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UK Veterinary Antibiotic Resistance and Sales Surveillance Report

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UK-VARSS 2014

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Foreword

This is the third combined antibiotic resistance and sales report, published under the acronym UK-VARSS by the Veterinary Medicine Directorate (an executive agency of Defra), and covers data from 2010-2014 (sales), and 2012-2014 (resistance).

This year's report represents a significant step forward for UK veterinary antibiotic-related surveillance: results from EU harmonised monitoring carried out under Commission Implementing Decision 2013/652/EU are presented for the first time, and antibiotic sales data have been supplemented with usage data for the first time, supplied by the British Poultry Council. Both of these additions contribute towards a better understanding of antibiotic use and the development of resistance within the veterinary field.

The report is of relevance to policy formulation, and to vets and other healthcare professionals, farmers, policy writers, academics and members of the public with an interest in veterinary and public health. The VMD is dedicated to providing all available data relating to antibiotic resistance in an accurate and transparent way. It is our intention to provide as much information as possible so as to raise awareness and empower people to take action to slow the rise of resistance.

For both sales and resistance surveillance we have used the Heads of Medicines Agencies definition of antimicrobials and antibiotics[1] which have also been adopted by EPRUMA[2].

For EU harmonised monitoring of resistance data, resistance is defined based on both epidemiological cut-off values and human clinical breakpoints. For clinical surveillance data, resistance has been defined based on human clinical breakpoints. The intent, in the future, is to move towards agreed animal species clinical breakpoints for clinical surveillance. However, even for future reports, we will retain human clinical breakpoints for selective pathogens, such as food-borne pathogens, due to their relevance for human medicine.

Professor S.P. Borriello

[1] www.hma.eu/fileadmin/dateien/Veterinary_medicines/00-HMA_Vet/02-HMA_Task_Force/03_HMA_vet_TF_AMR/2012_11_HMA_agreed_AB_AM_definitions.pdf
[2] http://www.epruma.eu/component/downloads/downloads/76.html

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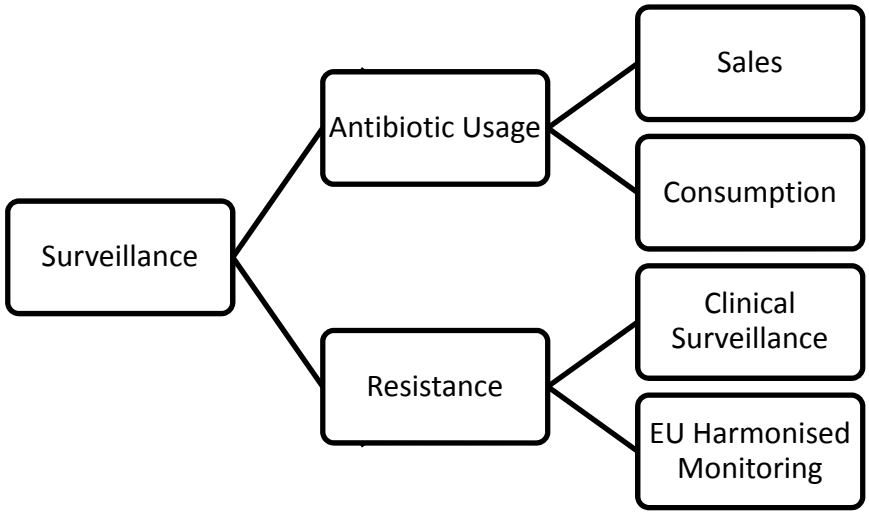
Executive Summary

This report contains four data chapters which follow the structure of our surveillance programmes:



Antibiotic Sales Data

The quantity of veterinary antibiotic medicines sold by veterinary pharmaceutical companies during the five year period spanning 2010 to 2014 is presented in **Chapter 2**, and represents complete data from the whole of the UK.

Antibiotic sales are converted to a proxy of use by using the Population Correction Unit (PCU), a theoretical unit of measure that considers the number and weight of food-producing animals at the most likely time of treatment. The tonnage of antibiotics sold is divided by the PCU to obtain a mg/PCU which is equivalent to mg/kg of food producing animals in the UK. Use of the PCU enables more meaningful year-on-year trend analysis than tonnage alone, and also permits comparison with other EU countries that use the same system.

The sales of veterinary antibiotics for food producing species in 2014 were 57 mg/PCU. This represents little change from 56 mg/PCU in 2013.

Fluoroquinolones and 3rd and 4th generation cephalosporins have been designated highest priority critically important antibiotics for human health by the World Health Organisation[3], and classified as antibiotics used in animals where the risk to public health is 'higher' (in scientific advice published by the European Medicines Agency[4]). In 2014 0.34 mg/PCU of fluoroquinolones and 0.20 mg/PCU of 3rd and 4th generation cephalosporins were sold for use in food producing species. These levels are low compared with other antibiotic classes authorised for use in animals. For fluoroquinolones a gradual increase was seen between 2008 and 2012 but the data from the last three years may suggest this is levelling out (2012-2015: range 0.34 – 0.36 mg/PCU). The mg/PCU result for 3rd and 4th generation cephalosporins has remained within the range 0.17 – 0.22 mg/PCU over the last five years reported.

[3] http://www.who.int/entity/foodsafety/publications/antimicrobials-third/en/index.html
[4]http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500170253

Antibiotic Consumption Data

Surveillance of consumption of antibiotics is a programme which is under development; **Chapter 3** reviews progress and reports for the first time some preliminary results.

The British Poultry Council has provided data collected from their members, representing 90% of the commercial meat poultry industry.

This new chapter also highlights the progress being made in other sectors including pigs and cattle, towards the collection of robust consumption data.

Antibiotic Resistance Data

Antibiotic resistance in bacteria isolated from animals is reported in **chapters 4 and 5**, reflecting the two distinct antibiotic resistance surveillance programmes in place for animals. Results are presented as epidemiological cut-off values (ECV) in **chapter 4** for consistency with recent European Food Safety Authority (EFSA) Summary Reports[5], and as human clinical breakpoints (CBP) in **chapter 5**.

- Epidemiological cut-off values represent the point at which bacteria have developed a higher level of resistance to an antibiotic than the background level of resistance that exists naturally in that bacterial species. A 'resistant' (or 'non-susceptible') ECV result does not necessarily imply a level of resistance which would correspond with clinical treatment failure.
- Clinical breakpoints relate laboratory results to clinical treatment success or failure. Therefore, 'resistant' results using clinical breakpoints correspond to a likelihood of treatment failure when using an antibiotic to treat a clinical infection caused by that bacterial isolate.

[5] http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/4036.pdf

EU Harmonised Monitoring

EU harmonised monitoring is a programme of structured surveillance set out in EU legislation. Its aim is to evaluate antibiotic resistance in bacteria of relevance to human health which have been isolated from healthy livestock animals. Samples which are utilised for EU harmonised monitoring originate from across the UK. For more detailed context of these bacterial species in terms of human health the reader is referred to the 'UK One Health Report'[6].

Campylobacter spp.

While most cases of *Campylobacter* infection in people are self-limiting and do not require treatment, when antibiotics are indicated, fluoroquinolones and macrolides are the antibiotic classes most typically prescribed for people.

All *C. jejuni* isolates from broilers and turkeys were susceptible to erythromycin.

Ciprofloxacin resistance in *C. jejuni* was identified in 44% (72/165) of isolates from broilers and 35% (55/157) of isolates from turkeys. In broilers this represents an increase compared to the results of a 2013 broiler survey which showed the level of ciprofloxacin resistance in *C. jejuni* in 2013 to be 31% (19/61 isolates). No earlier data for turkeys are available for comparison.

While the percentage of resistant isolates of *C. jejuni* was higher in broilers in 2014 compared with 2013, these represent two years' worth of data based on 61 isolates in 2013 and 165 isolates in 2014. Whether or not this represents a trend will be informed by future data.

Salmonella spp.

As with *Campylobacter*, *Salmonella* infection in people is frequently self-limiting and requires no treatment; however, antibiotics may be necessary in severe cases. Fluoroquinolones and 3rd and 4th generation cephalosporins are important classes of antibiotics for treating *Salmonella* infections in people where treatment is necessary.

In 2014, 64% (108/168) of *Salmonella* spp. isolates from broilers were fully sensitive to all antibiotics tested; comparable to the levels seen in 2013 (63%). In laying hens, 93% (54/58) of the *Salmonella* tested were fully sensitive to all antibiotics tested; an increase on the percentage fully sensitive seen in 2013 (84%). In fattening turkeys, 31% (51/162) of isolates were fully sensitive to all antibiotics tested; an increase on the percentage fully sensitive seen in 2013 (14%). No *Salmonella* from broilers, layers and turkeys were resistant to meropenem, cefotaxime or ceftazidime in 2014.

Escherichia coli

Gram-negative commensal organisms such as *E. coli* are commonly regarded as 'indicator organisms' to monitor antibiotic resistance in the intestinal flora. *E. coli* are thought to constitute a reservoir of antibiotic resistance in any given bacterial population. This is problematic as *E. coli* may transfer these genes to other bacteria, including pathogenic varieties.

[6] https://www.gov.uk/government/publications/uk-one-health-report-antibiotics-use-in-humans-and-animals

No resistance was detected in *E. coli* isolated from broilers or turkeys to the following antibiotics: cefotaxime, ceftazidime, colistin, meropenem and tigecycline. Resistance to ciprofloxacin was found in 25% (39/159) of *E. coli* isolates from broilers and 17% (29/168) from turkeys.

Clinical surveillance

Clinical surveillance is a programme of passive surveillance. Its aim is to evaluate antibiotic resistance in bacteria of relevance to animal health which have been isolated from clinical diagnostic samples from animals. This programme relies on the submission of carcases or other diagnostic samples by private veterinary surgeons to the Animal and Plant Health Agency (APHA) veterinary laboratories. These laboratories are situated in England and Wales with the exception of APHA Lasswade, in Scotland. Similar programmes are conducted in Scotland and Northern Ireland. Data from the Scottish and Northern Irish clinical surveillance programmes are not included in this report.

Salmonella spp.

A total of 7769 *Salmonella* isolates were identified between 2012 and 2014. In 2014, 69.3% of 2347 isolates from a range of sources (see **Annex 20**) were susceptible to all antibiotics. This is an increase compared to 2013 (64.2%) and 2012 (59.7%). In 2014, 1% (23/2347) of all *Salmonella* isolates were resistant to ciprofloxacin. None of the *Salmonella* isolates tested showed resistance to cefotaxime or ceftazidime.
Resistance to gentamicin in *Salmonella* isolated from sheep, pigs and chickens was a maximum of 8.8% in 2014. Resistance to gentamicin was highest in all isolates from pigs at 8.8%, which is similar to the level seen in 2013 (8.4%) and a reduction from 2012 levels (26.4%).

Escherichia coli

Clinical resistance to cefotaxime in *E. coli* from neonatal calves and lambs in 2014 was 15% and 3% respectively, whilst cefpodoxime resistance in *E. coli* in the same year was 0% in neonatal piglets, 4% in chickens and 0% in turkeys. Cefpodoxime resistance in clinical diagnostic *E. coli* from chickens was 14% in 2012, 8% in 2013 and 4% in 2014. Enrofloxacin resistance was 12%, 18%, 1%, 5% and 14% in *E. coli* from calves, piglets, lambs, chickens and turkeys respectively.

LA-MRSA

Livestock-associated methicillin-resistant *S. aureus* (MRSA) ST398, *spa*-type t034, was detected in skin lesions on two piglets, from one incident, from a breeder-finisher farm in eastern England[7].

Mastitis Pathogens

Resistance demonstrated by mastitis pathogens in 2014 were broadly similar to previous years. In *E. coli* resistance to amoxicillin/clavulanic acid and ampicillin was seen in 7% and 24% of isolates, respectively – which represent marginal decreases compared to 2013 levels. Resistance to enrofloxacin was observed in 3% of *E. coli* isolates which is a small increase when compared with 2013 (0%) and 2012 (2%). Resistance to cefpodoxime also increased to 2% of all *E. coli* isolates; resistance had been seen at levels of <1% in 2013 and 2012. No resistance was seen to

[7] http://veterinaryrecord.bmj.com/content/176/6/151.3.full

amoxicillin/clavulanic acid or ampicillin in *S. dysgalactiae* isolates (as in previous years) and tetracycline resistance in *S. dysgalactiae* decreased but remained high with 85% of isolates demonstrating resistance (91% in 2013, 80% in 2012). Similarly no resistance to amoxicillin/clavulanic acid or ampicillin was seen in *S. uberis* isolates in 2014. *Staphylococcus aureus* isolates were frequently (35% of 82 isolates) resistant to ampicillin; resistance to other antibiotics was less common. No MRSA isolates were detected in cattle in 2014.

Respiratory Pathogens

All isolates of *M. haemolytica*, *P. multocida, Bibersteinia trehalosi* or *Histophilus somni* from cattle, sheep or pigs in 2014 were sensitive to enrofloxacin. Trimethoprim/sulphonamide resistance (1/14 isolates) and tetracycline resistance (2/24 isolates) was detected in 2014 – this is the first time that resistance to these antibiotics has been detected under the clinical surveillance programme.

Other Veterinary Pathogens

Penicillin resistance was detected in two *Streptococcus suis* isolates from pigs out of a total of 177 tested between 2012-2014. The proportion of isolates of *Brachyspira hyodysenteriae* resistant to tiamulin (applying clinical breakpoints) increased in 2012-2014 compared to previous years, although only low numbers of isolates (nine in 2012, eight in 2013 and four in 2014) were available for testing.

Chapter 1 – Introduction

The past year has seen the high profile of antimicrobial resistance (AMR) continue to grow. The adoption in 2015 of the World Health Organisation's Global Action Plan on AMR was reinforced by AMR resolutions adopted by the World Organisation for Animal Health (OIE) and the United Nations Food and Agriculture Organisation (FAO). Two priority areas which have been widely recognised in these documents are the need for countries to develop national action plans, and the need to strengthen surveillance systems for antibiotic use and resistance, in animals and in people. The scope of action is global and so is the potential benefit to taking a joined up international approach. Nevertheless, accomplishing change at an international level has its origin in co-ordinated domestic action.

The UK's national action plan is the UK 5 Year AMR Strategy, published in 2013[8]. In the action plan published with the first annual progress report on the UK 5 year AMR strategy in December 2014[9], three aspirations of direct relevance to the VARSS report were set out for the period to 2018. These were to "reduce antimicrobial use in livestock production in real terms over the next four years", "ensure that sales of fluoroquinolone and modern cephalosporin classes of antibiotics remain low and reduce further as a proportion of total antibiotic sales", and to "aim to improve access to sensitivity data to inform optimal veterinary prescribing". In addition, we set out commitments to undertake work to understand factors that influence veterinary prescribing behaviour, and the uptake of good biosecurity and husbandry practices.

The sales of veterinary antibiotics indicate a static picture for 2014. The many limitations of sales data, a recurring theme of **chapter 2**, illustrate that while this information permits a high level description of veterinary antibiotics in the UK it does not meaningfully support more detailed analysis. For this, data on which antibiotics are prescribed/administered to which animals are needed. Engagement with the veterinary profession and groups representing different animal species is a key part of the VMD's efforts to promote the message of responsible use in relation to the aspirations of the UK 5 year AMR strategy action plan, and this continues.

Antibiotic consumption data supplied by the British Poultry Council represents good progress in surveillance of veterinary antibiotic use, and other groups are also working hard to develop equivalent systems suitable for the species for which they are responsible. There will be many benefits of usage data through provision of a more accurate and detailed picture than sales data, but usage surveillance also has potential to be also valuable at the practical clinical level. In particular, a common theme in goals around AMR, articulated internationally, is to pursue reduction of use of antibiotics. This is likely necessary, but by how much and in which species or production groups before animal health and welfare start to be at risk are important considerations. A more considered approach would be to set the emphasis on prudent use of antibiotics, though this is very hard to define in a measurable way in the field. There is a potential opportunity for data on consumption of antibiotics to be collected together with information on health/disease status of the animals and more, so that the answer to the question "how low is possible and acceptable?" might be explored.

[8] https://www.gov.uk/government/publications/uk-5-year-antimicrobial-resistance-strategy-2013-to-2018
[9] https://www.gov.uk/government/publications/progress-report-on-the-uk-five-year-amr-strategy-2014

The EU harmonised monitoring programme, which evaluates resistance in bacteria of public health importance which have been isolated from healthy animals, recognises the potential for certain bacteria to present a route of AMR transmission from animals to people. These data have been presented together with corresponding AMR data from bacteria isolated from humans in the One Health Report published in July 2015[10], and the ten recommendations from that report will inform how our UK surveillance systems evolve to improve their value across disciplines.

The final chapter in this report maintains the long standing UK focus on resistance in bacteria isolated from clinical cases in veterinary patients. This is an 'early warning system' for emerging resistance patterns. In this report, these data are only presented from England, Wales, and a small minority of samples from Scotland, reflecting the distribution of Animal and Plant Health Agency laboratories. Similar programmes are conducted in Scotland and Northern Ireland, and we intend to explore bringing all UK clinical AMR surveillance data together into the VARSS report in the future.

At present, disease in animals which is untreatable by antibiotics authorised for veterinary use is still rare. Those identified by our surveillance remain limited to a small number of cases of swine dysentery (caused by *Brachyspira hyodysenteriae*). Our goal is to keep clinically relevant veterinary resistance to a minimum, and our hope is that this is where antibiotic consumption surveillance has the potential to play a role as a clinical tool which will help farmers and vets implement best practice responsible use of antibiotics based on local, relevant, farm-level data.

We look forward to the ongoing refinement of our surveillance programmes in partnership with colleagues and stakeholders from the veterinary/animal sector and beyond.

[10] https://www.gov.uk/government/publications/uk-one-health-report-antibiotics-use-in-humans-and-animals

Chapter 2 – Sales of Antibiotics Authorised for use as Veterinary Medicines

Introduction

The quantity of authorised veterinary antibiotics sold throughout the UK has been reported to the VMD by pharmaceutical companies since 1998. Initially data were provided on a voluntary basis, but since 2005 it has been a statutory requirement set out in the UK Veterinary Medicines Regulations[11]. The data represented do not take into account wastage, imports or exports of veterinary antibiotics but they serve as the best currently available approximation of the quantity of antibiotics administered to animals in the UK. These sales data are submitted yearly to the European Medicines Agency where they are compiled with equivalent data from other European countries and published in the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) report on sales of veterinary antibiotics in the European Union (EU) and European Economic Area (EEA). In keeping with most other European countries, we do not have a comprehensive system which can collect and collate data on antibiotic use by animal species. However, such systems are under development and are discussed further in **Chapter 3**.

Method

Annual sales of all authorised veterinary medicines are supplied by Marketing Authorisation Holders (MAH) to the Veterinary Medicines Directorate (VMD) where they are collated and validated. From these data the total weight in tonnes of each antibiotic active substance is calculated.

Since total annual tonnage does not permit useful trend analysis by year due to variation in animal populations over time, adjustment is made using the population correction unit (PCU). This is a standard technical unit of measurement adopted by EU countries. It represents the estimated weight at treatment for each species and the estimated numbers of each species which will have been eligible for treatment over a 12 month period, using a standard formula developed by the European Medicines Agency. PCUs are set by species groups; the top level whole-country PCU incorporates data from across the livestock species populations. Companion animal (non-food) species are excluded from this formula. Using the PCU, the overall sales of products authorised for use in food producing species can be presented as mg/PCU. This enables year-on-year comparison to see whether sales for livestock are changing in real terms. Further details of these calculations are presented in **Annex 1**; full technical details on PCU methodology can be found in the 2009 ESVAC report[12].

From the sales data alone it is not possible to identify the species in which the antibiotics were actually used. This is for two reasons:

1. Many products are authorised for use in more than one animal species. In particular a large number of products are authorised for use in both pigs and poultry.
2. The 'prescribing cascade'[13] makes provision that under certain circumstances medicines may legally be administered to species for which they have not been authorised. This is sometimes known as 'off-label' use. There is no way of knowing what proportions of

[11] https://www.gov.uk/guidance/veterinary-medicines-regulations
[12] http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/09/WC500112309.pdf
[13] http://www.legislation.gov.uk/uksi/2013/2033/schedule/4/made

products sold have been administered under the cascade in this way. More details on the cascade are available in **Annex 2**.

Contributing pharmaceutical companies are listed in **Annex 23**.

Key messages

- The trend for overall livestock mg/PCU is currently stable.
- The trend for mg/PCU for 3rd and 4th generation cephalosporins for livestock species is currently stable.
- The trend for mg/PCU for fluoroquinolones had been increasing gradually before 2012 but has been stable for the past three years.

In 2014 a total of 429 tonnes of authorised veterinary antibiotics[14] were sold in the UK. Tetracyclines accounted for 40% of this figure by weight. Of this total, 369 tonnes were accounted for by products authorised for food producing species only[15]. The sales of veterinary antibiotics for food producing species adjusted by the food producing animal population were 57 mg/PCU. This represents little change from 2013 (an increase of nine tonnes and an increase of 1 mg/PCU).

Fluoroquinolones and 3rd and 4th generation cephalosporins have been designated highest priority critically important antibiotics for human health by the World Health Organisation[16], and classified as antibiotics used in animals where the risk to public health is 'higher' in scientific advice published by the European Medicines Agency[17]. In 2014 0.34 mg/PCU fluoroquinolones and 0.20 mg/PCU 3rd and 4th generation cephalosporins were sold for use in food producing species. These levels are low compared with other antibiotic classes authorised for use in animals. For fluoroquinolones a gradual increase was seen between 2008 and 2012 but the data from the last three years may suggest this is levelling out (2012-2015: range 0.34 – 0.36 mg/PCU). The mg/PCU result for 3rd and 4th generation cephalosporins has remained within the range 0.17 – 0.22 mg/PCU over the last five years reported.

What the results do not tell us: the extent to which prescribing was appropriate or inappropriate cannot be inferred from sales data. The number of treatments administered cannot be inferred from sales data; neither can the duration of treatment nor the dose of antibiotic. The latter two are particularly pertinent since reducing treatment duration or dose would reduce sales but would be likely to represent inappropriate prescribing. The results do not tell us whether antibiotics were prescribed for treatment, metaphylaxis or preventive use. The extent to which antibiotics were used off-label cannot be inferred from sales data.

[14] This figure relates to weight of active antibiotic chemical substances, not weight of medicines as packaged for sale.
[15] Veterinary antibiotics authorised for a combination of livestock and companion animals are not included in this figure.
[16] http://www.who.int/entity/foodsafety/publications/antimicrobials-third/en/index.html
[17] http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500170253

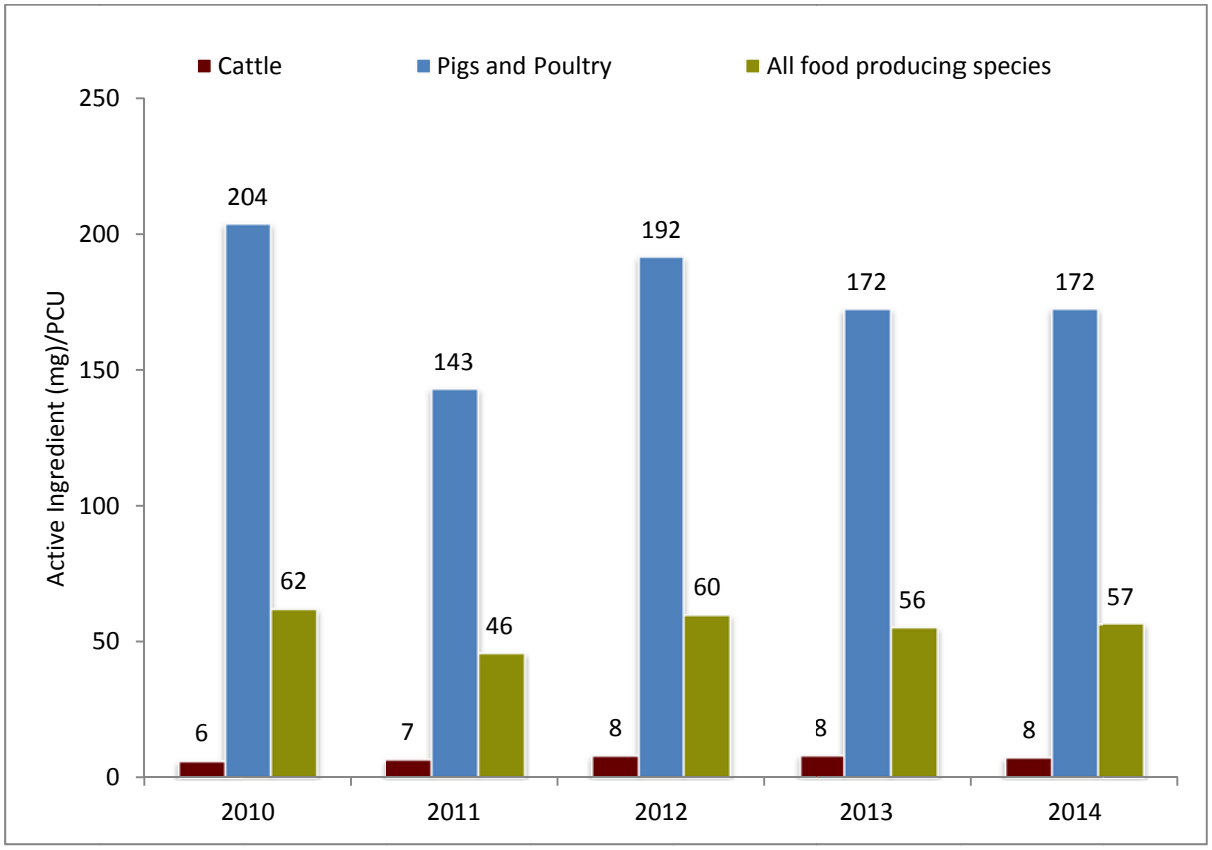
Results

Sales by Animal Species PCU

As indicated in the method, and in more detail in **Annex 1**, the total tonnage of antibiotics sold is divided by the PCU to give the mg/PCU figure. This is the most meaningful parameter to use when comparing antibiotic sales year on year as it adjusts for fluctuations in animal populations. The mg/PCU can be thought of as the quantity of antibiotic active substance sold per kilogram bodyweight of food producing animals in the UK over the course of the year. It is a theoretical measure and should not be misinterpreted as the actual quantity given to any one animal; sales data do not give this level of information.

Figure 2.1 shows the amount of antibiotic sold in the UK in mg/PCU for 2010–2014. The bars representing use in all food producing species show data from products authorised for use in any individual livestock species or any combination of livestock species, but exclude products authorised for a mixture of livestock and companion animal species. The data for cattle represent products authorised for use only in cattle and no other species. The data for pigs and poultry represent products authorised for use in just pigs, just poultry, for pigs and poultry but no other species. In the UK the role of horses is predominantly as a companion or sport animal, so this species is not included as a livestock/food-producing species.

Figure 2.1: Milligrams (mg) of active substance sold for food producing animals per Population Correction Unit (PCU) 2010–2014



There was little change in mg/PCU between 2013 and 2014. The results for cattle and for combined pigs/poultry were the same for both years while the overall livestock result was greater in 2014 by 1 mg/PCU.

The mg/PCU figure for all food producing species remained relatively stable between 2010 and 2014 with an average for the five year period of 56.2 mg/PCU/year. The sharp decrease observed in 2011 has been discussed in previous reports, and details are provided in **UK-VARSS 2012**[18].

When considering the mg/PCU figures in different species groups it is apparent that considerably smaller quantities of active substance are sold per kg for use in cattle than for pigs/poultry. This difference is seen each year and may reflect a number of factors including production type, husbandry, and disease prevalence[19]. However, more detailed interpretation by species is not supported by the data due to the limitations of using antibiotic sales as a proxy for actual usage data (for detail of the limitations of sales data, please refer to **Annex 4**)

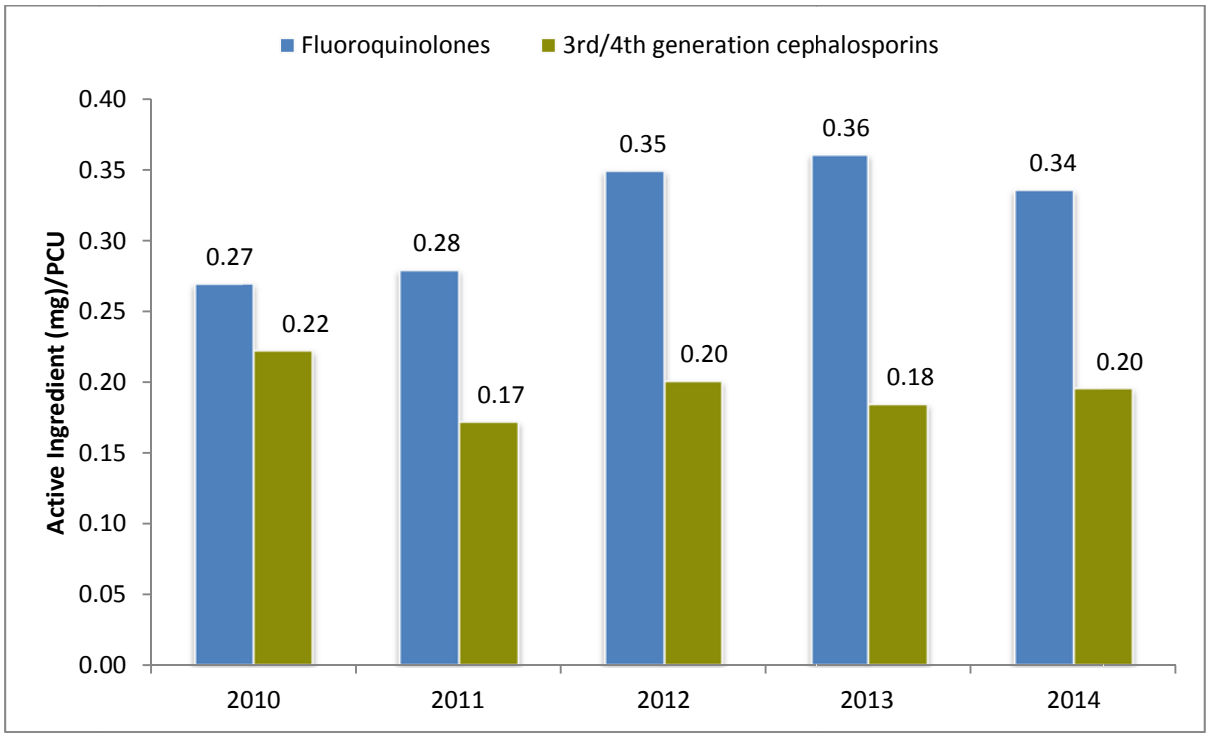
[18] http://webarchive.nationalarchives.gov.uk/20140909112428/http://www.vmd.defra.gov.uk/pharm/antibiotic_salesdata.aspx

[19] Information on changes in livestock disease patterns that may have influenced sales of antibiotics can be found in Defra funded disease surveillance reports available at: http://www.defra.gov.uk/APHA-en/category/publications/disease-surv/surv-reports/

Antibiotics of particular relevance to human health:

Certain antibiotic classes are categorised by the World Health Organisation (WHO) as critically important antibiotics (CIA) for human use, of which several are designated 'highest priority critically important antibiotics' (HP-CIA)[20]. In December 2014, the European Medicines Agency (EMA) published scientific advice on the risk to humans from resistance in bacteria from animals to antibiotics classed as CIA by the WHO. This advice was prepared by an expert group composed of representatives and experts from human and animal disciplines[21]. The EMA scientific advice classed macrolides as category 1, where the risk of use in animals to public health is low or limited. The scientific advice did not make recommendations for avoiding use of macrolides in animal health beyond what is consistent with responsible use principles. The same document classed fluoroquinolones and 3rd and 4th generation cephalosporins as category 2, or "antimicrobials used in veterinary medicine where the risk for public health is higher". On this basis, in the present VARSS report presentation of more detailed information of antibiotics of relevance to human health has focused on fluoroquinolones and 3rd and 4th generation cephalosporins. **Figure 2.2** shows the sales of these veterinary antibiotics of 'highest priority critically important antibiotics for humans', in mg/PCU.

Figure 2.2: **Milligrams (mg) of active substance for 'highest priority critically important antibiotics for humans' sold for food producing animals only per population correction Unit (PCU) for 2010-2014***



[20] http://www.who.int/entity/foodsafety/publications/antimicrobials-third/en/index.html

[21] The antimicrobial advice ad hoc expert group (AMEG) included representation from European Medicines Agency (EMA) and its Committee for Medicinal Products for Veterinary Use and Antimicrobials Working Party (CVMP/AWP) and its Committee for Medicinal Products for Human Use and Infectious Disease Working Party (CHMP/IDWP), the European Food Safety Authority (EFSA), the European Centre for Disease Prevention and Control (ECDC) and the Joint Interagency Antimicrobial Consumption and Resistance Analysis Report (JIACRA).

**These results exclude fish because there are no products containing HP-CIAs authorised for use in fish; inclusion of these species within the PCU figure would skew the results.*

Sales of HP-CIAs make up a small proportion of the 57 mg/PCU overall all-antibiotic result in livestock: in 2014, 0.34 mg/PCU fluoroquinolones and 0.20 mg/PCU 3rd and 4th generation cephalosporins were sold for use in livestock species. While the sales of fluoroquinolones in mg/PCU have increased compared with older data going back to 2008, results from the last three years have stabilised (2012-2015: range 0.34 – 0.36). The mg/PCU result for 3rd and 4th generation cephalosporins has remained stable. Historical data is shown in **Annex 5**.

Sales of Intramammary Antibiotic Products

Sales of intramammary antibiotic products for cattle ranged from 10.1 to 11.8 million tubes (2,756 to 3,605 kg of active substance) and 1.54g to 1.99g average/cow between 2010 and 2014 (**Table 2.1**). Sales of products for lactating cows increased by 0.1 million tubes (1,268 kg) and sales of dry cow therapy products increased by 0.4 million tubes (1,766 kg) from 2013 to 2014. However, there is no clear increasing or decreasing trend over the five year period.

Table 2.1: Sales in kg of active ingredient and (grams active ingredient/dairy cow*) of antibiotic intramammary products 2010-2014

	2010	2011	2012	2013	2014
Dry Cow Products	1882 (1.02)	1686 (0.93)	1885 (1.04)	1593 (0.89)	1766 (0.96)
Lactating Cow Products	1649 (0.89)	1400 (0.77)	1720 (0.95)	1163 (0.65)	1268 (0.69)
Total	3531 (1.91)	3086 (1.70)	3605 (1.99)	2756 (1.54)	3034 (1.65)

**based on number of dairy cows in the national herd in each respective year*

The proportion of intramammary products sold which contain 3rd and 4th generation cephalosporins remained stable between 2013 and 2014. In 2013, 8.3% of intramammary products sold contained these active ingredients compared to 8.9% in 2014.

Total Sales and Sales by Antibiotic Group for Food and Non-Food Animals

The total quantities of antibiotic active substance in products sold between 2010 and 2014 and their breakdown by chemical grouping are shown in **Table 2.2**. Definitions of these groups can be found in the "Glossary of Terms" at **Annex 22**. The total quantity of antibiotics sold in 2014 was 429 tonnes. There was no consistent pattern in total sales between 2010 and 2014, with a difference of 23% between the highest and lowest sales years. Antibiotic sales were highest in 2010 at 7% above the 5 year mean of 417 tonnes. As previously discussed, tonnage is a less meaningful way of monitoring trends than mg/PCU as it does not take account of variations in UK livestock populations.

Table 2.2: Sales (tonnes active ingredient) of total antibiotic products by chemical grouping 2010 – 2014 and total sales 2010–2014

	2010	2011	2012	2013	2014
Tetracyclines	200	110	190	184	173
Trimethoprims/ Sulphonamides	75	72	80	61	70
Trimethoprims	12	12	13	10	11
Sulphonamides	63	60	66	51	59
ß-lactams	93	86	90	89	91
$1^{st}/2^{nd}$ Generation Cephalosporins	6	5	6	5	6
$3^{rd}/4^{th}$ Generation Cephalosporins (t)	1	1	1	1	1
(kg)*	1,455	1,172	1,332	1,189	1,335
Penicillins**	17	20	8	20	12
Other Penicillins***	69	60	75	63	72
Aminoglycosides	22	19	20	21	22
streptomycins	8	7	8	8	7
neomycin and framycetin	<1	<1	<1	<1	1
others****	14	12	12	13	14
Macrolides	35	37	41	43	48
Fluoroquinolones (t)	2	2	2	3	3
(kg)*	2,232	2,085	2,434	2,610	2,596
Other	20	20	21	19	22
Total	**447**	**346**	**445**	**420**	**429**

*Because of the heightened interest in HP-CIA classes, fluoroquinolones and $3^{rd}/4^{th}$ generation cephalosporins the kg active substance are shown in addition to the rounded tonnage.
**includes benzylpenicillin, benzathine penicillin, phenoxymethylpenicillin, procaine penicillin
***includes amoxyxillin (including in combination with clavulanic acid), ampicllin, cloxacillin, nafcillin
****includes gentamycin, kanamycin, spectinomycin, spiramycin

The sales of different chemical groups of antibiotics between 2010 and 2014 are shown in **Figure 2.3** and represent the main chemical groups of veterinary antibiotics sold in the UK. In all years, tetracyclines, ß-lactams (including penicillin) and trimethoprim/sulphonamides accounted for the majority of antibiotic active substances sold in veterinary medicines. In 2014, these groups combined accounted for 78% of sales, with tetracyclines accounting for 40%, ß-lactams 21% and trimethoprim/sulphonamides 16%. The majority of tetracycline products sold were authorised for use in pigs, poultry and cattle.

Figure 2.3: Sales (tonnes active ingredient) of total antibiotic products by chemical group 2010–2014

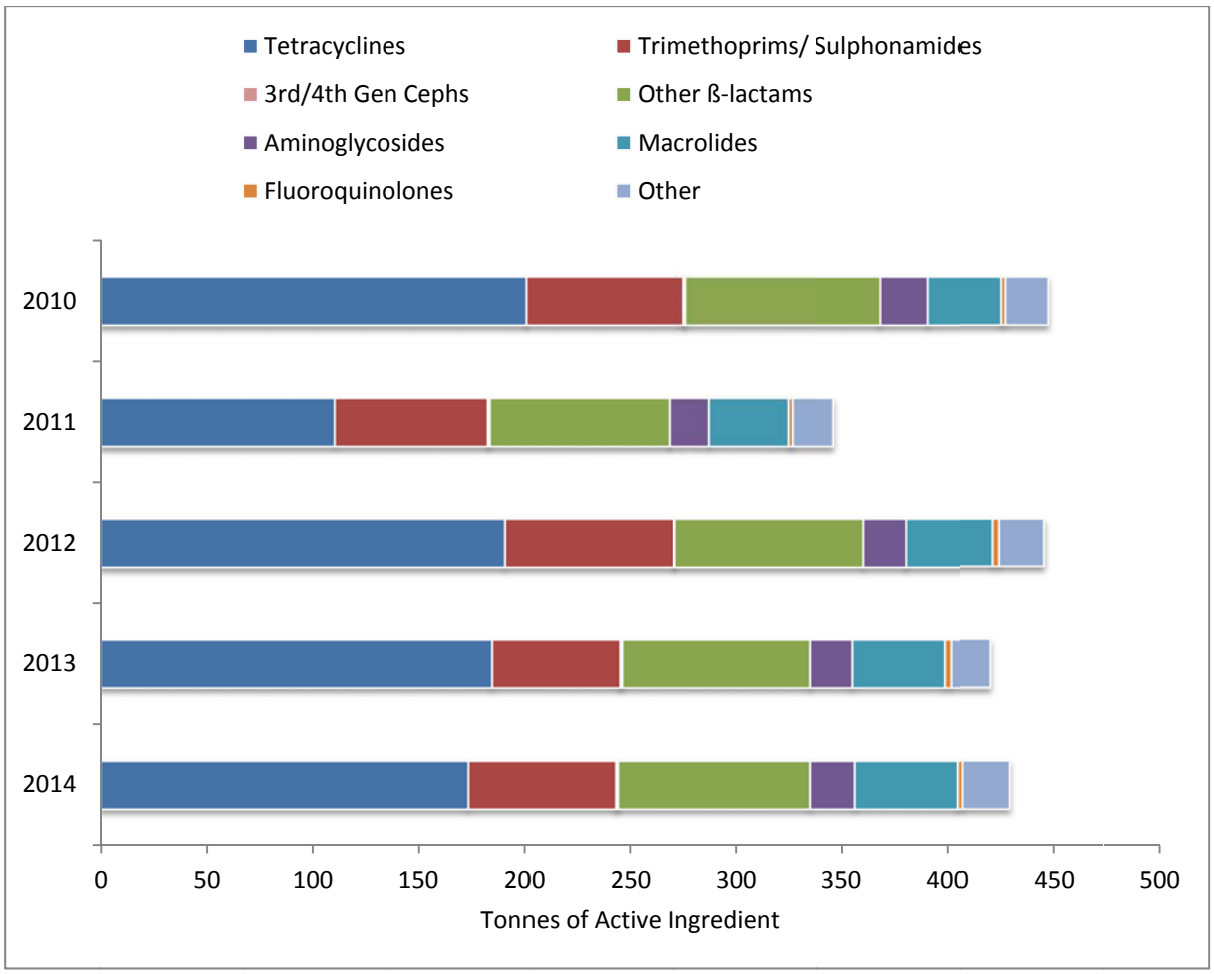


Table 2.2, and **Figure 2.3** indicate that while the sales of most classes of antibiotics has been stable over the past five years, there has been a steady year-on-year increase in sales of macrolides during this time. Tetracycline sales fluctuated over the period, with the greatest variation observed between 2010 and 2011. Sales of tetracycline products increased in 2012 but have decreased since by six tonnes in 2013 and a further 11 tonnes in 2014.

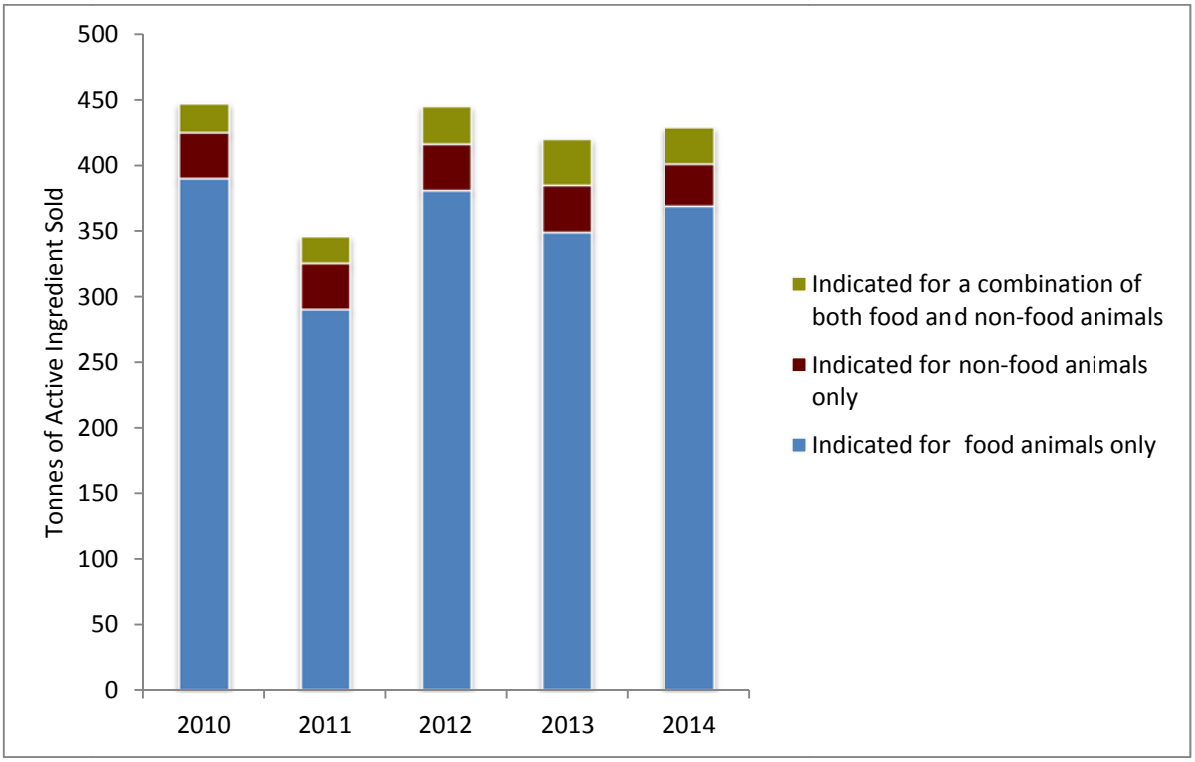
Sales by Animal Species Indicated

The quantities of antibiotic active substance in products sold between 2010 and 2014 are shown in **Table 2.3** and **Figure 2.4**, differentiated by the classes or combination of classes of species in which they are authorised for use (livestock only, companion animals only, or a mixture of both).

Table 2.3: Sales in tonnes active ingredient and (% of total sales) of antibiotics 2010–2014, in the categories of food animals only, non-food animals only and combined food and non-food animals

	2010	2011	2012	2013	2014
Indicated for food animals only	390 (87%)	290 (84%)	381 (86%)	355 (84%)	369 (86%)
Indicated for non-food animals only	35 (8%)	35 (10%)	35 (8%)	36 (9%)	32 (7%)
Indicated for a combination of both food and non-food animals	22 (5%)	21 (6%)	29 (6%)	29 (7%)	28 (7%)
Total sales of antibiotics	447	346	445	420	429

Figure 2.4: Sales for animal use of antibiotic products (tonnes active ingredient) 2010–2014



The proportions of antibiotics sold across each of the three categories above have remained broadly similar over the past five years.

The breakdown by species of the sales of antibiotics in products authorised only for food animals (data shown in the first row of **Table 2.3**) is shown in **Table 2.4**. In 2014, 83% of active substance from antibiotic products authorised only for food animals were indicated for use in both pigs and poultry, and no other species. Multi-species products (excluding those authorised for pigs and poultry only) accounted for 12.5% of sales of antibiotics sold for food producing animals in 2014.

Table 2.4: Sales (tonnes active substance) of antibiotics authorised only for food-producing animals, by species 2010–2014

Product indicated exclusively for:	2010	2011	2012	2013	2014
Cattle	11	12	14	14	13
Pigs	47	62	65	61	64
Poultry	50	23	22	19	19
Sheep	<1	<1	<1	<1	<1
Fish	1	2	2	1	2
Pigs and Poultry	252	162	245	226	225
Other livestock species	29	29	33	34	46
Total	390	290	381	355	369

We are currently working towards more accurate methods of data collection to permit analysis of antibiotic consumption by animal species and production type, in particular for the priority species pigs, poultry and cattle. This is presented in **Chapter 3**: Consumption Data.

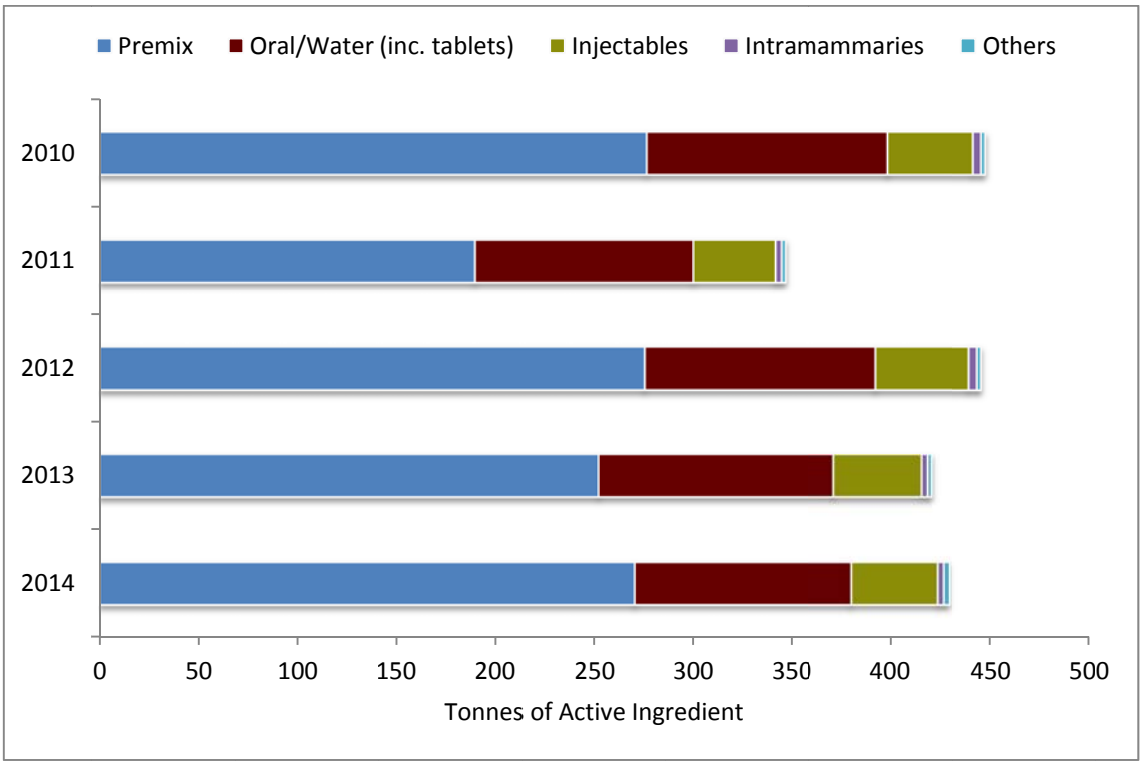
Sales by Route of Administration

The main routes of administration of veterinary antibiotics sold for all species in 2010–2014 are listed in **Table 2.5** and **Figure 2.5**. Premixes and oral/water soluble products (including tablets) accounted respectively for 63% and 26% of the total antibiotics sold in 2014. Injectable, intramammary, and other antibiotic products (creams, aerosols, drops etc.) contributed 10%, 0.7% and 0.7% respectively.

Table 2.5: Sales of in tonnes active ingredient, all species, and (% of total sales) by route of administration 2010–2014

	2010	2011	2012	2013	2014
Premix	276 (62%)	189 (55%)	275 (62%)	252 (60%)	270 (63%)
Oral/Water	122 (25%)	111 (32%)	117 (26%)	119 (28%)	110 (26%)
Injectable	43 (10%)	41 (12%)	47 (11%)	44 (10%)	43 (10%)
Intramammary	4 (<1%)	3 (<1%)	4 (<1%)	3 (<1%)	3 (<1%)
Others	2 (<1%)	2 (<1%)	2 (<1%)	2 (<1%)	3 (<1%)
Total	447	346	445	420	429

Figure 2.5: Sales of total antibiotics (tonnes active ingredient, all species) by route of administration 2010–2014



* *Others include aerosols, creams, and ear and eye medications.*

Chapter 3 – Consumption Data

Introduction

As discussed in **chapter 2**, antibiotic sales data have many limitations and are not suitable for assessing use in each species. Consumption data, i.e. the amount of antibiotics purchased, prescribed and/or administered, have the potential to provide much more precise estimates. The VMD is currently working in partnership with key livestock sectors to develop a system for the collection of antibiotic consumption data in food producing animals, facilitating and coordinating sector-led collection systems for the priority livestock sectors (pigs, poultry and cattle). This chapter focuses on description of progress achieved so far: representatives from each of the priority livestock sectors have provided updates on activities surrounding data collection. Also, for the first time, total antibiotic consumption data have been provided by the British Poultry Council (BPC) (**Annex 6**). Text contributed by external bodies is presented in italics to distinguish it from the authors' text.

Poultry

Contribution from the British Poultry Council:

*The British Poultry Council's (BPC) Antibiotic Stewardship Programme was established in 2011, representing more than 90% of the UK poultry meat sector. The BPC formed this working group to identify a programme of work designed to promote the responsible use of antibiotics. One of the first actions of this working group in 2012 was to ban the use of all cephalosporins in flocks used for poultry meat production and established its commitment to reduce the prophylactic use of fluoroquinolones in day old broilers. Another action of this group was to voluntarily submit data on antibiotic usage, collected from poultry producers, to the VMD to allow for accurate monitoring and analysis. The data disclosed to the VMD (***Annex 6***) show a reduction in usage from 2013 to 2014 in poultry raised for meat.*

Pigs

Contribution from the Pig Health and Welfare Council Antimicrobial Usage Sub-group

The PHWC Antimicrobial Usage Sub-group is working to implement an action plan developed from an industry wide workshop held in October 2014, to optimise the responsible use of antimicrobials in UK pig production. In its first year the sub-group has concentrated on how to collect data on the actual usage of antimicrobials on UK pig farms and, with funding from AHDB-Pork and the VMD, is now developing a medicines hub. Pig farmers will be able to report their antibiotic usage to the hub, which will enable them to monitor their use of antibiotics over time. The hub will have the ability to provide trend reports to farmers and to provide aggregated, anonymised data to VMD, to assist in interpretation of the sales data already collected from pharmaceutical companies and for submission to the European Commission when Member State reporting is required. It will also help farmers meet their obligations under farm quality assurance schemes. The hub is being designed in such a way as to enable future expansion to allow capture of data about antibiotic use in other livestock species.

Cattle

Contribution from the Cattle Health and Welfare Group

In 2014 the VMD commissioned the Cattle Health & Welfare Group (CHAWG) to undertake a scoping study to ascertain what antimicrobial usage data are currently being collected and what should be done to develop data collection systems in the UK cattle sector (both dairy and beef). The study concluded that currently there is no central data collection point for medicine usage within the cattle industry, although there are a number of individual initiatives evolving through veterinary practices, universities and milk recording schemes. For the future a two stage process is suggested that initially utilises data from veterinary practice records followed by an industry agreed approach to extracting farm level data. To make this happen a small working group of selected individuals working through CHAWG will be tasked with this role. The group is currently being established.

Future Plans

In the coming year the focus of activity will be around completion of the medicines hub for the pig sector and the establishment of central co-ordination for initiatives in the cattle sectors. The medicines hub for the pig sector is under construction, with a pilot of the live system planned for January 2016 and the target date for launch of the system April 2016. The CHAWG is currently in discussion with the VMD and key industry partners in the dairy and beef production sectors on the establishment of a working group to facilitate and co-ordinate the development of UK-wide approaches to data collection.

Chapter 4 – EU Harmonised Monitoring of Antibiotic Resistance

Introduction

EU harmonised monitoring is a programme set out in EU legislation which aims to evaluate antibiotic resistance in bacteria of relevance to human health which have been isolated from healthy animals. It is sometimes referred to as 'structured surveillance' because the survey is specifically designed to collect samples which are representative of the population over a defined period of time.

Results are presented as epidemiological cut-off values (ECV) in this chapter for consistency with recent European Food Safety Authority (EFSA) AMR Summary Reports[22].

- Epidemiological cut-off values represent the point at which bacteria have developed a higher level of resistance to an antibiotic than the background level of resistance that exists naturally in that bacterial species. A 'resistant' (or 'non-susceptible') ECV result does not necessarily imply a level of resistance which would correspond with clinical treatment failure.
- Clinical breakpoints relate laboratory results to clinical treatment success or failure. Therefore, 'resistant' results using clinical breakpoints correspond to a likelihood of treatment failure when using an antibiotic to treat a clinical infection caused by that bacterial isolate.

Results using both ECV and human clinical breakpoints are provided in full in **Annexes 10, 11,** and **12**.

What surveillance activities do we conduct under EU harmonised monitoring?

EU harmonised monitoring for AMR in the UK is conducted in accordance with Commission Decision 2013/652/EU[23] 'on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria'. This piece of legislation came into force in January 2014 and mandates all EU Member States to monitor AMR in specified bacteria in food producing animals at slaughter, and food products at retail. An overview of this sampling plan, by year, is summarised in **Annex 7**.

In 2014 Member States were mandated to monitor AMR in *Salmonella* spp. isolated from flocks of broilers, layers and turkeys, and also in *Campylobacter jejuni* and *Escherichia coli* isolated from broilers and turkeys at slaughter. The monitoring of AMR in *Campylobacter coli* and *Enterococcus* spp. from broilers was voluntary in 2014 and was not undertaken by the UK. Please refer to **Annex 8** for a summary of the sources of samples which were tested under this EU monitoring.

Prior to the introduction of Decision 2013/652/EU, *Salmonella* from the poultry National Control Programmes (NCPs) were annually tested for AMR, in accordance with protocols set out by the EFSA. Results from these NCP data are presented for years prior to 2014.

In 2013, *Campylobacter jejuni* were isolated from broiler caecal samples collected within a UK abattoir survey, which was based on the EU technical specifications in Decision 2007/516/EC.

[22] http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/4036.pdf
[23] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:303:0026:0039:EN:PDF

Selection of isolates for susceptibility testing was based on the criteria laid down in EU technical specifications (Decision 2007/516/EC of 21/7/2007).

No monitoring for *E. coli* resistance was systematically conducted using the EFSA protocol prior to 2014 in the UK; consequently, a single year's worth of *E. coli* resistance data is presented in this chapter.

The importance of these EU surveillance activities and the relevant legislation is three-fold:

- The zoonotic organisms for which the legislation outlines monitoring provisions – such as *Salmonella* and *Campylobacter* – are of direct relevance to human health. Additionally, the panel of antibiotics against which these organisms must be tested includes antibiotics that are highest-priority critically important antibiotics for human health as defined by the WHO (e.g. 3rd and 4th generation cephalosporins and fluoroquinolones).

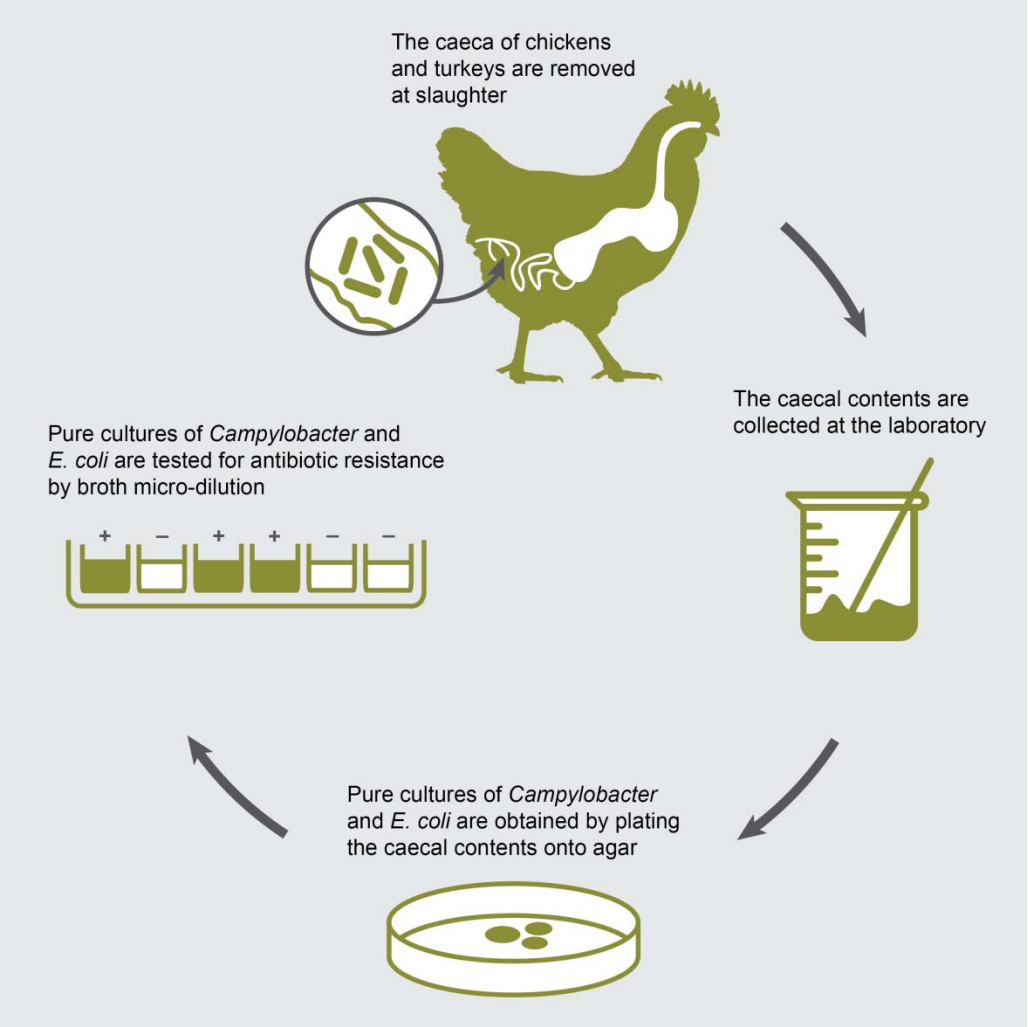
- The legislation and accompanying technical specifications[24] provide a standardised and harmonised sampling methodology which will provide comparable and robust resistance data for a representative proportion of food producing animals and food products across the EU as the monitoring progresses.

- The legislation provides a harmonised set of EUCAST epidemiological cut-off values (ECV) and human clinical breakpoints to interpret susceptibility to antibiotics. Access to these two sets of breakpoints will enable the future comparison of animal resistance data with similar data generated by human health, both within the UK and across the EU.

[24] http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/3686.pdf

Method

Figure 4.1: The EU Harmonised Monitoring process in 2014



Susceptibility tests against the antibiotic panels defined in the legislation[25] were conducted by the network of APHA veterinary laboratories situated throughout Great Britain.

Isolates recovered for EU harmonised monitoring were selected for susceptibility testing based on the criteria specified in the EU technical specifications (Commission Decisions 2007/516/EC [26]and 2013/652/EU). *Campylobacter jejuni, Salmonella* spp. and *E. coli* susceptibility testing was performed using a standardised broth microdilution method in accordance with recommendations from EFSA (EFSA, 2007 and EFSA, 2008). Resistance was determined using the EUCAST epidemiological cut-off values (ECVs) as described in Commission Decision 2013/652/EU.

Multiple antibiotic resistance is defined in this report as resistance to four or more antibiotics which were tested for a particular isolate. There is no internationally agreed definition of multiple resistance and the term has been used differently in different studies (EFSA, 2012, Schwarz *et al*., 2010).

[25] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:303:0026:0039:EN:PDF
[26] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32007D0516&from=EN

Key Messages

Results described as "resistant" in this chapter do not necessarily indicate that an infection in a patient would not respond to treatment.

***Campylobacter* spp.**

While most cases of *Campylobacter* infection in people are self-limiting and do not require treatment, when antibiotics are indicated, fluoroquinolones and macrolides are the antibiotic classes most typically prescribed for people.

All *C. jejuni* isolates from broilers and turkeys were susceptible to erythromycin.

Ciprofloxacin resistance in *C. jejuni* was identified in 44% (72/165) of isolates from broilers and 35% (55/157) of isolates from turkeys. In broilers this represents an increase compared to the results of a 2013 broiler survey which showed the level of ciprofloxacin resistance in *C. jejuni* in 2013 to be 31% (19/61 isolates). No earlier data for turkeys are available for comparison.

While the percentage of resistant isolates of *C. jejuni* was higher in broilers in 2014 compared with 2013, these represent two years' worth of data based on 61 isolates in 2013 and 165 isolates in 2014. Whether or not this represents a trend will be informed by future data.

***Salmonella* spp.**

As with *Campylobacter*, *Salmonella* infection in people is frequently self-limiting and requires no treatment; however, antibiotics may be necessary in severe cases. Fluoroquinolones and 3rd and 4th generation cephalosporins are important classes of antibiotics for treating *Salmonella* infections in people where treatment is necessary.

In 2014, 64% (108/168) of *Salmonella* spp. isolates from broilers were fully sensitive to all antibiotics tested; a slight increase on the levels seen in 2013 (63%). In laying hens, 93% (54/58) of the *Salmonella* tested were fully sensitive to all antibiotics tested; an increase on the percentage fully sensitive seen in 2013 (84%). In fattening turkeys, 31% (51/162) of isolates were fully sensitive to all antibiotics tested; an increase on the percentage fully sensitive seen in 2013 (14%). No *Salmonella* from broilers, layers and turkeys were resistant to meropenem, cefotaxime or ceftazidime in 2014.

Escherichia coli

Gram-negative commensal organisms such as *E. coli* are commonly regarded as 'indicator organisms' to monitor AMR in the intestinal flora. *E. coli* are thought to constitute a reservoir of antibiotic resistance in any given bacterial population. This is problematic as *E. coli* may transfer these genes to other bacteria, including pathogenic varieties.

No resistance was detected in *E. coli* isolated from broilers or turkeys to the following antibiotics: cefotaxime, ceftazidime, colistin, meropenem and tigecycline. Resistance to ciprofloxacin was found in 25% (39/159) of *E. coli* isolates from broilers and 17% (29/168) from turkeys.

Results

Antibiotic resistance in *Campylobacter jejuni, Salmonella* and *E. coli* have been interpreted using EUCAST epidemiological cut-off values. Results from the same samples interpreted using EUCAST clinical break-points are presented in **Annexes 10**, **11** and **12**.

Results described as "resistant" in this chapter do not necessarily indicate that an infection in a patient would not respond to treatment.

Campylobacter spp.

- In 2014, all isolates of *C. jejuni* from broilers were susceptible to erythromycin, streptomycin and gentamicin.

- Resistance to both streptomycin and gentamicin was detected in two *C. jejuni* isolates from turkeys. A single isolate from a turkey was resistant to erythromycin and this isolate was also resistant to ciprofloxacin.

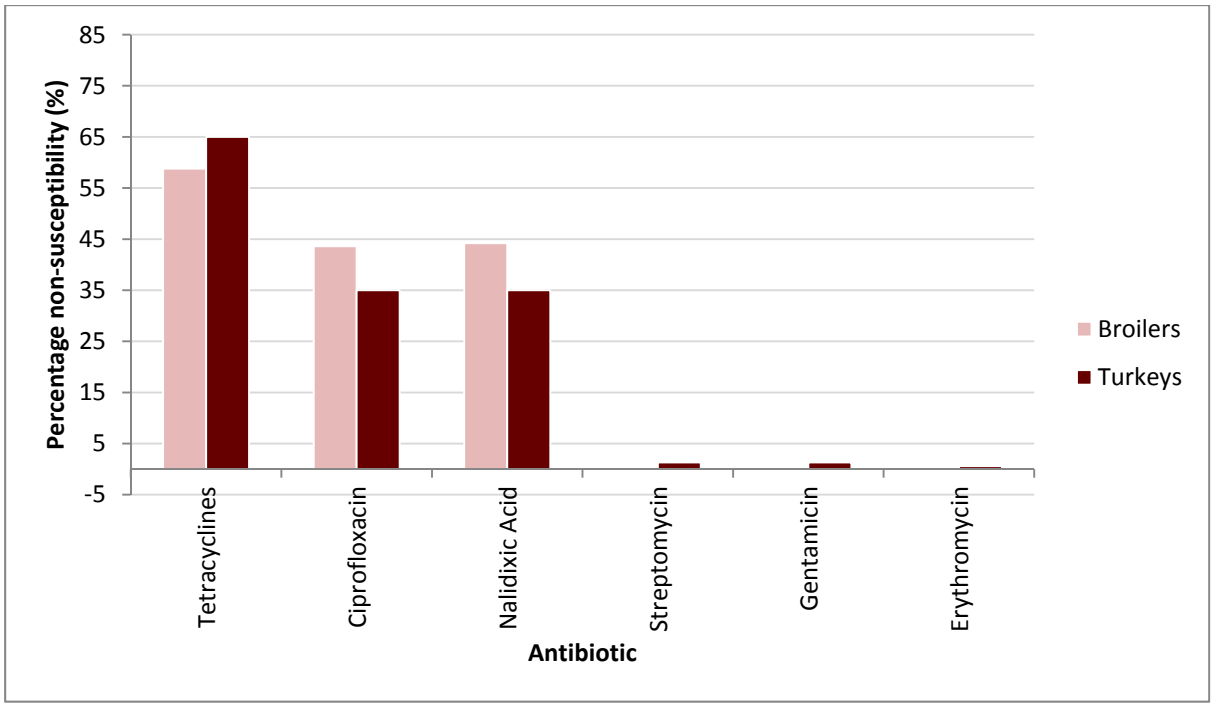
- Ciprofloxacin resistance was demonstrated in 44% (72/165) of *C. jejuni* isolates from broilers and all of these isolates were also resistant to nalidixic acid. A single isolate was resistant to nalidixic acid but susceptible to ciprofloxacin. This is an increase in resistance compared to the results of a 2013 broiler survey (VARSS, 2014) which showed that the level of ciprofloxacin resistance in *C. jejuni* in 2013 was 31% (19/61 isolates).

- Ciprofloxacin resistance was demonstrated in 35% (55/157) of *C. jejuni* isolates from turkeys, and all of these isolates were also resistant to nalidixic acid.

- Of the 72 *C. jejuni* isolates from broilers which were resistant to ciprofloxacin 65/72 (90%) were also resistant to tetracyclines. Of the 55 *C. jejuni* isolates from turkeys which were resistant to ciprofloxacin, 49/55 (89%) were also resistant to tetracyclines, a similar situation to that seen in broilers.

- Tetracycline resistance was observed in 65% and 58% of *C. jejuni* from turkeys and broilers, respectively. With regards to tetracycline resistance in broilers, this resistance level is an increase compared to the results of a 2013 broiler survey which demonstrated that resistance was observed in 48% (29/61) of isolates.

Figure 4.2: Percentage non-susceptibility (interpreted using EUCAST ECVs) in *Campylobacter jejuni* isolates from broilers (n=165) and turkeys (n=157) in 2014



Escherichia coli

- In 2014, 159 isolates of *E. coli* were examined from broilers and 168 isolates from turkeys.

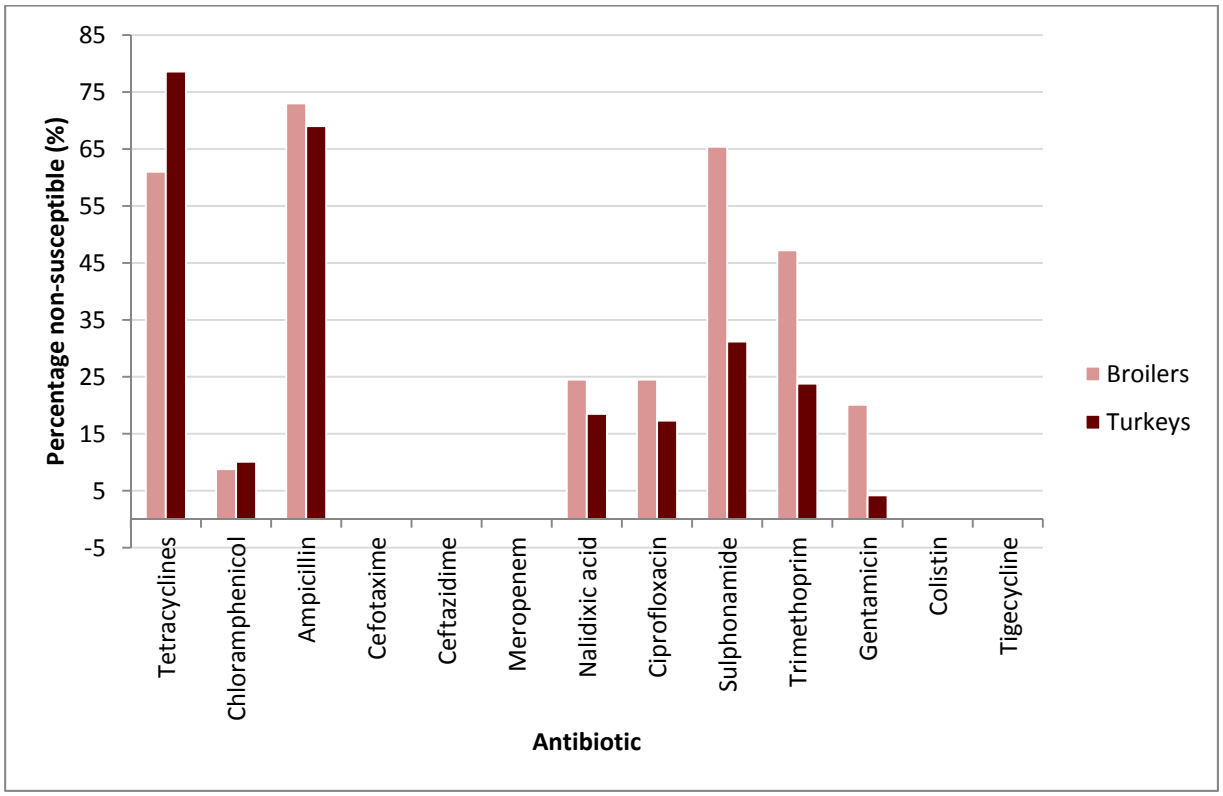
- Considering antibiotics of critical importance to human medicine, no resistance was detected to cefotaxime, ceftazidime, colistin, meropenem or tigecycline: all *E. coli* isolates from broilers and from turkeys were fully susceptible to these substances.

- Resistance to ciprofloxacin was observed in 25% and 17% of *E. coli* isolates from broilers and turkeys, respectively. All isolates which were resistant to ciprofloxacin were also resistant to nalidixic acid, apart from two *E. coli* isolates from turkeys which were resistant to nalidixic acid, but susceptible to ciprofloxacin.

- Seventeen of 168 *E. coli* isolates from turkeys were resistant to chloramphenicol; of these, most were also resistant to ampicillin (16/17), tetracyclines (16/17), sulphonamides (15/17) or trimethoprim (13/17). Fifty-four of 168 *E. coli* isolates from turkeys were resistant to sulphonamides; of these, most (52/54) were also resistant to tetracyclines; whilst 36/54 were also resistant trimethoprim and 46/54 were also resistant to ampicillin.

- The position was similar in *E. coli* from broilers, with 14 out of 159 isolates demonstrating resistance to chloramphenicol – most of the chloramphenicol isolates (13/14) were also resistant to ampicillin. Thirteen out of 14 isolates were also resistant to sulphonamides and 13/14 to tetracyclines, whilst 10/14 were resistant to trimethoprim. Of the 104/159 *E. coli* isolates from broilers which were resistant to sulphonamides, 84/104 were also resistant to tetracyclines, 87/104 were also resistant to ampicillin and 74/104 were also resistant to trimethoprim.

Figure 4.3: Percentage (%) non-susceptibility (interpreted using EUCAST ECVs) in *Escherichia coli* isolates from broilers (n=159) and turkeys (n=168) in 2014



Salmonella spp.

Broilers

- In 2014, no isolates of *Salmonella* from broilers were resistant to meropenem, cefotaxime, ceftazidime or colistin.

- Sixty-four percent (108/168) of *Salmonella* spp. isolates from broilers were fully sensitive to all antibiotics against which they were tested – comparable to the levels seen in 2013 (63%). No isolates of *S*. Enteritidis or *S*. Typhimurium recovered from broilers were detected.

- One isolate of monophasic *Salmonella* Typhimurium was tested and showed ampicillin, sulphonamide, tetracycline, trimethoprim and gentamicin resistance.

- The most prevalent serovars from broilers were *S*. Mbandaka (51 isolates) and *S*. Kedougou (29 isolates). Seventy-five percent of *S.* Mbandaka isolates (38/51) were susceptible to all of the antibiotics tested.

- The *Salmonella* Kedougou isolates from broilers were mostly (24/29; 83%) resistant to sulphonamides and trimethoprim, with many of these (10 isolates) also resistant to tetracyclines.

- Ten *Salmonella* isolates from broilers had an MIC to tigecycline of 2mg/l, just above the epidemiological cut-off value. These isolates were all *S*. Kedougou, which were also resistant to tetracyclines, suggesting that tetracycline resistance may be linked to the observed low-level tigecycline resistance in this serovar.

- Six *Salmonella* isolates (4% of the total, as seen in 2013) were resistant to ciprofloxacin and these comprised mainly *Salmonella* Indiana (2), Mbandaka (1) and Senftenberg (1), together with two isolates of a rough strain. All of these isolates were also resistant to nalidixic acid.

Layers

- No *Salmonella* isolates recovered from layers in 2014 (or 2013) were resistant to meropenem, cefotaxime, or ceftazidime.

- Ninety-three percent (54/58) of the *Salmonella* isolates tested were fully sensitive to all antibiotics against which they were tested – an increase on the percentage fully sensitive seen in 2013 (85%).

- Seven isolates of *S.* Enteritidis were recovered; of which four were fully sensitive. Two isolates were resistant to colistin and one of these was also resistant to tetracyclines. A single isolate was resistant to ciprofloxacin and nalidixic acid.

- There were four *S*. Dublin isolates recovered from all layers and one of these isolates was resistant to colistin. The three *Salmonella* isolates from layers which were microbiologically resistant to colistin each had colistin MICs of 4mg/l, just above the ECV. *Salmonella* Dublin and *S.* Enteritidis are group D *Salmonella* isolates and it has been

suggested that group D *Salmonellae* are less susceptible in their wild-type normal distribution for colistin than other *Salmonella* isolates.

- There were no *S*. Typhimurium isolates recovered from layers.

- Nine isolates of *Salmonella* Newport and two isolates of monophasic *Salmonella* (4,5,12:i) were fully susceptible to the panel of antibiotics tested.

Turkeys

- Resistance to meropenem, cefotaxime, ceftazidime or colistin was not detected in *Salmonella* isolates from turkeys in 2014.

- Thirty-one percent (51/162) of *Salmonella* isolates were fully sensitive to all antibiotics which they were tested against – an increase on the percentage fully sensitive seen in 2013 (14%).

- There were no *S*. Enteritidis isolates recovered from turkeys. A single isolate of *Salmonella* Typhimurium was resistant to ampicillin, sulphonamides and tetracyclines. Thirteen isolates of the monophasic *Salmonella* 4,5,12:i:- were recovered from turkeys and of these 10/13 were resistant to ampicillin, sulphonamides and tetracyclines, with one also resistant to ciprofloxacin and nalidixic acid.

- Resistance to ciprofloxacin was detected in 33 isolates (20%), belonging to serotypes Newport (18), Senftenberg (10), Bardo (3), Agona (1) and a monophasic Typhimurium (1). All of these isolates were also resistant to nalidixic acid. In 2013, resistance to ciprofloxacin was detected in 14% of *Salmonella* from turkeys.

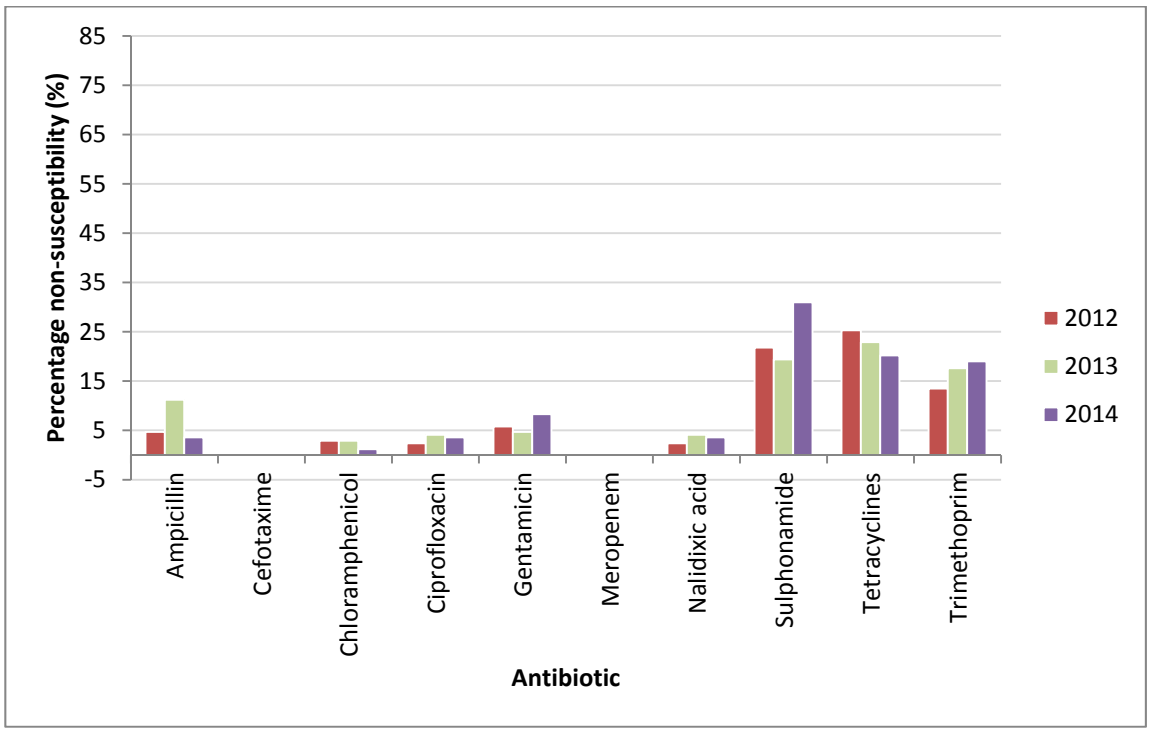
- Of the *S.* Newport isolates recovered, 77% (17/22) were resistant to ciprofloxacin, nalidixic acid and ampicillin.

- There were 40 isolates of *Salmonella* Derby isolated and 34 (85%) were resistant to sulphonamides and tetracyclines.

- Of 29 isolates of *Salmonella* Kedougou examined, 25 were resistant to sulphonamides and most of these (24/25) were also resistant to tetracyclines. Similar to the situation with *S.* Kedougou from broilers, 13/29 *S*. Kedougou isolates from turkeys had tigecycline MICs just above the epidemiological cut-off value and were therefore classed as showing microbiological resistance to tigecycline. These *S*. Kedougou were also all resistant to tetracyclines, suggesting that tetracycline resistance may be linked to the observed low-level tigecycline resistance in this serovar.

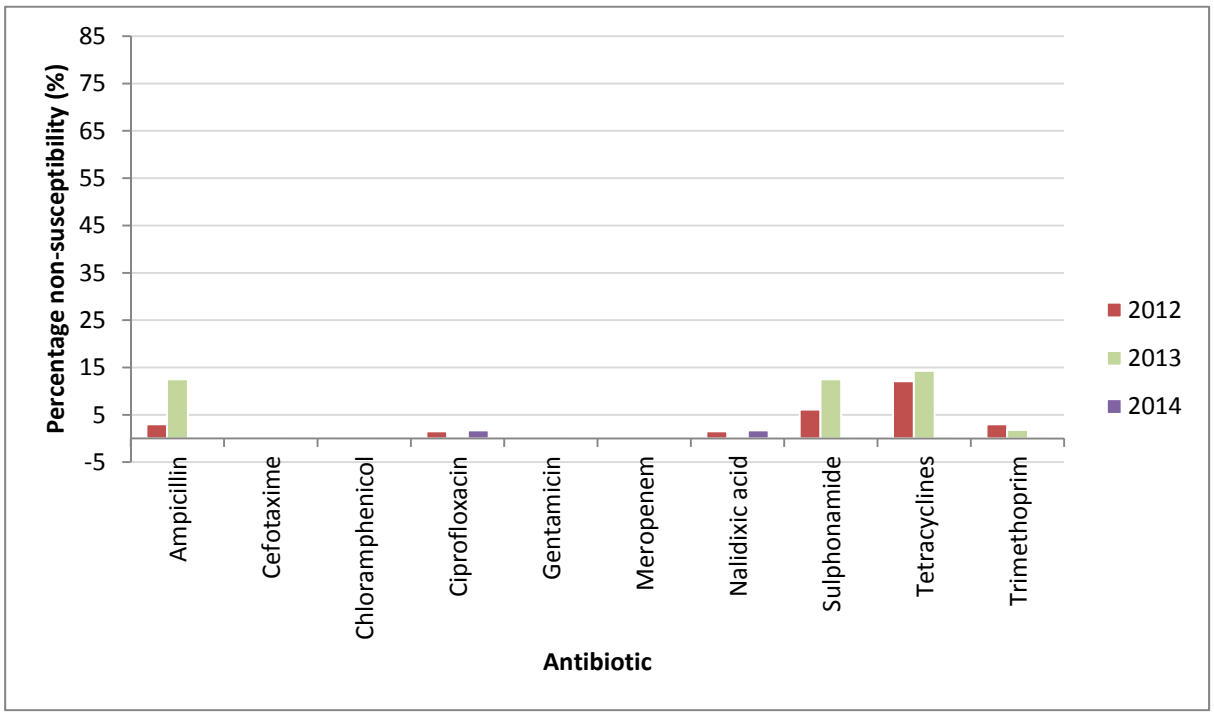
Annual resistance data for *Salmonella* isolates from the NCP have been published previously in the 2011 and 2013 UK-VARSS reports, but for completeness these datasets can also be found in **Annex 12**. The isolates submitted to EFSA in accordance with 2013/653/EU can be compared to isolates collected under the NCP in previous years:

Figure 4.4: Percentage non-susceptibility (interpreted using ECVs) in *Salmonella* isolates recovered from broilers in 2012 (n=170), 2013 (n=170) and 2014 (n=168)



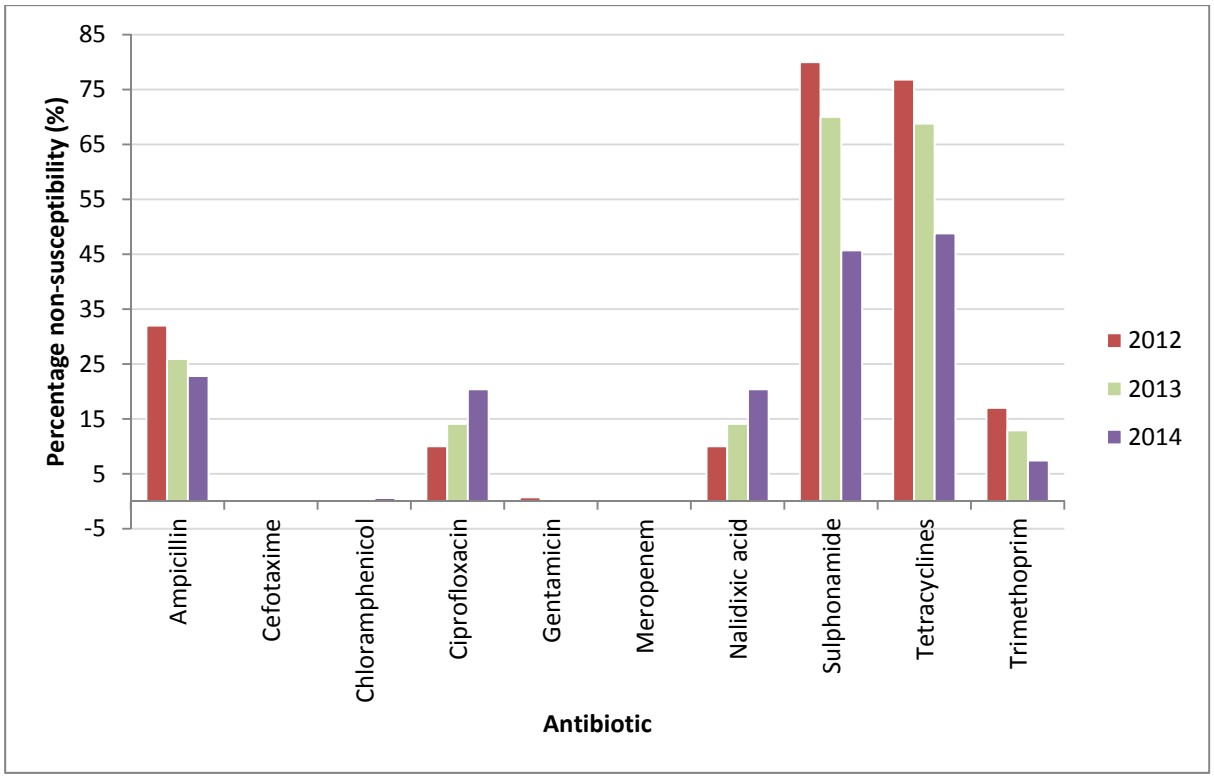
Note: Resistance to meropenem was tested in 2014 only – the percentage non-susceptibility was 0%

Figure 4.5: Percentage non-susceptibility (interpreted using ECVs) in *Salmonella* isolates recovered from laying hens in 2012 (n=66), 2013 (n=56) and 2014 (n=58)



Note: Resistance to meropenem was tested in 2014 only – the percentage non-susceptibility was 0%

Figure 4.6: Percentage of non-susceptibility (interpreted using ECVs) in *Salmonella* isolates recovered from turkeys in 2012 (n=142), 2013 (n=170) and 2014 (n=162)



Note: Resistance to meropenem was tested in 2014 only – the percentage non-susceptibility was 0%

Chapter 5 – Clinical Surveillance of Antibiotic Resistance

Introduction

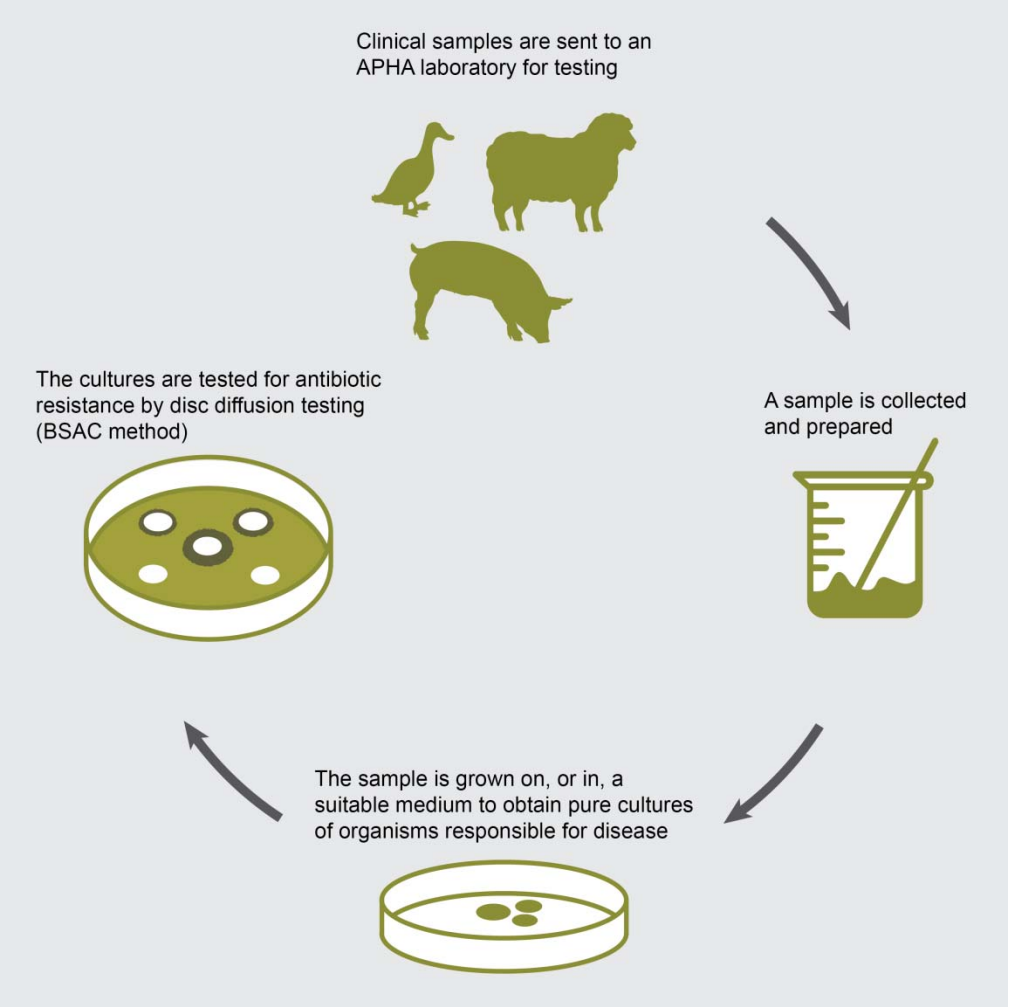
Clinical surveillance is a programme of passive surveillance. Its aim is to evaluate antibiotic resistance in bacteria of relevance to animal health which have been isolated from clinical diagnostic samples from animals. This programme relies on the submission of carcases or other diagnostic samples by private veterinary surgeons to the Animal and Plant Health Agency (APHA) veterinary laboratories. These laboratories are situated in England and Wales with the exception of APHA Lasswade, in Scotland. Similar programmes are conducted in Scotland and Northern Ireland. Data from the Scottish and Northern Irish clinical surveillance programmes are not included in this report.

Where it is clinically relevant, culture and sensitivity testing are undertaken on isolates recovered from submitted samples. Since clinical surveillance is a passive form of surveillance, findings may not be representative of the wider population, but it serves as a useful means to investigate resistance of importance to animal health and welfare.

Method

How were samples collected?

Figure 5.1: Diagram of the clinical surveillance process



How was antibiotic susceptibility testing conducted?

Susceptibility tests were conducted by a network of APHA veterinary laboratories situated throughout Great Britain.

For isolates recovered through the clinical surveillance scheme, the susceptibility tests described were performed (unless otherwise stated) using a disc diffusion technique on Isosensitest Agar (Oxoid) with appropriate media supplementation, where necessary, for fastidious organisms. The disc concentrations used are as stated in **Annex 9**. Resistance was interpreted using human clinical breakpoints as published by BSAC. Isolates have been classed as either sensitive or resistant; under the BSAC guidelines intermediate isolates are considered resistant. For some veterinary 'drug/bug' combinations there are no published BSAC breakpoints available – in these cases, a historical APHA veterinary breakpoint (13mm zone size diameter) has been used to define sensitive and resistant strains.

Multiple antibiotic resistance is defined in this chapter as resistance to four or more antibiotics which were tested for a particular isolate. There is no internationally agreed definition of multiple resistance and the term has been used differently in different studies (EFSA, 2012, Schwarz *et al*., 2010).

Key Messages

Salmonella spp.

A total of 7769 *Salmonella* isolates were identified between 2012 and 2014. In 2014, 69.3% of 2347 isolates from a range of sources (see **Annex 20**) were susceptible to all antibiotics. This is an increase compared to 2013 (64.2%) and 2012 (59.7%). In 2014, 1% (23/2347) of all *Salmonella* isolates were resistant to ciprofloxacin. None of the *Salmonella* isolates tested showed resistance to cefotaxime or ceftazidime.
Resistance to gentamicin in *Salmonella* isolated from sheep, pigs and chickens did not exceed 8.8% in 2014. Resistance to gentamicin was highest in all isolates from pigs at 8.8%, which is similar to the level seen in 2013 (8.4%) and a reduction from 2012 levels (26.4%).

Escherichia coli

Clinical resistance to cefotaxime in *E. coli* from neonatal calves and lambs in 2014 was 15% and 3% respectively, whilst cefpodoxime resistance in *E. coli* in the same year was 0% in neonatal piglets, 4% in chickens and 0% in turkeys. Cefpodoxime resistance in clinical diagnostic *E. coli* from chickens was 14% in 2012, 8% in 2013 and 4% in 2014. Enrofloxacin resistance was 12%, 18%, 1%, 5% and 14% in *E. coli* from calves, piglets, lambs, chickens and turkeys respectively.

LA-MRSA

Livestock-associated methicillin-resistant *S. aureus* (MRSA) ST398, *spa*-type t034, was detected in skin lesions on two piglets from a breeder-finisher farm in eastern England[27].

Mastitis Pathogens

Resistance demonstrated by mastitis pathogens in 2014 were broadly similar to previous years. In *E. coli* resistance to amoxicillin/clavulanic acid and ampicillin was seen in 7% and 24% of isolates, respectively – which represent marginal decreases compared to 2013 levels. Resistance to enrofloxacin was observed in 3% of *E. coli* isolates which is an increase when compared with 2013 (0%) and 2012 (2%). Resistance to cefpodoxime also increased to 2% of all *E. coli* isolates; resistance has been seen at levels of <1% in 2013 and 2012. No resistance was seen to amoxicillin/clavulanic acid or ampicillin in *S. dysgalactiae* isolates (as in previous years) and tetracycline resistance in *S. dysgalactiae* decreased but remained high with 85% of isolates demonstrating resistance (91% in 2013, 80% in 2012). Similarly no resistance to amoxicillin/clavulanic acid or ampicillin was seen in *S. uberis* isolates in 2014. *Staphylococcus aureus* isolates were frequently (35% of 82 isolates) resistant to ampicillin; resistance to other antibiotics was less common. No MRSA isolates were detected in cattle in 2014.

Respiratory Pathogens

All isolates of *M. haemolytica*, *P. multocida, Bibersteinia trehalosi* or *Histophilus somni* from cattle, sheep or pigs in 2014 were sensitive to enrofloxacin. Trimethoprim/sulphonamide resistance (1/14

[27] http://veterinaryrecord.bmj.com/content/176/6/151.3.full

isolates) and tetracycline resistance (2/24 isolates) was detected in 2014 – this is the first time that resistance to these antibiotics has been detected under the clinical surveillance programme.

Other Veterinary Pathogens

Penicillin resistance was detected in two *Streptococcus suis* isolates from pigs out of a total of 177 tested between 2012-2014. The proportion of isolates of *Brachyspira hyodysenteriae* resistant to tiamulin (applying clinical breakpoints) increased in 2012-2014 compared to previous years, although only low numbers of isolates (nine in 2012, eight in 2013 and four in 2014) were available for testing.

Results

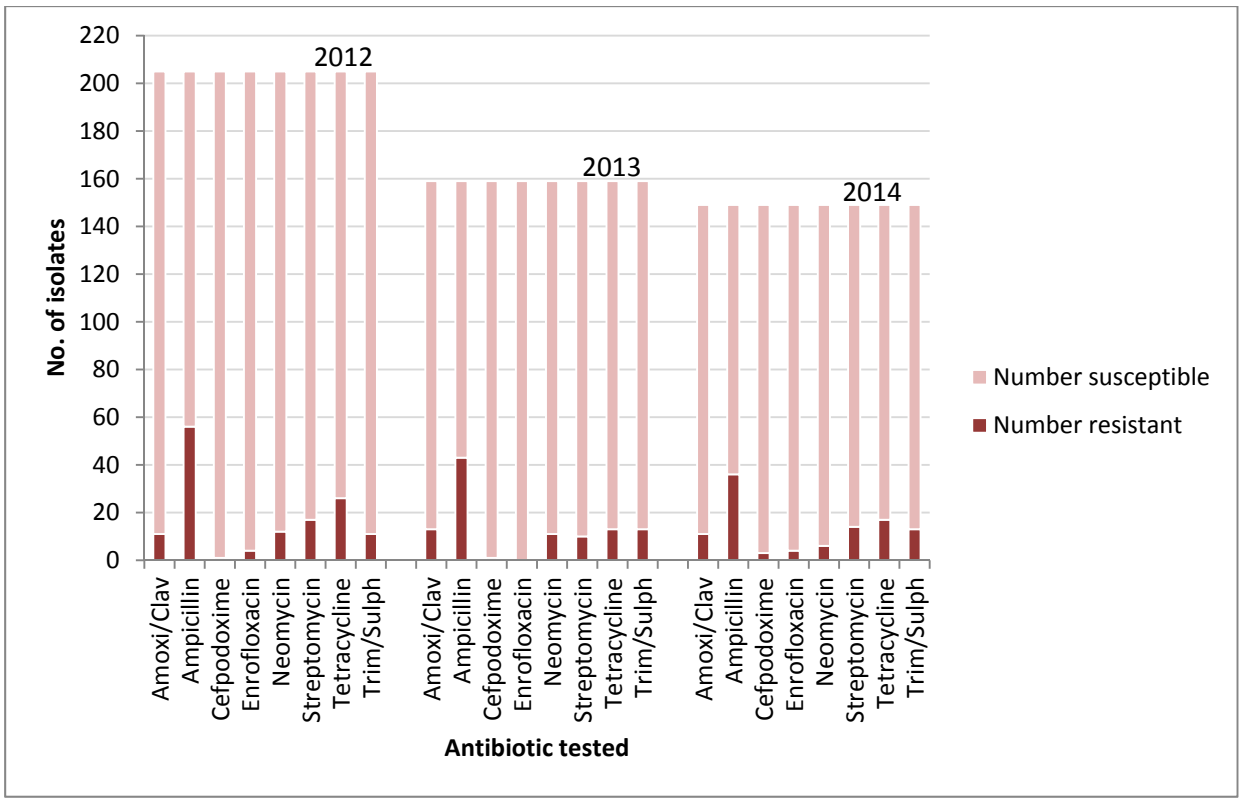
Where more than 20 isolates of any pathogen were recovered per year the results are presented graphically in the main body and the numerical data is available in the annex, where fewer than 20 isolates the results are only presented in the annex and not in the main body of the text.

Veterinary Pathogens – Mastitis Pathogens

Escherichia coli

Gram-negative pathogens such as *E. coli* and other coliforms are one of the three main causes of bovine mastitis. Most strains originate from the immediate environment of the cow, and are most likely to be of faecal origin. It is thought that no special virulence factors are required to infect the mammary gland. The isolates presented in this report therefore represent the normal types of bacterium which are present in the immediate environment of adult dairy cattle, particularly in the cattle sheds and cubicle houses. It is noteworthy that in 2014 the percentage of isolates resistant to cefpodoxime in mastitis *E. coli*/coliform isolates (2%) is much lower than the percentage resistance to ceftazidime (7%) or cefotaxime (15%) observed in non-mastitis *E. coli*/coliform isolates from calves (**Table A19.4, Annex 19**).

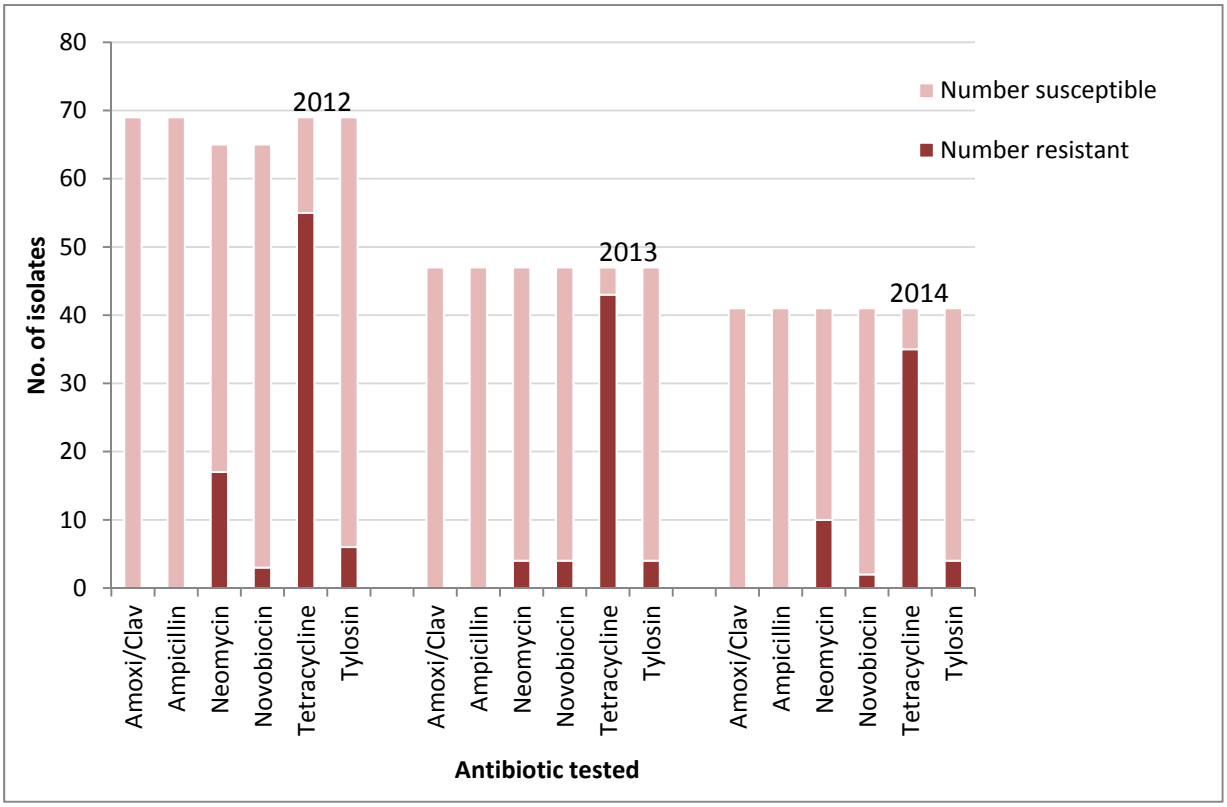
Figure 5.2: Resistance and susceptibility (interpreted using BSAC human clinical breakpoints) of *E. coli* mastitis isolates, 2012-2014



Streptococcus dysgalactiae

Streptococcus dysgalactiae is a Lancefield Group C streptococcus and a commensal of the mucous membranes of cattle; it is a cause of mastitis and occasionally other diseases in cattle. It is not considered a zoonosis and Group S streptococci that can cause disease in humans are considered to constitute a separate population. No resistance to ampicillin or amoxicillin/clavulanate was identified over the reporting period 2012-2014 (**Figure 5.3**). Resistance to neomycin is to be expected as this organism has been noted to demonstrate intrinsic resistance to neomycin. Tetracycline resistance is also recognised as being common in this species and was detected in 80% to 91% of isolates in 2012-2014 (**Table A13.2, Annex 13**).

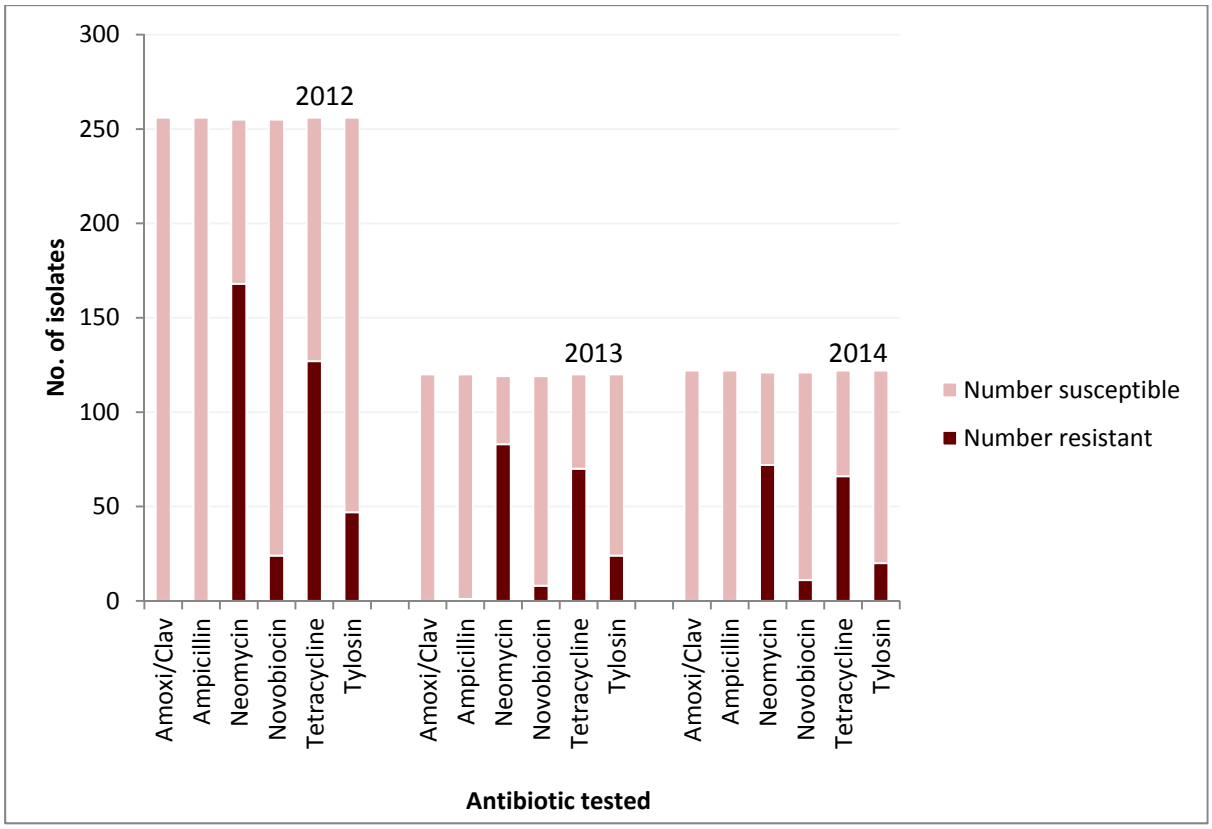
Figure 5.3: Resistance and susceptibility (interpreted using BSAC human clinical breakpoints) of *S. dysgalactiae* mastitis isolates, 2012-2014



Streptococcus uberis

Streptococcus uberis is widely distributed in the environment and a normal commensal resident of the bovine vagina, tonsil and skin. It is a common cause of mastitis and not regarded as zoonotic. Ampicillin and amoxicillin/clavulanate resistance were not detected in *S. uberis* in 2014 (**Figure 5.4**). In 2012 – 2014, 16 to 20% of *S. uberis* strains were resistant to tylosin (**Annex 13**). Resistance to tetracyclines was also detected in *S. uberis* isolates in 2012–2014 and ranged from 50% to 58%.

Figure 5.4: Resistance and susceptibility of *S. uberis* mastitis isolates (interpreted using BSAC human clinical breakpoints) 2012-2014



Resistance to tylosin in *S. uberis* can be mediated by the induction of a plasmid-encoded enzyme which methylates the 20S ribosomal RNA sub-unit and prevents binding of the macrolide to the bacterial ribosome, and so disrupts protein synthesis.

Staphylococcus aureus

Staphylococcus aureus is normally resident on the skin and mucous membranes of cattle and is a common cause of mastitis. It is not generally regarded as zoonotic and although both Meticillin Resistant *Staphylococcus aureus* (MRSA) and a recently-described variant form of MRSA have been detected in cattle (Vanderhaeghen *et al*. 2010, García-Álvarez *et al*., 2011), the possible role of cattle as a source of human infection has not been well-defined. Other strains of *S. aureus* are for the most part considered to be generally host species-specific. Isolates of *S. aureus* from non-mastitis cases are detailed further in **Annex 17**.

Between 2012 and 2014, a large proportion of isolates (29 – 39%) were resistant to ampicillin, and amoxicillin/clavulanate resistance fluctuated between 14–25% (**Annex 13**).

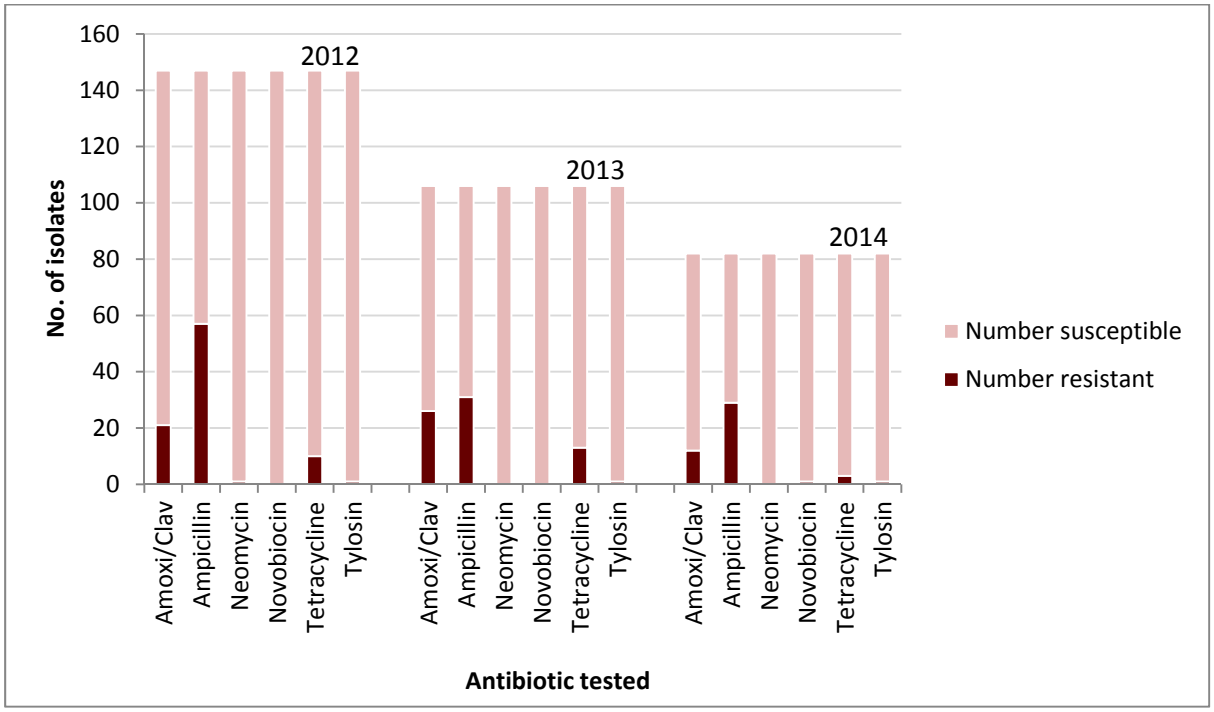
Penicillin resistance in bovine *S. aureus* is thought to occur mainly via the production of beta-lactamases that degrade both penicillin and ampicillin. The genes encoding beta-lactamases can be located on plasmids and often on transposons and may be readily transferable by conjugation. Any *S. aureus* isolates which are resistant to ampicillin are currently screened for susceptibility to cefoxitin to detect the variant *mecA* gene (now described as *mecC*) as well as isolates of classical MRSA.

Tylosin (macrolide) resistance was recorded in a small proportion (1%) of isolates. Resistance to tetracycline remained at or below 12% over the monitoring period (**Annex 13**).

There are several possible mechanisms for the development of macrolide resistance in *S. aureus*, the most important of which is production of enzymes that alter the ribosomal binding site by methylation, and possession of an efflux pump. Genes for these enzymes may be on plasmids or transposons and may be readily transferable.

No MRSAs were detected in cattle over the period 2012–2014. The variant *mecA* gene *mecC* was recently described in bovine *S. aureus* isolates from the UK (García-Álvarez *et al*., 2011), whilst classical MRSA has been detected in bovine mastitis on the continent of Europe (Vanderhaeghen *et al*., 2010).

Figure 5.5: Resistance and susceptibility of *S. aureus* isolates (interpreted using BSAC human clinical breakpoints), 2012-2014



Veterinary Pathogens – Respiratory Pathogens

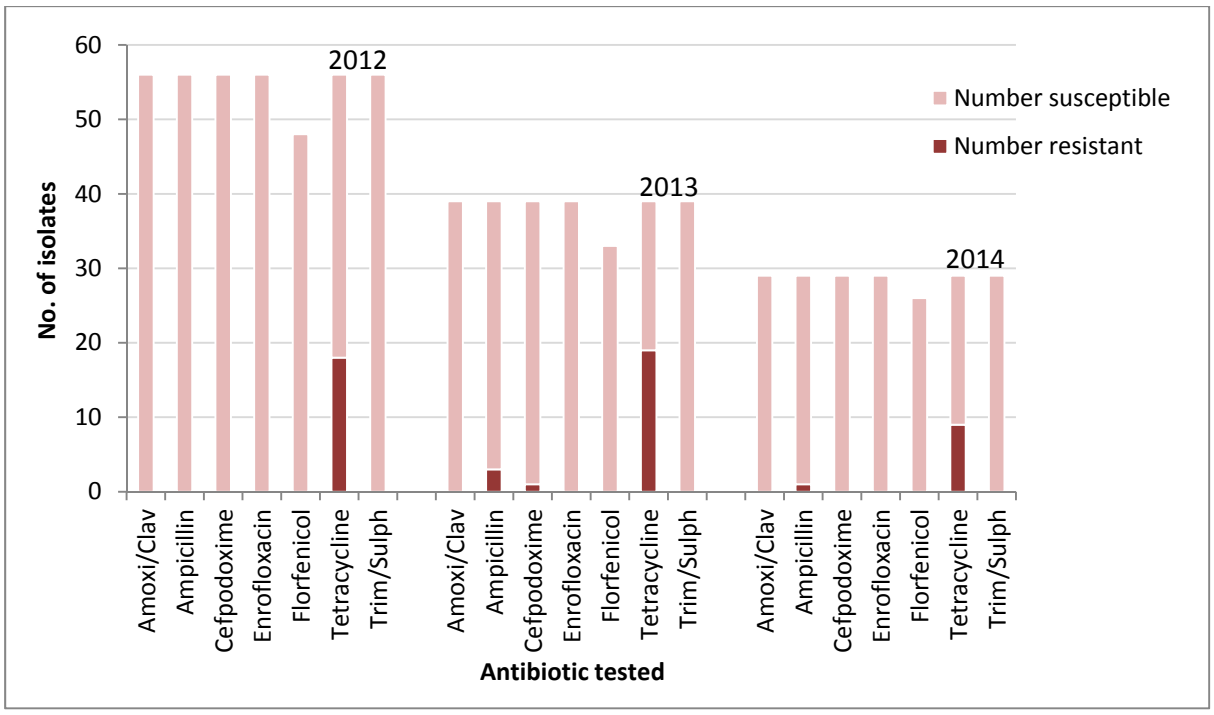
Pasteurella multocida

Pasteurella multocida is a relatively uncommon cause of respiratory or systemic disease in cattle in the UK (the incidence of disease caused by this bacterium is much greater in North America and certain other parts of the world) however good resistance data for this organism are available via UK clinical surveillance activities. Toxigenic strains of *P. multocida* are responsible for the development of atrophic rhinitis in pigs and some strains of the organism can also affect poultry (fowl cholera), however it is a rare pathogen of sheep in the UK (**Annex 15**). There is probably carriage in the upper respiratory tract of some animals and bovine strains are likely to be distinct from those infecting other species.

Cattle

Resistance to ampicillin and tetracyclines was found in bovine isolates over the monitoring period (**Figure 5.6**), including a single isolate was reported as resistant to cefpodoxime in 2013 (this has not been confirmed by follow-up testing). There was no resistance detected to enrofloxacin or florfenicol in any of the domestic species between 2012 and 2014.

Figure 5.6: Resistance and susceptibility (interpreted using BSAC human clinical breakpoints) of *P. multocida* isolates from respiratory infections of cattle, 2012-2014

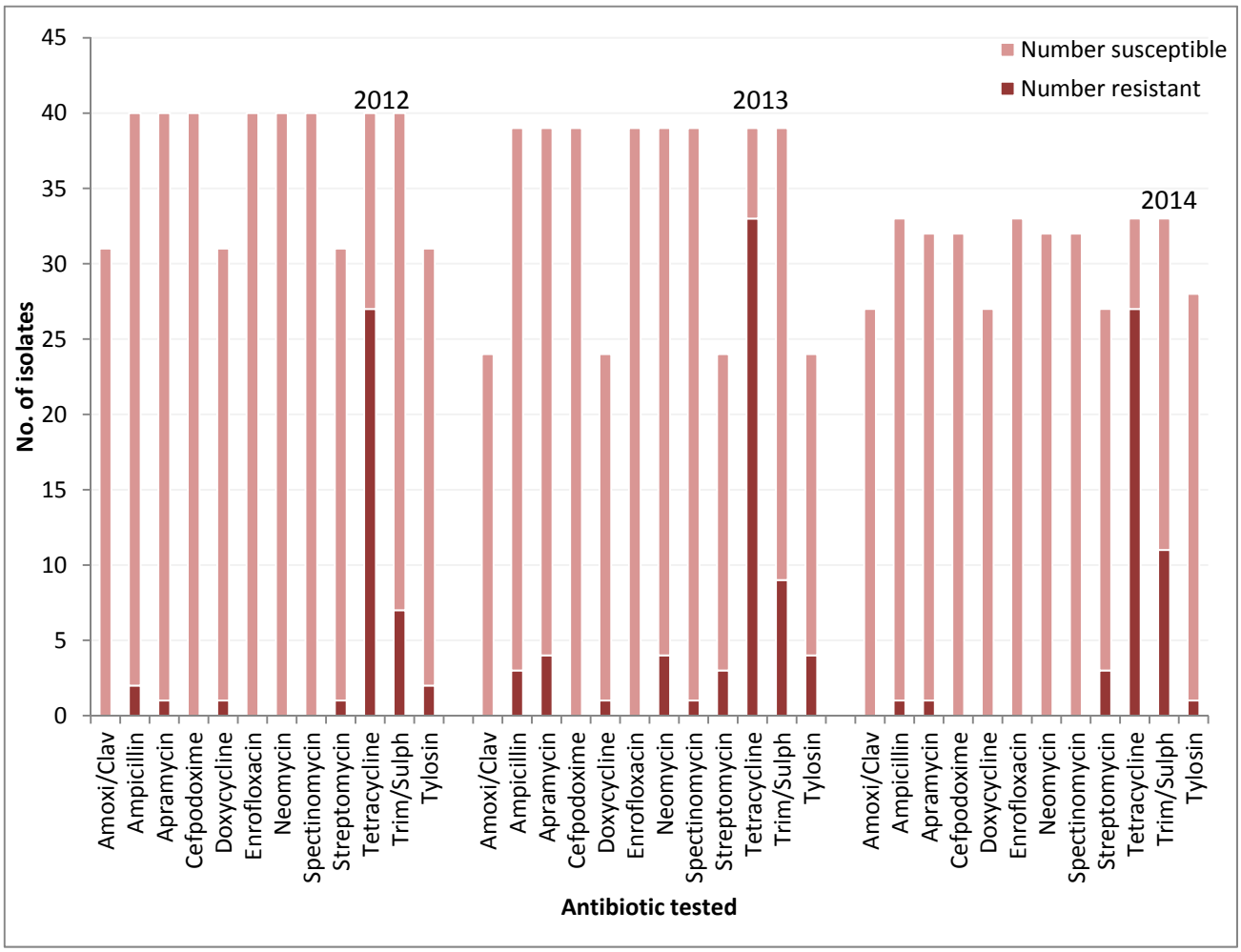


Pigs

Ampicillin resistance was observed in 5%, 8% and 3% of isolates of *P. multocida* in 2013, 2013, and 2014 respectively (**Annex 16**). Tetracycline resistance was frequent in *P. multocida* from pigs, although isolates were mostly susceptible to doxycycline.

This relationship between tetracycline and doxycycline resistance may reflect the resistance mechanism(s) involved; some genes have been shown to confer resistance to tetracyclines but not to doxycycline.

Figure 5.7: Resistance and susceptibility (interpreted using BSAC human clinical breakpoints) of *P. multocida* isolates from respiratory infections of pigs, 2012-2014



Mannheimia haemolytica

Mannheimia (Pasteurella) haemolytica is a common cause of respiratory disease in both cattle and sheep in the UK, although different serotypes predominantly affect each species. There is carriage in the upper respiratory tract in healthy animals and ovine *Mannheimia* strains can also cause bovine mastitis.

Sheep

M. haemolytica isolates recovered over the 2012-2014 period were mostly sensitive to the reported panel of antibiotics, with only a few isolates resistant to either trimethoprim/ sulphonamides (1/14 isolates) or tetracyclines (2/24 isolates) in 2014 – this is, however, the first time that resistance to these antibiotics has been detected under the clinical surveillance programme. For further information please see **Table A15.2, Annex 15**.

Veterinary Pathogens – Other Pathogens

Brachyspira hyodysenteriae

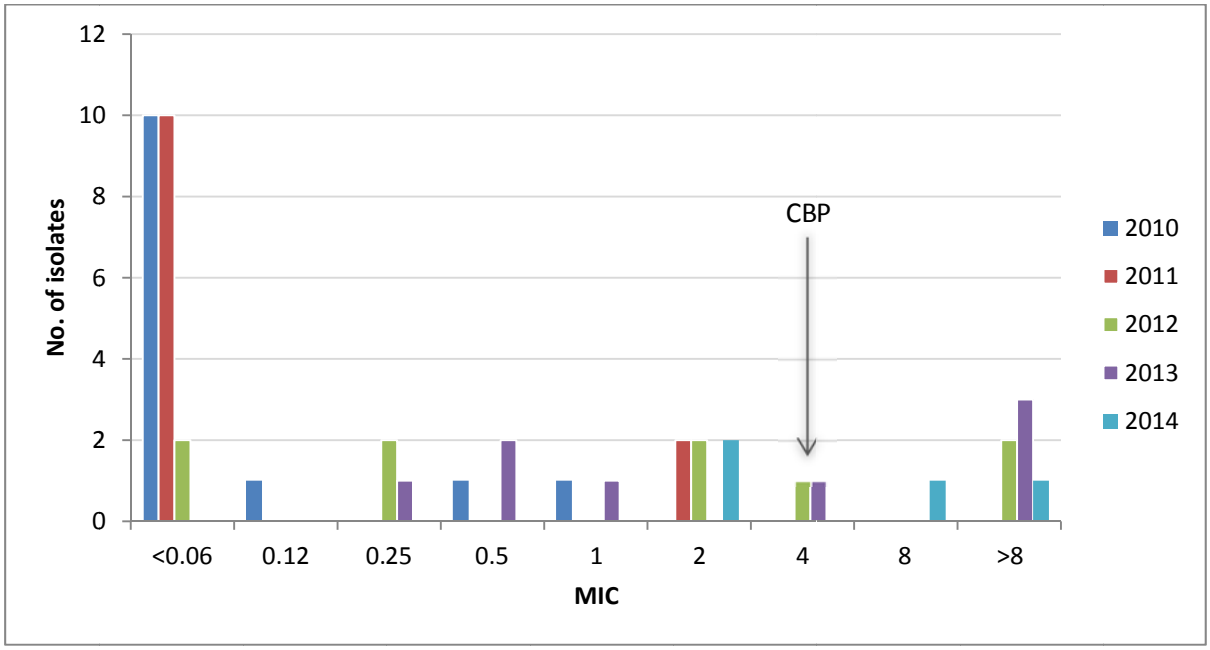
Brachyspira hyodysenteriae is the causative organism of swine dysentery, an enteric disease of pigs, resulting in serious ill-thrift in its chronic form. A limited range of antibiotics is available for the treatment of swine dysentery and since resistance arises through mutation, reliance on on-going medication without addressing other aspects of disease control, such as hygiene and herd husbandry (for example, all-in/all-out management or periodic depopulation) carries the attendant risk that mutational resistance may arise.

Tiamulin is an important antibiotic used for the treatment of swine dysentery, and as such isolates recovered via clinical surveillance activities are tested for susceptibility to it. Tiamulin-resistance in *B. hyodysenteriae*, in conjunction with resistance to other available therapeutic compounds remains extremely uncommon. Tiamulin-resistant isolates might, however, show resistance to some or all of the other antibiotics currently used for treatment. When resistance occurs to all of the available therapeutic antibiotics then important animal welfare considerations arise, since affected pigs can respond poorly to treatment and fail to thrive. In such instances, the only practical option may eventually be to depopulate herds, with serious economic implications for the farmer.

For the isolates reported here, an agar plate dilution method was used to determine the tiamulin MIC. The tiamulin MICs for selected *B. hyodysenteriae* isolates tested over the period 2010-2014 are shown in **Figure 5.8**. This includes some "repeat" isolates (i.e. isolates recovered from the same farm premises over a period of time) and two isolates are included from 2013 from the same premises which had a tiamulin MIC >8mg/l.

Figure 5.8 shows an increase in the proportion of isolates with a tiamulin MIC above the clinical breakpoint (CBP) of 4mg/l (Rønne and Szancer, 1990) in 2012, 2013 and 2014, although the number of isolates tested each year is low.

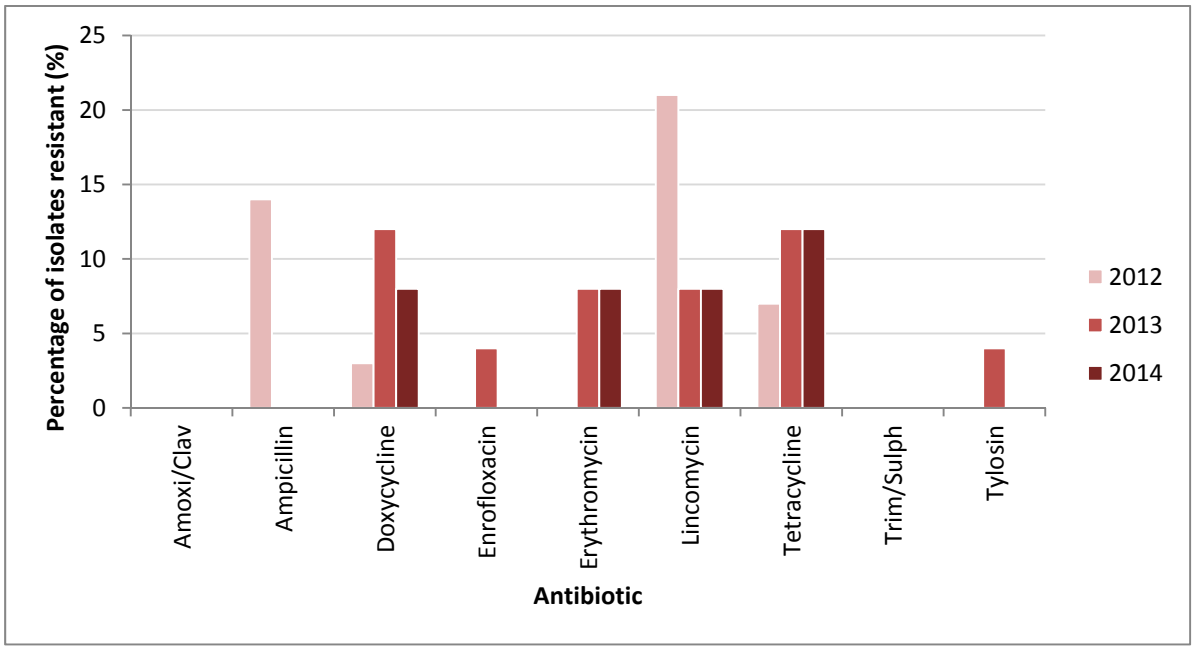
Figure 5.8: Tiamulin minimum inhibitory concentration (MIC) of selected *Brachyspira hyodysenteriae* isolates from England and Wales, 2010-2014



Staphylococcus aureus

Staphylococcus aureus causes a number of infections in poultry and game birds, including septicaemia, yolk sac infection, arthritis and osteomyelitis. Resistance to ampicillin, tetracyclines, doxycycline, enrofloxacin, macrolides and lincomycin was detected in isolates of *S. aureus* from chickens, though resistance to amoxicillin/clavulanate and trimethoprim/sulphonamide was not. For data on *S. aureus* isolates responsible for bovine mastitis cases see **page 52**.

Figure 5.9: Percentage of *S. aureus* isolates from chickens resistant to antibiotics, in 2012 (n=23-29), 2013 (n=25-26) and 2014 (n=25-26)



In addition to the 26 cultures of *S. aureus* from chickens in 2014, one isolate was also recovered from a turkey, and one from a pheasant. The isolate from a turkey was resistant to amoxicillin/clavulanic acid, ampicillin, doxycycline, lincomycin, tetracycline, and tylosin. The isolate from a pheasant was resistant to ampicillin, doxycycline and tetracycline.

There was one incident of livestock-associated meticillin resistant *Staphylococcus aureus* (LA-MRSA) in food producing animals in Great Britain in 2014[28].

S. aureus isolates were recovered from two piglets presenting with skin lesions similar to those observed in exudative epidermitis ("greasy pig disease"). The *S. aureus* were found to be MRSA ST398, *spa*- type t034. The piglets were from a breeder-finisher farm, located in eastern England. These porcine isolates were resistant to cefoxitin, penicillin, amoxicillin/ clavulanate, tetracyclines and lincomycin.

[28] http://veterinaryrecord.bmj.com/content/176/6/151.3.extract

Zoonotic Bacteria

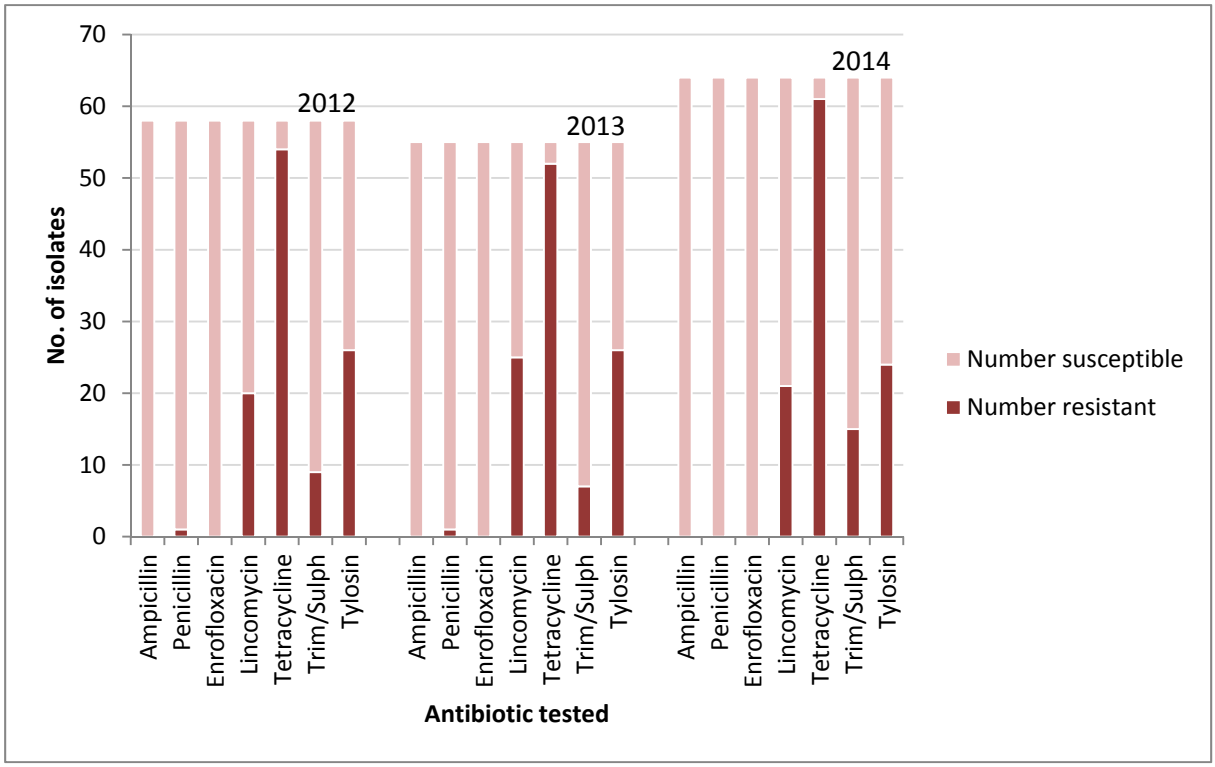
Streptococcus suis

Streptococcus suis is a pathogen of pigs that can cause pneumonia, meningitis and arthritis. It can also rarely infect man.

177 isolates have been isolated from pigs via clinical surveillance activities between 2012 and 2014. In 2012 and 2013, single isolates of *S. suis* were detected which were resistant to penicillin (**Figure 5.10**). Considering the other antibiotics tested throughout this period, isolates resistant to trimethoprim/ sulphonamide, tylosin and lincomycin were all recorded. Resistance to tetracycline was consistently high in isolates in 2012 (93%), 2013 (95%) and 2014 (95%). Please see **Annex 18** for further information.

Penicillin MIC determinations have been performed on 100 archived recent *S. suis* isolates and two isolates from 2009/2010 from cases of clinical streptococcal disease in pigs. These isolates were found to have penicillin MICs of >0.25 mg/l, equivalent to the BSAC human clinical breakpoint for resistance in beta-haemolytic streptococci. Considering that the majority of *S. suis* isolates tested had penicillin MICs of 0.006 to 0.064 mg/l, this finding is considered to confirm reduced penicillin susceptibility.

Figure 5.10: A graph to show resistance and susceptibility (interpreted using BSAC human clinical breakpoints) of *S. suis* isolates from pigs, 2012-2014



Escherichia coli

E. coli is an important bacterium as it is ubiquitous in farm animal species and has a zoonotic potential. *E. coli* can, however, occur as a commensal organism in animals and humans, and has the capacity to function as a reservoir of transferable resistance determinants.

This section of the report includes all isolates of *Escherichia coli* and coliform bacteria presumptively identified as *E. coli* through clinical surveillance activities, with the exception of isolates recovered from milk which are included in the previous section on mastitis organisms. The majority of isolates reported in this section were recovered from faeces or intestinal contents, and includes strains which are both animal pathogens and commensal strains. Collated data for the major food-producing animals tested are shown in **Table 5.1**, and resistance data split by species are shown in **Figures 5.11-5.14**.

Table 5.1: Susceptibility of all *Escherichia coli* isolates from cattle, pigs, sheep, broilers and turkeys (all ages, combined) to highest-priority critically important antibiotics for human health, 2012-2014

	***E. coli,* all food producing animals (all ages)**		
	2012	**2013**	**2014**
Total available / % multi-resistant	1571 / 54%	1404 / 51%	1150 / 57%
Cefotaxime	125/846 (15%)	98/857 (11%)	80/593 (13%)
Cefpodoxime	55/534 (10%)	27/434 (6%)	19/481 (4%)
Ceftazidime	55/846 (7%)	53/857 (6%)	44/593 (7%)
Enrofloxacin	103/1507 (7%)	114/1400 (8%)	93/1144 (8%)

*Note: A table detailing the full breakdown of proportion of non-susceptibility to all antibiotics (not just those of importance in the treatment of human clinical infections) in all livestock species can be found in **Annex 19**.*

For some livestock species the age of the animal at the time of sampling can have a large impact on the percentage of resistant isolates detected; there is a general trend towards decreasing resistance in adult livestock. Therefore, when interpreting the total resistance data presented in this section of the report please note that large differences in the levels of resistance observed in the main livestock groups may reflect the differing proportions of the age-classes of animals which have contributed to the figures.

Figure 5.11: Susceptibility of *E. coli* from cattle to highest-priority critically important antibiotics for human health in 2012 (n=901), 2013 (n=782) and 2014 (n=539)

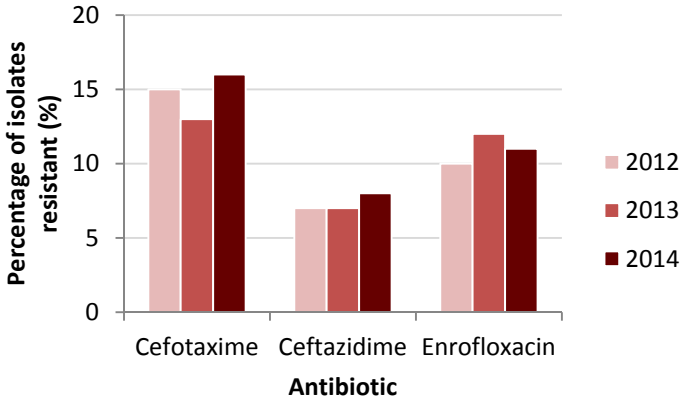


Figure 5.12: Susceptibility of *E. coli* from pigs to highest-priority critically important antibiotics for human health in 2012 (n=134), 2013 (n=102) and 2014 (n=180)

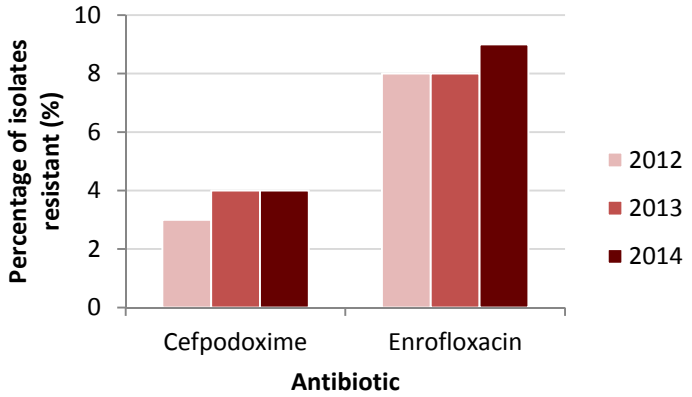


Figure 5.13:Susceptibility of *E. coli* from sheep to highest-priority critically important antibiotics for human health in 2012 (n=165), 2013 (n=225) and 2014 (n=130)

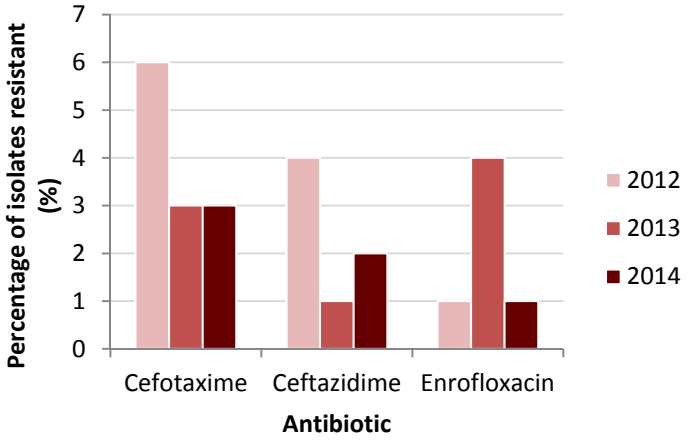
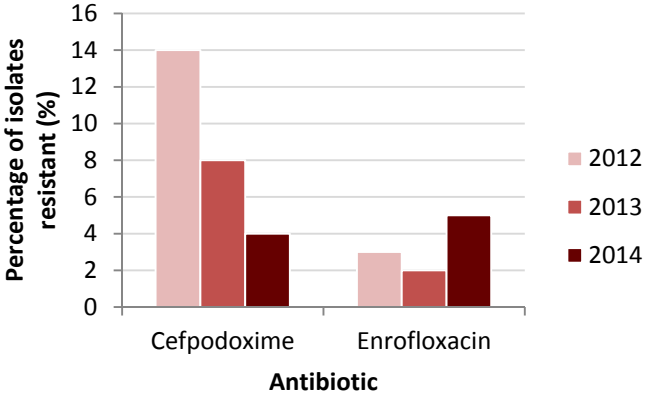


Figure 5.14: Susceptibility of *E. coli* from chickens to highest-priority critically important antibiotics for human health in 2012 (n=338), 2013 (n=289) and 2014 (n=294)



***Escherichia coli* in neonatal, post-weaning and adult cattle, pigs and sheep**

As indicated on **page 60**, there is a general trend towards decreasing resistance in isolates from older animals in all species, as compared to younger animals of the same species. This observation is consistent with previous surveillance data and with studies recorded in the literature (Hinton, 1986). Resistance in *E. coli* from neonatal calves, pigs and lambs are presented on **pages 63-65**, and resistance data for all *E. coli* isolates from cattle, pigs and sheep are presented in tabular format in **Annex 19.** Due to differences in the number of isolates available from each age group, only the resistance observed in isolates from neonates are presented in the main body of the report.

Resistance to third generation cephalosporins (cefotaxime, ceftazidime or cefpodoxime) detected in *E. coli/*coliforms in animals will include resistance mediated by both ESBL and AmpC resistance mechanisms. The higher prevalence of resistance to cefotaxime versus ceftazidime observed, for example, in neonatal calves (**Figure 5.15**), may reflect the occurrence of ESBL enzymes which are cefotaximases, rather than ceftazidimases. The relatively high frequency at which *E. coli* isolates resistant to ampicillin are recovered from young calves may reflect the use of dry cow intra-mammary infusions in the dam and transfer of residual antibiotics to calves in colostrum, which may then exert a selective pressure on the intestinal bacterial flora of the neonatal calf.

Cefpodoxime resistance in *E. coli* isolates from pigs shows an interesting age distribution with resistance detected in neonatal animals but less so in piglets post weaning. Resistance to cefpodoxime declined from 9% to 0% in neonatal pigs over the period 2012-2014.

In general, lower levels of resistance to most antibiotics are consistently observed in sheep than in pigs and cattle. Cefotaxime and ceftazidime resistance were detected in neonatal lambs, the former at a higher prevalence; as in calves, this may reflect the occurrence of ESBL enzymes which are cefotaximases, rather than ceftazidimases.

Over the reporting period, enrofloxacin resistance was detected in 10% to 12% of *E. coli* from neonatal calves, in 11% to 18% of isolates from neonatal pigs and 1% to 3% of isolates from neonatal lambs.

Resistance to aminoglycosides in *E. coli* showed some fluctuations over the period 2012-2014; neomycin resistance increased from 37% to 49% in isolates from neonatal calves, whereas it declined from 20% to 2% in *E. coli* from post-weaning pigs. Spectinomycin resistance increased from 24% to 51% in *E. coli* from neonatal pigs.

Figure 5.15: Susceptibility of *E. coli* from neonatal calves, between 2012-2014

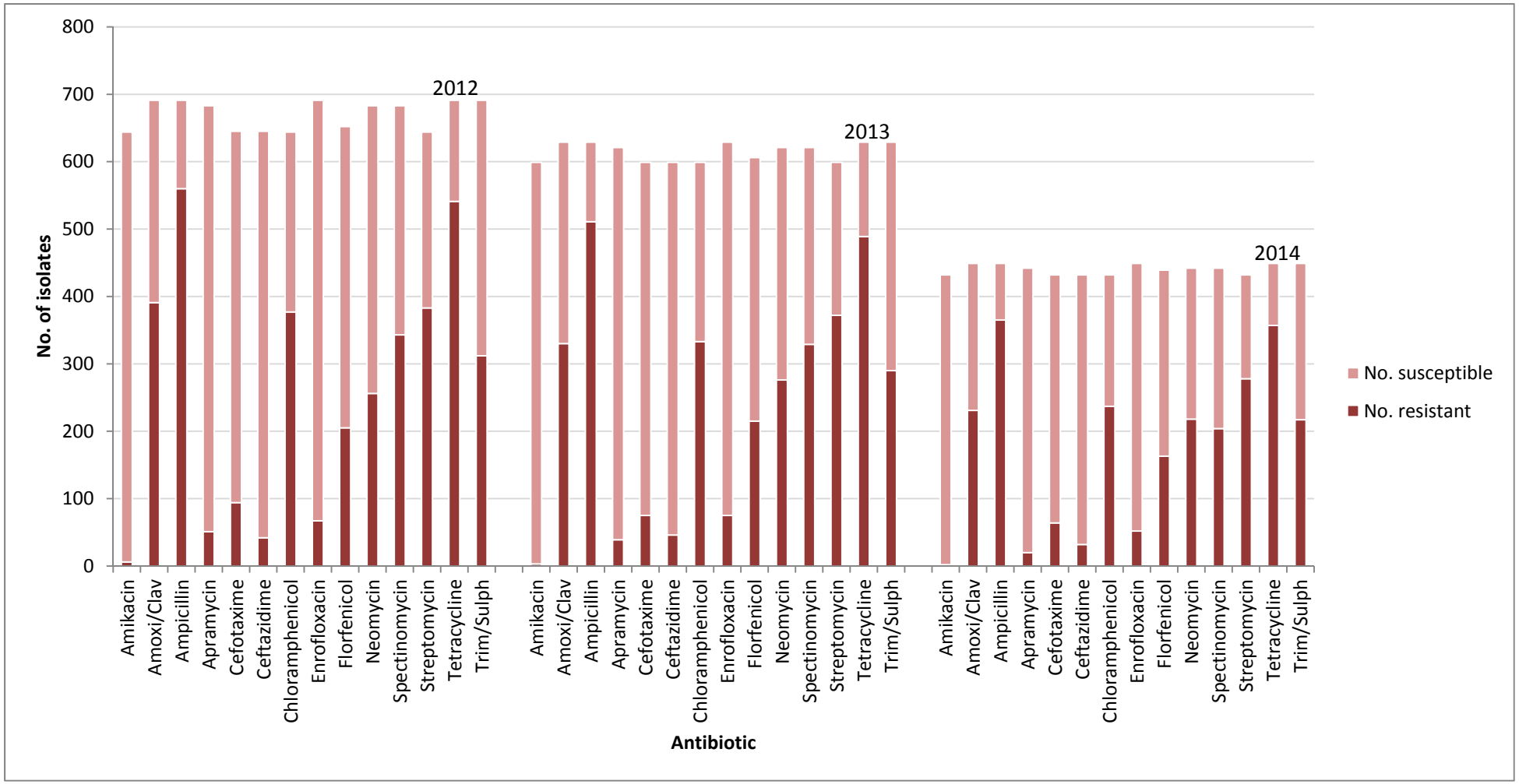


Figure 5.16: Susceptibility of *E. coli* from neonatal pigs, between 2012-2014

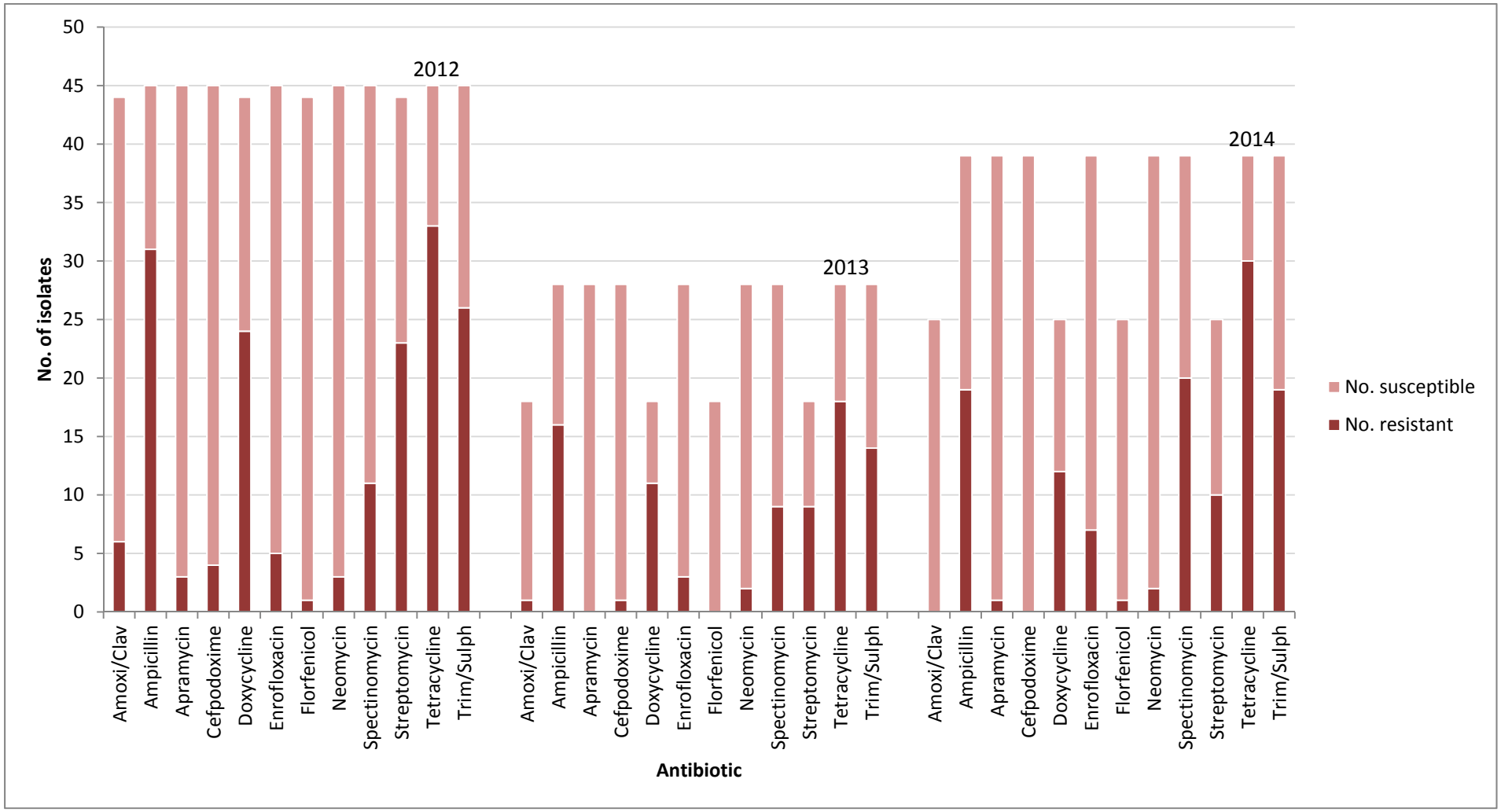
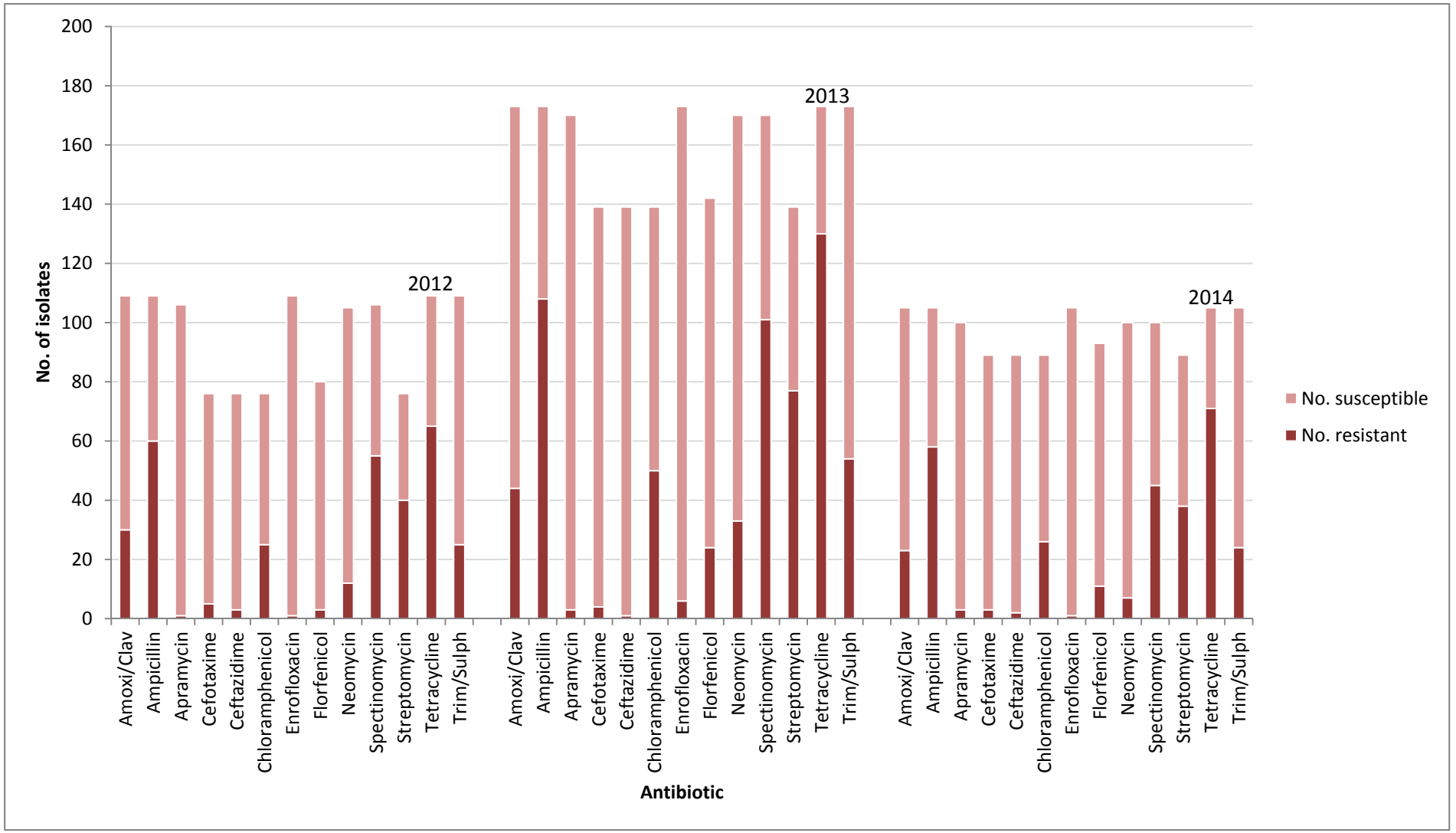


Figure 5.17: Susceptibility of *E. coli* from neonatal lambs, between 2012-2014



Salmonella spp.

There is a National Control Programme in place in the UK to reduce the prevalence of *Salmonella* in poultry, under which isolates of *Salmonella* are routinely collected for surveillance purposes. The isolates collected under the NCP are all subject to serotyping and antibiotic susceptibility testing. *Salmonella* is also reportable under the Zoonosis Order[29]. Any laboratory that isolates *Salmonella* from a food producing animal is required to inform APHA and make the isolate available for further testing if requested, as a result of this the clinical surveillance of *Salmonella* is enhanced.. This section of the report presents an overview of all of the clinical surveillance *Salmonella* isolates that were tested for resistance in 2012-2014, as well as those isolates which originate from the National Control Programme.

Due to the importance of *Salmonella* as a zoonotic pathogen it is considered useful to look at the serotype and even phage type of an isolate when investigating potential epidemiological links between animal and human cases – as such, individual serotypes are also reported in this section. Considering the findings of this report in relation to *Salmonella*, resistance to third generation cephalosporins and fluoroquinolones is considered of most importance, since these antibiotics are particularly relevant for the treatment of human salmonellosis, where this is required. Most cases of non-typhoidal *Salmonella* infection in humans are non-invasive and limited to the gastro-intestinal tract and therefore do not require antibiotic treatment.

Where resistance to third generation cephalosporins and fluoroquinolones is detected in a food producing animal(s), attempts are made to visit the farms, in order to explain the significance of the findings and provide appropriate advice on control. The number of cultures received from any one farm varies enormously, especially in the case of those received from poultry premises. Some poultry companies have a continuous monitoring programme in place and thus large numbers of *Salmonella* isolates may be received from a particular company. In that situation the numbers of isolates of a particular serotype and their antibiotic susceptibility may not reflect the prevalence in the animal population as a whole but rather the intensity of the monitoring programme on a farm or group of farms. Therefore, to indicate better the prevalence of resistance, only the first isolate of a given serotype or phage definitive type (DT) from each incident has usually been tested from each incident.

The *Salmonella* isolates reported in this section have been tested for their *in vitro* sensitivity to 16 antibiotics as defined in Annex 20. The choice of antibiotics, which is reviewed by APHA periodically, is designed to comprise a core set which are used in veterinary practice, as well as in human medicine.

[29] http://www.legislation.gov.uk/uksi/1989/285/contents/made

All *Salmonella* – Summary

A total of 7769 isolates were identified between 2012 and 2014. In 2014, 69.3% of 2347 isolates were susceptible to all antibiotics, compared to 64.2% of 2886 isolates and 59.7% of 2536 isolates, in 2012 and 2013 respectively.

In 2014, only 1% of all *Salmonella* isolates were resistant to ciprofloxacin and resistance to the 3rd generation cephalosporins, cefotaxime or ceftazidime, was not detected. Ciprofloxacin resistance was not detected in *S.* Typhimurium, one of the serotypes of particular public health importance. Resistance to highest-priority critically important antibiotics for human health in *Salmonella* from livestock is detailed below in **Table 5.2**; resistance to all antibiotics tested is presented in tabular format in **Table A20.1, Annex 20**.

No resistance to cefotaxime or ceftazidime was detected in isolates from cattle, sheep, chickens or turkeys, though 0.6% of isolates from pigs were resistant to these antibiotics. Resistance to ciprofloxacin and gentamicin was a little more common (**Table 5.2**).

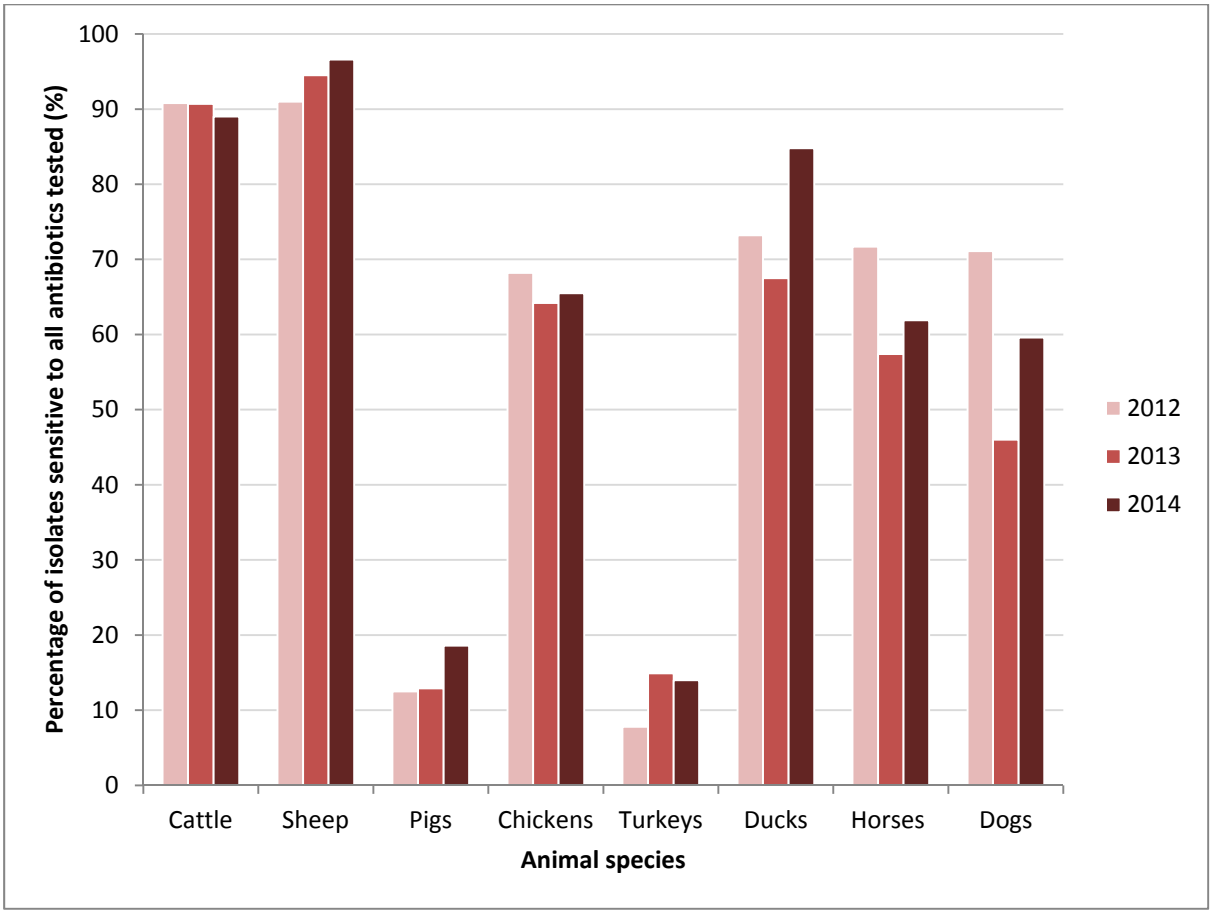
Table 5.2: Percentage of *Salmonella* isolates from cattle, sheep, pigs, chickens and turkeys that were resistant to highest-priority critically important antibiotics for human health, 2012-2014

Livestock species	Percentage susceptible to antibiotics (%)		
	2012	2013	2014
	Ciprofloxacin		
Cattle	0	0	0
Sheep	0	0	0
Pigs	0.5	0	0
Chickens	0.6	1.4	0.6
Turkeys	2.4	7	11.2
	Gentamicin		
Cattle	0	0.2	0
Sheep	0	1.1	1.7
Pigs	26.4	8.4	8.8
Chickens	4.2	3.5	2.9
Turkeys	0.2	0.4	0

Salmonella – By Animal Species

Figure 5.17 shows the percentage of *Salmonella* isolates recovered from key animal species that were fully sensitive to all antibiotics tested. The data used to produce this figure are presented in tabular format, in full, in **Table A20.1, Annex 20**.

Figure 5.17: Percentage of all *Salmonella* isolates from key animal species that were fully sensitive to all antibiotics tested, 2012-2014



Cattle – In 2014, 89% of *Salmonella* isolates were fully susceptible to all antibiotics tested. This is a slight decrease compared to 2013 (90.7%) and 2012 (90.8%). Of the 427 isolates recovered in 2014, the highest levels of resistance were to streptomycin (8.2%) and tetracycline (8.2%); a slight increase on the levels seen in 2013 (6.2% for both antibiotics). Resistance to sulphonamide compounds and ampicillin were observed at levels of 7.7% and 7.5%, respectively, in 2014 – compared with levels of 5.4% and 5% in 2013.

Sheep – In 2014, as in previous years, resistance in *Salmonella* from sheep was low; 96.6% of all isolates were fully susceptible to all antibiotics tested. This is an increase on the percentage fully susceptible seen in 2013 (94.5%). Of the 59 isolates recovered in 2014 the highest levels of resistance were observed in streptomycin (1.7%), gentamicin (1.7%), sulphonamide compounds (1.7%), and tetracycline (1.7%).

Pigs – Considering all *Salmonella* isolates from pigs (n=204), the percentage of fully susceptible isolates rose from 12.5% in 2012 and 12.9% in 2013, to 18.6% in 2014. In 2014, tetracycline

resistance was most commonly observed in *Salmonella* isolates originating from pigs (74.5%). This was also the situation for resistance to ampicillin (68.1%), sulphonamides (74.5%) and streptomycin (68.6%). 8.8% of isolates were resistant to apramycin in 2014, compared with 7.9% in 2013. Apramycin resistance occurred mainly in monophasic Typhimurium; in 2014, 2% of *S*. Typhimurium (n=102), 26% of 4,12:i:- isolates (n=27) and 16% of 4,5,12:i:- isolates (n=50) were resistant to apramycin. Sulphamethoxazole/trimethoprim resistance in *Salmonella* isolates from pigs was 46.1% in 2014. The serotype which contributed most to this total resistance figure was *S.* Typhimurium (67% resistant, n=102).

Chickens – In 2014, 65.5% of *Salmonella* isolates were fully susceptible to all antibiotics tested, a figure close to the previous two years. Of the 525 isolates recovered in 2014, some of the highest levels of resistance were to sulphonamide compounds (19.2%) and tetracycline (14.5%); which are decreases on the levels observed in 2013, where resistance to sulphonamide compounds and tetracycline were seen at 21.8% and 20.9%, respectively. Resistance to ciprofloxacin was seen at levels <1%, whilst gentamicin resistance was detected in 2.9% of isolates, which is a slight decrease on levels seen in 2013 (3.5%) and 2012 (4.2%).

Turkeys – Of all *Salmonella* isolates from turkeys in 2014 (n=143), 14% were fully susceptible to all antibiotics tested. This is a similar level to that seen in 2013 (14.9%) and an increase on the level seen in 2012 (7.8%). Resistance to streptomycin (65%), sulphonamide compounds (64.3%) and tetracycline (60.1%) were particularly high. Of all sources of *Salmonella,* resistance to naladixic acid (18.2%) and ciprofloxacin (11.2%) were highest in turkey isolates – all of the ciprofloxacin resistant isolates from turkeys were *S.* Newport. The resistance to ciprofloxacin in 2014 (11.2%) is an increase on the levels seen in 2013 (7%) and 2012 (2.4%). No resistance was seen to gentamicin.

Ducks – Of 197 isolates cultured in 2014, 84.8% of *Salmonella* were fully susceptible to all antibiotics tested. No resistance was seen to naladixic acid or ciprofloxacin. The highest level or resistance was seen to furazolidone – 12.7% of isolates were resistant to this antibiotics, which is a decrease on the levels seen in 2013 (23%) and 2012 (15.2%).

Horses – Of 84 *Salmonella* isolates cultured from horses in 2014, 61.9% of isolates were fully susceptible to all antibiotics tested; compared with 57.4% in 2013 and 71.7% in 2012. No resistance was observed to gentamicin, ciprofloxacin, or the 3rd generation cephalosporins. The highest levels of resistance were seen for tetracycline (34.5%), streptomycin (26.2%), the sulphonamide compounds (26.2%) and ampicillin (22.6%) – all of which were a reduction on the levels seen in 2013.

Dogs – 59.6% of all *Salmonella* isolates from dogs were fully sensitive to all antibiotics tested; this is an increase on the percentage of 46% fully susceptible in 2013, but is not as high as the level seen in 2012 (71.1%). As was observed in *Salmonella* from horses, the highest resistances in *Salmonella* from dogs were to tetracycline (34%), streptomycin (27.7%), sulphonamide compounds (34%) and ampicillin (34%).

Salmonella Dublin

Of the 286 *Salmonella* Dublin cultures tested during 2014, 96.5% were susceptible to all 16 antibiotics (**Table A20.2, Annex 20**). The percentage of *S.* Dublin isolates sensitive to all 16 antibiotics has shown only slight fluctuations over the period 2005-2014 and the majority of isolates remain susceptible; this has been the situation since surveillance began in 1971.

Most *S.* Dublin isolates (94%) originated from cattle in 2014 and this was also similar to the situation recorded in previous years. Isolates from species other than cattle in 2014 were all fully susceptible to the panel of 16 antibiotics tested.

Resistance to ampicillin, which had been observed for the first time for several years in a very low number of bovine isolates in 2000, was not recorded in 2001 or 2002 but then re-appeared consistently in 2003-2014 (**Table 5.18**). Resistance to furazolidone was not detected in 2010-2013, but re-appeared in 2014 in a single isolate. Similarly, there were no isolates resistant to trimethoprim/sulphonamides detected in 2007-2013; though a single resistant isolate was detected in 2014. Resistance to streptomycin was the most frequent resistance observed in *S.* Dublin in 2014, though only in 2.4% of isolates. Neomycin resistance was observed in a single isolate from cattle, whilst nalidixic acid resistance was not observed in 2014. Of the ten *S.* Dublin isolates which demonstrated antibiotic resistance, six were only resistant to a single antibiotic in the panel of antibiotics tested (neomycin or streptomycin).

Table 5.18: *Salmonella* Dublin: percentage of resistant isolates, 2012-2014

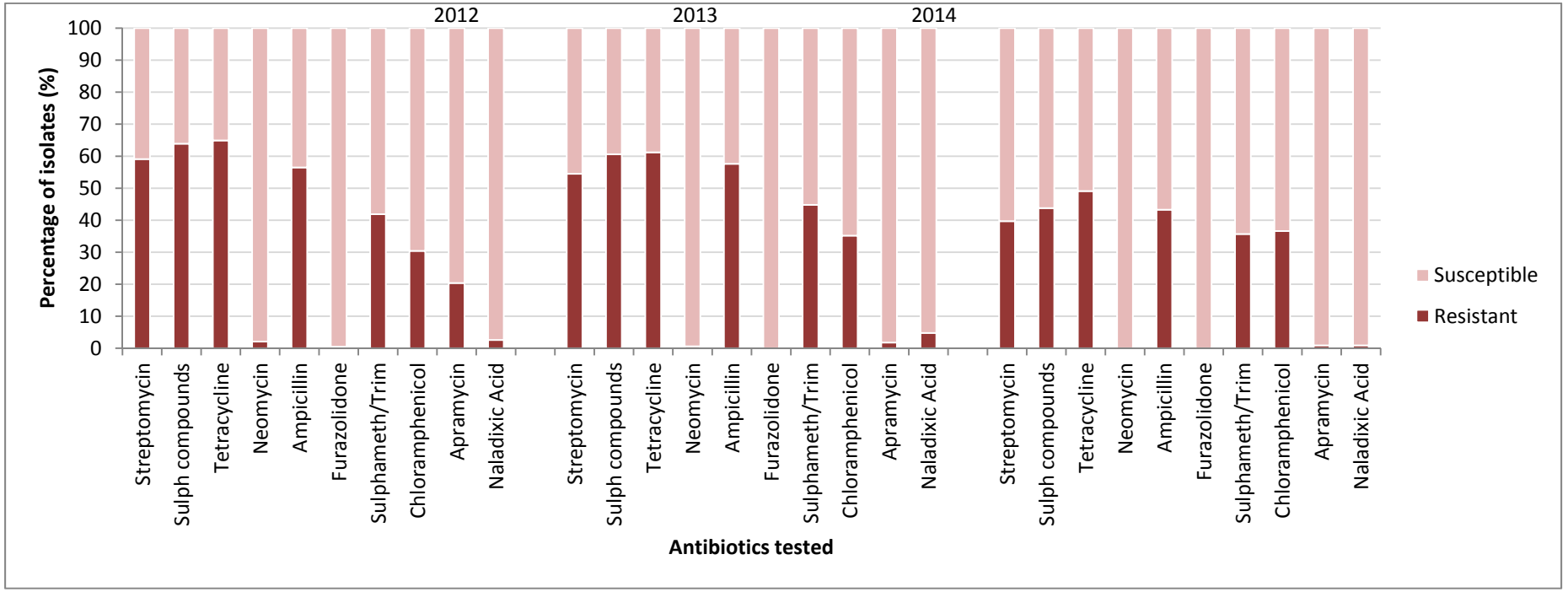
	Percentage of isolates resistant (%)		
Antibiotic	**2012**	**2013**	**2014**
Streptomycin	1.8	1.3	2.4
Chloramphenicol	0.3	0	0
Sulphonamide compounds	0	0	0.7
Tetracycline	0.3	0	1.1
Neomycin	0	0.3	0.3
Ampicillin	0.6	0.3	0.7
Furazolidone	0	0	0.3
Sulphamethoxazole/Trimethoprim	0	0	0.7
Naladixic Acid	0.6	1	0

Salmonella Typhimurium

224 isolates of *Salmonella* Typhimurium were subjected to antibiotic susceptibility testing in 2014. 44.2% of all *Salmonella* Typhimurium isolates investigated were sensitive to all of the antibiotics tested (**Figure 5.19**), which is a large increase from the figure of 30.3% observed in 2013, and 27.2% in 2012. The higher proportion of fully susceptible *S*. Typhimurium isolates has also influenced the figures for resistance to individual antibiotics in **Table A20.3** (**Annex 20**), with a decline in resistance evident for all antibiotics except chloramphenicol. There were no *Salmonella* Typhimurium isolates resistant to ceftazidime, cefotaxime, ciprofloxacin, amoxicillin/clavulanate, furazolidone, neomycin or amikacin in 2014.

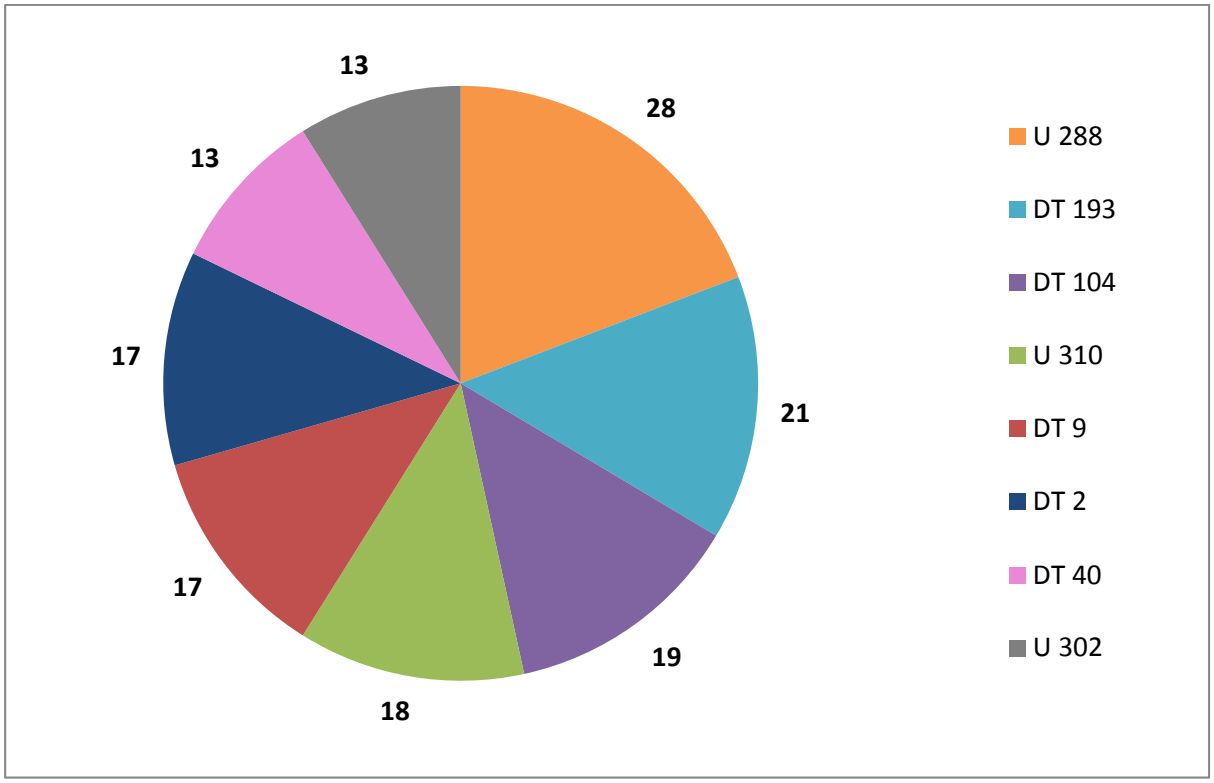
Considering all *S*. Typhimurium, a marked increase in resistance to sulphamethoxazole/trimethoprim from levels of around 16-24% in 1996-2001, to 32.7% to 57.9% in 2002-2007 has been observed, and discussed in previous reports. In 2008, the prevalence of resistance to sulphamethoxazole/trimethoprim was 26.4%, though in 2009 this increased to 40.7%; it was 27.1% in 2010, 37.5% in 2011, 41.9% in 2012, 44.8% in 2013 and 35.7% in 2014.

Figure 5.19: *Salmonella* Typhimurium: percentage of resistant isolates (n=224) between 2012-2014



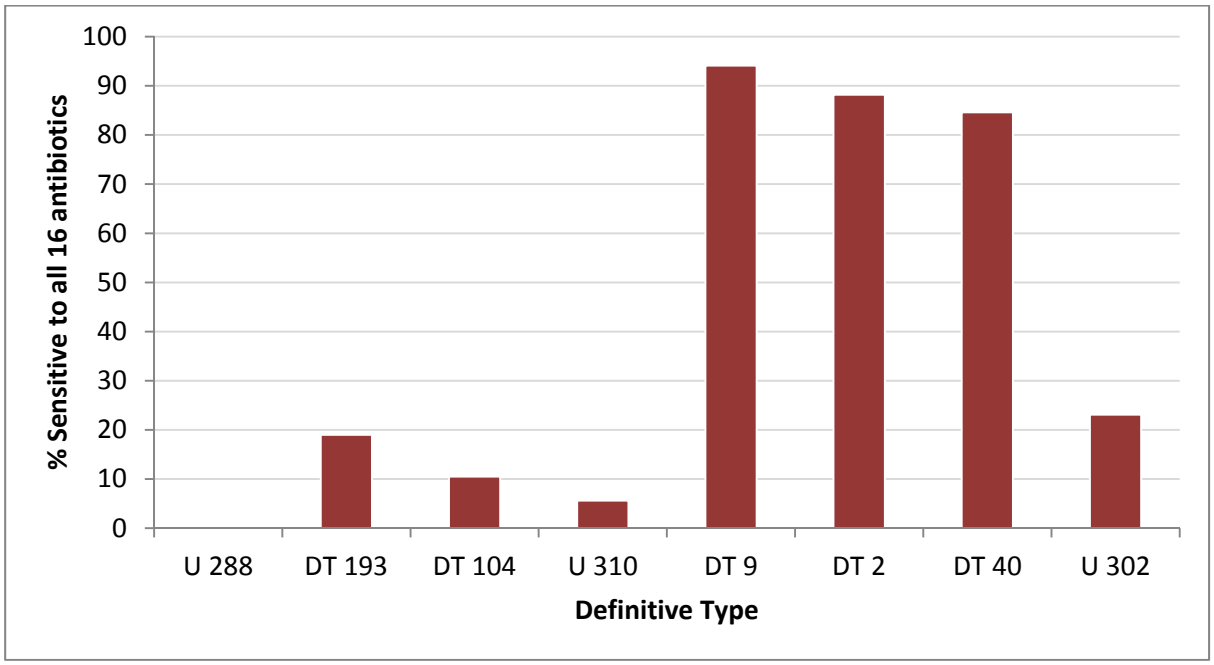
The generally high level of resistance of *Salmonella* Typhimurium isolates observed in recent years has partly been a reflection of the contribution of Typhimurium DT104 and its variants, DT104B and U302, which have contributed more than a quarter of isolates in some years in the previous decade. However, when considering the number of *Salmonella* Typhimurium isolates comprising DT104 and its variants over a longer time period, there has been a significant decline. A breakdown of the eight most frequent definitive or undefined types subjected to susceptibility testing in 2014 are presented in **Figure 5.20** – for more information on phage types prior to 2013 please see the *Salmonella* in Livestock Production Report.[30]

Figure 5.20: Number of isolates of *Salmonella* Typhimurium of the eight most frequent definitive or undefined types subjected to susceptibility testing in 2014



[30] https://www.gov.uk/government/statistics/salmonella-in-livestock-production-in-great-britain-2013

Figure 5.21: Percentage sensitivity of the most frequent definitive or undefined types of *Salmonella* Typhimurium subjected to susceptibility testing in 2014



In 2014, only 15% (5/33) of DT104, DT104B and U302 isolates were sensitive to all the antibiotics tested (**Figure 5.21**). Furthermore, 0% (0/20) of DT104 and 104B isolates from all sources were resistant to nalidixic acid and 20% (4/20) were resistant to sulphamethoxazole/trimethoprim. The sulphamethoxazole/trimethoprim resistant isolates originated from cattle (two), with single isolates from a pig (DT104B) and a horse. No isolates of DT104 were recovered from turkeys in 2012 to 2014; isolates from this source have commonly shown nalidixic acid resistance in previous years.

S. Typhimurium U288 and DT193 from pigs comprised 12.5% (28) and 5.8% (13) of the total numbers of *S*. Typhimurium isolates respectively; none of the U288 and DT193 isolates from pigs were fully susceptible in 2014. AmCSSuTTm was the commonest resistance pattern observed in both DT 193 isolates (ten isolates) and U288 isolates (23 isolates) from pigs. In *S*. Typhimurium DT104 and 104B, the commonest resistance pattern seen was the typical pentavalent resistance pattern AmCSSuT, which occurred in 11/20 isolates; three further isolates had this pentavalent resistance pattern with additional resistance to trimethoprim/sulphonamides.

Considering all *S.* Typhimurium types, apramycin resistance, which had increased in *S*. Typhimurium in 2011 to 20.4%, was 20.4% again in 2012. This was a notable change in comparison with preceding years where apramycin resistance has been consistently less than 5%. In 2013, apramycin resistance was 1.8% in *S.* Typhimurium, and then it 2014 it was 0.9%; a marked decline compared to 2011 and 2012. Over this period, isolates resistant to apramycin were also resistant to gentamicin.

Multiple antibiotic resistance was detected in definitive and undefined phage types 104, 193 and U302 from cattle; in phage types 193 from turkeys and in phage types 32, 104, 104B, 120, 193, U288, U302 and U308 from pigs. Of the 25 different definitive and undefined phage types detected, ten (namely 1, 7, 7variant, 29, 36, 41, 41B, 66A, 193A and U323) were fully susceptible to all of the antibiotics tested.

Monophasic *Salmonella* Serotypes

Fifty-nine isolates of the monophasic *Salmonella* 4,12:i:- were examined, belonging to phage types 20A (n=1), 120 (n=6), 193 (n=41) and U311 (n=3); eight isolates were not typable. Most isolates were from pigs (46%) with feed the next most common source of origin (10%). The commonest pattern of resistance observed was AmSSuT occurring in 27/41 DT 193 isolates, 3/3 U311 isolates, the single 20A isolate and 2/8 of the isolates which were not typable with phages. 39/41 DT 193 isolates (95%) had the basic AmSSuT resistance pattern alone or with one or more additional resistances.

A total of 133 isolates of the monophasic *Salmonella* 4,5,12:i:- were examined, including phage types 40 (n=1), 120 (n=5), 138 (n=1), 193 (n=109), 193A (n=1) and U311 (n=10); six isolates were un-typable. The commonest resistance pattern in DT 193 isolates was AmSSuT, occurring in 72% of isolates (79/109). Most isolates of DT 193 were from pigs (41%) and turkeys (18%).

Salmonella other than Dublin or Typhimurium

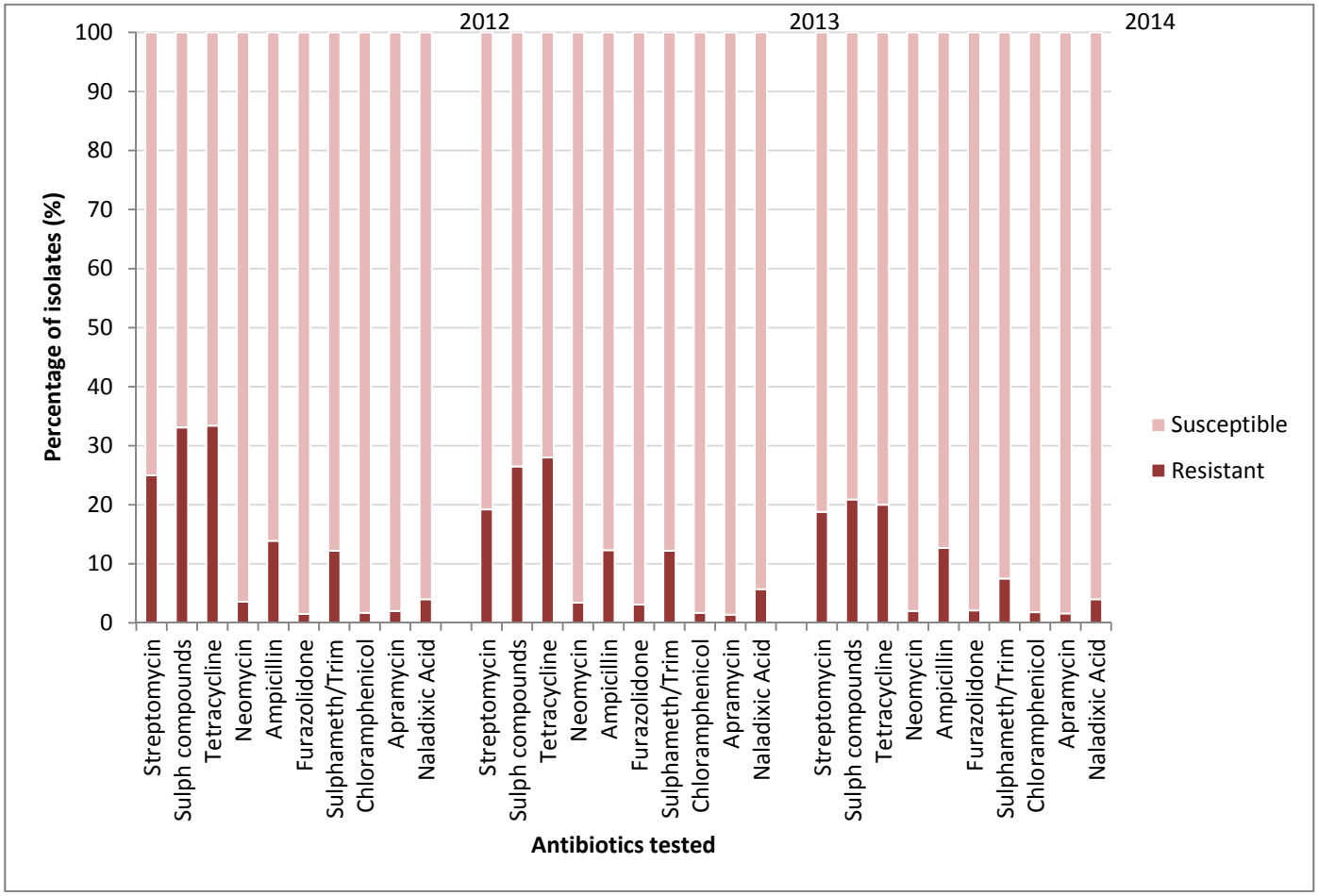
Of the 1,837 isolates of serotypes other than *S*. Dublin and *S*. Typhimurium tested, 68% were sensitive to all the antibiotics in the panel (**Table A20.4**, **Annex 20**), an increase on the figure recorded in 2013, when 61% were fully sensitive. Thirty-two (1.7%) of these isolates were *S.* Enteritidis and of these 29/32 (91%) were fully susceptible. *S*. Enteritidis DT8 was the only phage type which showed resistance to the panel of antibiotics tested and of ten isolates examined, 2/2 from horses were resistant to nalidixic acid and 1/2 from unknown mammalian species was resistant to tetracyclines; the remaining isolates were fully susceptible. The other phage types of *S.* Enteritidis isolates which were tested and in which resistance was not detected belonged to phage types 1b, 2, 4, 4b, 9a, 9b, 11, 13a, 20 and 23.

The percentage of *Salmonella* isolates (other than Dublin or Typhimurium) sensitive to the panel of 16 antibiotics is presented below in **Figure 5.22**. In 2014, neomycin resistant isolates originated mainly from ducks (191 isolates; 8.4% resistant), chickens (521 isolates; 1.7% resistant) and pigs (101 isolates; 7.9% resistant). The majority of the neomycin-resistant isolates from chickens were *Salmonella* Ohio (the same situation prevailed in 2011 - 2013). In ducks, *S*. Indiana was the main serotype showing resistance to neomycin (14/70 isolates resistant). The *S*. Indiana isolates from ducks were also frequently resistant to furazolidone (19/70 isolates).

The apparent increase in the prevalence of resistance to streptomycin, sulphonamides and tetracycline which was observed following 2009 reflected in part the increased monitoring of turkeys that has occurred in 2010-2013 under the Control of *Salmonella* in Turkeys Order. Considering *Salmonella* isolates other than Typhimurium and Dublin from turkeys in 2014 (n=142), 65% were resistant to streptomycin, 64% to sulphonamides and 60% to tetracyclines, similar to the equivalent figures for pigs in 2013 (72-78%), but higher than those for chickens (15-19%) or cattle (12-14%).

In 2014, the proportion of *Salmonella* isolates originating from feed increased from 1% to 22% and in both 2013 and 2014 most of these isolates (83-93%) were fully susceptible.

Figure 5.22: Salmonellas other than Dublin and Typhimurium, percentage of isolates resistant to antibiotics tested (n=1837), between 2012-2014



References

European Food Safety Authority (EFSA). 2007. Report including a proposal for a harmonized monitoring scheme for antimicrobial resistance in *Salmonella* in fowl (*Gallus gallus*), turkeys, and pigs and *Campylobacter jejuni* and *C. coli* in broilers. *The EFSA Journal*. 96:1-46.

European Food Safety Authority (EFSA). 2008. Report from the Task Force of Zoonoses Data Collection including guidance for harmonized monitoring and reporting of antimicrobial resistance in commensal *Escherichia coli* and *Enterococcus* spp. from food animals. *The EFSA Journal*. 141:1-44.

European Food Safety Authority and European Centre for Disease Prevention and Control. 2012. The European Union Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2010. The *EFSA Journal*. 10:2598 [233 pp.] doi:10.2903/j.efsa.2012.2598.

European Food Safety Authority (EFSA). 2012. Technical specifications for the analysis and reporting of data on antimicrobial resistance in the European Union Summary Report. The *EFSA Journal.* 10(2):2587. [53 pp.] doi:10.2903/j.efsa.2012.2587

García-Álvarez, L., Holden, M.T., Lindsay, H., *et al.* (2011). Methicillin-resistant *Staphylococcus aureus* with a novel *mecA* homologue in human and bovine populations in the UK and Denmark: a descriptive study. *Lancet Infectious Diseases.* 11:595–603.

Hinton, M. (1986). The ecology of *Escherichia coli* in animals including man with particular reference to drug resistance. *Veterinary Record.* 119:420-426.

Rønne, H., Szancer, J. (1990) In vitro susceptibility of Danish field isolates of *Treponema hyodysenteriae* to chemotherapeutics in swine dysentery (SD) therapy. Interpretation of MIC results based on the pharmacokinetic properties of the antibacterial agents. Proceedings of the 11th IPVS Congress. Lausanne, Switzerland, July 1 to 5, 1990. p 126

Schwarz, S., Woodford, N., van Duijkeren, E., Johnson, A.P., Gaastra, W. 2010. Assessing the antimicrobial susceptibility of bacteria obtained from animals. *Veterinary Microbiology*. 141:1-4.

Vanderhaeghen, W., Cerpentier, T., Adriaensen, C., Vicca, J., Hermans, K., and Butaye, P. (2010). Methicillin-resistant *Staphylococcus aureus* (MRSA) ST398 associated with clinical and subclinical mastitis in Belgian cows. *Veterinary Microbiology.* 144:166-171.

Veterinary Medicines Directorate. 2013. UK Veterinary Antibiotic Resistance and Sales Surveillance Report. *http://webarchive.nationalarchives.gov.uk/20140909112428/http://www.vmd.defra.gov.uk/pharm/antibiotic_salesdata.aspx*

Veterinary Medicines Directorate. 2014. UK Veterinary Antibiotic Resistance and Sales Surveillance Report. *https://www.gov.uk/government/publications/veterinary-antimicrobial-resistance-and-sales-surveillance-2013*

Annex 1 – European Population Correction Unit (PCU)

When assessing antibiotics sales it is important that the demographics of the animal population potentially exposed to treatment are also taken in to account, (see "data limitations"). **Table A1.1** shows the living population of UK food-producing animals recorded each year in Defra's June Census for each of the last five reporting years. All figures are quoted in thousands of individual animals and are not adjusted to take into account seasonality or for animals whose lives are shorter than a year.

Table A1.1: Numbers of Livestock (in 000s) in 2010–2014 by species

	2010	2011	2012	2013	2014*
Cattle	10112	9933	9900	9844	9837
Pigs	4460	4441	4481	4885	4815
Sheep	31084	31634	32215	32856	33743
Poultry	163867	162551	160061	162609	169684**

2013 Data have been validated since the previous report.

*2014 Data are provisional as they have not been fully validated at the time of printing.
**Census data is likely to be a large underestimate of the poultry population.

It is also necessary to take into account the varying weight of different animal species and the weight of each particular species at the time when they are most likely to have been treated with antibiotic products, since this is likely to be different to their weight at the time of slaughter. This is achieved through use of the PCU, a technical unit of measurement representing the estimated weight at treatment of livestock (1 PCU = 1 kg of different categories of livestock). The PCU also takes account of slaughtered animals over the course of a year, and is therefore a more accurate estimate of weight of livestock eligible for treatment over a year than raw census data would be. The annual ESVAC (European Surveillance of Veterinary Antimicrobial Consumption) report uses the PCU in order to estimate temporal trends in use or sales of antibiotics across different EU Member States. The PCU figures used in the analysis below are taken from the ESVAC scheme.

Table A1.2 shows the calculated combined UK PCU value for all food producing species, with subcategories showing the PCU for pigs, poultry and cattle. The standard formula used for calculation of the PCU for poultry does not include population figures for egg producers (laying hens) so the poultry PCU is likely to be an underestimate. In the UK the role of horses is predominantly as a companion or sport animal, so this species is excluded from the livestock PCU figure. The PCU for each reported animal category was calculated by multiplying the total number of each category of livestock animals in the UK (see foot-note to **Table A1.2**) by their theoretical weight at the age when antibiotic treatment is most likely to take place. The calculation takes into account animals exported from the UK for slaughter, or imported to the UK for fattening. Full details on the methodology of calculation of the PCU can be found in the 2009 ESVAC report, as can the average weight of each category of animal at treatment, as used in the PCU calculation.[31]

[31] http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/09/WC500112309.pdf

Table A1.2: Population correction unit (PCU) (in 1,000 tonnes) of the animal population, 2010–2014

	2010	2011	2012	2013	2014*
Total food producing species PCU (excluding horses)[1]	6275	6330	6354	6404	6518
- **Pig only PCU**	705	717	733	716	745
- **Poultry only PCU**	1009	1012	1040	1059	1042
- **Cattle only PCU**	1750	1767	1708	1692	1731

[1] *Total food producing species PCU includes cattle, pigs, sheep, goats, poultry (broilers) and fish.*

**PCU calculation for 2013 is based on import/export figures obtained from TRACES and EUROSTAT provided by ESVAC and Defra census data; at the time of publication these had nott undergone full ESVAC validation and therefore are provisional. Data from 2013 have undergone validation and have been updated since the previous report.*

Individual values for sheep and fish are not shown because the total amount of antibiotics sold for these species is small (less than three tonnes), (see section on antibiotic sales data; **Table x**). Companion animals are not included in the PCU as reliable population data cannot be collected, therefore antibiotic products authorised for use in both food and non-food animals are not included in the analysis.

Annex 2 – Cascade Prescribing

The Cascade is a legislative provision in the Veterinary Medicines Regulations that allows a veterinary surgeon to prescribe unauthorised medicines that would not otherwise be permitted e.g. imported medicines or a medicine licensed for human use. The principle of the Cascade is that, if there is no suitable veterinary medicine authorised in the UK to treat a condition, the veterinary surgeon responsible for the animal may in particular, to avoid causing unacceptable suffering, treat with an unauthorised medicine. Food producing animals may only be treated under the Cascade with medicines whose pharmacologically active substances are listed in the Table of Allowed Substances in Commission Regulation EU No 37/2010.

The data used in this report do not include data on sales of human antibiotics used in animals in accordance with the prescribing cascade, as currently there is no mechanism by which such information can be obtained. However, the understanding is that use of human products in food producing species is not extensive, due to issues with withdrawal periods.

The VMD continues to explore methods that can accurately incorporate information on the amounts of antibiotics imported into/exported from the UK and methods that can accurately incorporate sales of antibiotics licensed for humans that are sold for animal use under the Cascade prescribing system.

Annex 3 – European Surveillance of Veterinary Antimicrobial Consumption (ESVAC)

The European Commission (EC) has requested the European Medicines Agency (EMA) to take the lead in collating data collected on the use of antimicrobial agents in animals in the European Union. The EMA is developing a harmonised approach for the collection and reporting of data based on national sales figures. This is designed to be comparable with usage data of human antimicrobials.

Published ESVAC reports are available from:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000302.jsp

The ESVAC publication report sales figures in a slightly different way to the approach used in the UK. Currently the ESVAC project utilises data on antimicrobial products with specific Anatomical Therapeutic Chemical (ATC) codes, and these do not at the current time encompass the same breadth of products as the UK report. In addition, ESVAC methods for calculation of active ingredient relate directly to information held within the Summary of Product Characteristics (SPC) which does not always mean the calculation will report quantity of active moiety. The UK calculation always converts ingredients to the active moiety. Therefore, figures reported in the UK report(s) are not directly comparable with the UK data cited in the ESVAC report(s). We intend to continue to use the current reporting format for the UK sales data report, but periodically review the UK report as the ESVAC project develops.

For the calculation of the Population Control Unit (PCU), the UK-VARSS report does not include horses as a food producing animal, for the calculation used in the ESVAC report horses are included in this classification. In order to calculate the mg/PCU the UK-VARSS report takes into account those products which are authorised for use in food producing animals only, however this is not possible for the ESVAC report as not all Member States provide species level information. Therefore in the ESVAC report antibiotics administered as a tablet are excluded from the mg/PCU calculation and all other formulations are included. This is because it is considered that tablets are primarily used in the treatment of non-food producing animals. The above demonstrate why the mg/PCU figures in the ESVAC and UK-VARSS report are not directly comparable.

Annex 4 – Data limitations

Sales data

Antibiotic sales data are considered to be an overestimate of use

- Sales data do not permit accurate analysis of antibiotic consumption by animal species or production category. Some formulations of antibiotics are authorised with indications for use in more than one species, eg pigs and poultry. It is not possible to ascertain from sales data in which species the product was used.
- A given quantity of antibiotic may represent many doses in small animals or few doses in large animals. It is not possible to predict the number of doses represented by the quantity sold.
- Changes in quantities of veterinary antibiotics sold should be considered in parallel with changes in the UK animal population over the corresponding time period. The populations of animal species are an important denominator and may vary quite markedly from year to year depending on market conditions for livestock derived food. Similarly variations in the size of the animals being treated should be taken into consideration as larger animals will require a larger relative quantity of antibiotics over a treatment period.
- To try and address the variation in animal populations and demographics, over time and between countries, the ESVAC project has developed a Population Correction Unit (PCU), a calculation that estimates the weight of the animal (or group of animals) receiving an antibiotic at the most likely time of administration. This unit is now used across EU member states and is currently the best approximation of consumption. We have used this form of analysis in this report.
- Sales data in general over estimate use, as not all antibiotics sold will be used. There is natural wastage resulting from pack sizes that do not meet dose need, and from drug expiry.
- Some products may be sold to UK feed mills for inclusion in feed which is then exported outside of the UK, currently there is no method for separating these sales from the total UK sales data, resulting in an over estimate of use in UK feed.
- Medication sold for use in humans may be used in animals under certain circumstances, according to the prescribing cascade; figures on such use are not included in the data presented. Further information on cascade prescribing can be found in **Annex 2.**

Population data:

- The food-producing animal population figures presented in this report are based on a single point in time “census”. While these figures can be considered accurately reflective of the total annual cattle population, they are less so for other animal species. The figures are least representative for poultry raised for meat where the total number at any one time only represent a small percentage of the total raised each year. The sheep population also varies significantly pre and post lambing season each year. These factors are taken into consideration when the PCU is calculated (see **Annex 1**).
- The population figures used in this report vary slightly to those used in the ESVAC report, which means the figures in this report cannot be directly compared with figures from the ESVAC reports (see **Annex 3**).

Resistance data, clinical surveillance

There are a number of limitations associated with the antibiotic resistance data reported here and they should be borne in mine when interpreting results. Isolates that are obtained through the clinical surveillance programme cannot be considered to accurately reflect the bacterial populations present within the general animal populations in the UK:

- This method of obtaining isolates is a "passive" form of surveillance; the samples obtained are not randomly selected and are susceptible to bias.

- Veterinary surgeons have the option to submit samples to private laboratories rather than APHA laboratories. The proportion of samples that APHA tests compared to other laboratories is not known, and therefore we cannot know how representative the samples processed by APHA are of total diagnostic submissions.

- Furthermore, geographical proximity of a farm or veterinary practice to an APHA diagnostic laboratory may have an impact on the submission rate of samples; clinical surveillance may therefore, naturally, over-represent the animal populations within certain geographical areas.

- It is also possible that the levels of resistance demonstrated by the clinical surveillance isolates presented in this report are higher than those seen in the wider bacterial populations present within animals in the UK as samples are more likely to be submitted from animals that have been unresponsive to initial antibiotic therapy, and thus the isolates recovered may have already been exposed to antibiotic pressure(s).

- Isolates from companion animals which are submitted to APHA are only investigated for antibiotic resistance if there is a public health concern, and therefore bacteria from these animal groups are under-represented in this report.

- The clinical surveillance section of the report details the number of bacterial isolates that underwent sensitivity testing, but not the number of animals from which samples were submitted for examination. Several bacteria may have been cultured from an individual animal.

- The diagnostic tests performed on any sample received through the clinical surveillance programme are dependent on the individual case; i.e. isolates of the same bacterial species are not always tested against the same panel of antibiotics. Therefore, if resistance is not detected in one isolate, it may not mean that resistance is not present, just that it was not tested for. This is especially true of commensal organisms.

- As explained in the Method (**page 45**), the breakpoints used for determining resistance for isolates recovered under the clinical surveillance programme are those as recommended by BSAC. These breakpoints were originally determined for human medicine and their use in veterinary medicine is based on the assumption that the concentration of antibiotic at the site of infection is the same in animals as it is in humans**.** Currently it is not known if this assumption is always correct, especially as different dosing regimens may be used in different animals and pharmacokinetics may vary between species.

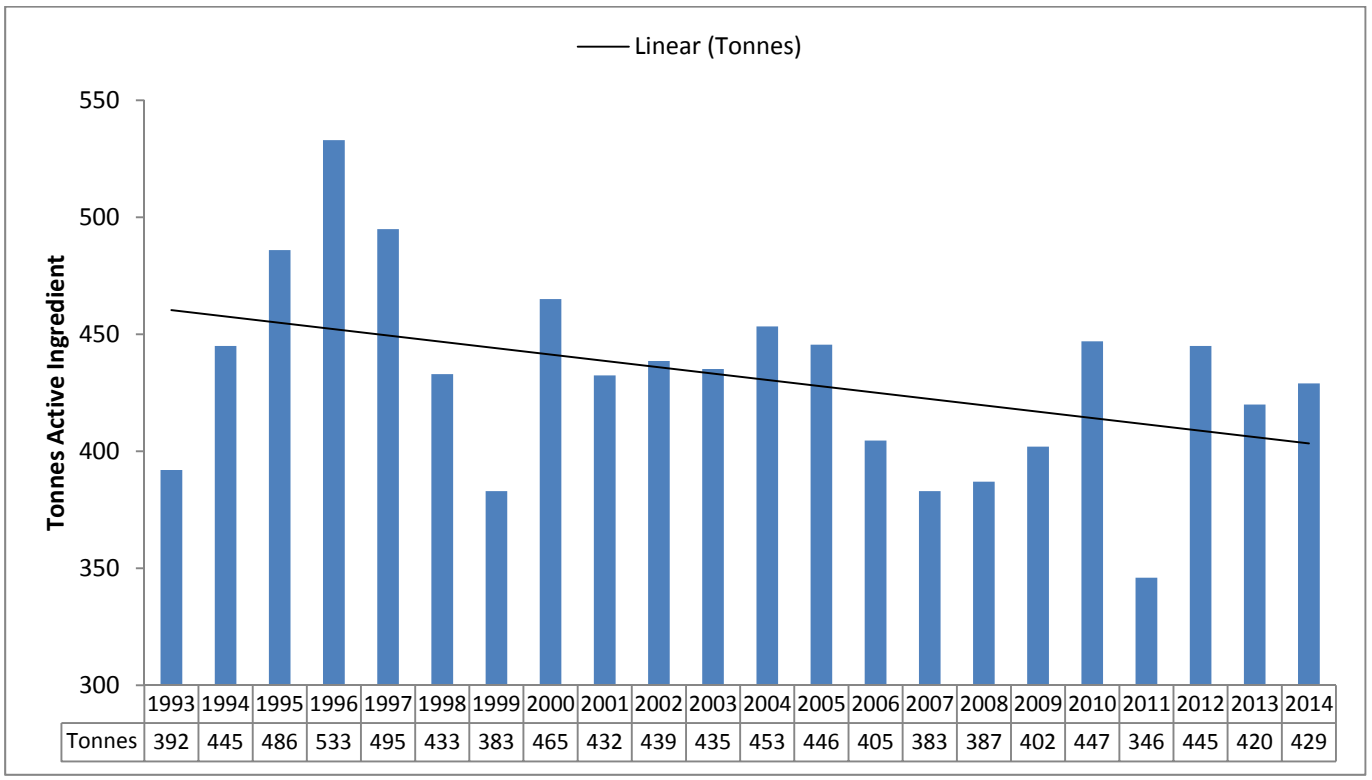
- As detailed in the Method section and **Annex 9**, in the case of some veterinary drug/bug combinations a BSAC cut-off may not exist; in which case a uniform APHA cut-off of 13mm is used to define resistance. The consequence of this is that some isolates that are considered to

be resistant based upon a BSAC breakpoint may actually be sensitive in a clinical veterinary setting, and vice-versa.

Annex 5 – Historical Data

The total quantities of antibiotic active ingredient sold between 1993 and 2014 are shown in **Figure A5.1.** Data have been collected from Market Authorisation Holders since 1993; from 2005 onwards data were provided as a statutory requirement. Data shown in **Figure A5.1** represent sales of antibiotics for therapeutic use only, and do not contain sales of products marketed as growth promoters which were banned in 2006.

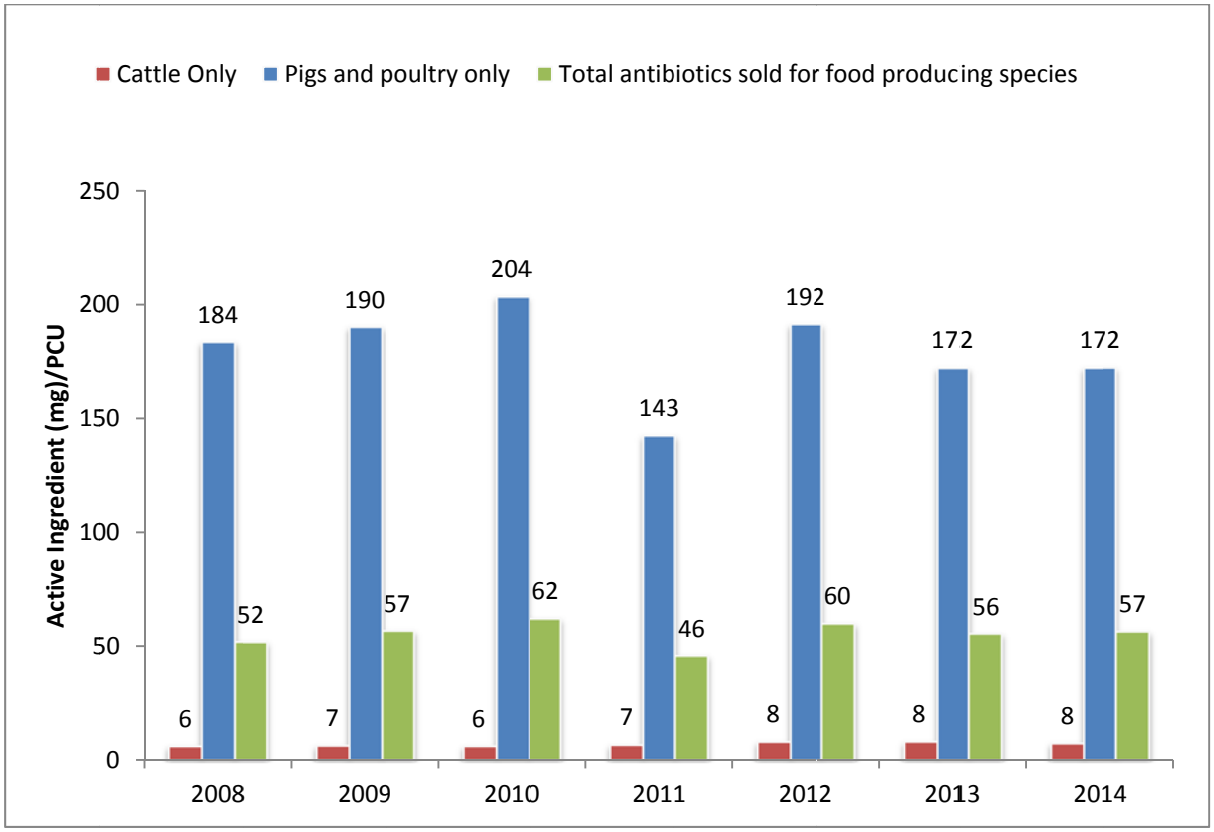
Figure A5.1: Sales (tonnes active ingredient) of antibiotic products 1993-2014



	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Tonnes	392	445	486	533	495	433	383	465	432	439	435	453	446	405	383	387	402	447	346	445	420	429

The European technical unit, PCU, has been adopted for the UK-VARSS report since 2012 however validated data are available from 2008 onwards, this data is presented in **Figure A5.2**.

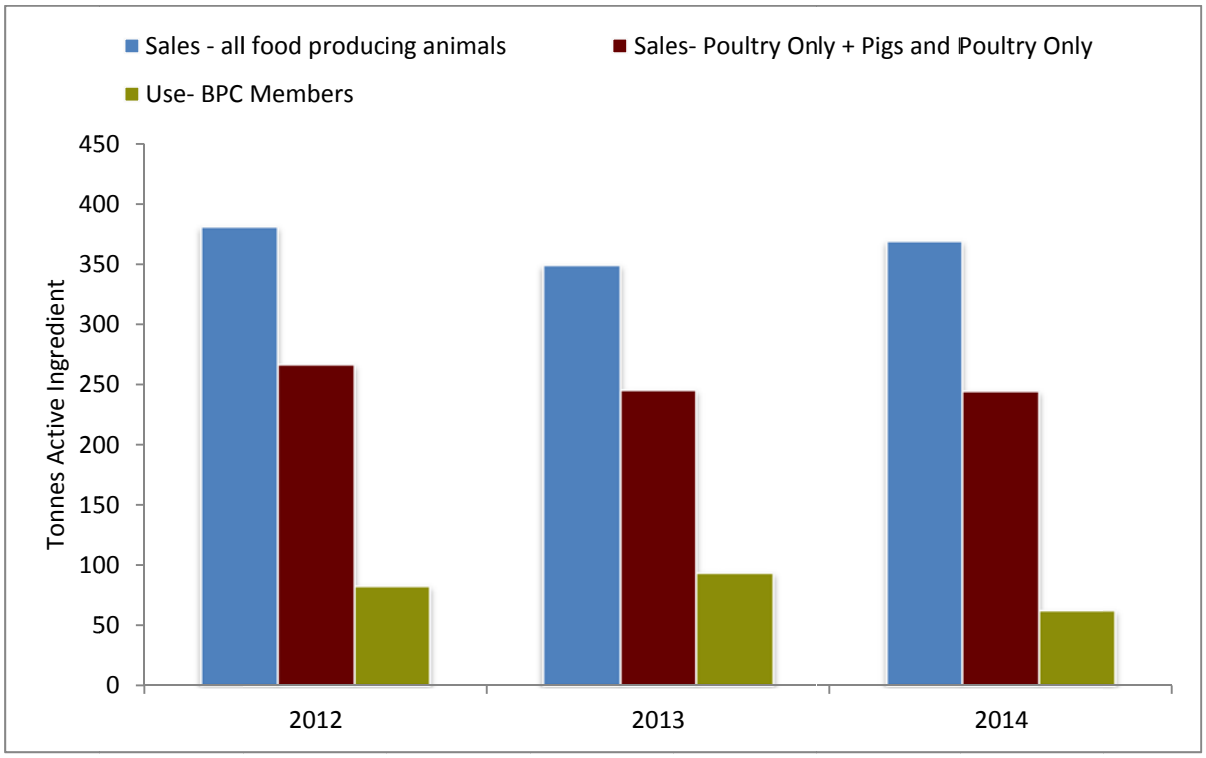
Figure A5.2: Milligrams (mg) of active ingredient of critically important antibiotics sold for food producing animals per population correction unit (PCU) for 2008-2014



Annex 6 – Antibiotic Consumption Data from the British Poultry Council

In 2014 BPC members used 62 tonnes of antibiotic active substance. ***Figure A6.1*** *shows the use of antibiotics recorded by BPC members, presented alongside sales of antibiotics for use in food producing animals, and sales of products indicated for use in poultry only or pigs and poultry only.*

Figure A6.1: Sales and use of antibiotics (tonnes active substance) 2012-2014



The limitations of sales data are again apparent when interpreting the information in this figure: the pig/poultry sales data shown in the red bar excludes products authorised for poultry in combination with non-poultry species (except pigs). In contrast, the BPC data in the green bar, representing actual use, may reflect any or all veterinary antibiotics authorised for chickens and/or turkeys and/or ducks (authorised in combination with other species or not), and may also include cascade (off-label) use of products not authorised for any poultry species. The data are thus presented together for interest only.

Focusing on the BPC data, **Figure A6.1** shows some variation in use of antibiotics recorded by BPC members since 2012. The highest use was recorded for 2013: 93 tonnes of antibiotic active substance. In 2014, this decreased by 31 tonnes to 62 tonnes, the lowest value over the three years BPC have been collecting these data. BPC have indicated that a reason for the higher overall use of antibiotics in meat poultry in 2013 may have been associated with quality of feed raw materials. The nutritional quality of locally produced raw materials used in poultry feed, wheat and barley, are heavily dependent on the weather conditions during the growing and harvest periods. Poorer quality feed is less easily digested and utilised by the birds and impacts significantly on the intestinal health of the birds. Feed quality was poor in 2012 and 2013 but improved in 2014. It is also interesting that the UK poultry population looks to have increased in size in 2014 compared with the two earlier years (see **Annex 1**; 2014 data not yet fully validated). Given that BPC members represent

approximately 90% of the UK poultry population, the reduction in use of antibiotics recorded during 2014 is encouraging.

Annex 7 – Summary of the EU Harmonised Monitoring Requirements of 2013/652/EU

	Sampling Year						
	2014	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Salmonella spp. - Broilers	x		x		x		x
Salmonella spp. - Layers	x		x		x		x
Salmonella spp. - Fattening Turkeys	x		x		x		x
Salmonella spp. - Broiler Carcases	x		x		x		x
Salmonella spp. - Fattening Turkey Carcases	x		x		x		x
Salmonella spp. - Pig Carcases		x		x		x	
Campylobacter jejuni - Broilers	x		x		x		x
Campylobacter jejuni - Fattening Turkeys	x		x		x		x
E. coli - Broiler Caeca	x		x		x		x
E. coli - Turkey Caeca	x		x		x		x
E. coli - Pig Caeca		x		x		x	
ESBL, AmpC and Carbapenemase producing *E. coli* - Broiler Caeca	x		x		x		x
ESBL, AmpC and Carbapenemase producing *E. coli* - Turkey Caeca	x		x		x		x
ESBL, AmpC and Carbapenemase producing *E. coli* - Pig Caeca		x		x		x	
ESBL, AmpC and Carbapenemase producing *E. coli* - Fresh broiler meat, pig meat and bovine meat gathered at retail	x	x	x	x	x	x	x
Campylobacter coli - Broilers	x		x		x		x
Campylobacter coli - Pigs		x		x		x	
E. faecium and *E. faecalis* - Broilers, Fattening Turkeys, Fattening Pigs, Bovines <1yr age	x	x	x	x	x	x	x

Key:
x = Mandatory
x = Voluntary
Pig and Bovine
Poultry

Note: The UK is exempt from the monitoring of resistance in isolates of bovine origin as we do not meet the cattle (<1 year of age) slaughter throughput as specified in the legislation.

Annex 8 – Sources of the bacteria to meet the EU Harmonised Monitoring Requirements of 2013/652/EU

Campylobacter spp.

Monitoring of *Campylobacter jejuni* in broilers and turkeys in 2014 was carried out as directed by the technical specifications outlined in Commission Decision 2013/652/EU.

Isolates of *Campylobacter jejuni* were cultured from caecal samples collected at slaughter from UK broilers (between January and December 2014) and turkeys (between June and December 2014). In accordance with the sampling framework, each isolate taken forward for resistance testing originated from a different flock of broilers or turkeys.

These results were submitted to EFSA and are expected to be published in the EU Summary Report on Antimicrobial Resistance for 2014 (EFSA and ECDC, in preparation).

Escherichia coli

Monitoring of antibiotic resistance in indicator *E. coli* recovered from healthy broilers and turkeys in 2014 was also based on the EU technical specifications in Commission Decision 2013/652/EU.

Similarly to the *Campylobacter* isolates, these *E. coli* were isolated from caecal samples collected at slaughter from UK broilers (between January – December 2014) and turkeys (between June – December 2014). In accordance with the sampling framework as specified in the legislation, each isolate taken forward for resistance testing originated from a different flock of broilers or turkeys.

These results were submitted to EFSA and are expected to be published in the EU Summary Report on Antimicrobial Resistance for 2014 (EFSA and ECDC, in preparation).

Salmonella spp.

A subset of Isolates collected under the *Salmonella* National Control Plans from broilers, layers and turkeys throughout 2014 were randomly selected and tested for antibiotic resistance in accordance with the recommendations of EFSA (EFSA, 2007) to fulfil the requirements of Commission decision 2013/652/EU.As for *Campylobacter* and *E. coli*, the *Salmonella* isolates discussed in this report originate from poultry from all parts of the UK. Flocks are sampled on-farm, via the collection of 'boot swab' samples from a representative proportion of the poultry house in accordance with Reg (EU) No 200/2012[32].

As with the *Campylobacter* and *E. coli* data, these results have been submitted to EFSA and will be published in the EU Summary Report on Antimicrobial Resistance for 2014 (EFSA and ECDC, in preparation).

[32] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:071:0031:0036:EN:PDF

Annex 9 – Disc diffusion breakpoints, corresponding MIC breakpoints and breakpoints under review for the clinical surveillance isolates included in this report

Antibiotic	Disc charge (micrograms)	*Escherichia coli*, Enterobacteriaceae	*Salmonella*	*Staphylococci*	*Streptococci*	*Pasteurella, Mannheimia, Histophilus, Actinobacillus*
Amikacin (AK)	30	R ≤ 18mm R ≥ 16mg/l	R ≤ 18mm R ≥ 16mg/l	NA	NA	NA
Amoxicillin/ clavulanic acid (AMC)	20/10	R ≤ 14mm R > 8mg/l	R ≤ 14mm R > 8mg/l	NA	NA	R ≤ 13mm
Amoxicillin/ clavulanic acid	2/1	NA	NA	R ≤ 17mm R > 1mg/l	R ≤ 13mm	NA
Ampicillin (AM)	10	R ≤ 14mm R > 8mg/l	R ≤ 14mm R > 8mg/l	R ≤ 13mm	R ≤ 13mm	R ≤ 29mm R > 1mg/l
Apramycin (APR)	15	R ≤ 13mm R ≥ 32 mg/l	R ≤ 13mm R ≥ 32 mg/l	NA	NA	R ≤ 13mm[†]
Cefotaxime (CTX)	30	R ≤ 29mm R ≥ 2mg/l	R ≤ 29mm R ≥ 2mg/l	NA	NA	NA
Cefpodoxime	10	R ≤ 19mm R > 1mg/l	NA	NA	NA	R ≤ 13mm
Ceftazidime (CAZ)	30	R ≤ 26mm	R ≤ 26mm	NA	NA	NA

		R ≥ 2mg/l	R ≥ 2mg/l			
Cefalexin	30	R ≤ 15mm R > 16mg/l	NA	R ≤ 13mm	R ≤ 24mm R > 2mg/l	R ≤ 13mm
Chloramphenicol (C)	30	R ≤ 20mm R > 8mg/l	R ≤ 20mm R > 8mg/l	NA	NA	NA
Ciprofloxacin (CIP)	1	NA	R ≤ 16mm R ≥ 1mg/l	NA	NA	NA
Doxycycline	30	R ≤ 13mm	NA	R ≤ 30mm R ≥ 2mg/l	NA	R ≤ 13mm
Erythromycin	5	NA	NA	R ≤ 19mm R ≥ 2mg/l	R ≤ 21mm* R ≥ 0.5mg/l	R ≤ 13mm
Enrofloxacin	5	R ≤ 13mm R ≥ 4mg/l	NA	R ≤ 13mm	R ≤ 13mm	R ≤ 13mm
Florfenicol	30	R ≤ 13mm R > 32mg/l	NA	NA	R ≤ 13mm	R ≤ 13mm
Furazolidone (FR)	15	NA	≤13mm	NA	NA	NA
Gentamicin (CN)	10	NA	R ≤ 19mm R ≥ 4mg/l	NA	NA	NA
Lincomycin	10	NA	NA	R ≤ 13mm	R ≤ 13mm	R ≤ 13mm

Nalidixic acid (NA)	NA	NA	≤ 13mm	NA	NA	NA
Neomycin (N)	10	R ≤ 13mm R > 8mg/l	R ≤ 13mm R > 8mg/l	NA	NA	NA
Neomycin	30	NA	NA	R ≤ 13mm	R ≤ 13mm	NA
Novobiocin	30	NA	NA	R ≤ 13mm	R ≤ 13mm	NA
Penicillin	1IU	NA	NA	R ≤ 24mm R > 0.12mg/l	R ≤ 19mm** R > 0.25mg/l	R ≤ 21mm R > 0.12 mg/l
Spectinomycin	25	R ≤ 13mm	NA	NA	NA	R ≤ 13mm†
Streptomycin (S)	10	R ≤ 12mm R > 8mg/l	R ≤ 13mm R > ~8mg/l	NA	NA	R ≤ 13mm†
Sulphonamide compounds (SU)	300	NA	≤ 13mm	NA	NA	NA
Tetracycline (T)	10	R ≤ 13mm R > 8mg/l	R ≤ 13mm R > 8mg/l	R ≤ 19mm R ≥ 2mg/l	R ≤ 19mm*** R ≥ 2mg/l	R ≤ 25mm
Trimethoprim/ sulphonamide (TM)	25	R ≤ 15mm R ≥ 4mg/l	R ≤ 15mm R ≥ 4mg/l	R ≤ 16mm R ≥ 4mg/l	R ≤ 19mm R ≥ 2mg/l	R ≤ 13mm
Tylosin	30	NA	NA	R ≤ 13mm	R ≤ 13mm	R ≤ 13mm

Key:

BSAC human clinical breakpoint.

Animal and Plant Health Agency (APHA) historical veterinary disc diffusion zone size breakpoint and MIC corresponding to that zone size breakpoint.

Animal Health and Veterinary Laboratories Agency (AHVLA) historical veterinary breakpoint (under ongoing review).

Notes:

- Where zone size disc diffusion data collected using the BSAC method and MIC data are both available then it is possible to draw regression lines and investigate the MIC which approximately corresponds to the historical veterinary breakpoint of 13mm. This has been done for several compounds (highlighted in blue in the table above).
- BSAC state that all *Salmonella* isolates should be reported as resistant to gentamicin and amikacin; resistance traits are used for epidemiological purposes (correlation with particular resistance mechanisms) in this report.
- The 16 antibiotics with antibiotic code e.g. amikacin (AK) are the set used for *Salmonella* susceptibility testing.
- Some *Haemophilus-Pasteurella-Actinobacillus* i.e. "HPA" organisms, for example *Actinobacillus pleuropneumoniae*, show a degree of intrinsic resistance to aminoglycosides.

* Erythromycin R $\leq$ 21mm for beta-haemolytic streptococci; R $\leq$ 19mm for other streptococci.
** Penicillin R $\leq$ 19mm for beta-haemolytic streptococci; R $\leq$ 16mm for other streptococci.
*** Tetracycline R $\leq$ 19mm for beta-haemolytic streptococci; R $\leq$ 23mm for other streptococci.

Annex 10 – EU Harmonised Monitoring, *Campylobacter jejuni* data

Table A10.1: Percentage non-susceptibility in *Campylobacter jejuni* isolates from broilers in 2013 and 2014, and from turkeys in 2014

Antibiotic	Percentage (%) of isolates non-susceptible in 2013 (n=61) (Broilers)	Percentage (%) of isolates non-susceptible in 2014 (n=165) (Broilers)	Percentage (%) of isolates non-susceptible in 2014 (n=157) (Turkeys)
Tetracyclines	47.5	58.8	65
Ciprofloxacin	31.1	43.6	35
Nalidixic Acid	31.1	44.2	35
Streptomycin	0	0	1.3
Gentamicin	0	0	1.3
Erythromycin	0	0	<1%

Annex 11 – EU Harmonised Monitoring, *E. coli* data

Table A11.1: Proportion of non-susceptible *Escherichia coli* isolates from broilers and turkeys in 2014

Antibiotic	Number of isolates non-susceptible using human clinical breakpoints (EUCAST)		Number of isolates non-susceptible using ECVs (EUCAST)	
	Broilers	Turkeys	Broilers	Turkeys
Tetracyclines	97/159 (61%)	132/168 (78.6%)	97/159 (61%)	132/168(78.6%)
Chloramphenicol	20/159 (12.6%)	20/168 (11.9%)	14/159 (8.8%)	17/168(10.1%)
Ampicillin	116/159 (73.0%)	116/168 (69.0%)	116/159 (73.0%)	116/168 (69.0%)
Cefotaxime	0/159 (0%)	0/168 (0%)	0/159 (0%)	0/168 (0%)
Ceftazidime	0/159 (0%)	0/168 (0%)	0/159 (0%)	0/168 (0%)
Meropenem	0/159 (0%)	0/168 (0%)	0/159 (0%)	0/168 (0%)
Nalidixic acid	39/159 (24.5%)	31/168 (18.5%)	39/159 (24.5%)	31/168 (18.5%)
Ciprofloxacin	6/159 (3.8%)	12/168 (7.1%)	39/159 (24.5%)	29/168 (17.3%)
Sulphonamide	*	*	104/159 (65.4%)	54/168 (32.1%)
Trimethoprim	75/159 (47.2%)	40/168 (23.8%)	75/159 (47.2%)	40/168 (23.8%)
Gentamicin	31/159 (19.5%)	7/168 (4.2%)	32/159 (20.1%)	7/168 (4.2%)
Azithromycin	*	*	**	**
Colistin	0/159 (0%)	0/168 (0%)	0/159 (0%)	0/168 (0%)
Tigecycline	0/159 (0%)	0/168 (0%)	0/159 (0%)	0/168 (0%)

* denotes that a BSAC human clinical breakpoint is not available for this antibiotic
** denotes that a EUCAST epidemiological cut-off value (ECV) is not available for this antibiotic

Annex 12 – EU Harmonised Monitoring, *Salmonella* data

Table A12.1: Proportion of non-susceptible *Salmonella* isolates from broilers, laying hens and turkeys sampled under the National Control Programme in 2014

Antibiotic	Number of isolates non-susceptible using human clinical breakpoints (EUCAST)			Number of isolates non-susceptible using ECVs (EUCAST)		
	Broilers	Laying Hens	Turkeys	Broilers	Laying Hens	Turkeys
Tetracyclines	34/168 (20.2%)	0/58 (0%)	79/162 (48.8%)	34/168 (20.2%)	0/58 (0%)	79/162 (48.8%)
Chloramphenicol	12/168 (7.1%)	1/58 (1.7%)	25/162 (15.4%)	2/168 (1.2%)	0/58 (0%)	1/162 (0.6%)
Ampicillin	6/168 (3.6%)	0/58 (0%)	37/162 (22.8%)	6/168 (3.6%)	0/58 (0%)	37/162 (22.8%)
Cefotaxime	0/168 (0%)	0/58 (0%)	0/162 (0%)	0/168 (0%)	0/58 (0%)	0/162 (0%)
Ceftazidime	0/168 (0%)	0/58 (0%)	0/162 (0%)	0/168 (0%)	0/58 (0%)	0/162 (0%)
Meropenem	0/168 (0%)	0/58 (0%)	0/162 (0%)	0/168 (0%)	0/58 (0%)	0/162 (0%)
Nalidixic acid	6/168(3.6%)	1/58 (1.7%)	33/162 (20.4%)	6/168(3.6%)	1/58 (1.7%)	33/162 (20.4%)
Ciprofloxacin	0/168 (0%)	0/58 (0%)	0/162 (0%)	6/168 (3.6%)	1/58 (1.7%)	33/162 (20.4%)
Sulphonamide	*	*	*	52/168 (31.0%)	0/58 (0%)	74/162 (45.7%)
Trimethoprim	32/168 (19.0%)	0/58 (0%)	12/162 (7.4%)	32/168 (19.0%)	0/58 (0%)	12/162 (7.4%)
Gentamicin	12/168 (7.2%)	0/58 (0%)	0/162 (0%)	14/168 (8.3%)	0/58 (0%)	0/162 (0%)
Azithromycin	*	*	*	**	**	**
Colistin	0/168 (0%)	3/58 (5.2%)	0/162 (0%)	0/168 (0%)	3/58 (5.2%)	0/162 (0%)
Tigecycline	0/168 (0%)	0/58 (0%)	3/162 (1.9%)	10/168 (6.0%)	0/58 (0%)	13/162 (8.0%)

* denotes that a EUCAST clinical breakpoint is not available for this antibiotic
** denotes that a EUCAST epidemiological cut-off value (ECV) is not available for this antibiotic

Table A12.2: Proportion of non-susceptibility in *Salmonella* isolates from broilers sampled under the National Control Programme, in 2012, 2013 and 2014

Antibiotic	Percentage non-susceptibility (interpreted using ECVs)		
	2012	2013	2014
Tetracyclines	43/170 (25.3%)	39/170 (22.9%)	34/168 (20.2%)
Chloramphenicol	5/170 (2.9%)	5/170 (2.9%)	2/168 (1.2%)
Ampicillin	8/170 (4.7%)	19/170 (11.2%)	6/168 (3.6%)
Cefotaxime	0/170 (0%)	0/170 (0%)	0/168 (0%)
Nalidixic acid	4/170 (2.4%)	7/170 (4.1%)	6/168(3.6%)
Ciprofloxacin	4/170 (2.4%)	7/170 (4.1%)	6/168 (3.6%)
Sulphonamide	37/170 (21.8%)	33/170 (19.4%)	52/168 (31.0%)
Trimethoprim	23/170 (13.5%)	30/170 (17.6%)	32/168 (19.0%)
Gentamicin	10/170 (5.8%)	8/170 (4.7%)	14/168 (8.3%)

Table A12.3: Proportion of non-susceptibility in *Salmonella* isolates from laying hens sampled under the National Control Programme, in 2012, 2013 and 2014

Antibiotic	Percentage non-susceptibility (interpreted using ECVs)		
	2012	2013	2014
Tetracyclines	8/66 (12.1%)	8/56 (14.3%)	0/58 (0%)
Chloramphenicol	0/66 (0%)	0/56 (0%)	0/58 (0%)
Ampicillin	2/66 (3%)	7/56 (12.5%)	0/58 (0%)
Cefotaxime	0/66 (0%)	0/56 (0%)	0/58 (0%)
Nalidixic acid	1/66 (1.5%)	0/56 (0%)	1/58 (1.7%)
Ciprofloxacin	1/66 (1.5%)	0/56 (0%)	1/58 (1.7%)
Sulphonamide	4/66 (6.1%)	7/56 (12.5%)	0/58 (0%)
Trimethoprim	2/66 (3.0%)	1/56 (1.8%)	0/58 (0%)
Gentamicin	0/66 (0%)	0/56 (0%)	0/58 (0%)

Table A12.4: Proportion of non-susceptibility in *Salmonella* isolates from turkeys sampled under the National Control Programme, in 2012, 2013 and 2014

Antibiotic	Percentage non-susceptibility (interpreted using ECVs)		
	2012	2013	2014
Tetracyclines	109/142 (76.8%)	117/170 (68.8%)	79/162 (48.8%)
Chloramphenicol	1/142 (<1%)	0/170 (0%)	1/162 (0.6%)
Ampicillin	45/142 (32.0%)	44/170 (25.9%)	37/162 (22.8%)
Cefotaxime	0/142 (0%)	0/170 (0%)	0/162 (0%)
Nalidixic acid	14/142 (9.9%)	24/170 (14.1%)	33/162 (20.4%)
Ciprofloxacin	14/142 (9.9%)	24/170 (14.1%)	33/162 (20.4%)
Sulphonamide	113/142 (79.6%)	119/170 (70%)	74/162 (45.7%)
Trimethoprim	24/142 (16.9%)	22/170 (12.9%)	12/162 (7.4%)
Gentamicin	1/142 (<1%)	0/170 (0%)	0/162 (0%)

Annex 13 – Clinical surveillance data for isolates from bovine mastitis cases

Table A13.1: Proportion of non-susceptibility (interpreted using BSAC human clinical breakpoints) in *Escherichia coli* mastitis isolates, from 2012-2014

	Mastitis Pathogens - *E. coli*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	5	8	9
Amoxicillin/Clavulanic acid	11/205 (5%)	13/159 (8%)	11/149 (7%)
Ampicillin	56/205 (27%)	43/159 (27%)	36/149 (24%)
Cefotaxime	-	-	-
Cefpodoxime	1/205 (<1%)	1/159 (<1%)	3/149 (2%)
Ceftazidime	-	-	-
Cefalexin	-	-	-
Enrofloxacin	4/205 (2%)	0/159 (0%)	4/149 (3%)
Streptomycin	17/205 (8%)	10/159 (6%)	14/149 (9%)
Tetracycline	26/205 (13%)	13/159 (8%)	17/149 (11%)
Trimethoprim/Sulphonamide	11/205 (5%)	13/159 (8%)	13/149 (9%)

Table A13.2: Proportion of non-susceptibility (interpreted using BSAC human clinical breakpoints) in *Streptococcus dysgalactiae* mastitis isolates, from 2012-2014

	Mastitis Pathogens - *S. dysgalactiae*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	0	0	0
Amoxicillin/Clavulanic acid	0/69 (0%)	0/47 (0%)	0/41 (0%)
Ampicillin	0/69 (0%)	0/47 (0%)	0/41 (0%)
Neomycin	17/65 (26%)	4/47 (9%)	10/41 (24%)
Novobiocin	3/65 (5%)	4/47 (9%)	2/41 (5%)
Tetracycline	55/69 (80%)	43/47 (91%)	35/41 (85%)
Tylosin	6/69 (9%)	4/47 (9%)	4/41 (10%)

Table A13.3: Proportion of non-susceptibility (interpreted using BSAC human clinical breakpoints) in *Streptococcus uberis* (and *S. agalactiae* – see foot-note) mastitis isolates, from 2012-2014

	Mastitis Pathogens - *S. uberis*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	2	3	1
Amoxicillin/Clavulanic acid	0/256 (0%)	0/120 (0%)	0/122 (0%)
Ampicillin	0/256 (0%)	1/120 (1%)	0/122 (0%)
Neomycin	168/255 (66%)	83/119 (70%)	72/121 (60%)
Novobiocin	24/255 (9%)	8/119 (7%)	11/121 (9%)
Tetracycline	127/256 (50%)	70/120 (58%)	66/122 (54%)
Tylosin	47/256 (18%)	24/120 (20%)	20/122 (16%)

Note: One *S. agalactiae* isolate was recovered in 2013 – it was resistant to Novobiocin but sensitive to all other antibiotics tested.

Table A13.4: Proportion of non-susceptibility (interpreted using BSAC human clinical breakpoints) in *Staphylococcus aureus* mastitis isolates, from 2012-2014

	Mastitis Pathogens - *S. aureus*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	4	6	4
Amoxicillin/Clavulanic acid	21/147 (14%)	26/106 (25%)	12/82 (15%)
Ampicillin	57/147 (39%)	31/106 (29%)	29/82 (35%)
Neomycin	1/147 (1%)	0/106 (0%)	0/82 (0%)
Novobiocin	0/147 (0%)	0/106 (0%)	1/82 (1%)
Tetracycline	10/147 (7%)	13/106 (12%)	3/82 (4%)
Tylosin	1/147 (1%)	1/106 (1%)	1/82 (1%)

Table A13.5: Proportion of non-susceptibility (interpreted using BSAC human clinical breakpoints) in *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* mastitis isolates, from 2012-2014

	Mastitis pathogens					
	K. pneumoniae			*P. aeruginosa*		
Antibiotic	2012	2013	2014	2012	2013	2014
Amoxicillin/Clavulanic acid	0/3	3/12	1/7	4/4	5/5	3/3
Ampicillin	2/3	11/12	4/7	4/4	5/5	3/3
Cefotaxime	-	3/4	1/1	3/4	0/5	0/1
Cefpodoxime	-	-	-	4/4	5/5	3/3
Ceftazidime	-	3/4	1/1	0/4	0/5	0/1
Cefalexin	-	3/3	1/1	4/4	5/5	1/1
Enrofloxacin	0/3	0/12	0/7	0/4	0/5	0/3
Neomycin	0/2	1/9	1/7	2/4	1/4	2/3
Streptomycin	0/2	2/7	0/7	0/4	0/4	0/3
Tetracycline	0/3	4/12	2/7	4/4	5/5	3/3
Trimethoprim/Sulphonamide	0/3	1/12	1/7	3/4	4/5	3/3

Table A13.6: Proportion of non-susceptibility (interpreted using BSAC human clinical breakpoints) in *Trueperella pyogenes* mastitis isolates, from 2012-2014

	Mastitis Pathogens - *T. pyogenes*		
Antibiotic	2012	2013	2014
Amoxicillin/Clavulanic acid	0/22 (0%)	0/11	0/16
Ampicillin	0/22 (0%)	0/11	0/16
Neomycin	7/22 (32%)	2/11	3/16
Novobiocin	0/22 (0%)	0/11	0/16
Tetracycline	12/22 (55%)	7/11	7/16
Tylosin	5/22 (23%)	0/11	1/16

Annex 14 – Clinical surveillance data for isolates from respiratory infections of cattle, sheep, and pigs

Table A14.1: Susceptibility of *Pasteurella multocida* isolates from respiratory infections of cattle (interpreted using BSAC human clinical breakpoints), 2012-2014

	Respiratory Pathogens - Cattle, *P. multocida*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	0	3	0
Amoxicillin/Clavulanic acid	0/56 (0%)	0/39 (0%)	0/29 (0%)
Ampicillin	0/56 (0%)	3/39 (8%)	1/29 (3%)
Cefalexin	-	0/1	-
Cefpodoxime	0/56 (0%)	1/39 (3%)	0/29 (0%)
Enrofloxacin	0/56 (0%)	0/39 (0%)	0/29 (0%)
Florfenicol	0/48 (0%)	0/33 (0%)	0/26 (0%)
Tetracycline	18/56 (32%)	19/39 (49%)	9/29 (31%)
Trimethoprim/Sulphonamide	0/56 (0%)	0/39 (0%)	0/29 (0%)
Tylosin	-	-	-

Table A14.2: Susceptibility of *Mannheimia haemolytica* isolates from respiratory infections of cattle (interpreted using BSAC human clinical breakpoints), 2012-2014

	Respiratory Pathogens - Cattle, *M. haemolytica*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	0	n/a	n/a
Amoxicillin/Clavulanic acid	0/26 (0%)	0/17	0/12
Ampicillin	0/26 (0%)	0/17	0/12
Cefalexin	-	-	-
Cefpodoxime	0/26 (0%)	0/17	0/12
Enrofloxacin	0/26 (0%)	0/17	0/12
Florfenicol	0/26 (0%)	0/17	2/12
Tetracycline	2/26 (8%)	1/17	3/12
Trimethoprim/Sulphonamide	1/26 (4%)	0/17	0/12
Tylosin	-	-	-

Table A14.3: Susceptibility of *Histophilus somni* isolates from respiratory infections of cattle (interpreted using BSAC human clinical breakpoints), 2012-2014

	Respiratory Pathogens - Cattle, *H. somni*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	4	n/a	n/a
Amoxicillin/Clavulanic acid	1/26 (4%)	0/14	0/10
Ampicillin	1/26 (4%)	0/14	0/10
Cefalexin	0/1	-	-
Cefpodoxime	1/26 (4%)	0/14	0/10
Enrofloxacin	0/26 (0%)	0/14	0/10
Florfenicol	0/26 (0%)	0/14	0/10
Tetracycline	1/26 (4%)	0/14	0/10
Trimethoprim/Sulphonamide	0/26 (0%)	0/14	0/10
Tylosin	0/1	-	-

Table A14.4: Susceptibility of *Trueperella pyogenes* isolates from respiratory infections of cattle (interpreted using BSAC human clinical breakpoints), 2012-2014

	Respiratory Pathogens - Cattle, *T. pyogenes*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	0	n/a	n/a
Amoxicillin/Clavulanic acid	0/23 (0%)	0/12	0/13
Ampicillin	0/23 (0%)	0/12	0/13
Cefalexin	0/23 (0%)	0/12	0/13
Cefpodoxime	-	-	-
Enrofloxacin	-	-	-
Florfenicol	1/23 (4%)	0/12	0/13
Tetracycline	13/23 (57%)	7/12	8/13
Trimethoprim/Sulphonamide	8/23 (35%)	6/12	3/13
Tylosin	2/23 (9%)	0/12	0/13

Annex 15 – Clinical surveillance data for isolates from respiratory infections of sheep

Table A15.1: Susceptibility of *Pasteurella multocida* isolates from respiratory infections of sheep (interpreted using BSAC human clinical breakpoints), 2012-2014

	Respiratory Pathogens - Sheep, *P. multocida*		
Antibiotic	**2012**	**2013**	**2014**
Amoxicillin/Clavulanic acid	0/2	0/5	0/2
Ampicillin	0/2	0/5	0/2
Cefalexin	-	-	-
Cefpodoxime	0/2	0/5	0/2
Enrofloxacin	0/2	0/5	0/2
Florfenicol	0/2	0/5	0/2
Tetracycline	0/2	1/5	0/2
Trimethoprim/Sulphonamide	0/2	0/5	0/2
Tylosin	-	-	-

Table A15.2: Susceptibility of *Mannheimia haemolytica* isolates from respiratory infections of sheep (interpreted using BSAC human clinical breakpoints), 2012-2014

	Respiratory Pathogens - Sheep, *M. haemolytica*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	0	0	0
Amoxicillin/Clavulanic acid	0/33 (0%)	0/20 (0%)	0/24 (0%)
Ampicillin	0/33 (0%)	0/20 (0%)	0/24 (0%)
Cefpodoxime	0/33 (0%)	0/20 (0%)	0/24 (0%)
Enrofloxacin	0/33 (0%)	0/20 (0%)	0/24 (0%)
Florfenicol	0/33 (0%)	0/19	0/23 (0%)
Tetracycline	0/33 (0%)	0/20 (0%)	2/24 (8%)
Trimethoprim/Sulphonamide	0/33 (0%)	0/20 (0%)	1/24 (4%)

Table A15.3: Susceptibility of *Bibersteinia trehalosi* isolates from respiratory infections of sheep (interpreted using BSAC human clinical breakpoints), 2012-2014

	Respiratory Pathogens - Sheep, *B. trehalosi*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	0	n/a	0
Amoxicillin/Clavulanic acid	0/30 (0%)	0/18	0/21 (0%)
Ampicillin	0/30 (0%)	0/18	0/21 (0%)
Cefalexin	-	-	-
Cefpodoxime	0/30 (0%)	0/18	0/21 (0%)
Enrofloxacin	0/30 (0%)	0/18	0/21 (0%)
Florfenicol	0/30 (0%)	0/18	0/21 (0%)
Tetracycline	2/30 (7%)	1/18	0/21 (0%)
Trimethoprim/Sulphonamide	0/30 (0%)	0/18	0/21 (0%)
Tylosin	0	-	-

Table A15.4: Susceptibility of *Trueperella pyogenes* isolates from respiratory infections of sheep (interpreted using BSAC human clinical breakpoints), 2012-2014

	Respiratory Pathogens - Sheep, *T. pyogenes*		
Antibiotic	**2012**	**2013**	**2014**
Amoxicillin/Clavulanic acid	0/14	0/5	0/10
Ampicillin	0/14	0/5	0/10
Cefalexin	0/14	0/5	0/10
Cefpodoxime	-	-	-
Enrofloxacin	-	-	-
Florfenicol	0/13	0/5	0/9
Tetracycline	1/14	2/5	2/10
Trimethoprim/Sulphonamide	7/13	0/5	4/9
Tylosin	0/14	0/5	0/10

Annex 16 – Clinical surveillance data for isolates from respiratory infections of pigs

Table A16.1: Susceptibility of *Pasteurella multocida* isolates from respiratory infections of pigs (interpreted using BSAC human clinical breakpoints), 2012-2014

	Respiratory Pathogens - Pigs, *P. multocida*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	3	5	0
Amoxicillin/Clavulanic acid	0/31 (0%)	0/24 (0%)	0/27 (0%)
Ampicillin	2/40 (5%)	3/39 (8%)	1/33 (3%)
Apramycin	1/40 (3%)	4/39 (10%)	1/32 (3%)
Cefpodoxime	0/40 (0%)	0/39 (0%)	0/32 (0%)
Doxycycline	1/31 (3%)	1/24 (4%)	0/27 (0%)
Enrofloxacin	0/40 (0%)	0/39 (0%)	0/33 (0%)
Florfenicol	0/31 (0%)	0/24 (0%)	0/27 (0%)
Lincomycin	-	-	-
Neomycin	0/40 (0%)	4/39 (10%)	0/32 (0%)
Spectinomycin	0/40 (0%)	1/39 (3%)	0/32 (0%)
Streptomycin	1/31 (3%)	3/24 (13%)	3/27 (11%)
Tetracycline	27/40 (68%)	33/39 (85%)	27/33 (82%)
Trimethoprim/Sulphonamide	7/40 (18%)	9/39 (23%)	11/33 (33%)
Tylosin	2/31 (6%)	4/24 (17%)	1/28 (4%)

Table A16.2: Susceptibility of *Actinobacillus pleuropneumoniae* isolates from respiratory infections of pigs (interpreted using BSAC human clinical breakpoints), 2012-2014

	Respiratory Pathogens - Pigs, *A. pleuropneumoniae*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	50	n/a	n/a
Amoxicillin/Clavulanic acid	0/17	0/15	0/14
Ampicillin	3/22 (14%)	3/17	0/14
Apramycin	12/22 (55%)	8/17	4/14
Cefpodoxime	0/22 (0%)	0/17	0/14
Doxycycline	0/17	1/15	0/14
Enrofloxacin	0/22 (0%)	0/17	0/14
Florfenicol	0/17	0/15	0/14
Lincomycin	-	-	-
Neomycin	16/22 (73%)	7/17	5/14
Spectinomycin	12/22 (55%)	6/17	4/14
Streptomycin	12/17	5/15	5/14
Tetracycline	7/22 (32%)	6/17	4/14
Trimethoprim/Sulphonamide	4/22 (18%)	5/17	0/14
Tylosin	9/17	8/15	13/14

Table A16.3: Susceptibility of *Trueperella pyogenes* isolates from respiratory infections of pigs (interpreted using BSAC human clinical breakpoints), 2012-2014

	Respiratory Pathogens - Pigs, *T. pyogenes*		
Antibiotic	**2012**	**2013**	**2014**
Amoxicillin/Clavulanic acid	-	-	-
Ampicillin	0/5	0/2	0/5
Apramycin	-	-	-
Cefpodoxime	-	-	-
Doxycycline	-	-	-
Enrofloxacin	0/5	0/2	0/5
Florfenicol	-	-	-
Lincomycin	1/5	1/2	0/5
Neomycin	-	-	-
Spectinomycin	-	-	-
Streptomycin	-	-	-
Tetracycline	0/5	0/2	1/5
Trimethoprim/Sulphonamide	1/5	1/2	1/5
Tylosin	2/5	1/2	0/5

Annex 17 – 'Other Veterinary Pathogens' – clinical surveillance data for *S. aureus* from chickens

Table A17.1: Percentage non-susceptibility of *S. aureus* isolates from chickens, 2012-2014

	Chickens, *S. aureus*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	0	0	0
Amoxicillin/Clavulanic acid	0/23 (0%)	0/25 (0%)	0/25 (0%)
Ampicillin	4/29 (14%)	0/26 (0%)	0/26 (0%)
Doxycycline	1/29 (3%)	3/26 (12%)	2/26 (8%)
Enrofloxacin	0/29 (0%)	1/26 (4%)	0/26 (0%)
Erythromycin	0/25 (0%)	2/25 (8%)	2/25 (8%)
Lincomycin	6/29 (21%)	2/26 (8%)	2/26 (8%)
Tetracycline	2/29 (7%)	3/26 (12%)	3/26 (12%)
Trimethoprim/Sulphonamide	0/29 (0%)	0/26 (0%)	0/26 (0%)
Tylosin	0/29 (0%)	1/26 (4%)	0/26 (0%)

Annex 18 – 'Other Veterinary Pathogens' – clinical surveillance data for *S. suis* from pigs

Table A18.1: Susceptibility of *Streptococcus suis* isolates from pigs (interpreted using BSAC human clinical breakpoints), 2012-2014

	Pigs, *S. suis*		
Antibiotic	**2012**	**2013**	**2014**
Percent multi-resistant (%)	2	4	6
Ampicillin	0/58 (0%)	0/55 (0%)	0/64 (0%)
Penicillin	1/58 (2%)	1/55 (2%)	0/64 (0%)
Cefalexin	-	-	-
Enrofloxacin	0/58 (0%)	0/55 (0%)	0/64 (0%)
Lincomycin	20/58 (34%)	25/55 (45%)	21/64 (33%)
Tetracycline	54/58 (93%)	52/55 (95%)	61/64 (95%)
Trimethoprim/Sulphonamide	9/58 (16%)	7/55 (13%)	15/64 (23%)
Tylosin	26/58 (45%)	26/55 (47%)	24/64 (38%)

Annex 19 – Clinical surveillance data for *E. coli*

Table A19.1: Susceptibility of all *Escherichia coli* isolates from cattle, pigs, sheep, chickens and turkeys (all ages, combined) between 2012-2014

	All species, total, *E. coli*		
Antibiotic	**2012**	**2013**	**2014**
Total available / % multi-resistant	1571 / 54%	1404 / 51%	1150 / 57%
Amikacin	8/839 (<1%)	4/856 (<1%)	2/590 (<1%)
Amoxicillin/Clavulanic acid	555/1369 (41%)	447/1296 (34%)	314/1045 (30%)
Ampicillin	1020/1507 (68%)	892/1400 (64%)	733/1144 (64%)
Apramycin	107/1476 (7%)	85/1360 (6%)	73/1118 (7%)
Cefotaxime	125/846 (15%)	98/857 (11%)	80/593 (13%)
Cefpodoxime	55/534 (10%)	27/434 (6%)	19/481 (4%)
Ceftazidime	55/846 (7%)	53/857 (6%)	44/593 (7%)
Chloramphenicol	467/839 (56%)	440/856 (51%)	298/590 (51%)
Doxycycline	145/475 (31%)	86/371 (23%)	157/452 (35%)
Enrofloxacin	103/1507 (7%)	114/1400 (8%)	93/1144 (8%)
Florfenicol	270/969 (28%)	295/969 (30%)	209/764 (27%)
Neomycin	369/1360 (27%)	398/1282 (31%)	287/1049 (27%)
Spectinomycin	549/1476 (37%)	565/1360 (42%)	441/1118 (39 %)
Streptomycin	559/947 (59%)	556/933 (60%)	442/742 (60%)
Tetracycline	1005/1507 (67%)	932/1400 (67%)	779/1144 (68%)
Trimethoprim/Sulphonamide	546/1507 (36%)	508/1400 (36%)	442/1144 (39%)

Table A19.2: Susceptibility of all *Escherichia coli* isolates from cattle, pigs and sheep (all ages) between 2012-2014

Antibiotic	Cattle			Pigs			Sheep		
	2012	2013	2014	2012	2013	2014	2012	2013	2014
Total available / % multi-resistant	901 / 69%	782 / 73%	539 / 75%	134 / 59%	102 / 51%	180 / 67%	165 / 31%	225 / 46%	130 / 42%
Amikacin	8/757 (1%)	4/706 (1%)	2/492 (<1%)	-	-	-	0/82 (0%)	0/150 (0%)	0/98 (0%)
Amoxicillin/ Clavulanic acid	454/850 (53%)	385/780 (49%)	271/533 (51%)	11/104 (11%)	3/76 (4%)	6/151 (4%)	35/155 (23%)	48/224 (21%)	26/130 (20%)
Ampicillin	673/850 (79%)	617/780 (79%)	431/533 (81%)	88/131 (67%)	51/101 (50%)	104/180 (58%)	75/155 (48%)	125/224 (56%)	71/130 (55%)
Apramycin	59/831 (7%)	50/761 (7%)	22/517 (4%)	21/131 (16%)	14/101 (14%)	34/180 (19%)	2/143 (1%)	3/204 (1%)	3/120 (3%)
Cefotaxime	117/760 (15%)	94/707 (13%)	77/495 (16%)	-	-	-	5/82 (6%)	4/150 (3%)	3/98 (3%)
Cefpodoxime	-	-	-	4/131 (3%)	4/101 (4%)	7/180 (4%)	-	-	-
Ceftazidime	51/760 (7%)	52/707 (7%)	42/495 (8%)	-	-	-	3/82 (4%)	1/150 (<1%)	2/98 (2%)
Chloramphenicol	440/757 (58%)	386/706 (55%)	271/492 (55%)	-	-	-	27/82 (33%)	54/150 (36%)	27/98 (28%)
Doxycycline	-	-	-	57/104 (55%)	45/76 (59%)	90/151 (60%)	-	-	-
Enrofloxacin	81/850 (10%)	93/780 (12%)	60/533 (11%)	10/131 (8%)	8/101 (8%)	17/180 (9%)	1/155 (1%)	8/224 (4%)	1/130 (1%)
Florfenicol	258/776 (33%)	262/724 (36%)	190/507 (37%)	7/104 (7%)	5/76 (7%)	8/151 (5%)	5/95 (5%)	28/169 (17%)	11/106 (10%)
Neomycin	325/831 (39%)	332/761 (44%)	250/517 (48%)	16/131 (12%)	10/101 (10%)	7/180 (4%)	16/142 (11%)	36/205 (18%)	9/121 (7%)
Spectinomycin	402/831	380/761	231/517	38/131	34/101	86/180	62/143	108/204	52/120

	(48%)	(50%)	(45%)	(29%)	(34%)	(48%)	(43%)	(53%)	(43%)
Streptomycin	461/757 (61%)	439/706 (62%)	316/492 (64%)	55/104 (53%)	33/76 (43%)	82/151 (54%)	43/82 (52%)	84/151 (56%)	44/99 (44%)
Tetracycline	659/850 (78%)	595/780 (76%)	424/533 (80%)	95/131 (73%)	75/101 (74%)	142/180 (79%)	86/155 (55%)	153/224 (68%)	89/130 (68%)
Trimethoprim/ Sulphonamide	387/850 (46%)	359/780 (46%)	261/533 (49%)	63/131 (48%)	51/101 (50%)	102/180 (57%)	28/155 (18%)	62/224 (28%)	28/130 (22%)

Table A19.3: Susceptibility of all *Escherichia coli* isolates from chickens and turkeys (all ages) between 2012-2014

Antibiotic	Chickens 2012	Chickens 2013	Chickens 2014	Turkeys 2012	Turkeys 2013	Turkeys 2014
Total available / % multi-resistant	338 / 29%	289 / 15%	294 / 25%	33 / 27%	6	7
Amikacin	-	-	-	-	-	-
Amoxicillin/ Clavulanic acid	55/251 (22%)	11/215 (5%)	11/230 (5%)	0/9	0/1	0/1
Ampicillin	166/338 (49%)	94/289 (33%)	124/294 (42%)	18/33 (55%)	5/6	3/7
Apramycin	23/338 (7%)	18/288 (6%)	14/294 (5%)	2/33 (6%)	0/6	0/7
Cefotaxime	-	-	-	-	-	-
Cefpodoxime	49/338 (14%)	23/288 (8%)	12/294 (4%)	0/33 (0%)	0/6	0/7
Ceftazidime	-	-	-	-	-	-
Chloramphenicol	-	-	-	-	-	-
Doxycycline	73/338 (22%)	40/289 (14%)	65/294 (22%)	15/33 (45%)	1/6	2/7
Enrofloxacin	9/338 (3%)	5/289 (2%)	14/294 (5%)	2/33 (6%)	0/6	1/7
Florfenicol	-	-	-	0/1	-	-
Neomycin	12/248 (5%)	20/214 (9%)	21/230 (9%)	0/8	0/1	0/1
Spectinomycin	42/338 (12%)	43/288 (15%)	71/294 (24%)	5/33 (15%)	0/6	1/7
Streptomycin	-	-	-	0/1	-	-
Tetracycline	146/338 (43%)	104/289 (36%)	120/294 (41%)	19/33 (58%)	5/6	4/7
Trimethoprim/ Sulphonamide	61/338 (18%)	36/289 (12%)	50/294 (17%)	7/33 (21%)	0/6	1/7

Table A19.4: Susceptibility of all *Escherichia coli* isolates from neonatal, pre-weaning and adult cattle, between 2012-2014

	Neonatal			Pre-weaning			Adult		
Antibiotic	**2012**	**2013**	**2014**	**2012**	**2013**	**2014**	**2012**	**2013**	**2014**
Total available / % multi-resistant	735 / 70%	630 / 75%	452 / 75%	80 / 66%	86 / 70%	44 / 64%	14	17	11
Amikacin	6/644 <1%	3/599 1%	2/432 0.5%	2/51 4%	0/61 0%	0/28 0%	0/6	0/3	0/3
Amoxicillin/ Clavulanic acid	391/691 57%	330/629 52%	231/449 51%	31/79 39%	36/86 42%	20/44 45%	2/13	2/16	2/8
Ampicillin	560/691 81%	511/629 81%	365/449 81%	60/79 76%	69/86 80%	32/44 73%	5/13	5/16	6/8
Apramycin	51/683 7%	39/621 6%	20/442 5%	2/72 3%	5/78 6%	2/37 5%	1/11	1/14	0/7
Cefotaxime	94/645 15%	75/599 13%	64/432 15%	11/51 22%	12/61 20%	7/28 25%	1/7	0/4	4/6
Ceftazidime	42/645 7%	46/599 8%	32/432 7%	3/51 6%	4/61 7%	5/28 18%	0/7	0/4	3/6
Chloramphenicol	377/644 59%	333/599 56%	237/432 55%	33/51 65%	34/61 56%	12/28 43%	2/6	2/3	3/3
Enrofloxacin	67/691 10%	75/629 12%	52/449 12%	5/79 6%	9/86 10%	4/44 9%	1/13	2/16	2/8
Florfenicol	205/652 31%	215/606 35%	163/439 37%	29/58 50%	33/69 48%	10/35 29%	1/8	1/5	2/3
Neomycin	256/683 37%	276/621 44%	218/442 49%	34/72 47%	38/78 49%	18/37 49%	2/11	1/14	1/7
Spectinomycin	343/683 50%	329/621 53%	204/442 46%	30/72 42%	28/78 36%	11/37 30%	3/11	4/14	1/7
Streptomycin	383/644 59%	372/599 62%	278/432 64%	37/51 73%	43/61 70%	14/28 50%	3/6	2/3	2/3
Tetracycline	541/691 78%	489/629 78%	357/449 80%	67/79 85%	67/86 78%	37/44 84%	5/13	7/16	5/8
Trimethoprim/ Sulphonamide	312/691 45%	290/629 46%	217/449 48%	39/79 49%	46/86 53%	22/44 50%	4/13	4/16	3/8

Table A19.5: Susceptibility of all *Escherichia coli* isolates from neonatal, post-weaning and adult pigs, between 2012-2014

	Neonatal			Post-weaning			Adult		
Antibiotic	**2012**	**2013**	**2014**	**2012**	**2013**	**2014**	**2012**	**2013**	**2014**
Total available / % multi-resistant	47 / 66%	28 / 46%	39 / 51%	45 / 62%	36 / 69%	84 / 79%	4	6	7
Amoxicillin / Clavulanic acid	6/44 14%	1/18	0/25 0%	3/33 9%	2/31 6%	3/78 4%	0/2	0/4	0/6
Ampicillin	31/45 69%	16/28 57%	19/39 49%	36/45 80%	20/35 57%	51/84 61%	0/4	3/6	3/7
Apramycin	3/45 7%	0/28 0%	1/39 3%	17/45 38%	9/35 26%	31/84 37%	0/4	1/6	0/7
Cefpodoxime	4/45 9%	1/28 4%	0/39 0%	0/45 0%	1/35 3%	1/84 1%	0/4	0/6	0/7
Doxycycline	24/44 55%	11/18	12/25 48%	20/33 61%	20/31 65%	51/78 65%	0/2	1/4	3/6
Enrofloxacin	5/45 11%	3/28 11%	7/39 18%	0/45 0%	2/35 6%	5/84 6%	0/4	0/6	1/7
Florfenicol	1/44 2%	0/18	1/25 4%	3/33 9%	4/31 13%	4/78 5%	0/2	0/4	0/6
Neomycin	3/45 7%	2/28 7%	2/39 5%	9/45 20%	5/35 14%	2/84 2%	0/4	1/6	1/7
Spectinomycin	11/45 24%	9/28 32%	20/39 51%	18/45 40%	17/35 49%	44/84 52%	0/4	1/6	3/7
Streptomycin	23/44 52%	9/18	10/25 40%	17/33 52%	16/31 52%	49/78 63%	0/2	0/4	3/6
Tetracycline	33/45 73%	18/28 64%	30/39 77%	35/45 78%	26/35 74%	69/84 82%	1/4	4/6	5/7
Trimethoprim / Sulphonamide	26/45 58%	14/28 50%	19/39 49%	22/45 49%	21/35 60%	54/84 64%	1/4	2/6	2/7

Table A19.6: Susceptibility of all *Escherichia coli* isolates from neonatal, pre-weaning and adult sheep, between 2012-2014

	Neonatal			Pre-weaning			Adult		
Antibiotic	**2012**	**2013**	**2014**	**2012**	**2013**	**2014**	**2012**	**2013**	**2014**
Total available / % multi-resistant	119 / 38%	174 / 54%	105 / 46%	19	15	12	18	18	5
Amoxicillin/Clavulanic acid	30/109 28%	44/173 25%	23/105 22%	4/19	2/15	0/12	1/18	0/18	1/5
Ampicillin	60/109 55%	108/173 62%	58/105 55%	8/19	4/15	4/12	4/18	6/18	2/5
Apramycin	1/106 1%	3/170 2%	3/100 3%	0/14	0/10	0/11	0/15	0/9	0/2
Cefotaxime	5/76 7%	4/139 3%	3/89 3%	0/4	0/3	0/3	-	0/1	-
Ceftazidime	3/76 4%	1/139 <1%	2/89 2%	0/4	0/3	0/3	-	0/1	-
Chloramphenicol	25/76 33%	50/139 36%	26/89 29%	1/4	2/3	0/3	-	0/1	-
Enrofloxacin	1/109 <1%	6/173 3%	1/105 <1%	0/19	0/15	0/12	0/18	1/18	0/5
Florfenicol	3/80 4%	24/142 17%	11/93 12%	1/9	2/8	0/4	0/3	0/10	0/2
Neomycin	12/105 11%	33/170 19%	7/100 7%	2/14	2/10	1/11	1/15	0/9	0/3
Spectinomycin	55/106 52%	101/170 59%	45/100 45%	3/14	2/10	3/11	3/15	2/9	1/2
Streptomycin	40/76 53%	77/139 55%	38/89 43%	3/4	2/3	1/3	-	1/1	1/1
Tetracycline	65/109 60%	130/173 75%	71/105 68%	9/19	9/15	8/12	5/18	7/18	3/5
Trimethoprim/Sulphonamide	25/109 23%	54/173 31%	24/105 23%	2/19	4/15	1/12	0/18	2/18	1/5

Annex 20 – Clinical surveillance data for *Salmonella* spp.

Table A20.1: Percentage sensitivity of all *Salmonella* isolates from clinical and structured surveillance in 2014

Origin of isolates	No. of cultures	Percentage sensitive to all 16 antibiotics (%)	Na	Cip	S	N	Apr	Cn	Su	Tm	Am	Amc	Caz	Ctx	Fr	T	C
Cattle	427	89	0	0	8.2	0.2	0	0	7.7	2.1	7.5	0	0	0	0.5	8.2	2.8
Sheep	59	96.6	0	0	1.7	0	0	1.7	1.7	0	0	0	0	0	0	1.7	0
Pigs	204	18.6	1	0	68.6	3.9	8.8	8.8	74.5	46.1	68.1	0	0	0	0.5	74.5	36.8
Chickens	525	65.5	5.7	0.6	15.6	1.7	2.3	2.9	19.2	9.3	6.1	0	0	0	1.3	14.5	3.6
Turkeys	143	14	18.2	11.2	65	0	0	0	64.3	7	40.6	0	0	0	0	60.1	0.7
Ducks	197	84.8	0	0	10.2	8.1	0	0	1.5	1.5	2	0	0	0	12.7	8.6	0
Horses	84	61.9	2.4	0	26.2	1.2	0	0	26.2	4.8	22.6	0	0	0	0	34.5	1.2
Dogs	47	59.6	0	0	27.7	0	2.1	2.1	34	12.8	34	0	0	0	0	34	12.8
Other non-avian species	169	87	1.2	0	8.9	0	0	0	5.9	1.2	4.1	0	0	0	0	6.5	0
Other avian species	66	60.6	16.7	4.5	10.6	0	0	0	15.2	7.6	15.2	1.5	0	0	0	15.2	1.5
Feed	417	83.5	0.5	0	2.9	0.7	0.2	0.5	10.3	8.9	3.8	0	0	0	0.7	11.3	0
Environment	9	66.7	11.1	11.1	11.1	0	0	0	0	0	11.1	0	0	0	22.2	0	0
Total	2347	69.3	3.2	1	18.8	1.6	1.4	1.6	20.6	9.3	14.2	0.04	0	0	1.7	20.5	4.9

*Note: antibiotic codes e.g. Cip, Cn, Amc, are provided in **Annex 9**.*

Table A20.2: *Salmonella* Dublin, antibiotic sensitivity monitoring, 2005-2014

Year	No. of isolates	Percentage sensitive to all 16 antibiotics (%)	Percentage of isolates resistant to:								
			S	C	SU	T	N	AM	FR	TM	NA
2005	365	98.1	1.1	0.3	0.3	0.3	0	0.8	0	0	0
2006	468	96.4	0.4	0.6	1.3	0.6	0.2	0.9	0	0.2	1.5
2007	381	98.7	0.8	0	0	0.2	0	0.2	0	0	0
2008	404	96.0	3.2	0.3	0.3	0.5	0	0.3	0.3	0	0.3
2009	560	92.3	7.0	0.4	0.5	0.9	0	0.5	0.2	0	0.4
2010	630	95.7	2.7	0.2	0.5	0	0	0.2	0	0	1.3
2011	453	96.0	3.3	0.4	0.4	0.4	0	0.2	0	0	0.4
2012	327	97.2	1.8	0.3	0	0.3	0	0.6	0	0	0.6
2013	393	96.9	1.3	0	0	0	0.3	0.3	0	0	1.0
2014	286	96.5	2.4	0	0.7	1.1	0.3	0.7	0.3	0.7	0

Table A20.3: *Salmonella* Typhimurium, antibiotic sensitivity monitoring, 2005-2014

Year	No. of isolates (DT104)*	Percentage sensitive to all 16 antibiotics (%)	Percentage of isolates resistant to:									
			S	SU	T	N	AM	FR	TM	C	APR	NA
2005	552 (144)	24.1	60.0	71.6	71.0	1.3	67.2	4.2	36.1	53.1	0.7	8.9
2006	1136 (316)	24.2	54.2	70.2	69.2	5.1	65.9	1.0	39.8	57.0	1.0	6.9
2007	1057 (181)	11.4	70.6	85.3	81.6	4.5	78.4	0.6	57.9	58.8	1.5	4.5
2008	709 (171)	19.6	65.7	70.7	73.8	1.6	66.2	0	26.4	43.0	1.0	3.5
2009	440 (64)	25.7	60.7	67.5	65.7	3.0	61.1	0.2	40.7	46.1	1.1	4.1
2010	328 (45)	33.5	54.6	56.7	58.2	3.0	51.2	0.3	27.1	36.3	4.0	5.2
2011	427 (52)	34.4	51.3	56.2	57.4	3.5	49.2	0	37.5	24.6	20.4	4.9
2012	191 (35)	27.2	59.1	63.9	64.9	2.1	56.5	0.5	41.9	30.4	20.4	2.6
2013	165 (47)	30.3	54.5	60.6	61.2	0.6	57.6	0	44.8	35.2	1.8	4.8
2014	224 (33)	44.2	39.7	43.8	49.1	0	43.3	0	35.7	36.6	0.9	0.9

*Note: * Includes the variants of DTI04, DT104B and U302.*

Table A20.4: Salmonellas other than Dublin and Typhimurium, antibiotic sensitivity monitoring, 2005-2014

Year	No. of isolates	Percentage sensitive to all 16 antibiotics (%)	Percentage of isolates resistant to:									
			S	SU	T	N	AM	FR	TM	C	APR	NA
2005	2683	65.6	10.9	23.7	23.6	4.2	4.6	6.2	12.3	2.5	0.1	2.2
2006	2727	58.7	15.8	25.1	28.8	6.9	7.2	5.7	14.2	3.2	0.2	4.0
2007	2248	63.4	12.8	22.2	28.8	4.0	7.7	3.5	11.9	2.2	0.2	3.4
2008	2474	67.3	14.0	17.5	23.7	3.2	5.0	1.3	8.1	1.8	0.3	1.8
2009	1990	64.0	16.4	23.2	24.4	4.1	8.1	2.9	12.6	2.5	1.7	2.1
2010	2126	56.7	29.1	35.7	32.5	3.4	12.9	0.8	11.2	1.3	0.7	1.8
2011	1982	56.4	27.2	35.1	31.1	2.7	16.3	0.2	13.6	3.6	3.2	2.6
2012	2018	75.0	25.0	33.1	33.4	3.6	13.9	1.5	12.2	1.7	2.0	4.0
2013	2328	61.2	19.2	26.5	28.0	3.4	12.3	3.1	12.2	1.7	1.4	5.7
2014	1837	68.2	18.8	20.9	20.0	2.0	12.7	2.1	7.5	1.8	1.6	4.0

Annex 21 – Data sources

Sales data

Marketing Authorisation Holders (MAHs) –Marketing Authorisation Holders of manufactured antibiotics are mandated to provide the Veterinary Medicines Directorate with total annual sales figures for each antibiotic product sold within the UK. Data are collated, verified and then transported into a bespoke spreadsheet for analysis. The total weight, in tonnes, of each active ingredient sold for each antibiotic is then calculated. There is currently no system available to collect and collate data on antibiotic use centrally, antibiotic sales data are collected as a proxy for use.

Periodic Safety Update Reports (PSURs) - Sales figures submitted by MAHs in PSURs for the purpose of Pharmacovigilance, were used to validate sales figures published in this report. Where a PSUR had been returned to the VMD Pharmacovigilance team in the 2014 calendar year reported sales were compared to those returned to the AMR team and any discrepancies were queried.

In order to calculate the Population Correction Unit data is supplied by:

Defra Statistics division – The live weight of animals slaughtered for food are calculated by Defra. The population numbers of food producing animals are supplied by Defra via the Agriculture in the UK report.

CEFAS – The annual live weight of fish at slaughter for the UK is supplied by CEFAS (Centre for Environment, Fisheries and Aquaculture Science).

TRACES – Import and export figures obtained from TRACES are provided by European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) and used in the calculation of the PCU.

Resistance data

APHA Diagnostic Submissions – Private veterinary surgeons or farmers in England and Wales can submit carcasses and other diagnostic samples to the Animal and Plant Health Agency (APHA) veterinary investigation centres for diagnostic investigation. Where it is clinically relevant, culture and antibiotic sensitivity testing are carried out on selected diagnostic samples. The results of such sensitivity tests are compiled; providing data for the "clinical surveillance" element of the AMR surveillance programme.

The Zoonoses Order (1989) – In accordance with the Zoonoses Order of 1989[33] any laboratory isolating *Salmonella* from domestic livestock in Great Britain (GB) is required to notify Defra, and to submit the isolate(s) to APHA for examination. *Salmonella* isolates submitted in compliance with this order are presented in the *Salmonella* section (**page 59**).

National Control Programme for *Salmonella* in Poultry – In order to comply with the requirement of the Zoonoses regulation (EC) No 2160/2003 the UK conducts a National Control Programme (NCP) for *Salmonella* in poultry. Under the NCP samples are required to be taken from flocks according to the criteria stated in the Control of *Salmonella* in Broilers, Poultry and Turkeys Orders.[34] [35] The first

[33] http://www.legislation.gov.uk/uksi/1989/285/contents/made
[34] http://www.legislation.gov.uk/uksi/2009/260/contents/made

isolate of each *Salmonella* serovar that is received from an animal or group of animals from one holding is tested for antibiotic susceptibility; the results of this sensitivity testing are presented in the *Salmonella* section on **page 96.**

VMD *Campylobacter* and *E. coli* Fattening Turkey Abattoir Survey (2014) – The VMD implemented a structured survey in 2014 to collect fattening turkey caecal samples at slaughter for the purposes of monitoring antimicrobial resistance in *Campylobacter jejuni* and *E. coli* isolates in accordance with Commission Decision 2013/652/EU[36]. The results of this survey are presented on **page 36**.

FSA *Campylobacter* Broiler Abattoir Survey (2014) – The Food Standards Agency (FSA) carried out a structured survey in 2014 to identify the prevalence of *Campylobacter jejuni* and *Campylobacter coli* in broiler chicken caecal samples. The sampling was carried out in accordance with EU technical specifications in Commission Decision 2007/516/EC[37]. Antibiotic susceptibility testing was performed on the *Campylobacter* spp. isolates recovered in the study, and the results are presented in **page 36.**

[35] http://www.legislation.gov.uk/uksi/2009/3271/made
[36] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:303:0026:0039:EN:PDF
[37] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32007D0516&from=EN

Annex 22 – Glossary of Terms

a.i.	Active Ingredient; the part of an antibiotic medicine that acts against the bacterial infection.
AHDB	Animal Health and Development Board
Aminoglycosides	A closely related group of bactericidal antibiotics derived from bacteria of the order Actinomycetales. Polycationic compounds that contain an aminocyclitol with cyclic amino-sugars attached by glycoside linkages. Sulphate salts are generally used. They have broadly similar toxicological features.
Antibiotic	A term synonymous with anti-bacterials.
Antimicrobial	A general term for any compound with a direct action on micro-organisms used for treatment or prevention of infections. Antimicrobials are inclusive of antibacterials, antivirals, antifungals and antiprotozoals.
Antimicrobial Resistance	The ability of a micro-organism to grow or survive in the presence of an antimicrobial that is usually sufficient to inhibit or kill micro-organisms of the same species.
β-Lactam	Semi-synthetic antibiotics derived from penicillin G or cephalosporin C, natural antibiotics produced by the mould *Cephalosporium acremonium*. Bactericidal products that act by inhibiting synthesis of the bacterial cell wall.
BPC	British Poultry Council
CBP	Clinical Break Point
CHAWG	Cattle Health and Welfare Group
Critically Important Antibiotics	These are antibiotics which; are the sole or one of few available treatments for serious human disease; and are used to treat diseases caused by organisms that may be transmitted to humans from non-human sources or, human diseases caused by organisms that may acquire resistance genes from non-human sources, (WHO definition). They include the following classes of antibiotics; fluoroquinolones; 3rd and 4th generation cephalosporins; and macrolides.
HP-CIA	Highest Priority Critically Important Antibiotics
Defra	Department for Environment, Food and Rural Affairs.
ECDC	European Centre for Disease Prevention and Control
ECV	Epidemiological cut-off value

EFSA	European Food Safety Authority
EMA	European Medicines Agency
Eurostat	Eurostat is the statistical office of the European Union.
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
FAO	Food and Agriculture Organisation of the United Nations.
Fluoroquinolone	A sub-group of the quinolone compounds, having the addition of a fluorine atom and the 7-piperazinyl group. Broad-spectrum antibacterials with properties more suited to the treatment of systemic infections.
Food Animals	Animals used for food production including: cattle, sheep, pigs, poultry, salmon, trout and bees.
Injectable Product	A product which is administered to animals via injection.
Intramammary Product	A product which is administered into the udder.
Macrolide	A large group of antibiotics mainly derived from *Streptomyces* spp. Weak bases that are only slightly soluble in water. They have low toxicity and similar antibiotic activity with cross-resistance between individual members of the group. Thought to act by interfering with bacterial protein synthesis.
Medicated Feeding stuff	Feeding stuffs that contain a veterinary medicine and that are intended for feeding to animals without further processing.
Metaphylaxis	The treatment of a group of animals where one or more individuals within the group has received a clinical diagnosis.
Non-Food Animals	Animals not reared for food. These are mainly companion animals including, dogs, cats, horses, small mammals, rabbits and birds.
OIE	World Organisation for Animal Health.
PHWC	Pig Health and Welfare Council
Population Correction Unit (PCU)	This is a technical unit of measurement which is used to represent the estimated weight at treatment of livestock and slaughtered animals. 1 PCU = 1 kg of different categories of livestock and slaughtered animals.
Sulphonamide	A group of bacteriostatic compounds that interfere with folic acid synthesis of susceptible organisms. They all have similar antibiotic activity but different pharmacokinetic properties.
Tetracycline	A group of antibiotics derived from *Streptomyces* spp. They are usually bacteriostatic at concentrations achieved in the body and act by

	interfering with protein synthesis in susceptible organisms. All have a broad spectrum of activity.
TRACES	European Commission's Director General Health and Consumer owned - The 'TRAde Control and Expert System' (TRACES) is a management tool for tracking the movements of animals, products of animal and non-animal origin and since version 6.00 also of plants, from both outside the European Union and within its territory.
Trimethoprim	Compounds with a similar action to sulphonamides, acting by interfering with folic acid synthesis, but at a different stage in the metabolic pathway. Display a similar spectrum of activity to, and are often used in combination with, sulphonamides.
VMD	Veterinary Medicines Directorate, an Executive Agency of the Department for Environment, Food and Rural Affairs (Defra).
Water/Oral Product	A product that is administered to animals orally. Includes tablets, boluses, capsules, dissolvable powders and sachets, solutions, etc.
WHO	World Health Organisation.

Annex 23 – Contributors

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Boehringer Ingelheim Ltd
Ceva Animal Health Ltd
Chanelle Animal Health Ltd
Continental Farmaceutica SL.
CP Pharma Handelsgesellschaft mbH
Cross Vetpharm Group Ltd
Cyton Biosciences Ltd
Dechra Ltd
Divasa – Farmavic S.A.
Dopharma Research B.V.
ECO Animal Health
Ecuphar N.V.
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Emdoka bvba
Eurovet Animal Health B.V.
Fort Dodge Animal Health Ltd
Forte Healthcare Ltd
Forum Products Limited
Franklin Pharmaceuticals Ltd
Globamed
Global Vet Health S.L
Harkers Ltd
Huvepharma N.V.
I.C.F. Sri Industria Chimica Fine
Industrial Veterinaria S.A.
Intervet UK Ltd
Janssen-Cilag Ltd
Kela N.V.
Krka Dd
Laboratorios Calier S.A.
Laboratorios Hipra S.A.
Laboratorios Karizoo S.A.
Laboratorios SYVA S.A.U
Laboratorios Velvian, S.L.

Lavet Pharmaceuticals Ltd
Le Vet B.V.
Merial Animal Health Ltd
Miklich Laboratorios S.L
Minster Veterinary Practice
Nimrod Veterinary Products Ltd
Norbrook Laboratories Ltd
Novartis Animal Health UK Ltd
Oropharma N.V.
Pharmaq Ltd
Phibro Animal Health SA
Quvera Ltd
Qalian Ltd
Sogeval S.A.
SP Veterinaria, S.A.
Triveritas Ltd
Tulivin Laboratories Ltd
Universal Farma S.L
Univet Ltd
Vétoquinol UK Ltd
Vetpharma Animal Health S.L
Virbac S.A
VMD NV
Zoetis

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