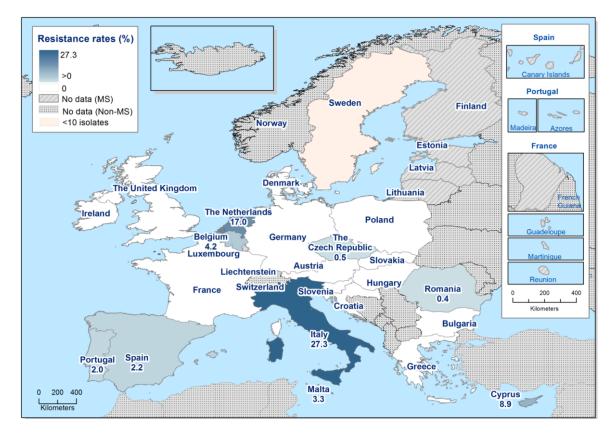


Figure 25: Spatial distribution of cefotaxime resistance among *Salmonella* spp. from broilers in countries reporting MIC data in 2014



Country	Ampicillin		Azithromycin		Cefotaxime		Ceftazidime		Chloramphenicol		Ciprofloxacin		Colistin ^(a)	
	N	% Res	N	% Res	Ν	% Res	Ν	% Res	N	% Res	Ň	% Res	Ν	% Res
Austria	113	1.8	113	0.9	113	0	113	0	113	0.9	113	50.4	113	19.5
Belgium	167	28.7	167	0.6	167	4.2	167	3	167	1.2	167	26.3	167	2.4
Bulgaria	17	47.1	_	_	17	0	17	0	17	35.3	17	94.1	_(a)	-
Croatia	126	7.1	126	4.0	126	0	126	0	126	0	126	62.7	126	0
Cyprus	45	35.6	45	0	45	8.9	45	8.9	45	0	45	68.9	45	0
Czech Republic	212	7.5	212	0.5	212	0.5	212	0.5	212	0	212	24.5	212	35.8
Denmark	26	30.8	26	0	26	0	26	0	26	0	26	0	26	0
France	36	2.8	36	0	36	0	36	0	36	0	36	2.8	36	2.8
Germany	28	14.3	28	3.6	28	0	28	0	28	0	28	42.9	28	0
Greece	20	5	20	5	20	0	20	0	20	0	20	25.0	20	0
Hungary	169	5.3	169	3.6	169	0	169	0	169	6.5	169	81.1	169	4.7
Ireland	16	12.5	17	0	17	0	16	6.3	19	0	15	0	17	0
Italy	66	43.9	66	1.5	66	27.3	66	25.8	66	6.1	66	54.5	66	0
Malta	60	40	_	_	60	3.3	60	16.7	60	8.3	20	50.0	-	-
Netherlands	88	39.8	88	0	88	17	88	17	88	6.8	88	31.8	88	15.9
Poland	85	22.4	85	0	85	0	85	0	85	2.4	85	67.1	85	0
Portugal	51	15.7	51	2.0	51	2	51	2	51	3.9	51	51.0	51	5.9
Romania	554	23.3	554	4.3	554	0.4	554	0.4	554	6.3	554	78.0	_(a)	-
Slovakia	19	10.5	19	0	19	0	19	0	19	0	19	78.9	19	15.8
Slovenia	85	8.2	85	1.2	85	0	85	0	85	1.2	85	83.5	85	2.4
Spain	135	40	135	0	135	2.2	135	2.2	135	11.1	135	63.0	135	3.7
United Kingdom	168	3.6	168	0	168	0	168	0	168	1.2	168	3.6	168	0
Total (MSs 22)	2,286	19.1	2,210	1.9	2,287	2.3	2,286	2.6	2,289	4.0	2,245	53.5	1,656	8.3
Iceland	16	0	16	0	16	0	16	0	16	0	16	0	16	0

Table 14: Occurrence of resistance to selected antimicrobials in *Salmonella* spp. isolates from broilers in 2014, using harmonised ECOFFs



Country	Genta	micin	Nalidixic acid		Sulfamethoxazole		Tetracycline		Tigecycline		Trimethoprim	
	Ν	% Res	Ν	% Res	N	% Res	N	% Res	N	% Res	Ν	% Res
Austria	113	0	113	50.4	113	49.6	113	50.4	113	1.8	113	0
Belgium	167	1.8	167	24.6	167	24.6	167	7.2	167	1.8	167	79.6
Bulgaria	17	5.9	17	100	17	100	17	100	17	17.6	17	64.7
Croatia	126	0.8	126	64.3	126	15.1	126	11.1	126	0	126	4.0
Cyprus	45	20.0	45	66.7	45	68.9	45	68.9	45	15.6	45	53.3
Czech Republic	212	1.4	212	23.1	212	22.6	212	20.3	212	1.9	212	0.9
Denmark	26	0	26	0	26	26.9	26	30.8	26	0	26	0
France	36	0	36	2.8	36	5.6	36	5.6	36	2.8	36	2.8
Germany	28	0	28	42.9	28	32.1	28	25.0	28	0	28	21.4
Greece	20	0	20	10	20	20.0	20	15.0	20	0	20	10.0
Hungary	169	2.4	169	79.9	169	68.0	169	67.5	169	30.2	169	0
Ireland	18	0	17	0	15	13.3	16	6.3	16	0	16	0
Italy	66	0	66	53.0	66	50.0	66	53.0	66	6.1	66	45.5
Malta	60	5	60	30.0	60	36.7	60	35.0	_	_	60	10.0
Netherlands	88	1.1	88	29.5	88	43.2	88	30.7	88	4.5	88	19.3
Poland	85	0	85	57.6	85	20.0	85	21.2	85	0	85	1.2
Portugal	51	3.9	51	31.4	51	11.8	51	9.8	51	0	51	7.8
Romania	554	14.8	554	71.8	553	67.5	554	62.6	554	16.8	554	17.5
Slovakia	19	0	19	78.9	19	68.4	19	68.4	19	5.3	19	0
Slovenia	85	0	85	84.7	85	83.5	85	82.4	85	24.7	85	1.2
Spain	135	21.5	135	40.0	135	39.3	135	33.3	135	1.5	135	10.4
United Kingdom	168	8.3	168	3.6	168	31.0	168	20.2	168	6.0	168	19.0
Total (MSs 22)	2,288	6.6	2,287	48.7	2,284	45.1	2,286	40.4	2,226	9.3	2,286	16.9
Iceland	16	0	16	0	16	43.8	16	0	16	0	16	0

All Salmonella isolates tested were susceptible to meropenem.

N: number of isolates tested; % Res: percentage of microbiologically resistant isolates; -: no information available; MSs: Member States. (a): A number of colistin-resistant isolates are undergoing testing for the presence of *mcr-1* gene. The reported occurrence of colistin resistance is unlikely to equate to the occurrence of *mcr-1*.



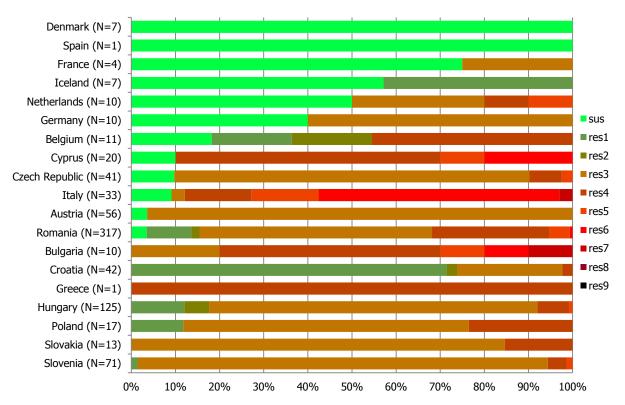
Antimicrobial resistance in certain *Salmonella* serovars in broiler flocks

Resistance levels in S. Infantis isolates from broiler flocks

S. Infantis is the most frequently reported serovars in broiler flocks, accounting for 36.5% of the *Salmonella* isolates serotyped (N=2,417). In *S.* Infantis isolates from broilers (19 MSs, Table 16), resistance to sulfamethoxazole and tetracycline was mostly high to extremely high (overall 82.7% and 81.3%, respectively), whereas resistance to ampicillin overall was moderate (10.9%), but varied considerably from none to extremely high. Only five MSs observed resistance to chloramphenicol and gentamicin (overall 3.6% and 2.9%, respectively). The Czech Republic and Italy recorded resistance to cefotaxime (15.0% and 54.5%, respectively) and three MSs reported resistance to ceftazidime resulting in an overall low occurrence (2.6%). Extremely high levels of resistance to ciprofloxacin and nalidixic acid were found in *S.* Infantis from most MSs, except Denmark and Spain. It is notable that isolates from Romania represented 39.8% of the *S.* Infantis isolates.

Multidrug resistance in S. Infantis isolates from broiler flocks

Most (> 80%) of the *S*. Infantis isolates from broilers (19 MSs, N=797) included in the MDR analysis were multiresistant (Figure 26). 'Microbiological' co-resistance to ciprofloxacin and cefotaxime was detected by Cyprus (15%) and Italy (54.5%) (Tables <u>COMINFANBR</u>).



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

Figure 26: Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in *Salmonella* Infantis from broilers in MSs in 2014

Spatial trends in resistance among S. *Infantis from broiler flocks*

The levels of resistance to ciprofloxacin in *S*. Infantis from broilers were extremely high at 100% in some MSs from eastern and southern Europe (Bulgaria, Croatia, Hungary, Slovakia and Slovenia), and very high in all other MSs (Figure 27). Resistance to cefotaxime was reported by only two MSs (Figure 29).





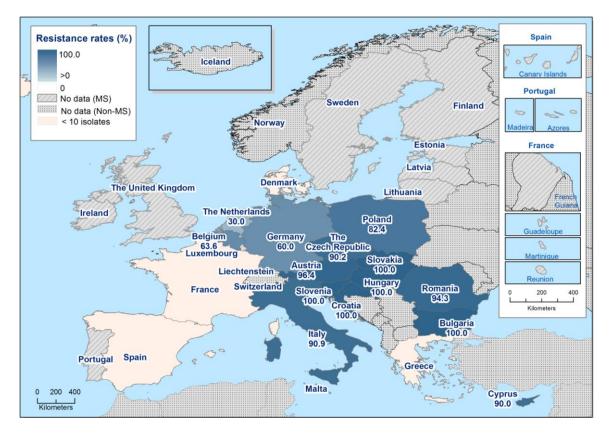


Figure 27: Spatial distribution of ciprofloxacin resistance among *Salmonella* Infantis from broilers in countries reporting MIC data in 2014

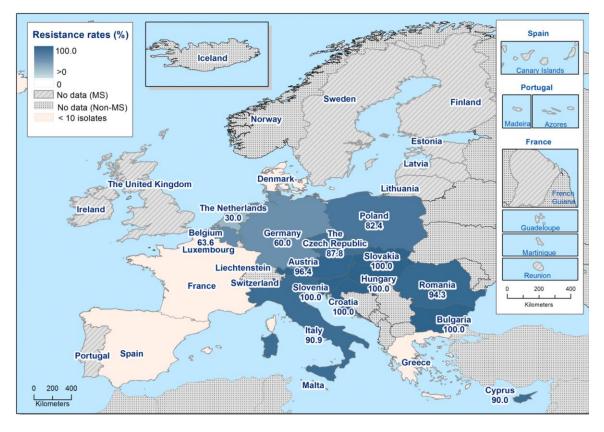


Figure 28: Spatial distribution of nalidixic acid resistance among *Salmonella* Infantis from broilers in countries reporting MIC data in 2014



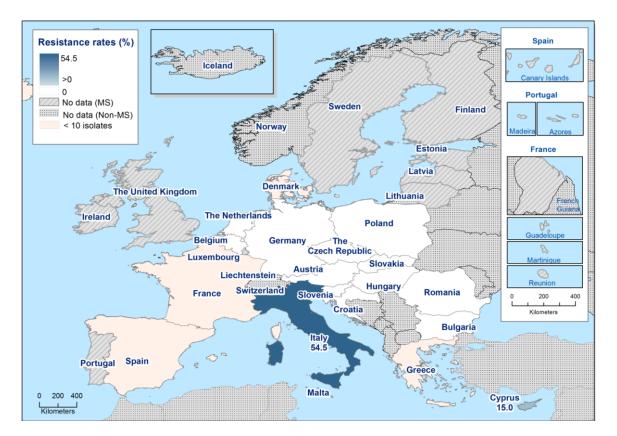


Figure 29: Spatial distribution of cefotaxime resistance among *Salmonella* Infantis from broilers in countries reporting MIC data in 2014

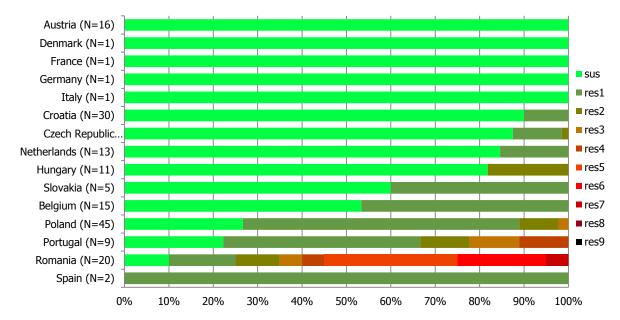
Resistance levels in S. Enteritidis isolates from broiler flocks

S. Enteritidis is the second most frequently reported serovars in broiler flocks, accounting for 13.5%, of the *Salmonella* isolates serotyped (N=2,417). Among *S.* Enteritidis isolates from broilers (15 MSs, Table 15), the overall resistance to ampicillin, chloramphenicol, gentamicin, sulfamethoxazole and tetracycline was at low levels; Romania being the only MS reporting high to very high levels of resistance to all these antimicrobials. High levels of resistance to ampicillin and gentamicin were reported by Portugal. Overall, resistance to nalidixic acid and ciprofloxacin were high in *S.* Enteritidis (24.6% and 23.3%, respectively), ranging from none to 100% in individual MSs.

Multidrug resistance in S. Enteritidis isolates from broiler flocks

'Microbiological' resistance to cefotaxime and ceftazidime was only reported by Portugal in a single isolate of *S*. Enteritidis. Most of the *S*. Enteritidis isolates (70.1%) were fully susceptible to all nine antimicrobials classes included in the MDR analysis for broilers (14 MSs, N=304) (Figure 30). However, only 26.7% and 22.2% of the *S*. Enteritidis from broilers in Poland and Portugal, respectively, were fully susceptible. 65.0% of the *S*. Enteritidis from Romania were multiresistant. 'Microbiological' co-resistance to ciprofloxacin and cefotaxime was detected in one isolate of *S*. Enteritidis from Portugal (Tables <u>COMENTERBR</u>). In broilers, resistance to colistin was noted in 40% of *S*. Enteritidis isolates.





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

Figure 30: Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in *Salmonella* Enteritidis from broilers in MSs in 2014

Spatial trends in resistance among S. Enteritidis from broiler flocks

Low levels of ciprofloxacin resistance (<10.0%) were reported by only two MSs Croatia and the Czech Republic (Figure 31). The levels of resistance to nalidixic acid in *Salmonella* spp. from broilers were extremely high (>70%) in two MSs,Poland and Romania, moderate in Hungary and the Netherlands and low Croatia and the Czech Republic (Figure 32). The resistance to cefotaxime was reported by only one country, but with less than 10 isolates tested (Figure 33).



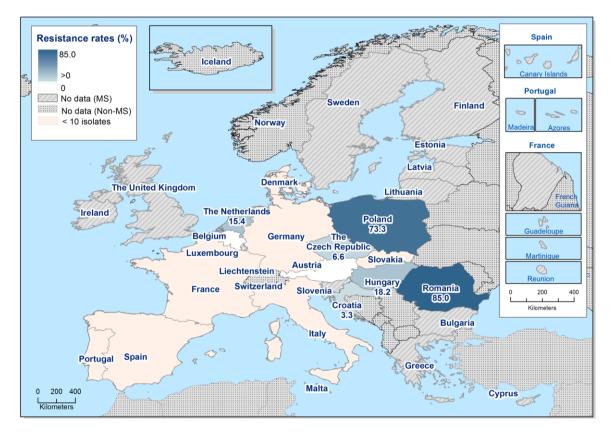


Figure 31: Spatial distribution of ciprofloxacin resistance among *Salmonella* Enteritidis from broilers in countries reporting MIC data in 2014

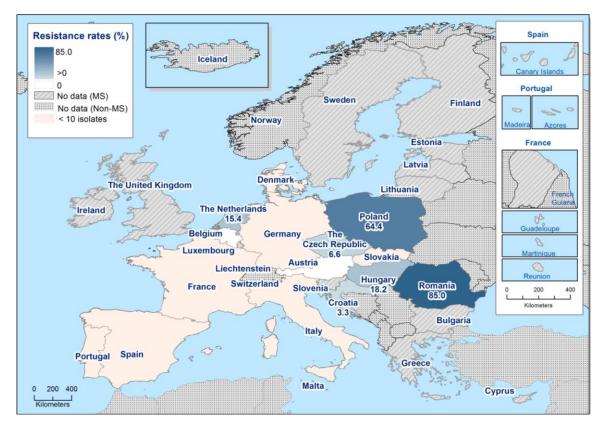


Figure 32: Spatial distribution of nalidixic acid resistance among *Salmonella* Enteritidis from broilers in countries reporting MIC data in 2014



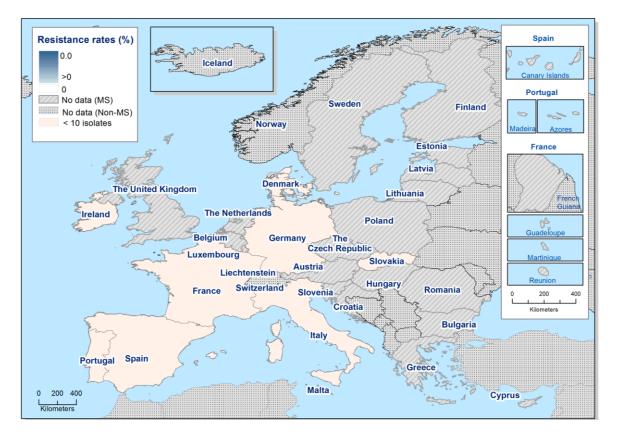


Figure 33: Spatial distribution of cefotaxime resistance among *Salmonella* Enteritidis from broilers in countries reporting MIC data in 2014

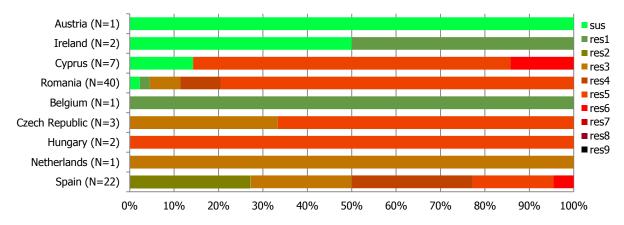
Resistance levels in S. Kentucky isolates from broiler flocks

S. Kentucky is the fourth most frequently reported serovars in broiler flocks, accounting for 4.8% of the *Salmonella* isolates serotyped (N=2,417). In *S.* Kentucky isolates from broilers (10 MSs, Table <u>KENTBRD</u>), overall, high to extremely high levels of resistance to ampicillin, ciprofloxacin, gentamicin, nalidixic acid, sulfamethoxazole and tetracycline were reported, whereas resistance varied markedly between MSs from none to 100%. Conversely, resistance to chloramphenicol, colistin, tigecycline and trimethropim was overall low. Two of the ten reporting MSs registered low to moderate levels of resistance to cefotaxime and ceftazidime. It is of note that Romania accounted for 38.3% of the *S.* Kentucky isolates analysed.

Multidrug resistance in S. Kentucky isolates from broiler flocks

In *S.* Kentucky isolates from broilers (eight MSs, N=82) 85.4% of the isolates included in the MDR analysis were multiresistant (Figure 34, Tables <u>COMKENBR</u>). 'Microbiological' and clinical co-resistance to ciprofloxacin and cefotaxime was detected in Spain (4.5%) (Tables <u>COMKENBR</u>).





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

Figure 34: Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in *Salmonella* Kentuky from broilers in MSs in 2014

Resistance levels in S. Typhimurium and monophasic S. Typhimurium isolates from broiler flocks

Resistance levels to ampicillin, sulfamethoxazole and tetracycline (overall 33.3–42.5%) in *S.* **Typhimurium** isolates from broilers (Table <u>TYPHIBRD</u>) were found to mainly be high to extremely high. Chloramphenicol resistance varied from none to 100% (overall 16.1%), whereas resistance to gentamicin was reported by only one MS. Resistance to cefotaxime and ceftazidime was reported only by Belgium, whereas nalidixic acid and ciprofloxacin resistance varied markedly between MSs from none to 100% (Romania). In broilers, 32.5% (17 MSs, N=83) of the *S.* Typhimurium isolates were multiresistant. 'Microbiological' co-resistance to ciprofloxacin and cefotaxime was only reported for one isolate by Belgium (Tables <u>COMTYPHIBR</u>).

Resistance levels to ampicillin, sulfamethoxazole and tetracycline (overall 79.4–82.4%) in **monophasic** *S.* **Typhimurium** isolates from broilers (Table <u>MONTPHIYBRD</u>) were found to mainly be high to extremely high. Chloramphenicol resistance was registered only by Malta (50.0%), whereas resistance to gentamicin was reported only by the United Kingdom. Resistance to cefotaxime and ceftazidime was reported only by Malta (50.0%) and the Netherlands (20.0%), whereas nalidixic acid and ciprofloxacin resistance was reported only by Belgium. In broilers, 74.2% (eight MSs, N=31) of the monophasic *S.* Typhimurium isolates were multiresistant. 'Microbiological' co-resistance to ciprofloxacin and cefotaxime was not reported. (Tables <u>COMMONTYPHIBR</u>).



Country	Amp	bicillin	Azithı	romycin	Cefo	taxime	Cefta	zidime	Chloran	nphenicol	Cipro	floxacin	Coli	istin ^(a)
-	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res	N	% Res	N	% Res
Austria	16	0	16	0	16	0	16	0	16	0	16	0	16	100
Belgium	15	0	15	0	15	0	15	0	15	0	15	0	15	13.3
Croatia	30	3.3	30	0	30	0	30	0	30	0	30	3.3	30	0
Czech Republic	136	5.1	136	0	136	0	136	0	136	0	136	6.6	136	55.1
Denmark	1	0	1	0	1	0	1	0	1	0	1	0	1	0
France	1	0	1	0	1	0	1	0	1	0	1	0	1	0
Germany	1	0	1	0	1	0	1	0	1	0	1	0	1	0
Hungary	11	0	11	0	11	0	11	0	11	0	11	18.2	11	45.5
Italy	1	0	1	0	1	0	1	0	1	0	1	0	1	0
Netherlands	13	0	13	0	13	0	13	0	13	0	13	15.4	13	69.2
Poland	45	11.1	45	0	45	0	45	0	45	0	45	73.3	45	0
Portugal	9	33.3	9	0	9	11.1	9	11.1	9	0	9	77.8	9	33.3
Romania	20	70	20	0	20	0	20	0	20	55.0	20	85	_	_
Slovakia	4	0	4	0	4	0	4	0	4	0	4	50	4	75.0
Spain	2	0	2	0	2	0	2	0	2	0	2	100	2	100
Total (MSs 15)	305	9.8	305	0	305	0.3	305	0.3	305	3.6	305	24.6	285	40.4

Table 15: Occurrence of resistance to selected antimicrobials in *Salmonella* Enteritidis isolates from broilers in 2014



Country	Genta	amicin	Na	idixic acid	Sulfame	thoxazole	Tetrac	cycline	Tige	cycline	Trime	thoprim
-	N	% Res	Ν	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Austria	16	0	16	0	16	0	16	0	16	0	16	0
Belgium	15	0	15	0	15	0	15	0	15	0	15	46.7
Croatia	30	0	30	3.3	30	3.3	30	0	30	0	30	0
Czech Republic	136	0	136	6.6	136	2.2	136	0	136	0	136	0
Denmark	1	0	1	0	1	0	1	0	1	0	1	0
France	1	0	1	0	1	0	1	0	1	0	1	0
Germany	1	0	1	0	1	0	1	0	1	0	1	0
Hungary	11	0	11	18.2	11	0	11	18.2	11	0	11	0
Italy	1	0	1	0	1	0	1	0	1	0	1	0
Netherlands	13	0	13	15.4	13	0	13	0	13	0	13	0
Poland	45	0	45	64.4	45	0	45	2.2	45	0	45	0
Portugal	9	22.2	9	77.8	9	0	9	0	9	0	9	0
Romania	20	20.0	20	85.0	20	55.0	20	60.0	20	0	20	30.0
Slovakia	4	0	4	50.0	4	0	4	0	4	0	4	0
Spain	2	0	2	100	2	0	2	0	2	0	2	0
Total (MSs 15)	305	2.0	305	23.3	305	4.9	305	4.9	305	0	305	4.3

All Salmonella isolates tested were susceptible to meropenem. N: number of isolates tested; % Res: percentage of microbiologically resistant isolates.

(a): A number of colistin-resistant isolates are undergoing testing for the presence of the *mcr-1* gene. The reported occurrence of colistin resistance does not equate to the occurrence of *mcr-1*.

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Country	Amp	bicillin	Azith	romycin	Cefot	axime	Cefta	zidime	Chloram	ohenicol	Ciprofl	oxacin	Colist	in ^(a)
-	N	% Res	Ν	% Res	Ν	% Res	Ν	Ν	% Res	Ν	% Res	N	% Res	Ν
Austria	56	0	56	1.8	56	0	56	0	56	0	56	96.4	56	3.6
Belgium	11	0	11	0	11	0	11	0	11	0	11	63.6	11	0
Bulgaria	10	40.0	_	_	10	0	10	0	10	20	10	100	_(a)	_
Croatia	42	4.8	42	11.9	42	0	42	0	42	0	42	100	42	0
Cyprus	20	30	20	0	20	15	20	15.0	20	0	20	90	20	0
Czech Republic	41	9.8	41	2.4	41	0	41	0	41	0	41	90.2	41	0
Denmark	7	0	7	0	7	0	7	0	7	0	7	0	7	0
France	4	0	4	0	4	0	4	0	4	0	4	25	4	0
Germany	10	0	10	0	10	0	10	0	10	0	10	60	10	0
Greece	1	0	1	0	1	0	1	0	1	0	1	100	1	0
Hungary	125	3.2	125	4	125	0	125	0	125	7.2	125	100	125	1.6
Italy	33	75.8	33	0	33	54.5	33	51.5	33	9.1	33	90.9	33	0
Malta	7	14.3	_	_	7	0	7	14.3	7	0	3	100	_	_
Netherlands	10	20.0	10	0	10	0	10	0	10	10	10	30	10	0
Poland	17	35.3	17	0	17	0	17	0	17	0	17	82.4	17	0
Romania	317	8.5	317	4.1	317	0	317	0	317	4.1	317	94.3	_(a)	_
Slovakia	13	15.4	13	0	13	0	13	0	13	0	13	100	13	0
Slovenia	71	5.6	71	1.4	71	0	71	0	71	1.4	71	100	71	2.8
Spain	1	0	1	0	1	0	1	0	1	0	1	0	1	0
Total (MSs 19)	796	10.9	779	3.3	796	2.6	796	2.6	796	3.6	792	92.7	462	1.3
Iceland	7	0	7	0	7	0	7	0	7	0	7	0	7	0

Table 16: Occurrence of resistance to selected antimicrobials in *Salmonella* Infantis isolates from broilers in 2014, using harmonised ECOFFs



Countral	Genta	amicin	Nali	dixic acid	Sulfam	ethoxazole	Tetra	cycline	Tige	cycline	Trime	thoprim
Country	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res
Austria	56	0	56	96.4	56	96.4	56	96.4	56	3.6	56	0
Belgium	11	0	11	63.6	11	63.6	11	45.5	11	27.3	11	63.6
Bulgaria	10	10.0	10	100	10	100	10	100	10	30	10	70.0
Croatia	42	0	42	100	42	26.2	42	26.2	42	0	42	0
Cyprus	20	5.0	20	90.0	20	90	20	90.0	20	35.0	20	90.0
Czech Republic	41	2.4	41	87.8	41	90.2	41	90.2	41	9.8	41	0
Denmark	7	0	7	0	7	0	7	0	7	0	7	0
France	4	0	4	25.0	4	25.0	4	25.0	4	25	4	0
Germany	10	0	10	60.0	10	60.0	10	60.0	10	0	10	0
Greece	1	0	1	100	1	100	1	100	1	0	1	100
Hungary	125	1.6	125	100	125	84.0	125	83.2	125	37.6	125	0
Italy	33	0	33	90.9	33	87.9	33	90.9	33	12.1	33	84.8
Malta	7	0	7	42.9	7	42.9	7	42.9	-	-	7	0
Netherlands	10	0	10	30.0	10	50.0	10	40.0	10	20.0	10	30.0
Poland	17	0	17	82.4	17	88.2	17	88.2	17	0	17	5.9
Romania	317	5.7	317	94.3	317	86.1	317	83.6	317	21.8	317	22.4
Slovakia	13	0	13	100	13	100	13	100	13	7.7	13	0
Slovenia	71	0	71	100	71	98.6	71	98.6	71	29.6	71	0
Spain	1	0	1	0	1	0	1	0	1	0	1	0
Total (MSs 19)	796	2.9	796	92.1	796	82.7	796	81.3	789	20.8	796	17.1
Iceland	7	0	7	0	7	42.9	7	0	7	0	7	0

All Salmonella isolates tested were susceptible to meropenem.

N: number of isolates tested; % Res: percentage of microbiologically resistant isolates; -: no information available; MSs: Member States. Issues with quality of data (a): A number of colistin-resistant isolates are undergoing testing for the presence of *mcr-1* gene. The reported occurrence of colistin resistance is unlikey to equate to the occurrence of *mcr-1*.

EFSA Journal



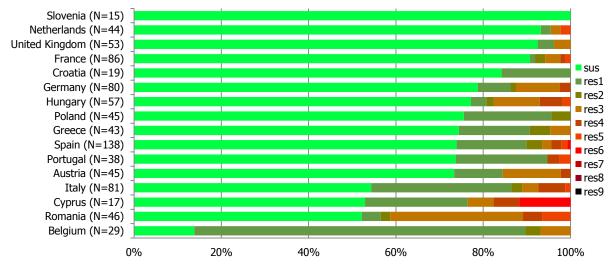
Antimicrobial resistance in *Salmonella* spp. in flocks of laying hens

Resistance levels in Salmonella spp. isolates from laying hen flocks

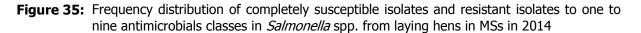
In 2014, 15 MSs reported data on *Salmonella* spp. in laying hens (Table 17). Most MSs registered low to moderate levels of resistance to ampicillin, ciprofloxacin, nalidixic acid, sulfamethoxazole and tetracycline, whereas four MSs reported high levels of resistance to at least one of these antimicrobials. Resistance to chloramphenicol and gentamicin was generally low. Resistance to cefotaxime and ceftazidime was low, and only three *Salmonella* spp. isolates, from three MSs, showed resistance to both antimicrobials. Compared with isolates from broilers, with the exception of colistin resistance, lower levels of resistance were reported in *Salmonella* spp. from laying hens.

Multidrug resistance in Salmonella spp. isolates from laying hen flocks

Most (74.1%) of the *Salmonella* spp. isolates included in the MDR analysis (22 MSs, N=858) were fully susceptible to the 11 antimicrobials considered (Figure 35), and between none and 41.3% of the *Salmonella* spp. isolates were multiresistant in reporting MSs (overall MDR, 9.7%). 'Microbiological' corresistance to ciprofloxacin and cefotaxime was very low at 0.12%, as it was observed in only one isolate from Romania (Table <u>COMSALMLAY</u>).



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



Spatial trends in resistance among Salmonella spp. from laying hen flocks

The levels of resistance to ciprofloxacin in *Salmonella* spp. from laying hens were high in some MSs from Eastern and Southern Europe (Cyprus, Hungary, Italy and Romania), and low to moderate in other reporting MSs (Figure 36). The levels of resistance to nalidixic acid were very similar to the levels of resistance to ciprofloxacin (Figure 37). Low level of resistance to cefotaxime was reported only by France, Poland and Romania, whereas no resistance was reported from other 13 MSs across Europe (Figure 38).





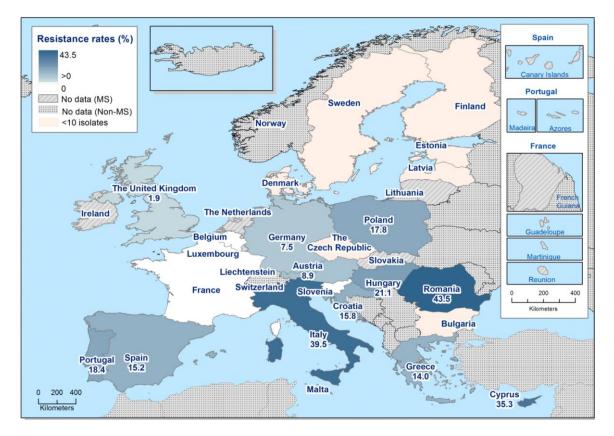


Figure 36: Spatial distribution of ciprofloxacin resistance among *Salmonella* spp. from laying hens in countries reporting MIC data in 2014

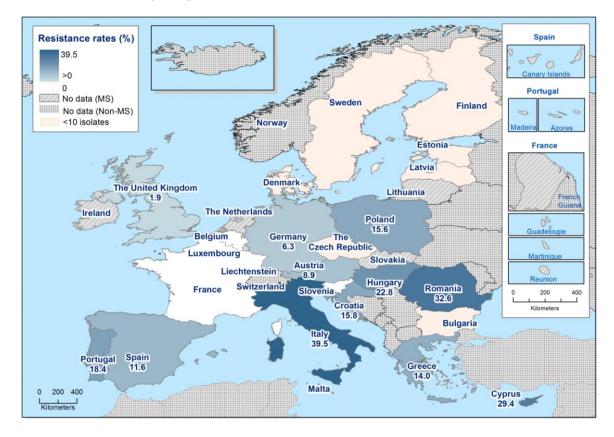


Figure 37: Spatial distribution of nalidixic acid resistance among *Salmonella* spp. from laying hens in countries reporting MIC data in 2014



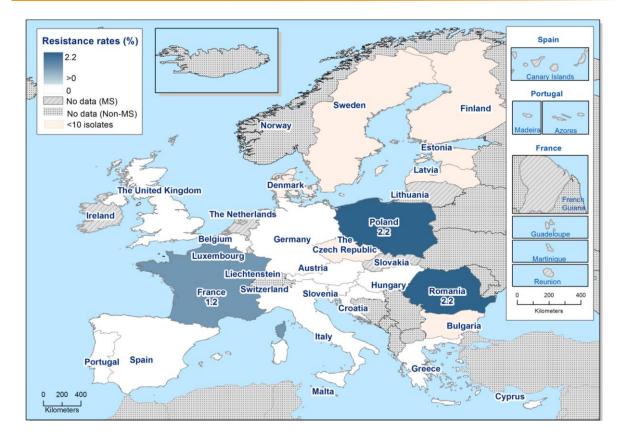


Figure 38: Spatial distribution of cefotaxime resistance among *Salmonella* spp. from laying hens in countries reporting MIC data in 2014

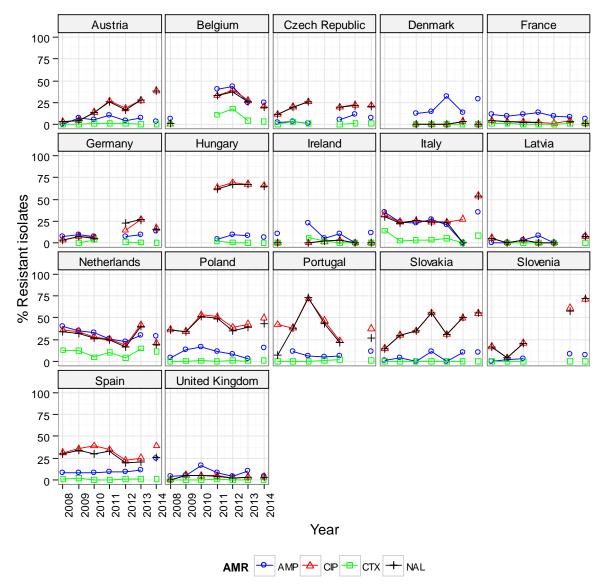
Temporal trends in resistance among Salmonella spp. from Gallus gallus

Seventeen MSs provided resistance data on 5 years or more to be included in the statistical analysis. Over the 7 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 five MSs, whereas statistically decreasing trends were observed in four other MSs. Statistically significant increasing trends in resistance to ciprofloxacin and/or nalidixic acid were registered in seven MSs, whereas statistically significant decreasing trends were observed in two MSs. Within each MS, similar levels of resistance to ciprofloxacin and nalidixic acid were observed from 2008 to 2014. Resistance to cefotaxime is generally very low; however, a statistically significant increasing trend was observed in one MSs, whereas the trend in five MSs was decreasing (Figure 39).

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 2008 to 2014 within each MS, although slight but statistically significant increases occurred in two MSs (Figure 40). 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 three MSs. Resistance to ciprofloxacin and nalidixic acid was comparable within MSs from 2008 to 2014.

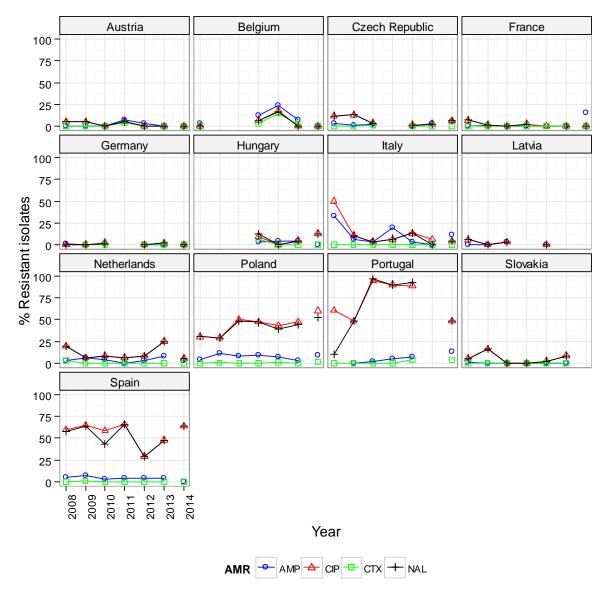




A statistically significant trend for 5 or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for ciprofloxacin and nalidixic acid in Austria (\uparrow), Belgium (\uparrow), Germany (\uparrow), Italy (\uparrow), Slovakia (\uparrow), Slovenia (\uparrow), for ampicillin in Belgium (\downarrow), the Czech Republic (\uparrow), Denmark (\uparrow), Italy (\downarrow), the Netherlands (\downarrow), Slovakia (\uparrow), Slovenia (\uparrow), Spain (\uparrow) and the United Kingdom (\downarrow), for ciprofloxacin in Portugal (\downarrow), for cefotaxime in Belgium (\downarrow), the Czech Republic (\downarrow), France (\downarrow), Germany (\downarrow), the Czech Republic (\downarrow), France (\downarrow), Germany (\downarrow), Italy (\downarrow) and the Netherlands (\uparrow). A statistically significant trend was observed for ciprofloxacin in Portugal (\uparrow), for nalidixic acid in Portugal (\uparrow) and Spain (\downarrow).

Figure 39: Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested *Salmonella* spp. isolates from *Gallus gallus* in reporting MSs, 2008–2014, quantitative data





A statistically significant trend for 5 or more years, as tested by a logistic regression model ($p \le 0.05$), was observed in the Czech Republic (\downarrow), France (\downarrow), Poland (\uparrow) and Portugal (\uparrow) for both ciprofloxacin and nalidixic acid, for ampicillin in France (\uparrow) and Portugal (\uparrow), for ciprofloxacin in Italy (\downarrow) and for cefotaxime in the Netherlands (\downarrow) and Portugal (\uparrow).

Figure 40: Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested *Salmonella* Enteritidis isolates from *Gallus gallus* in reporting MSs, 2008–2014, quantitative data



Country	Amp	icillin	Azithı	omycin	Cefo	axime	Cefta	zidime	Chlorar	nphenicol	Ciprof	oxacin	Coli	stin ^(a)
-	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	N	% Res	Ň	% Re:	Ν	% Res
Austria	45	6.7	45	0	45	0	45	0	45	2.2	45	8.9	45	17.8
Belgium	29	10.3	29	0	29	0	29	0	29	0	29	0	29	41.4
Croatia	19	0	19	0	19	0	19	0	19	0	19	15.8	19	0
Cyprus	17	11.8	17	0	17	0	17	0	17	0	17	35.3	17	0
France	86	7	86	0	86	1.2	86	1.2	86	2.3	86	0	86	15.1
Germany	80	13.8	80	1.3	80	0	80	0	80	0	80	7.5	80	10
Greece	43	4.7	43	0	43	0	43	0	43	0	43	14	43	0
Hungary	57	8.8	57	0	57	0	57	0	57	0	57	21.1	57	12.3
Italy	81	11.1	81	0	81	0	81	0	81	2.5	81	39.5	81	11.1
Poland	45	2.2	45	0	45	2.2	45	2.2	45	2.2	45	17.8	45	0
Portugal	38	7.9	38	0	38	0	38	0	38	5.3	38	18.4	38	13.2
Romania	46	23.9	46	2.2	46	2.2	46	2.2	46	0	46	43.5	46	8.7
Slovenia	15	0	15	0	15	0	15	0	15	0	15	0	15	0
Spain	138	8.7	138	0.7	138	0	138	0	138	2.2	138	15.2	138	8.7
United Kingdom	53	3.8	53	0	53	0	53	0	53	0	53	1.9	53	9.4
Total (MSs 15)	792	8.8	792	0.4	792	0.4	792	0.4	792	1.4	792	15.9	792	10.5

able 17: Occurrence of resistance to selected antimicrobials in <i>Salmonella</i> spp. isolates from laying hens in 2014, using harmonised ECOFFs



Country	Gent	amicin	Na	alidixic acid	Sulfam	ethoxazole	Tetra	acycline	Tigecy	ycline	Trim	ethoprim
-	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Austria	45	0	45	8.9	45	17.8	45	24.4	45	0	45	0
Belgium	29	0	29	0	29	6.9	29	0	29	0	29	86.2
Croatia	19	0	19	15.8	19	0	19	0	19	0	19	0
Cyprus	17	11.8	17	29.4	17	23.5	17	29.4	17	0	17	23.5
France	86	0	86	0	86	8.1	86	7	86	0	86	1.2
Germany	80	1.3	80	6.3	80	15	80	11.3	80	0	80	1.3
Greece	43	0	43	14	43	11.6	43	9.3	43	0	43	0
Hungary	57	1.8	57	22.8	57	14	57	17.5	57	5.3	57	3.5
Italy	81	1.2	81	39.5	81	9.9	81	9.9	81	0	81	3.7
Poland	45	0	45	15.6	45	2.2	45	2.2	45	0	45	0
Portugal	38	0	38	18.4	38	5.3	38	2.6	38	0	38	5.3
Romania	46	6.5	46	32.6	46	28.3	46	43.5	46	2.2	46	2.2
Slovenia	15	0	15	0	15	0	15	0	15	0	15	0
Spain	138	2.9	138	11.6	138	8.7	138	8.7	138	0.7	138	2.9
United Kingdom	53	0	53	1.9	53	3.8	53	5.7	53	0	53	0
Total (MSs 15)	792	1.5	792	14.4	792	10.6	792	11.4	792	0.6	792	5.4

Note: All Salmonella isolates tested were susceptible to meropenem N: number of isolates tested; % Res: percentage of microbiologically resistant isolates; MSs: Member States

(a): A number of colistin-resistant isolates are undergoing testing for the presence of *mcr-1* gene. The reported occurrence of colistin resistance is unlikely to equate to the occurrence of *mcr-1*.

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Antimicrobial resistance in certain Salmonella serovars in laying hen flocks

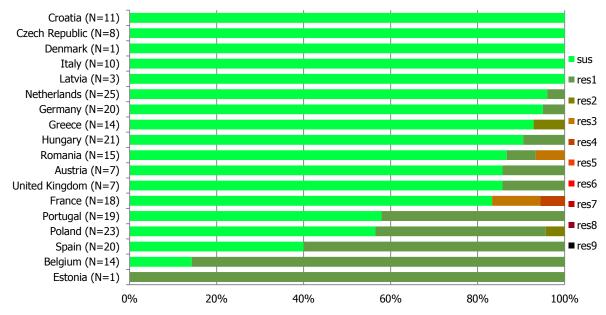
The most commonly reported serovars in laying hen flocks were *S*. Enteritidis (27.3%), *S*. Typhimurium (7.9%) and *S*. Infantis (7.6%) (Table <u>SERLAY</u>). Considering all of the serotyped isolates submitted from laying hens, there were five or fewer isolates for 54 serovars and single isolates belonging to 33 different serovars.

Resistance levels in S. Enteritidis isolates from laying hen flocks

S. Enteritidis was the most common serovar identified (27.3%) from laying hen flocks in 2014. In *S.* Enteritidis isolates from laying hens (17 MSs, Table 18), the overall resistance to ampicillin, chloramphenicol, sulfamethoxazole and tetracycline was at low levels. Resistance to azithromycin and gentamicin was not reported by any of MSs. Overall, resistance to nalidixic acid and ciprofloxacin were moderate in *S.* Enteritidis (15.2% and 14.8%, respectively). 'Microbiological' resistance to cefotaxime and ceftazidime was reported at low levels only by Poland in *S.* Enteritidis.

Multidrug resistance in S. Enteritidis isolates from laying hen flocks

Most of the *S*. Enteritidis isolates (77.1%) were fully susceptible to all 11 antimicrobials included in the MDR analysis for laying hens (17 MSs, N=236) (Figure 41). Multiresistant isolates were only reported by France and Romania. 'Microbiological' co-resistance to ciprofloxacin and cefotaxime was not reported (Tables <u>COMENTERLAY</u>). In layers, resistance to colistin was noted in 31.9% of *S*. Enteritidis isolates.



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

Figure 41: Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in *Salmonella* Enteritidis from laying hens in MSs in 2014

Spatial trends in resistance among S. Enteritidis from laying hen flocks

Low levels of ciprofloxacin resistance (< 10.0%) were reported by two MSs (Hungary and Romania) (Figure 42). The levels of resistance to nalidixic acid in *S*. Enteritidis from laying hens were low in Hungary and Romania, high in Portugal and Poland and very high in Spain (Figure 43). Resistance to cefotaxime was reported by only Poland (Figure 44).





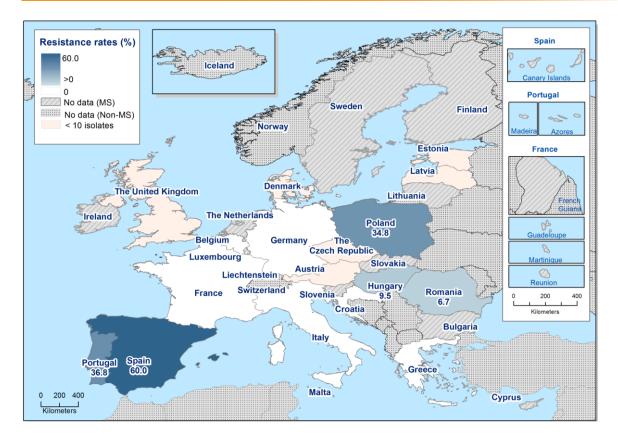


Figure 42: Spatial distribution of ciprofloxacin resistance among *Salmonella* Enteritidis from laying hens in countries reporting MIC data in 2014

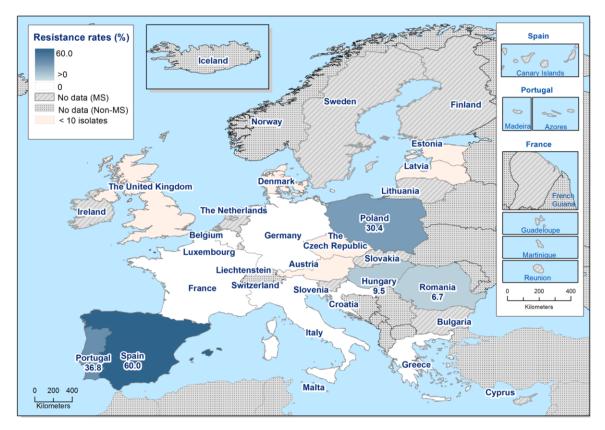


Figure 43: Spatial distribution of nalidixic acid resistance among *Salmonella* Enteritidis from laying hens in countries reporting MIC data in 2014



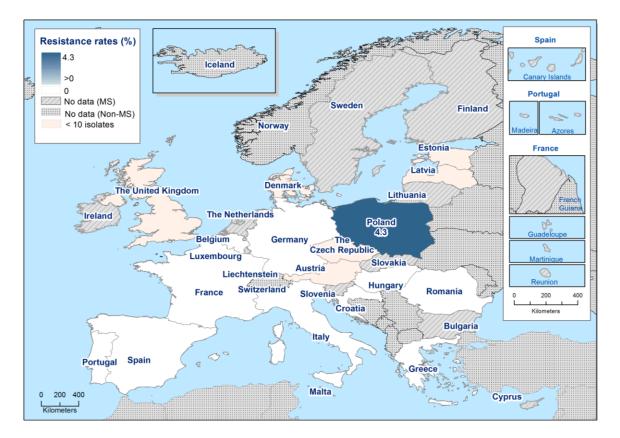


Figure 44: Spatial distribution of cefotaxime resistance among *Salmonella* Enteritidis from laying hens in countries reporting MIC data in 2014

Resistance and multidrug resistance in S. Typhimurium isolates from laying hen flocks

Resistance levels to ampicillin, sulfamethoxazole and tetracycline (overall 18.8–26.6%) in *S***. Typhimurium** isolates from laying hens (Table <u>TYPHILAYD</u>) were found to be moderate to very high levels. The overall resistance to chloramphenicol and trimethoprim was reported at low levels (6.3–4.7%) whereas the resistance to the other antimicrobials tested required by the legislation was not detected.

In laying hen flocks, 16.4% (18 MSs, N=67) of the *S*. Typhimurium isolates were multiresistant. 'Microbiological' co-resistance to ciprofloxacin and cefotaxime was not detected by any of the reporting MSs (Tables <u>COMTYPHILAY</u>).

Resistance and multidrug resistance in monophasic S. Typhimurium isolates from laying hen flocks

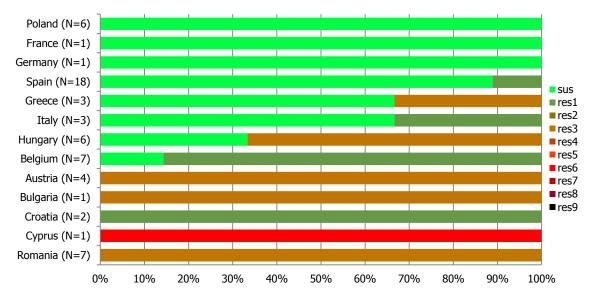
Resistance levels to ampicillin, sulfamethoxazole and tetracycline (overall 37.5–87.5%) in **monophasic** *S.* **Typhimurium** isolates from laying hens (Table <u>MONTYPHILAYD</u>) were observed at very to extremely high levels. Resistance to chloramphenicol and trimethoprim was not reported, whereas resistance to ciprofloxacin and nalidixic acid was registered only in one MS.

In laying hen flocks, 66.7% (three MSs, N=6) of the monophasic *S*. Typhimurium isolates were multiresistant. 'Microbiological' co-resistance to ciprofloxacin and cefotaxime was not detected by any of the reporting MSs (Tables <u>COMMONTYPHILAY</u>).

Resistance and multi-drug resistance in S. Infantis isolates from laying hen flocks

The overall resistances in *S.* Infantis isolates from laying hens (14 MSs, Table 19), were much lower than the one registered in broilers. Only 31.7% of the *S.* Infantis isolates from laying hens (13 MSs, N=60) included in the MDR analysis were multiresistant (Figure 45, Tables <u>COMINFANLAY</u>).



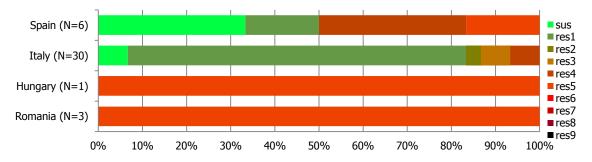


MS: Member State; N: total number of isolates tested for susceptibility against the whole common antimicrobial set for *Salmonella*; sus: susceptible to all antimicrobial classes of the common set for *Salmonella*; res1–res9: resistance to one antimicrobial classes/resistance to nine antimicrobial classes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

Figure 45: Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in *Salmonella* Infantis from laying hens in MSs in 2014

Resistance and multidrug resistance in S. Infantis isolates from laying hen flocks

The overall resistances in *S.* Kentucky isolates from laying hens (five MSs, Table <u>KENTLAYD</u>), were lower than those registered in broilers. 27.5% of the *S.* Kentucky isolates from laying hens (four MSs, N=40) included in the MDR analysis were multiresistant (Figure 46, Tables <u>COMINFANLAY</u>).



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

Figure 46: Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in *Salmonella* Kentucky from laying hens in MSs in 2014



Country	Am	picillin	Azith	romycin	Cefo	taxime	Cefta	zidime	Chloram	phenicol	Ciprof	oxacin	Colis	stin ^(a)
-	Ν	% Res	Ν	% Res	N	% Res	N	Ν	% Res	N	% Res	Ν	% Res	Ν
Austria	7	0	7	0	7	0	7	0	7	0	7	0	7	85.7
Belgium	14	0	14	0	14	0	14	0	14	0	14	0	14	85.7
Croatia	11	0	11	0	11	0	11	0	11	0	11	0	11	0
Czech Republic	8	0	8	0	8	0	8	0	8	0	8	0	8	50.0
Denmark	1	0	1	0	1	0	1	0	1	0	1	0	1	100
Estonia	1	0	1	0	1	0	1	0	1	0	1	100	1	0
France	18	16.7	18	0	18	0	18	0	18	5.6	18	0	18	16.7
Germany	20	0	20	0	20	0	20	0	20	0	20	0	20	35.0
Greece	14	7.1	14	0	14	0	14	0	14	0	14	0	14	0
Hungary	21	0	21	0	21	0	21	0	21	0	21	9.5	21	28.6
Italy	10	0	10	0	10	0	10	0	10	0	10	0	10	80.0
Latvia	1	0	1	0	1	0	1	0	1	0	1	0	1	100
Poland	23	4.3	23	0	23	4.3	23	4.3	23	0	23	34.8	23	0
Portugal	19	5.3	19	0	19	0	19	0	19	0	19	36.8	19	26.3
Romania	15	6.7	15	0	15	0	15	0	15	0	15	6.7	15	6.7
Spain	20	0	20	0	20	0	20	0	20	0	20	60	20	55.0
United Kingdom	7	0	7	0	7	0	7	0	7	0	7	14.3	7	28.6
Total (MSs 17)	210	3.3	210	0	210	0.5	210	0.5	210	0.5	210	15.2	210	31.9

Table 18: Occurrence of resistance to selected antimicrobials in Salmonella Enteritidis isola



EUSR on AMR in zoonotic and indicator bacteria from humans, animals and food 2014

Country	Genta	amicin	Nali	dixic acid	Sulfam	ethoxazole	Tetra	cycline	Tigeo	cycline	Trime	thoprim
-	Ν	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Austria	7	0	7	0	7	14.3	7	0	7	0	7	0
Belgium	14	0	14	0	14	0	14	0	14	0	14	85.7
Croatia	11	0	11	0	11	0	11	0	11	0	11	0
Czech Republic	8	0	8	0	8	0	8	0	8	0	8	0
Denmark	1	0	1	0	1	0	1	0	1	0	1	0
Estonia	1	0	1	100	1	0	1	0	1	0	1	0
France	18	0	18	0	18	16.7	18	16.7	18	0	18	5.6
Germany	20	0	20	0	20	5	20	0	20	0	20	0
Greece	14	0	14	0	14	0	14	7.1	14	0	14	0
Hungary	21	0	21	9.5	21	0	21	0	21	4.8	21	0
Italy	10	0	10	0	10	0	10	0	10	0	10	0
Latvia	1	0	1	0	1	0	1	0	1	0	1	0
Poland	23	0	23	30.4	23	4.3	23	0	23	0	23	0
Portugal	19	0	19	36.8	19	0	19	0	19	0	19	0
Romania	15	0	15	6.7	15	6.7	15	6.7	15	6.7	15	0
Spain	20	0	20	60.0	20	0	20	0	20	0	20	0
United Kingdom	7	0	7	14.3	7	0	7	0	7	0	7	0
Total (MSs 17)	210	0	210	14.8	210	3.3	210	2.4	210	1.0	210	6.2

Note: All Salmonella isolates tested were susceptible to meropenem. N: number of isolates tested; % Res: percentage of microbiologically resistant isolates; MSs: Member States

(a): A number of colistin-resistant isolates are undergoing testing for the presence of *mcr-1* gene. The reported occurrence of colistin resistance is unlikely to equate to the occurrence of *mcr-1*.

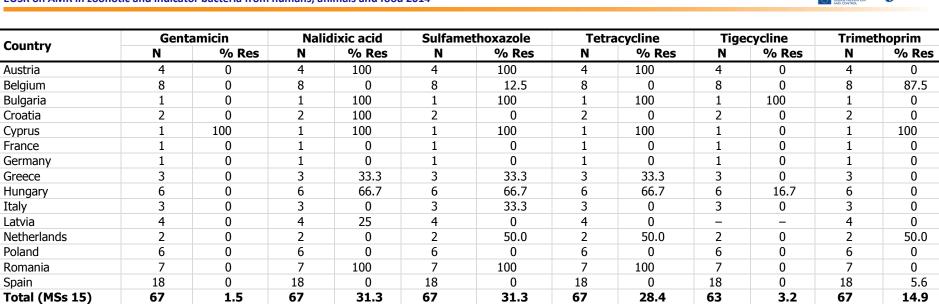
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Countral	Amp	bicillin	Azithr	omycin	Cefo	taxime	Cefta	azidime	Chloran	nphenicol	Cipro	floxacin	Coli	stin ^(a)
Country	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ň	% Res	Ν	% Res
Austria	4	0	4	0	4	0	4	0	4	0	4	100	4	0
Belgium	8	0	8	0	8	0	8	0	8	0	8	0	8	0
Bulgaria	1	0	_	_	1	0	1	0	1	0	1	100	1	0
Croatia	2	0	2	0	2	0	2	0	2	0	2	100	2	0
Cyprus	1	100	1	0	1	0	1	0	1	0	1	100	1	0
France	1	0	1	0	1	0	1	0	1	0	1	0	1	0
Germany	1	0	1	0	1	0	1	0	1	0	1	0	1	0
Greece	3	0	3	0	3	0	3	0	3	0	3	33.3	3	0
Hungary	6	0	6	0	6	0	6	0	6	0	6	66.7	6	0
Italy	3	0	3	0	3	0	3	0	3	0	3	0	3	0
Latvia	4	0	_	_	4	0	4	0	4	0	4	25.0	4	0
Netherlands	2	50.0	2	0	2	0	2	0	2	50	2	0	2	0
Poland	6	0	6	0	6	0	6	0	6	0	6	0	6	0
Romania	7	0	7	14.3	7	0	7	0	7	0	7	100	7	0
Spain	18	5.6	18	0	18	0	18	0	18	0	18	0	18	0
Total (MSs 15)	67	4.5	62	1.6	67	0	67	0	67	1.5	67	31.3	67	0

Table 19: Occurrence of resistance to selected antimicrobials in *Salmonella* Infantis isolates from laying hens in 2014, using harmonised ECOFFs





All Salmonella isolates tested were susceptible to meropenem.

N: number of isolates tested; % Res: percentage of microbiologically resistant isolates; -: no information available; MSs: Member States.

(a): A number of colistin-resistant isolates are undergoing testing for the presence of mcr-1 gene. The reported occurrence of colistin resistance is unlikely to equate to the occurrence of mcr-1.

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Antimicrobial resistance in *Salmonella* spp. in flocks from fattening turkeys

Resistance levels in Salmonella *spp. isolates from fattening turkey flocks*

In 2014, nine MSs reported quantitative MIC data on *Salmonella* spp. isolates from fattening turkeys (Table 20). Most MSs reported high to extremely high levels of resistance to ampicillin, ciprofloxacin, nalidixic acid, sulfamethoxazole and tetracycline, with the notable exception of Germany where no resistance to ampicillin and low levels of resistance to ciprofloxacin and nalidixic acid were registered, although in a low number of 13 isolates. Overall, the levels of resistance to these five antimicrobials ranged between 43.7% and 68.3% (Table 20). Contrasting levels of resistance to chloramphenicol and gentamicin were observed. As in previous years, chloramphenicol resistance was either not recorded or observed at low levels in most MSs, with the exception of Spain which reported high resistance (28.8%). Although moderate to high resistance levels to gentamicin were reported by five MSs, the overall gentamicin resistance was low at 7.7%. Cefotaxime and ceftazidime resistance was not recorded, whereas the overall resistance to azithromycin and tigecycline was low.

Multidrug resistance in Salmonella spp. isoaltes from fattening turkey flocks

Overall, MDR was assessed at 58.1% and the level of MDR varied considerably (from 7.7% to 96.0%) between the 12 MSs which submitted data (N=743) (Figure 51, Tables <u>COMSALMTURK</u>).

Resistance levels in S. Derby and S. Kentucky isolates from fattening turkey flocks

High to extremely high levels of resistance to ampicillin, ciprofloxacin, gentamicin, nalidixic acid, sulfamethoxazole and tetracycline were found in the *S*. **Kentucky** isolates included in the analysis (six MSs, Table 20). In contrast, resistance to azithromycin, cefotaxime, ceftazidime, colistin and trimethoprim was absent. In fattening turkeys, 69.1% of the *S*. Kentucky isolates (six MSs, N=55) included in the MDR analysis were multiresistant and none of these isolates was found fully susceptible (Tables <u>COMKENTURK</u>).

It is notable that isolates from Spain and the United Kingdom represented 96.9% of the *S.* **Derby** isolates and the resistance to the antimicrobial tested varied remarkably between these two MSs (Table 20). Spain reported MDR in all (145) *S.* Derby isolates (Tables <u>COMDERBYTURK</u>).

Temporal trends in resistance among Salmonella *from turkeys*

Six MSs which reported data from 5 years or more were included in the statistical analysis. Statistically significant increasing trends in resistance to ciprofloxacin, nalidixic acid and/or to ampicillin were observed in one MS each. All reporting MSs observed a similarity in their trends in resistance to ciprofloxacin and nalidixic acid. In Poland and Spain, higher levels of resistance to ciprofloxacin than to nalidixic acid were observed in 2014, probably reflecting the spread of plasmid-mediated genes leading to fluoroquinolone resistance. In Poland in 2014, this was a feature in only five isolates, whereas, in Spain, this was observed in 140 isolates, most of which (128 isolates; 91.4%) were *S*. Derby. 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 involved in the analysis.

Spatial trends in resistance among Salmonella spp. from turkeys

The spatial distribution of ciprofloxacin in *Salmonella* spp. isolated from fattening turkeys in 2014 show great variation across the EU (Figure 48). Except for Germany, high to extremely high levels of nalidixic acid resistance were observed across Europe (Figure 49), the highest occurrence being observed in Hungary and Austria. Resistance to cefotaxime was not reported by any of MSs (Figure 50).

Country	Am	picillin	Azithr	omycin	Cefo	taxime	Ceft	azidime	Chloran	nphenicol	Ciprof	loxacin	Colis	stin ^(a)
-	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ň	% Res	Ν	% Res
Salmonella spp.														
Austria	14	50.0	14	0	14	0	14	0	14	0	14	71.4	14	7.1
Czech Republic	19	63.2	19	5.3	19	0	19	0	19	0	19	68.4	19	0
France	58	29.3	58	0	58	0	58	0	58	5.2	58	41.4	58	3.4
Germany	13	0	13	7.7	13	0	13	0	13	0	13	7.7	13	0
Hungary	170	53.5	170	4.1	170	0	170	0	170	2.9	170	90.6	170	0.6
Italy	35	62.9	35	0	35	0	35	0	35	2.9	35	28.6	35	8.6
Poland	29	72.4	29	0	29	0	29	0	29	6.9	29	79.3	29	0
Spain	226	94.7	226	0.9	226	0	226	0	226	28.8	226	92.9	226	2.7
United Kingdom	162	22.8	162	0	162	0	162	0	162	0.6	162	20.4	162	0
Total (MSs 9)	726	58.0	726	1.5	726	0	726	0	726	10.6	726	65.8	726	1.8
<i>Salmonella</i> Kent	ucky													
Cyprus	2	100	2	0	2	0	2	0	2	0	2	100	2	0
Czech Republic	10	100	10	0	10	0	10	0	10	0	10	100	10	0
Hungary	28	100	28	0	28	0	28	0	28	7.1	28	96.4	28	0
Italy	1	100	1	0	1	0	1	0	1	0	1	100	1	0
Poland	9	100	9	0	9	0	9	0	9	0	9	100	9	0
Spain	5	60	5	0	5	0	5	0	5	0	5	100	5	0
Total (MSs 6)	55	96.4	55	0	55	0	55	0	55	3.6	55	98.2	55	0
Salmonella Derb	у													
Czech Republic	1	0	1	0	1	0	1	0	1	0	1	0	1	0
France	3	0	3	0	3	0	3	0	3	0	3	0	3	0
Hungary	2	0	2	0	2	0	2	0	2	0	2	0	2	0
Spain	145	100	145	0.7	145	0	145	0	145	37.9	145	95.2	145	2.1
United Kingdom	41	2.4	41	0	41	0	41	0	41	0	41	0	41	0
Total (MSs 5)	192	76.0	192	0.5	192	0	192	0	192	28.6	192	71.9	192	1.6

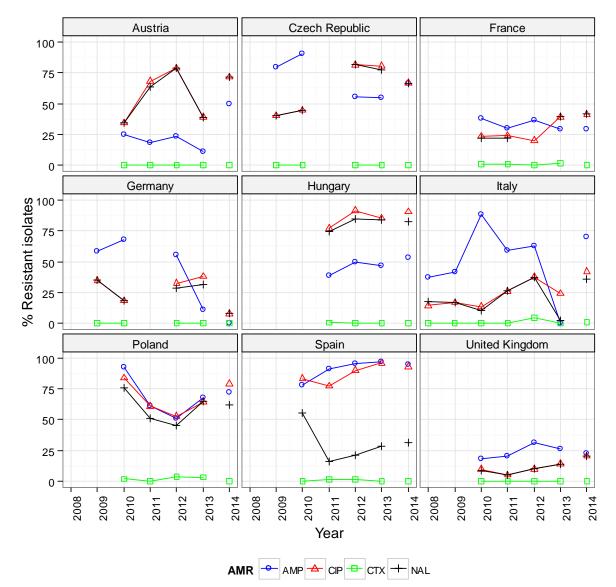
Table 20: Occurrence of resistance to selected antimicrobials in Salmonella spp., Salmonella Kentucky and Salmonella Derby isolates from turkeys in 2014



Country	Gentamicin		Nalidixic acid		Sulfamethoxazole		Tetracycline		Tigecycline		Trimethoprim	
	Ν	% Res	Ν	% Res	Ν	% Res	N	% Res	N	% Res	Ν	% Res
Salmonella spp.												
Austria	14	35.7	14	71.4	14	14.3	14	35.7	14	0	14	14.3
Czech Republic	19	15.8	19	68.4	19	26.3	19	31.6	19	0	19	5.3
France	58	0	58	41.4	58	29.3	58	34.5	58	1.7	58	20.7
Germany	13	0	13	7.7	13	23.1	13	15.4	13	0	13	0
Hungary	170	11.2	170	82.4	170	38.2	170	72.4	170	24.7	170	10.0
Italy	35	31.4	35	22.9	35	62.9	35	71.4	35	0	35	17.1
Poland	29	31.0	29	62.1	29	37.9	29	58.6	29	0	29	0
Spain	226	4.0	226	31	226	73.9	226	96.9	226	0.9	226	69.0
United Kingdom	162	0	162	20.4	162	45.7	162	48.8	162	8	162	7.4
Total (MSs 9)	726	7.7	726	43.7	726	50.4	726	68.3	726	8	726	28.4
Salmonella Kentu	cky											
Cyprus	2	100	2	100	2	100	2	100	2	0	2	0
Czech Republic	10	30	10	100	10	30.0	10	30	10	0	10	0
Hungary	28	67.9	28	96.4	28	67.9	28	71.4	28	3.6	28	0
Italy	1	100	1	100	1	100	1	100	1	0	1	0
Poland	9	77.8	9	100	9	77.8	9	77.8	9	0	9	0
Spain	5	100	5	100	5	100	5	100	5	0	5	0
Total (MSs 6)	55	67.3	55	98.2	55	67.3	55	69.1	55	1.8	55	0
Salmonella Derby												
Czech Republic	1	0	1	0	1	0	1	0	1	0	1	0
France	3	0	3	0	3	66.7	3	66.7	3	0	3	0
Hungary	2	0	2	0	2	0	2	0	2	0	2	0
Spain	145	0	145	6.9	145	100	145	100	145	1.4	145	99.3
United Kingdom	41	0	41	0	41	85.4	41	87.8	41	0	41	0
Total (MSs 5)	192	0	192	5.2	192	94.8	192	95.3	192	1.0	192	75.0

All *Salmonella* isolates tested were susceptible to meropenem. N: number of isolates tested; % Res: percentage of microbiologically resistant; MSs: Member States. (a): A number of colistin-resistant isolates are undergoing testing for the presence of *mcr-1* gene. The reported occurrence of colistin resistance is unlikely to equate to the occurrence of *mcr-1*.





A statistically significant trend was observed for both ciprofloxacin and nalidixic acid in Austria (\uparrow), France (\uparrow), Italy (\uparrow), Poland (\downarrow), Spain (\uparrow) and United Kingdom (\uparrow), for ampicillin in Italy (\uparrow), Poland (\downarrow), Spain (\uparrow) and United Kingdom (\uparrow), and Spain (\downarrow).

Figure 47: Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested *Salmonella* spp. isolates from turkeys in reporting MSs, 2008–2014, quantitative data





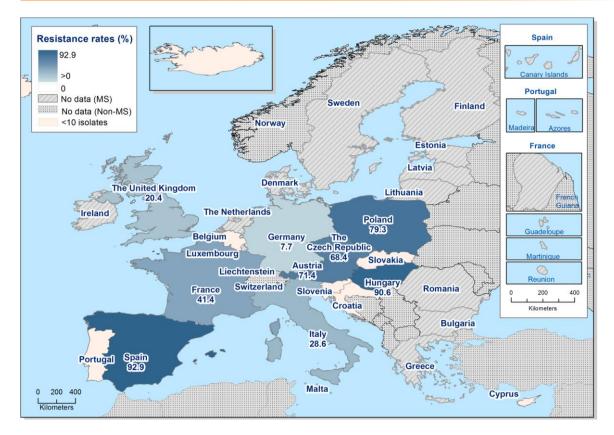


Figure 48: Spatial distribution of ciprofloxacin resistance among *Salmonella* spp. from fattening turkeys in 2014

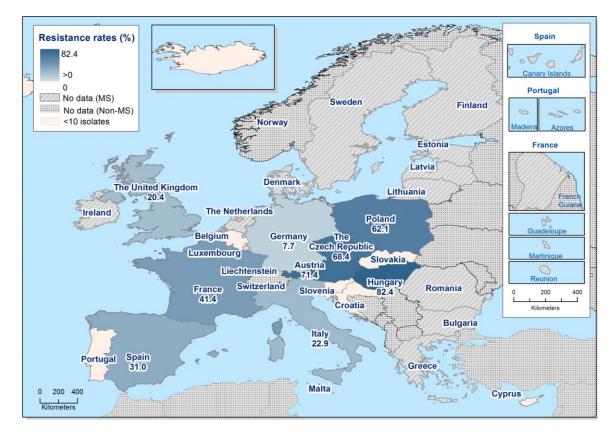


Figure 49: Spatial distribution of nalidixic acid resistance among *Salmonella* spp. from fattening turkeys in 2014



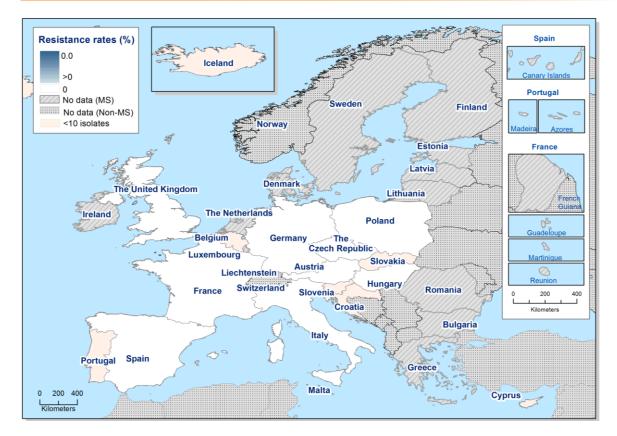
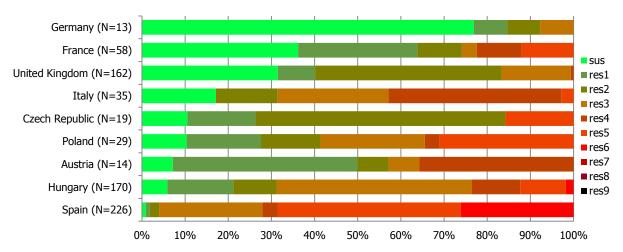


Figure 50: Spatial distribution of cefotaxime resistance among *Salmonella* spp. from fattening turkeys in 2014



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

Figure 51: Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in *Salmonella* spp. from fattening turkeys in 2014



Comparison of 'clinical' and 'microbiological' resistance to cefotaxime

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 may be used for treatment of animals, and the high levels of ciprofloxacin resistance observed among *Salmonella* spp. in some animal species are of concern. It is of note that, according to the EU legislation, antimicrobials shall not be used as a specific method to control *Salmonella* in poultry.

In *Salmonella* spp. from broilers an overall low level of 'microbiological' resistance to cefotaxime (2.3%) was reported, and two MSs (the Netherlands and Italy) recorded moderate and high levels, (17.0% and 27.3%, respectively). Low levels of cefotaxime resistance were reported in Belgium, Cyprus, Malta, Portugal and Spain and cefotaxime resistance was not detected in isolates from 15 reporting countries. Applying the EUCAST CBPs, 'clinical' resistance was found in 8 out of 26 MSs, contributing to an overall low level of 'clinical' resistance to cefotaxime (2.0%). This is despite a moderate occurrence of 'clinical' resistance in isolates from the Netherlands, representing 17.0% of all isolates and a high 'clinical' resistance in isolates from Italy (Table 21:). The 'microbiological' and 'clinical' resistance to cefotaxime in *Salmonella* spp. from laying hens was very low (overall 0.3%), and only three MSs reported low levels of resistance to cefotaxime. Cefotaxime resistance at 'microbiological' levels was not found in the isolates from fattening pigs.

The term 'microbiological' resistance is used when resistance is interpreted using the 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. Plasmid mediated quinolone resistance (PMQR) can be caused by the the action of efflux pumps (*qepA* genes), enzymatic modifications (*aac(6')-Ib-cr* gene, which also confers resistance to kanamycin), and protection of the DNA gyrase (*qnrA*, *qnrB*, *qnrD* and *qnrS* genes) (Cavaco et al., 2009).

The presence of two single point mutations in the QRDR will usually confer 'clinical' resistance to ciprofloxacin (minimum inhibitory concentration (MIC) > 0.064 mg/L) as well as to nalidixic acid (MIC > 16mg/L). In contrast, isolates harbouring only one single point mutation in the QRDR will usually show 'clinical' resistance to nalidixic acid, whereas the susceptibility to ciprofloxacin is reduced to only a 'microbiological' resistance level.

In absence of other mechanisms, the presence of PMQR determinants (i.e. *qnr* genes) in a bacterium, will confer only 'microbiological' resistance to ciprofloxacin, but the isolate will be susceptible to nalidixic acid.



Table 21: Occurrence of resistance to	cefotaxime among Salmonella spi	p. from broilers, lay	aying hens and fattening	turkeys in 2014, using harmonised
ECOFFs and EUCAST CBPs				

Country	Broilers						Laying hens					Fattening turkeys				
	N	n res ECOFF	% res ECOFF	n res CBP	% res CBP	N	n res ECOFF	% res ECOFF	n res CBP	% res CBP	N	n res ECOFF	% res ECOFF	n res CBP	% res CBP	
Austria	113	0	0	0	0	45	0	0	0	0	14	0	0	0	0	
Belgium	170	7	4.1	4	2.4	29	0	0	0	0	6	0	0	0	0	
Bulgaria	17	0	0	0	0	3	0	0	0	0	-	_	-	_	-	
Croatia	126	0	0	0	0	19	0	0	0	0	7	0	0	0	0	
Cyprus	45	4	8.9	4	8.9	17	0	0	0	0	5	0	0	0	0	
Czech Republic	212	1	0.5	1	0.5	8	0	0	0	0	19	0	0	0	0	
Denmark	26	0	0	0	0	2	0	0	0	0	-	_	-	_	-	
Estonia	-	-	-	_	-	2	0	0	0	0	-	_	-	_	-	
Finland	-	-	_	_	_	1	0	0	0	0	-	—	-	_	-	
France	36	0	0	0	0	86	1	1.2	1	1.2	58	0	0	0	0	
Germany	28	0	0	0	0	80	0	0	0	0	13	0	0	0	0	
Greece	20	0	0	0	0	43	0	0	0	0	-	_	-	_	-	
Hungary	169	0	0	0	0	57	0	0	0	0	170	0	0	0	0	
Ireland	17	0	0	0	0	-	-	-	-	-	-	_	-	_	-	
Italy	66	18	27.3	18	27.3	81	0	0	0	0	35	0	0	0	0	
Latvia	-	-	_	_	-	9	0	0	0	0	-	_	-	_	-	
Malta	60	2	3.3	0	0	5	0	0	0	0	-	_	-	_	-	
Netherlands	88	15	17.0	15	17.0	44	0	0	0	0	7	0	0	0	0	
Poland	85	0	0	0	0	45	1	2.2	1	2.2	29	0	0	0	0	
Portugal	51	1	2.0	1	2.0	38	0	0	0	0	1	0	0	0	0	
Romania	554	2	0.4	2	0.4	46	1	2.2	1	2.2	-	_	-	_	-	
Slovakia	20	0	0	0	0	4	0	0	0	0	1	0	0	0	0	
Slovenia	85	0	0	0	0	15	0	0	0	0	4	0	0	0	0	
Spain	135	3	2.2	2	1.5	138	0	0	0	0	226	0	0	0	0	
Sweden	2	0	0	0	0	2	0	0	0	0	-	_	-	_	-	
United Kingdom	168	0	0	0	0	53	0	0	0	0	162	0	0	0	0	
Total (MSs 26)	2,293	53	2.3	47	2.0	872	3	0.3	3	0.3	757	0	0	0	0	
Iceland	16	0	0	0	0	-	_	-	_	_	-	_	_	_	-	

ECOFFs: epidemiological cut-off values; EUCAST: European Committee on Antimicrobial Susceptibility Testing; N: number of isolates tested; n: number of isolates resistant; % res: percentage of resistant isolates; CBP: cllinical breakpoint.



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>HIGHSALMBRMEAT</u>, <u>HIGHSALMTURKMEAT</u>, <u>HIGHSALMLAY</u> and <u>HIGHSALMTURK</u>.

Most of the *Salmonella* isolates that displayed high-level resistance to ciprofloxacin originated from fattening turkeys (7.3%), broiler meat (4.6%) and broilers (4.2%). No isolates from turkey meat displayed high-level resistance; only eight *S*. Kentucky and one *S*. Kottbus isolates from laying hens from Hungary, Romania and Spain exhibited such high-level resistance, comprising 1.4% of all *Salmonella* isolates from layers.

One quarter of the *Salmonella* spp. isolates from broilers included in the analysis originated from Romania, where 9.4% of the isolates showed high-level resistance (mainly *S*. Kentucky) (Table <u>HIGHSALMBR</u>). Among the other 19 MSs included in the analysis of broiler isolates, high-level resistance was reported by Bulgaria (5.9%, N=17), Croatia (0.8%, N=126), Cyprus (17.8%, N=45), the Czech Republic (1.4%, N=212), Hungary (1.2%, N=169), Poland (1.2%, N=85) and Spain (17.0%, N=135). Reflecting the generally lower levels of resistance in *Salmonella* from laying hens, high-level ciprofloxacin resistance was observed in only three of the 12 included MSs: Hungary (1.8%, N=57), Romania (8.7%, N=46) and Spain (2.9%, N=138). In addition, from Hungary and Spain, isolates from broiler meat (4.3%, N=47 and 18.5%, N=130) displayed high-level ciprofloxacin resistance.

In fattening turkeys, high-level ciprofloxacin resistance was observed in the Czech Republic (52.6%, N=19), Hungary (15.3%, N=170), Italy (2.9%, N=35), Poland (34.5%, N=29) and Spain (2.7%, N=226) (Table <u>HIGHSALMTURK</u>).

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 *S*. Kentucky isolates from *Gallus gallus* in Cyprus, Hungary, Italy, Romania and Spain and turkeys in the Czech Republic, Hungary, Italy, Poland and Spain and in broiler meat from Hungary and Spain. Most of the *S*. Kentucky isolates with high-level ciprofloxacin resistance (n=161) were multiresistant (73.3%), and most isolates (65.3%) were also resistant to gentamicin, ampicillin, nalidixic acid, sulfamethoxazole and tetracycline often also streptomycin (Gen-Cip-Amp-Nal-Smx-Tet). Resistance to several, or even all, other antimicrobials included in the MDR analysis were also observed. Only Spain reported one isolates of *S*. Kentucky showed only high-level resistance to ciprofloxacin and nalidixic acid resistance but were otherwise susceptible to the antimicrobials tested.

Estonia reported high-level ciprofloxacin resistance in a single isolate of *S*. Worthington from a pig.

S. Infantis also displayed high-level resistance to ciprofloxacin (n=11), and was encountered in broilers from Bulgaria, Croatia, Cyprus, the Czech Republic and Romania and broiler meat from Hungary. 91.0% of the isolates were multiresistant and, besides the high-level ciprofloxacin resistance, most *S*. Infantis isolates were also resistant to nalidixic acid, sulfamethoxazole, tetracycline and, in most cases, trimethoprim and ampicillin. **S. Enteritidis** was reported in broilers by Poland (n=1) and Romania (n=3), whereas a single isolate of the serovar *S*. Kottbus was reported from laying hens and **S. Bonariensis** was reported from fattening turkeys.

Multidrug resistance patterns 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 AMR. 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.

The patterns of AMR exhibited by all reported *Salmonella* isolates revealed numerous combinations of resistance to the nine different antimicrobial agents included in the analysis. The reported MSs occurrence of specific MDR profiles in meat and animals are presented in the MDR patterns tables. In broiler flocks, eight serovars (Infantis, Enteritidis, Mbandaka, Kentucky, Senftenberg, Typhimurium, Agona and Montevideo) accounted for 74.1% of *Salmonella* spp. (Table <u>SERBR</u>). A further 102 serovars were reported from broilers and 44 of these were represented by only single isolates. In laying hen flocks, eight serovars (Enteritidis, Typhimurium, Infantis, Kentucky, Montevideo, Mbandaka, Senftenberg and Livingstone) accounted for 62.3% of *Salmonella* spp (Table <u>SERLAY</u>). There were a further 75 serovars reported from laying hen flocks. In fattening turkey flocks, eight serovars (Derby, Kentucky, Newport, Hadar, Infantis, Saintpaul, Bredeney and Stanley) accounted for 68.1% of *Salmonella* spp. (Table <u>SEROFATTURK</u>). There were a further 40 serovars reported from fattening turkeys.

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, where 982/2223 (44.2%) of isolates were MDR (Table MULTISALMBR) and broiler meat where 148/564 (26.2%) of isolates were MDR (Table MULTISALMBRMEAT), the most common resistance pattern was a combination of ciprofloxacin/nalidixic acid, sulfamethoxazole and tetracycline, followed by the same pattern with the addition of tigecycline, both patterns accounting for 22.4% of the broiler isolates and 19.2% of the broiler meat isolates included in the analysis. The majority of isolates with these patterns of resistance both from broilers (95.8% of isolates with this pattern) and from broiler meat (95.4% of isolates with this pattern) were S. Infantis. These resistant profiles were predominately reported in broilers by Austria (98.2%), the Czech Republic (81.4%), Hungary (83.9%) and Slovakia (84.6%) and in meat from broilers by Austria and the Czech Republic (100%), Hungary (89.2%), Slovakia (77.8%) and Slovenia (92.9%). In laying hens the most common resistance pattern was the same as in broilers: ciprofloxacin/nalidixic acid, sulfamethoxazole and tetracycline, followed by ampicillin, ciprofloxacin/nalidixic acid and tetracycline (Table MULTISALMLAY). As in broilers, most of the isolates (15/17, 88.2%) with resistance to ciprofloxacin/nalidixic acid, sulfamethoxazole and tetracycline were S. Infantis.

In turkeys, where 432/726 (59.5%) of isolates were MDR, three serovars accounted for more than 50% of the MDR isolates, namely *S*. Derby (n=145 MDR isolates), *S*. Infantis (n=46 MDR isolates) and *S*. Kentucky (n=38 MDR isolates). The most common patterns were related to single MSs such as the most common pattern: ampicillin, ciprofloxacin/nalidixic acid, sulfamethoxazole, tetracycline and trimethoprim being reported by Spain (representing 94.7% of total isolates reported with this pattern). Most (92.6%) of the isolates with this MDR pattern were *S*. Derby. The second and third most common patterns were mainly reported also by Spain: ampicillin, ciprofloxacin/nalidixic acid, sulfamethoxazole, tetracycline and tetracycline (55.7%), and the MDR pattern ampicillin, chloramphenicol, ciprofloxacin/nalidixic acid, sulfamethoxazole, tetracycline and trimethoprim (98.2%). In turkey meat, where 73/226 (32.3%) of isolates were MDR, the two most common resistance patterns were ampicillin, chloramphenicol, sulfamethoxazole, tetracycline, trimethoprim and ampicillin, ciprofloxacin/nalidixic acid, tetracycline, each accounting for 17.8% of the total number of MDR isolates from turkey meat (Table <u>MULTISALMTURKMEAT</u>).

Salmonella Enteritidis

Information on MDR was sparsely available for S. Enteritidis isolates and only reported from broilers (16/74,21.6%) of isolates showed MDR and 16/305 (5.2%) of total S. Enteritidis isolates reported with MDR isolates originating from Poland, from broilers, Portugal and Romania (Table MULTIENTERBR) and laying hens (4/33,12.1%) of isolates showed MDR and 4/210 (1.9%) of total S. Enteritidis isolates reported from laying hens, MDR isolates from France and Romania (Table MULTIENTERLAY). One isolate from laying hens showed resistance to ampicillin, chloramphenicol, sulfamethoxazole, tetracycline and trimethoprim. In broilers, 11/72 (15.3%) of isolates were resistant to 5 or more antimicrobials, although MDR remains uncommon in S. Enteritidis isolates. Most of the S. Enteritidis isolates from broilers (70.1%), broiler meat (64.0%) and laying hens (77.1%) were fully susceptible to the 11 antimicrobials addressed in the analysis. 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 travel-related cases in the United Kingdom (Rodriquez et al., 2012). Streptomycin is however no longer included in the monitoring.

Salmonella Typhimurium

MDR *S.* Typhimurium isolates were reported in turkey meat (9 isolates were MDR out of 9 *S.* Typhimurium isolates reported) (Table <u>MULTITYPHITURKMEAT</u>), broilers (27 isolates were MDR out of 87 *S.* Typhimurium isolates reported, 31.0%) (Table <u>MULTITYPHIBR</u>), laying hens (11 isolates were MDR out of 64 *S.* Typhimurium isolates reported, 17.2%) (Table <u>MULTITYPHILAY</u>) and fattening turkeys (9 isolates were MDR out of 21 *S.* Typhimurium isolates reported, 42.9%) (Table <u>MULTITYPHITURK</u>). A wide range of different MDR patterns were reported in all sources. The most frequent MDR pattern was resistance to ampicillin, sulfamethoxazole and tetracycline in most sources. However, penta-, hexa- and hepta-valent resistance were reported in few isolate from broilers and one from fattening turkeys. Resistance to cefotaxime/ceftazidime was reported with only one isolate from broilers but was absent in all other sources. Ciprofloxacin resistance was not reported in *S.* Typhimurium MDR isolates form laying hens.

Monophasic Salmonella *Typhimurium*

The MDR patterns for monophasic *S.* Typhimurium isolates were reported from broilers (23 isolates were MDR out of 34 isolates reported, 67.6%) (Table <u>MULTIMONTYPHIBR</u>) and laying hens (3 isolates were MDR out of 8 isolates reported, 37.5%) (Table <u>MULTIMONTYPHIBR</u>). The most frequent core pattern of resistance observed was resistance to ampicillin, sulfamethoxazole and tetracycline occurring in all MDR isolates from broilers laying hens.

Salmonella Kentucky

The patterns of MDR for *S.* Kentucky isolates were reported from meat from broilers (5 isolates were MDR out of 33 isolates reported, 15.2%) (Table <u>MULTIKENBRMEAT</u>), meat from turkeys (4 isolates were MDR out of 7 isolates reported, 57.1%) (Table <u>MULTIKENTUCKYTURKMEAT</u>), broilers (70 isolates were MDR out of 115 isolates reported, 60.9%) (Table <u>MULTIKENTBR</u>), laying hens (11 isolates were MDR out of 44 isolates reported, 25.0%) (Table <u>MULTIKENTLAY</u>) and fattening turkeys (38 isolates were MDR out of 55 isolates reported, 69.1%) (Table <u>MULTIKENTURK</u>). About 55.7% of the isolates from broilers had the core pattern of pentavalent resistance to ampicillin, ciprofloxacin/nalidixic acid, gentamicin, sulfamethoxazole and tetracycline reported by the Cyprus, the Czech Republic, Hungary, Romania and Spain. This core pentavalent resistance pattern was most observed also in isolates in laying hens, fattening turkeys and turkey and broiler meat.

Salmonella Infantis

MDR patterns for *S*. Infantis were available from broiler meat (118 isolates were MDR out of 147 isolates reported, 80.3%) (Table MULTIINFANBRMEAT), turkey meat (7 isolates were MDR out of 9 isolates reported, 77.8%) (Table MULTIINFANBRMEAT), broilers (649 isolates were MDR out of 796 isolates reported, 81.5%) (Table MULTIINFANBR), laying hens (18 isolates were MDR out of 64 isolates reported, 28.1%) (Table MULTIINFANBR), laying hens (18 isolates were MDR out of 53 isolates reported, 86.8%) (Table MULTIINFANLAY) and fattening turkeys (46 isolates were MDR out of 53 isolates reported, 86.8%) (Table MULTIINFANTURK). In fattening turkeys most of the isolates originated from Hungary (90.2%). *S*. Infantis displayed a wide range of different MDR patterns; however, almost all MDR patterns (> 97%) included resistance to ciprofloxacin and/or nalidixic acid, as well as resistance to sulfamethoxazole and tetracycline. Resistance to ciprofloxacin/nalidixic acid, sulfamethoxazole and tetracycline was the most common pattern in *S*. Infantis from broiler meat (74.6%), broilers (54.6%), laying hens (78.9%) and fattening turkeys (43.5%). All other multiresistant *S*. Infantis isolates having resistance to cefotaxime and/or ceftazidime originated from Cyprus (16.7%, n=3) and Italy broilers (60.0%, n=18).



3.1.3. Discussion

Antimicrobial resistance in *Salmonella* in humans

Although there has been a significant decline in human salmonellosis cases from 2007 to 2014, 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 be mainly attributed to the reduction in the prevalence of *Salmonella* in flocks of laying hens and 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, 2015).

In 2014, information on AMR in *Salmonella* isolates from human cases was reported by 21 MSs and one non-MS. Resistance in human *Salmonella* isolates was high to ampicillin, sulfamethoxazole and tetracycline, and moderate to high for nalidixic acid. These antimicrobials or other agents of the same class are used commonly for treating infections in animals and humans (although not usually for treating *Salmonella* infections in humans). For ampicillin, sulfonamides and tetracyclines, 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).

Because of the compulsory AST of isolates from poultry and poultry products in 2014, the human data analysis also focused on the serovars that are the most frequent and/or have the highest resistance levels among serovars found in poultry, besides S. Typhimurium and monophasic S. Typhimurium. Among these, human S. Kentucky isolates exhibited very high to extremely high resistance levels to ampicillin, ciprofloxacin, gentamicin, nalidixic acid, sulfamethoxazole and tetracycline, which is consistent with the dissemination of the ciprofloxacin-resistant S. Kentucky ST198 strain in Europe, and elsewhere, since 2010 (Le Hello et al., 2013). Resistance to nalidixic acid and ciprofloxacin was commonly associated with S. Infantis and S. Enteritidis. Resistance to third-generation cephalosporins was also more common in S. Infantis and particularly high levels were observed in Italy which is due to the circulation of a multiresistant and ESBL-producing (CTX-M type) clone of S. Infantis in Italy (Ida Luzzi, Istituto Superiore di Sanità, personal communication, August 2015). Based on the animal and food data, this clone also seems to prevail in Italian broilers. Resistance to colistin was commonly detected in S. Enteritidis both among human and poultry isolates. It has been suggested that elevated resistance to colistin is an intrinsic trait among some serovars, including S. Enteritidis (Agersø et al, 2012). As the CBP is at the same concentration as the ECOFF applied in the analysis, the observed colistin resistance is of concern since the last-resort drug might no longer be effective for treating severe human infections with the most common Salmonella serovar.

For the 2014 report, ECDC and EFSA agreed to include the same antimicrobial classes in the MDR analysis for better comparison between the two sectors. For the human data analysis, this meant including also carbapenems which had not been possible in 2013 when too few countries reported on this class. Among the ten MSs reporting on all nine antimicrobial classes in 2014, slightly more than half of the human isolates were susceptible to all of them. About 30% of the isolates exhibited MDR, i.e. they were non-susceptible to at least three different antimicrobial classes. Isolates from one country (France) exhibited much higher MDR levels (> 60%) which could be a bias introduced by sampling and testing strategies, e.g. an overrepresentation of serovars with high MDR due to targeted surveillance (e.g. of *S.* Kentucky), and testing of the full panel only on isolates expressing resistance to ampicillin. Among separate serovars, MDR was extremely high in *S.* Kentucky, very high in monophasic *S.* Typhimurium and *S.* Infantis, whereas being low in *S.* Enteritidis and *S.* Derby.

Clinical and microbiological co-resistance to the critically important therapeutic antimicrobials ciprofloxacin and cefotaxime were reported from six and seven countries, respectively, out of the ten included in the MDR analysis, and represented 0.5% and 0.6% of reported isolates. This was higher than in 2013, most likely due the lowered CBP for ciprofloxacin as the proportion of cefotaxime resistance remained the same in both years. MSs are encouraged to monitor for resistance to reserve agents, such as meropenem, colistin, azithromycin and tigecycline 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 2014. Whereas 15 countries were reporting data on meropenem in 2014, only two to four countries reported



data on the other last-resort drugs, probably because the EU protocol for harmonised monitoring of AMR in human *Salmonella* and *Campylobacter* isolates lists meropenem among the priority antimicrobials and the others as optional (ECDC, 2014). 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 food-producing 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 terms of data quality and comparability, major improvements in harmonising data between countries and across sectors have been made in the last two reports. In the data collection for the 2013 report, for the first time, countries could report measured values (quantitative AST data as opposed to interpreted categories) to ECDC, and seven countries were then able to submit Salmonella data in this way. For 2014, 12 countries were able to provide quantitative AST data, with four countries changing from qualitative reporting and one country reporting AST data for the first time. The quantitative 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 'nonsusceptible' group. 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' category. Thus, this approach further improves the comparability of human and nonhuman data. For countries submitting categorical data, only four were using other criteria than EUCAST or did not communicate which criteria they were using. For future reports, EFSA and ECDC hope that more countries will report measured values. More harmonisation is also needed when it comes to the selection of isolates for testing and reporting at the EU level, as, in many countries, the sampling and the antimicrobials tested for a particular selection are not random and represent different fractions of all isolates identified in a country.

In 2014, some aspects of the reported human data remained difficult to interpret. For some countries, the reported percentage of isolates resistant to ciprofloxacin was very low whereas the reported percentage resistant to nalidixic acid was high. Whereas the proportion of isolates resistant to fluoroquinolones might be expected to be slightly lower compared to quinolones, this difference was considerable in some countries, and in two countries even as large as 20-fold and more than 100-fold. Perhaps, some countries using disk diffusion (which applied to the majority of the human laboratories) had not yet adopted the EUCAST recommendation, issued in early 2014, to screen for pefloxacin susceptibility instead of ciprofloxacin in order to detect low-level fluoroquinolone resistance. It could also be that some countries reporting interpreted results had not yet adapted to the new, significantly lower CBP for ciprofloxacin, which was also introduced in 2014. The EU protocol will be updated on these two points.

Antimicrobial resistance in Salmonella from poultry and meat thereof

In *Salmonella* isolates from poultry and meat, harmonised isolate-based data were reported by 27 MSs and one non-MS in 2014. The isolate-based data enable the analysis of MDR patterns, high level of resistance to ciprofloxacin and co-resistance to ciprofloxacin and cefotaxime, agents critically important for treating human salmonellosis. 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 subdivision of resistance data allows for more accurate analysis and as required by the legislation, all MSs included information on serovars and production type.

In 2014, MSs collected *Salmonella* isolates for susceptibility testing according to the new harmonised monitoring plan (Commission implementing Decision 2013/652/EU). In line with this decision, the antimicrobial agents included in the test panels were changed; most importantly, testing of resistance to streptomycin was not required, which had an impact on how MDR patterns were interpreted. The animal and meat sections in this chapter focus primarily on *Salmonella* from poultry and poultry meat, reflecting the monitoring plan for 2014 set out in the Decision.

Antimicrobials such as ampicillin, sulfamethoxazole and tetracycline 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, sulfamethoxazole and tetracycline, as well as to chloramphenicol, were recorded in *Salmonella* isolates from fattening turkeys and meat



from turkeys. Considering all reporting MSs, isolates from laying hens displayed the lowest levels of resistance to these antimicrobials. Levels of resistance were generally higher in *S*. Enteritidis from broiler flocks than from laying hen flocks, particularly in the case of resistance to chloramphenicol, tetracycline and sulfamethoxazole. This may reflect that laying hens are usually less frequently treated with antimicrobials than broilers, although trimethoprim showed the reverse pattern. 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 in layers may reflect that this is one of the compounds available (although it is also available for the treatment of broilers) or may possibly reflect an association of particular *S*. Enteritidis phage types which show low-level ciprofloxacin resistance with laying hens.

Colistin-resistant *Salmonella* isolates were detected by several MSs originating from broilers, laying hens and fattening turkeys. Further information is provided in the Summary/Main findings section.

The occurrence of resistance to fluoroquinolones (ciprofloxacin) was in general particularly related to certain animal species and sources – fattening turkeys, broilers, and meat thereof – combined with a clearly defined geographical distribution, including the following countries: Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Hungary, Italy, Malta, Poland, Portugal, Romania, Slovenia, Slovakia and 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 suggestive 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). Although genetic typing of isolates would be required for definitive confirmation, the predominance of particular MDR or other resistance patterns in isolates of Infantis and Kentucky as well as published national reports also support clonal expansion.

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. In the single MS where it was detected (Spain), co-resistance to these antimicrobials occurred in a single *S*. Kentucky isolate from broilers, which showed high-level resistance to fluoroquinolones.

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 also reported probably indicating the occurrence of plasmid-mediated *qnr* genes leading to fluoroquinolone, but not nalidixic acid, resistance. This was particularly a feature of *Salmonella* isolates from broilers in Malta, Portugal and Spain and from turkeys in Hungary and Spain, although it was also present to a lesser extent in isolates from layers from some MSs.

MDR, defined as resistance to three or more of eleven antimicrobial classes, was generally higher in *Salmonella* spp. from broilers (46.3% of isolates) and turkeys (59.5% of isolates) than in layers (11% of isolates). In broilers, the proportion of all isolates showing MDR, was greatly influenced by the occurrence of MDR *S*. Infantis, this serovar accounting for approximately 31% of the MDR isolates in broilers. Particular MDR patterns were associated with *S*. Infantis and because this serovar was prevalent in many countries, these patterns greatly influenced the overall resistance figures. This is exemplified by resistance to ciprofloxacin/nalidixic acid, sulfamethoxazole and tetracycline which occurred as an MDR pattern without additional resistances in 355/762 (46.5%) of *S*. Infantis isolates; Infantis represented 762/2,122 (35.9%) of all *Salmonella* isolates examined from broilers. 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 multiresistant strains of *Salmonella* occurring in several MSs. High-level ciprofloxacin resistance (MIC > 4) was observed in multiresistant *S.* Kentucky isolates from broilers, laying hens and turkeys, and in *S.* Infantis from broilers. It was displayed by much lower numbers of other serovars (Enteritidis, Bonariensis, Kottbus) and was also detected in *S.* Kentucky from broiler and turkey meat, and in *S.* Infantis from broiler meat. The MSs reporting high levels of ciprofloxacin-resistant *S.* Kentucky and *S.* Infantis isolates in 2014 also reported similar findings in 2013 (the Czech Republic, Hungary, Romania and Spain); however, more MSs provided in 2014 isolate data suitable for the analysis of high-level ciprofloxacin resistance, therefore more MSs found isolates with high-level resistance to ciprofloxacin. High-level ciprofloxacin



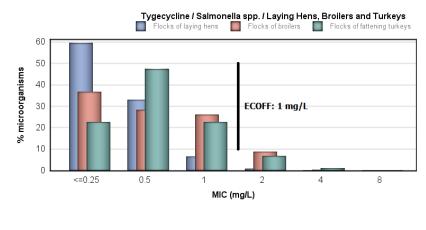
resistance is usually related to chromosomal mutations and therefore provides strong evidence for clonal expansion of particular strains of *Salmonella*.

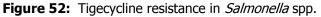
There were no *Salmonella* isolates recovered from poultry in 2014 which were resistant to carbapenems, a class of antimicrobials which is not used therapeutically in food-producing animals, but which is reserved for use in man. Supplementary testing of those *Salmonella* isolates which were resistant to the indicator cephalosporins (cefotaxime and ceftazidime) with a further panel of antimicrobials revealed the presence of isolates with ESBL, AmpC and combined ESBL plus AmpC phenotypes. Most MSs reported low numbers of isolates with these phenotypes, though in two MSs, two serovars (Infantis with an ESBL phenotype in Italy; Heidelberg with an ampC phenotype in the Netherlands) contributed to moderate or high levels of cephalosporin resistance in *Salmonella* from broilers. The occurrence of *S*. Infantis with an ESBL phenotype and *S*. Heidelberg with an AmpC phenotype in restricted geographical regions of Europe suggests clonal expansion and spread within broilers in these regions.

Within a given MS, any attempt to relate AMR in human *Salmonella* isolates to AMR 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.

Tigecycline resistance in *Salmonella* spp.

Microbiological resistance to tigecycline was reported in 9.3% of 2,293 *Salmonella* spp. from broilers, 0.6% of 872 isolates from laying hens and 8% of 757 isolates from turkeys. There was a marked association of tigecycline microbiological resistance with *S*. Infantis in poultry and most microbiologically resistant strains had MICs just above the ECOFF at 2 or 4 mg /l. The maximal MIC of 8 mg/l was observed in only two isolates (*S*. Infantis from layers and *S*. Tennessee from broilers). Resistance to tigecycline in *Salmonella* is thought to be mediated by increased activity of efflux pumps, principally through modifications to the expression of efflux pump regulatory genes and this may explain the distribution of MICs which was obtained. However, determining the susceptibility of tigecycline is not entirely straightforward as the method can be affected by oxidation of the test reagents and the results are being further investigated by the EU-RL for AMR in case methodological issues have influenced the monitoring results in 2014.







3.2. Antimicrobial resistance in *Campylobacter*

Human infections with *Campylobacter*

Campylobacter causes many 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, 2015). In 2014, 241,170 laboratory-confirmed cases of campylobacteriosis were reported in the EU/EEA. *C. jejuni* and *C. coli* accounted for 99.7% of cases with species information. Patients may experience mild to severe illness. Symptoms may include (bloody) diarrhoea, abdominal pain, fever, headache and nausea. The mean duration of illness is 2 to 5 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 required, 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.

In 2014, 13 MSs and Norway provided data on human *Campylobacter* isolates for 2014. Eight countries (Austria, Estonia, Italy, Luxembourg, Norway, Portugal, Romania and Slovenia) reported quantitative isolate-based AST results as measured values of either inhibition zone diameters or MICs. Six countries reported case-based AST results interpreted as susceptible (S), intermediate (I) or resistant (R) according to the CBPs applied. Countries reporting resistance in *Campylobacter* from humans in 2014 are presented in Tables <u>CAMPJEOVERVIEW</u> and <u>CAMPCOOVERVIEW</u>. The report only addressed data on *C. jejuni* and *C. coli* for comparison with AST data on food-producing animals and food, and as these *Campylobacter* species are the most commonly identified cause of campylobacteriosis in humans in the EU. Quantitative isolate-based data on AMR in *Campylobacter* isolates from poultry and meat derived thereof were reported by 26 MSs and two non-MSs Iceland and Switzerland. 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* (Tables <u>CAMPJEOVERVIEW</u> and <u>CAMPCOOVERVIEW</u> and <u>CAMPCOOVERVIEW</u>).

3.2.1. Antimicrobial resistance in *Campylobacter* isolates from humans

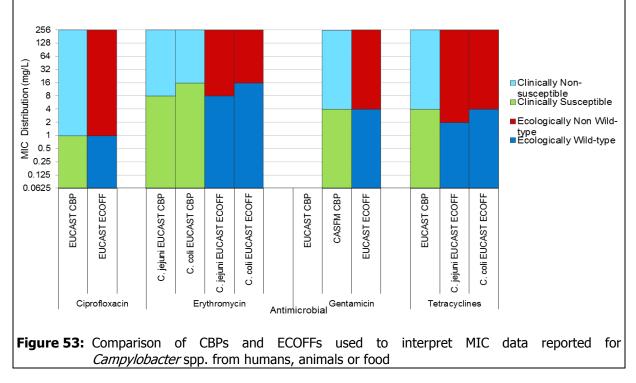
Since resistance levels differ substantially between *C. jejuni* and *C. coli*, data are reported separately for the two species. Results are presented for the three first-priority antimicrobials currently included in the harmonised panel of antimicrobials to be tested with *Campylobacter* isolates from humans (ciprofloxacin, erythromycin and tetracycline) and for two optional agents (co-amoxiclav and gentamicin) (ECDC, 2014). 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: all countries except one tested all three priority antimicrobials, seven also tested gentamicin and three tested co-amoxiclav.

Interpretation of data must take account of the wide variation in the numbers of *Campylobacter* isolates reported by MSs. Whereas this may in part be related to true differences in the incidence of campylobacteriosis, it is also likely to be greatly influenced by practices 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 4, Material and methods chapter. Quantitative data were interpreted by ECDC based on the EUCAST epidemiological cut-off (ECOFF) values, where available. In the absence of ECOFFs, CBPs from the French Society for Microbiology (CA-SFM) were applied. For the qualitative SIR data, the intermediate and resistant results were combined into a 'non-susceptible' category. For the four antimicrobials reported for both human and animal/food isolates, the commonly used interpretive criteria were aligned (Figure 53). 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 total concordance across interpretive categories, except for the EUCAST CBP for *C. jejuni* for tetracyclines, which is one doubling dilution higher than the EUCAST ECOFF.



Antimicrobial resistance in *Campylobacter jejuni* from humans

Resistance levels in Campylobacter jejuni isolates from humans

As in previous years, *C. jejuni* was the most common *Campylobacter* species identified in 2014, with 102,663 cases reported in the EU/EEA. AST data were reported for 12.3% of these cases in 2014 by 13 MSs and Norway. A very high proportion (60.2%) of human isolates were resistant to ciprofloxacin in 2014 (13 MSs, Table 22) with extremely high proportions observed in several countries, most noticeably in Portugal (97.9%), followed by Lithuania (87.4%) and Spain (87.4%). The lowest proportion of isolates resistant to ciprofloxacin was reported by Norway (29.7%). Similar observations were made regarding the levels of resistance to tetracyclines which were high overall (46.4%) with the highest proportion of resistance reported by Spain (81.3%) and Portugal (77.1%). The level of resistance to erythromycin was overall relatively low, at 1.5%, but varied between countries. The highest proportion of erythromycin-resistant isolates was reported by Malta (27.5%). This is substantially higher than the level of resistance reported by any other country, although Italy (13.0%) also reported a higher level than other countries. Resistance to gentamicin was generally very low (0.4%) but substantially higher in Slovakia, although only a low number of isolates (n=23) had been tested.



Country	Ciprofl	oxacin	Co-am	oxiclav	Erythr	omycin	Gent	amicin	Tetrac	yclines
	Ν	% Res	Ν	% Res	N	% Res	N	% Res	N	% Res
Austria ^(a)	357	69.7	-	-	357	0	357	0.3	357	31.1
Estonia ^(a)	31	80.6	-	-	31	0	-	-	31	64.5
France	4,627	55.4	4624	1.0	4,623	0.3	4,531	0.2	4,264	54.2
Italy ^(a)	69	81.2	-	-	69	13.0	_	_	69	69.6
Lithuania	198	87.4	-	-	275	1.5	-	-	80	51.3
Luxembourg ^(a)	761	64.5	340	8.8	762	0.3	-	-	762	47.9
Malta	182	69.8	-	-	182	27.5	_	_	-	-
Netherlands	3,033	59.8	-	-	2,612	1.9	-	-	1,957	43.2
Portugal ^(a)	96	97.9	-	-	96	5.2	96	0.0	96	77.1
Romania ^(a)	16	50.0	-	-	16	0	16	0	16	43.8
Slovakia	1,211	50.6	202	1.5	1,278	1.1	23	39.1	1,258	25.6
Slovenia ^(a)	1,028	69.5	-	-	1,026	1.5	-	-	1,026	36.2
Spain	246	87.4	-	-	246	3.3	246	2.0	246	81.3
Total (MSs 13)	11,855	60.2	5,166	1.5	11,573	1.5	5,269	0.4	10,162	46.4
Norway ^(a)	145	29.7	_	-	145	3.4	145	2.8	145	20.0

Table 22: Antimicrobial resistance in Campylobacter jejuni from humans per country in 2014

N: number of isolates tested; % Res: percentage of resistant isolates (either non-wild type by ECOFFs or clinically nonsusceptible by combining resistant and intermediate categories); -: no data reported.

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

MDR among Campylobacter jejuni isolates from humans

Five MSs and Norway tested at least ten isolates of *C. jejuni* for resistance to the four antimicrobial classes included in the MDR analysis. Overall, 20.5% of human *C. jejuni* isolates in the five reporting MSs were susceptible to all four antimicrobial classes (5 MSs, Table <u>COMCAMPJEHUM</u>). Particularly low levels of susceptibility were reported from Portugal (1.0%) and Spain (8.5%) (Figure 54). MDR was, on average, very low in the five MSs (0.4%) with the highest MDR observed in Portugal (3.1%) and Spain (2.8%). A very low proportion of isolates (0.3%) in the five MSs exhibited 'microbiological' as well as 'clinical' resistance to both ciprofloxacin and erythromycin, but slightly higher levels were observed in Portugal, Norway and Spain. Spain reported two isolates resistant to all four antimicrobial classes.

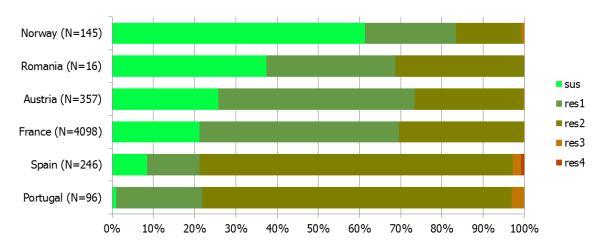


Figure 54: Frequency distribution of *Campylobacter jejuni* isolates from humans completely susceptible or resistant to one to four antimicrobial classes in 2014

Spatial distribution of resistance among Campylobacter jejuni isolates from human cases

The spatial distribution of ciprofloxacin resistance in *C. jejuni* isolates from human cases (Figure 55) shows that the highest proportion of resistance was reported by southern European and Baltic countries, whereas northern and central European countries reported lower levels. Erythromycin resistance levels were higher in the southern European countries and in Norway (Figure 56).



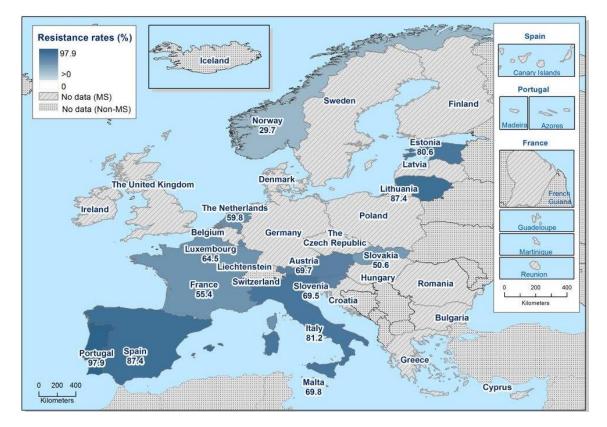


Figure 55: Spatial distribution of ciprofloxacin resistance among *Campylobacter jejuni* from human cases in reporting countries in 2014

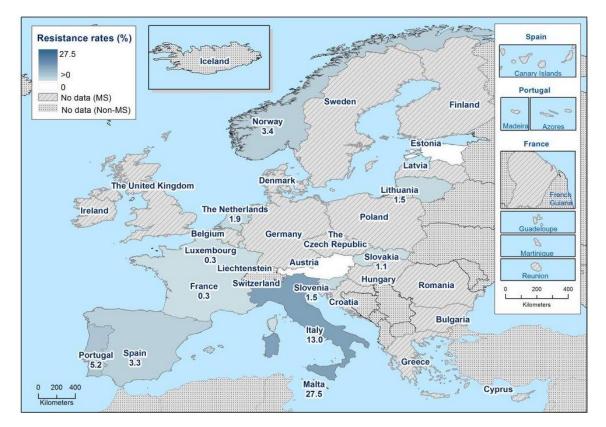


Figure 56: Spatial distribution of erythromycin resistance among *Campylobacter jejuni* from human cases in reporting countries in 2014



Antimicrobial resistance in Campylobacter coli from humans

Resistance levels in Campylobacter coli isolates from humans

C. coli was the second most common Campylobacter species identified in 2014, with 9,098 cases reported in the EU/EEA. AST data were reported for 17.4% of these cases in 2014 by 13 MSs and Norway. Very high proportions of resistance were observed for ciprofloxacin (68.9%) and tetracyclines (53.8%), with extremely high proportions (> 70%) resistant to ciprofloxacin in Portugal, Spain, Lithuania, Malta, Austria and Slovenia (13 MSs, Table 23). Proportions of isolates resistant to erythromycin and gentamicin were also markedly higher in C. coli than in C. jejuni (14.6% vs. 1.5% and 1.7% vs 0.4%, respectively). Portugal, Spain and Malta reported the highest levels of resistance to erythromycin (57.6%, 44.8% and 42.5%, respectively).

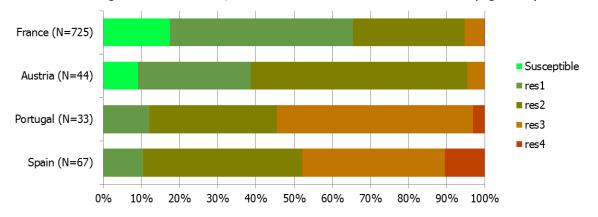
Table 23: Antimicrobial resistance in Campylobacter coli from hu	umans per country in 2014
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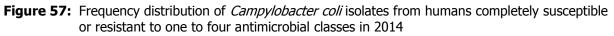
Country	Ciprof	loxacin	Co-ar	noxiclav	Erythr	omycin	Gen	tamicin	Tetracyclines		
	N	% Res	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	
Austria ^(a)	44	84.1	-	-	44	4.5	44	0	44	68.2	
Estonia ^(a)	2	NA	-	_	2	NA	_	_	2	NA	
France	812	63.1	811	0.9	812	10.1	800	0.8	753	49.0	
Italy ^(a)	6	NA	-	-	6	NA	-	-	6	NA	
Lithuania	16	87.4	-	_	21	4.8	_	_	4	NA	
Luxembourg ^(a)	73	69.9	39	15.4	73	9.6	_	_	73	69.9	
Malta	80	86.3	_	_	80	42.5	2	NA	3	NA	
Netherlands	203	65.5	-	_	167	17.4	-	-	129	62.0	
Portugal ^(a)	33	97.0	-	_	33	57.6	33	3.0	33	87.9	
Romania ^(a)	7	NA	_	_	7	NA	7	NA	7	NA	
Slovakia	70	61.4	28	3.6	85	5.9	-	-	80	31.3	
Slovenia ^(a)	87	80.5	-	_	87	4.6	-	-	87	46.0	
Spain	67	97.0	_	_	67	44.8	67	13.4	67	92.5	
Total (MSs 13)	1,500	68.9	878	1.6	1,484	14.6	953	1.7	1,288	53.8	
Norway ^(a)	6	NA	_	_	6	NA	6	NA	6	NA	

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

MDR among Campylobacter coli isolates from humans

Overall, 15.0% of the human C. coli isolates were susceptible to all four antimicrobial classes, with no susceptible isolates reported by Portugal and Spain (Figure 57, Table COMCAMPCOHUM). The level of MDR was overall moderate (10.4%) but ranged from 4.5% to 54.5% between countries, with a country average of 28.0%. The overall level of microbiological and clinical co-resistance to ciprofloxacin and erythromycin was 13.6% and 13.5%, respectively. Spain reported seven isolates and France and Portugal one isolate each, resistant to all four antimicrobial classes (Figure 57).







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 2014 are presented in Table <u>CAMPCOOVERVIEW</u> and <u>CAMPJEOVERVIEW</u>. Antimicrobials selected by the different MSs, and non-MSs, for susceptibility testing of *C. jejuni* and *C. coli* are shown in presented in Material and methods section.

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 (Denmark) were based mainly on the random collection of broiler meat samples obtained at slaughterhouses, processing plants or retail outlets. Data on antimicrobial resistance in *Campylobacter* isolates from meat from turkeys were submitted by Austria, Germany and Portugal and from meat from pigs by Belgium and Portugal. Portugal reported data on antimicrobial resistance in *C. jejuni* isolates from meat from bovine animals.

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

For 2014, four MSs provided antimicrobial resistance data on *C. jejuni* and *C. coli* isolates from broiler meat (Table 24). 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. 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 very low level (0.6%). For those antimicrobials of particular importance in treating human *Campylobacter* infections, resistance to ciprofloxacin was in general very 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. In contrast to the other two reporting MSs, Denmark recorded a moderate resistance level (15.4%) to ciprofloxacin and nalidixic acid in *C. jejuni*, although a low number of isolates was tested. The recorded levels of resistance to erythromycin considering *C. jejuni* and *C. coli* were contrasting, with higher resistance observed in *C. coli*.

MDR 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.



Country	Cipro	floxacin	Eryth	romycin	Genta	amicin	Nalid	ixic acid	Strept	tomycin	Tetracycline	
-	N	%	N	%	N	%	N	%	N	%	N	%
Campylobacter je	juni											
Meat from broiler	S											
Austria	102	71.6	102	0	102	0	102	67.6	102	0	102	26.5
Denmark	26	15.4	26	0	26	0	26	15.4	26	0	26	11.5
Germany	180	69.4	180	3.3	180	0.6	180	65	180	1.1	180	46.1
Total (MSs 3)	308	65.6	308	1.9	308	0.3	308	61.7	308	0.6	308	36.7
Meat from turkey	s	•	•	•		•	·		·		•	
Austria	13	92.3	13	0	13	0	13	84.6	13	0	13	38.5
Germany	61	60.7	61	0	61	0	61	54.1	61	1.6	61	52.5
Total (MSs 2)	74	66.2	74	0	74	0	74	59.5	74	1.4	74	50.0
Campylobacter co	oli											
Meat from broiler												
Austria	45	88.9	45	11.1	45	0	45	88.9	45	11.1	45	60.0
Germany	72	80.6	72	15.3	72	0	72	79.2	72	2.8	72	79.2
Portugal	17	100	17	41.2	17	0	17	100	17	5.9	17	88.2
Total (MSs 3)	134	85.8	134	17.2	134	0	134	85.1	134	6.0	134	73.9
Meat from turkey		1	1	1	1	1	1	1	1	1	1	
Germany	37	86.5	37	29.7	37	0	37	83.8	37	13.5	37	70.3

Table 24: Occurrence of resistance to selected antimicrobials in *Campylobacter coli* and *Campylobacter jejuni* from meat in 2014, using harmonised ECOFFs

ECOFFs: epidemiological cut-off values; N: number of isolates tested; %: percentage of resistant isolates per category of susceptibility or multiple resistance; MSs: Member States.



Antimicrobial resistance in *Campylobacter* isolates from broilers

Representative monitoring

In 2014, the implementation of Commission Implementing Decision 2013/652/EU, which sets out the requirements for monitoring resistance in *C. jejuni* in broilers, resulted in comprehensive monitoring in 25 MSs and one non-MS (Iceland) on *C. jejuni* and *C. coli* isolates from broilers (Table 25). On a voluntary basis, eight MSs also monitored resistance in *C. coli* in broilers. Further information on the representative sampling of carcases of healthy broilers at the slaughterhouse may be found in the Material and methods section.

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

As seen in previous years, the occurrence of resistance to the antimicrobials studied varied greatly between the reporting countries in 2014.

Considering *C. jejuni*, in general, the overall observed levels of resistance to tetracyclines (overall 54.4%), nalidixic acid (overall 65.1%) and ciprofloxacin (overall 69.8%) were high to extremely high, whereas those of resistance to streptomycin (overall 6.9%) and erythromycin (overall 5.9%) were low to moderate. Exceptions to this general pattern of resistance to these substances were observed for isolates from Sweden and Iceland which reported the lowest occurrence of resistance (at low levels), and those from Latvia, which recorded resistance to nalidixic acid and ciprofloxacin in all the isolates tested. Another exception to this general pattern of resistance was observed for isolates from Denmark, which recorded moderate levels of resistance to ciprofloxacin, nalidixic acid (both at 17.6%) and tetracycline (12.1%) and for isolates from Finland, which reported moderate resistance to tetracyclines (17.0%). In contrast, gentamicin resistance was either undetected or reported at low levels (overall 0.9%).

The results in *C. coli* isolates from broilers were similar, with high to extremely high levels of resistance to ciprofloxacin (overall 74.3%), nalidixic acid (overall 69.5%) and tetracyclines (overall 59.6%) for most MSs, with the exception of Croatia (2.2%). Streptomycin overall resistance was generally higher in *C. coli* (22.0%), than in *C. jejuni* (6.9%) from broilers at the MS level. Overall resistance to erythromycin was higher in *C. coli* (14.5%) than in *C. jejuni* (5.9%) for all reporting MSs and at the MS level for most MSs, with the exception of three central and south-eastern European countries, the Czech Republic, Romania and Slovakia.

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.

Country	Cipro	floxacin	Eryth	romycin	Gent	amicin	Nalid	lixic acid	Strep	tomycin	Tetracycline	
-	N	%	N	%	N	%	N	%	N	%	N	%
Campylobacter jeji	ıni											
Austria	193	75.1	193	0	193	0	193	67.9	193	2.1	193	23.8
Belgium	92	60.9	92	1.1	92	0	92	60.9	92	0	92	52.2
Bulgaria	110	87.3	110	39.1	110	4.5	110	85.5	110	27.3	110	69.1
Croatia	65	26.2	65	0	65	4.6	65	26.2	65	0	65	13.8
Cyprus	69	72.5	69	11.6	69	2.9	69	71.0	69	21.7	69	73.9
Czech Republic	47	78.7	47	4.3	47	0	47	61.7	47	10.6	47	36.2
Denmark	165	17.6	165	0.6	165	0	165	17.6	165	4.8	165	12.1
Finland	88	25.0	88	0	88	0	88	25.0	88	0	88	17.0
France	175	61.1	175	0	175	0	175	59.4	175	0.6	175	72.6
Germany	195	66.7	195	3.6	195	0	195	55.9	195	0	195	51.3
Greece	80	91.3	80	0	80	0	80	77.5	80	21.3	80	71.3
Hungary	150	93.3	150	0	150	0	150	91.3	150	1.3	150	58.0
Ireland	99	27.3	99	1.0	99	0	99	27.3	99	5.1	99	28.3
Italy	261	90.0	261	3.1	261	0.8	261	75.5	261	3.4	261	78.9
Latvia	92	100	92	1.1	92	3.3	92	100	92	1.1	92	23.9
Lithuania	37	89.2	37	2.7	37	0	37	89.2	37	13.5	37	59.5
Netherlands	98	64.3	98	0	98	0	98	61.2	98	0	98	50.0
Poland	179	94.4	179	0.6	179	0.6	179	83.8	179	20.7	179	73.7
Portugal	240	95.4	240	11.7	240	0	240	96.3	240	1.7	240	84.6
Romania	447	76.5	447	20.4	447	3.4	447	71.6	447	17.4	447	62.0
Slovakia	11	72.7	11	18.2	11	0	11	63.6	11	9.1	11	27.3
Slovenia	77	81.8	77	0	77	0	77	77.9	77	5.2	77	51.9
Spain	80	95.0	80	0	80	0	80	78.8	80	3.8	80	87.5
Sweden	102	3.9	102	0	102	0	102	7.8	102	1.0	102	1.0
United Kingdom	165	43.6	165	0	165	0	165	44.2	165	0	165	58.8
Total (MSs 25)	3,317	69.8	3,317	5.9	3,317	0.9	3,317	65.1	3,317	6.9	3,317	54.4
Iceland	28	3.6	28	0	28	0	28	3.6	28	0	28	0
Campylobacter coll	i											
Croatia	93	10.8	93	0	93	2.2	93	10.8	93	4.3	93	2.2
Czech Republic	52	86.5	52	0	52	0	52	50.0	52	28.8	52	51.9
Germany	111	82.9	111	23.4	111	0	111	80.2	111	12.6	111	82.0
Netherlands	39	51.3	39	2.6	39	0	39	51.3	39	12.8	39	59.0
Romania	316	82.3	316	16.1	316	3.8	316	78.8	316	21.2	316	60.4
Slovakia	36	91.7	36	2.8	36	0	36	91.7	36	19.4	36	44.4
Slovenia	30	83.3	30	3.3	30	0	30	83.3	30	30.0	30	63.3
Spain	90	94.4	90	34.4	90	6.7	90	90.0	90	53.3	90	97.8
Total (MSs 8)	767	74.3	767	14.5	767	2.6	767	69.5	767	22.0	767	59.6

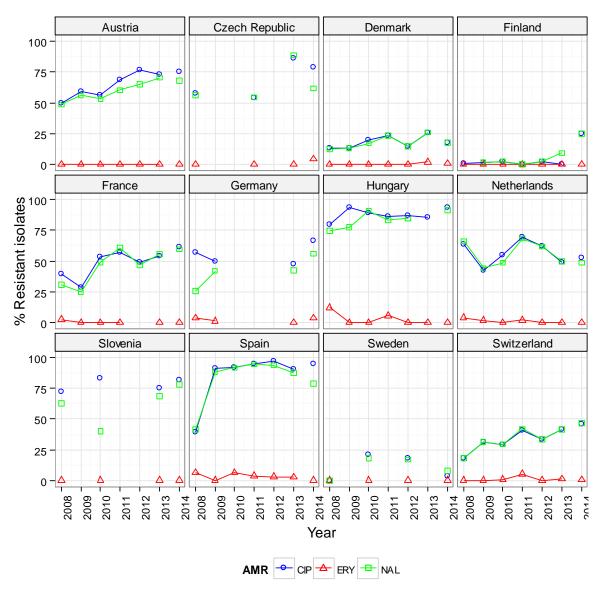
Table 25: Occurrence of resistance to selected antimicrobials in *Campylobacter* from broilers in 2014, using harmonised ECOFFs

ECOFFs: epidemiological cut-off values; N: number of isolates tested; %: percentage of resistant isolates per category of susceptibility or multiple resistance; MSs: Member States.



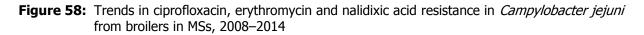
Temporal trends in resistance among Campylobacter jejuni isolates from broilers

Eleven MSs and one non-MS provided resistance data on 5 years or more to be included in the trend analysis of antimicrobial resistance. The trends observed in *C. jejuni* from broilers over the 2008–2014 period (Figure 58) show, for ciprofloxacin and nalidixic acid resistance, statistically significant increases in Austria, Finland, France, Hungary, Spain and Switzerland, although, in both Austria and Spain, this increase seems to have levelled off since 2012, whereas, in Finland, the increase has started to take off only over the last 2 years. Although resistance to erythromycin in *C. jejuni* remained relatively stable at low levels over the study period, France, Hungary, the Netherlands and Spain registered significantly decreasing resistance, whereas, conversely, Switzerland recorded a slightly increasing resistance. In Switzerland, significant increases in resistance to both ciprofloxacin/nalidixic acid and erythromycin were observed over the period, whereas, in the Netherlands, both trends in resistance to the same substances were decreasing over the period.

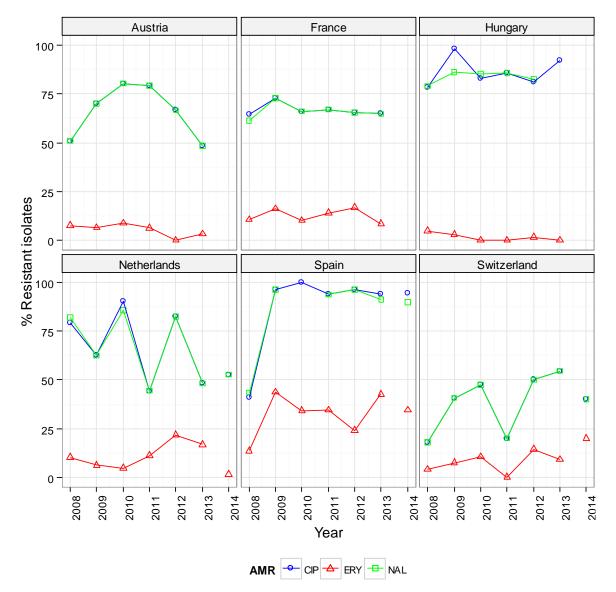


MS: Member State.

Note:A statistically significant increasing trend over 5 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), Finland (\uparrow), France (\uparrow), Hungary(\uparrow), Spain (\uparrow) and Switzerland (\uparrow). A statistically significant decreasing trend over five or more years for erythromycin was observed in France (\downarrow), Hungary (\downarrow), the Netherlands (\downarrow) and Spain (\downarrow) and for ciprofloxacin in the Netherlands (\downarrow).







MS: Member State.

- Note: A statistically significant trend over 5 or more years, as tested by a logistic regression model ($p \le 0.05$), was observed for both ciprofloxacin and nalidixic acid in Austria (\downarrow), Spain (\uparrow),Switzerland (\uparrow) and the Netherlands (\downarrow). A statistically significant trend over 5 or more years for erythromycin was observed in Spain (\uparrow) and Hungary (\downarrow) and the Netherlands (\downarrow).
- **Figure 59:** Trends in ciprofloxacin, erythromycin and nalidixic acid resistance in Campylobacter *coli* from broilers in MSs, 2008–2014

Spatial distribution of resistance among Campylobacter jejuni isolates from broilers

The spatial distributions of ciprofloxacin resistance in *C. jejuni* isolates from broilers (Figure 60 and Figure 61) show that the highest levels of resistance to this substance were reported in eastern and southern Europe, whereas northern European countries reported lower resistance levels. Although erythromycin resistance was generally registered at low to very low levels across Europe, much higher resistance was observed in south-eastern Europe.



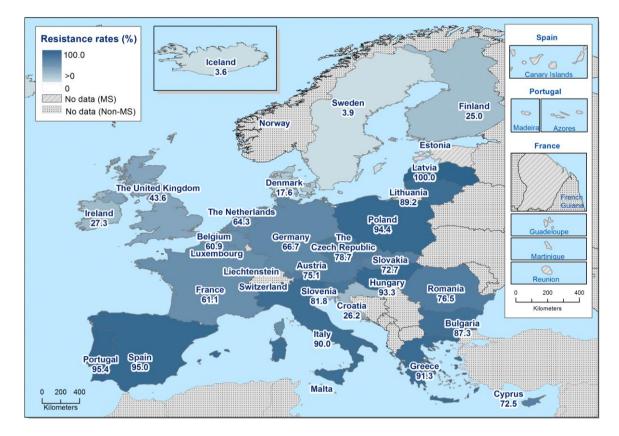


Figure 60: Spatial distribution of ciprofloxacin resistance among *Campylobacter jejuni* from broilers of *Gallus gallus* in reporting countries in 2014

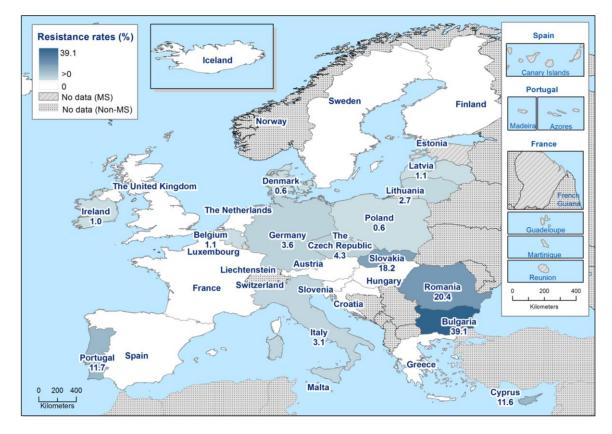


Figure 61: Spatial distribution of erythromycin resistance among *Campylobacter jejuni* from broilers of *Gallus gallus* in reporting countries in 2014



Multidrug resistance among Campylobacter jejuni and Campylobacter coli isolates from broilers

A large variation in the levels of complete susceptibility to the common set of antimicrobials for *Campylobacter* (four 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 91.2% in Sweden and 96.4% in Iceland, whereas in Bulgaria, Cyprus, Greece, Hungary, Italy, Poland, Portugal and Spain, the proportion of fully susceptible isolates was much lower (under 10.0%). The overall complete susceptibility of the *C. jejuni* isolates was assessed at 23.1%. MDR in *C. jejuni* isolates was recorded in 11 countries (out of 26 reporting data), generally at low levels, although, in Bulgaria, 29.1% of isolates exhibited MDR. The overall MDR of the *C. jejuni* isolates was 4.6% (Table <u>COMCAMPJEBR</u>).

The important co-resistance¹⁵ for public health to both ciprofloxacin and erythromycin in *C. jejuni* was detected in 14 out of 26 reporting countries, with Bulgaria reporting the highest occurrence of co-resistance in 34.5% of isolates. The overall co-resistance to ciprofloxacin and erythromycin in *C. jejuni* was 4.8% for all reporting MSs.

In *C. coli*, complete susceptibility was generally lower (18.3%) than that observed in *C. jejuni* and the occurrence of MDR was greater (18.3%) than that reported in *C. jejuni* isolates (Table <u>COMCAMPCOBR</u>). In *C. coli* isolates, co-resistance to ciprofloxacin and erythromycin was detected in six out of nine MSs, with Spain reporting the highest occurrence in 33.3% of isolates; resulting in an overall co-resistance in *C. coli* of 18.3%.

The frequency distributions of the numbers of antimicrobials to which individual isolates were resistant (Figure 62 and Figure 63) showed marked variation between different reporting countries. Although most of the reporting countries detected resistance to a maximum of two antimicrobial classes in *C. jejuni*, Portugal, Romania and Bulgaria reported MDR levels ranging between 10 and nearly 30% (Figure 62). Conversely, in reporting MSs, *C. coli* isolates displayed more frequently resistance to three different classes of antimicrobials (Figure 63), notably in Germany and Spain where the occurrence of MDR exceeded 20%.

Patterns of multidrug resistance in Campylobacter jejuni and Campylobacter coli isolates from broilers

Considering *C. jejuni*, isolate-based data were available from 25 contributing MSs and one non-MS, which in total reported details of 3,345 isolates. The isolates reported by 14 MSs (44.5% from the total number of the isolates reported) and Iceland are not addressed in the Table <u>MULTICAMPJEGBR</u>, as they were not multiresistant. Considering *C. coli*, analysis of the patterns of resistance to erythromycin, ciprofloxacin/nalidixic acid, tetracyclines and gentamicin was possible for 622 *C. coli* isolates from six contributing MSs (Table <u>MULTICAMPCOBR</u>).

Among the 1,842 *C. jejuni* isolates from broilers from the reporting MSs submitting isolates which were multiresistant, 8.4% (n=155) exhibited MDR (Table <u>MULTICAMPJEGBR</u>). The most common pattern of MDR was resistance to ciprofloxacin/nalidixic acid, erythromycin and tetracyclines, occurring in 135 out of 155 resistant isolates (and constituting the core resistance pattern in a further 13 isolates, which also showed gentamicin resistance) reported by submitting MSs. The situation regarding the patterns was similar in *C. coli* (Table <u>MULTICAMPCOBR</u>), but with a higher percentage (16.9%) of the isolate displayed MDR of all isolates were available (N=622). Gentamicin resistance, as a component of MDR patterns in *C. coli*, was observed only in Romania and Spain. Romania 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.

¹⁵ 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.



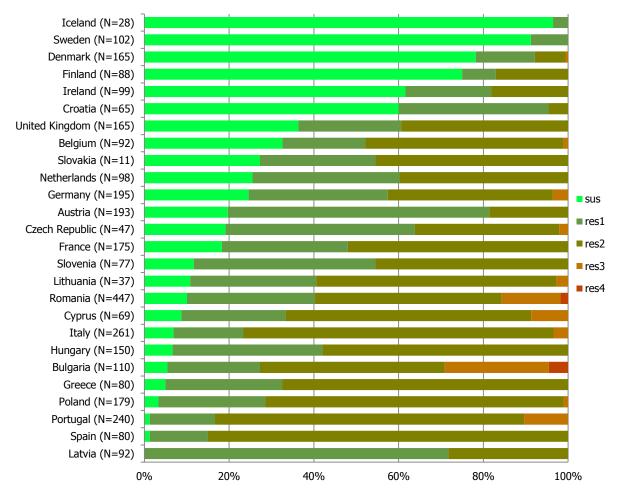


Figure 62: Frequency distribution of *Campylobacter jejuni* isolates completely susceptible and resistant to one to four antimicrobials, in broilers in MSs, 2014

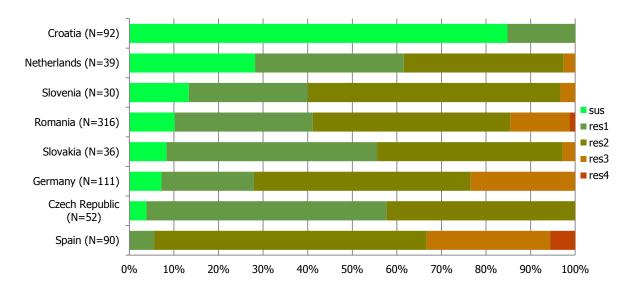


Figure 63: Frequency distribution of *Campylobacter coli* isolates completely susceptible and resistant to one to four antimicrobials, in broilers in MSs, 2014



Antimicrobial resistance in Campylobacter isolates from fattening turkeys

Representative monitoring

For 2014, resistance data on *Campylobacter* isolates from fattening turkeys (Table 26) were provided by 10 MSs. Commission Implementing Decision 2013/652/EU lays down that monitoring resistance in *C. jejuni* in fattening turkeys is mandatory in those MSs where the production of turkey meat is greater than 10,000 tonnes slaughtered per year. Three MSs also reported data on *C. coli* in fattening turkeys. Further information on the representative sampling of carcases of healthy broilers at the slaughterhouse may be found in the Material and methods section.

Resistance levels among Campylobacter jejuni isolates from fattening turkeys

In *C. jejuni* isolates, the range of resistance to ciprofloxacin, nalidixic acid and tetracycline generally varied from very high to extremely high. The overall resistance to erythromycin and streptomycin was low and to gentamicin was very low. Resistance levels to antimicrobials were higher in *C. coli* than in *C. jejuni* for fattening turkeys.

Temporal trends in resistance among Campylobacter jejuni from fattening turkeys isolates

None of MSs provided resistance data for *C. jejuni* from fattening turkeys isolates on 5 years or more to be included in the statistical analysis.

Spatial distribution of resistance among Campylobacter jejuni isolates from fattening turkeys

The spatial distributions of ciprofloxacin and erythromycin resistance in *C. jejuni* isolates from fattening turkeys (Figure 64 and Figure 65) show that the highest levels of resistance to these substances were reported by southern European countries, whereas northern European countries reported lower levels.



	Cipro	floxacin	Erythr	omycin	Genta	amicin	Nalid	ixic acid	Strep	tomycin	Tetra	cycline
Country	N	%	N	%	N	%	N	%	N	%	N	%
Campylobacter je	juni											
Austria	73	63.0	73	0	73	0	73	60.3	73	1.4	73	35.6
France	174	55.7	174	0.6	174	0	174	52.3	174	0	174	71.8
Germany	187	62.6	187	2.1	187	0	187	56.1	187	3.2	187	56.7
Hungary	87	95.4	87	0	87	0	87	94.3	87	2.3	87	58.6
Italy	153	86.3	153	5.9	153	0.7	153	64.7	153	3.3	153	78.4
Poland	171	83.0	171	1.8	171	0	171	77.8	171	13.5	171	57.9
Portugal	72	90.3	72	8.3	72	0	72	87.5	72	2.8	72	87.5
Romania	14	85.7	14	0	14	0	14	78.6	14	21.4	14	71.4
Spain	37	89.2	37	10.8	37	0	37	75.7	37	5.4	37	94.6
United Kingdom	153	34.6	153	0.7	153	1.3	153	34	153	1.3	152	64.5
Total (MSs 10)	1,121	69.6	1,121	2.5	1,121	0.3	1,121	63.2	1,121	4.1	1,120	65.4
Campylobacter co	oli											
Germany	235	91.5	235	37	235	0.4	235	87.7	235	14.5	235	88.1
Romania	22	100	22	4.5	22	0	22	100	22	27.3	22	45.5
Spain	133	98.5	133	60.9	133	9.8	133	93.2	133	60.2	133	100
Total (MSs 3)	390	94.4	390	43.3	390	3.6	390	90.3	390	30.8	390	89.7

Table 26: Occurrence of resistance to selected antimicrobials in *Campylobacter* from fattening turkeys in 2014, using harmonised ECOFFs

ECOFFs: epidemiological cut-off values; N: number of isolates tested; %: percentage of resistant isolates per category of susceptibility or multiple resistance; MSs: Member States.



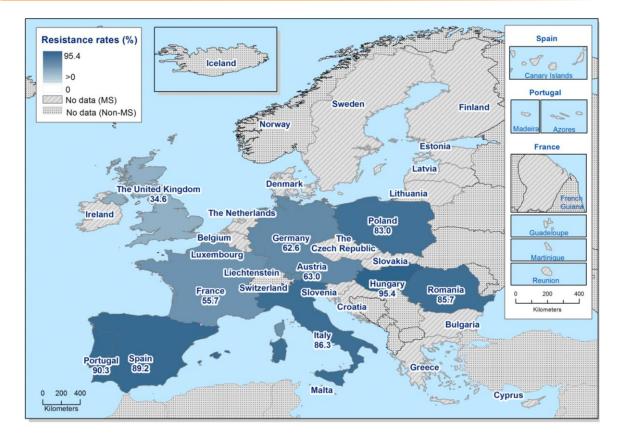


Figure 64: Spatial distribution of ciprofloxacin resistance among *Campylobacter jejuni* from fattening turkeys in reporting countries in 2014

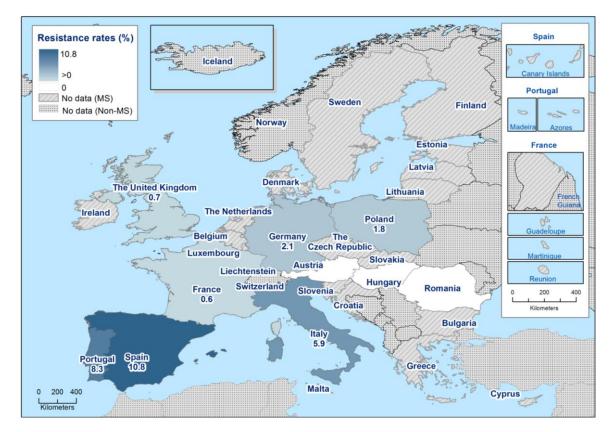
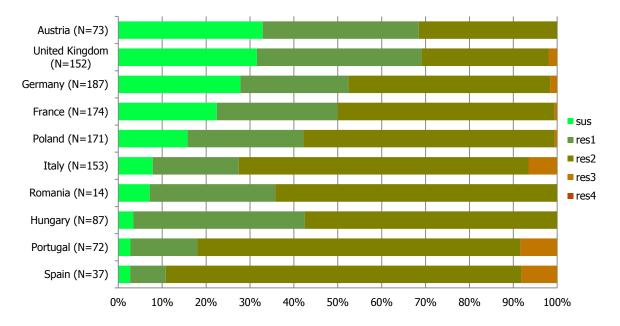


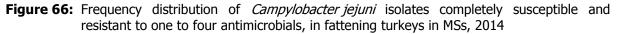
Figure 65: Spatial distribution of erythromycin resistance among *Campylobacter jejuni* from fattening turkeys in reporting countries in 2014



MDR among Campylobacter jejuni isolates from fattening turkeys

Isolates exhibiting MDR accounted for about 8.0% of isolates in Portugal and Spain, whereas, in France and Poland, they represented less than 1% (Table <u>COMCAMPJETURK</u>). The frequency distributions (Figure 66) showed an important diversity between the reporting countries; most of them detected resistance to a maximum of three antimicrobial classes. In addition, a low proportion of isolates showing co-resistance to ciprofloxacin and erythromycin was observed in isolates from Germany, Italy, Poland, Portugal and Spain and overall the co-resistance equalled 2.4%.





Patterns of multi-drug resistance in Campylobacter jejuni isolates from fattening turkeys

Isolate-based data were available for 1,121 *C. jejuni* isolates from fattening turkeys, provided by 10 reporting MSs, and of these 794 (70.8%) exhibited MDR (Table <u>MULTICAMPJEGTURK</u>). The most common MDR pattern observed in fattening turkeys was resistance to ciprofloxacin/nalidixic acid, erythromycin and tetracyclines, occurring in 88.9% of the total number of isolates. The other most frequent pattern of MDR was resistance to the ciprofloxacin/nalidixic acid, gentamicin and tetracyclines. Resistance to ciprofloxacin/nalidixic acid and tetracyclines was observed in all of the multiresistant *C. jejuni* isolates from fattening turkeys.

3.2.3. Discussion

Antimicrobial resistance in *Campylobacter* in humans

Information on antimicrobial resistance in *Campylobacter* isolates from human cases of campylobacteriosis was available from 13 MSs and Norway in 2014. The proportion of human *C. jejuni* isolates resistant to erythromycin¹⁶ was low overall (> 1.0% to 10.0%), but moderately high (> 10.0– 20.0%) in *C. coli* and high (> 20.0–50.0%) to very high (> 50.0–70.0%) in a few reporting countries. Very high to extremely high (> 70.0%) resistance levels to ciprofloxacin¹⁷ were reported in human *Campylobacter* isolates from all MSs (although lower in Norway). The level of acquired resistance to fluoroquinolones in some MSs is so high that this agent can no longer be considered appropriate for routine empirical treatment of human *Campylobacter* infection. The highest proportion of ciprofloxacin resistance in *C. jejuni* isolates from human cases was reported by southern European and Baltic

¹⁶ A representative of the macrolides commonly used in the treatment of human campylobacteriosis.

¹⁷ A representative of the fluoroquinolones commonly used in the treatment of human campylobacteriosis.



countries, whereas northern and central European countries reported lower levels. A similar spatial distribution was observed in isolates from broilers.

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, preparing and consuming broiler meat or can be attributed to the chicken reservoir as a whole (EFSA BIOHAZ Panel, 2010a), this is a compelling example of the impact of acquired antimicrobial resistance in food and animals on the availability of effective antimicrobial agents for treating some zoonotic human infections.

Human antimicrobial susceptibility data were available for all antimicrobials included in the MDR analysis from five MSs and Norway for *C. jejuni* and from four MSs for *C. coli*. Overall, only one in five human *C. jejuni* isolates and one in six human *C. coli* isolates were fully susceptible to all tested antimicrobials. Multi-drug resistance¹⁸ was low (0.4%) in *C. jejuni* but significantly higher (10.4%) in *C. coli* with two of four countries reporting MDR in about half of the isolates (though the number of tested isolates were low). It is important to emphasise that all antimicrobials included in the MDR analysis since the 2013 report are of clinical relevance. Clinical and microbiological co-resistance to the critically important antimicrobials ciprofloxacin and erythromycin was low in *C. jejuni* but moderate in *C. coli* with two countries reporting high to very high co-resistance levels to the two primary agents used for treatment.

In terms of data quality and comparability, major improvements in harmonising data between countries and across sectors have been made during the last two data collections. In the data collection for the 2013 report, for the first time, countries could report measured values (quantitative AST data as opposed to interpreted categories) to ECDC and five countries did so. For 2014, eight countries provided quantitative AST data, with three countries changing from qualitative reporting, one country reporting AST data for the first time and one country that did not report, compared to 2013. The quantitative 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 'nonsusceptible' group. With this approach, the ECOFF-based category of 'wild type' corresponds fully to the 'susceptible' category and the ECOFF-based category of 'non-wild type' corresponds closely to the 'non-susceptible' category with only one exception for tetracyclines and *C. jejuni*. Thus, this approach further improves the comparability of human and non-human data. Of countries submitting categorical data, all but one was using EUCAST criteria in 2014, a significant stride towards harmonisation compared with 2012. For future reports, EFSA and ECDC hope that more countries will report measured values. More harmonisation is also needed when it comes to the sampling of isolates for testing and reporting at the EU level, as, in many countries, the sampling and the antimicrobials tested for a particular sample are not random, and represent different fractions of all isolates identified in a country.

As in the two previous reports, isolates from cases notified as having been acquired while travelling abroad were excluded from the analysis. The rationale is to facilitate assessment of the relationship between antimicrobial resistance in *Campylobacter* isolates from food and food-producing animals with antimicrobial resistance in human isolates of *Campylobacter* spp. As imported or traded food 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 remains complex.

Antimicrobial resistance in *Campylobacter* in poultry and meat thereof

Commission Implementing Decision 2013/652/EU sets out the requirements for monitoring resistance in *C. jejuni* in broilers and fattening turkeys in 2014 and resulted in comprehensive monitoring in these animal populations. The data relating to the susceptibility of *Campylobacter* of animal origin reported by MSs were well harmonised with almost all MSs followed the requirements of the Decision 2013/652/EU and adopting the EFSA guidelines and recommendations. Testing of streptomycin susceptibility of *Campylobacter* was voluntary in 2014 and results were not included in the MDR analysis.

¹⁸ MDR is defined as microbiological resistance to at least three of the four different antimicrobial classes tested.



Overall, the levels of antimicrobial resistance in *Campylobacter* isolates from food in 2014 were higher than those observed in 2013, although fewer countries reported data in 2014, comparing with 2013. Because of the marked differences in the levels of resistance observed between some countries, variation in those countries which report data each year can add to the variability observed in overall figures for all reporting MSs. The monitoring of antimicrobial resistance in *C. jejuni* isolates from broilers was mandatory in 2014 and therefore, the majority of the MSs (25) reported data, compared with 2013, when only 11 MSs reported data. Levels of resistance in *C. jejuni* isolates from broilers were higher than those observed in 2013.

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 resistance was not detected, whereas, for *C. coli*, there was again a wide variation in levels or resistance at the MS level, irrespective of the source of the isolates.

In 2014, ciprofloxacin resistance in C. jejuni isolates from humans was 60.2% for all contributing MSs (range: 50.6–47.9%), 69.8% in broilers (range: 3.9–100%) and 69.6% in fattening turkeys (range: 34.6–95.4%). The picture is clearly complex in relation to the sources of human infections because these may be related to consumption of broilers or turkeys meat (as well as other sources). International trade also means that consumers may be exposed to meat produced in a number of different countries. Despite the fact that imported food can contribute to cases of *Campylobacter* infection, there were striking parallels in the observed occurrence of resistance to ciprofloxacin, erythromycin, gentamicin and tetracyclines in *C. jejuni* isolates from broiler meat, broilers and man in Austria, and in C. coli isolates from broiler meat and man in Portugal, with similar levels of resistance to each antimicrobial seen in isolates originating from these different sources within each country. Austria and Portugal were the only MSs which reported results for Campylobacter isolates from meat and from human cases of infection. Interestingly, Austria also reported results for C. jejuni from meat from turkeys and fattening turkeys; isolates from turkeys also closely paralleled the results obtained for isolates from human cases, whereas ciprofloxacin resistance was rather higher in isolates from turkey meat. From 2008 to 2014, statistically significant increasing trends in ciprofloxacin and nalidixic acid resistance in C. jejuni from broilers were observed over 5 or more years in six reporting countries; this was also observed in *C. coli* from broilers in two reporting countries.

Regarding resistance to erythromycin — in all reporting MSs, erythromycin resistance in *C. jejuni* from broilers and fattening turkeys was 5.9% and 0.7%, respectively, whereas, in *C. coli* resistance was 14.5% and 43.3%, respectively. Erythromycin resistance showed increasing trends in *C. coli* from broilers in two countries, whereas erythromycin resistance showed a decreasing trend in *C. jejuni* from broilers in four countries. The range of dilutions over which erythromycin is currently tested is limited and thus, 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. Recently, transferable macrolide resistance has been detected and this confers high level macrolide resistance (further information is presented in the text box below).

Campylobacter can develop resistance to several of the different antimicrobials in the common test panel by different mechanisms. 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; Luangtongkum et al., 2009). The efflux pump CmeABC acting alone has also 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 British 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 humans¹⁹, showed resistance to erythromycin, ciprofloxacin and tetracyclines, raising the possibility that CmeABC may

¹⁹ Of the human *Campylobacter* isolates in 2014, 42 *C. jejuni* and 48 *C. coli* isolates were resistant to all these three substances (data not shown in the section).



have been responsible for or contributed to the observed pattern of resistance. Only 14/3,317 (0.4%) of *C. jejuni*, 10/767 (1.3%) of *C. coli* from broilers and 1/1,121 (0.09%) of *C. jejuni* from turkeys were resistant to the combination erythromycin, ciprofloxacin and tetracyclines, without showing nalidixic acid resistance. CmeABC may also have contributed to the MDR patterns of resistance shown by isolates which were resistant to erythromycin, ciprofloxacin, nalidixic acid and tetracyclines, but in which *gyrA* mutations were also present conferring both ciprofloxacin and nalidixic acid resistance.

The frequently high levels of tetracycline resistance observed in *Campylobacter* may in part be a consequence of the presence of the tetracycline resistance gene *tet(O)* on a transferable plasmid facilitating dissemination of tetracycline resistance (Wieczorek and Osek, 2013), although *tet(O)* may also be chromosomally located in *Campylobacter* (Piddock et al., 2008). Recently, a transferable plasmid bearing the macrolide resistance gene *erm*(B) which confers high-level macrolide resistance, has been described (Wang et al. 2014). This is an important development, because macrolide resistance up to this point appears to have been mutational rather than related to transferable, plasmid-mediated resistance mechanisms in *Campylobacter* and the occurrence of plasmid-mediated resistance may allow the much wider dissemination of macrolide resistance than has previously been observed. AS the *erm*(B) gene confers erythromycin MICs of \geq 512 mg/L, it may be necessary in the future to review the dilution range of erythromycin which is tested. In 2014, 75/3,504 (2.1%) *C. jejuni* and 71/795 (8.9%) *C. coli* isolates from broilers, as well as 11/1,123 (1.0%) *C. jejuni* and 134/390 (34.4%) *C. coli* isolates from turkeys had MICs of >128mg/L (the highest dilution tested), so if *erm*(B) is present in these *Campylobacter* isolates, from the current monitoring, an upper ceiling can be placed on the proportion of the total number of isolates which might carry this gene.

Gentamicin resistance in *Campylobacter* was uncommon in broilers and fattening turkeys isolates, but where it did occur in multiple-resistant isolates of *C. coli* and *C. jejuni*, streptomycin resistance was usually also observed in previous years. Streptomycin is now tested on a voluntary basis and was not included in the MDR analysis for 2014. Recently a cluster of aminoglycoside-modifying enzymes has been reported in *C. coli* from broiler chickens in China (Qin et al., 2012). An increase in gentamicin resistance in *C. coli* from retail chicken the USA has recently been observed (FDA, 2011), with most isolates originating from the western region of the USA and apparently related to the clonal expansion of a particular *C. coli* lineage. The resistance gene *aph(2'')-Ig* was responsible for conferring gentamicin resistance in these USA retail chicken *C. coli* isolates and was colocated on a plasmid which also carried *tet*(O) resistance (Zhao et al., 2015). Gentamicin resistance was detected in *C. jejuni* from broilers and turkeys, and *C. coli* from broilers in EU MSs in 2014, although whether clonal expansion of strains is also playing any role in the occurrence of gentamicin resistance in these *Campylobacter* isolates is not known.

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.



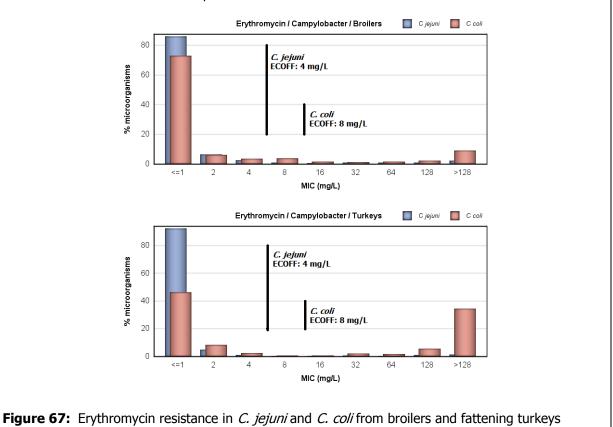
High-level Erythromycin Resistance in *Campylobacter* spp.

Macrolides are important compounds for the treatment of human *Campylobacter* infections. In broilers, 5.9% of *C. jejuni* isolates from 25 MSs and 14.5% of *C. coli* from eight MSs, were microbiologically resistant to erythromycin. In turkeys, 2.5% of *C. jejuni* from 10 MSs and 43.3% of *C. coli* from three MSs were erythromycin resistant. The occurrence of resistance to erythromycin in *Campylobacter* spp. varied markedly between individual MSs.

Resistance to macrolides in *Campylobacter* spp. has generally been the result of mutations in ribosomal RNA or ribosomal proteins and these mutations are thought to have incurred fitness costs, accounting for the low occurrence of erythromycin resistance in many countries (Wang et al., 2014). Ribosomal mutations can confer high-level erythromycin resistance (Gibreel and Taylor, 2006). Transferable resistance to erythromycin was first described in *Campylobacter* isolates from food-producing animals (including pigs, chickens and ducks) from China in 2014 (Qin et al., 2014, Wang et al., 2014) and frequently resulted in high level resistance to erythromycin, with MICs recorded at > 512 mg/L. Resistance is conferred by the rRNA methylase gene *erm*(B), which can be associated with either chromosomal multidrug resistance islands or transferable plasmids.

The recent emergence of transferable macrolide resistance in *Campylobacter* may provide a means whereby macrolide resistance can spread rapidly in *Campylobacter*. The situation may be compared to tetracycline resistance, which is frequently plasmid mediated in *Campylobacter*, and is frequently detected in many EU MSs at high levels.

Although transferable erythromycin resistance conferred by *erm*(B) generally results in high-level resistance to erythromycin, mutational resistance can also result in high-level resistance to erythromycin, but may equally result in lower MICs (still above the ECOFF), dependent on the particular mutations which have occurred. The distribution of erythromycin MICs can be used to identify the numbers of isolates which have higher levels of resistance to erythromycin. These isolates may have transferable or mutational erythromycin resistance and fluctuations in the number detected will provide an early indication of changes in the occurrence of high-level macrolide resistance in *Campylobacter*. Genetic investigation of isolates will be necessary for definitive characterisation of the resistance mechanisms which are present.





3.3. Antimicrobial resistance in indicator *Escherichia coli*

Rationale for monitoring AMR in indicator *E. coli* in food-producing animals and food

Commensal *E. coli* is typically chosen as an indicator of antimicrobial resistance in Gram-negative bacteria, as it is commonly present in animal faeces, may be 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 food-producing animals, can constitute 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* is also helpful as representative of the Enterobacteriaceae to monitor the emergence and changes in the proportion of bacteria producing ESBLs. Since 2014, the mandatory monitoring of AMR in indicator *E. coli* from food-producing animals and food thereof has laid down inthe EU legislation.

In total, 27 MSs and two non-MSs reported quantitative MIC data in commensal (indicator) *E. coli* isolates from poultry populations in 2014 (Table <u>ESCHEOVERVIEW</u>). Two of these countries provided MIC data on isolates collected from poultry meat. Antimicrobial susceptibility data were interpreted using ECOFFs laid down in Commission implementing Decision 2013/652/EC to determine organisms exhibiting reduced susceptibility, i.e. showing 'microbiological' resistance (as opposed to 'clinical' resistance).²⁰

For further information on antimicrobials tested by the reporting countries and the reported MIC distributions for *E. coli* in 2014, please refer to Table 5 and Table 7 in the Material and methods chapter and to the submitted and validated MS data published on the EFSA website, respectively.

Azithromycin newly inserted in the harmonised set of antimicrobial substances tested

Azithromycin replaced streptomycin in the test panel for Salmonella and E, coli in 2014. A number of important MDR patterns included resistance to streptomycin and an adverse consequence of this change is that these patterns can no longer be so readily detected. Azithromycin is a macrolide used in the treatment of certain human invasive Salmonella infections; it has also been used in the treatment of some other human enterobacterial infections, for example, Shigella spp. (Boumghar-Bourtchai et al., 2008). Breakpoints to discriminate between azithromycin resistant and susceptible populations of *E. coli* were proposed in a study looking at the epidemiology of mass drug treatment of human patients with azithromycin to control trachoma infection (Seidman et al., 2014). The same cutoff value (\geq 32 mg/L – which is equivalent to the cut-off value of > 16 mg/L used in this report) has been used in epidemiological studies of *E. coli* in animals (Schmidt et al., 2015). The azithromycin resistance results may therefore be considered to have relevance in treatment of certain invasive infections of humans, to detect reservoirs of macrolide resistance genes and in an epidemiological context. The macrolide efflux pump Mef(B) confers high level resistance to azithromycin and was first described in *E. coli* recovered from pigs in the UK (Liu et al., 2009), where it was co-located on plasmids which also carried the sul3 gene conferring sulfonamide resistance. In human medicine, macrolide resistance genes have been detected in E. coli isolates from patients who had received antimicrobial drugs or been hospitalized (Nguyen et al., 2009). E. coli carrying macrolide resistance genes can be associated with ESBL-producing E. coli and were also detected in E. coli co-resistant to trimethoprim/sulfonamides and amoxicillin; such human E. coli isolates may constitute a reservoir of macrolide resistance genes for Salmonella or Shigella (Nguyen et al., 2009).

²⁰ 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 animals

Antimicrobial resistance in indicator *Escherichia coli* isolates from broilers

In 2014, 27 MSs and one non-MS provided data in indicator *E. coli* isolates from broilers (Table 27). All MSs collected indicator *E. coli* isolates based on the requirements lay down in Decision 2013/652/EC. As Romania, where the resistance levels observed were among the highest reported, accounted for 17% of the *E. coli* isolates from broilers included in the analysis, the resistance rates presented at the reporting MS group level are impacted by the occurrence of resistance recorded in Romania.

Resistance levels among Escherichia coli *isolates from broilers*

Typically, the occurrence of resistance in *E. coli* isolates from broilers varied markedly between reporting countries. Resistance to ampicillin, sulfamethoxazole, tetracyclines and trimethoprim was high to very or extremely high in most reporting countries (overall resistance equalling 58.7%, 53.1%, 50.1%, 40.6%, respectively), with the striking exception of the Nordic countries (Denmark, Finland, Norway and Sweden) which registered low to moderate resistance to the above mentioned antimicrobials. Resistance to chloramphenicol ranged widely from low to very high, with the Nordic countries and Slovenia reporting no resistance. The gentamicin resistance was reported at very low to low levels, with the exceptions of Bulgaria, Greece, Lithuania, Romania, Spain and the United Kingdom, recording moderate and high resistance. Resistance to colistin was overall very low at 0.9%, and recorded only in six countries.

Resistance to ciprofloxacin and nalidixic acid was generally high to very or extremely high among the reporting countries (overall resistance equalling 65.7% and 62.6%, respectively), with the exception of Denmark and Sweden, which reported moderate resistance and Finland and Norway, which recorded low resistance to these substances. 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 and ceftazidime was generally low in most reporting countries, although four MSs reported moderate and three high levels of resistance. Cefotaxime and ceftazidime resistance were either similar or cefotaxime resistance slightly exceeded ceftazidime resistance in most countries, although, in a few countries (Lithuania, Malta and the Netherlands), ceftazidime resistance exceeded cefotaxime resistance.



Country	Amp	oicillin	Azithr	omycin	Cefot	axime	Cefta	zidime	Chloran	nphenicol	Cipro	floxacin	Colis	stin ^(a)
	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res
Austria	176	28.4	176	0.6	176	1.1	176	1.1	176	6.8	176	59.7	176	0
Belgium	158	72.8	158	4.4	158	8.2	158	7	158	20.9	158	69.6	158	0
Bulgaria	85	88.2	-	-	85	0	85	0	85	51.8	85	92.9	_(a)	_
Croatia	170	56.5	170	1.8	170	0.6	170	0.6	170	11.2	170	80.6	170	0
Cyprus	87	69.0	87	8.0	87	32.2	87	29.9	87	21.8	87	75.9	87	0
Czech Republic	196	33.2	196	0	196	1.0	196	1.0	196	2.6	196	68.9	196	0
Denmark	191	14.1	191	0	191	0	191	0	191	0	191	12.0	191	0
Estonia	71	88.7	71	8.5	71	4.2	71	2.8	71	22.5	71	88.7	71	1.4
Finland	175	4.6	175	0	175	0	175	0	175	0	175	4.6	175	0
France	226	55.8	226	2.7	226	4.0	226	4.0	226	3.1	226	44.2	226	1.8
Germany	227	55.9	227	10.1	227	1.3	227	1.3	227	18.9	227	47.6	227	7.0
Greece	172	69.8	172	9.3	172	2.9	172	2.9	172	35.5	172	89.0	172	0
Hungary	170	42.9	170	4.7	170	2.9	170	2.9	170	9.4	170	72.9	170	0
Ireland	167	69.5	167	6.6	167	4.2	167	3.6	167	6.6	167	41.3	167	0
Italy	170	86.5	170	2.9	170	6.5	170	5.9	170	45.9	170	67.6	170	5.3
Latvia	147	53.1	147	0	147	30.6	147	29.9	147	32.7	147	91.8	143	0
Lithuania	85	83.5	85	5.9	85	31.8	85	36.5	85	35.3	85	97.6	85	1.2
Malta	60	45.0	-	-	60	15.0	60	20.0	60	25	32	75.0	-	-
Netherlands	377	62.1	377	2.1	377	2.9	377	3.2	377	13.5	377	46.4	377	0
Poland	179	72.6	179	0.6	179	2.2	179	2.2	179	19	179	87.7	179	0
Portugal	201	75.6	201	4.0	201	5.5	201	5.5	201	33.8	201	90.5	201	2.5
Romania	859	73.1	859	19.0	859	1.7	859	1.7	859	49.4	859	93.1	_(a)	_
Slovakia	85	67.1	85	12.9	85	12.9	85	11.8	85	11.8	85	94.1	85	0
Slovenia	85	65.9	85	0	85	9.4	85	9.4	85	0	85	70.6	85	0
Spain	170	72.4	170	17.1	170	14.7	170	14.7	170	18.8	170	85.3	170	0
Sweden	197	9.1	197	0	197	0	197	0	197	0	197	11.2	197	0
United Kingdom	159	73.6	159	5.0	159	0	159	0	159	8.8	159	24.5	159	0
Total (MSs 27)	5,045	58.6	4,900	6.7	5,045	5.1	5,045	5.0	5,045	21.6	5,017	65.7	4037	0.9
Norway	205	6.3	205	0	205	1.5	205	1.5	205	0	205	3.4	205	0

Table 27: Occurrence of resistance to selected antimicrobials in indicator *Escherichia coli* from broilers in MSs reporting data in 2014



Country	Gent	amicin	Nalidixic acid		Sulfame	Sulfamethoxazole		Tetracycline		Tigecycline		Trimethoprim	
	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	
Austria	176	2.3	176	56.8	176	33.0	176	29.0	176	0	176	22.7	
Belgium	158	5.7	158	63.3	158	58.2	158	45.6	158	0	158	49.4	
Bulgaria	85	41.2	85	92.9	85	97.6	85	96.5	85	1.2	85	80.0	
Croatia	170	5.3	170	74.7	170	44.7	170	43.5	170	0	170	28.8	
Cyprus	87	9.2	87	74.7	87	66.7	87	78.2	87	0	87	57.5	
Czech Republic	196	0.5	196	63.8	196	24.5	196	24.0	196	0	196	14.3	
Denmark	191	3.1	191	11.0	191	13.1	191	5.8	191	0	191	7.3	
Estonia	71	0	71	77.5	71	40.8	71	18.3	71	0	71	46.5	
Finland	175	0.6	175	4.6	175	6.9	175	10.9	175	0	175	5.1	
France	226	1.8	226	42.0	226	48.2	226	63.3	226	0	226	42.9	
Germany	227	7.0	227	44.5	227	53.7	227	33.9	227	0	227	37.0	
Greece	172	12.8	172	86.0	172	70.3	172	68.0	172	0	172	61.6	
Hungary	170	5.3	170	73.5	170	43.5	170	39.4	170	0.6	170	23.5	
Ireland	167	6.0	167	41.9	167	49.7	167	52.7	167	0	167	39.5	
Italy	170	8.2	170	64.1	170	77.6	170	73.5	170	0	170	62.9	
Latvia	147	2.7	147	86.4	147	51.0	147	53.1	147	0	147	36.1	
Lithuania	84	25.0	85	90.6	85	76.5	82	56.1	85	0	85	61.2	
Malta	60	5.0	60	65.0	60	51.7	60	45.0	-	-	60	36.7	
Netherlands	377	6.4	377	44.6	377	52.5	377	42.4	377	0	377	44.6	
Poland	179	3.9	179	79.3	179	58.1	179	62.0	179	0	179	38.5	
Portugal	201	10	201	88.6	201	69.2	201	66.2	201	0	201	54.2	
Romania	859	30.5	859	88.5	859	76.8	859	73.8	859	0	859	57.4	
Slovakia	85	5.9	85	94.1	85	45.9	85	43.5	85	0	85	36.5	
Slovenia	85	0	85	64.7	85	37.6	85	31.8	85	0	85	34.1	
Spain	170	32.9	170	84.1	170	50.0	170	60.6	170	0	170	37.1	
Sweden	197	0	197	11.2	197	12.7	197	9.6	197	0	197	7.6	
United Kingdom	159	20.8	159	25.2	159	64.8	159	60.4	159	0	159	46.5	
Total (MSs 27)	5,044	11.6	5,045	62.6	5,045	53.1	5,043	50.1	4,985	0	5,045	40.6	
Norway	205	0	205	3.4	205	3.4	205	1.5	205	0	205	3.4	

Note: All E. coli isolates tested were susceptible to meropenem.

MSs: Member States; N: number of isolates tested; % Res: percentage of resistant isolates;-: no information available. (a): A number of colistin-resistant isolates are undergoing testing for the presence of *mcr-1* gene. The reported occurrence of colistin resistance is unlikely to equate to the occurrence of *mcr-1*.



Temporal trends in resistance among indicator Escherichia coli isolates from broilers

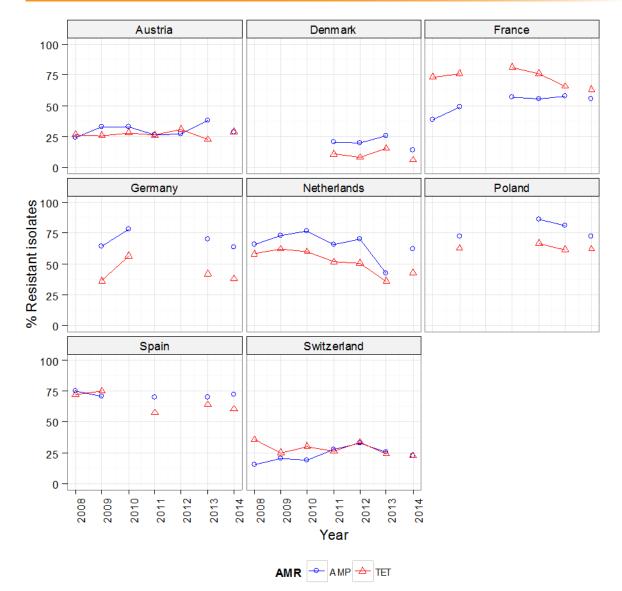
Temporal trends in resistance to selected antimicrobials in indicator *E. coli* isolates from broilers over the 7-year study period from 2008 to 2014 are displayed on Figure 68 and Figure 69. Four MSs and Switzerland provided resistance data on 5 years or more to be included in the statistical analysis.

Marked discrepancies in resistance levels between reporting MSs was observed for many of the antimicrobials. France, 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 2014, and France, Spain and the Netherlands registered the highest resistance to tetracyclines from 2008 to 2014. 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. Such inter-annual evolutions need to be confirmed by longer term trends.

Although resistance to many of the antimicrobials was 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 5 or more years were discerned. France and Switzerland recorded significant increases in resistance to ampicillin, ciprofloxacin and nalidixic acid, and cefotaxime only by France, while, contrastingly, the Netherlands reported significant declines in resistance to ampicillin, cefotaxime, ciprofloxacin, nalidixic acid and tetracyclines over the last 5 years.



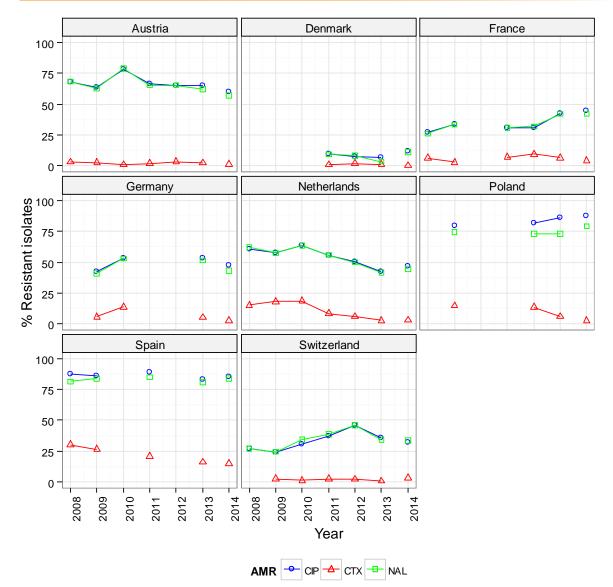


MS: Member State.

Statistically significant increasing trends over 5 or more years, as tested by a logistic regression model ($p \le 05$), were observed for ampicillin in France (\uparrow) and Switzerland (\uparrow). Statistically significant decreasing trends over five or more years were observed for ampicillin and tetracycline in the Netherlands (\downarrow) and for tetracycline in France (\downarrow).

Figure 68: Trends in ampicillin and tetracyclines resistance in indicator *Escherichia coli* from broilers in reporting countries, 2008–2014





MS: Member State.

Statistically significant increasing trends over 5 or more years, as tested by a logistic regression model ($p \le 05$), were observed for cefotaxime, ciprofloxacin and nalidixic acid in France (\uparrow) and for ciprofloxacin and nalidixic acid Switzerland (\uparrow). Statistically significant decreasing trends over 5 or more years were observed for cefotaxime, ciprofloxacin and nalidixic acid in the Netherlands (\downarrow), for ciprofloxacin and nalidixic acid in Austria (\downarrow).

Figure 69: Trends in cefotaxime, ciprofloxacin and nalidixic acid resistance in indicator *Escherichia coli* from broilers in reporting countries, 2008–2014

Spatial distribution of resistance among indicator Escherichia coli from broilers

The spatial distributions of ciprofloxacin, nalidixic acid and cefotaxime resistance in *E. coli* from broilers are shown in Figure 70, Figure 71 and Figure 72. The Nordic countries reported the lowest levels of resistance to both antimicrobials. The highest resistance to cefotaxime tended to be reported by the most western countries, whereas the spatial pattern for nalidixic acid was less clear.



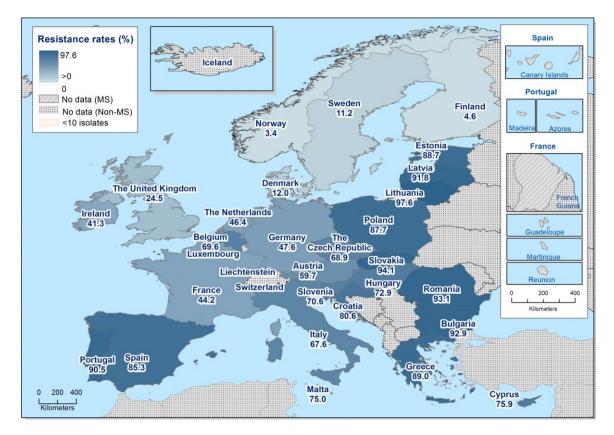


Figure 70: Spatial distribution of ciprofloxacin resistance among indicator *Escherichia coli* from broilers in reporting countries, in 2014

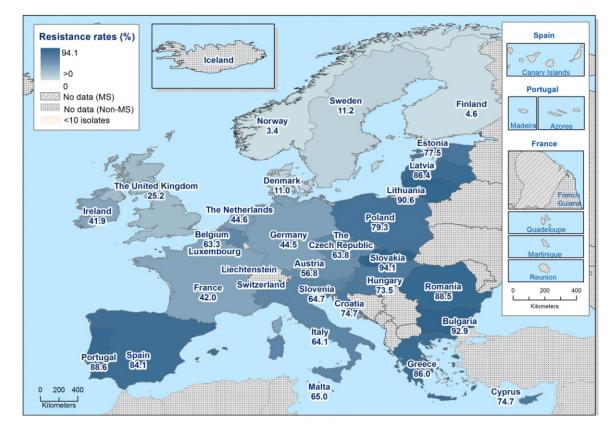


Figure 71: Spatial distribution of nalidixic acid resistance among indicator *Escherichia coli* from broilers in reporting countries, in 2014



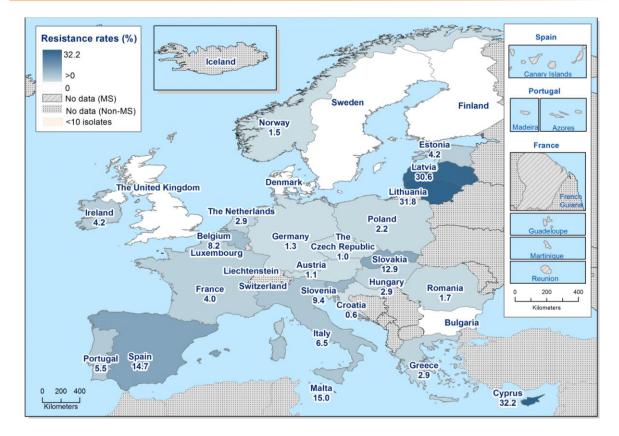


Figure 72: Spatial distribution of cefotaxime resistance among indicator *Escherichia coli* from broilers in reporting countries, in 2014

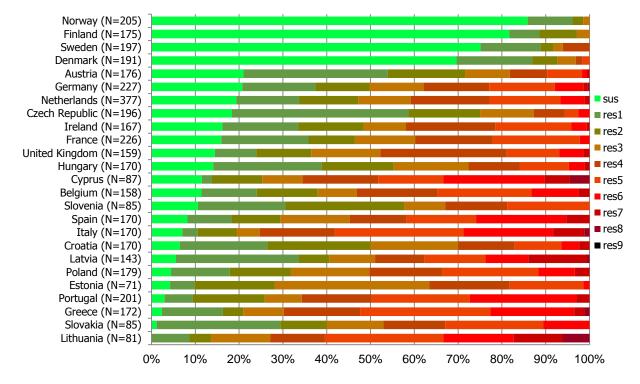
Multiple resistance among indicator Escherichia coli isolates from broilers

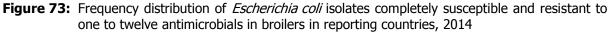
For 2014, 26 MSs and one non-MS provided data regarding resistance in indicator *E. coli* in broilers. Among the reporting countries, marked variations were observed in the percentages of completely susceptible isolates, which varied from none in Bulgaria and Lithuania to 81.7% in Finland and 85.9% in Norway.

Although all reporting countries recorded multiresistant isolates, the proportion differed substantially between them, reaching up to 95.3% in Bulgaria (Table COMESCHEBR). The frequency distributions (Figure 73) showed that isolates resistant to as many as five antimicrobials were reported from all reporting countries, except Finland, Norway and Sweden, and eight MSs reported a few isolates resistant to eight substances and two isolates reported by two MSs were resistant to nine substances.

Co-resistance to cefotaxime and ciprofloxacin was detected at high (Cyprus) to very low levels (Hungary) in the MSs, when CBPs were applied (Table <u>COMESCHEBR</u>).







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. The same behaviour was found for the isolates which were resistant to ceftazidime and were also resistant to cefotaxime. Considering the resistance patterns of isolates co-resistant to ciprofloxacin and cefotaxime (210 isolates), a number of isolates (125 out of 210 or 59.5%) were also resistant to ampicillin, sulfamethoxazole and tetracyclines, with or without additional resistances. Trimethoprim resistance was also commonly observed in isolates co-resistant to ciprofloxacin and cefotaxime, whereas resistance to nalidixic acid and ampicillin was expected in such co-resistant isolates. A variety of resistance patterns was observed in co-resistant isolates, each pattern occurring at a low frequency. 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 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.

Table 28:	Co-resistance	to	(fluoro)quinolones	and	third-generation	cephalosporins	in	indicator
	Escherichia co	<i>oli</i> fr	om broilers in MSs,	2014				

Country	N	MDR patterns of isolates resistant to both CIP and CTX (number of isolates)	CIP a	nt to both nd CTX, g ECOFFs	Resistant to both CIP and CTX, applying CBPs		
			Ν	% Res	Ν	% Res	
Austria	176	CTX-CAZ-CIP-AMP-NAL(1)	1	0.6	-	-	
Belgium	158	CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET(2)	13	8.2	4	2.5	
		CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)					
		CTX-CAZ-CIP-AMP-NAL(1)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(2)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TMP(3)					
		CTX-CIP-AMP-NAL-SMX-TET-TMP(1)					
		CTX-CIP-AMP-NAL-SMX-TMP(1)					



Country	N	MDR patterns of isolates resistant to both CIP and CTX (number of isolates)	CIP a	nt to both nd CTX, g ECOFFs	Resistant to both CIP and CTX, applying CBPs		
		(number of isolates)	N	% Res	N	% Res	
		GEN-CHL-CTX-CAZ-CIP-AMP-NAL(1)		70 1100		70	
		GEN-CTX-CAZ-CIP-AMP-NAL-SMX-TET(1)					
Croatia	170	GEN-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)	1	0.6	_	_	
Cyprus	87	CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(2)	28	32.2	18	20.7	
eypi do	0,	CTX-CAZ-CIP-AMP-NAL(4)	20	5212	10	2017	
		CTX-CAZ-CIP-AMP-NAL-SMX-TET(1)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(11)					
		CTX-CAZ-CIP-AMP-NAL-TET(1)					
		CTX-CAZ-CIP-AMP-NAL-TET-TMP(1)					
		CTX-CIP-AMP-NAL-SMX-TET-TMP(2)					
		GEN-CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(4)					
		GEN-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(2)					
Czech	196	CTX-CAZ-CIP-AMP-NAL(2)	2	1.0	_	_	
Republic			_				
Estonia	71	CTX-CAZ-CIP-AMP-NAL(2)	3	4.2	_	_	
Locoma	, 1	CTX-CIP-AMP-NAL(1)	J				
France	226	CTX-CAZ-CIP-AMP-NAL-SMX-TET(3)	4	1.8	_	_	
	220	CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)		1.0			
Germany	227	CHL-CTX-CAZ-CIP-AMP-COL-NAL-SMX-TMP(1)	2	0.9	_	_	
Germany	227	CHL-CTX-CAZ-CIP-AMP-COL-NAL-SMX-TMP(1) CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)	2	0.9			
Greece	172	CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1) CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)	4	2.3	4	2.3	
Greece	172	GEN-CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)	4	2.5	4	2.5	
		.,					
		GEN-CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TMP(1)					
llungen (170	GEN-CHL-CTX-CAZ-CIP-AMP-SMX-TET-TMP(1)	4	2.4	- 1	0.6	
Hungary	170	CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)	4	2.4	1	0.6	
Tualand	107	CTX-CAZ-CIP-AMP-NAL(3)	2	1.2			
Ireland	167	CTX-CAZ-CIP-AMP-NAL-SMX-TET(1)	2	1.2	-	-	
Th	170	CTX-CIP-AMP-NAL-SMX-TET(1)	_	2.0	2	1.2	
Italy	170	CHL-CTX-CAZ-CIP-AMP-COL-NAL-SMX-TET-TMP(1)	5	2.9	2	1.2	
		CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)					
		CTX-CIP-AMP-NAL-SMX-TET-TMP(1)					
		GEN-CHL-CTX-CAZ-CIP-AMP-SMX-TET(1)					
Latvia	143	CHL-CTX-CAZ-CIP-AMP-NAL-SMX(4)	43	30.1	15	10.5	
		CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET(4)					
		CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(18)					
		CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TMP(4)					
		CHL-CTX-CIP-AMP-NAL-SMX-TET-TMP(1)					
		CTX-CAZ-CIP-AMP-NAL(3)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(3)					
		CTX-CAZ-CIP-AMP-NAL-TET(1)					
		CTX-CAZ-CIP-AMP-SMX-TET(1)					
		CTX-CAZ-CIP-AMP-TET(1)					
		CTX-CAZ-CIP-NAL(1)					
		CTX-CIP-AMP-NAL-TET(1)					
		GEN-CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)					
Lithuania	81	CHL-CTX-CAZ-CIP-AMP-NAL-SMX(1)	26	32.1	14	17.3	
		CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET(1)					
		CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)					
		CHL-CTX-CIP-AMP-SMX-TMP(1)					
		CTX-CAZ-CIP-AMP-COL-NAL-SMX-TET(1)					
		CTX-CAZ-CIP-AMP-NAL(6)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(2)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TMP(1)					
		CTX-CAZ-CIP-AMP-NAL-TET(1)					
		CTX-CAZ-CIP-AMP-SMX-TET(1)					
		GEN-CHL-CTX-CAZ-CIP-AMP-NAL-SMX(1)					
		GEN-CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(5)					
		GEN-CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TMP(2)					
		GEN-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(2)					
Netherlands	377	CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)	2	0.5	_	_	
actionalius	577	CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1) CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TMP(1)	۷	0.5			
		CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TMP(1) CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET(1)	4	2.2	3	1.7	





Country	N	MDR patterns of isolates resistant to both CIP and CTX (number of isolates)	CIP a	nt to both nd CTX, g ECOFFs	Resistant to both CIP and CTX, applying CBPs		
		(number of isolates)	N	% Res	Ν	% Res	
		CTX-CAZ-CIP-AMP-NAL-SMX-TET(1)					
		CTX-CAZ-CIP-AMP-NAL-TET(2)					
Portugal	201	CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(2)	10	5.0	3	1.5	
		CTX-CAZ-CIP-AMP-COL-NAL-SMX(1)					
		CTX-CAZ-CIP-AMP-NAL(1)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TET(3)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(2)					
		GEN-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)					
Slovakia	85	CHL-CTX-CAZ-CIP-AMP-NAL-SMX(1)	10	11.8	8	9.4	
		CTX-CAZ-CIP-AMP-NAL-SMX-TET(2)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)					
		CTX-CAZ-CIP-AMP-NAL-TET(2)					
		CTX-CIP-AMP-NAL-SMX-TMP(3)					
		GEN-CTX-CAZ-CIP-AMP-NAL-SMX-TET(1)					
Slovenia	85	CTX-CAZ-CIP-AMP(1)	5	5.9	_	_	
		CTX-CAZ-CIP-AMP-NAL(1)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TMP(1)					
		CTX-CAZ-CIP-AMP-TET(2)					
Spain	170	CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET(1)	25	14.7	15	8.8	
•		CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)					
		CTX-CAZ-CIP-AMP-NAL(5)					
		CTX-CAZ-CIP-AMP-NAL-SMX(1)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TET(3)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(2)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TMP(3)					
		CTX-CAZ-CIP-AMP-NAL-TET(3)					
		CTX-CAZ-CIP-AMP-NAL-TET-TMP(1)					
		GEN-CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET(1)					
		GEN-CTX-CAZ-CIP-AMP-NAL-SMX(1)					
		GEN-CTX-CAZ-CIP-AMP-NAL-SMX-TET(1)					
		GEN-CTX-CAZ-CIP-AMP-NAL-SMX-TMP(1)					
		GEN-CTX-CAZ-CIP-AMP-NAL-TMP(1)					
Total (MSs 20)	3,311		194	5.9	87	2.6	

N: number of isolates tested; CIP: ciprofloxacin; CTX: cefotaxime; ECOFFs: epidemiological cut-off values; % Res: percentage of resistant isolates; CBPs: clinical breakpoints; CAZ: ceftazidime; NAL: nalidixic acid; AMP: ampicillin; TET: tetracycline; GEN: gentamicin; CHL: chloramphenicol; COL: colistin; SMX: sulfamethoxazole; TMP: trimethoprim; MSs: Member States.-: no information available.



A 'new' summary indicator of resistance in broilers at the EU level

A summary indicator of resistance in indicator *E. coli* from broilers at the EU level was calculated on the basis of the weighted mean by 'population correction unit-broiler' (PCU-broiler) of the proportions of resistant isolates observed in each of the 27 reporting MSs (Table 29 displays percentages of resistance). The population correction unit (PCU) is a specific indicator of animal population size which has been developed by the EMA primarily to estimate sales corrected by the animal population in individual countries. PCU is used as a proxy for the size of the animal population domestically produced at risk of being treated and is purely a technical unit of measurement. In the case of PCU-broiler, 1 PCU = 1 kg of broilers domestically produced and slaughtered. The data sources used and the methodology for the calculation of PCU are comprehensively described in Appendix 2 to EMA's report 'Trends in the sales of veterinary antimicrobial agents in nine European countries: 2005–2009' (EMA/ESVAC, 2011). For the year 2014, the PCU-broilers were computed by the EMA based on data reported by the MSs and provided to EFSA (Table 29).

Country	PCU-Broilers (in Kg)	weight PCU-Broilers
Belgium	200912716	0.032076388
Bulgaria	43136880	0.006886947
Croatia	34675704	0.005536092
Cyprus	10746150	0.001715659
Czech Republic	117238012	0.018717441
Denmark	118734540	0.018956367
Estonia	373748	5.96701E-05
Finland	63161160	0.010083891
France	835393588	0.133373385
Germany	830028816	0.132516882
Greece	114100540	0.018216534
Hungary	129355559	0.020652048
Ireland	_	-
Italy	508036793	0.081109776
Latvia	18506859	0.002954682
Lithuania	46878274	0.007484274
Malta	2242740	0.000358061
Netherlands	414665914	0.066202803
Poland	816079584	0.13028984
Portugal	183147322	0.029240084
Romania	9859665	0.001574129
Slovakia	12221144	0.001951147
Slovenia	34422847	0.005495723
Spain	621756469	0.099265503
Sweden	88917800	0.014196025
United Kingdom	942327808	0.150445792
Total (MSs 27)	6263570396	1

Table 29: PCU-broilers, in 27 MSs, 2014

Compared with the proportion of resistant isolates at the EU level (computed as the fraction of the total number of resistant isolates out of the total number of tested isolates in the group of reporting MSs) typically presented in this EU Summary Report, the summary indicator better accounts for the structure of the broiler populations within the EU i.e. the distribution of the broiler population per reporting MS. More weight is given to the resistance observed in the broiler populations of important size. Table 30 presents the resistance assessed by using 'totals' and the 'summary indicator' expressed in percentages of resistant indicator *E. coli* isolates from broilers. Similar results are obtained, although the 'summary indicator' is generally slightly lower than the 'Total'.



Table 30: Resistance in indicator *E. coli* from broilers assessed by the percentage of resistant isolates (Total) and 'summary indicator' (weighted mean of the proportions of resistant isolates in the reporting MSs) in the EU, 27 MSs, 2014

EU MSs 27	Ampicillin	Azithromycin	Cefotaxime	Ceftazidime	Chloramph	enicol	Ciproflox	acin	Colistin
Total (%)	58.7	6.7	5.1	5	21.	.6	65.7	7	3.7
Indicator (%)	64.2	5.3	4.2	4.2	16.	7	57.2	7	2.0
EU MSs 27	Gentamicin	Nalidixic acid	Sulfamethox	cazole Tet	tracycline	Tigecyo	cline	Trimet	hoprim
EU MSs 27 Total (%)	Gentamicin 11.6		Sulfamethox		tracycline 50.1	Tigecyo	cline		t hoprim 40.6

Antimicrobial resistance in indicator Escherichia coli isolates from fattening turkeys

In 2014, 11 MSs provided antimicrobial resistance data on indicator *E. coli* in fattening turkeys which were included in the following analysis (Table 31).

Resistance levels among indicator Escherichia coli isolates from fattening turkeys

In 2014, resistance to ampicillin, sulfamethoxazole and tetracyclines in *E. coli* isolates from fattening turkeys was generally very high among reporting MSs, ranging from 16.9% to 87.6%, whereas resistance to chloramphenicol and trimethoprim was overall high at the reporting MSs level. Conversely, resistance to azithromycin and gentamicin was low to moderate in most reporting countries, with the notable exception of Italy and Romania, which reported high resistance. The colistin resistance was generally recorded at low to very low levels. Resistance to ciprofloxacin and nalidixic acid was high and very high among almost all reporting countries, ranging between 1.7% and 89.5%. The resistance to cefotaxime and ceftazidime was either not detected or reported at low levels in all reporting countries.

Temporal trends in resistance among indicator Escherichia coli isolates from fattening turkeys

There were not enough data to present the trends in resistance to selected antimicrobials in indicator *E. coli* from fattening turkeys from 2008 to 2014.

Spatial distribution of resistance among indicator Escherichia coli isolates from fattening turkeys

The spatial distribution of ciprofloxacin, nalidixic acid and cefotaxime resistance in indicator *E. coli* from fattening turkeys is shown in Figure 74, Figure 75 and Figure 76, respectively. For nalidixic acid, most countries reported moderate and high levels of resistance so the spatial pattern was less clear. Figure 76 illustrates the variability in levels of cefotaxime resistance in *E. coli* across the EU and the absence of a clear spatial distribution.

Country	Amp	oicillin	Azithr	omycin	Cefo	taxime	Cefta	azidime	Chloran	nphenicol	Ciprof	loxacin	Colis	tin ^(a)
	N	% Res	Ν	% Res	N	% Res	N	% Res	Ν	% Res	N	% Res	N	% Res
Austria	125	48.0	125	0.8	125	1.6	125	0.8	125	9.6	125	28.0	125	0
France	238	64.3	238	0.8	238	0.4	238	0.4	238	16.4	238	21.0	238	5.9
Germany	170	64.7	170	8.8	170	2.4	170	1.8	170	25.9	170	37.6	170	4.7
Hungary	170	61.2	170	1.8	170	1.8	170	1.8	170	18.8	170	62.9	170	0
Italy	170	78.8	170	3.5	170	1.2	170	1.2	170	26.5	170	60.0	170	22.9
Poland	170	75.9	170	1.2	170	2.4	170	1.8	170	22.9	170	70.0	170	2.9
Portugal	185	80.0	185	4.9	185	2.7	185	2.7	185	52.4	185	79.5	185	27.0
Romania	38	86.8	38	21.1	38	0	38	0	38	78.9	38	89.5	38	2.6
Spain	170	85.3	170	3.5	170	10.0	170	10.0	170	47.6	170	85.9	170	3.5
Sweden	59	25.4	59	0	59	1.7	59	1.7	59	3.4	59	3.4	59	0
United Kingdom	168	69.0	168	1.2	168	0	168	0	168	11.3	168	18.5	168	0
Total (MSs 11)	1,663	69.0	1,663	3.2	1,663	2.3	1,663	2.2	1,663	26.5	1,663	50.3	1,663	7.4

Table 31: Occurrence of resistance to selected antimicrobials in indicator *Escherichia coli* from fattening turkeys in reporting countries, in 2014

Country	Gentamicin		Nali	dixic acid	Sulfame	ethoxazole	Tetra	cycline	Tige	cycline	Trime	ethoprim	
	N	% Res	N	% Res	Ν	% Res	N	% Res	N	% Res	N	% Res	
Austria	125	0	125	18.4	125	19.2	125	40.8	125	0	125	12	
France	238	4.2	238	19.7	238	45.8	238	75.2	238	0	238	37.4	
Germany	170	10.6	170	31.8	170	52.4	170	56.5	170	0	170	30.6	
Hungary	169	6.5	170	52.9	170	50.6	170	64.1	170	0.6	170	20	
Italy	170	21.8	170	49.4	170	62.4	170	77.6	170	0	170	58.8	
Poland	170	11.8	170	58.8	170	55.9	170	73.5	170	0	170	41.2	
Portugal	185	14.6	185	73.5	185	71.9	185	85.9	185	0	185	49.7	
Romania	38	47.4	38	76.3	38	73.7	38	84.2	38	0	38	52.6	
Spain	170	11.2	170	76.5	170	67.1	170	87.6	170	0	170	42.4	
Sweden	59	0	59	1.7	59	16.9	59	23.7	59	0	59	5.1	
United Kingdom	168	4.2	168	17.3	168	32.7	168	79.2	168	0	168	25	
Total (MSs 11)	1,662	10.0	16,63	43.5	1,663	51.1	1,663	70.9	1,663	0.1	1,663	35.4	

All E. coli isolates tested were susceptible to meropenem.

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

(a): A number of colistin-resistant isolates are undergoing testing for the presence of mcr-1 gene. The reported occurrence of colistin resistance is unlikely to equate to the occurrence of mcr-1.



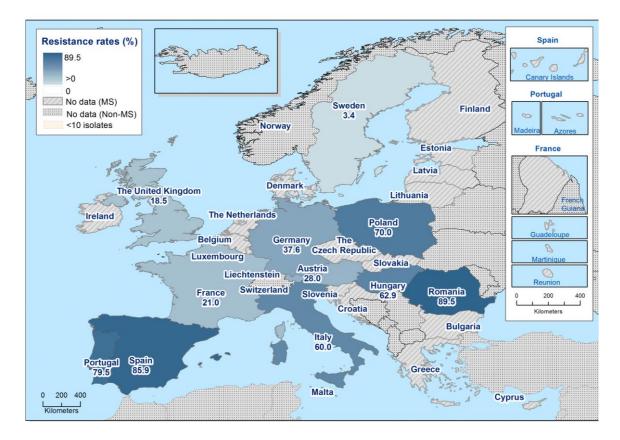


Figure 74: Spatial distribution of ciprofloxacin resistance among indicator *Escherichia coli* from fattening turkeys in reporting countries, in 2014

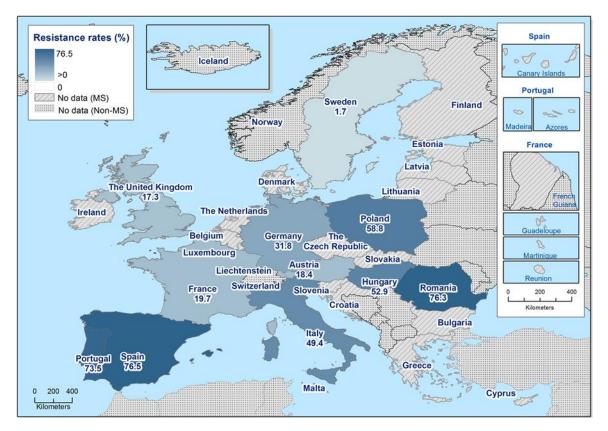


Figure 75: Spatial distribution of nalidixic acid resistance among indicator *Escherichia coli* from fattening turkeys in reporting countries, in 2014



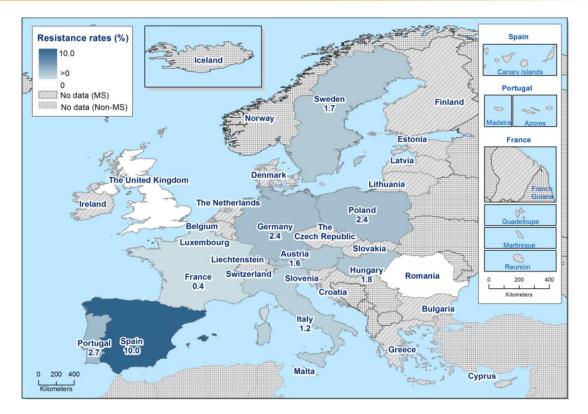
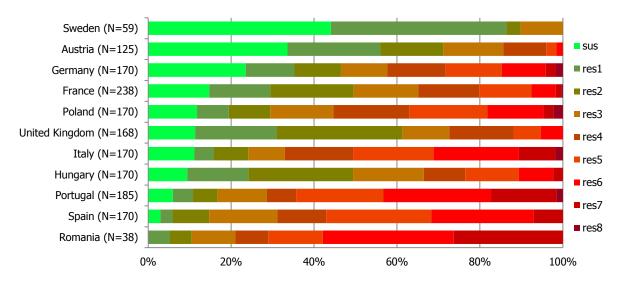
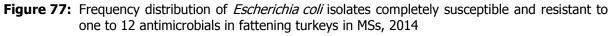


Figure 76: Spatial distribution of cefotaxime resistance among indicator *Escherichia coli* from fattening turkeys in reporting countries, in 2014

Multiple resistance among indicator Escherichia coli isolates from fattening turkeys

Eleven MSs reported isolate-based data from fattening turkeys. Around 14.0% of the isolates tested were susceptible to the panel tested. In Sweden, 44.1% of the isolates 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>COMESCHETURK</u>). The frequency distributions (Figure 77) showed that except Sweden all reporting countries detected MDR to as six antimicrobial classes. Very few isolates (14 isolates out of 1,663 isolates tested) exhibited co-resistance to cefotaxime and ciprofloxacin using either ECOFFs or CBPs as interpretive criteria (Table <u>COESCHETURK</u>).







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

Indicator *E. coli* isolates resistant to cefotaxime and ciprofloxacin using CBPs were observed in few isolates from Germany, Italy, Poland and Spain, and ampicillin, sulfamethoxazole and tetracycline resistance was often present in the isolates tested (Table 32 and Table <u>MULTIESCHETURK</u>). These additional resistances (together with trimethoprim resistance in some cases) were noted in *E. coli* isolates showing high-level ciprofloxacin resistance (Table <u>CIPESCHETURK</u>).

Country	N	Multidrug Resistance patterns of isolates resistant to both CIP and CTX	CIP a	nt to both and CTX, ag ECOFFs	Resistant to both CIP and CTX, applying CBPs		
		(number of isolates)	N	% Res	Ν	% Res	
Austria	125	CTX-CAZ-CIP-AMP-TET(1)	1	0.8	-	-	
France 238 CTX-CAZ-CIP-AMP-COL-NAL-TMP(CTX-CAZ-CIP-AMP-COL-NAL-TMP(1)	1	0.4	_	-	
Germany	170	CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)	3	1.8	2	1.2	
		GEN-CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET- TMP(2)					
Hungary	170	CTX-CAZ-CIP-AMP-NAL(1)	2	1.2	_	-	
		CTX-CAZ-CIP-AMP-NAL-SMX-TET(1)					
Italy	170	CTX-CAZ-CIP-AMP-NAL-TET-TMP(1)	2	1.2	1	0.6	
		CTX-CAZ-CIP-AMP-SMX-TET-TMP(1)					
Poland	170	CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)	4	2.4	1	0.6	
		CHL-CTX-CAZ-CIP-AMP-SMX-TET(1)					
		GEN-CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET- TMP(1)					
		GEN-CHL-CTX-CIP-AMP-NAL-SMX-TET-TMP(1)					
Portugal	185	CHL-CTX-CAZ-CIP-AMP-NAL-SMX(1)	4	2.2	_	-	
		CHL-CTX-CAZ-CIP-AMP-COL-NAL-SMX-TET(2)					
		CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(1)					
Spain	170	CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET(6)	15	8.8	10	5.9	
		CHL-CTX-CAZ-CIP-AMP-NAL-SMX-TET-TMP(4)					
		CHL-CTX-CAZ-CIP-AMP-SMX-TET(2)					
		CTX-CAZ-CIP-AMP-NAL(1)					
		CTX-CAZ-CIP-AMP-NAL-SMX-TMP(1)					
		CTX-CAZ-CIP-AMP-NAL-TET-TMP(1)					
Total (MSs 8)	1,398		32	2.3	14	1	

Table 32: Co-resistance to fluoroquinolones and third-generation cephalosporins in indicator

 Escherichia coli from fattening turkeys in MSs, 2014

N: number of isolates tested; CIP: ciprofloxacin; CTX: cefotaxime; ECOFFs: epidemiological cut-off values; % Res: percentage of resistant isolates; CBPs: clinical breakpoints; CAZ: ceftazidime; NAL: nalidixic acid; AMP: ampicillin; TET: tetracycline; GEN: gentamicin; CHL: chloramphenicol; COL: colistin; SMX: sulfamethoxazole; TMP: trimethoprim; MSs: Member States.-: no information available.

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

The MDR patterns in indicator *E. coli* from broilers and fattening turkeys are shown in Tables <u>MULTIESCHEBR</u> and <u>MULTIESCHETURK</u>.

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 (148 different patterns displayed by 2,834 isolates), reflecting the diverse nature of the *E. coli* strains tested (Table <u>MULTIESCHEBR</u>). Resistance to ampicillin, ciprofloxacin/nalidixic acid, sulfamethoxazole, tetracyclines and trimethoprim was observed as a core pattern in 41.2% of all *E. coli* isolates from broilers and was the predominant MDR pattern (9.6%). This is similar with the data from previous year, a common core of resistance to ampicillin, sulfamethoxazole 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/ceftazidime; cefotaxime/ceftazidime resistance occurred as a component of infrequent MDR patterns in 8.7% of the isolates showing MDR. Ciprofloxacin/nalidixic acid resistance frequently occurred as a component of MDR in *E. coli* from broilers and was a component of 103 of the 148 MDR patterns detected (70.0%) and was observed in 84.6% of MDR isolates (2,397 out of 2,834).

Multiple drug resistance in *Escherichia coli* isolates from fattening turkeys

The overall range of different MDR patterns observed in indicator E. coli isolates from fattening turkeys in MSs reporting isolate-based data were similar to that seen in broilers, with a large number of different resistance patterns evident (97 different patterns displayed by 986 isolates), again reflecting the diverse nature of the *E. coli* strains which have been tested (Table MULTIESCHETURK). Particular MDR patterns were predominant in fattening turkeys, with one pattern (resistance to ampicillin, chloramphenicol, ciprofloxacin/nalidixic acid, tetracyclines, sulfamethoxazole and trimethoprim) occurring at a frequency of 21.1% among the MDR patterns obtained and 12.5% of all E. coli from turkeys. In fattening turkeys, E. coli with three MDR patterns (including a common core pattern of resistance to ampicillin, ciprofloxacin/nalidixic acid and tetracyclines) accounted for approximately 40.0% of the total number of multiresistant E. coli isolates for which data were available. Resistance to ampicillin, ciprofloxacin/nalidixic acid and tetracyclines also occurred as a recurring core pattern in isolates showing additional resistances. Considering those resistance patterns occurring at a higher frequency in fattening turkeys, these did not generally include resistance to cefotaxime/ceftazidime; however, cefotaxime/ceftazidime resistance occured as a component of infrequent resistance patterns in 4.0% of MDR isolates. Ciprofloxacin/nalidixic acid resistance occurred less frequently than in broilers as a component of MDR in fattening turkeys, occurring in 61 of the 97 (62.9%) resistance patterns observed and was present in 74.1% of fattening turkeys MDR E. coli isolates (731 out of 986).

Resistance to colistin in *E. coli* from broilers and turkeys (see also main findings section)

Monitoring of colistin resistance has recently assumed greater importance with the discovery of transferable resistance to colistin, conferred by the gene *mcr-1* in China (Liu et al., 2015). The *mcr-1* gene encodes a phosphoethanolamine transferase, which adds a phosphoethanolamine moiety to the lipid A of the lipopolysaccharide component of the bacterial cell wall. Historically, resistance to colistin was related to chromosomal alterations, which also affected lipid A and reduced the binding of colistin to the cell wall, but these chromosomal alterations were not transferable. 2014 was the first year in which the monitoring of colistin resistance in *E. coli* from animals was mandatory, and 0.9% and 7.4% of the *E. coli* isolated from broilers and turkeys, respectively, were resistant to this antimicrobial.

Where colistin resistance is conferred by chromosomal alterations, then isolates with such alterations either arise by mutation or through clonal expansion of resistant strains. In plasmid-mediated colistin resistance, depending on the transmissibility and promiscuity of the plasmid and any other resistance genes which are carried by the pasmid, then a different progression in the development of resistance might be expected. In the case of promiscuous plasmids, this might involve rapid and extensive dissemination to a wide range of *E. coli* strains.

As this report was being prepared, a number of countries worldwide reported the presence of *mcr-1* in enterobacteriaceae recovered from humans, food or animals. Such reports demonstrated that *mcr-1* was present in *E. coli* in food-producing animals (pigs and cattle) in Belgium in 2011-2012 (Malhotra-Kumar et al., 2016) in France in veal calves in 2005 (Haenni et al., 2016) and in Germany in pigs in 2010 (Falgenhauer et al., 2016). Furthermore, the *mcr-1* gene with or without the truncated mobile genetic element IS*Apl1* in some cases occurred on a plasmid different from that reported in China, which indicated that the *mcr-1* gene has been transferred between different plasmids (Malhotra-Kumar et al., 2016). These studies also showed that plasmids carrying *mcr-1* had transferred between different bacteria, because unrelated *E. coli* strains carried *mcr-1* (Haenni et al., 2016). *E. coli* isolates reported from pigs in Germany and veal calves in France also produced extended-spectrum beta-lactamases (Falgenhauer et al., 2016; Haenni et al., 2016); although isolates from animals in Belgium did not produce ESBLs, one which was sequenced showed multi-drug resistance (Malhotra-Kumar et al., 2016). Although enterobacteriaceae from animals in Europe have not so far been reported which carry *mcr-1* and which are resistant to carbapenems, this has been reported in human clinical isolates (Poirel et al., 2016).



3.3.3. 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 multiresistant organisms.

A total of 27 MSs and two non-MSs provided quantitative *E. coli* MIC data in 2014 for at least one of the livestock species. Reported antimicrobial resistance data in *E. coli* isolates from food-producing animals, 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 broilers and fattening turkeys observed between 2008 and 2014, 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.

Resistance levels were generally higher among *E. coli* isolates from broilers than isolates from fattening turkeys. This was the fourth year that resistance data were reported separately for different production types of *Gallus gallus* and it was the first year that mandatory AMR monitoring in indicator *E. coli* broilers was in place.

Generally, similar 'microbiological' resistance levels were identified for ampicillin, sulfamethoxazole 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 higher in broilers (11.6%) than in fattening turkeys (10.0%). 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 found at higher levels in *E. coli* isolates from broilers than from fattening turkeys. 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 fluoroguinolone 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 fattening turkeys. 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.

'Microbiological' resistance to third-generation cephalosporins (cefotaxime and ceftazidime) – another class categorised as critically important in human medicine – was infrequently detected in 2014 in *E. coli* from fattening turkeys where levels were < 2.3% in all reporting MSs. A number of reporting MSs recorded high to moderate levels in *E. coli* from broilers, and resistance was typically higher in isolates from broilers than in fattening turkeys. 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.



The levels of MDR²¹ in most reporting countries were relatively high in indicator *E. coli* isolates from both broilers (8.1–95.3%) and fattening turkeys (10.2–89.5%), they were overall at very high levels of resistance (54.3% in broilers and 58.9% in turkeys); 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, Finland, Sweden and Norway were the only reporting countries with > 70% full susceptibility, while, in fattening turkeys, Sweden and Austria were the only reporting MSs with >30% full susceptibility. Considering clinical resistance, corresistance to cefotaxime and ciprofloxacin was detected at very low to high levels in broilers in 12 MSs and at very low to low levels in four MSs in fattening turkeys in 2014. These *E. coli* isolates were randomly chosen from non-selective culture plates and they may have limited direct relevance to human medicine; however 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 fattening turkeys from MSs reporting isolate-based data have again been included in this report. Resistance to ampicillin, ciprofloxacin, sulfamethoxazole, tetracyclines and trimethoprim was observed in 9.8% of all *E. coli* isolates from broilers and was the predominant MDR pattern. Particular MDR patterns were predominant in fattening turkeys, with one pattern occurring at a frequency of 15.9% amongst the MDR patterns obtained. Two other MDR patterns each accounted more than 9.0% of the total MDR 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*. Strain typing of selected *E. coli* isolates and detailed examination of *E. coli* plasmids would assist in differentiating between clonal expansion of MDR *E. coli* strains and the spread of promiscuous MDR plasmids between different *E. coli* strains by bacterial conjugation. The findings indicate some differences between fattening turkeys 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 and also in fattening turkeys, 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 84.7% of MDR *E. coli* isolates from broilers (2,386 out of 2,818), whereas ciprofloxacin resistance also occurred frequently as a component of MDR in fattening turkeys and was present in 74.4% (728 out of 979) of MDR *E. coli* isolates. Considering the resistance patterns occurring at a higher frequency in broilers, and fattening turkeys, these did not generally include resistance to cefotaxime; however, cefotaxime resistance did occur as a component of infrequent resistance patterns.

Tigecycline resistance was infrequently detected in *E. coli* isolates from broilers and turkeys. There are technical issues in relation to testing tigecycline susceptibility and the isolates identified as showing microbiological resistance will be subjected to further investigation at the EURL-AR. Marked differences were evident between the results obtained for *E. coli* (where resistance was rare) and *Salmonella* where resistance occurred more frequently and was associated with certain serovars, for example, *S.* Infantis.

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, nalidixic acid, cefotaxime, ceftazidime and ampicillin. This occurred in 0.6% of the total number of *E. coli* isolates from broilers and was detected in 11 MSs which reported co-resistant to ciprofloxacin and cefotaxime. 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 applying microbiological breakpoints was less common in fattening turkeys (2.3% of all *E. coli* isolates) than in broilers (5% of all *E. coli*).

²¹ Proportions of isolates showing reduced susceptibility to at least three antimicrobial classes according to epidemiological cutoff values.



A variety of resistance patterns was observed in high-level ciprofloxacin-resistant *E. coli* isolates from broilers and fattening turkeys, with each pattern occurring at a low frequency. This may suggest that, in fattening turkeys and broilers, there is random mutation occurring in diverse strains of *E. coli*, which are accumulating mutations and acquiring resistance. The possible occurrence of plasmid-mediated quinolone resistance genes in those isolates, as suggested by the phenotypic patterns, calls for confirmation.

Integrons can be associated with particular antimicrobial resistance genes and, in the Spanish study,²² both class 1 and class 2 integrons were detected in fattening turkeys 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, whereas 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 ampicillin for resistance purposes) and tetracyclines. The common core patterns of resistance to ampicillin, sulfamethoxazole, tetracyclines and trimethoprim (and combinations thereof) frequently observed in the monitoring of *E. coli* isolates are probably therefore related to the presence of integrons.

Full resistance to all of the antimicrobials in the test panel was not observed in any isolates from broilers and fattening turkeys. Although no *E. coli* isolates from broilers or turkeys were resistant to meropenem, further testing with the supplementary panel of cephalosporins and carbapenems revealed that a number of isolates from broilers and a single isolate from turkeys were resistant to ertapenem. The phenotypic resistance patterns were suggestive of permeability changes to the bacterial cell wall (loss of porins) acting in association with AmpC or ESBL enzymes and are discussed further in Chapter 3.6 on cephalosporin resistance.

²² High prevalence of multiple resistance to antibiotics in *Salmonella* serovars isolated from a poultry slaughterhouse in Spain, Vet Microbiol. 2004 Nov 30;104(1-2):133–9.



3.4. Meticillin-resistant *Staphylococcus aureus*

Meticillin-resistant *Staphylococcus aureus* (MRSA)

MRSA has been recognised as an important cause of infections in humans for decades. Strains of MRSA causing infections in humans can be divided into three broad categories, healthcareassociated (HA-), community-associated (CA-) and livestock-associated (LA-) MRSA. LA-MRSA has been detected in pigs and poultry, as well as some other farm animal species in many countries worldwide. HA-MRSA and CA-MRSA include strains which predominantly affect humans, and these generally do not involve food-producing animals, although LA-MRSA may also be harboured by humans, especially where there is occupational contact with affected livestock. LA-MRSA may cause illness in human, although transmissibility between humans has been shown to be very limited, even in healthcare facilities.¹

Antimicrobial susceptibility in European invasive *Staphylococcus aureus* isolates is reported by the MSs to the European Antimicrobial Resistance Surveillance Network (EARS-Net) hosted by ECDC. Molecular typing data are not reported and thus, where there may be possible links to the animal reservoir of LA-MRSA, these cannot be detected easily with current monitoring procedures, at least at the European level. The EU/EEA population-weighted mean MRSA percentage was 17.4.0% in 2014. Although a significantly decreasing trend was observed from 2011 to 2014, the decrease was less pronounced compared with what was observed for the period from 2009 to 2012. MRSA remains a human public health priority, as the percentage of MRSA remains above 25.0% in 7 out of 19 countries, mainly in southern and south-eastern Europe (ECDC, 2015).

A principal recommendation (EFSA, 2009a, 2009c and 2012b) 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. Isolates representative of various animal and food origins should be analysed for lineage determination, antimicrobial susceptibility and virulence-associated traits. Monitoring of MRSA in animals and food is currently performed by MSs voluntarily.

3.4.1. Meticillin-resistant Staphylococcus aureus in food and animals

LA-MRSA isolates are the principal focus of this section, which summarises the MRSA prevalence and resistance results in various foodstuffs and food-producing animal species/populations reported by six MSs to EFSA in 2014 (Table <u>MRSAOVERVIEW</u>). Data on AMR of MRSA isolates from food-producing animals were reported by only two countries in 2014; these countries also reported molecular typing data. This section also includes occurrence data reported on companion animals. To date, methods for the isolation of MRSA from food and animals have not been harmonised at the EU level and therefore, the methods used by individual reporting MSs may differ in sensitivity.

Meticillin-resistant Staphylococcus aureus in food

In 2014, four MSs (Germany, Slovakia, Poland and Spain) and Switzerland reported information on the occurrence of MRSA in various categories of food (Table 33). Germany investigated a wide range of meat from turkeys, recording a high level (42.5%) of MRSA prevalence in this food category. Spain examined a range of food products for MRSA, and positive isolates were obtained from fresh meat from pigs (one isolate, 3.2%) and meat products from pigs (28 isolates, 12.9%). Switzerland investigated 319 samples of fresh broiler meat, among which 22 samples (6.9%) tested positive isolates were reported without specifying *spa*-type. Switzerland reported the corresponding *spa*-typing for all the positive results. Generally, meat from several different sources proved positive for MRSA, including meat from broilers, turkeys and pigs, at various levels of prevalence.

²³ 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 (EMA) on MRSA in livestock, companion animals and food (EFSA, 2009a) provide more background information and recommendations on MRSA. 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 multiresistance profile of MRSA in food-producing animals and food thereof (EFSA, 2012b).



Food categories	Description	Sample unit	Number		
Country			Units tested	(%) Positive for MRSA	
Cheeses ma	ade from cows' milk				
Poland	Soft and semi-soft, processing plant, surveillance	Single	3	0	
Cheeses ma	ade from goats' milk				
Poland	Hard, processing plant, surveillance	Single	1	0	
	Soft and semi-soft, farm/processing plant, surveillance	Single	5	0	
Confectione	ery products and pastes				
Slovakia	Processing plant, monitoring	Single	2	0	
Meat from I	bovine animals				
Spain	Meat products/minced meat, surveillance	Single	8	0	
Meat from I	broilers				
Spain	Meat products/Meat preparation, surveillance	Single	21	0	
Switzerland	Fresh, retail, monitoring	Batch	319	22 ^(a) (6.9%)	
Meat from o	lucks and geese				
Spain	Fresh, surveillance	Single	11	0	
Meat from	pigs				
Spain	Fresh, surveillance	Single	31	1 (3.2%)	
	Meat products, surveillance	Single	217	28 (12.9%)	
	Minced meat, Surveillance	Single	17	0	
Meat from t	turkey				
Germany	Fresh, retail, monitoring – active	Single	339	144 (42.5%)	
Spain	Meat preparation, surveillance	Single	2		
Milk					
Poland	Raw milk for manufacture, processing plant, monitoring	Single	4	0	
Spain	Raw milk, surveillance	Single	2	0	
	essed food products and prepared dishes				
Slovakia	Noodles/sandwiches/ready-to-eat salads, catering/processing plant, monitoring/surveillance	Single	11	0	
Vegetables					
Slovakia	Pre-cut, catering/processing plant, monitoring	Single	4	0	
Spain	Surveillance	Single	3	0	

(a): Isolates belonged to the *spa*-type t011 (3 isolates), t032 (3), t034 (14), t571 (1), t899 (1).

Meticillin-resistant *Staphylococcus aureus* in animals

Monitoring meticillin-resistant Staphylococcus aureus in food-producing animals

For 2014, Belgium, Germany, the Netherlands, Iceland, Norway, Sweden and Switzerland reported data on the prevalence of MRSA in food-producing animals and/or their environment (Table 34).

The MRSA prevalence in fattening pigs in Switzerland was assessed at 26.5% and, although only the limited number of 5 animals were investigated in the Netherlands, 3/5 animals tested positive. The prevalence reported in Norway, which tested a very large number of samples from pig farms, was very low at 0.1%.

Germany reported a low prevalence of 9.7% in bulk tank milk from dairy herds, whereas the Netherlands, testing a large number of dairy cows, registered a moderate prevalence of 16.9%.

A holding prevalence of 0.6% and 3.0%, respectively, was recorded in breeding flocks of chickens and flocks of laying hens in Belgium. Germany reported a high prevalence of turkey flocks positive for MRSA (21.9%) in investigating turkeys sampled on the farm.



A number of different *spa*-types were reported (Table 34).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. The other *spa*-types detected in pigs in Switzerland were single isolates of t899, which can be associated with ST9 or CC398 (Guardabassi et al., 2009), t2741, which can be associated with CC11 or CC398 (EFSA, 2009b; Köck et al. 2013) and t208, which is associated with ST49 in Switzerland (Overesch et al., 2011). Belgium provided *spa*-type data for MRSA isolates recovered from *Gallus gallus*: t1985, which was detected in a single breeding flock of *Gallus gallus* in Belgium, is associated with MRSA CC398, whereas t011, which is also associated with CC398, was detected in laying hens.

Table 34:	Meticillin-resistant	Staphylococcus	aureus	in	food-producing	animals	(excluding	clinical
	investigations), 20)14						

Production type/Description	Sample unit	Number		
		Units tested	(%) Positive for MRSA	
ne animals)			·	
Dairy cows, farm, monitoring – active	Herd (bulk tank milk)	372	36 (9.7%)	
Dairy cows, farm, monitoring		12,075	2,045 (16.9%)	
s (fowl)				
Breeding flocks, farm, monitoring – active	Holding	159	1 ^(a) (0.6%)	
Laying hens, farm, monitoring - active	Holding	233	7 ^(b) (3.0%)	
Fattening pigs, slaughterhouse, monitoring	Slaughter batch	24	0	
Fattening pigs, farm, monitoring	Animal	5	3 (60.0%)	
Farm, control and eradication programmes	Herd	986	$1^{(c)}(0.1\%)$	
Fattening pigs, slaughterhouse, monitoring	Animal	298	79 ^(d) (26.5%)	
			· · · ·	
Farm, monitoring – active	Flock	192	42 (21.9%)	
	De animals) Dairy cows, farm, monitoring – active Dairy cows, farm, monitoring 5 (fowl) Breeding flocks, farm, monitoring – active Laying hens, farm, monitoring - active Fattening pigs, slaughterhouse, monitoring Fattening pigs, farm, monitoring Farm, control and eradication programmes Fattening pigs, slaughterhouse, monitoring	Dairy cows, farm, monitoring – active Herd (bulk tank milk) Dairy cows, farm, monitoring Herd (bulk tank milk) Dairy cows, farm, monitoring Holding s (fowl) Breeding flocks, farm, monitoring – active Holding Breeding flocks, farm, monitoring – active Holding Laying hens, farm, monitoring – active Holding Fattening pigs, slaughterhouse, monitoring Slaughter batch Fattening pigs, farm, monitoring Animal Farm, control and eradication programmes Herd Fattening pigs, slaughterhouse, monitoring Animal	Units Units Dairy cows, farm, monitoring – active Herd (bulk tank milk) 372 Dairy cows, farm, monitoring 12,075 Construction 12,075 Strength 159 Breeding flocks, farm, monitoring – active Holding 159 Laying hens, farm, monitoring – active Holding 233 Fattening pigs, slaughterhouse, monitoring Slaughter batch 24 Fattening pigs, farm, monitoring Animal 5 Farm, control and eradication programmes Herd 986 Fattening pigs, slaughterhouse, monitoring Animal 298	

(b): Isolates belonged to the *spa*-type t011 (2 isolates) and unspecified (5).

(c): Isolate belonged to the *spa*-type t011.

(d): Isolates belonged to the spa-type t011 (19 isolates), t034 (57), t208 (1), t2741 (1), t899 (1).

Survey on the prevalence of meticillin-resistant *Staphylococcus aureus* (MRSA) in breeding pig holdings with in Sweden

To assess the occurrence and the diversity of MRSA in pig breeding holdings (holdings housing and selling mainly breeding pigs) in Sweden, a survey was carried out to determine the prevalence of holdings positive for MRSA in Sweden in September–December 2014. The survey involved all 39 nucleus and multiplying pig holdings in Sweden. The weaned pigs of 5–12 weeks of age were investigated for MRSA colonisation. Six pigs per box and 15 boxes per herd were sampled. Sampling was performed by scrubbing the skin behind one ear with a sterile compress. The same compress was used to sample six pigs in the same box, constituting a pooled sample. Samples were tested for the presence of MRSA by using the laboratory method used within the framework of the EU baseline survey (EFSA, 2009), including a two-step selective enrichment, followed by plating on selective media and blood agar plates.

MRSA was not detected in any sample and holdings investigated. There are reasons to believe that the MRSA situation in the Swedish pig population still is favourable. The low number of notified human cases of MRSA CC398 supports this opinion.

In accordance with the Swedish legislation, MRSA in food-producing animals is notifiable to the Swedish Board of agriculture, which, in the case of findings of MRSA in such animals, shall decide on actions to be taken.



Clinical investigations for meticillin-resistant Staphylococcus aureus in food-producing animals

Typically, clinical investigations differ from monitoring data in food-producing animals, as 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 level, it is still considered relevant to report the range of animal species/populations which can be affected. In 2014, Hungary, Ireland, the Netherlands and Slovakia reported data on clinical investigations for MRSA in different kinds of food-producing animals (Table 35).

Table 35: Meticillin-resistant *Staphylococcus aureus* in food-producing animals, clinical investigations, 2014

Animal species	Production type/Description	Sample unit	Number			
Country			Units tested	(%) positive for MRSA		
Cattle (bovi	ne animals)					
Hungary	Farm	Animal	1	1 (100%)		
	Farm	Herd	71	33(46.5%)		
Ireland	Dairy cows, farm	Animal	3,254	0		
Slovakia	Calves (under 1 year)/Dairy cows, farm	Animal	128	0		
Deer						
Ireland	Farmed, Farm	Animal	14	0		
Gallus gallu	s (fowl)			·		
Hungary	Farm	Animal	89	63 (70.9%)		
Ireland	Breeding flocks for broiler production line/broilers, Farm	Animal	273	0		
Goats						
Ireland	Mixed herds, farm	Animal	91	0		
Slovakia	Animals over 1 year, farm	Animal	5	0		
Pheasants	· · · · · · · · · · · · · · · · · · ·					
Hungary	Meat production flocks, farm	Animal	1	1 (100%)		
Pigs						
Hungary	Farm	Animal	35	16(45.7%)		
Ireland	Breeding animals/Fattening pigs farm	Animal	789	0		
Slovakia	Farm	Animal	1	0		
Rabbits		1				
Hungary	Farmed, farm	Animal	17	3(17.6%)		
Netherlands		Animal	17	4(23.5%)		
Sheep		1	1			
Hungary	Farm	Animal	1	1 (100%)		
Ireland	Meat production animals, farm	Animal	24	0		
Slovakia	Animals under 1 year (lambs)/milk ewes, farm	Animal	5	0		
Turkeys		,				
Hungary	Farm	Animal	5	4 (80%)		
Ireland	Fattening flocks, farm	Animal	60	0		



Clinical investigations for meticillin-resistant Staphylococcus aureus in companion animals

Four MSs (Hungary, Ireland, the Netherlands and Slovakia) reported data on MRSA in companion animals in 2014 (Table 36). The corresponding *spa*-typing data were not available.

Table 36: Meticillin-resistant *Staphylococcus aureus* in companion animals, clinical investigations, 2014

Animal species	Production type	Sample unit	Number		
Country			Units tested	(%) Positive for MRSA 1 (100%) 0 4 (8.9%) 0	
Cats		·		·	
Hungary	Pet animals	Animal	1	1 (100%)	
Ireland	Pet animals	Animal	6	0	
Netherlands	Pet animals	Animal	45	4 (8.9%)	
Slovakia	Pet animals	Animal	7	0	
Dogs					
Hungary	Pet animals	Animal	3	3 (100%)	
Ireland	Pet animals	Animal	152	0	
Netherlands	Pet animals	Animal	56	9 (16.1%)	
Slovakia	Pet animals	Animal	137	0	
Solipeds, doi	nestic				
Netherlands	Horses	Animal	28	14 (50.0%)	
Slovakia	Horses	Animal	3	0	

Temporal trends in the occurrence of meticillin-resistant Staphylococcus aureus

Switzerland reported results on the yearly prevalence of MRSA in fattening pigs from 2009 to 2014 (Table 37). Prevalence has increased annually, rising from 2.2% in 2009 to 26.5% in 2014. 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.



Table 37:	Temporal occurrence	e of meticillin-resistant Staphyloc	<i>occus aureus</i> in animals

Country	Year	Production type/Description	Sample	N	umber
_			unit	tested	(%) Positive for MRSA
Switzerland	2009	Fattening pigs, at slaughterhouse, nasal swabs	Animal	405	8 (2.2) ^(a)
	2010	Fattening pigs, at slaughterhouse, nasal swabs	Animal	392	23 (5.9) ^(b)
	2011	Fattening pigs, at slaughterhouse, nasal swabs, monitoring	Animal	392	22 (5.6) ^(c)
	2012	Fattening pigs, at slaughterhouse, nasal swabs, monitoring	Animal	397	72 (18.1) ^(d)
	2013	Fattening pigs, at slaughterhouse, nasal swabs, monitoring	Animal	351	73 (20.8) ^(e)
	2014	Fattening pigs, at slaughterhouse, nasal swabs, monitoring	Animal	298	79 (26.5) ^(f)

(a): In 2009, isolates were reported as unspecified genotypes.

(b): In 2010, 17 isolates were of genotype ST398-t034-V, one was of genotype ST398-t011-V and five were of genotype ST49t208-V.

(c): In 2011, 19 isolates were of genotype ST398-t034-V, one was of genotype ST398-t011-V, one was of genotype ST49t208-V and one was of genotype ST1-t2279-IVc.

(d): In 2012, 61 isolates belonged to genotype CC398-t034, nine belonged to genotype CC398-t011 and two belonged to genotype ST49-t208.

(e): In 2013, 63 isolates belonged to genotype CC398-t034 and 10 belonged to genotype CC398-t011.

(f): In 2014, 57 isolates belonged to genotype CC398-t034, 19 belonged to genotype CC398-t011, and one was genotype ST49-t208, one was spa-type t2741 and one belonged to the spa-type t899.

Susceptibility testing of meticillin-resistant *Staphylococcus aureus* isolates

In 2014, data on the antimicrobial susceptibility of MRSA isolates were reported only by Belgium and Switzerland (Table 38). Both countries used a broth dilution method and applied EUCAST ECOFFs to determine the susceptibility of isolates. All MRSA strains isolated were resistant to penicillin and to cefoxitin (data not shown).

Tetracycline resistance was common in the MRSA isolates tested 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).

Among the low numbers of MRSA isolates from *Gallus gallus* were tested by Belgium, chloramphenicol resistance was observed in 71.4% of isolates from layers.

Considering the susceptibility of MRSA isolates²⁴ from meat from broilers reported by Switzerland, most isolates were resistant to tetracyclines (86.4%) (Table 38).

Among MRSA isolates (N=79) from fattening pigs in Switzerland, resistance was not detected to chloramphenicol, fusidic acid, linezolid mupirocin or vancomycin (Table 38). Resistance was reported at extremely high levels to tetracycline (100%), clindamycin (79.7%), tiamulin (78.5%), erythromycin (75.9%) and trimethoprim (74.7%), and at low levels for kanamycin and ciprofloxacin (8.9%), gentamicin (6.3%), sulfamethoxazole (3.8%) and rifampicin (1.3%).

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 pigs, layers, breeding chickens or meat from broilers, was resistant to neither vancomycin nor linezolid.

²⁴ The corresponding *spa*-type are presented in the footnote of.



Table 38: Occurrence of resistance (%) to selected antimicrobials in MRSA from food and animals, 2014

Country	Chloran	nphenicol	Cipro	floxacin	Cline	damycin	Eryth	romycin	Fusio	lic acid
-	N	% Res	Ň	% Res	Ν	% Res	Ň	% Res	N	% Res
Gallus gallus (fowl) bree	ding flocks									
Belgium	1	0	1	100	1	100	1	100	1	0
Gallus gallus (fowl) layin	g hens									
Belgium	- 7	71.4	7	14.3	7	42.9	7	85.7	7	28.6
Meat from broilers (Galla	<i>us gallus</i>) fresh	1								
Switzerland	22	0	22	22.7	22	86.4	22	72.7	22	0
Pigs fattening pigs										
Switzerland	79	0	79	8.9	79	79.7	79	75.9	79	0
Country	Genta	amicin	Kana	mycin	Lir	nezolid	Mu	pirocin	-	nupristin/ fopristin
	N	% Res	Ν	% Res	Ν	% Res	N	% Res	N	% Res
Gallus gallus (fowl) bree	ding flocks									
Belgium	1	0	1	0	1	0	1	0	1	0
Gallus gallus (fowl) lavin	a hens									

Belgium	7	14.3	7	71.4	7	0	7	14.3	7	14.3
Meat from broilers (Gallus	<i>s gallus</i>) fresh	1								
Switzerland	22	0	22	0	22	0	22	0	_	_
Pigs fattening pigs										
Switzerland	79	6.3	79	8.9	79	0	79	0	_	_

Country	Rif	ampicin	Strep	tomycin	Sulfame	thoxazole	Tetra	acyclines	Ti	amulin	Trim	ethoprim
-	Ν	% Res	N	% Res	N	% Res	Ν	% Res	Ν	% Res	Ν	% Res
Gallus gallus	(fowl)	breeding	flocks									
Belgium	1	0	1	0	1	0	1	100	1	0	1	100
Gallus gallus	(fowl)	laying he	ens									
Belgium	7	71.4	7	71.4	7	71.4	7	85.7	7	28.6	7	28.6
Meat from b	roilers	(Gallus ga	<i>allus</i>) fr	esh								
Switzerland	22	0	22	18.2	22	13.6	22	86.4	22	77.3	22	86.4
Pigs fattenin	g pigs											
Switzerland	79	1.3	79	59.5	79	3.8	79	100	79	78.5	79	74.7

-: no information available;

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

All MRSA isolates tested were also resistant to penicillin and cefoxitin as expected. All isolates were susceptible to vancomycin and linezolid.

3.4.2. Discussion

Monitoring of MRSA in animals and food is currently voluntary and only a limited number of countries reported MRSA data to EFSA in 2014. A number of MRSA strains have been detected in animals and animal products, indicating that animals can acquire and disseminate MRSA strains other than those which might strictly be regarded as LA-MRSA (Normanno et al., 2015; Battisti et al., 2010).

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 food included chicken, pork and meat from turkeys in 2014. It should be underlined that the laboratory techniques used to detect MRSA employ selective bacterial culture and thus, very low levels of contamination can be detected. LA-MRSA is considered a poor coloniser of humans and occurs uncommonly in persons without direct or indirect contact with livestock or carcases derived thereof (Graveland et al., 2010). Only low numbers of samples of some food were tested and prevalence estimates are therefore likely to have wide confidence intervals, as a result of the small sample sizes. Cross-contamination between carcases on slaughterhouse lines or during production processes may result in a higher prevalence in meat produced from animals than in the animals themselves. It is also noteworthy that prevalence measures may be obtained in relation to the contamination of individual carcases, meat or other products, but for colonised animals, prevalence measures may be determined at the flock or holding level, rather than by determining the status of individual animals.



Considering trends in the occurrence of MRSA in food, the monitoring of MRSA in meat products from pigs in Spain showed an increase in prevalence of MRSA over the period 2012–2014, from 0% in 2012 to 8.5% in 2013 and 12.9% in 2014. In Germany, the prevalence of MRSA in fresh retail meat from turkeys was assessed at similar levels of 37.7% and 42.5% in 2012 and 2014, respectively.

Switzerland reported *spa*-typing results for MRSA isolates from meat from broilers and most isolates (19/22) belonged to *spa*-types associated with LA-MRSA CC398 (t011, t034, t571 and t899²⁵). Although *S. aureus* belonging to *spa*-type t571 has been associated with severe disease in humans, a particular clone of meticillin-susceptible *S. aureus* (MSSA) differing from that occurring in animals is responsible (Cuny et al., 2013). The *spa*-type t571 isolates reported by Switzerland are meticillin-resistant and are therefore likely to be related to LA-MRSA, rather than the human MSSA t571 clone. Three isolates from broiler meat at retail were *spa*-type t032, which is a *spa*-type associated with the HA-MRSA, EMRSA-15, belonging to CC22. *Spa*-type t032 is therefore usually associated with a healthcare-associated strain of MRSA, not commonly reported from food-producing animals. Contamination of meat with HA-MRSA from persons in contact with the meat at some point is a possible explanation for its occurrence.

In food-producing animals in 2014, most of the MRSA spa-types detected were associated with LA-MRSA CC398. Switzerland detected single isolates of spa-types t899 and t2741, which can also be associated with CC398, but which may also associated with either ST9 or CC11, respectively. Although the likelihood is that these isolates were also associated with CC398, the findings illustrate the limitations of *spa*-typing as a single method of definitively assigning all of the animal isolates which were recovered by reporting countries to particular MRSA lineages. Spa-type t208, which is associated with ST49 in Switzerland, has been considered to have emerged in the Swiss fattening pig population by acquisition of the SCC_{mec} element by MSSA belonging to ST49 (Overesch et al., 2011). Switzerland has performed annual surveillance for MRSA in pigs since 2009 (Table 37:). MRSA ST49 has persisted in pigs over this monitoring period and, although it was initially reported from seven different farms, it has not subsequently increased in prevalence, whereas it is noteworthy that those spa-types associated with CC398 have shown a steady increase in prevalence. Data relating to colonisation by MRSA CC398 in humans in European countries show a similar trend in some countries, for example, an increase in MRSA CC398 cases as a proportion of all MRSA cases detected in nasopharyngeal swabbing of patients at 39 hospitals from 14% in 2008 to 29% in 2012 was noted in north-western Germany (Köck et al., 2013). In the Netherlands, 15% of human carriers of MRSA CC398 do not report direct contact with pigs or veal calves; indirect transmission from animals or direct transmission from colonised humans are possible sources (Lekkerkerk et al., 2015). Although LA-MRSA CC398 is considered a poor coloniser of human (Graveland et al., 2010), it can cause serious, fatal infections in humans, especially in patients who are prone to acquire staphylococcal infections (Berning et al. 2015). Berning et al. reported case details of two fatal infections, both of which occurred in persons with direct links to pig farms or pig farming.

Considering the three broad epidemiological classes of MRSA (LA-MRSA, HA-MRSA and CA-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 2014. *Spa*-types associated with healthcare-associated MRSA were much less frequent and those associated with CA-MRSA were not reported. 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. Susceptibility data for MRSA isolates were provided by Belgium and Switzerland who did not detect resistance to either vancomycin or linezolid, important antimicrobials for treatment of human patients. The high proportion of MRSA isolates from pigs showing resistance to tiamulin and trimethoprim presumably reflects the relatively common usage of these compounds in pig medicine in many European countries.

Norway tested a large number of pig herds (N=986) in 2014, as part of a surveillance and eradication programme for LA-MRSA (outlined at http://www.vetinst.no/eng/Surveillance-programmes/Swine-MRSA). National eradication programmes for LA-MRSA have not been attempted in other European countries. Norway has consistently demonstrated a very low/zero prevalence of MRSA-positive pig

²⁵ *Spa*-type t899 can be associated with either MRSA ST9 or CC398.



herds in surveillance performed since 2008 and this situation is likely to be favourable to achieving the goal of eradicating and then maintaining freedom from LA-MRSA. The eradication programme involves slaughter and depopulation of affected herds, followed by thorough cleaning and disinfection and then re-stocking with pigs free from LA-MRSA.

S. aureus isolates belonging to CC398 can be divided into 'human' and 'animal' lineages based on characteristics including susceptibility to meticillin and tetracyclines (animal lineages are resistant; human lineages are susceptible) and possession of the φSA3 prophage, *scn* and *chp* virulence genes, features which have been associated with the meticillin-susceptible lineages of CC398 affecting humans (Smith and Wardyn, 2015, Chroboczek et al. 2013). The results reported here relate to MRSA isolates from animals and food and considering the rapid developments which have occurred in recent years relating to the occurrence of MRSA in animals and the emergence of LA-MRSA, it seems likely that further evolution will occur. *Spa*-typing provides a convenient method for preliminary characterisation of isolates described in this report, but may not always contain sufficient information to fully interpret the significance of isolates.



3.5. Third-generation cephalosporin and carbapenem resistance in *Escherichia coli* and *Salmonella*

Resistance to third-generation cephalosporins: the importance of extended-spectrum beta-lactamases (ESBLs), AmpC enzymes and carbapenemases

Occurrence of ESBLs and acquired AmpC (aAmpC) beta-lactamases is considered to be an important emerging issue in Gram-negative bacteria of public health significance. ESBLs and AmpC are enzymes that hydrolyse extended-spectrum betalactam antimicrobials. Bacteria which produce ESBL/aAmpC enzymes are usually resistant to third-generation cephalosporins, which are critically important antimicrobials for the treatment of systemic or invasive Gram-negative bacterial infections in humans. Apart from their wide use to treat *E. coli* infections, these drugs play a critical role in the treatment of certain invasive *Salmonella* infections, particularly in children and immunosuppressed patients.

Enterobacteria may become resistant to third-generation cephalosporins by several different mechanisms. Among these different mechanisms, the most common is the production of betalactamases. These enzymes are encoded by genes which can be located on either plasmids (small covalently closed circles of DNA), which can be transferred between bacteria (i.e. during bacterial conjugation), or the chromosome. There are different types of beta-lactamase which can confer resistance to third-generation cephalosporins. Based on structural similarities (aminoacid content) they are subdivided into four classes, designated A to D: ESBL enzymes of the TEM, SHV and CTX-M families belong to class A, ESBL enzymes of the OXA-family are included in Class D, while class C includes the AmpC beta-lactamases. The beta-lactamase encoding genes can be chromosomal and intrinsic i.e. present naturally in the bacterial species (often referred as chromosomal, 'c'), or acquired ('a'), gained by transfer between bacteria.

The occurrence of beta-lactamases in *Salmonella* and *E. coli* (both pathogens and commensals) is mostly due to the acquisition of genes usually from other Enterobacteriaceae through transfer of plasmids (conjugation) and in a lesser extent, bacteriophages acting as vectors (transduction), or to the clonal spread of carrier bacteria. Wild-type *Salmonella* do not possess endogenous beta-lactamase encoding genes. Although all four different types of beta-lactamase classes have been found in *Salmonella*, within the EU, the most important mechanism of resistance to third-generation cephalosporins in *Salmonella* is the production of ESBLs followed by the production of aAmpCs. *E. coli* also possesses endogenous AmpC beta-lactamase encoding genes, that in some circumstances can be activated (i.e. mutations in the promotor regions), and also confer resistance to third-generation cephalosporins in *E. coli* is primarily the production of ESBLs, followed by that of aAmpC. Commensal bacteria, such as indicator *E. coli*, may contribute to the dissemination of ESBLs/aAmpC, as these resistance mechanisms are usually transferable.

The emergence during the last years of resistance to carbapenems, last line antimicrobials for human medicine is considered as an important public health concern. Carbapenems are used for the treatment of highly resistant infections in humans, including, for example, the treatment of infections with Gram-negative bacteria producing ESBLs. Resistance to carbapenems in Gram-negative bacteria is mainly related to the production of carbapenemases (beta-lactamases) and the acquisition of carbapenemase encoding genes, although other mechanisms (i.e. related to cell permeability) also exist. The most frequent beta-lactamases with carbapenemase activity can be found in the class A (KPC), class D (OXA-type carbapenemases) and Class B (metallo beta-lactamases like NDM, VIM and IMI) of Ambler's classification. 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.



Considering the public health relevance of resistance to third-/fourth-generation cephalosporins, and carbapenem compounds, the new legislation on harmonised monitoring of antimicrobial resistance in food-producing animals and food (Commission implementing Decision 2013/652/EU) has laid down the mandatory monitoring of resistance to representative substances of these antimicrobial classes in *Salmonella* and indicator *E. coli* in 2014 onwards. All *Salmonella* and indicator *E. coli* isolates exhibiting microbiological resistance to cefotaxime, ceftazidime or meropenem have had to be subsequently subjected to further testing using a supplementary panel of substances to obtain more detailed phenotypic characterisation of any resistance detected to third-generation cephalosporins and/or the carbapenem compound meropenem.

Rationale for the choice of certain substances included in the supplementary panel

- Cefotaxime and ceftazidime have been included in the supplementary panel because, although most ESBL confer resistance to both compounds, some ESBL primarily confer resistance to one or the other compound.
- Confirmatory synergy testing has been also foreseen so that a presumptive ESBL phenotype may be identified.
- Cefoxitin has been also included so that a presumptive AmpC phenotype may be identified.
- Meropenem, imipenem and ertapenem have been included so that putative carbapenemase producers may be identified.
- Temocillin (6-a-methoxy-ticarcillin) efficacy is unaffected by most ESBL and AmpC enzymes and this substance may be particularly useful in human medicine to treat urinary tract infections caused by ESBL-producing Gram-negative organisms (Livermore and Tulkens, 2009). Susceptibility to temocillin enables further phenotypic characterisation of carbapenemases.

From the results of such further testing, it has thus been possible to infer the presumptive class of beta-lactamase enzyme which was responsible for conferring the phenotypic profile of resistance to third-generation cephalosporins or meropenem detected, providing additional epidemiological information. This monitoring primarily addressed in this chapter was performed in accordance with the legislation and did not utilise selective primary isolation media containing cephalosporins so the results generally relate to organisms selected at random from primary culture media.

In 2014, the 'specific' monitoring of ESBL-/AmpC-/Carbapenemases-producing *E. coli* (by using selective media containing cephalosporins) was also performed on a voluntary basis by a limited number of reporting countries. The corresponding results have also been briefly presented below, and the results of the 'routine' and 'specific' monitoring were put in perspective, if possible. Italy also reported results of a 'specific' monitoring of carbapenemase-producing microorganisms (by using selective media containing carbapenems), performed voluntarily.

Identification of presumptive phenotypes of ESBL-, AmpC- and/or carbapenemase producers (also see material and methods section)

To infer the presumptive class of beta-lactamase enzyme responsible for conferring the phenotypic profile of resistance to third-generation cephalosporins or meropenem detected, the EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance (EUCAST, 2013) were applied. A screening breakpoint for cefotaxime and/or ceftazidime (> 1 mg/L) was applied to screen for ESBL and AmpC-producers, as these isolates typically (with only a few exceptions) show MICs for cefotaxime and/or ceftazidime > 1 mg/L, whereas different resistance mechanisms are expected in the resistant isolates (MIC > ECOFFs) exhibiting MICs lower than the screening breakpoint. Some of the countries also voluntarily reported results from the detection of ESBL-/AmpC-resistance genes in the third generation cephalosporin resistant isolates. These data were compared with the classifications made on the phenotypic basis.



3.5.1. Third-generation cephalosporin and carbapenem resistance in *Salmonella* isolates from food and animals (routine monitoring)

In 2014, third-generation cephalosporin resistance was identified in a range of *Salmonella* serovars. Occurrence data in *Salmonella* spp. are presented in Table 39 below and further results at the serovar level are also tabulated in appendices.

Third-generation cephalosporin and carbapenem resistance in Salmonella from food

Resistance levels to carbapenems in Salmonella isolated from meat from broilers and turkeys

None of the *Salmonella* isolates from meat from broilers or turkeys were microbiologically resistant to meropenem, ertapenem or imipenem.

Resistance levels to cefotaxime and ceftazidime in Salmonella from broilers meat

In the eleven reporting MSs, resistance to cefotaxime or ceftazidime in *Salmonella* spp. isolates from broiler meat was either not detected or reported at low levels (Table <u>SALMBRMEATD</u>) in Belgium (three isolates resistant to cefotaxime, two isolates resistant to ceftazidime, accounting for 3.7% and 2.5% of the isolates tested, respectively) and in Spain (one isolate resistant to both antimicrobials, representing 0.8% of the isolates tested) (Table <u>SALMBRMEATD</u>).

The resistant isolates belonged to serovars *S*. Enteritidis (Table <u>ENTERBRMEATD</u>), *S*. Paratyphi and *S*. Cerro. Resistance to cefotaxime or ceftazidime was not detected in *S*. Infantis, *S*. Kentucky, *S*. Indiana isolates from meat from broilers (Table <u>INFANBRMEATD</u>, <u>KENTUBRMEATD</u>, <u>INDIANABRMEATD</u>).

Resistance levels to cefotaxime and ceftazidime in Salmonella from turkey meat

In the three reporting MSs, no *Salmonella* isolates from turkey meat were resistant to cefotaxime or ceftazidime in 2014 (Table <u>SALMTURKMEATD</u>) and therefore, no supplementary beta-lactam or carbapenem susceptibility testing was performed on isolates.

Third-generation cephalosporin and carbapenem resistance in *Salmonella* from animals

Resistance levels to carbapenems in Salmonella from flocks of broilers, laying hens and turkeys

None of the *Salmonella* isolates from broiler, laying hen and turkey flocks which were subjected to supplementary testing were microbiologically resistant to ertapenem, imipenem or meropenem.

Resistance levels to cefotaxime and ceftazidime in Salmonella from broiler flocks

Low levels of resistance to cefotaxime at 2.3% and to ceftazidime at 2.6% were 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>SALMBRD</u>). Only Italy and the Netherlands recorded much higher levels of resistance to both antimicrobials (above 10.0%), whereas Malta recorded a resistance to ceftazidime above 10.0%.

The resistance to cefotaxime and ceftazidime in *S*. Enteritidis isolates from broilers was generally not detected in reporting MSs (Table <u>ENTERBRD</u>). Resistance to both cefotaxime and ceftazidime in *S*. Enteritidis was reported only by Portugal in 1/9 isolates tested.

Resistance levels to cefotaxime and ceftazidime in Salmonella from laying hen flocks

The levels of resistance in laying hen flocks were generally lower than those reported in broiler flocks. In *Salmonella* spp. from laying hens, only three MSs (France, Poland and Romania) detected resistance to third-generation cephalosporins out of the 15 reporting MSs, respectively.

Considering isolates from laying hens resistance to cefotaxime and ceftazidime in *S*. Enteritidis was detected by Poland (Table <u>ENTERLAYD</u>). *S*. Typhimurium isolates from laying hens (Table <u>TYPHILAYD</u>) were tested by 17 MSs; none of the reporting countries detected resistance to cefotaxime or to ceftazidime in *S*. Typhimurium.



Resistance levels to cefotaxime and ceftazidime in Salmonella from fattening turkey flocks

There were no *Salmonella* isolates from turkey flocks which were resistant to cefotaxime or ceftazidime in the nine reporting MSs in 2014 (Table <u>SALMFATTURKD</u>) and therefore, no supplementary beta-lactam susceptibility testing was performed on isolates.

Resistance phenotypes identified in Salmonella spp. from broiler flocks

Salmonella spp. isolates with a presumptive ESBL phenotype were detected in broiler flocks in five MSs and of these, 10% (3/30) demonstrated synergy only with cefotaxime (Table 40). The proportion of *Salmonella* spp. isolates from broiler flocks exhibiting a presumptive ESBL phenotype was low in all countries, except in Italy, where 25.8% of *Salmonella* spp. isolates showed a presumptive ESBL phenotype. Three MSs reported isolates with a presumptive ESBL and AmpC phenotype in broilers and six MSs reported isolates with a presumptive AmpC phenotype, including the Netherlands, which registered moderate numbers of isolates (12.5%) having a presumptive AmpC phenotype. A presumptive AmpC phenotype was detected in laying hen flocks at a low level by three MSs and in meat from broilers at a very low level by one MS, with a further MS reporting a presumptive AmpC and ESBL phenotype.

Most *Salmonella* spp. isolates from broiler flocks exhibiting a presumptive ESBL phenotype belonged to *S*. Infantis (60%, 18/30) with *S*. Paratyphi B var. Java comprising a further 20% (6/30). Considering those isolates with a presumptive AmpC phenotype, 50% (9/18) belonged to *S*. Heidelberg, whereas single isolates of *S*. Infantis and *S*. Paratyphi B var. Java had a presumptive AmpC phenotype. *Salmonella* spp. from broiler flocks with a presumptive 'AmpC and ESBL' phenotype included three isolates of *S*. Infantis and a single isolate of *S*. Entertitidis (Table ENTERBRD).

Three *Salmonella* isolates from laying hen flocks with a presumptive AmpC phenotype belonged to serovars *S.* Enteritidis, *S.* Anatum and *S.* Glostrup.

	Total number of	1	Number s	ubjected t	o supple	ementa	ary testir	ng and	number	resistan	t ^(a)
Country	Salmonella spp.		taxime	Ceftazi			xitin		oime ^(b)	Temo	
-	tested	Ν	n Res	Ν	n Res	Ν	n Res	N	n Res	Ν	n Res
Meat from broi	lers										
Belgium	81	3	2	3	2	3	2	3	2	3	0
Hungary	47	1	0	1	0	1	0	1	0	1	0
Spain	130	1	1	1	1	1	1	1	1	1	0
Total (MSs 3)	258	5	3	5	3	5	3	5	3	5	0
Broilers											
Belgium	167	7	7	7	6	7	1	7	7	7	0
Cyprus	45	4	4	4	4	4	2	4	4	4	1
Czech Republic	212	1	1	1	1	1	1	1	1	1	0
Hungary	169	3	0	3	0	3	0	3	0	3	0
Ireland	16	1	1	1	1	1	1	1	1	1	1
Italy	66	18	18	18	17	18	1	18	18	18	0
Netherlands	88	15	15	15	15	15	11	15	14	15	0
Portugal	51	1	1	1	1	1	1	1	1	1	0
Romania	554	2	2	2	2	2	2	2	2	2	0
Spain	135	3	3	3	3	3	2	3	3	3	0
Total (MSs 10)	1,503	55	52	55	50	55	22	55	51	55	2
Laying hens											
France	86	1	1	1	1	1	1	1	1	1	0
Poland	45	1	1	1	1	1	1	1	1	1	0
Romania	46	1	1	1	1	1	1	1	1	1	1
Total (MSs 3)	177	3	3	3	3	3	3	3	3	3	1

Table 39: Occurrence of resistance to beta-lactam compounds in *Salmonella* spp. isolates from broilers, laying hens and meat from broilers collected within the routine monitoring and subjected to supplementary testing (panel 2) in 2014

ECOFFs: epidemiological cut-off values; N: number of isolates tested; n Res: number of the isolates resistant; MSs: Member States.

(a): No resistance to carbapenems was reported.

(b): Interpretive cut-off applied for cefepime: > 0.125mg/L.

(c): Interpretive cut-off applied for temocillin: > 32 mg/L.

Table 40: Presumptive ESBL and AmpC phenotypes identified in *Salmonella* spp. isolates from broilers, laying hens and meat from broilers collected within the routine monitoring and subjected to supplementary testing (panel 2) in 2014^(a)

Country	Total	Number of				Presumpt	tive Resistand	e Phenotype				
	number of <i>Salmonella</i>	with nella supplementary	with ESBL ^(b) supplementary		with clavula	BL nic-SYN only CTX ^(c)		BL Ilanic-SYN		pC ^(e)	AmpC +	ESBL ^(f)
	tested	testing	n	% ^(g)	n	% ^(g)	n	% ^(g)	n	% ^(g)	n	% ^(g)
Meat from Broil	ers											
Belgium	81	3									2 ^(h)	2.5
Spain	130	1							1	0.8		
Broiler flocks												
Belgium	167	7	6	3.6	2	1.2			1	0.6		
Cyprus	45	4	2	4.4							2	4.4
Czech Republic	212	1 ^(h)							1	0.5		
Ireland	16	1							1	6.3		
Italy	66	18 ^(h)	17	25.8	1	1.5					1	1.5
Netherlands	88	15	4	4.5					11	12.5		
Portugal	51	1									1	1.9
Romania	554	2							2	0.4		
Spain	135	3 ^(h)	1	0.7					2	1.5		
Total MSs 9	1,334	52	30	2.2	3	0.2			18	1.3	4	0.29
Norway		1							1			
Laying hen floc	ks											
France	86	1							1	1.2		
Poland	45	1							1	2.2		
Romania	46	1							1	2.2		
Total MSs 3	177	3							3	1.7		

ESBL: extended spectrum beta-lactamase; n= isolates with this phenotype; %: percentage of isolates with this phenotype from the total tested; SYN: synergy; CTX: cefotaxime; CAZ: ceftazidime; MSs: Member States

(a): According to EUCAST Guidelines (EUCAST, 2013), only isolates showing an MIC > 1 mg/ml for ceftaxime and/or ceftazidime (screening breakpoint) were considered (see Chapter 1.2.5).

(b): All isolates with an ESBL phenotype, i.e. showing clavulanate synergy with cefotaxime or ceftazidime or synergy with both compounds.

(c): Isolates showing synergy with cefotaxime only, suggesting the presence of an ESBL with cefotaximase activity.

(d): Isolates showing synergy with ceftazidime only, suggesting the presence of an ESBL with ceftazidimase activity.

(e): Isolates with microbiological resistance to cefoxitin.

(f): Isolates showing synergy with cefotaxime or ceftazidime and with microbiological resistance to cefoxitin

(g): Percentage of the total number of *Salmonella* isolates tested (with panel 1).

(h): Molecular data were reported. For Belgium, only data for the meat isolates were reported, being both isolates positive for CTX-M enzymes with an MIC =16 mg/L for cefoxitin. Regarding the poultry isolates: for the Czech Republic, the isolate was in fact CMY-2 positive; for Italy, all isolates were CTX-M positive, one of them also with a MIC =16 for cefoxitin. For Spain, one isolate was positive for CTX-M, the other two isolates for CMY-2 encoding genes.



3.5.2. Third-generation cephalosporin and carbapenem resistance in indicator *Escherichia coli* isolates from food and animals (routine monitoring)

Third-generation cephalosporin resistance in indicator *E. coli* isolates from food

For 2014, Denmark reported results on resistance to cefotaxime and ceftazidime in indicator *E. coli* isolates from meat from broilers, pigs and bovine animals, whereas Germany reported data on meat from broilers and meat from turkeys. Overall, resistance to third-generation cephalosporins was either not detected or reported at low levels ranging, between 0.7% and 5.9% (Table <u>ESCHEMEAT</u>).

Third-generation cephalosporin resistance in indicator *E. coli* isolates from animals

Resistance to cefotaxime, ceftazidime and carbapenem compounds, and presumptive ESBL and AmpC phenotypes identified in indicator E. coli *isolates from broilers*

Resistance to cefotaxime in indicator *E. coli* isolates from broilers were reported by 27 reporting MSs and Norway (Table <u>ESCHEBR</u> and Table 41). The levels of resistance recorded were generally low, although Malta, Slovakia and Spain observed moderate levels of resistance in broilers, whereas Cyprus, Latvia and Lithuania registered high resistance levels, above 30%. In Bulgaria, Denmark, Finland, Sweden and the United Kingdom, resistance to cefotaxime and ceftazidime was not detected in isolates from broilers. Overall, resistance levels in reporting countries were low at 5.1% for cefotaxime and 5.0% for ceftazidime.

Ertapenem-resistant indicator *E. coli* isolates from broilers (Table 41) were reported by Lithuania (3 isolates), Latvia (1), Poland (1), Slovakia (1), Slovenia (1) and Spain (2) and each of these isolates exhibited a presumptive AmpC or ESBL phenotype (Table 42). Loss of porins in conjunction with ESBL or AmpC enzyme production is therefore considered to account for resistance to ertapenem in the absence of resistance to the other carbapenems tested.

Indicator *E. coli* isolates with a presumptive ESBL phenotype were detected in broilers from 21 MSs and Norway. Significant numbers of isolates showed synergy with only one of the two indicator cephalosporins (cefotaxime and ceftazidime) used in combination with clavulanate to detect synergy. The proportion of all *E. coli* isolates from broilers with a presumptive ESBL phenotype was low or very low in most countries, except Cyprus, Latvia, Lithuania, Malta, Slovakia and Spain, where more than 10% of the indicator *E. coli* isolates tested had a presumptive ESBL phenotype. Four MSs reported *E. coli* with both a presumptive ESBL and AmpC phenotype from broilers, whereas 14 MSs reported isolates with a presumptive AmpC phenotype, although the proportion of total *E. coli* with this phenotype was less than 10% in all MSs, except Lithuania, where it was 22.4% (Table 42).

Resistance to cefotaxime, ceftazidime and carbapenem compounds, and presumptive ESBL and AmpC phenotypes identified in E. coli *isolates from fattening turkeys*

Data on resistance in indicator *E. coli* isolates from fattening turkeys were reported by 11 reporting MSs. The levels of resistance recorded for third generation cephalosporins were generally low; Romania and the United Kingdom did not detect any resistance. Overall, resistance levels in reporting countries were lower in fattening turkeys than in those from broilers, at 2.3% for cefotaxime and 2.2% for ceftazidime (Table <u>ESCHETURK</u> and Table 43).

A single ertapenem-resistant indicator *E. coli* isolate was reported by France and this isolate exhibited a presumptive AmpC phenotype (Table 44). Loss of porins in conjunction with AmpC enzyme production is therefore considered to account for resistance to ertapenem in the absence of resistance to the other carbapenems tested.

Indicator *E. coli* isolates with a presumptive ESBL phenotype were detected in fattening turkeys in six MSs and three non-MSs. Significant numbers of isolates showed synergy with cefotaxime only. The proportion of all *E. coli* isolates from broilers with a presumptive ESBL phenotype was low or very low in most countries, except in Spain where 10% of the *E. coli* sampled exhibited a presumptive ESBL phenotype. Three MSs reported *E. coli* isolates with a presumptive AmpC phenotype in fattening turkeys, although those isolates accounted for less than 2% of indicator *E. coli* investigated in each MS. No presumptive `ESBL and AmpC' phenotype was detected in fattening turkeys (Table 44).



Table 41: Occurrence of resistance to beta-lactam and carbapenem compounds in indicator *E. coli* isolates from broiler flocks collected within the routine monitoring and subjected to supplementary testing (panel 2) in 2014

Country	Total number	Number subjected to supplementary testing and number resistant											
•	of	Cef	otaxime		azidime		oxitin		epime		penem	Tem	ocillin
	E. coli tested	Ν	n Res	Ν	n Res	Ν	n Res	Ν	n Res	Ν	n Res	Ν	n Res
Austria	176	2	2	2	2	2	0	2	2	2	0	2	0
Belgium	158	13	13	13	12	13	5	13	11	13	0	13	0
Croatia	170	1	1	1	1	1	0	1	1	1	0	1	0
Cyprus	87	35	28	35	26	35	15	35	25	35	0	35	0
Czech Republic	196	2	2	2	2	2	0	2	2	2	0	2	2
Estonia	71	3	3	3	1	3	2	3	1	3	0	3	0
France	226	9	9	9	9	9	0	9	9	9	0	9	0
Germany	227	5	3	5	3	5	1	5	3	5	0	5	0
Greece	172	5	5	5	5	5	2	5	5	5	0	5	0
Hungary	170	5	5	5	5	5	3	5	4	5	0	5	0
Ireland	167	7	7	7	6	7	2	7	7	7	0	7	0
Italy	170	11	11	11	9	11	3	11	11	11	0	11	0
Latvia	147	48	45	48	43	48	15	48	40	48	1	48	0
Lithuania	85	32	27	32	31	32	20	32	24	32	3	32	0
Netherlands	377	10	10	10	10	10	0	10	10	10	0	10	0
Poland	179	4	4	4	4	4	3	4	4	4	1	4	0
Portugal	201	11	11	11	11	11	1	11	11	11	0	11	0
Romania	859	15	15	15	15	15	8	15	10	15	0	15	0
Slovakia	86	16	11	16	6	16	4	16	11	16	1	16	0
Slovenia	85	8	8	8	8	8	7	8	6	8	1	8	0
Spain	170	25	25	25	25	25	7	25	25	25	2	25	0
Total (21 MSs)	4,179	267	245	267	234	267	98	267	222	267	9	267	2
Norway	205	3	3	3	3	3	3	3	0	3	0	3	0

No *E. coli* isolates from broilers were resistant to meropenem.

Interpretive cut-off applied for temocillin: > 32 mg/L.

ECOFFs: epidemiological cut-off values; N: number of the isolates tested; n Res: number of the isolates resistant; MSs: Member States



Country	Total number	Number of				Presum	ptive Resistaı	nce Phenotype				
-	of <i>E. coli</i> tested	<i>E. coli</i> with supplementary	ES	BL ^(b)	ESBL with cla only for	vulanic-SYN	ESBL with	clavulanic-SYN for CAZ ^(d)	Amp	рС ^(е)	AmpC +	ESBL ^(f)
		testing	n	% ^(g)	n	% ^(g)	n	% ^(g)	n	% ^(g)	n	% ^(g)
Austria	176	2	2	1.1	2	1.1						
Belgium	158	13 ^(h)	7	4.4	2	1.3	1	0.6	5	3.2		
Croatia	170	1	1	0.6	1	0.6						
Cyprus	87	35	13	14.9	8	9.2			8	9.2	7	8.0
Czech Republic	196	2 ⁽ⁱ⁾	2	1.0								
Estonia	71	3 ^(h)	1	1.4	1	1.4						
France	226	9	9	4.0	3	1.3	1	0.4				
Germany	227	5	3	1.3			2	0.9				
Greece	172	5	3	1.7	2	1.2			2	1.2		
Hungary	170	5	2	1.2	1	0.6	1	0.6	3	1.8		
Ireland	167	7 ^(h)	4	2.4	3	1.8			2	1.2		
Italy	170	11 ⁽ⁱ⁾	8	4.7	2	1.2	1	0.6	3	1.8		
Latvia	147	48	30	20.4	8 ^(j)	5.4	8	5.4	7	4.8	8	5.4
Lithuania	85	32 ^(j)	12	14.1	5	5.9	3	3.5	19 ^(j)	22.4	1	1.2
Netherlands	377	10	10	2.7	4	1.1						
Poland	179	4	1	0.6					3 ^(j)	1.7		
Portugal	201	11	10	5.0	1	0.5			1	0.5		
Romania	859	15 ^(h)	6	0.7					8	0.9		
Slovakia	86	16	9	10.5	6	7.0			2 ^(j)	2.3		
Slovenia	85	8	1	1.2					7 ^(j)	8.2		
Spain	170	25 ^(i,j)	18	10.6	2	1.2			3	1.8	4	2.4
Total (21 MSs)) 4,179	267	152	3.6	51	1.2	17	0.4	73	1.7	20	0.5

Table 42: Presumptive ESBL and AmpC phenotypes identified in indicator *E. coli* isolates from broiler flocks collected within the routine monitoring and subjected to supplementary testing (panel 2) in 2014^(a)

ESBL: extended spectrum beta-lactamase; n= isolates with this phenotype; %: percentage of isolates from the total tested; SYN: synergy; CTX: cefotaxime; CAZ: ceftazidime; MSs: Member States.

(a): According to EUCAST Guidelines (EUCAST, 2013), only isolates showing an MIC > 1 mg/ml for cefotaxime and/or ceftazidime (screening breakpoint) were considered (see Chapter 1.2.5).

(b): All isolates with an ESBL phenotype, i.e. showing clavulanate synergy with cefotaxime or ceftazidime or synergy with both compounds.

(c): Isolates showing synergy with cefotaxime only, suggesting the presence of an ESBL with cefotaximase activity.

(d): Isolates showing synergy with ceftazidime only, suggesting the presence of an ESBL with ceftazidimase activity.

(e): Isolates with microbiological resistance to cefoxitin.

(f): Isolates showing synergy with cefotaxime or ceftazidime and with microbiological resistance to cefoxitin. nel 1).

(g): Percentage of the total number of *E. coli* isolates tested (with panel 1).

(h): Isolates microbiologically resistant to cefotaxime and/or ceftazidime but with MIC =< 1 mg/L for both antimicrobials (suggesting the presence of other mechanisms, but not further classified) were reported by Belgium (1 isolate), Romania (1), Estonia (2) and Ireland (1).

(i): Molecular data were reported by the Czech Republic, Italy, and Spain. Almost all isolates were reported as positive the ESBL CTX-M, SHV, TEM- or AmpC CMY-2 encoding genes tested, according to their phenotypes. For Italy, one isolate reported positive for SHV showed an MIC = 16 mg/L (suggesting the presence of a chromosomal AmpC) but no synergy, thus was classified in the AmpC-phenotype group and not in the putative ESBL- nor ESBL+AmpC-phenotypes ones. For Spain, the isolates classified in the ESBL+AmpC phenotype groups, showed a cefoxitin MIC = 16 mg/L, suggesting the presence of cAMPc together with the CTX-M reported. Two of the three Spanish isolates exhibiting AmpC phenotype were reported as CMY-2 positive, but, for the third isolate placed in this group because of exhibiting an MIC = 64 mg/L for cefoxitin and no synergy, no CMY-2 encoding gene was reported.

(j): Included isolates with ertapenem resistance (MIC = 0.12-0.25 mg/L).



Table 43: Occurrence of resistance to beta-lactam and carbapenem compounds in indicator *E. coli* isolates from fattening turkeys collected within the routine monitoring and subjected to supplementary testing (panel 2) in 2014

Country	Total number			Nu	mber subjec	ted to su	pplementa	ry testin	Number subjected to supplementary testing and number resistant											
-	of <i>E. coli</i> tested	Cefo	taxime		azidime		oxitin		epime		benem	Tem	ocillin							
		Ν	n Res	N	n Res	N	n Res	N	n Res	N	n Res	Ν	n Res							
Austria	125	2	2	2	1	2	0	2	2	2	0	2	0							
France	238	1	1	1	1	1	1	1	1	1	1	1	0							
Germany	170	6	4	6	3	6	0	6	4	6	0	6	0							
Hungary	170	4	3	4	3	4	2	4	2	4	0	4	0							
Italy	170	2	2	2	2	2	0	2	2	2	0	2	0							
Poland	170	3	2	3	2	3	3	3	3	3	0	3	0							
Portugal	185	5	5	5	5	5	0	5	5	5	0	5	0							
Spain	170	17	17	17	17	17	0	17	17	17	0	17	0							
Sweden	59	1	1	1	1	1	0	1	0	1	0	1	0							
Total MSs (9)	1,457	41	37	41	35	41	6	41	36	41	0	41	0							

No *E. coli* isolates from fattening turkeys were resistant to imipenem or meropenem.

Interpretive cut-off applied for temocillin: > 32 mg/L.

ECOFFs: epidemiological cut-off value; MSs: Member States.



Table 44: Presumptive ESBL and AmpC phenotypes identified in indicator *E. coli* isolates from fattening turkeys collected within the routine monitoring and subjected to supplementary testing (panel 2) in 2014^(a)

Country	Total number	Number of	Presumptive Resistance Phenotype											
of <i>E. coli</i> tested	indicator <i>E. coli</i> with supplementary testing	ESBL ^{(b}		ESBL with clavulanic- SYN only for CTX ^(c)		ESBL with clavulanic-SYN only for CAZ ^{)(d)}		AmpC ^(e)		Am ES	pC + BL ^(f)			
			n	% ^(g)	n	% ^(g)	n	% ^(g)	n	% ^(g)	n	% ^(g)		
Austria	125	2 ^(h)	1	0.8										
France	238	1							1 ⁽ⁱ⁾	0.4				
Germany	170	6	4	2.4	1	0.6								
Hungary	170	4	1	0.6	1	0.6			2	1.2				
Italy	170	2 ^(j)	2	1.2	2	1.2								
Poland	170	3							3	1.8				
Portugal	185	5	5	2.7										
Spain	170	17 ^(j)	17	10.0	1	0.6								
Sweden	59	1												
Total MSs (9)	1,457	41	30	2.1	5	0.3			6	0.4				

ESBL: extended spectrum beta-lactamase; n= isolates with this phenotype; %: percentage of isolates with this phenotype from the total tested; SYN: synergy; CTX: cefotaxime; CAZ: ceftazidime; MSs: Member States.

(a): According to EUCAST Guidelines (EUCAST, 2013), only isolates showing an MIC > 1 mg/L for cefotaxime and/or ceftazidime (screening breakpoint) were considered (see chapter 1.2.5).

(b): All isolates with an ESBL phenotype, i.e. showing clavulanate synergy with cefotaxime or ceftazidime or synergy with both compounds.

(c): Isolates showing synergy with cefotaxime only, suggesting the presence of an ESBL with cefotaximase activity.

(d): Isolates showing synergy with ceftazidime only, suggesting the presence of an ESBL with ceftazidimase activity.

(e): Isolates with microbiological resistance to cefoxitin.

(f): Isolates showing synergy with cefotaxime or ceftazidime and with microbiological resistance to cefoxitin.

(g): Percentage of the total number of *E. coli* isolates tested (with panel 1).

(h): One isolate was microbiologically resistant to cefotaxime and/or ceftazidime but with MIC =< 1 mg/L for both antimicrobials (not further classified).

(i): This isolate also showed resistance to ertapenem (MIC = 0.012 mg/L)

(j): Molecular data were reported. For Italy, both isolates showing an ESBL-phenotype were found positive for CTX-M encoding genes. For Spain, all isolates were found positive for SHV ESBLs, excepting one isolate positive for CTX-M.

172



3.5.3. Specific monitoring of ESBL-/AmpC-/carbapenemase-producing E. coli

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. For 2014, the specific ESBL-/AmpC-/carbapenemase-producing monitoring was performed on a voluntary basis by four MSs and 2 non-MSs (Table 48, Table 49, Table 50. Finland, Italy, Slovenia, Sweden, and Iceland and Switzerland reported data on specific monitoring in broilers. Italy and Sweden reported data on specific monitoring in turkeys.

Finland and Sweden reported data on the results obtained for both antimicrobial resistance Panels (Panel 1 and Panel 2). Slovenia reported results only for Panel 2. Italy reported data for results obtained with Panel 1 and positive results from the molecular data analyses. Switzerland reported data on isolates collected from caecal swabs, whereas the rest of the MSs/non-MSs reported data from caecum samples (Commission Implementing Decision 2013/652). Sweden also provided positive results from molecular data analyses.

The prevalence of ESBL/AmpC in the samples analysed within the specific monitoring was not assessed, as data on positive/negative samples were not collected by EFSA mandatorily in 2014, and all but one (Italy) reporting countries did not provide with the data. Thus, only occurrence of ESBLs *vs*. AmpC is presented below (Table 50).

Voluntarily reported results from Italy derived from thespecific carbapenemase-producing microorganism monitoring, the specific ESBL-/AmpC-/carbapenemase-producing monitoring (on *E. coli* but also for *Salmonella* spp.) and the assessment of the prevalence of ESBL-,AmpC- and carbapenemase-producers in the samples analysed, are presented in a specific text box below,

Specific ESBL-/AmpC-/carbapenemase-producing *E. coli* monitoring in broilers

Although Finland, Iceland and Sweden did not detect any cephalosporin/carbapenem resistance in the *E. coli* isolates from broilers tested within the framework of the mandatory routine monitoring, cephalosporin resistant isolates were recovered by performing the specific monitoring of ESBL-/AmpC-/carbapenemase-producing *E. coli*. In Sweden (72 isolates tested) and Iceland (3 isolates tested), almost only presumptive AmpC phenotype (98.6% and 100%, respectively) was present in the isolates analysed. In Finland (25 isolates analysed), both presumptive AmpCphenotype (60%) and ESBLphenotype (44%) were frequent among the isolates analysed. The presumptive ESBL+AmpC-phenotype was also present among the isolates tested.

Slovenia reported eight *E. coli* isolates resistant to third-generation cephalosporins recovered within the routine monitoring in broilers. Most of these isolates showed an AmpCphenotype (87.5% vs 12.5% with an ESBL phenotype). Conversely, when performing specific ESBL-/AmpC-/Carbapenemase-producing monitoring, most of the 28 isolates analysed showed a presumptive ESBL phenotype (96.4% vs none with an AmpC phenotype).

Switzerland reported seven *E. coli* isolates resistant to third-generation cephalosporins recovered from the routine monitoring in broilers (42.8% and 28.5% ESBL- and AmpC-phenotype, respectively). From specific monitoring, 124 isolates were analysed, with 55.6%, 44.3% and 4% of them exhibiting a presumptive ESBL-, AmpC- of ESBL+AmpC-phenotype, respectively.

In the isolates recovered from the specific monitoring ESBL-/AmpC-/carbapenemase-producing *E. coli* in broilers, low ertapenem resistance (MIC = 0.012-0.25 mg/L) was reported in Finland (1 isolate), Slovenia (3) and Switzerland (22), and each of these isolates exhibited a presumptive AmpC or ESBL phenotype.

Specific ESBL-/AmpC-/carbapenemase-producing *E. coli* monitoring in turkeys

Sweden reported data on 12 isolates collected within this specific monitoring in turkeys, five of them showing a presumptive AmpC phenotype (with MIC = 16 mg/L for cefoxitin) and none of them a presumptive ESBL phenotype (Table 50).



Specific monitorings of ESBL-/AmpC-/carbapenemase-producing and carbapenemaseproducing *E. coli* and *Salmonella* in broilers and fattening turkeys in Italy in 2014

In Italy, the specific monitoring of ESBL-/AmpC-/carbapenemase-producing *E. coli* and *Salmonella* in caecal samples from broilers and fattening turkeys at slaughter was performed and reported on a voluntary basis in 2014, in accordance with the Commission Implementing Decision 2013/652/EU and using the caecal samples investigated for *Campylobacter* spp. under that Decision.

The objectives were (1) to assess the occurrence of extended spectrum cephalosporin resistant-(ESC-R) and carbapenemase-resistant (CPE-R) *Salmonella* spp. and *E. coli* in broilers and fattening turkeys – in a context of increasing trends of ESC-R *Salmonella* occurrence within the *Salmonella* National Control Programme in broilers – and (2) to provide a comparison with the occurrence of ESC-R and CPE-R Enterobacteriaceae in humans, as recently reported (ECDC, 2013). Samples were examined by the NRL-AR in accordance with the protocols developed by the EURL-AR. Suspect ESC-R or CPE-R isolates were further investigated to confirm the phenotype of resistance observed by consensus international molecular methods.

Specific monitoring of carbapenemase-producing E. coli

No carbapenemase-producing *E. coli* were detected in broilers or fattening turkeys (see table below).

Table 45: Prevalence of carbapenemase-producing *E. coli* from broilers and fattening turkeys collected within the specific carbapenemase-producing microorganisms monitoring in Italy in 2014

Poultry population	Number of caecal samples tested on selective culture media	Number of caecal samples tested positive for carbapenemase-producing <i>E. coli</i>	Prevalence (95% CI)
Broilers	300	0	0.0% (0.0, 1.2)
Fattening turkeys	300	0	0.0% (0.0, 1.2)

This study provides baseline information of utmost interest, as in Italy, CPE-R Enterobacteriaceae in humans are widespread and are currently considered a major burden among healthcare-associated infectious diseases.

Specific monitoring of ESBL-/AmpC-producing E. coli

ESC-R *E. coli* were confirmed as ESBL-/AmpC-producing *E. coli* by performing relevant Polymerase Chain Reaction (PCR) tests. Corresponding prevalence in broilers and fattening turkeys is shown in the table below.

Table 46: Prevalence of ESBL-/AmpC-producing *E. coli* from broilers and fattening turkeys within the specific ESBL-/AmpC-producing *E. coli* monitoring in Italy in 2014

Poultry population	Number of caecal samples tested on selective culture media	samples tested on elective culture mediapositive for ESBL-/AmpC-producing <i>E. coli</i>				
Broilers	300	244 ^(a)	81.3% (76.5, 85.6)			
Fattening turkeys	300	224 ^(b)	74.7% (69.5, 79.5)			
clinical resistance (b): Nearly 96% were CTX-M-1). Transi	e to cefotaxime or ceftazidime. Am e ESBL-producing <i>E. coli</i> , with 73% ferable AmpC genes, encoding CM	Y-2, were found in 13.1% of isolates. All isolat ong these ESC-R isolates, 95.1% were multi-d b harbouring genes of the CTX-M family (mostl Y-2, were found in 2.7% of isolates. All isolate n the range of clinical resistance for cefotaxime	rug resistant. y encoding the enzyme s had MICs above the			

It should be noted that, when using selective culture methods, the occurrence of ESBL/AmpCproducing *E. coli* in broilers and fattening turkeys is assessed with much greater sensitivity than when using non-selective culture methods. Considering randomly selected isolates of indicator commensal *E. coli* (n=170) from the same caecal samples, cultured on non-selective media, the occurrence of



ESBL/AmpC-producing *E. coli* was 6.47% (11/170) in broilers and 1.18% (2/170) in turkeys, respectively.

The difference is most likely explained by the fact that the ESC-R population may be still subdominant among the *E. coli* populations in the gut flora of these food-producing animals, so that the probability of randomly picking an ESC-R *E. coli* from non-selective agar plates is not high for the majority of samples tested.

Third- and fourth-generation cephalosporins have never been licensed for use in poultry in Italy, and off-label use is currently prohibited, according to the EU legislation. Selection pressure exerted by the use of high amounts of other antimicrobial classes (*e.g.* tetracyclines, sulfonamides, aminopenicillins, (fluoro)quinolones), may also contribute to co-selection of ESC-R, since ESC-R isolates can show multiple drug resistance.

Monitoring of ESBL-/AmpC-/carbapenemase-producing Salmonella *at slaughter*

Cultures for *Salmonella* spp. according to the ISO standards were also performed on the samples collected according to Commission implementing Decision 2013/652/EU. All isolates were serotyped and susceptibility tested, with molecular confirmation of phenotype by PCR.

Table 47: Prevalence of ESBL-/AmpC-producing Salmonella from broilers and fattening turkeys within national specific ESBL-/AmpC-producing Salmonella monitoring in Italy in 2014

Poultry population	Number of caecal samples tested on selective culture media	Number of caecal samples tested positive for ESBL-/AmpC-/carbapenemase- producing <i>Salmonella</i>	Prevalence (95% CI)
Broilers	709	90	12.7% (10.3, 15.4)
Fattening turkeys	558	146	26.2% (22.6, 30.0)

A total 89 isolates from broilers were available for AST testing. No CPE-R *Salmonella* was detected (prevalence: 0.0%, 95% CI: 0.0, 0.52%). ESC-R isolates comprised 3.37% of the total (3/89), and were multiresistant serovar Infantis isolates. This serovar represented 75% of all isolates detected in the survey. *S*. Infantis is also the most frequent serovar reported as ESC-R among isolates tested in the national control programme (NCP) in broiler chicken (27.27% ESC-R in 2014, the vast majority of which are due to an emerging ESBL, CTX-M-1-producing *S*. Infantis clone).

A total 145 isolates from turkeys were available for AST testing. ESC-R isolates were 0.69% (1/145), a low figure which is in agreement with susceptibility data from the NCP in turkeys.

Although the data sets from the two different types of study (survey at slaughter *vs.* NCP) are not directly comparable, monitoring trends in AMR in *Salmonella* spp. (including MDR and resistance to Critically Important Antimicrobials), using both approaches (Census and Objective sampling strategies) may contribute to provide a more accurate picture of the epidemiology of AMR in *Salmonella* spp. in Italy.



Table 48: Occurrence of resistance to selected antimicrobials in *Escherichia coli* from broilers and fattening turkeys in reporting countries collected within thespecific ESBL-/Ampc-/carbapenemase-producing monitoring (Panel 1), in 2014

Country	Amp	Ampicillin		Azithromycin		Cefotaxime		Ceftazidime		nphenicol	Ciprofloxacin		Colistin	
	Ν	% Res	Ν	% Res	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res
Broilers														
Finland	25	100	25	0	25	100	25	96	25	0	25	52.0	25	0
Italy	244	100	244	4.1	244	100	244	84.4	244	55.3	244	75.4	244	5.3
Sweden	72	100	72	0	72	100	72	100	72	0	72	9.7	72	0
Total (MSs 3)	341	100	341	2.9	341	100	341	88.6	341	39.6	341	59.8	341	3.8
Iceland	3	100	3	0	3	100	3	100	3	0	3	0	3	0
Switzerland	124	100	124	0	124	100	124	91.1	124	18.5	124	44.4	124	0
Fattening turkeys	s											1		
Italy	224	100	224	7.6	224	100	224	85.7	224	40.6	224	77.7	224	25.9
Sweden	12	100	12	0	12	100	12	100	12	0	12	0	12	0
Total (MSs 2)	236	100	236	7.2	236	100	236	86.4	236	38,6	236	73.7	236	24.6

Country	Gentamicin		Nalidixic acid		Sulfamethoxazole		Tetra	cycline	Tige	cycline	Trimethoprim	
	N	% Res	N	% Res	N	% Res	N	% Res	N	% Res	Ν	% Res
Broilers		•		•								
Finland	25	0	25	52	25	40	25	52	25	0	25	16
Italy	244	10.2	244	68	244	91.8	244	80.7	244	0.4	244	61.1
Sweden	72	0	72	6.9	72	19.4	72	9.7	72	0	72	0
Total (MSs 3)	341	7.3	341	54	341	72.7	341	63.6	341	0.3	341	44.9
Iceland	3	0	3	0			3	0	3	0	3	0
Switzerland	124	0	124	39.5	124	62.1	124	53.2	124	0	124	30.6
Fattening turkeys									1			
Italy	224	17.9	224	68.3	224	81.7	224	86.2	224	0	224	62.5
Sweden	12	0	12	0	12	0	12	100	12	0	12	0
Total (MSs 2)	236	16.9	236	64.8	236	77.5	236	86.9	236	0	236	59.3

All E. coli isolates tested were susceptible to meropenem.

ESBL: extended spectrum beta-lactamase; N: number of the isolates tested; % Res: percentage of resistant isolates; MS: Member States.



Table 49: Occurrence of resistance to selected antimicrobials in Escherichia coli from broilers and fattening turkeys in reporting countries collected within the specific ESBL-/Ampc-/carbapenemase-producing monitoring (Panel 1), in 2014

Country	Cef	Cefepime		Cefotaxime		Cefoxitin		Ceftazidime		Ertapenem		Imipenem		Meropenem		Temocillin	
	Ν	% Res	N	% Res	Ν	% Res	N	% Res	Ν	% Res	N	% Res	Ν	% Res	Ν	% Res	
Broilers		1		1			1			1	1						
Finland	25	80.0	25	100	25	44.0	25	96.0	25	4.0	25	0	25	0	25	0	
Italy	28	100	28	100	28	0	28	96.4	28	0	28	0	28	0	28	0	
Sweden	72	56.9	72	100	72	98.6	72	100	72	11.1	72	0	72	0	72	0	
Total (MSs 3)	125	71.2	125	100	125	65.6	125	98.4	125	7.2	125	0	125	0	125	0	
Iceland	3	100	3	100	3	100	3	100	3	0	3	0	_	-	_	-	
Switzerland	124	85.5	124	100	124	44.4	124	91.1	124	17.7	124	0	124	0	124	0	
Fattening turke	ys			1			1	1		1	1						
Sweden	12	8.3	12	100	12	41.7	12	91.7	12	0	12	0	12	0	12	0	

Interpretive cut-off applied for temocillin: > 32 mg/L ESBL: extended spectrum beta-lactamase; N: number of the isolates tested; % Res: percentage of resistant isolates; -: no information available; MSs: Member States



Table 50: Presumptive ESBL and AmpC phenotypes identified in *E. coli* isolates from meat from broilers, broilers and fattening turkeys collected within the specific ESBL-/Ampc-/carbapenemase-producing monitoring and subjected to supplementary testing or molecular typing confirmation in 2014^(a)

Country	Total		Presumptive Resistance Phenotype													
-	number of <i>E. coli</i>	ES	SBL ^(b)		r clavulanic- y for CTX ^(c)	ESBL with o SYN only f	AmpC ^(e)		AmpC +	ESBL ^(f)						
	tested	n	% ^(g)	n	% ^(g)	n	% ^(g)	n	% ^(g)	n	% ^(g)					
Meat from broi	ilers															
Slovenia	20	20	100	5	25.0	4	20.0	-	-	-	-					
Iceland	4 ^(h)	-	-	-	-	-	-	4	100	-	-					
Switzerland	232 ^(h)	107	46.1	48	20.7	25	10.8	122	52.6	-	-					
Broilers																
Finland	25	15	60.0	7	28.0	1	4.0	11	44.0	1	4.0					
Italy	244 ⁽ⁱ⁾	209	85.6	-	-			32	13.11							
Slovenia	28 ^(h)	27	96.4	8	28.6	7	25.0									
Sweden	72 ⁽ⁱ⁾	1	1.4	1	1.4			71	98.6							
Total MSs 4	341	252	73.9	-	-	-	-	114	33.4	1	0.3					
Iceland	3	-	-	-	-	-	-	3	100	-	-					
Switzerland	124 ^(h)	69	55.6	32	25.8	11	8.9	55	44.3	5	4.0					
Fattening turk	eys	· · · · · · · · · · · · · · · · · · ·														
Italy	224 ⁽ⁱ⁾	215	96.0	-	-	-	-	6	2.7	-	-					
Sweden	12 ^(h)	-	-	-	-	-	-	5	41.7	-	-					
Total MSs 2	236	215	91.1	-	-	-	-	11	4.7	-	-					

ESBL: extended spectrum beta-lactamase; n= isolates with this phenotype; %: percentage of isolates with this phenotype from the total tested; SYN: synergy; CTX: cefotaxime; CAZ: ceftazidime; MSs: Member States

(a): According to EUCAST Guidelines (EUCAST, 2013), only isolates showing an MIC > 1 mg/L for cefotaxime and/or ceftazidime (screening breakpoint) were considered (see Chapter 1.2.5).

(b): All isolates with an ESBL phenotype, i.e. showing clavulanate synergy with cefotaxime or ceftazidime or synergy with both compounds.

(c): Isolates showing synergy with cefotaxime only, suggesting the presence of an ESBL with cefotaximase activity.

(d): Isolates showing synergy with ceftazidime only, suggesting the presence of an ESBL with ceftazidimase activity.

(e): Isolates with microbiological resistance to cefoxitin.

(f): Isolates showing synergy with cefotaxime or ceftazidime and with microbiological resistance to cefoxitin. Most of these isolates exhibited a MIC=16 mg/L for cefoxitin, suggesting the expression of a cAmpC.

(g): Percentage of the total number of *E. coli* isolates tested (with panel 1).

(h): Isolates with 'other phenotype': Isolates showing an MIC >1 mg/L for cefotaxime and/or ceftazidime but without synergy with clavulanic acid nor resistance to cefoxitin were reported by Sweden (5 isolates from turkeys). Isolates microbiologically resistant to cefotaxime and/or ceftazidime but with MIC =< 1 mg/L for both antimicrobials (not further classified) were reported by Switzerland (12 from broiler meat; 5 from broiler) and Slovenia (1 isolate from broiler)

(i): Molecular data were reported. For Italy, all isolates, excepting three from broilers and three from turkeys, were found positive for the ESBL CTX-M, SHV, TEM- or AmpC CMY-2 encoding genes tested. For Sweden, all isolates from poultry, excepting one isolate with AmpC-phenotype (cefoxitin MIC = 32) were confirmed positive for CMY-2 or CTX-M.



3.5.4. Comparison of cefotaxime resistance in *Salmonella* spp. and indicator *Escherichia coli* isolates from animals

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 (clonal spread) will also play a major part in influencing the occurrence of third-generation cephalosporin resistance. Clonal spread of resistant *Salmonella* can occur subsequent to the acquisition of cephalosporin resistance genes and for reasons other than the selective pressure of usage of antimicrobials, for example, through animal movements or because resistance has occurred at the top of production pyramids in breeding animals. There are also differences in the way that *E. coli* and *Salmonella* are obtained for sampling in the monitoring programme and in the diversity of strains which occur in the intestine of animals. Thus, *E. coli* are present in a diverse array of strains, one of which is chosen from non-selective culture plates for further examination, whereas *Salmonella* tends to occur not as multiple different serovars in each animal but as one or a few single serovars in a flock, which is recovered from the animals using a *Salmonella* selective agar.

Considering the prevalence of resistance to cefotaxime and ceftazidime 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 2014, the prevalence of resistance is higher in *E. coli* than it is in *Salmonella* spp. with the exception of Italy and the Netherlands isolates for broilers where clonal spread of the servars Infantis (Italy) and Heidelberg (the Netherlands) is suspected. Table 51: summarises the data and illustrates some interesting observations relating to the occurrence of cefotaxime and ceftazidime 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 and ceftazidime 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 *E. coli*. However, the correlation does 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. at the primary reservoir of beta-lactamase resistance, which is less frequently observed in *Salmonella* spp. a bacterial species in which clonal spread is of major importance.

Ten out of the twenty-two MSs (45.5%) reporting data on *Salmonella* spp. detected resistance to cefotaxime and ceftazidime in broilers, and the occurrence ranged from 0.4% to 27.3%. In *E. coli*, 22 out of the 27 reporting MSs (81.5%) detected resistance to the same substances and the occurrence ranged from 0.6% to 32.2%. For these isolates, the total prevalence of ESBLs vs AmpCs (considering isolates both classified as ESBL/ESBL+AmpC *vs*. or AmpC/ESBL+AmpC) for *Salmonella* (2.49 vs 1.6%; 65.3% vs 43.6% for the cephalosporin resistant isolates) was slightly lower than the one detected for indicator *E. coli* (4.1% vs 2.2%; 64.3% vs 34.7% for the cephalosporin resistant isolates).



Table 51:	Resistance (%) to cefotaxime and ceftazidime in Salmonella spp. and indicator E. coli isolates in MSs in 2014 testing both back	cterial species in
	broilers or fattening turkeys	

Country				Bro	ilers				Fattening turkeys							
•		Salmone			E. coli				Salmonella spp.				E. coli			
	Cefotaxime Ceftazidime			Cefotaxime Ceftazidime				Cefotaxime Ceftazidime				Cefot	axime	Ceftazidime		
	N	% Res	N	% Res	N	% Res	Ν	% Res	Ν	% Res	Ν	% Res	N	% Res	Ν	% Res
Austria	113	0	113	0	176	1.1	176	1.1	14	0	14	0	125	1.6	125	0.8
Belgium	167	4.2	167	3	158	8.2	158	7.0	_	_	_	_	_	_	_	_
Bulgaria	17	0	17	0	85	0	85	0	_	_	_	-	-	-	_	-
Croatia	126	0	126	0	170	0.6	170	0.6	_	_	_	_	_	_	_	_
Cyprus	45	8.9	45	8.9	87	32.2	87	29.9	_	_	_	-	_	_	_	-
Czech Republic	212	0.5	212	0.5	196	1.0	196	1.0	19	0	19	0	_	_	_	-
Denmark	26	0	26	0	191	0	191	0	_	_	_	_	_	_	_	_
Estonia	_	-	_	_	71	4.2	71	2.8	_	_	_	-	_	_	_	-
Finland	_	-	-	-	175	0	175	0	_	_	_	-	_	_	_	-
France	36	0	36	0	226	4.0	226	4	58	0	58	0	238	0.4	238	0.4
Germany	28	0	28	0	227	1.3	227	1.3	13	0	13	0	170	2.4	170	1.8
Greece	20	0	20	0	172	2.9	172	2.9	_	_	_	-	_	_	_	-
Hungary	169	0	169	0	170	2.9	170	2.9	170	0	170	0	170	1.8	170	1.8
Ireland	17	0	16	6.3	167	4.2	167	3.6	_	_	_	-	_	_	_	-
Italy	66	27.3	66	25.8	170	6.5	170	5.9	35	0	35	0	170	1.2	170	1.2
Latvia	-	-	-	-	147	30.6	147	29.9	-	-	_	-	-	-	-	-
Lithuania	_	-	_	-	85	31.8	85	36.5	_	_	_	-				
Malta	60	3.3	60	16.7	60	15.0	60	20.0	_	_	_	-	-	-	_	-
Netherlands	88	17.0	88	17.0	377	2.9	377	3.2	-	-	_	-	-	-	-	-
Poland	85	0	85	0	179	2.2	179	2.2	29	0	29	0	170	2.4	170	1.8
Portugal	51	2.0	51	2.0	201	5.5	201	5.5	_	_	_	-	185	2.7	185	2.7
Romania	554	0.4	554	0.4	859	1.7	859	1.7	-	-	_	-	38	0	38	0
Slovakia	19	0	19	0	86	12.8	86	11.6	_	_	_	-	_	-	_	_
Slovenia	85	0	85	0	85	9.4	85	9.4	_	_	_	-	_	-	_	_
Spain	135	2.2	135	2.2	170	14.7	170	14.7	226	0	226	0	170	10.0	170	10.0
Sweden	_	_	_	_	197	0	197	0	_	_	_	-	59	1.7	59	1.7
United Kingdom	168	0	168	0	159	0	159	0	162	0	162	0	168	0	168	0
Total (MSs 27)	2,287	2.3	2,286	2.6	5,046	5.1	5,046	5.0	726	0	726	0	1,663	2.3	1,663	2.2
Iceland	16	0	16	0	205	1.5	205	1.5	_	_	_	-	_	-	_	_

MSs: Member states; N: number of the isolates tested; % Res: percentage of resistant isolates;-: no information available.



3.5.5. Discussion

Third-generation cephalosporins are antimicrobials of particular importance because they are frequently used as the first-line treatment in invasive Gram-negative infections, for example infections caused by *E. coli* or *Salmonella*. In 2014, 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 broilers, laying hens and fattening turkeys 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. EFSA recommended that both cefotaxime and ceftazidime should be included in the harmonised mandatory monitoring to ensure optimal detection of all ESBLs (including also SHV-, TEM- and OXA-variants) (EFSA, 2012a), and this was implemented in 2014, as surveillance procedures should anticipate possible changes in the status of different ESBL enzymes. The value of this approach is evident in the cephalosporin resistance figures presented for broilers, where some isolates were detected which showed synergy with either cefotaxime or ceftazidime alone.

The results have been presented by animal production type. 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. Occurrence of resistance to cefotaxime or/and ceftazidime in Salmonella spp. was higher in broilers than in laying hens (whenever resistance was detected) for all MSs (9/22 vs. 3/15 reporting MSs). Laying hens tend to be infrequently treated with antimicrobials, especially once in lay. The three MSs reporting cefotaxime or ceftazidime resistance in *Salmonella* spp. from laying hens, each reported only single isolates of serovars Enteritidis, Paratyphi and Cerro. The situation differed in relation to Salmonella spp. resistant to third-generation cephalosporins in broilers, where, of the nine MSs reporting resistant isolates, only two reported single isolates the remainder detected more than one isolate and Italy (S. Infantis) and the Netherlands (S. Heidelberg) in particular reported multiple isolates of the same serovar, indicating likely clonal dissemination of these serovars in broilers in those MSs. S. Enteritidis from broilers and layers were mostly susceptible to cefotaxime and ceftazidime from most MSs, with the exception of single S. Enteritidis isolates from broilers from Portugal and from layers from Poland. Malta reported isolates resistant to ceftazidime, but susceptible to cefotaxime, in broilers, 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 fattening turkeys where no resistance to third-generation cephalosporins was detected. Although resistance to thirdgeneration cephalsporins was not detected in Salmonella spp. from fattening turkeys, only nine MSs reported results for turkeys, whereas 22 MSs reported results for Salmonella spp. from broilers. 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, S. Enteritidis 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.



Considering the 4,179 E. coli isolates reported from broilers, 5% showed co-resistance to cefotaxime and ciprofloxacin using ECOFFs and 2.3% using clinical breakpoints. Figures for the 2,293 Salmonella spp. isolates from broiler flocks were rather similar, with 2.3% co-resistance to cefotaxime and ciprofloxacin detected using ECOFFs and 2.0% co-resistance detected using clinical breakpoints. In laying hen flocks, where E. coli data were not available, co-resistance in Salmonella occurred at the much lower level of 0.3%. Differences in the pattern of usage of antimicrobials in broiler and laying hen flocks may account for the lower level of co-resistance observed in Salmonella isolates from laying hens. Similarly, of 1,398 E. coli isolates from fattening turkeys, the figures were 2.3% and 1% for coresistance to cefotaxime and ciprofloxacin using ECOFFs and clinical breakpoints, respectively, whereas co-resistance was not detected in Salmonella spp. from turkeys. These differences between E. coli and Salmonella spp. in relation to the observed levels of resistance to cephalosporins and of coresistance to cefotaxime and ciprofloxacin may relate to a number of factors. Clonal expansion of Salmonella spp. is suspected in isolates from broilers from Italy and the Netherlands, where one Salmonella serovar is dominant among those showing resistance. Clonal expansion will be more readily detected in Salmonella than in E. coli because of the primary culture methods which are used, in which E. coli are selected at random from the total E. coli population which is present.

The emerging serovar *S*. Kentucky was the only serovar to show high-level resistance to ciprofloxacin, and resistance to cefotaxime and ceftazidime, with a single isolate from broilers in Spain detected with such resistance. Resistance to both first-line compounds used for treatment of invasive salmonellosis is undesirable because both first-line treatments are likely to be ineffective.

Third-generation cephalosporin resistance in *Salmonella* was very low or absent for most of the MSs, but when present, there were some differences on the resistance mechanisms found depending on the animal species. In *Salmonella* from laying hen flocks, AmpC enzyme producers were detected at a very low level, whereas in *Salmonella* from broiler flocks, ESBL enzyme producers predominate in most MSs, although AmpC enzyme producers were majority in the Netherlands, but also occurred in some other MSs. The occurrence of only a few serovars having acquired these types of resistance (*S.* Infantis, *S.* Heidelberg and *S.* Java) may be related to the prevalence of these serovars in those MSs, where resistance was detected or may be related to particular features which have allowed them to develop resistance or enabled them to spread. In *E. coli* from both broilers and fattening turkeys, isolates with a presumptive ESBL phenotype were more common than isolates with a presumptive AmpC phenotype. Ertapenem resistance was observed in some isolates with an ESBL or AmpC phenotype and this is presumed to be related to ESBL or AmpC enzyme production in conjunction with loss of porins.

Temocillin (6-a-methoxy-ticarcillin) was included in the supplementary panel of antimicrobials for any isolates showing resistance to cefotaxime, ceftazidime or meropenem in 2014. Temocillin can allow further phenotypic characterisation of carbapenemase-producing isolates²⁶. Temocillin is unaffected by most ESBL and AmpC enzymes and may be particularly useful in human medicine to treat urinary tract infections caused by ESBL-producing Gram-negative organisms (Livermore and Tulkens, 2009). Resistance to temocillin in ESBL- and AmpC-producing *E. coli* detected in poultry was rare and was not observed in *E. coli* from fattening turkeys in any MS. In *E. coli* from broilers, it was only detected in one MS in two isolates, which were both phenotypically ESBL-producers. The significance of *E. coli* infections in humansis the subject of debate (Bélanger et al., 2011). Irrespective of any possible direct significance of these organisms for humans, resistance in commensal *E. coli* in animals constitutes a reservoir of resistance genes and a low prevalence of cephalosporin resistance is therefore desirable.

For the routine AMR monitoring in commensal indicator *E. coli*, the examination of a single randomlyselected *E. coli* isolate from non-selective culture plates was performed. This approach enables the assessment of the proportion of randomly selected *E. coli* that is resistant to cephalosporins, as categorized as presumptive ESBL/ampC/carbapenemase producers. It provides a lower degree of sensitivity, particularly where ESBL-producing *E. coli* constitutes a small proportion of the total *E. coli* flora, than that obtained using specific monitoring based on selective media. The approach is useful for consumers risk assessment, as it is consider that *E. coli* will be transferred along the food chain in a random fashion (EFSA, 2012a).

²⁶ For example, those isolates producing the enzyme OXA-48 in which high-level resistance to temocillin can be observed (Woodford et al., 2013).



Conversely, for the specific ESBL/AmpC/carbapenemase monitoring, culture methods using a nonselective enrichment and a selective medium for the detection of producer *E. coli* (protocol recommended by the EURL-AR) shall be used. The method would allow the detection of ESBL/AmpC within samples (determination of the proportion of samples contaminated with ESBL-/AmpC-/carbapenemases-producing *E. coli*). The sensitivity to detect the producer *E. coli* by this approach is higher than that obtained when performing the (random) routine monitoring, especially when investigating populations with a low prevalence of ESBL-producing *E. coli*. If large numbers of AmpCproducing *E. coli* are present in samples, they may obscure the concomitant presence of ESBLproducing *E. coli* in the same samples. It should be taken into account that for MDR data analyses, only a subpopulation of *E. coli* would be represented (EFSA, 2012a).

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. Categorising isolates which are resistant to third-generation cephalosporins and/or carbapenems according to their presumptive ESBL, AmpC and or carbapenemase phenotype provides useful epidemiological information on the reservoirs of the different types of resistance present in *E. coli* in different food-producing animal populations and categories of foodstuffs. For those countries providing molecular data on the occurrence of selected acquired genes (i.e. bla_{CTX-M} , bla_{SHV} ESBLs, bla_{CMY-2}), the classification of the isolates according to their presumptive phenotypes based on the EUCAST criteria (EUCAST, 2013) was supported in most of the appropriateness of the criteria applied. The main differences were found for the isolates classified as presumptive ESBL + AmpC-producers for which the reported MIC values for cefoxitin (low resistance, values close to the ECOFF) could be related, at least in *E. coli*, with the putative expression of intrinsic AmpC genes (Table 40, Table 42, Table 44 and Table 49).

Regarding carbapenem non-susceptibility and detection of putative carbapenemase-producers within indicator *E. coli* and/or *Salmonella*, after validation of data (retesting of antimicrobial susceptibility and species identification by several MSs), none of the data reported for the isolates collected within the routine monitoring suggested the presence of these isolates. Only a few countries reported, on voluntary basis, data on specific monitoring on ESBL-/AmpC-/carbapenemases-producing *E. coli* and/or on the specific monitoring on carbapenemase-producer indicator *E. coli* isolates were identified. Whereas this initial data is reassuring, carefulness is advisable until a general overview is performed through specific monitoring in all MSs in 2015 onwards, as required by the legislation. It shall be also taken into account that the isolation methods applied for the mandatory ESBL-/AmpC-/carbapenemases-producing *E. coli* specific monitoring (selective media containing cefotaxime 1 mg/L, protocol of EURL-AR) would provide a better sensitivity for the selection of ESBL-/AmpC-producers.



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List of abbreviations

%	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
APHA	Animal and Plant Health 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
СР	carbapenemase producer
CTX-M	cefotaximase
DD	disk diffusion method
DL	dilution method
DIN	Deutsches Institut für Normung
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
ESBL	extended spectrum beta-lactamase
ETEC	enterotoxigenic <i>E. coli</i>
EUCAST	European Committee on Antimicrobial Susceptibility Testing
EURL-AR	EU Reference Laboratory for Antimicrobial Resistance (www.crl-ar.eu)
FWD	food- and waterborne diseases and zoonoses
HACCP	hazard analysis and critical control point
HPA	Health Protection Agency (UK)
Ι	intermediate
IZD	inhibition zone diameter
MDR	multiple drug resistance
MIC	minimum inhibitory concentration
MRSA	meticillin-resistant Staphylococcus aureus
MSSA	meticillin-susceptible Staphylococcus aureus
MS	Member State
NA	not applicable
NCP	National Control Programme
NRL	National Reference Laboratory
Q	quantitative
R	resistant
res1-res9	resistance to one antimicrobial substance/resistance to nine antimicrobial substances of the common set for <i>Salmonella</i>
S	susceptible
SIR	susceptible, intermediate, resistant



ST	sequence type
TESSy	The European Surveillance System
VTEC	vero(cyto)toxigenic <i>E. coli</i>
WHO	World Health Organization

Antimicrobial substances

AMC	amoxicillin/clavulanate
AMP	ampicillin
AZM	azithromycin
CAZ	ceftazidime
CHL	chloramphenicol
CIP	ciprofloxacin
CLI	clindamycin
CST	colistin
CTX	cefotaxime
ERY	erythromycin
FUS	fusidic acid
GEN	gentamicin
KAN	kanamycin
LZD	linezolid
MER	meropenem
MUP	mupirocin
NAL	nalidixic acid
QD	quinupristin/dalfopristin
RIF	rifampicin
SUL	sulfonamides
STR	streptomycin
SXT	sulfamethoxazole
TGC	tigecycline
TIA	tiamulin
TET	tetracycline
TMP	trimethoprim

MSs of the EU and other reporting countries in 2014

Austria	AT	
Belgium	BE	
Bulgaria	BG	
Croatia	HR	
Cyprus	CY	
Czech Republic	CZ	
Denmark	DK	
Estonia	EE	

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EUSR on AMR in zoonotic and indicator bacteria from humans, animals and food 2014



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

Non-MSs reporting, 2014

Iceland	IS	
Norway	NO	
Switzerland	СН	

Definitions

'Antimicrobial-resistant isolate'	In the case of quantitative data, an isolate was defined as 'resistant' to a selected 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 the cut-off value. The cut-off values, used to interpret MIC distributions (mg/L) for bacteria from animals and food, are shown in Material and methods, Table 5, Table 6 and Table 7.	
		ualitative data, an isolate was regarded as resistant when the I it as resistant using its own cut-off value or break point
`Level of antimicrobial resistance'	The percentage	of resistant isolates among the tested isolates
'Reporting MS group'	MSs (MSs) that provided data and were included in the relevant table for antimicrobial resistance data for the bacteria–food/animal category– antimicrobial combination	
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%



Appendix: List of usable data

1. Summary

Table abbreviation	Table name
SUMTABL1	Summary of phenotypic characterisation of third generation cephalosporin resistance in Salmonella from poultry in 2014
SUMTABL2	Summary of phenotypic characterisation of third generation cephalosporin resistance in <i>E. coli</i> from poultry in 2014

Figure abbreviation	Figure name
FIG1	Breakdown of serovars in <i>Salmonella</i> isolates from broiler flocks tested for antimicrobial susceptibility in the EU, 2014
FIG2	Proportions of isolates fully susceptible, resistant to one to two classes of substances and multiresistant in the most commonly recovered Salmonella serovars in broiler flocks in the EU, 2014
FIG3	Colistin resistance in Salmonella
FIG4	Colistin resistance in indicator <i>E. coli</i>
FIG5	Erythromycin resistance in C. jejuni and C. coli from broilers
FIG6	Erythromycin resistance in C. jejuni and C. coli from fattening turkeys

2. Matherial and Methods

Table abbreviation	Table name
MMTABL1	Antimicrobials reported, methods used, type of data reported and interpretive criteria
	applied by MSs for human Salmonella AST data in 2014
MMTABL2	Antimicrobials reported, method used, type of data reported and interpretive criteria
	applied by MSs for human Campylobacter AST data in 2014
MMTABL3	Panel of antimicrobial substances included in AMR monitoring, EUCAST ECOFFs and
	concentration ranges tested in Salmonella spp. and indicator commensal E. coli (first
	panel)
MMTABL4	Panel of antimicrobial substances included in AMR monitoring, EUCAST ECOFFs and
	concentration ranges tested in <i>C. jejuni</i> and <i>C. coli</i>
MMTABL5	Panel of antimicrobial substances, EUCAST ECOFFs and concentration ranges used for
	testing only Salmonella spp. and indicator commensal E. coli isolates resistant to
	cefotaxime, ceftazidime or meropenem (second panel)

3.1. Salmonella

3.1.1. Antimicrobial resistance in Salmonella isolates from humans

Table abbreviation	Table name
BOVISHUM	Antimicrobial resistance in <i>Salmonella</i> Bovismorbificans from humans per country in 2014
BREDENEYHUM	Antimicrobial resistance in Salmonella Bredeney from humans per country in 2014
CHESTERHUM	Antimicrobial resistance in Salmonella Chester from humans per country in 2014
COMDERBYHUM	Complete susceptibility, MDR and co-resistance in <i>Salmonella</i> Derby from humans in 2014
COMENTERHUM	Complete susceptibility, MDR and co-resistance in <i>Salmonella</i> Enteritidis from humans in 2014
COMINFANHUM	Complete susceptibility, MDR and co-resistance in <i>Salmonella</i> Infantis from humans in 2014
COMKENTHUM	Complete susceptibility, MDR and co-resistance in <i>Salmonella</i> Kentucky from humans in 2014
COMMONTYPHIHUM	Complete susceptibility, MDR and co-resistance in monophasic <i>Salmonella</i> Typhimurium from humans in 2014
COMSALMHUM	Complete susceptibility, MDR and co-resistance in <i>Salmonella</i> spp. from humans in 2014

EUSR on AMR in zoonotic and indicator bacteria from humans, animals and food 2014



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COMTYPHIHUM	Complete susceptibility, MDR and co-resistance in Salmonella Typhimurium
	from humans in 2014
CORVALLISHUM	Antimicrobial resistance in Salmonella Corvallis from humans per country in 2014
DERBYHUM	Antimicrobial resistance in <i>Salmonella</i> Derby from humans per country in 2014
ENTERHUM	Antimicrobial resistance in <i>Salmonella</i> Enteritidis from humans per country in 2014
HADARHUM	Antimicrobial resistance in <i>Salmonella</i> Hadar from humans per country in 2014
INDIANAHUM	Antimicrobial resistance in <i>Salmonella</i> Indiana from humans per country in 2014
INFANHUM	Antimicrobial resistance in <i>Salmonella</i> Infantis from humans per country in 2014
KENTHUM	Antimicrobial resistance in <i>Salmonella</i> Kentucky from humans per country in 2014
MBANDAKAHUM	Antimicrobial resistance in Salmonella Mbandaka from humans per country in 2014
MIKAWAHUM	Antimicrobial resistance in Salmonella Mikawasima from humans per country in 2014
MM1	Antimicrobials reported, methods used, type of data reported and interpretive criteria applied by MS for human <i>Salmonella</i> AST data in 2014
MONTYPHIHUMD	Antimicrobial resistance in monophasic <i>Salmonella</i> Typhimurium 1,4,[5],12:i:- from humans per country in 2014
MUENCHENHUM	Antimicrobial resistance in <i>Salmonella</i> Muenchen from humans per country in 2014
NEWPORTHUM	Antimicrobial resistance in <i>Salmonella</i> Newport from humans per country in 2014
PARATYPHIBJAVAHUM	Antimicrobial resistance in <i>Salmonella</i> Paratyphi B var. L+ tartrate+ (Java) from humans per country in 2014
RISSENHUM	Antimicrobial resistance in Salmonella Rissen from humans per country in 2014
SALMHUM	Antimicrobial resistance in <i>Salmonella</i> spp. (all non-typhoidal serovars) from humans per country in 2014
SALMTRAVHUMAN	Proportion of tested <i>Salmonella</i> spp. isolates from human cases associated with travel, domestic cases and cases with unknown travel information by country in 2014
SENFTHUM	Antimicrobial resistance in Salmonella Senftenberg from humans per country in 2014
STANLEYHUM	Antimicrobial resistance in <i>Salmonella</i> Stanley from humans per country in 2014
TYPHIHUMD	Antimicrobial resistance in <i>Salmonella</i> Typhimurium from humans per country in 2014
VIRCHOVHUM	Antimicrobial resistance in Salmonella Virchow from humans per country in 2014

Figure abbreviation	Figure name
FIG7	Comparison of CBPs for non-susceptibility (intermediate and resistant categories
	combined) and ECOFFs used to interpret MIC data reported for Salmonella spp.
	from humans, animals or food
FIG8	Frequency distribution of Salmonella spp. isolates from humans completely
	susceptible or resistant to one to eight antimicrobial classes in 2014
FIG9	Frequency distribution of Salmonella Enteritidis isolates from humans completely
	susceptible or resistant to one to nine antimicrobial classes in 2014
FIG10	Spatial distribution of ciprofloxacin resistance among S. Enteritidis from human
	cases in reporting countries in 2014
FIG11	Spatial distribution of nalidixic acid resistance among S. Enteritidis from human
	cases in reporting countries in 2014
FIG12	Spatial distribution of cefotaxime resistance among S. Enteritidis from human
	cases in reporting countries in 2014
FIG13	Frequency distribution of Salmonella Infantis isolates from humans completely
	susceptible or resistant to one to nine antimicrobial classes in 2014
FIG14	Spatial distribution of ciprofloxacin resistance among S. Infantis from human
	cases in reporting countries in 2014
FIG15	Spatial distribution of nalidixic acid resistance among S. Infantis from human
	cases in reporting countries in 2014
FIG16	Spatial distribution of cefotaxime resistance among S. Infantis from human cases
	in reporting countries in 2014



FIG17	Frequency distribution of <i>Salmonella</i> Kentucky isolates from humans completely susceptible or resistant to one to nine antimicrobial classes in 2014
FIG18	<u>Frequency</u> distribution of <i>Salmonella</i> Typhimurium isolates from humans completely susceptible or resistant to one to nine antimicrobial classes in 2014
FIG19	<u>Frequency distribution of monophasic Salmonella</u> Typhimurium 1,4,[5],12:i:- isolates from humans completely susceptible or resistant to one to eight antimicrobial classes in 2014

3.1.2. Antimicrobial resistance in Salmonella isolates from animals and food

Table abbreviation	Table name
BREDENEYTURKMEATD	Occurrence of resistance to selected antimicrobials, Panel 1, in <i>Salmonella</i> Bredeney from meat from turkeys in 2014, using harmonis ed epidemiological cut-off values
CEFOCOM	Occurrence of resistance to cefotaxime,Panel 1, in <i>Salmonella</i> spp. from broilers, laying hens, fattening turkeys, fattening pigs and calves (under 1 year) in 2014, u sing harmonised ECOFFs and EUCAST CBPs
COMDERBYLAY	Complete susceptibility and MDR in <i>Salmonella</i> Derby from laying hens in 2014
COMDERBYTURKMEAT	Complete susceptibility and MDR in <i>Salmonella</i> Derby from meat from turkeys in 2 014
COMDERBYTURK	Complete susceptibility and MDR in <i>Salmonella</i> Derby from fattening turkeys in 20 14
COMENTERBREED	Complete susceptibility and MDR in <i>Salmonella</i> Enteriditis from breeding hens in 2 014
COMENTERBRMEAT	Complete susceptibility and MDR in <i>Salmonella</i> Enteritidis from meat from broilers in 2014
COMENTERBR	Complete susceptibility and MDR in <i>Salmonella</i> Enteriditis from broilers in 2014
COMENTERLAY	Complete susceptibility and MDR in <i>Salmonella</i> Enteriditis from laying hens in 201 4
COMINFANBRMEAT	Complete susceptibility and MDR in <i>Salmonella</i> Infantis from meat from broilers in 2014
COMINFANBR	Complete susceptibility and MDR in <i>Salmonella</i> Infantis from broilers in 2014
COMINFANITURK	Complete susceptibility and MDR in <i>Salmonella</i> Infantis from fattening turkeys in 2 014
COMINFANLAY	Complete susceptibility and MDR in <i>Salmonella</i> Infantis from laying hens in 2014
COMINFTURKMEAT	Complete susceptibility and MDR in <i>Salmonella</i> Infantis from meat from turkeys i <u>n 2014</u>
COMKENBRMEAT	Complete susceptibility and MDR in <i>Salmonella</i> Kentucky from meat from broilers i <u>n 2014</u>
COMKENBR	Complete susceptibility and MDR in <i>Salmonella</i> Kentucky from broilers in 2014
COMKENLAY	Complete susceptibility and MDR in <i>Salmonella</i> Kentucky from laying hens in 201 4
COMKENTUCKYTURKMEAT	<u>Complete susceptibility and MDR in <i>Salmonella</i> Kentucky from meat from turkeys in 2014</u>
COMKENTURK	Complete susceptibility and MDR in <i>Salmonella</i> Kentucky from fattening turkeys in 2014
COMMONTYPHIBR	Complete susceptibility and MDR in monophasic Salmonella Typhimurium from br oilers in 2014
COMMONTYPHILAY	Complete susceptibility and MDR in monophasic Salmonella Typhimurium from lay ing hens in 2014
COMPSALMBRMEAT	Complete susceptibility and MDR in <i>Salmonella</i> spp. from meat from broilers in 20 14
COMSALMBREED	Complete susceptibility and MDR in <i>Salmonella</i> spp. from breeding hens in 2014
COMSALMBR	Complete susceptibility and MDR in Salmonella spp. from broilers in 2014
COMSALMLAY	Complete susceptibility and MDR in <i>Salmonella</i> spp. from laying hens in 2014
COMSALMPIGMEAT	Complete susceptibility, MDR and index of diversity in <i>Salmonella</i> spp. from pig m eat in 2014



COMSALMTURKMEAT	Complete susceptibility and MDR in <i>Salmonella</i> spp. from meat from turkeys in 20
COMSALMTURK	14 Complete susceptibility and MDR in Salmonella spp. from fattening turkeys in 201
COMSTANTURK	Complete susceptibility and MDR in <i>Salmonella</i> Stanley from fattening turkeys in 2 014
COMTYPHIBR	Complete susceptibility and MDR in <i>Salmonella</i> Typhimurium from broilers in 201 4
COMTYPHILAY	Complete susceptibility and MDR in <i>Salmonella</i> Typhimurium from laying hens in 2 014
COMTYPHIPIGMEAT	Complete susceptibility and MDR in <i>Salmonella</i> Typhimurium from meat from pigs in 2014
COMTYPHITURKMEAT	Complete susceptibility and MDR in <i>Salmonella</i> Typhimurium from meat from turk eys in 2014
COMTYPHITURK	Complete susceptibility and MDR in <i>Salmonella</i> Typhimurium from fattening turke ys in 2014
COSALM	<u>Co-</u> resistance to cefotaxime and ciprofloxacin (applying EUCAST clinical breakpoints)
DERBYTURKD	Occurrence of resistance to selected antimicrobials, Panel 1, in <i>Salmonella</i> Derby isolates from fattening turkeys in 2014, using harmo nised epidemiological cut-off values
ENTERBRD	Occurrence of resistance to selected antimicrobials, Panel 1, in <i>Salmonella</i> Enteritidis isolates from broilers in 2014, using harmonised epidemiological cut-off values
ENTERBRD2	Occurrence of resistance to selected antimicrobials, Panel 2, in <i>Salmonella</i> Enteritidis isolates from broilers in 2014, using harmonised epidemiological cut-off values
ENTERBRMEATD	Occurrence of resistance to selected antimicrobials, Panel 1, in <i>Salmonella</i> Enteritidis from meat from broilers in 2014, using harmonis ed epidemiological cut-off values
ENTERBRMEATD2	Occurrence of resistance to selected antimicrobials, Panel 2, in <i>Salmonella</i> Enteritidis from meat from broilers in 2014, using harmonis ed epidemiological cut-off values
ENTERLAYD	Occurrence of resistance to selected antimicrobials, Panel 1, in <i>Salmonella</i> Enteritidis isolates from laying hens in 2014, using harmoni sed epidemiological cut-off values
ENTERLAYD2	Occurrence of resistance to selected antimicrobials, Panel 2, in <i>Salmonella</i> Enteritidis isolates from laying hens in 2014, using harmoni sed epidemiological cut-off values
ENTEROVERVIEW	Overview of countries reporting antimicrobial resistance data using MICs on <i>Salmo nella</i> Enteritidis from humans and various animal and food categories in 2014
ENTERTURKD	Occurrence of resistance to selected antimicrobials, Panel 1, in <i>Salmonella</i> Enteritidis isolates from fattening turkeys in 2014, using ha rmonised epidemiological cut-off values
FREQINFBR	Frequency distribution of completely susceptible isolates and resistant isolates to f rom one to nine antimicrobials classes in Salmonella Infantis from broilers in 2014 in 2014
FREQKENMBR	Frequency distribution of completely susceptible isolates and resistant isolates to f rom one to nine antimicrobials classes in Salmonella Kentuky from broilers in 2014 Kentuky
FREQSALMBR	Frequency distribution of completely susceptible isolates and resistant isolates to f rom one to nine antimicrobials classes in <i>Salmonella</i> spp. from broilers in 2014
FREQSALMLAY	Frequency distribution of completely susceptible isolates and resistant isolates to f rom one to nine antimicrobials classes in <i>Salmonella</i> spp. from laying hens in 2014
HADARTURKD	Occurrence of resistance to selected antimicrobials, Panel 1, in <i>Salmonella</i> Hadar isolates from fattening turkeys in 2014, using harmo nised epidemiological cut-off values



Frequency distribution of completely susceptible isolates and resistant isolates to f
rom one to nine antimicrobials
classes in Salmonella Enteritidis from meat from broilers (Gallus gallus) in 2014
Frequency distribution of completely susceptible isolates and resistant isolates to f
rom one to nine antimicrobials
classes in Salmonella Enteritidis from broilers in 2014
Frequency distribution of completely susceptible isolates and resistant isolates to f
rom one to nine antimicrobials
classes in Salmonella Infantis from laying hens in 2014
Frequency distribution of completely susceptible isolates and resistant isolates to f
rom one to nine antimicrobials
classes in Salmonella Kentuky from laying hens in 2014
Frequency distribution of completely susceptible isolates and resistant isolates to f
rom one to nine antimicrobials
classes in <i>Salmonella</i> spp. from meat from broilers (Gallus gallus) in 2014
Frequency distribution of completely susceptible isolates and resistant isolates to f
rom one to nine antimicrobials
classes in Salmonella spp. from meat from turkeys in 2014Frequency distribution of completely susceptible isolates and resistant isolates to f
rom one to nine antimicrobials
classes in Salmonella spp. from fattening turkeys in 2014
Ciprofloxacin resistance assessed at differing thresholds in
Salmonella serovars from broilers in 2014
Ciprofloxacin resistance assessed at differing thresholds
in <i>Salmonella</i> serovars from broiler meat in 2014
Ciprofloxacin resistance assessed at differing thresholds in <i>Salmonella</i> serovars fro
m laying hens in 2014
Ciprofloxacin resistance assessed at differing thresholds in
Salmonella serovars from fattening turkeys in 2014
Ciprofloxacin resistance assessed at differing thresholds in <i>Salmonella</i> serovars fro
m turkey meat in 2014
Occurrence of resistance to selected antimicrobials,
Panel 1, in <i>Salmonella</i> Indiana from meat from broilers in 2014, using harmonised
epidemiological cut-off values
Occurrence of resistance to selected antimicrobials,
Panel 1, in Salmonella Infantis isolates from broilers in 2014, using harmonised ep
idemiological cut-off values
Occurrence of resistance to selected antimicrobials,
Panel 2, in Salmonella Infantis isolates from broilers in 2014, using harmonised ep
idemiological cut-off values
Occurrence of resistance to selected antimicrobials,
Panel 1, in Salmonella Infantis from meat from broilers in 2014, using harmonised
_epidemiological cut-off values
Occurrence of resistance to selected antimicrobials,
Panel 2, in <i>Salmonella</i> Infantis from meat from broilers in 2014, using harmonised
epidemiological cut-off values
Occurrence of resistance to selected antimicrobials,
Panel 1, in <i>Salmonella</i> Infantis isolates from laying hens in 2014, using harmonise
d epidemiological cut-off values
Occurrence of resistance to selected antimicrobials, Panel1, in Salmonella Infantis isolates from fattening turkeys in 2014, using harm
onised epidemiological cut-off values
Occurrence of resistance to selected antimicrobials,
Panel1, in <i>Salmonella</i> Infantis from meat from turkeys in 2014, using harmonised
epidemiological cut-off values
Occurrence of resistance to selected antimicrobials,
Panel1, in <i>Salmonella</i> Kentucky isolates from broilers in 2014, using harmonised e
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pidemiological cut-off values

	Occurrence of registence to calcuted entimicrohiole
KENTLAYD	Occurrence of resistance to selected antimicrobials,
	Panel1, in <i>Salmonella</i> Kentucky isolates from laying hens in 2014, using harmonis ed epidemiological cut-off values
KENTTURKD	Occurrence of resistance to selected antimicrobials,
KENTTURKD	Panel1, in <i>Salmonella</i> Kentucky isolates from fattening turkeys in 2014, using har
	monised epidemiological cut-off values
KENTUBRMEATD	Occurrence of resistance to selected antimicrobials,
REINTODRIFIERTD	Panel1, in <i>Salmonella</i> Kentucky from meat from broilers in 2014, using harmonise
	<u>d epidemiological cut-off values</u>
KENTURKMEATD	Occurrence of resistance to selected antimicrobials,
	Panel 1, in <i>Salmonella</i> Kentucky from meat from turkeys in 2014, using harmonise
	d epidemiological cut-off values
MBANBRD	Occurrence of resistance to selected antimicrobials,
	Panel 1, in <i>Salmonella</i> Mbandaka isolates from broilers in 2014, using harmonised
	epidemiological cut-off values
MBANBRD2	Occurrence of resistance to selected antimicrobials,
	Panel 2, in <i>Salmonella</i> Mbandaka isolates from broilers in 2014, using harmonised
	epidemiological cut-off values
MONTYPHIBRD	Occurrence of resistance to selected antimicrobials,
	Panel 1, in monophasic Salmonella Typhimurium isolates from broilers in 2014, usi
	ng harmonised epidemiological cut-off values
MONTYPHILAYD	Occurrence of resistance to selected antimicrobials,
	Panel 1, in monophasic Salmonella Typhimurium isolates from laying hens in 2014
	, using harmonised epidemiological cut-off values
MULTIDERBYTURK	MDR patterns to selected antimicrobials,
	Panel 1, in Salmonella Derby from fattening turkeys in 2014
MULTIENTERBR	MDR patterns to selected antimicrobials, Panel
	1, in Salmonella Enteritidis from broilers in 2014
MULTIENTERLAY	MDR patterns to selected antimicrobials, Panel
	1, in Salmonella Enteritidis from laying hens in 2014
MULTIINFANBR	MDR patterns to selected antimicrobials, Panel
	<u>1, in Salmonella Infantis from broilers in 2014</u>
MULTIINFANBRMEAT	MDR patterns to selected antimicrobials,
	Panel 1, in <i>Salmonella</i> Infantis from meat from broilers in 2014
MULTIINFANLAY	MDR patterns to selected antimicrobials,
	Panel 1, in Salmonella Infantis from laying hens in 2014
MULTIINFANTURK	MDR patterns to selected antimicrobials,
	Panel 1, in Salmonella Infantis from fattening turkeys in 2014
MULTIINFBR	MDR patterns to selected antimicrobials, Panel
	1, in <i>Salmonella</i> Infantis from broilers in 2014
MULTIINFLAY	MDR patterns to selected antimicrobials, Panel 1,
MULTIINFTURKMEAT	in <i>Salmonella</i> Infantis from laying hens in 2014
MULTIINFTURKMEAT	MDR patterns to selected antimicrobials, Panel 1, in <i>Salmonella</i> Infantis from meat from turkeys in 2014
MULTIKENBRMEAT	
MULTIKENDRMEAT	MDR patterns to selected antimicrobials, Panel 1, in <i>Salmonella</i> Kentucky from meat from broilers in 2014
MULTIKENTBR	MDR patterns to selected antimicrobials, Panel
MOLTIKLINIBK	1, in <i>Salmonella</i> Kentucky from broilers in 2014
MULTIKENTLAY	MDR patterns to selected antimicrobials, Panel
MOLTIKLNTLAT	1, in <i>Salmonella</i> Kentucky from laying hens in 2014
MULTIKENTUCKYTURKMEAT	MDR patterns to selected antimicrobials,
MOLTIKENTOCKTTOKKMEAT	Panel 1, in <i>Salmonella</i> Kentucky from meat from turkeys in 2014
MULTIKENTURK	MDR patterns to selected antimicrobials,
	Panel 1, in <i>Salmonella</i> Kentucky from fattening turkeys in 2014
MULTIMONTYPHIBR	MDR patterns to selected antimicrobials,
	Panel 1, in monophasic Salmonella Typhimurium from broilers in 2014
MULTIMONTYPHILAY	MDR patterns to selected antimicrobials,
	Panel 1, in monophasic <i>Salmonella</i> Typhimurium from laying hens in 2014
MULTISALMBR	MDR patterns to selected antimicrobials, Panel
	1, in <i>Salmonella</i> spp. from broilers in 2014
MULTISALMBREED	MDR patterns to selected antimicrobials,
	Panel 1, in <i>Salmonella</i> spp. from breeding hens in 2014



MULTISALMBRMEAT	MDR patterns to selected antimicrobials, Panel 1, in <i>Salmonella</i> spp. from meat from broilers in 2014
MULTISALMLAY	MDR patterns to selected antimicrobials, Panel
	1, in Salmonella spp. from laying hens in 2014
MULTISALMTURKMEAT	MDR patterns to selected antimicrobials,
	Panel 1, in Salmonella spp. from meat from turkeys in 2014
MULTISALTURK	MDR patterns to selected antimicrobials,
MULTISTANTURK	Panel 1, in <i>Salmonella</i> spp. from fattening turkeys in 2014
MULTISTANTURK	MDR patterns to selected antimicrobials, Panel 1, in <i>Salmonella</i> Stanley from fattening turkeys in 2014
MULTISTANTURKMEAT	MDR patterns to selected antimicrobials,
	Panel 1, in <i>Salmonella</i> Stanley from meat from turkeys in 2014
MULTITYPHIBR	MDR patterns to selected antimicrobials,
	Panel 1, in Salmonella Typhimurium from broilers in 2014
MULTITYPHILAY	Multiresistance patterns to selected antimicrobials,
	Panel 1, in Salmonella Typhimurium from laying hens in 2014
MULTITYPHITURK	MDR patterns to selected antimicrobials,
MULTITYPHITURKMEAT	Panel 1, in <i>Salmonella</i> Typhimurium from fattening turkeys in 2014 MDR patterns to selected antimicrobials,
MULTITIFIITURNMLAT	Panel 1, in <i>Salmonella</i> Typhimurium from meat from turkeys in 2014
NEWPTURKD	Occurrence of resistance to selected antimicrobials,
	Panel 1, in <i>Salmonella</i> Newport isolates from fattening turkeys in 2014, using har
	monised epidemiological cut-off values
NEWPTURKD2	Occurrence of resistance to selected antimicrobials,
	Panel 2, in Salmonella Newport isolates from fattening turkeys in 2014, using har
	monised epidemiological cut-off values
NEWTURKMEATD	Occurrence of resistance to selected antimicrobials,
	Panel 1, in <i>Salmonella</i> Newport from meat from turkeys in 2014, using harmonise
RISSENBRD	<u>d epidemiological cut-off values</u> Occurrence of resistance to selected antimicrobials,
RISSLINDRD	Panel 1, in <i>Salmonella</i> Rissen isolates from broilers in 2014, using harmonised epi
	demiological cut-off values
SALMBRD	Occurrence of resistance to selected antimicrobials,
	Panel 1, in <i>Salmonella</i> spp. isolates from broilers in 2014, using harmonised epi
	demiological cut-off values
SALMBRD2	Occurrence of resistance to selected antimicrobials,
	Panel 2, in <i>Salmonella</i> spp. isolates from broilers in 2014, using harmonised epi demiological cut-off values
SALMBRMEATD	Occurrence of resistance to selected antimicrobials,
SALINDRINLATD	Panel 1, in <i>Salmonella</i> spp. from meat from broilers in 2014, using harmonised epi
	demiological cut-off value
SALMBRMEATD2	Occurrence of resistance to selected antimicrobials,
	Panel 2, in Salmonella spp. from meat from broilers in 2014, using harmonised epi
	demiological cut-off values
SALMFATTURKD	Occurrence of resistance to selected antimicrobials,
	Panel 1, in <i>Salmonella</i> spp. isolates from fattening turkeys in 2014, using harmoni
SALMFATTURKD2	sed epidemiological cut-off values Occurrence of resistance to selected antimicrobials,
SALMFATTURKDZ	Panel 2, in <i>Salmonella</i> spp. isolates from fattening turkeys in 2014, using harmoni
	sed epidemiological cut-off values
SALMLAYD	Occurrence of resistance to selected antimicrobials,
	Panel 1, in <i>Salmonella</i> spp. isolates from laying hens in 2014, using harmonised e
	pidemiological cut-off values
SALMLAYD2	Occurrence of resistance to selected antimicrobials,
	Panel 2, in <i>Salmonella</i> spp. isolates from laying hens in 2014, using harmonised e
	pidemiological cut-off values
	Overview of countries reporting antimicrobial resistance data using MICs on Salmo
SALMOVERVIEW	
SALMOVERVIEW	nella spp all serovars from humans and various animal and food categories in 20
	<i>nella</i> spp all serovars from humans and various animal and food categories in 20 <u>14</u>
SALMOVERVIEW	nella spp all serovars from humans and various animal and food categories in 20



d epidemiological cut-off value SENFBRD2 Occurrence of resistance to se Panel 2, in Salmonella Senften d epidemiological cut-off value SERBOVMEAT Frequency distribution of Salm animals tested for anticrobial se SERBR2 SERBR2 Frequency distribution of Salm anticrobial susceptibility to Par tested for anticrobial susceptibility to Par tested for anticrobial susceptibility	berg isolates from broilers in 2014, using harmonise s lected antimicrobials, berg isolates from broilers in 2014, using harmonise s conella serovars of isolates from meat from bovine susceptibility to Panel 1 substances in 2014 conella serovars of isolates from broilers tested for
d epidemiological cut-off value SENFBRD2 Occurrence of resistance to se Panel 2, in Salmonella Senften d epidemiological cut-off value SERBOVMEAT Frequency distribution of Salm animals tested for anticrobial se SERBR2 SERBR2 Frequency distribution of Salm anticrobial susceptibility to Par tested for anticrobial susceptibility to Par tested for anticrobial susceptibility	s lected antimicrobials, berg isolates from broilers in 2014, using harmonise s conella serovars of isolates from meat from bovine susceptibility to Panel 1 substances in 2014 conella serovars of isolates from broilers tested for nel 2 substances in 2014 conella serovars of isolates from meat from broilers
SENFBRD2 Occurrence of resistance to see Panel 2, in Salmonella Senften d epidemiological cut-off value SERBOVMEAT Frequency distribution of Salma SERBR2 Frequency distribution of Salma SERBRMEAT2 Frequency distribution of Salma SERBRMEAT2 Frequency distribution of Salma	lected antimicrobials, berg isolates from broilers in 2014, using harmonise is conella serovars of isolates from meat from bovine susceptibility to Panel 1 substances in 2014 conella serovars of isolates from broilers tested for nel 2 substances in 2014 conella serovars of isolates from meat from broilers
Panel 2, in Salmonella Senften d epidemiological cut-off value SERBOVMEAT Frequency distribution of Salm animals tested for anticrobial s SERBR2 Frequency distribution of Salm anticrobial susceptibility to Par SERBRMEAT2 Frequency distribution of Salm anticrobial susceptibility to Par	berg isolates from broilers in 2014, using harmonise s isolates from meat from bovine isolates from meat from bovine isolates from broilers tested for nel 2 substances in 2014 isonella serovars of isolates from broilers from broilers isolates from meat from broilers
d epidemiological cut-off value SERBOVMEAT Frequency distribution of Salmanials tested for anticrobial second se	s conella serovars of isolates from meat from bovine susceptibility to Panel 1 substances in 2014 conella serovars of isolates from broilers tested for nel 2 substances in 2014 conella serovars of isolates from meat from broilers
animals tested for anticrobial s SERBR2 Frequency distribution of Salman SERBRMEAT2 Frequency distribution of Salman tested for anticrobial susceptibility to Par	susceptibility to Panel 1 substances in 2014 sonella serovars of isolates from broilers tested for nel 2 substances in 2014 sonella serovars of isolates from meat from broilers
animals tested for anticrobial s SERBR2 Frequency distribution of Salman SERBRMEAT2 Frequency distribution of Salman tested for anticrobial susceptibility to Par	susceptibility to Panel 1 substances in 2014 sonella serovars of isolates from broilers tested for nel 2 substances in 2014 sonella serovars of isolates from meat from broilers
SERBR2 Frequency distribution of Salma anticrobial susceptibility to Par SERBRMEAT2 Frequency distribution of Salma tested for anticrobial susceptible	onella serovars of isolates from broilers tested for nel 2 substances in 2014 nonella serovars of isolates from meat from broilers
anticrobial susceptibility to Par SERBRMEAT2 Frequency distribution of Salm tested for anticrobial susceptible	nel 2 substances in 2014 sonella serovars of isolates from meat from broilers
tested for anticrobial susceptib	
	ility to Panel 2 substances in 2014
CEDDDMEAT Execution of Color	
SERBRMEAT <u>Frequency distribution of Salm</u>	onella serovars of isolates from meat from broilers
tested for anticrobial susceptib	ility to Panel 1 substances in 2014
SERBR <u>Frequency distribution of Salm</u>	onella serovars of isolates from broilers tested for
anticrobial susceptibility to Par	nel 1 substances in 2014
SERCALVES <u>Frequency distribution of Salm</u>	
	year) tested for anticrobial susceptibility to Panel 1
substances in 2014	
	onella serovars of isolates from cattle tested for
anticrobial susceptibility to Par	
	onella serovars of isolates from fattening pigs
	ility to Panel 1 substances in 2014
	onella serovars of isolates from Gallus gallus (fowl)
	ility to Panel 1 substances in 2014
	onella serovars of isolates from laying hens tested
for anticrobial susceptibility to	
	onella serovars of isolates from laying hens tested
for anticrobial susceptibility to	
SEROFATTURK Frequency distribution of Salm	
tested for anticrobial susceptib	
	onella serovars of isolates from fattening turkeys
	ility to Panel 2 substances in 2014
SEROTURK <u>Frequency distribution of Salma</u> anticrobial susceptibility to Par	onella serovars of isolates from turkeys tested for
	onella serovars of isolates from meat from pigs
	ility to Panel 1 substances in 2014
	<i>conella</i> serovars of isolates from meat from pigs
	ility to Panel 1 substances in 2014
	<i>onella</i> serovars of isolates from pigs tested for
anticrobial susceptibility to Par	
	onella serovars of isolates from meat from turkeys
	ility to Panel 1 substances in 2014
TYPHIBRD Occurrence of resistance to se	
	urium isolates from broilers in 2014, using harmonis
ed epidemiological cut-off value	
TYPHIBRD2 Occurrence of resistance to se	
	urium isolates from broilers in 2014, using harmonis
ed epidemiological cut-off valu	
TYPHILAYD Occurrence of resistance to se	
Panel 1, in Salmonella Typhim	urium isolates from laying hens in 2014, using harm
onised epidemiological cut-off	
	g antimicrobial resistance data using MICs on Salmo
	ns and various animal and food categories in 2014
TYPHITURKD Occurrence of resistance to se	
	urium isolates from fattening turkeys in 2014, using
harmonised epidemiological c	
TYPHITURKMEATD Occurrence of resistance to se	lected antimicrobials,
Panel1, in Salmonella Typhimu	rium from meat from turkeys in 2014, using harmo
nised epidemiological cut-off v	



Figure abbreviation	Figure name
FIG20	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobial classes in <i>Salmonella</i> spp. from broiler
FIG21	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobial classes in <i>Salmonella</i> spp. from fattening turkey meat in MSs in 2014
FIG22	<u>Frequency distribution of completely susceptible isolates and resistant isolates to one to</u> <u>nine antimicrobials classes in <i>Salmonella</i> spp. from broilers in MSs in 2014</u>
FIG23	Spatial distribution of ciprofloxacin resistance among <i>Salmonella</i> spp. from broilers in countries reporting MIC data in 2014
FIG24	Spatial distribution of nalidixic acid resistance among <i>Salmonella</i> spp. from broilers in countries reporting MIC data in 2014
FIG25	Spatial distribution of cefotaxime resistance among <i>Salmonella</i> spp. from broilers in countries reporting MIC data in 2014
FIG26	<u>Frequency distribution of completely susceptible isolates and resistant isolates to one to</u> nine antimicrobials classes in <i>Salmonella</i> Infantis from broilers in MSs in 2014
FIG27	Spatial distribution of ciprofloxacin resistance among <i>Salmonella</i> Infantis from broilers in countries reporting MIC data in 2014
FIG28	Spatial distribution of nalidixic acid resistance among <i>Salmonella</i> Infantis from broilers in countries reporting MIC data in 2014
FIG29	Spatial distribution of cefotaxime resistance among <i>Salmonella</i> Infantis from broilers in countries reporting MIC data in 2014
FIG30	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> Enteritidis from broilers in MSs in 2014
FIG31	Spatial distribution of ciprofloxacin resistance among <i>Salmonella</i> Enteritidis from broilers in countries reporting MIC data in 2014
FIG32	Spatial distribution of nalidixic acid resistance among <i>Salmonella</i> Enteritidis from broilers in countries reporting MIC data in 2014
FIG33	Spatial distribution of cefotaxime resistance among <i>Salmonella</i> Enteritidis from broilers in countries reporting MIC data in 2014
FIG34	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> Kentuky from broilers in MSs in 2014
FIG35	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> spp. from laying hens in MSs in 2014
FIG36	Spatial distribution of ciprofloxacin resistance among <i>Salmonella</i> spp. from laying hens in countries reporting MIC data in 2014
FIG37	Spatial distribution of nalidixic acid resistance among <i>Salmonella</i> spp. from laying hens in countries reporting MIC data in 2014
FIG38	Spatial distribution of cefotaxime resistance among <i>Salmonella</i> spp. from laying hens in countries reporting MIC data in 2014
FIG39	Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested <i>Salmonella</i> spp. isolates from <i>Gallus gallus</i> in reporting MSs, 2008–2014, quantitative data
FIG40	Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested Salmonella Enteritidis isolates from Gallus gallus in reporting MSs, 2008–2014, quantitative data
FIG41	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> Enteritidis from laying hens in MSs in 2014
FIG42	Spatial distribution of ciprofloxacin resistance among <i>Salmonella</i> Enteritidis from laying hens in countries reporting MIC data in 2014
FIG43	Spatial distribution of nalidixic acid resistance among <i>Salmonella</i> Enteritidis from laying hens in countries reporting MIC data in 2014
FIG44	Spatial distribution of cefotaxime resistance among <i>Salmonella</i> Enteritidis from laying hens in countries reporting MIC data in 2014
FIG45	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> Infantis from laying hens in MSs in 2014
FIG46	Frequency distribution of completely susceptible isolates and resistant isolates to one to nine antimicrobials classes in <i>Salmonella</i> Kentucky from laying hens in MSs in 2014
FIG47	Trends in ampicillin, cefotaxime, ciprofloxacin and nalidixic acid resistance in tested Salmonella spp. isolates from turkeys in reporting MSs, 2008–2014, quantitative data
FIG48	Spatial distribution of ciprofloxacin resistance among <i>Salmonella</i> spp. from fattening turkeys in 2014



FIG49	Spatial distribution of nalidixic acid resistance among <i>Salmonella</i> spp. from fattening turkeys in 2014
FIG50	Spatial distribution of cefotaxime resistance among <i>Salmonella</i> spp. from fattening turkeys in 2014
FIG51	<u>Frequency distribution of completely susceptible isolates and resistant isolates to one to</u> <u>nine antimicrobials classes in <i>Salmonella</i> spp. from fattening turkeys in 2014</u>
FIG52	Tigecycline resistance in Salmonella spp.

3.2. Campylobacter

3.2.1. Antimicrobial resistance in Campylobacter isolates from humans

Table abbreviation	Table name
САМРСОНИМ	Antimicrobial resistance in <i>Campylobacter coli</i> from humans per country in 2014
САМРЈЕНИМ	Antimicrobial resistance in <i>Campylobacter jejuni</i> from humans per country in 2014
CAMPTRAVHUM	Proportion of tested Campylobacter jejuni and C. coli isolates from human cases associated with travel, domestic cases and cases with unknown travel information by country in 2014
COMCAMPCOHUM	Complete susceptibility, MDR and co-resistance in Campylobacter coli from humans in 2014
COMCAMPJEHUM	Complete susceptibility, MDR and co-resistance in <i>Campylobacter jejuni</i> from humans in 2014
MM2	Antimicrobials reported, methods used, type of data reported and interpretive criteria applied by MS for human <i>Campylobacter</i> AST data in 2014

3.2.2. Antimicrobial resistance in Campylobacter isolates from animals and food

Table abbreviation	Table name
CAMPCOBRD	Occurrence of resistance to selected antimicrobials in <i>Campylobacter coli</i> from broilers
	in 2014, using harmonised epidemiological cut-off values
CAMPCOMEAT	Occurrence of resistance to selected antimicrobials in <i>Campylobacter coli</i> from meat in
	2014, using harmonised epidemiological cut-off values
CAMPCOOVERVIEW	Overview of countries reporting antimicrobial resistance data using MIC on <i>Campylobac</i>
	ter coli from humans and various animal and food categories in 2014
CAMPCOTURD	Occurrence of resistance to selected antimicrobials in <i>Campylobacter coli</i> from fattening
	turkeys in 2014, using harmonised epidemiological cutoff values
CAMPJEBRD	Occurrence of resistance to selected antimicrobials in <i>Campylobacter jejuni</i> from broiler
	s in 2014, using harmonised epidemiological cut-off values
CAMPJEMEAT	Occurrence of resistance to selected antimicrobials in <i>Campylobacter jejuni</i> from meat i
	n 2014, using harmonised epidemiological cut-off values
CAMPJEOVERVIEW	Overview of countries reporting antimicrobial resistance data using MIC on <i>Campylobac</i>
	ter jejuni from humans and various animal and food categories in 2014
CAMPJETURD	Occurrence of resistance to selected antimicrobials in <i>Campylobacter jejuni</i> from fatteni
	ng turkeys in 2014, using harmonised epidemiological cut-off values
COMCAMPCOBR	Complete susceptibility and MDR in Campylobacter coli from broilers in 2014
COMCAMPJEBR	Complete susceptibility and MDR in <i>Campylobacter jejuni</i> from broilers in 2014
COMCAMPJETURK	Complete susceptibility and MDR in <i>Campylobacter jejuni</i> from fattening turkeys in 201
	4
FREQCAMPCOBR	Frequency distribution of completely susceptible isolates and resistant isolates to from
	one to five antimicrobials in Campylobacter coli from broilers in 2014
FREQCAMPJEGBR	Frequency distribution of completely susceptible isolates and resistant isolates to from
	one to five antimicrobials in Campylobacter jejuni from broilers in 2014
FREQCAMPJEGTURK	Frequency distribution of completely susceptible isolates and resistant isolates to from
	one to five antimicrobials in Campylobacter jejuni from fattening turkeys in 201
	<u>4</u>
MULTICAMPCOBR	MDR patterns of selected antimicrobials, Panel
	<u>1, in <i>Campylobacter coli</i> from broilers in 2014</u>



MULTICAMPJEGBR	MDR patterns of selected antimicrobials,	Panel
	1, in <i>Campylobacter jejuni</i> from broilers in 2014	
MULTICAMPJEGTURK	MDR patterns of selected antimicrobials,	Panel
	1, in <i>Campylobacter jejuni</i> from fattening turkeys in 2014	

Figure abbreviation	Figure name
FIG53	Comparison of CBPs and ECOFFs used to interpret MIC data reported for <i>Campylobacter</i> spp. from humans, animals or food
FIG54	Frequency distribution of <i>Campylobacter jejuni</i> isolates from humans completely susceptible or resistant to one to four antimicrobial classes in 2014
FIG55	Frequency distribution of <i>Campylobacter jejuni</i> isolates from humans completely susceptible or resistant to one to four antimicrobial classes in 2014
FIG56	Spatial distribution of erythromycin resistance among <i>Campylobacter jejuni</i> from human cases in reporting countries in 2014
FIG57	Frequency distribution of <i>Campylobacter coli</i> isolates from humans completely susceptible or resistant to one to four antimicrobial classes in 2014
FIG58	Trends in ciprofloxacin, erythromycin and nalidixic acid resistance in <u>Campylobacter jejuni</u> from broilers in MSs, 2008–2014
FIG59	Trends in ciprofloxacin, erythromycin and nalidixic acid resistance in <i>Campylobacter coli</i> from broilers in MSs, 2008–2014
FIG60	Spatial distribution of ciprofloxacin resistance among <i>Campylobacter jejuni</i> from broilers of <i>Gallus gallus</i> in reporting countries in 2014
FIG61	Spatial distribution of erythromycin resistance among <i>Campylobacter jejuni</i> from broilers of <i>Gallus gallus</i> in reporting countries in 2014
FIG62	Frequency distribution of <i>Campylobacter jejuni</i> isolates completely susceptible and resistant to one to four antimicrobials, in broilers in MSs, 2014
FIG63	Frequency distribution of <i>Campylobacter coli</i> isolates completely susceptible and resistant to one to four antimicrobials, in broilers in MSs, 2014
FIG64	Spatial distribution of ciprofloxacin resistance among <i>Campylobacter jejuni</i> from fattening turkeys in reporting countries in 2014
FIG65	Spatial distribution of erythromycin resistance among <i>Campylobacter jejuni</i> from fattening turkeys in reporting countries in 2014
FIG66	Frequency distribution of <i>Campylobacter jejuni</i> isolates completely susceptible and resistant to one to four antimicrobials, in fattening turkeys in MSs, 2014
FIG67	Erythromycin resistance in <i>C. jejuni</i> and <i>C. coli</i> from broilers and fattening turkeys

3.3. Escherichia coli

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

Table abbreviation	Table name
CIPESCHEBR	<u>Ciprofloxacin resistance assessed at differing thresholds in</u> indicator <u>Escherichia coli</u> from broilers in 2014
CIPESCHETURK	Ciprofloxacin resistance assessed at differing thresholds in indicator <i>Escherichia coli</i> fro <u>m fattening turkeys in 2014</u>
COESCHEBR	Coresistance to cefotaxime and ciprofloxacin in indicator <i>Escherichia coli</i> from broilers i <u>n 2014</u>
COESCHETURK	<u>Co-</u> <u>resistance to cefotaxime and ciprofloxacin in indicator</u> <u>Escherichia coli</u> from fatt <u>ening turkeys in 2014</u>
COMESCHEBR	Complete susceptibility and MDR in indicator Escherichia coli from broilers in 2014



COMECCUETURY	Complete sussentibility and MDD in indicator in <i>Each wishin and ifteen fathering</i> to be and
COMESCHETURK	Complete susceptibility and MDR in indicator in <i>Escherichia coli</i> from fattening turkeys i
	<u>n 2014</u>
ESCHEBR2	Occurrence of resistance to selected antimicrobials, Panel 2, in indicator Escherichia coli
	from broilers in MSs reporting data in
	2014, using harmonised epidemiological cut-off values
ESCHEBRDESBL2	Specific monitoring of enzyme-producing <i>E. coli</i> from broilers in 2014:
	occurrence of resistance to selected antimicrobials,
	Panel 2, using harmonised epidemiological cut-off values
ESCHEBRDESBL	Specific monitoring of enzyme-producing <i>E. coli</i> from broilers in 2014:
ESCHEDICDESDE	occurrence of resistance to selected antimicrobials,
	Panel 1, using harmonised epidemiological cut-off values
	Panel 1, using harmonised epidemiological cut-on values
ESCHEBRMEATD2	Specific monitoring of enzyme-producing <i>E. coli</i> from broiler meat in 2014:
	occurrence of resistance to selected antimicrobials,
	Panel 2, using harmonised epidemiological cut-off values
ESCHEBRMEATESBL	Specific monitoring of enzyme-producing <i>E. coli</i> from broiler meat in 2014:
	occurrence of resistance to selected antimicrobials,
	Panel 1, using harmonised epidemiological cut-off values
ESCHEBR	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator <i>Escherichia coli</i>
LOCILER	from broilers in MSs reporting data in
	2014, using harmonised epidemiological cut-off values
ESCHEMEAT	Occurrence of resistance to selected antimicrobials in indicator <i>Escherichia coli</i> from
LIGCHEMEAT	meat in MSs reporting data in 2014, using harmonised epidemiological cut-
	off values
ESCHEOVERVIEWESBL	Overview of countries reporting antimicrobial resistance data using MIC on specific
LICHLOVERVIEWEIJE	monitoring of enzyme-producing <i>E. coli</i>
	from various animal and food categories in 2014
ESCHEOVERVIEW	Overview of countries reporting antimicrobial resistance data using MIC on indicator <i>Es</i>
LICITOVERVIEW	<u>cherichia coli</u> from various animal and food categories in 2014
ESCHETURK2	Occurrence of resistance to selected antimicrobials, Panel 2, in indicator
ESCHETURKZ	Escherichia coli isolates from fattening turkeys in 2014, using harmonised epid
	emiological cut-off values
ESCHETURKESBL2	Specific monitoring of enzyme-producing <i>E. coli</i> from fattening turkeys in 2014:
	occurrence of resistance to selected antimicrobials,
	Panel 2, using harmonised epidemiological cut-off values
ESCHETURKESBL	Specific monitoring of enzyme-producing <i>E. coli</i> from fattening turkeys in 2014:
	occurrence of resistance to selected antimicrobials,
	Panel 1, using harmonised epidemiological cut-off values
ESCHETURK	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator
ESCHETURK	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator <i>Escherichia coli</i> isolates from fattening turkeys in 2014, using harmonised epid
	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator <u>Escherichia coli</u> isolates from fattening turkeys in 2014, using harmonised epid <u>emiological cut-off values</u>
FREQESCHEBR	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator Escherichia coli isolates from fattening turkeys in 2014, using harmonised epid emiological cut-off values Frequency distribution of completely susceptible isolates and resistant isolates to from
	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator Escherichia coli isolates from fattening turkeys in 2014, using harmonised epid emiological cut-off values Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in commensal indicator Escherichia coli from broile
FREQESCHEBR	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator Escherichia coli isolates from fattening turkeys in 2014, using harmonised epid emiological cut-off values Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in commensal indicator Escherichia coli from broile rs in 2014 rs in 2014 rs in 2014
	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator Escherichia coli isolates from fattening turkeys in 2014, using harmonised epid emiological cut-off values Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in commensal indicator Escherichia coli from broile rs in 2014 Frequency distribution of completely susceptible isolates and resistant isolates to from
FREQESCHEBR	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator Escherichia coli isolates from fattening turkeys in 2014, using harmonised epid emiological cut-off values Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in commensal indicator Escherichia coli from broile rs in 2014 Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in <i>Escherichia coli</i> from fattening turkeys in 2014
FREQESCHEBR	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator Escherichia coli isolates from fattening turkeys in 2014, using harmonised epid emiological cut-off values Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in commensal indicator Escherichia coli from broile rs in 2014 Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in <i>Escherichia coli</i> from fattening turkeys in 2014
FREQESCHEBR	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator Escherichia coli isolates from fattening turkeys in 2014, using harmonised epid emiological cut-off values Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in commensal indicator Escherichia coli from broile rs in 2014 Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in <i>Escherichia coli</i> from fattening turkeys in 2014
FREQESCHEBR	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator Escherichia coli isolates from fattening turkeys in 2014, using harmonised epid emiological cut-off values Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in commensal indicator Escherichia coli from broile rs in 2014 Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in Escherichia coli from fattening turkeys in 2014 MDR patterns of selected antimicrobials, Panel n indicator Escherichia coli from broilers in 2014 MDR patterns of selected antimicrobials, Panel n indicator Escherichia coli from broilers in 2014
FREQESCHEBR FREQESCHETURK MULTIESCHEBR	Occurrence of resistance to selected antimicrobials, Panel 1, in indicator Escherichia coli isolates from fattening turkeys in 2014, using harmonised epid emiological cut-off values Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in commensal indicator Escherichia coli from broile rs in 2014 Frequency distribution of completely susceptible isolates and resistant isolates to from one to eleven antimicrobials in Escherichia coli from fattening turkeys in 2014 MDR patterns of selected antimicrobials, Panel 1,

Figure abbreviation	Figure name
FIG68	Trends in ampicillin and tetracyclines resistance in indicator <i>Escherichia coli</i> from broilers in reporting countries, 2008–2014
FIG69	Trends in cefotaxime, ciprofloxacin and nalidixic acid resistance in indicator <u>Escherichia coli</u> from broilers in reporting countries, 2008–2014
FIG70	Spatial distribution of ciprofloxacin resistance among indicator <i>Escherichia coli</i> from broilers in reporting countries, in 2014
FIG71	Spatial distribution of nalidixic acid resistance among indicator Escherichia coli from



	broilers in reporting countries, in 2014
FIG72	Spatial distribution of cefotaxime resistance among indicator Escherichia coli from
	broilers in reporting countries, in 2014
FIG73	Frequency distribution of Escherichia coli isolates completely susceptible and resistant
	to one to twelve antimicrobials in broilers in reporting
FIG74	Spatial distribution of ciprofloxacin resistance among indicator Escherichia coli from
	fattening turkeys in reporting countries, in 2014
FIG75	Spatial distribution of nalidixic acid resistance among indicator Escherichia coli from
	fattening turkeys in reporting countries, in 2014
FIG76	Spatial distribution of cefotaxime resistance among indicator Escherichia coli from
	fattening turkeys in reporting countries, in 2014
FIG77	Frequency distribution of Escherichia coli isolates completely susceptible and resistant
	to one to twelve antimicrobials in fattening turkeys in MSs, 2014

3.4. Meticillin-resistant Staphylococcus aureus (MRSA)

3.4.1. Meticillin-resistant Staphylococcus aureus in food and animals

Table abbreviation	Table name
MRSAAMR	Occurrence of resistance for selected antimicrobials in MRSA from food and animals in 2014, using harmonised epidemiological cut-off values
MRSAANIMALCLIN	MRSA in food-producing animals, clinical investigations, 2014
MRSAANIMAL	MRSA in food-producing animals (excluding clinical investigations), 2014
MRSACLINANIMAL	MRSA in companion animals, clinical investigations, 2014
MRSAFOOD	MRSA in food, 2014
MRSAOVERVIEW	Overview of countries reporting data on MRSA in animals and food in 2014
MRSATRENDANIMAL	Temporal occurrence of MRSA in animals
MULTIMRSABREEDGG	MDR patterns of selected antimicrobials in <i>Staphylococcus aureus</i> meticillin resistant fro m breeding <i>Gallus gallus</i> in 2014
MULTIMRSALH	MDR patterns of selected antimicrobials in <i>Staphylococcus aureus</i> meticillin resistant fro m laying hens in 2014.

3.5.1. Third-generation cephalosporin and carbapenem resistance in Escherichia coli and Salmonella

Table abbreviation	Table name
RESCEPH1	Occurrence of resistance to beta-lactam and carbapenem compounds among Salmonella spp. subject to supplementary testing from broilers, laying hens and meat from broilers in 2014, using harmonised ECOFFs
RESCEPH2	Resistance phenotypes identified in <i>Salmonella</i> spp. subjected to supplementary testing from broilers, laying hens and meat from broilers in MSs in 2014
RESCEPH3	Occurrence of resistance to beta-lactam and carbapenem compounds in indicator <u>E. coli</u> isolates from broiler flocks subject to supplementary testing in 2014, using harmonised ECOFFs
RESCEPH4	Presumptive ESBL and AmpC phenotypes identified in indicator <i>E. coli</i> isolates from broiler flocks subjected to supplementary testing in 2014
RESCEPH5	Occurrence of resistance to beta-lactam and carbapenem compounds in indicator <u>E. coli</u> isolates from fattening turkeys subject to supplementary testing in 2014, using harmonised ECOFFs
RESCEPH6	Presumptive ESBL and AmpC phenotypes identified in indicator <i>E. coli</i> isolates from fattening turkeys subjected to supplementary testing in 2014
RESCEPH7	Occurrence of resistance to selected antimicrobials in <i>Escherichia coli</i> from broilers and <u>fattening turkeys in reporting countries</u> , specific ESBL monitoring, Panel 2, in 2014



RESCEPH8	Occurrence of resistance to selected antimicrobials in <i>Escherichia coli</i> from broilers and fattening turkeys in reporting countries, specific ESBL monitoring, panel 2, in 2014
RESCEPH9	Presumptive ESBL and AmpC phenotypes identified in <i>E. coli</i> from broilers recovered from the specific monitoring on ESBLs/AmpC/Carbapenemases and subjected to supplementary testing or molecular typing confirmation in 2014
RESCEPH10	Resistance (%) to cefotaxime and ceftazidime in <i>Salmonella</i> spp. and indicator <i>E. coli</i> isolates in MSs in 2014 testing both bacterial species in broilers or fattening turkeys