



Veterinary
Medicines
Directorate



SALES DATA CORRECTIONS - SEE ERRATUM

**UK – Veterinary Antibiotic Resistance
and Sales Surveillance Report**



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Foreword

Following a very high profile last year for AMR on the international stage, 2017 has seen the international drive for action maintain its momentum. The year started with progressive AMR commitments from the G20 agriculture ministers which were followed closely by the G20 health ministers and leaders. In March the international Inter-Agency Coordination Group was launched to take forward the commitments of the Global AMR Action Plan (2015) and the UN General Assembly AMR Declaration (2016). In June the EU commission released its new AMR One Health Action Plan, and in July, the Codex Alimentarius Commission approved reopening of the AMR task force to look at developing guidance on integrated AMR surveillance and updating its code of practice on minimising the risk of AMR in the food chain. More recently, the G7 Chief Veterinary Officers Forum produced a consensus paper on agreed terms for definitions of terms relating to AMR to help international discussions take place using a common language.



At home in the UK we have entered the final year of the UK 5 Year AMR Strategy 2013-2018, and the VMD and colleagues across government have been working closely with stakeholders in the veterinary profession, agriculture industry and beyond to deliver on our shared AMR commitments.

Last year, in response to the recommendations of the O'Neill Review on AMR, we made three high profile government commitments around the introduction of targets for the reduction of antibiotic use in animals and strengthening veterinary stewardship of antibiotics, which are of greatest importance to human health. We committed to do this without compromising animal health or welfare, but through optimising animal health and the prevention of disease through alternative approaches to antibiotic use. We view this approach as essential in underpinning the sustainable and long-term success of our shared AMR ambitions.

Within this context this year's VARSS report marks several important milestones:

- The Government commitment to reduce antibiotic use in livestock and fish farmed for food to a multi-species average of 50 mg/kg by 2018, from 62 mg/kg in 2014, has been achieved two years early. Antibiotic use in food-producing animal species decreased by 27% to 45 mg/kg.
- The lowest UK veterinary antibiotic total sales figure recorded (337 tonnes) since regular UK antibiotic sales reporting began in 1993.
- Reductions across sales of all highest-priority critically important antibiotics (HP-CIAs), including an 83% reduction in sales of colistin use for food producing animals, from an already very low level.
- The report contains expanded data on antibiotic usage for a number of sectors and highlights the reductions achieved in 2016 by the pig and poultry sectors, with overall reductions of 34% in pigs, 37% in chickens, 57% in turkeys and 60% in ducks.
- As well as reductions in overall use, the pig and meat poultry sectors also achieved reductions in use of HP-CIAs by 73% and 78% respectively.

Beyond the results themselves, seeing all these datasets together in the VARSS report reinforces several messages. Firstly and most importantly, it demonstrates the commitment by the people who work in these sectors to delivering responsible reductions in the use of antibiotics in the

animals they raise. Further, their voluntary sharing of usage data demonstrates their commitment to transparency – showing where use is reducing, where there is still work to be done, and illustrating the different challenges faced by a diverse range of sectors.

Throughout the narrative of past years around how antibiotic use should be measured there have been various critiques of different metrics used. The more work done within our UK sectors the clearer it becomes that there is no 'one size fits all', no 'perfect' metric – but that the important thing is to understand what each metric actually measures and select the most appropriate one for informing how to improve responsible use of antibiotics in each set of circumstances. There will always be a need for a common metric (the way mg/kg has been used to date), but it is also important to generate relevant sector-specific metrics for feedback to vets and farmers to facilitate optimisation of their use of antibiotics. We can expect more work on this in the future.

Our measure of antibiotic resistance in bacteria from animals has continued this year through our surveillance and monitoring activities. The focus has been on bacterial pathogens that cause disease in animals, and bacteria that can be transmitted from healthy animals to humans via direct contact or through consumption of contaminated food. This shows a low or very low level of resistance in food-borne pathogens to most of the HP-CIAs for human medicine. However, levels of resistance to fluoroquinolones, one of the HP-CIAs, remain relatively high in *Campylobacter* and *E. coli* but at lower levels than in the past. Although, overall the rates of resistance have remained relatively stable for most of the bacteria and antibiotics tested, a decline has started to be seen, particularly in *E. coli* isolates from chickens, coinciding with a reduction in antibiotic use in poultry. This observation will need to be confirmed in the coming years as new data become available.

As the present 2013-2018 UK 5 Year AMR Strategy nears its close, we are drawing on the collaborations forged with our stakeholders and working with them to build the goals of the next strategy. At the same time, we have been reflecting back on what has been achieved since 2013. AMR is a long term threat which will never fully go away and there will always be work to be done, but we have been sincerely impressed by the way different sectors have risen, or are rising to the challenge. The results within this report show how change is possible where there is the will and a team effort to achieve it. We look forward to continuing to work in this spirit with our colleagues, both in the UK and abroad, and within and beyond government in the years ahead.



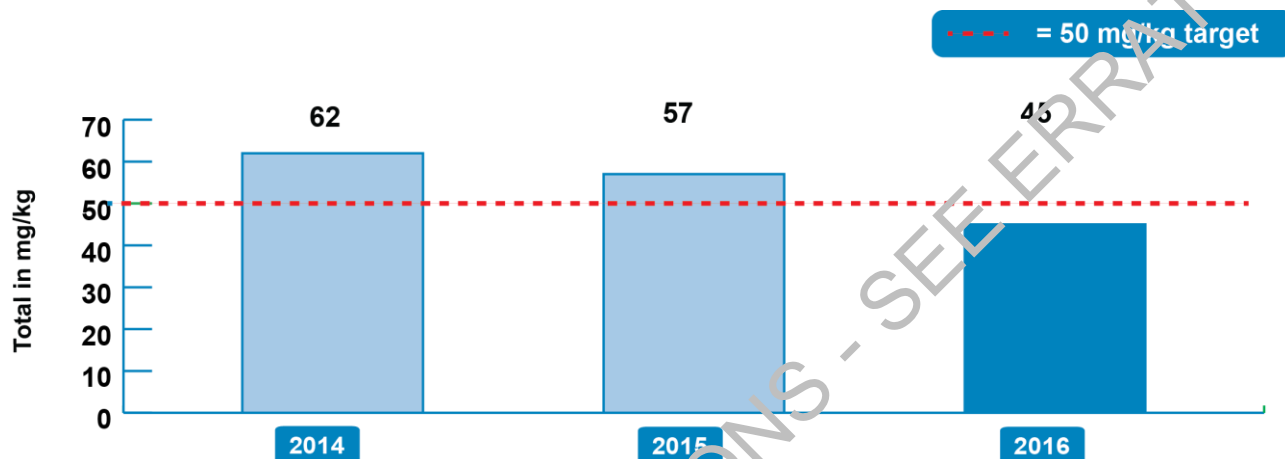
Professor S. Peter Borriello
Chief Executive Officer

Highlights

Antibiotic Sales

Overall trends in mg/kg

The Government committed to reduce antibiotic use in livestock and fish farmed for food to a multi-species average of 50 mg/kg by 2018, from 62 mg/kg in 2014. This has been achieved two years early, with antibiotic use in food-producing animal species decreasing by 27% to 45 mg/kg.

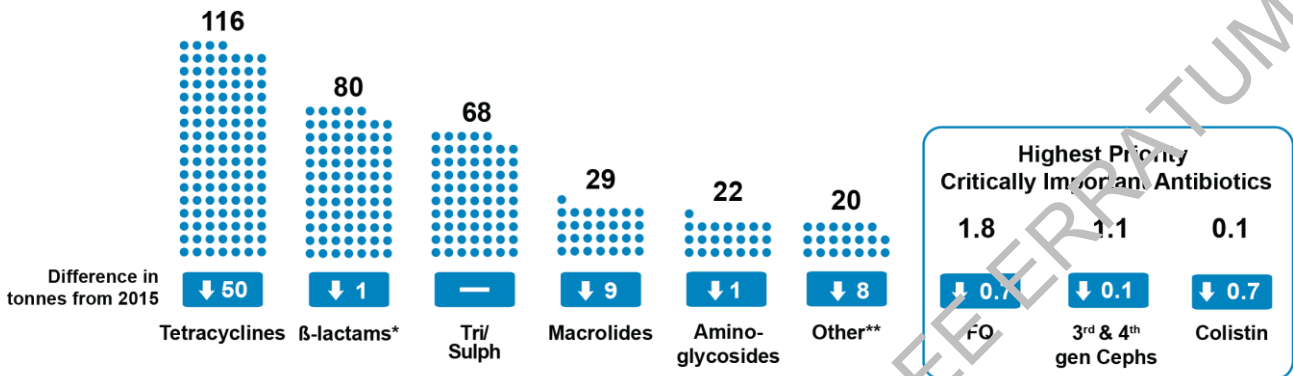


Sales of highest priority critically important antibiotics (HP-CIAs) have also reduced in 2016 from an already low level. Sales of 3rd/4th generation cephalosporins reduced by 12% to 0.15 mg/kg, fluoroquinolones reduced by 29% to 0.24 mg/kg, and colistin reduced by 83% to 0.02 mg/kg, which is considerably below the 1 mg/kg maximum target for colistin recommended by the European Medicines Agency.

	2012	2013	2014	2015	2016	Compared with 2015
Total (mg/kg)	66	62	62	57	45	↓ 21%
Fluoroquinolones (FQ) (mg/kg)	0.33	0.36	0.35	0.34	0.24	↓ 29%
3 rd /4 th gen Cephalosporins (mg/kg)	0.20	0.18	0.19	0.17	0.15	↓ 12%
Colistin (mg/kg)	0.09	0.11	0.12	0.12	0.02	↓ 83%
Total sales (tonnes)	464	436	445	408	337	↓ 17%

Total sales in tonnes of active ingredient by class for 2016

Tetracyclines, β -lactams and trimethoprim/sulphonamides accounted for the majority (78%) of active antibiotic ingredient sold. As with previous years, HP-CIAs (fluoroquinolones, colistin and 3rd/4th generation cephalosporins) accounted for a small proportion of the sales (<1%).



*includes 3rd & 4th gen Ceph








**other includes: amphenicols, lincomycins, pleuromutilins, steroidal antibiotics and polymyxins (including colistin)

FQ = fluoroquinolones

Antibiotic Usage

Antibiotic usage and data collection activities by livestock species

Antibiotic usage refers to the amount of antibiotics purchased, prescribed and/or administered. For the first time, this report includes antibiotic usage data from the pig, meat poultry, egg, gamebird and dairy industries, collected and provided on a voluntary basis.

		Total Coverage %*	2016 Total tonnage	2016 Total Usage**	Compared with 2015 %	HP-CIA usage	Compared with 2015 %
Pigs		62	89.3	183 mg/kg	↓ 34	0.3 mg/kg	↓ 73
Turkeys		90	23.7	86 mg/kg	↓ 57	0.12 mg/kg	↓ 78
Broilers				17 mg/kg	↓ 37		
Ducks				3 mg/kg	↓ 60		
Dairy		33	7.2	26 mg/kg (2.3 DCDVet)	↑ 9 (↓ 5 [†])	0.96 mg/kg	↓ 50
Layers		90	2.6	0.7 DD/100 eggs	—	15.2 kg	—
Gamebirds		90	20.2	—	—	64.1 kg	—

*represents the % of animals covered by the data, except for gamebirds where it represents an estimate of the % of total antibiotic sales

**mg/kg relates to the amount of active ingredient whereas Defined Course Doses (DCDVet) relates to the number of antibiotic courses administered, in both cases normalised by kg biomass and calculated using ESVAC methodology. ESVAC methodology is not available for eggs, gamebirds or ducks. The British Poultry Council (BPC) use a weight of 1.75kg per slaughter duck to estimate biomass whereas the British Egg Industry Council calculate the average number of antibiotic daily doses (DD) per chicken given over a 100 day period, using actual usage data.

[†]the reason for the increase in mg/kg but reduction in DCDVet is due to a switch away from HP-CIAs to non HP-CIAs, which have a higher amount of active ingredient per course than HP-CIAs

It is important to note that none of these datasets have 100% coverage and so the results presented here may not be fully representative of the industry, especially for pigs and dairy cattle where the UK coverage is 62% and 33% respectively. In pigs, the number of contributors to the electronic medicines book (eMB) is set to increase; Quality Meat Scotland required the use of eMB to record antibiotic usage from August 2016 and, as of 11th November 2017, this will now be a requirement under the Red Tractor assurance scheme. The Cattle Health and Welfare Group will also continue to work towards increasing the amount of antibiotic usage data available for the dairy industry, as well as obtaining usage data for the beef and sheep industries.

Antibiotic Resistance in Zoonotic and Commensal Bacteria from Healthy Animals at Slaughter

Resistance in *Escherichia coli* from broilers and turkeys

Of the highest priority critically important antibiotics for human medicine (HP-CIAs), no resistance was detected in indicator *E. coli* from broilers and turkeys at slaughter with the exception of a single isolate from turkeys resistant to cefotaxime and ceftazidime (3rd/4th generation cephalosporins) and the moderate resistance to fluoroquinolones reduced further from 2014 to 21.6% in broilers and 15.6% in turkeys.

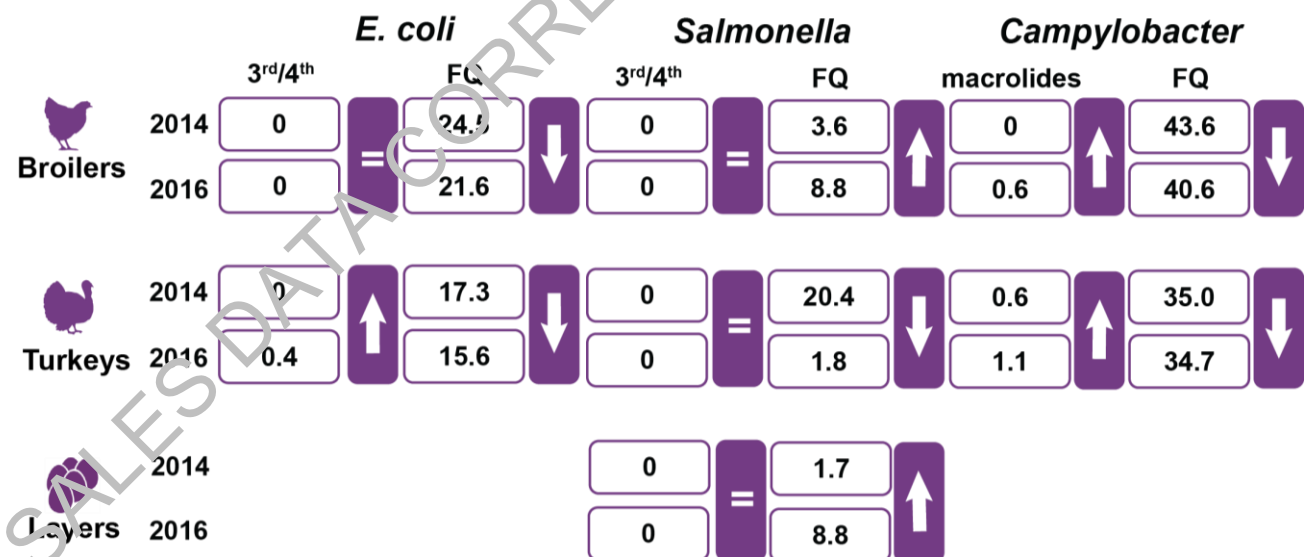
Resistance in *Salmonella* from laying hens, broilers and turkeys

No resistance to HP-CIAs was detected in *Salmonella* isolates from laying hens, broilers or turkeys, other than a relatively low level to fluoroquinolones (1.7%-8.8%). Compared to 2014 there was a big reduction in resistance to fluoroquinolones in isolates from turkeys and a small increase in those from broilers and layers.

Resistance in *Campylobacter jejuni* from broilers and turkeys

Resistance to fluoroquinolones was detected in a relatively high proportion of *C. jejuni* isolates from broilers (40.6%) and turkeys (34.7%), a small decrease in levels compared to 2014.

Resistance to erythromycin, which is the first-line treatment for *Campylobacter* infection in people, was very low in isolates from broilers (0.6%) and turkeys (1.1%).



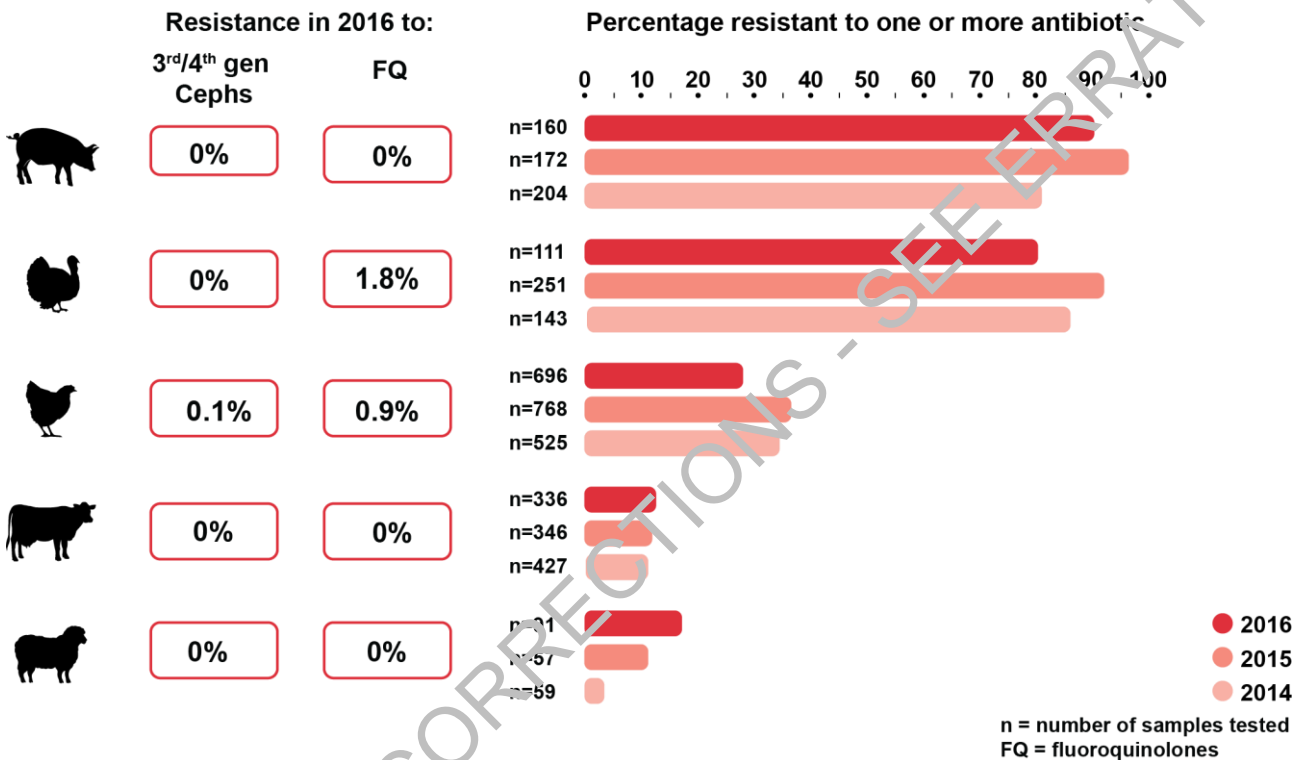
FQ = fluoroquinolones
3rd/4th = 3rd/4th generation cephalosporins

Antibiotic Resistance – Clinical Surveillance

Resistance in *Salmonella*

Overall, a high percentage of *Salmonella* isolates (69.0%) were susceptible to all the 16 antibiotics tested.

A very low level of resistance to fluoroquinolones (0.6%) and to 3rd/4th cephalosporins (0.4%) was observed, however none of the *Salmonella* Typhimurium isolates were resistant to these HP-CMs.

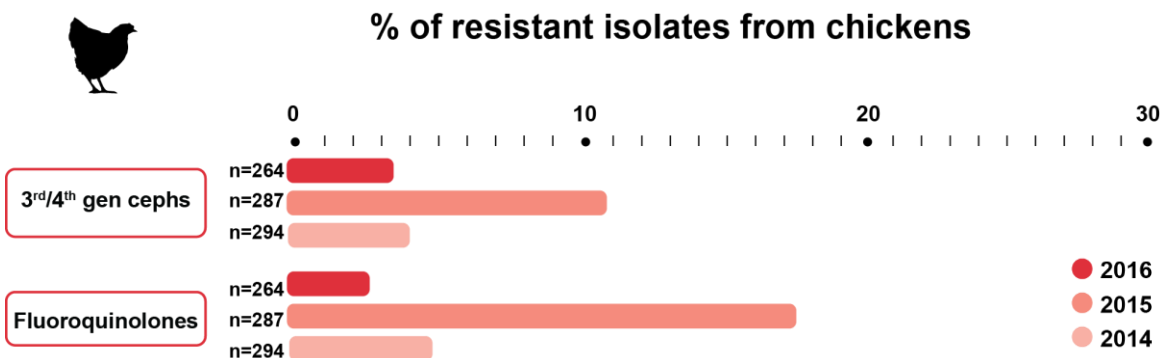


Resistance in *Escherichia coli*

Resistance in *E. coli* isolates from chickens, which has shown an upward trend since 2013, showed a marked decline in 2016 for several antibiotics, coinciding with a reduction in antibiotic use in broilers.

Resistance levels to 3rd/4th generation cephalosporins were relatively low in *E. coli* isolates from most livestock species (less than 3%) with the exception of isolates from calves which showed a higher resistance level (16%).

Colistin resistance was not detected.



Introduction

This report presents combined data on veterinary antibiotic sales and antibiotic resistance in bacteria from animals in the UK. The antibiotic sales data from 2005 to 2016 is presented in **Chapter 1** and is based on sales of antibiotics authorised for use in animals in the UK. Data are submitted by the veterinary pharmaceutical companies to the VMD. Sales data are generally used as an estimate for antimicrobial usage. However, as not all antibiotics sold will be used, and many antibiotics are authorised for use in multiple species, it is not possible to determine how much is used by each animal species. The VMD is working in partnership with key livestock sectors to develop, facilitate and coordinate antibiotic usage collection systems. Antibiotic usage data from meat poultry was presented for the first time in the 2014 VARSS report, and this year the report also includes usage data from the pig, gamebird, egg and dairy sectors (**Chapter 2**).

The VMD collates data from government laboratories on antibiotic resistance in bacteria from animals. The surveillance activities focus on the occurrence of antimicrobial resistance in pathogens that cause infections in animals, zoonotic bacteria that can develop resistance in the animal reservoir which may subsequently compromise treatment outcome when causing infection in people, and indicator bacteria such as *E. coli* due to their ubiquitous nature in animals, food and humans and their ability to readily develop or transfer antimicrobial resistance between these reservoirs. There are two different antimicrobial resistance surveillance programmes in the UK. One is the EU harmonised monitoring programme which is a legal requirement that involves the susceptibility testing of zoonotic (*Salmonella* and *Campylobacter*) and commensal (*E. coli*) bacteria from healthy animals sampled at slaughter. Results from the EU harmonised monitoring are presented in **Chapter 3**. The second programme is the clinical surveillance which relies on voluntary submission of samples by farmers and veterinary surgeons and involves the susceptibility testing of bacteria that cause disease in animals isolated from samples or carcasses submitted to government laboratories for diagnostic investigations. Based on the disease relevance, bacteria identified are tested for antibiotic susceptibility. Results from the clinical surveillance are presented in **Chapter 4**.

Details on methodology and results not presented in the report are included in the **Supplementary material** report. The supplementary material report and previous VARSS reports are available to download at www.gov.uk.

CHAPTER 1

Sales of Veterinary Antibiotics

SALES DATA CORRECTIONS - SEE ERRATUM

Chapter 1: Sales of Veterinary Antibiotics

1.1 Summary

The Department for Environment, Food and Rural Affairs (Defra) committed to a 20% reduction in antibiotic use in livestock and fish farmed for food to a multi-species average of 50 mg/kg by 2018, from a sales figure of 62 mg/kg in the baseline year of 2014 (HM Government, 2016). This target has been achieved two years early, with sales of antibiotics for use in food-producing animal species decreasing by 27% to 45 mg/kg in 2016.

When compared to 2015, the overall quantity of active antibiotic ingredient sold in 2016 for use in all animal species decreased by 17% to 337 tonnes, the lowest volume recorded since VMD began to record sales of veterinary antibiotics in 1993. Between 2015 and 2016 antibiotics for use across all food-producing animal species decreased by 21% (from 57 mg/kg to 45 mg/kg). In the same period, sales of products authorised for only pig and/or poultry use decreased by 36% (from 302 tonnes to 192 tonnes).

Sales (tonnes of active ingredient sold) of trimethoprim, sulphonamides, β -lactams and aminoglycosides remained stable between 2012 and 2016, but there were notable reductions observed for tetracyclines (30%) and macrolides (24%) between 2015 and 2016.

Sales of highest priority critically important antibiotics (HP-CIAs) also reduced in 2016, from an already low level. Sales of 3rd and 4th generation cephalosporins reduced by 12% to 0.15 mg/kg in 2016, sales of fluoroquinolones reduced by 29% to 0.24 mg/kg and sales of colistin reduced by 83% to 0.02 mg/kg in 2016 which is considerably below the 1 mg/kg maximum target for colistin recommended by the European Medicines Agency (EMA).

1.2 Introduction

Pharmaceutical companies have reported the quantity of authorised veterinary antibiotics sold throughout the UK to the VMD since 1993; this has been a statutory requirement since 2005 (S1.1 in supplementary materials for further details).

The data reported in this chapter do not take in to account wastage, nor imports or exports of veterinary antibiotics, but they serve as the best currently available approximation of the quantity of antibiotics administered to all animal species within the UK (further details on data limitations can be found in Annex A).

Note that, for ease of reading, the data have in some cases been rounded to the nearest integer. However, the percentage changes have been calculated using the exact number.

1.3 Methods

1.3.1 Data collection and validation

Pharmaceutical companies supplied annual sales of all authorised veterinary antibiotics to the VMD in accordance with the Veterinary Medicines Regulations 2013 (S.I. 2013 No.2033), schedule 1, paragraph 31 (3a). Upon receipt, data are collated and validated. To check the correctness and completeness, product data entries are compared to those submitted in previous years. If large discrepancies are observed between data provided in successive years, data validity is further investigated and queried with the pharmaceutical company. Sales data for antibiotic products returning Periodic Safety Update Reports (PSURs) are also compared to those sales data returned by the pharmaceutical companies, and any discrepancies investigated (further details can be found in Annex B).

1.3.2 Tonnes of active ingredient

The weight of antibiotic sold is an exact measurement obtained by multiplying the quantitative composition of active ingredient for each product, obtained from the Summary of Product Characteristics (SPC), by the number of units sold as reported by the MAH. For some active ingredients that are either prodrugs or expressed in International Units (IU), a conversion factor is applied to calculate the tonnes of antibiotic sold. These conversion factors are recommended by the European Medicines Agency (EMA) in the framework of the ESVAC project (ESVAC, 2016).

The data reported here are presented according to the Anatomical Therapeutic Chemical Classification System for veterinary medicinal products (ATCvet) as shown in Table 1.1 (www.whooc.no/atcvet/). Antibiotic agents for intestinal use, intrauterine use, systemic use and intramammary use are included, but sales of dermatological preparations and preparations for sensory organs (described as “other” route of administration in previous UK-VARSS reports) are not included (sales of these preparations are reported in S1.1 of supplementary material). This represents a maximum of three tonnes in any given year.

Table 1.1. Categories and ATCvet codes of antibiotic veterinary medicinal products included in the data.

Veterinary antibiotic category	ATCvet codes
Antibiotic agents for intestinal use	QA07AA; QA07AB
Antibiotic agents for intrauterine use	QG01AA; QG01AE; QG01BA; QG01BE; QG51AA; QG51AG
Antibiotic agents for systemic use	QJ01
Antibiotic agents for intramammary use	QJ51
Antibiotic agents for antiparasitic use (Solely sulphonamides)	QP51AG

1.3.3 Population Correction Unit (PCU)

Trends in sales of antibiotics over time cannot be determined without taking into consideration variations in the size and number of the animal population. Therefore sales data are analysed using the Population Correction Unit (PCU), a theoretical unit of measure formulated by the EMA and adopted by countries across Europe to standardise sales against an animal population denominator. Using the PCU, the overall sales of products authorised for use in **food-producing animal species** can be presented as mg/PCU.

The mg/PCU can be considered as the average quantity of active substance sold per kilogram bodyweight of food-producing animal in the UK over the course of a year based on an estimated weight at the point of treatment, and enables year-on-year comparisons to be made. Further details on these calculations are presented in S1.2 of supplementary material and full technical details on PCU methodology can be found in the 2009 ESVAC report (ESVAC, 2011). **Within this report, all reference to mg/kg equates to mg/PCU.**

1.3.4 Historical UK-VARSS reports

In UK-VARSS reports published before 2016 (2015 data), the methodology used for the calculation of tonnes of active antibiotic ingredient, and the mg/kg (also referred to as mg/PCU) calculation, differed from the European methodology. To provide harmonisation, all sales data published in this chapter, and in future reports, are reported using European methodology. An explanation of the changes in methodology, and comparative data can be found in S1.1 of the supplementary material.

1.3.5 Corrections for 2015 data

There have been minor revisions in the 2015 sales data provided by a number of MAHs. All data and figures within this report have been corrected to account for these. In particular, total antibiotic active ingredient sold in 2015 was 4 tonnes greater than originally reported, leading to an adjusted mg/kg figure for all food-producing species of 57 mg/kg (56 mg/kg previously reported).

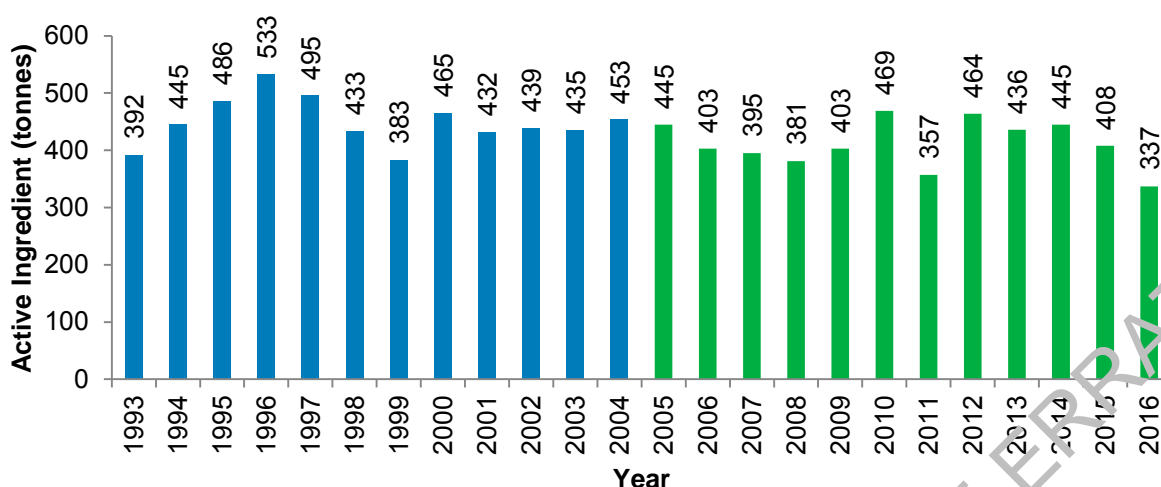
1.4 Results and discussion

1.4.1 Total sales of antibiotics for veterinary use in the UK

Total sales of antibiotic products for veterinary use within the UK from 1993 to 2016 is presented in Figure 1.1 which shows tonnes of active substance sold per given year.

Sales data analysed using the ESVAC methodology is unavailable for the years prior to 2005 as the ESVAC project wasn't launched until September 2009, with the first report publishing aggregated sales data for the years 2005-2009. Therefore, sales data for the years 1993-2004 reported using historical UK-VARSS methodology have also been included in Figure 1.1 for comparative purposes.

Figure 1.1. Total tonnes of active ingredient of antibiotic sold in the UK using UK-VARSS (■) and ESVAC (■) methodology, 1993-2016



The total quantity of active antibiotic ingredient sold in 2016 was 337 tonnes, the lowest total observed since 1993, when the VMD began recording veterinary antibiotic sales. This is despite the fact that the ESVAC methodology produces a higher figure than the VARSS methodology, as active ingredient calculations often include the weight of the salt, whereas the VARSS method does not (see S1.1 of the supplementary material for further details).

The total sales figure for active ingredient recorded in 2016 (337 tonnes) is 20% lower than the ten year mean for the preceding 2005 to 2015 period (mean 418.7 tonnes, range 357-469 tonnes). There was also a 17% reduction in antibiotic sales between 2015 and 2016.

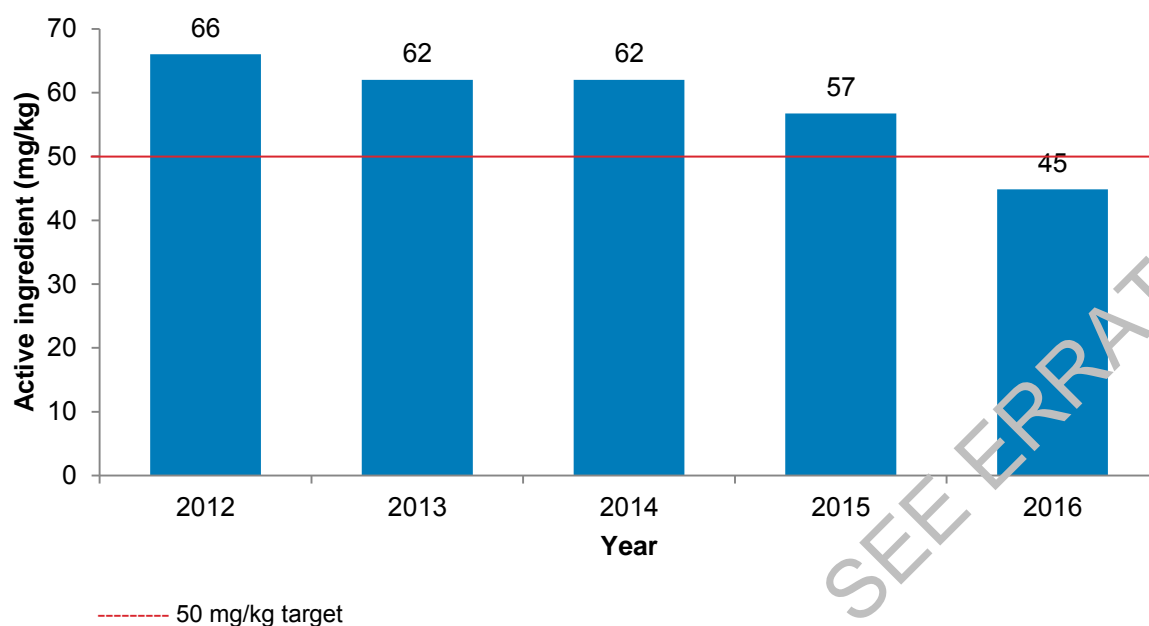
1.4.2 Sales of antibiotics by animal species indicated

1.4.2.1 Sales of antibiotics for food-producing species (mg/kg)

The mg/kg figure for products licensed for all food-producing species (including products authorised for use in horses) decreased by 12 mg/kg (21%) between 2015 and 2016 from 57 to 45 mg/kg (Figure 1.2). This is the lowest UK figure reported since regular sales reporting started in 2005 and is below the 50 mg/kg target set to be achieved by 2018.

Mg/kg figures for different food-producing species cannot be accurately calculated from sales data. This is because a large proportion of antibiotic products are authorised for use in either multiple food-producing species or a combination of both food- and non-food producing species. Usage data obtained from the key livestock sectors is presented in chapter 2, which addresses this problem of attribution.

Figure 1.2. Milligrams (mg) of active ingredient of antibiotic sold licensed for use in all food-producing species per kg, 2012-2016



1.4.2.2 Total sales of antibiotics by animal species indicated (tonnes)

The quantities of antibiotic active substance in products sold between 2012 and 2016 are shown in Table 1.2, differentiated by the species or combination of species for which they are indicated.

In the UK, the role of horses is predominantly as a companion or sport animal, and therefore horses pose limited public health risk for food-borne disease transmission. For this reason, in Table 1.2, 'horse only' products have been classified under 'indicated for non-food producing animals' for reporting tonnage. Similarly, all products that list horses as an authorised species in combination with farmed food-producing species are categorised under 'indicated for a combination of both food and non-food producing species'. However, when calculating overall mg/kg for livestock, horses are included as a food-producing species, in line with ESVAC methodology.

In 2016, 244 tonnes (72%) of total sales were attributed to antibiotic products authorised for food-producing animals only. Products sold exclusively for pigs and/or poultry accounted for 192 tonnes, reflecting a reduction of 110 tonnes (36%) compared with 2015 (302 tonnes). Products licensed for 'cattle only' increased by 4 tonnes (29%) in 2016, largely caused by an increase in sales of cattle oral antibiotics from 6.7 tonnes to 8.7 tonnes (30%) and an increase in intramammary sales from 3.2 to 3.7 tonnes (16%) (data not shown).

Sales of antibiotics specific for non-food producing animals increased between 2015 and 2016 by 73%. In particular, sales of products authorised for 'horses only' increased by 16 tonnes (from 13 tonnes to 29 tonnes). Sales of antibiotics for a combination of food and non-food producing animals also increased by 13 tonnes (37%).

Table 1.2. Tonnes and (% of total sales) of active ingredient of antibiotic sold for species category indicated, 2012-2016^x

		2012	2013	2014	2015	2016
1. Indicated for food producing animals only	- Pigs and Poultry only	235	217	235	214	127
	- Pigs only	66	63	66	50	39
	- Poultry only*	47	43	43	38	26
	- Cattle only	14	14	13	14	18
	- Fish only	2.1	0.8	2.4	0.7	1.6
	- Sheep only	0.2	0.2	0.1	0.2	0.2
	- Multiple food producing species**	32	30	24	30	33
	- Total	396 (85%)	368 (84%)	393 (86%)	347 (85%)	244 (72%)
2. Indicated for non-food producing animals only	- Companion animal only (excluding horse only)	14	14	16	13	16
	- Horse only	21	22	16	13	29
	- Total	35 (8%)	36 (8%)	32 (7%)	26 (6%)	45 (13%)
3. Indicated for a combination of both food and non-food producing animals	- Total	33 (7%)	32 (7%)	30 (7%)	35 (9%)	48 (14%)
Total sales of antibiotics^x		464	436	445	408	337

^x The totals were rounded to the nearest integer. This explains discrepancies between the sum of individual species categories and the totals presented.

*In reports prior to UK-VARSS 2015, products authorised for use in 'ducks' in combination with other poultry species have been included in the 'multiple livestock species' category. These products have been included in the 'poultry only' category in this table. This change affects those data reported in previous UK-VARSS reports for 'pig and poultry only', 'poultry only' and 'multiple farmed food producing species'.

** Not including products indicated for pigs and poultry only, horses or products indicated for a combination of both farmed food and non-food producing species.

1.4.3 Total sales of antibiotics by antibiotic class

1.4.3.1 Total sales by antibiotic group for all species (tonnes)

The total quantities of antibiotic active ingredient in veterinary products sold between 2012 and 2016 and their breakdown by class are presented in Table 1.3. Definitions of these classes and the active ingredients that are included within each group can be found in S1.3 of supplementary material.

Sales (tonnes of active ingredient sold) of trimethoprim, sulphonamides, β -lactams and aminoglycosides remained stable between 2012 and 2016, but there were notable reductions observed for tetracyclines (30%) and macrolides (24%) between 2015 and 2016.

In 2016, there was also a reduction in the sales of all antibiotic classes identified as Highest Priority Critically Important Antibiotics (HP-CIA), see section 1.4.3.3 for further details. Notably, total tonnes sold of colistin decreased by 85% between 2015 and 2016.

Table 1.3. Tonnes of active ingredient of antibiotic sold for all species by class, 2012-2016^x

	2012	2013	2014	2015	2016
Tetracyclines	201	194	181	166	116
Trimethoprim/ Sulphonamides	80	61	71	68	68
Trimethoprim	13	10	12	11	11
Sulphonamides	66	51	59	57	57
β-lactams	94	94	95	81	80
1 st /2 nd Generation Cephalosporins	5	5	5	5	5
3 rd /4 th Generation Cephalosporins (kg)*	(1328)	(1192)	(1332)	(1202)	(1071)
Penicillins**	19	20	12	9	17
Other Penicillins***	69	68	77	65	57
Aminoglycosides	22	24	24	23	22
Streptomycins	10	11	9	10	16
Neomycin and framycetin	1	1	1	1	1
Other aminoglycosides****	12	9	14	13	5
Macrolides	41	40	48	38	29
Fluoroquinolones (kg)*	(2381)	(2562)	(2590)	(2532)	(1796)
Other*****	24	21	24	28	20
Colistin (kg)*	(606)	(728)	(837)	(870)	(128)
Total ^x	464	436	445	408	337

^x The totals were rounded to the nearest integer. This explains the discrepancy between the overall total and the classes' totals.

*Because of the heightened interest in HP-CIA classes the sales of fluoroquinolones, 3rd and 4th generation cephalosporins and colistin are displayed in kg

**includes benzylpenicillin, benzathine penicillin, phenoxymethylpenicillin, procaine penicillin

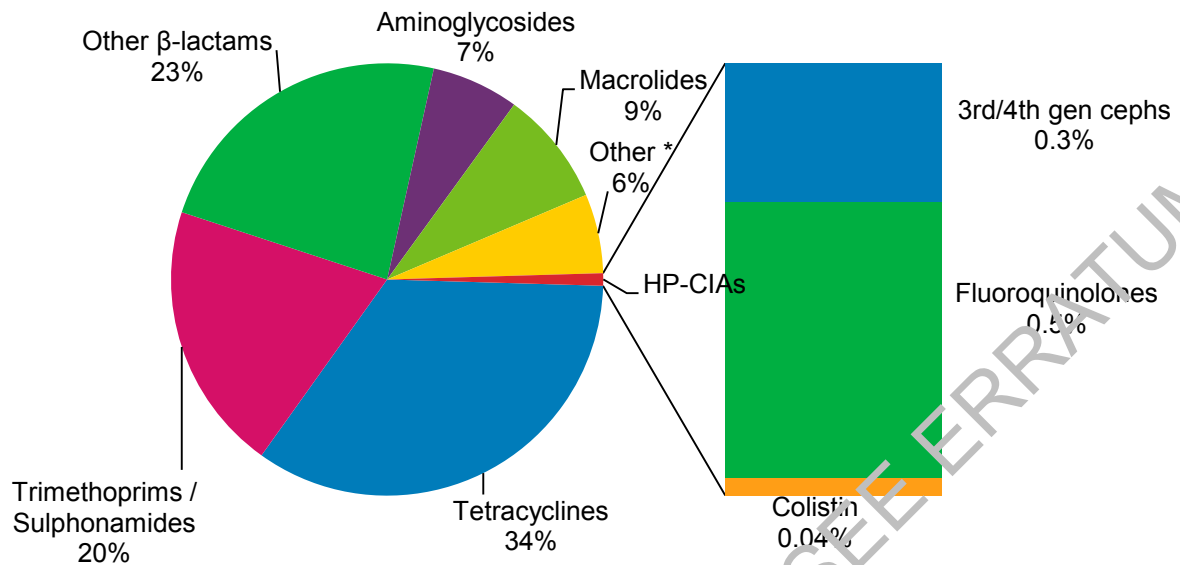
***includes amoxicillin (including in combination with clavulanic acid), ampicillin, cloxacillin, nafcillin

****includes apramycin, gentamicin, kanamycin, spectinomycin

*****includes: amphenicols, lincomycins, pleuromutilins, polymyxins and steroidal antibiotics. Colistin sales are included within this group.

Tetracyclines, β-lactams and trimethoprim/sulphonamides accounted for the majority (>75%) of active substance sold (Figure 1.3). As with previous years (see UK-VARSS 2015), HP-CIAs (fluoroquinolones, colistin and 3rd and 4th generation cephalosporins) accounted for a small proportion of the sales in 2016 (<1%).

Figure 1.3. Percentage (weight) of active ingredient of antibiotic by class sold for all species, 2016

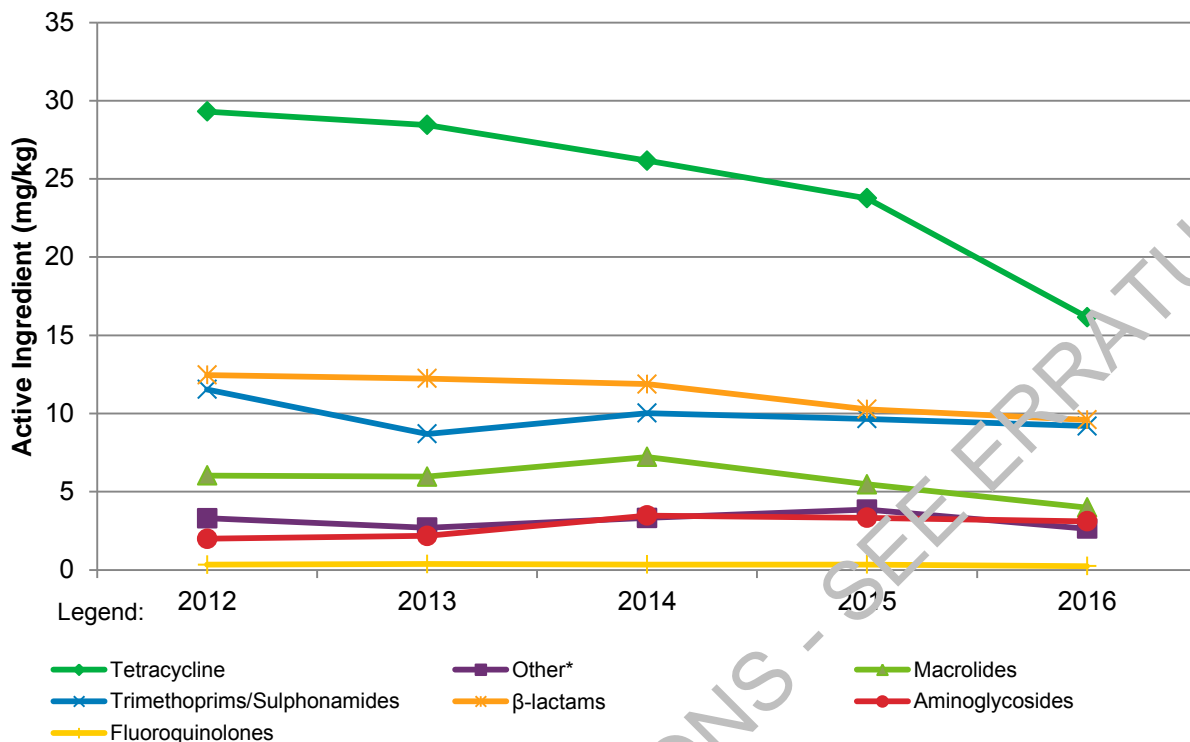


*Others includes: amphenicols, lincomycins, pleuromutilins, polymyxins (excluding colistin) and steroidal antibiotics.

1.4.3.2 Sales by antibiotic class for food producing species (mg/kg)

Sales of all classes of antibiotics declined between 2012 and 2016 (Fig. 1.4). Tetracyclines have remained the most sold class of products over the last five years, despite a steep decline of 8 mg/kg between 2015 and 2016.

Figure 1.4. Milligrams (mg) of active ingredient of antibiotic by class sold for food-producing species per kg by class, 2012-2016



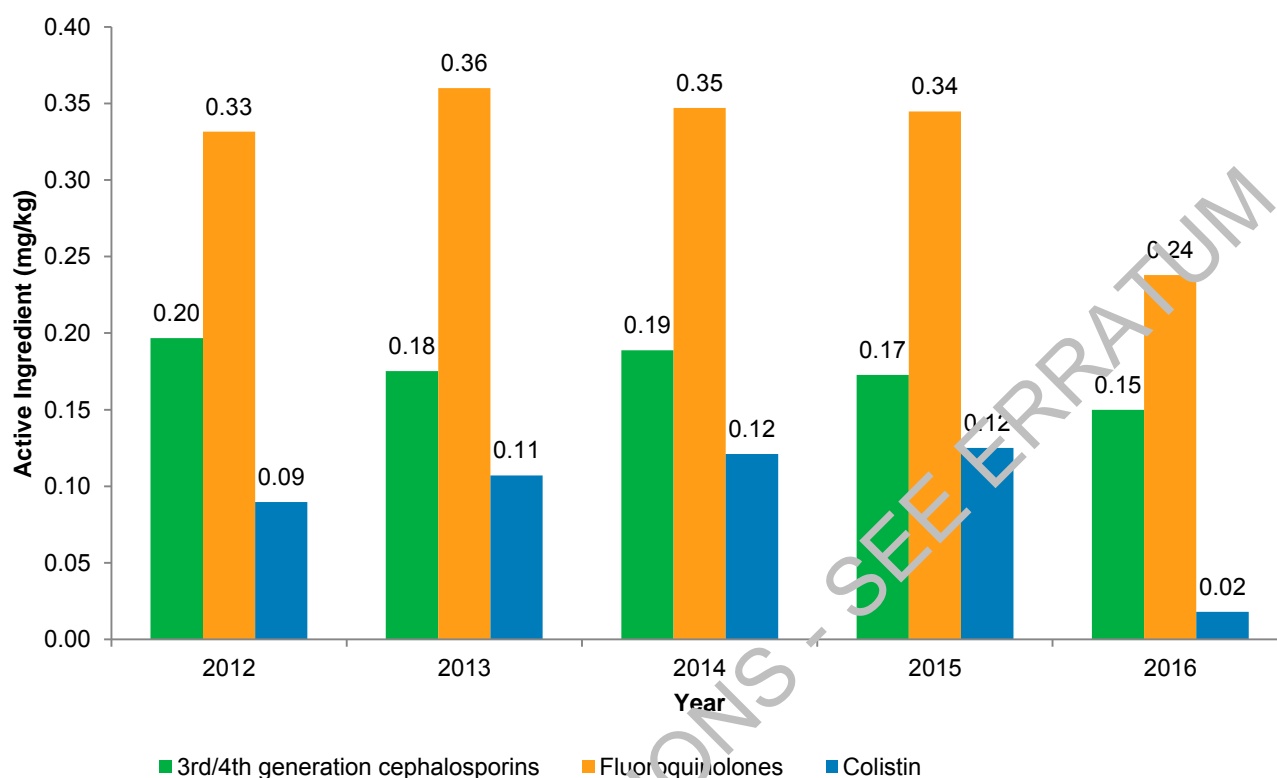
*Other includes: amphenicols, lincomycins, pleuromutilins, polymyxins (including colistin) and steroidal antibiotics.

1.4.3.3 Sales of antibiotics of particular relevance to human health (mg/kg)

In April 2013, the European Commission (EC) requested advice from the EMA on the impact of the use of antibiotics on human and animal health and measures to manage the possible risk to humans. Taking the World Health Organisation (WHO) list as a starting point, the EMA prepared a categorisation of HP-CIAs based on their degree of risk to people due to resistance development following use in animals in Europe. The advice classed fluoroquinolones and 3rd and 4th generation cephalosporins as category 2, which means the risk for public health is considered higher. Following the emergence of new data on colistin resistance, this advice was subsequently updated to include colistin as a category 2 antibiotic.

Sales of HP-CIAs represent a small proportion (<1%) of the 45 mg/kg overall antibiotic use in livestock. Sales of all three HP-CIA antibiotic classes decreased between 2015 and 2016, in particular colistin, which decreased by 83% (0.1 mg/kg) (Fig. 1.5).

Figure 1.5. Milligrams (mg)/kg of active ingredient of “highest priority critically important antibiotics” sold for food-producing species, 2012-2016



1.4.4 Total sales by administration route

1.4.4.1 Sales by administration route for all species

Of the main routes of administration of veterinary antibiotics (Table 1.4 and Fig. 1.6), premixes accounted for the majority of total sales in 2016 (44%), followed by oral/water products (29%).

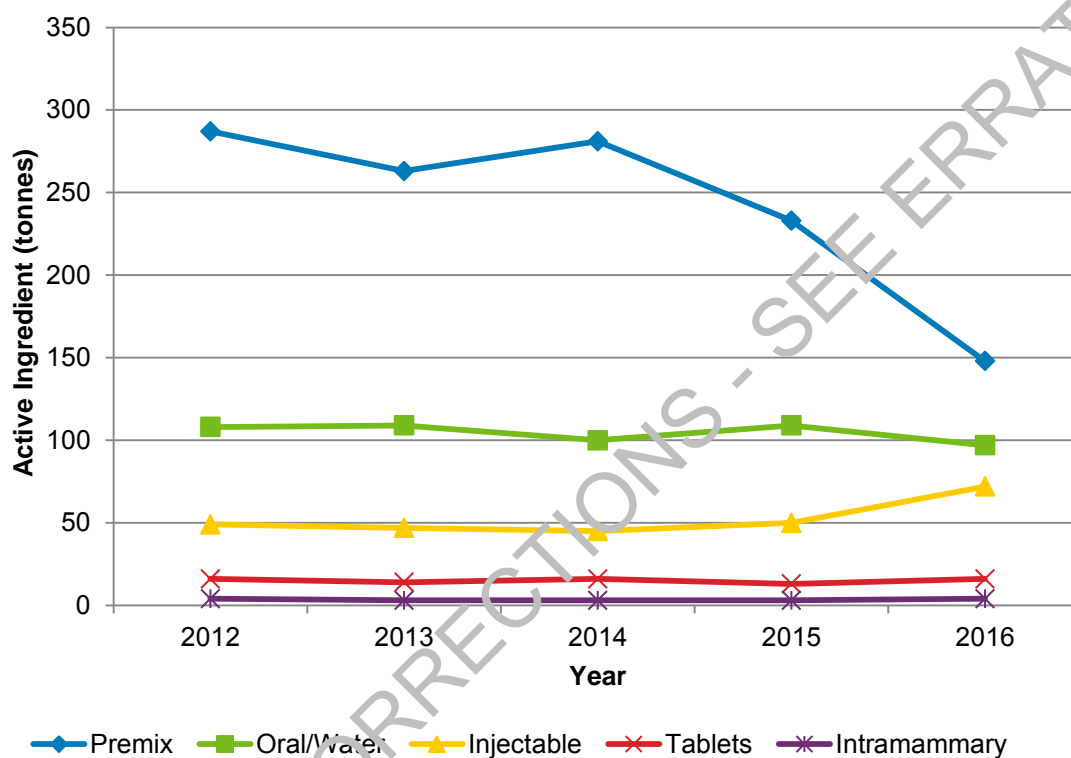
Table 1.4. Tonnes and (% of total sales) of active ingredient of antibiotic sold for all species by route of administration, 2012-2016

	2012	2013	2014	2015	2016
Premix	287 (62%)	263 (60%)	281 (63%)	233 (57%)	148 (44%)
Oral/Water*	108 (23%)	109 (25%)	100 (22%)	109 (27%)	97 (29%)
Injectable	49 (11%)	47 (11%)	45 (10%)	50 (12%)	72 (21%)
Tablets	16 (3%)	14 (3%)	16 (4%)	13 (3%)	16 (5%)
Intramammary	4 (<1%)	3 (<1%)	3 (<1%)	3 (1%)	4 (1%)
Total	464	436	445	408	337

*Excluding tablets, including bolus preparations

Sales of both premixes and oral/water soluble products decreased in 2016 by 36% and 11%, respectively (Table 1.4 and Fig.1.6). In contrast, sales of injectable preparations increased by 44% between 2015 and 2016. This was largely attributed to a rise in sales of injectable products licensed for a combination of both food and non-food producing animals (data not shown).

Figure 1.6. Tonnes of active ingredient of antibiotic sold for all species by route of administration, 2012-2016



1.4.4.2 Sales of intramammary antibiotic products

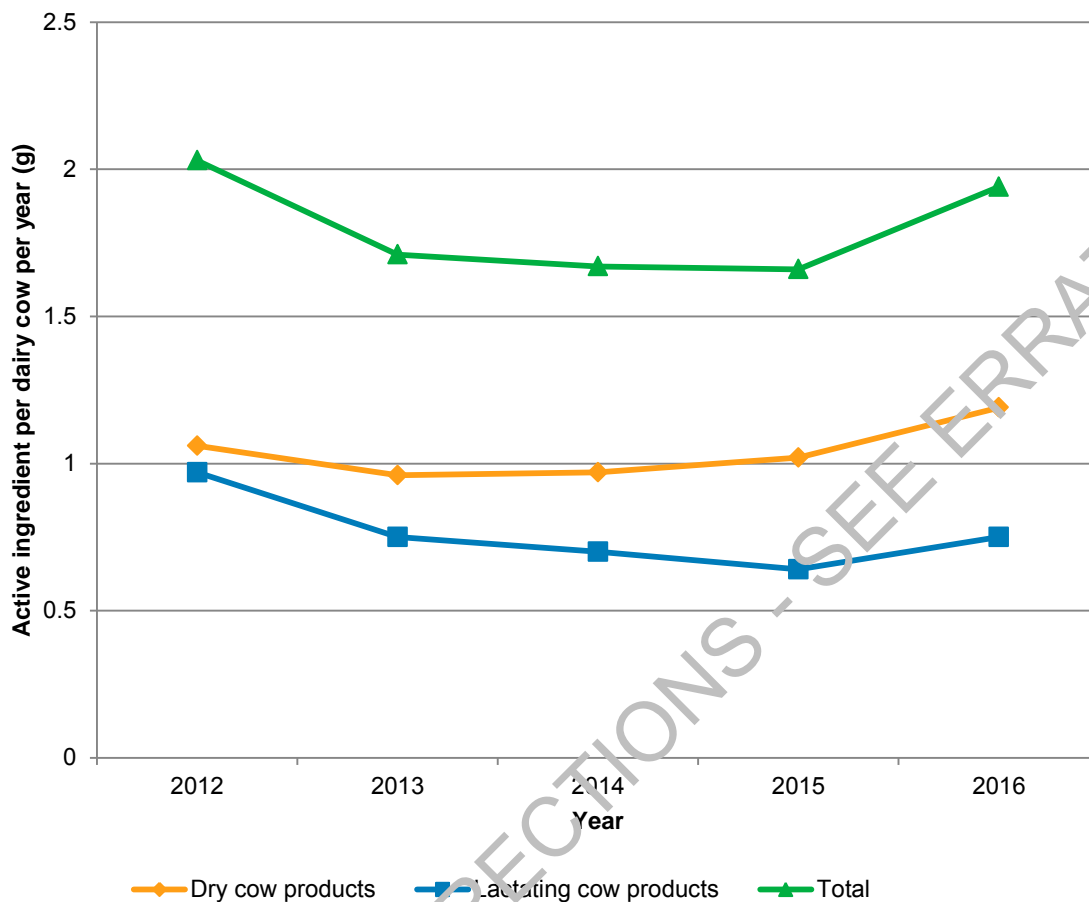
Table 1.5 and Fig. 1.7 show that the weight of active ingredient sold for dry cow intramammary treatment increased by 17% (326 kg of active substance or 0.18 g/animal) between 2015 and 2016. Sales of lactating cow products increased by 18% (221 kg of active substance or 0.12 g/animal).

Table 1.5. Total kilograms (kg) and (average amount in grams per dairy cow*) of active ingredient of intramammary antibiotics sold, 2012-2016

	2012	2013	2014	2015	2016
Dry Cow Products	1895 (1.06)	1716 (0.96)	1782 (0.97)	1941 (1.01)	2267 (1.19)
Lactating Cow Products	1750 (0.97)	1331 (0.75)	1289 (0.70)	1209 (0.63)	1430 (0.75)
Total	3645 (2.03)	3047 (1.71)	3072 (1.67)	3150 (1.64)	3697 (1.94)

*based on number of dairy cows in the national herd in each respective year, obtained from Agriculture in the United Kingdom, 2016

Figure 1.7. Average annual amount in grams (g) of active ingredient of intramammary antibiotic sold per dairy cow, 2012-2016



An assessment of courses given can be made based on the ESVAC defined course dose (DCDVet) methodology, where four tubes represents one course for dry cow therapy and three tubes represents one course for lactating cow therapy.

The number of DCDVet increased by 23% (from 0.80 to 0.98) for lactating cow therapy and by 2% (from 0.73 to 0.75) for dry cow therapy (data not shown). For dry cow therapy, the disparity between g/dairy cow (which increased by 17%) and number of DCDVet (which increased by 2%) is due by the fact that the average grams of active ingredient per dry cow tube sold increased from 0.35 to 0.40 between 2015 and 2016. This can be partly explained by a switch away from HP-CIAs, which have a lower amount of active ingredient per tube.

The amount of active ingredient from sales of HP-CIAs for intramammary use decreased by 19% (52 kg), and these reductions were primarily seen for dry cow therapy (data not shown). HP-CIAs now represent 5.9% of intramammary sales compared with 8.5% in 2015. In terms of course doses, this represents a 7% fall in use of HP-CIAs from 0.33 (22% of intramammary courses) to 0.31 (18% of intramammary courses).

1.4.4.3 Distribution of sales for the most-sold antibiotic classes and HP-CIAs by administration route

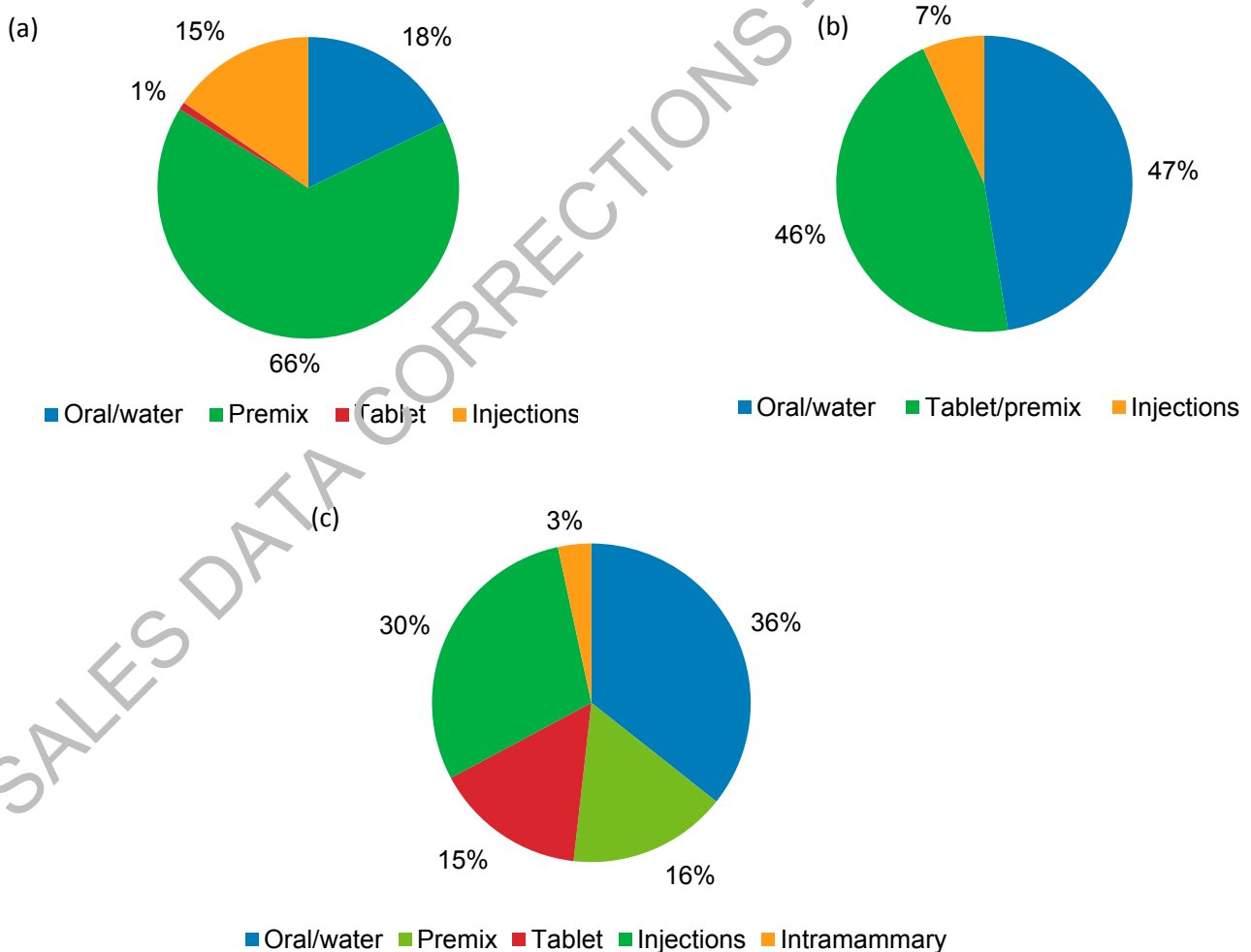
1.4.4.3.1 Most-sold antibiotics

The majority of sales for tetracyclines (66%) in 2016 were in premix form. The remainder of sales were attributed to oral/water (18%), injectable (15%) and tablet (1%) form, Fig 1.8a.

The majority of sales of sulphonamides in 2016 were used in oral/water (47%) and tablets/premix form (46%). Sales of tablets and premixes have been combined in Figure 1.8b for reasons of commercial sensitivity. A small proportion of sales containing sulphonamide as an active ingredient were also attributed to intramammaries.

The majority of β -lactams (including cephalosporins) in 2016 were in oral/water (36%) and injectable form (30%), Fig 1.8c.

Figure 1.8. Distribution of sales (tonnes) of most-sold antibiotic classes by the major pharmaceutical forms sold in 2016 for (a) tetracyclines, (b) sulphonamides, and (c) β -lactams



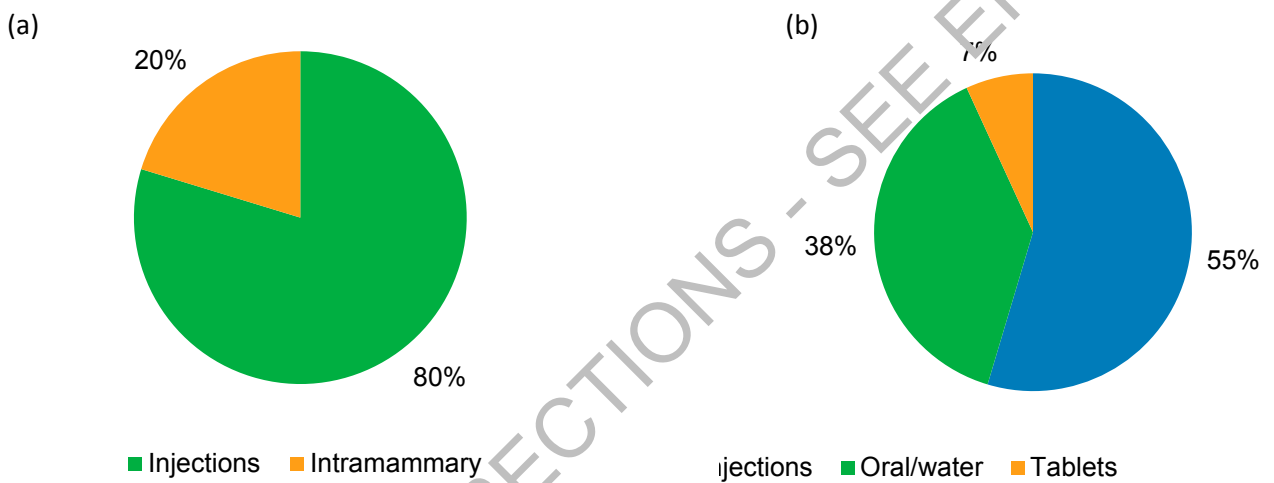
1.4.4.3.2 Highest Priority Critically Important Antibiotics

The majority of sales of 3rd and 4th generation cephalosporins in 2016 were for injectable formulations (80%) (Fig.1.9a).

The majority of fluoroquinolones in 2016 were injectable (55%) and oral/water (38%) formulations (Fig. 1.9b).

Sales of colistin in 2016 were solely via oral/water administration route.

Figure 1.9. Distribution of sales (tonnes) of HP-CIAs for all species, by the major pharmaceutical forms sold in 2016 (a) 3rd/4th generation cephalosporins, and (b) fluoroquinolones



CHAPTER 2

Antibiotic Usage Data Collection Activities by Livestock Species

SALES DATA CORRECTIONS - SEE ERRATUM

Chapter 2: Antibiotic Usage Data Collection Activities by Livestock Species

2.1 Summary

Antibiotic usage data from meat poultry was presented for the first time in the 2014 VARSS report, and this year the report also includes usage data from the pig, gamebird, egg and dairy sectors. This has been collected on a voluntary basis, and is testament to the hard work from the sectors in collecting these data and a strong willingness to share the data openly.

The report highlights the reductions achieved in 2016 by the pig and poultry sectors, with overall reductions in mg/kg of 34% in pigs, 37% in chickens, 57% in turkeys and 80% in ducks. As well as reductions in overall use, the pig and meat poultry sectors also managed to reduce Highest Priority Critically Important Antibiotics (HP-CIAs) by 73% and 78% respectively.

The report also presents important baseline data relating to the majority of the egg and game farm industry. Further work is needed to collect accurate usage data from the cattle and sheep sector, but results are presented here from a sample of 33% of dairy farms. These show that, although the mg/kg increased by 9%, there was a 5% reduction in the number of antibiotic courses administered. This was due to a switch away from HP-CIAs to non HP-CIAs, which have a higher amount of active ingredient per course than HP-CIAs.

2.2 Introduction

Many antibiotics are authorised for use in multiple species, so it is not possible to determine how much is used per species from sales data. The VMD worked in partnership with key livestock sectors to develop, facilitate and coordinate antibiotic usage collection systems.

Antibiotic usage refers to the amount of antibiotics purchased, prescribed and/or administered. The data have been obtained from producers (pig, poultry and egg sectors), feed companies (gamebirds) and veterinary practice sales records (gamebirds and dairy cattle).

Capturing antibiotic usage data per species will provide a baseline against which trends and the effect of interventions, such as those designed to reduce antibiotic use, can be measured. The data can also be used to investigate risk factors for high levels of antibiotic use and the effect of use on the development of resistance. Collection systems will also allow for benchmarking, enabling farmers to compare themselves with their peers and encouraging vets and farmers to identify and share good practice.

This chapter describes the progress achieved so far, with updates from the key livestock sectors. Note that, for ease of reading, the data have in some cases been rounded to the nearest integer. However, the percentage changes have been calculated using the exact number.

2.3 Antibiotic usage for the pig industry

2.3.1 Methods

The antibiotic usage data in pigs was extracted from the electronic Medicines Book for Pigs (eMB), developed by the pig sector with support from the VMD, and launched by the Agriculture and Horticulture Development Board Pork (AHDB) Pork in April 2016.

The scope and limitations of the data (as provided by AHDB-Pork) are presented below:

- These data are national, aggregated figures for antibiotic usage calculated from individual unit data held in the eMB for pig farms across the UK. To date, eMB uptake has been voluntary; therefore, this sample may not be representative for the whole of the UK.
- These eMB data cover 56% UK pig production for 2015 and 62% pig production in 2016. In terms of English pig production, these eMB data cover 61% of slaughter pigs for 2015 and 70% for 2016.
- Producers input their data and, although AHDB identified and queried clear outliers, it is not able to validate every individual producer's data. However, at a national, aggregated level, the data provide an estimation of national usage and allow year-on-year comparisons to be made.
- These data were extracted from eMB on 14 September 2017 and the figures will now be fixed as the reference levels for 2015 and 2016. Producers may still add 2015 and 2016 data to eMB for their own usage, but data entered or modified after this date will not be used to further amend the national aggregated figures.
- The eMB database and the calculations within it have recently been subject to a series of quality assurance checks to ensure national aggregated figures are as accurate as possible. As a result of this process, the eMB system is continuing to develop, and work to further improve data accuracy is ongoing.
- The calculations used for the eMB data are in-line with the methods used by the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project, to allow comparisons to be made with European counterparts.

2.3.2 Results and discussion

2.3.2.1 Statement from Pig Health and Welfare Council (PHWC) Antimicrobial Usage Subgroup

“The PHWC Antimicrobial Usage Sub-Group continues to work to implement the action plan to promote the responsible use of antibiotics in UK pig production. The antibiotic reductions highlighted here between 2015 and 2016 are testament to what has been achieved so far, although there is still further work to be done. The veterinary and farming industries, with support from the Pig Veterinary Society (PVS) and the National Pig Association (NPA), are committed to a rigorous ongoing plan to reduce and refine antibiotic use further within the sector, and this will be carried out alongside monitoring of the individual and collective health of pigs. Key focuses of this ongoing and ambitious programme include changing attitudes (the “courage to cut”) and promoting

responsible use strategies which, depending on the specific farm situation, include vaccination and disease elimination, as well as husbandry, environment and biosecurity improvements. In addition to overall use, the data from eMB highlight the significant reductions in Highest Priority Critically Important Antibiotics (HP-CIAs). Use of these products is constrained by the requirements of the PVS Prescribing Principles to which all veterinary surgeons attending Red Tractor assured farms are required to adhere to, and those attending QMS assured farms are recommended to adhere to. From October 2017, additional documented justification for such use on the Veterinary Health Plan will be required in all regions.

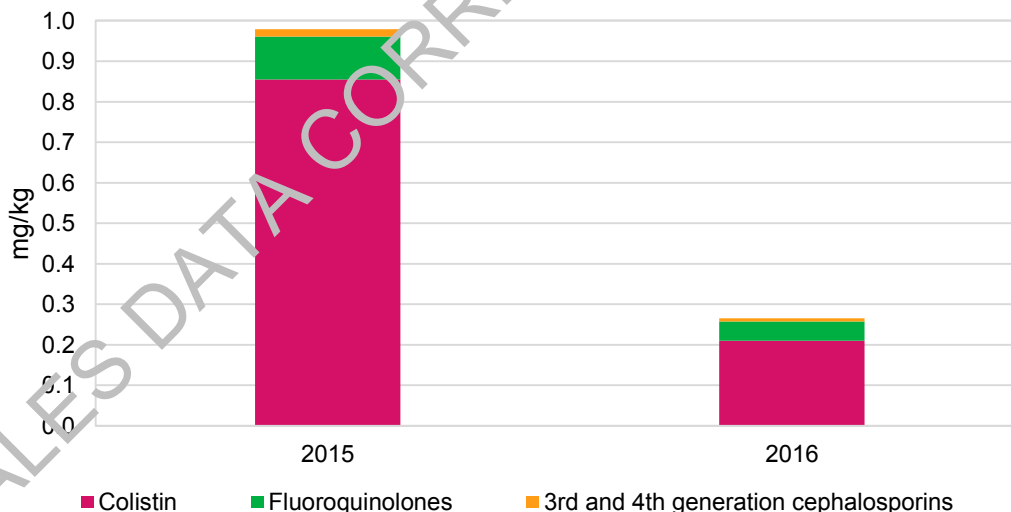
In the future, the amount of antibiotic usage data being added are also set to increase; QMS Scotland required the use of eMB pigs to record antibiotic usage from August 2016 and, as of 11th November 2017, this will now be a requirement under the Red Tractor assurance scheme. In addition, benchmarking facilities are being completed, and these will allow farms to compare their use with similar farm types around the UK.”

2.3.2.2 Antibiotics usage data from eMB Pigs

Total eMB recorded antibiotic usage in pigs was 89 tonnes in 2016 and this represents 62% of the UK pig population. When taking into account the weight of the pig population, usage decreased by 34% from 278 mg/kg in 2015 to 183 mg/kg in 2016.

Usage of HP-CIAs recorded in pigs decreased by 73% from 1.0 mg/kg in 2015 to 0.3 mg/kg in 2016 and these represent 0.1% of total antibiotic usage recorded in 2016. In particular, colistin usage decreased by 75% from 0.9 mg/kg in 2015 to 0.2 mg/kg in 2016 (Fig 2.1).

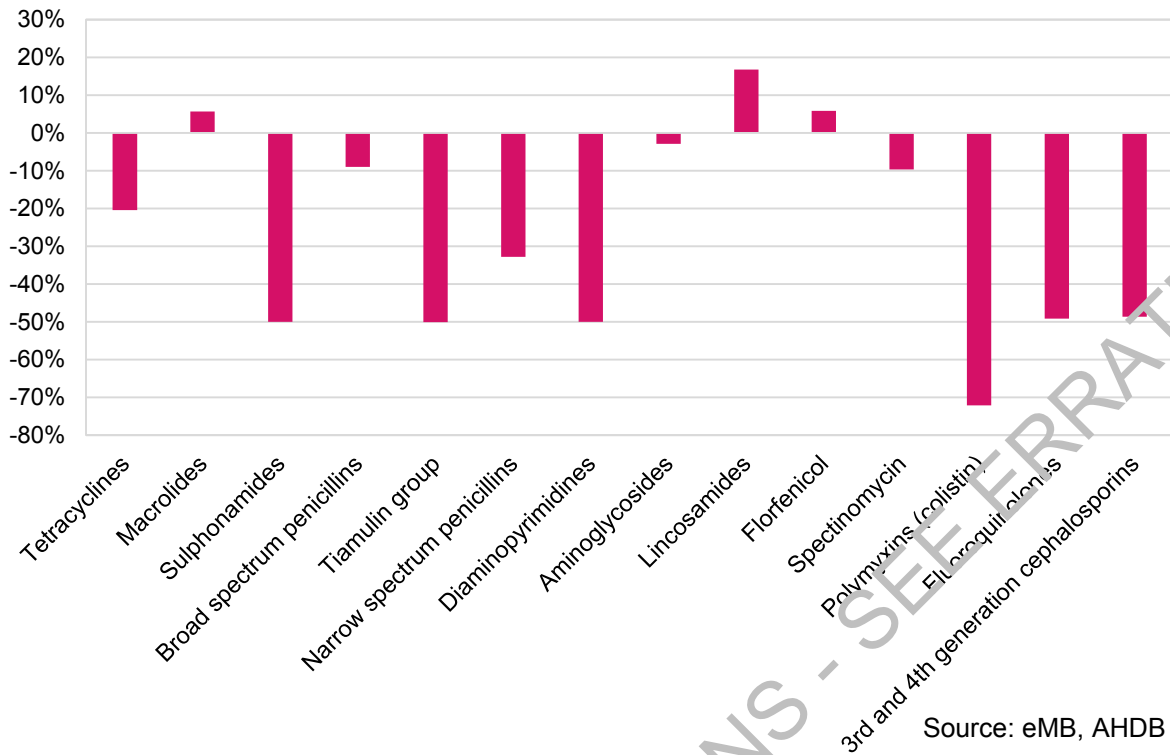
Figure 2.1. HP-CIA usage in pigs recorded in eMB by class, 2015-2016



Source: eMB, AHDB

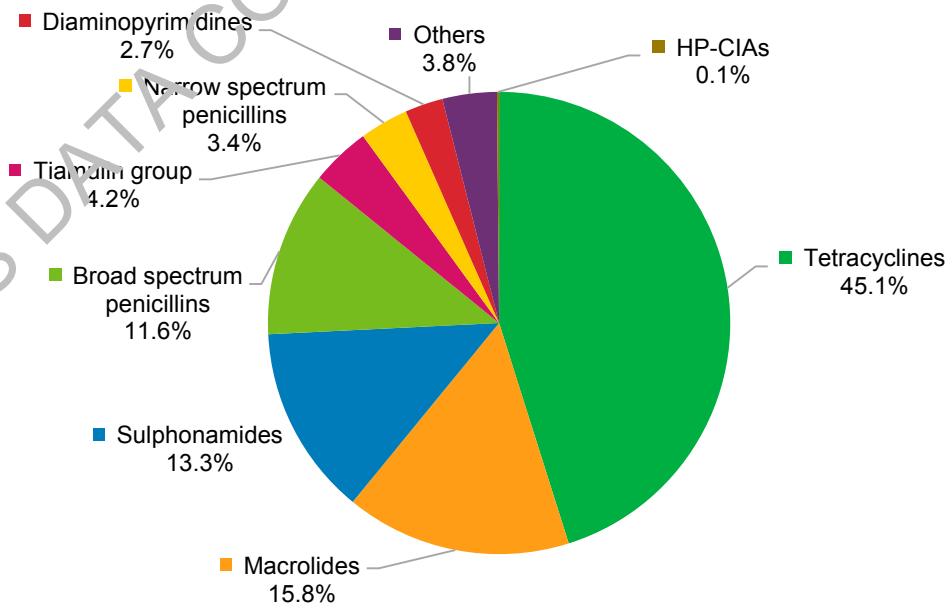
Recorded usage decreased across nearly all antibiotic classes between 2015 and 2016, except for macrolides, lincosamides and florfenicol (Fig. 2.2).

Figure 2.2. Change in antibiotic usage (%) recorded in eMB between 2015 and 2016 by class



Tetracyclines made up nearly half of usage (45%) followed by macrolides (16%) and Sulphonamides (13%) (Fig 2.3).

Figure 2.3. Antibiotic usage in pigs recorded in eMB for 2016 by class



2.4 Antibiotic usage for the meat poultry industry

2.4.1 Methods

The British Poultry Council (BPC) provided the antibiotic usage data for the meat poultry (chicken, turkey and duck) industries. It runs an antibiotic stewardship scheme that covers 90% of the industry. This process of data collection started in 2012 and producers are responsible for submitting quarterly (chicken) or annual (turkey and duck) antibiotic use data in the form of an aggregate spreadsheet. BPC then collate the data and report usage per sector in their annual report. This includes the overall annual amount of antibiotic active ingredient used (in tonnes), which includes breeders and producers. For the producers, this is then compared with the population at risk of treatment to create a mg/kg usage figure. BPC calculates the population at risk of treatment by using annual slaughter numbers and the following standardised estimated weights at time of treatment:

- **Chickens:** 1 kg (derived by ESVAC)
- **Turkeys:** 6.5 kg (derived by ESVAC)
- **Ducks:** 1.75 kg (derived by BPC based on ESVAC principles)

BPC carries out the calculations using ESVAC methodology. The process of calculating active ingredient has been validated by VMD.

2.4.2 Results and discussion

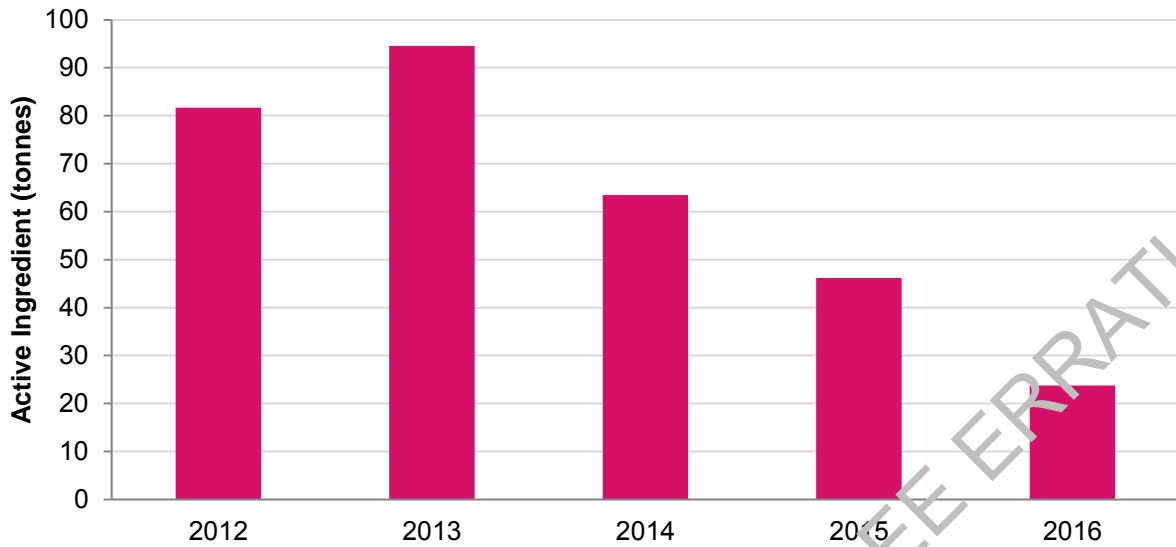
2.4.2.1 Statement from British Poultry Council

“The British Poultry Council Antibiotic Stewardship was set up in 2011 to continuously review on-farm management practices and ensure sustainable use of antibiotics throughout the supply chain. The Stewardship aims to ensure that antibiotic therapies are used only when necessary, to protect the health and welfare of the birds, to safeguard the efficacy of antibiotics, and to produce food consumers trust. An openness in the sector to accept change, encourage innovation and share best practice has resulted in a 71% reduction in the total use of antibiotics from 2012 to 2016. The poultry meat sector started an antibiotic usage collection system in 2012, stopped the prophylactic use of antibiotics as well as the use of colistin in 2016 and committed to use macrolides and fluoroquinolones only as a last resort. As part of the BPC’s clinical governance approach, any use of macrolides and fluoroquinolones is reported in detail to BPC, including case history and outcome of the treatment.”

2.4.2.2 Antibiotic usage data from British Poultry Council

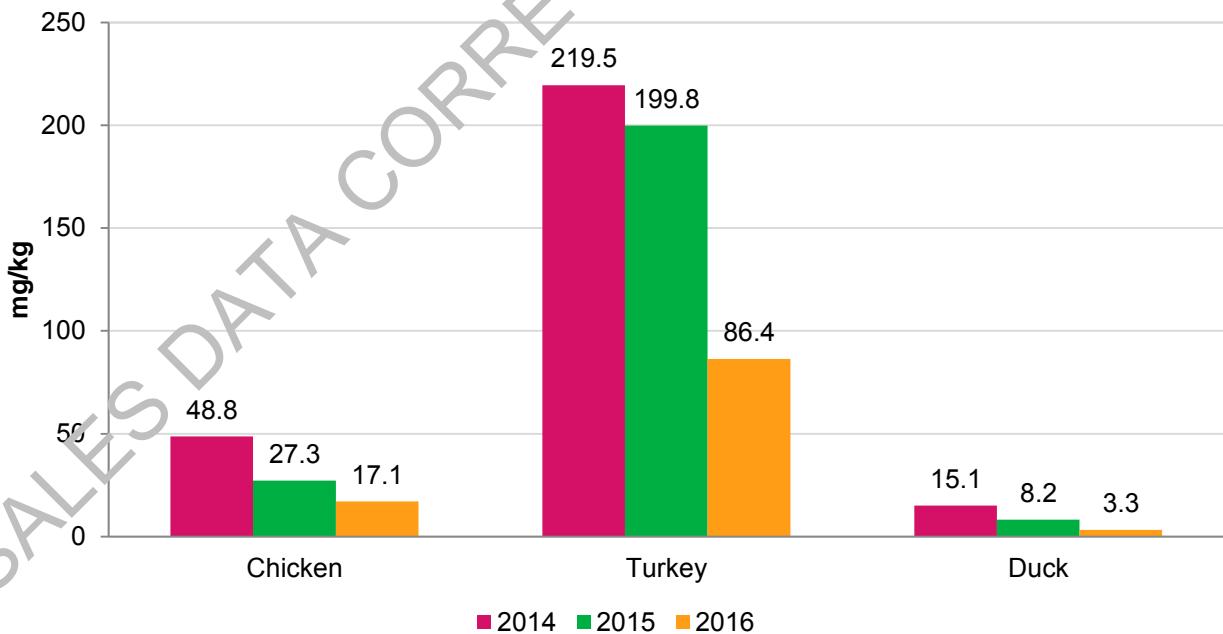
In 2016, the BPC reported the use of 23.7 tonnes of antibiotic active ingredient, which is a reduction of 22.5 tonnes (49%) compared with 2015. This also represents a reduction of 58 tonnes (71%) from 2012 and is the lowest recorded value over the four years that BPC has been collecting these data (Fig. 2.4).

Figure 2.4. Tonnes of active ingredient of antibiotic used by all members of the BPC Antibiotic Stewardship 2012-2016



For the first time, BPC has provided usage data split by species, (Fig. 2.5). This shows that since 2014 the chicken sector has reduced usage by 31.7 mg/kg (65%); the turkey sector has reduced usage by 133.1 mg/kg (61%); and the duck sector has reduced usage by 11.9 mg/kg (78%).

Figure 2.5. Mg/kg of active ingredient of antibiotic used by members of the BPC Antibiotic Stewardship, split by species (chicken, turkey and duck)



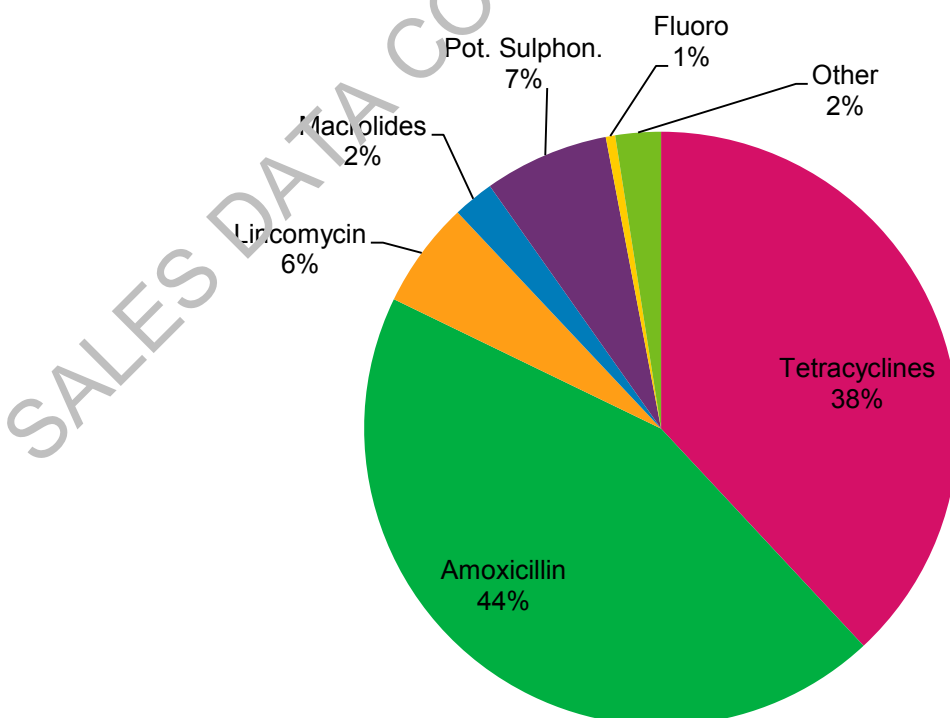
When analysed to level of active ingredient class, 82% were in the form of amoxicillin and tetracycline for 2016 (Table 2.1 and Fig. 2.6). Between 2015 and 2016, reductions were seen across all antibiotic classes except potentiated sulphonamides (Table 2.1). When considering the most used antibiotics, the use of amoxicillin reduced by 3.5 tonnes (25%) and tetracyclines reduced by 14.9 tonnes (62%). This reduction in tetracyclines is primarily driven by the turkey sector, which reduced its use from 15.2 tonnes to 4.3 tonnes (data not shown).

Table 2.1: Active ingredient of antibiotic (tonnes) used by members of the BPC Antibiotic Stewardship, by class 2015-2016

	2015 Tonnes (%)	2016 Tonnes (%)
Amoxicillin	14.0 (30)	10.5 (44)
Tetracyclines	23.9 (52)	9.0 (38)
Potentiated sulphonamides	1.0 (2)	1.6 (7)
Lincomycins	4.8 (10)	1.4 (6)
Macrolides	1.1 (2)	0.5 (2)
Fluoroquinolones**	0.5 (1)	0.1 (<1)
Other*	0.9 (2)	0.6 (2)
Colistin**	0.04 (<1)	0.008 (<1)
Total	46.2	23.7

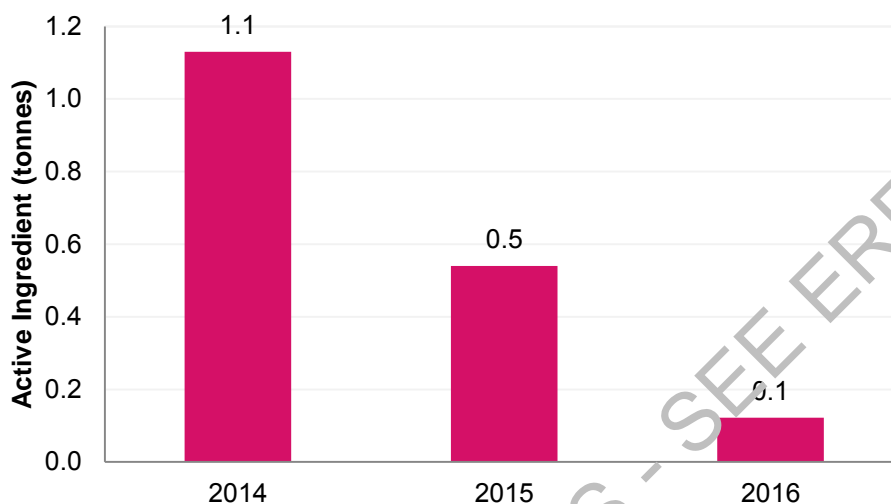
* - includes aminoglycosides, penicillin, pleuromutalin, colistin and products under the cascade
 ** - highest priority critically important antibiotics

Figure 2.6. Breakdown of active ingredient of antibiotic used by members of the BPC Antibiotic Stewardship, by class 2016



In terms of HP-CIAs, there was virtually no use of colistin (BPC stopped the use of products containing colistin during 2016). In addition, fluoroquinolone use now account for only 0.5% of antibiotics used and this has reduced by 78% since 2015 (Fig 2.7).

Figure 2.7. Tonnes of active ingredient of fluoroquinolones used by members of the BPC Antibiotic Stewardship, 2014-2016



When analysed to the level of species, the duck sector did not use any fluoroquinolones, the chicken sector have reduced usage by 96%, and the turkey sector have reduced usage by 76% (data not shown).

2.5 Antibiotic usage for the egg industry

2.5.1 Methods

The collection of antibiotic usage data is organised by the British Egg Industry Council (BEIC). Sharing these data with BEIC is obligatory through the Lion Scheme, which represents 90% of the UK egg industry. All egg producers, pullet rearers and breeding companies are required to report any use of an antibiotic to their subscriber. Producers report their data to the BEIC on a quarterly basis and denominator data are available from monthly records of the total number of birds in the scheme, averaged over the year. The BEIC collated the aggregate annual antibiotic pack level data and provided it to the VMD, who have carried out and validated the usage by active ingredient using ESVAC principles. The data published here as 'daily doses/100 chicken days at risk' represents the average number of doses administered per chicken over a 100 day period and is based on the actual number of doses administered, which is provided directly to BEIC.

2.5.2 Results and discussion

2.5.2.1 Statement from the British Egg Industry Council

“The usage data presented for 2016 confirms that the egg industry is a low user of antibiotics. Infectious disease is mainly controlled by good management, hygiene and, where appropriate, vaccination. The UK egg industry assurance scheme – the BEIC Lion Code of Practice – includes specific constraints on HP-CIAs – for example 3rd and 4th generation cephalosporins cannot be used, fluoroquinolones cannot be used on day-old chicks and, since 6th June 2016, colistin cannot be used. These constraints have been implemented by BEIC in consultation with veterinarians, with a view to reducing the risk of selection for antibiotic resistance in the egg food chain, which might be of clinical relevance in human medicine. BEIC is also in the process of rolling out a new formal training scheme for farm and hatchery staff involved in egg production (The Lion Training Passport). This will involve targeted training on many aspects of farm operations relevant to reducing the need to medicate. This scheme will be available to all members of staff on Lion Code farms and hatcheries.”

2.5.2.2 Antibiotic usage data from the British Egg Industry Council

Data for 2016 show that the egg industry used 2.6 tonnes of antibiotic active ingredient, which represents 0.73 daily doses/100 days (or % bird days treated). Note that a ‘mg/kg’ figure has not been calculated, as ESVAC do not provide a standardised method/weights for the egg sector.

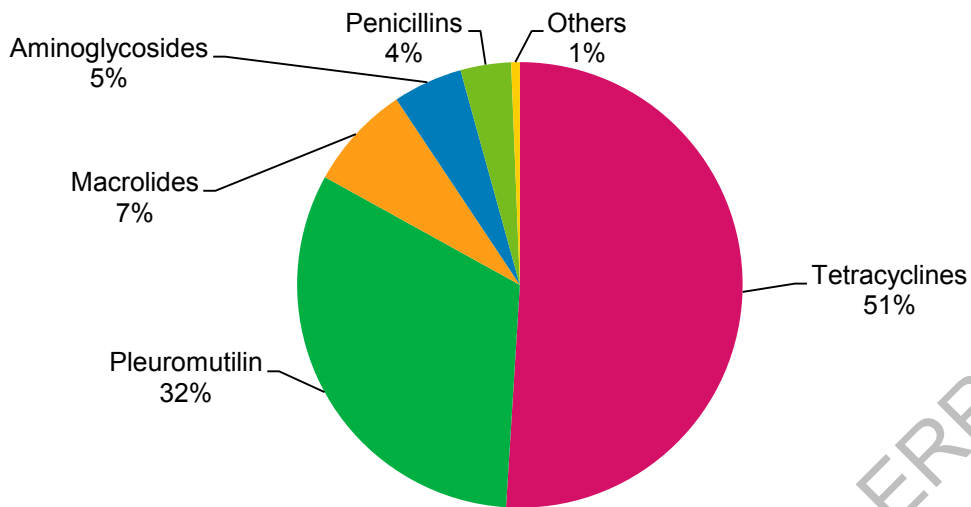
When analysed to the level of active ingredient class, tetracycline and pleuromutilins account for 83% of the use (Table 2.2 and Fig. 2.8).

Table 2.2. Tonnes of active ingredient used by members of the BEIC Lion Code 2016

Antibiotic	Tonnes (%)	Antibiotic	Tonnes (%)
Tetracyclines	1.33 (51)	Penicillins	0.10 (4)
Pleuromutilins	0.84 (32)	Colistin*	0.01 (<1)
Macrolides	0.20 (7)	Lincomycins	0.0012 (<1)
Aminoglycosides	0.13 (5)	Fluoroquinolones*	0.0002 (<1)

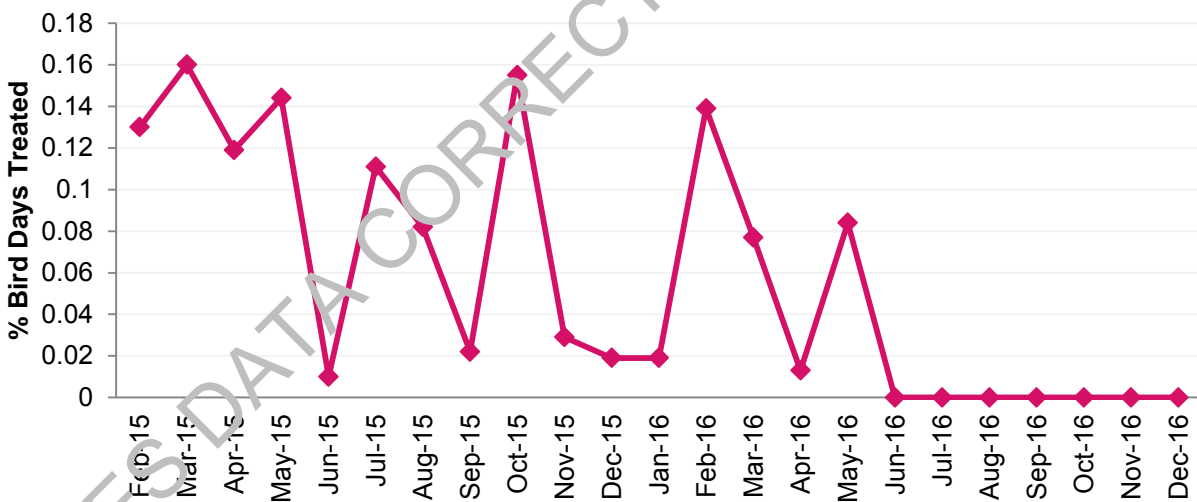
* Highest Priority Critically Important Antibiotics

Figure 2.8. Tonnes of active ingredient used by members of the BEIC Lion Code 2016



When considering the HP-CIAs, fluoroquinolone use is very low (<0.008% of antibiotics used). Colistin use accounts for less than 0.6% of antibiotics used, and since BEIC introduced a colistin ban on 6th June 2016, usage has dropped to zero use (Fig 2.9).

Figure 2.9. Monthly % bird days treated with colistin by members of the BEIC Lion Code



2.6 Antibiotic usage for the gamebirds industry

2.6.1 Methods

The Game Farmers Association (GFA) coordinated a comprehensive, voluntary usage data collection exercise to measure the use of antibiotics throughout the sector. This involved the collection of:

- In-feed incorporation records from all known game feed producers, which supply 95% of game farmers and rearers;
- Prescribing records from all known specialist gamebird vets, of which 75% of game farmers and rearers are clients.

Each of these companies was asked to provide a spreadsheet showing the amount of each antibiotic used in 2016. GFA aggregated the results and provided them to the VMD, who then used ESVAC methodology to calculate the amount of antibiotic active ingredient administered by the game sector.

2.6.2 Results and discussion

2.6.2.1 Statement from Game Farmers Association

“The Game Farmers Association voluntarily instituted data collection and is committed to bringing down antibiotic use, while ensuring bird health and welfare are preserved. A whole sector campaign to raise awareness on the importance of using as little antibiotic as possible has begun, and this has involved gamebird keepers, their vets and their feed companies. In May 2017, for example, all 19 specialist gamebird veterinary practices in the UK supported and circulated a Joint Communication summarising best practice requirements for antibiotic use and prescribing. This reinforced the message that no in-feed antibiotics should be prescribed to gamebirds unless the responsible vet has visited the birds and established through diagnosis a specific need to prescribe. Case studies are also being written up and disseminated, sharing best practice and highlighting the importance of, for example, scrupulous biosecurity, ploughing the ground between rearing seasons and careful management of stocking densities, lighting levels and ventilation.”

2.6.2.2 Antibiotic usage data from Game Farmers Association (GFA)

The verified data show that 20.2 tonnes of antibiotic active ingredient were reported through the GFA data collection programme for 2016. Note that a ‘mg/kg’ figure has not been included, as ESVAC do not provide standardised methods/ weights in order to calculate this for gamebirds.

GFA reported that 74% of antibiotic use was administered through feed and 26% in water (derived from Table 2.3). There are no licensed in-feed products for gamebirds, so these products are used under veterinary prescription via the cascade system.

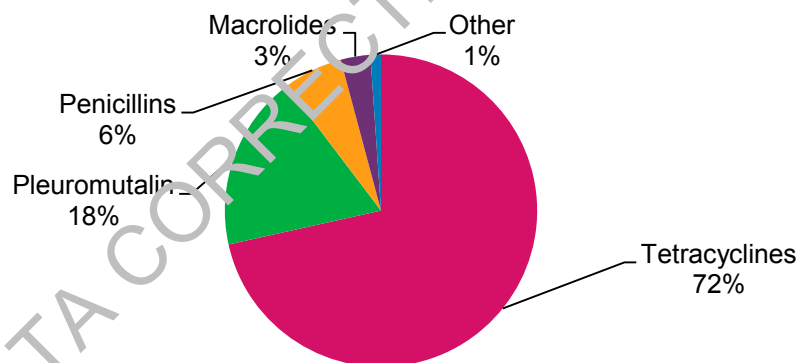
Table 2.3. Tonnes of active ingredient of antibiotics used by the gamebirds industry, as collected by GFA 2016

	Premix Tonnes	Water Tonnes
Tetracyclines	11.9	2.6
Pleuromutilins	2.7	1.0
Macrolides	0.4	0.2
Penicillins	0	1.2
Other, includes:	0	0.2
Fluoroquinolones*		63.5 kg
Colistin*		0.6 kg
Total	15.0	5.2

* Highest Priority Critically Important Antibiotics

Tetracyclines and pleuromutilins represent 90% of antibiotics used (Fig. 2.10). Tetracyclines are commonly used in gamebirds for treating protozoal rather than bacterial diseases. HP-CIAs, however are only used in water, and their use is low (representing 0.3% of all antibiotics used in the gamebird sector).

Figure 2.10. Percentage of active ingredient of antibiotics used by the gamebirds industry, as collected by GFA 2016



This is the first time that the gamebirds industry, through the GFA, collected and subsequently published antibiotic usage data for their sector. These figures will provide a baseline for monitoring the effect of the extensive programme of work that is being undertaken to reduce antibiotic use within the sector.

2.7 Antibiotic usage for the cattle industry

2.7.1 Methods

The data from dairy farms presented in this report have been taken from FarmVet Systems, a software company which extracts and cleanses sales data from Practice Management Systems and can determine whether the medicine has been delivered to a farm keeping cattle.

In this analysis, farms were considered dairy if they had more than 15 calves born to dairy dams, using information derived from movement records (British Cattle Movement Service (BCMS) for England, Wales and Scotland, and Animal Plant Health Inspection Service for Northern Ireland). The average number of dairy breed animals over 2 years of age was determined for each farm and used to calculate the mg/kg using ESVAC methodology.

The VMD converted the aggregate data into amount of active ingredient using standard ESVAC methodology, with topical antibiotics excluded from the analysis. However, in this sample of farms these accounted for a small proportion (<2%) of antibiotic active ingredient used in cattle.

Products that did not include 'cattle' in the license were excluded from the analysis. However, it is possible that some of the products excluded were used in cattle via the cascade system. It is important to note that products licensed for 'multi-species' – including cattle – may also have been used in other species kept on the farm. This is particularly the case for products (such as long acting tetracyclines), which are commonly used in sheep and cattle. However, the number of sheep only products was relatively small (representing 0.8% of total use of these products when compared with sales data) so the impact of sheep use of the "multi-species" products in this sample is also likely to be relatively small.

The beef data obtained during this process are not presented in this report. The antibiotic data collected for beef represented 11% of the industry. However, when comparing with the UK sales data, the use of sheep only products in these farms also represent 11% of total UK sales. This highlights how interlinked the sheep and beef industries are and work is currently ongoing to try to accurately determine sheep numbers in this sample of farms and assess the possibility of separating out which "multi-species" products are being used in beef and which are being used in sheep. This issue of beef and sheep highlights the importance of categorising accurately on Practice Management Systems whether a product is intended for use in beef or sheep. Another option is to collect usage data from the farm itself rather than relying on vet sales data.

2.7.2 Results and discussion

2.7.2.1 Statement from Cattle Health and Welfare Group (CHAWG)

“The sample data presented here have arisen from a collaboration between the Cattle Health and Welfare Antimicrobial Usage Data Collection Steering Group, the Agriculture and Horticulture Development Board (AHDB) and FarmVet Systems. While it may not be a truly representative sample, it does account for 33% of UK dairy cows and highlights some important trends for the dairy industry. The reduction in the use of HP-CIAs demonstrated by this sample of dairy farms reflects efforts by the cattle industries and the veterinary profession in working towards the December 2016 statement produced by the British Cattle Veterinary Association. This statement explains that these drugs “should only be used where they have been demonstrated by sensitivity testing to be the only suitable choice to avoid unnecessary suffering”. This is also consistent with the new Red Tractor Assurance scheme standards for beef, dairy and sheep, which from October 2017, state that “Highest Priority Critically Important Antibiotics (HP-CIAs) are used as a last resort under veterinary direction”.

In the future, the Antimicrobial Usage Steering Group will continue to work towards obtaining accurate, representative baseline data for the dairy, beef and sheep industries and developing standard protocols to aid in collection and analysis of farm and veterinary antibiotic usage data for benchmarking purposes. It will also strive for the creation of an industry-owned and managed data collection hub that can collate antibiotic usage data (from vet- and/or farm-level sources) in one place. Furthermore, from October 2017, the dairy Red Tractor standards will include a requirement that dairy farms collate data on antibiotic usage and review this with their vet on an annual basis. This review must also make recommendations towards responsible reduction of antibiotic use, selective dry cow therapy and a review of any antibiotic failures. As 98% of UK dairy herds are registered under this scheme, this is likely to provide considerable traction.”

2.7.2.2 Results

The dairy data for 2015 and 2016 represent just over 3000 farms. AHDB commissioned Bristol University to assess the representativeness of the sample, and it was found that, when looking at total number of dairy cattle, the sample covers 1/3 of all dairy cattle in the UK, although percentage coverage in the sample is higher in England and Northern Ireland than in Wales and Scotland (Table 2.4). The mean herd size in the sample (using the definition average number of dairy breed cattle > 2 years of age) is 211 for 2015 and 214 for 2016. BCMS record analysis shows that, for farms in Great Britain, the mean herd size in this sample is 36% higher than the overall mean (data not shown).

Table 2.4. A comparison of farms included in the FarmVet Systems sample for 2016

	Distribution of dairy cattle in sample (%)	National coverage (%)	Mean herd size (average number of cattle > 2 years of age)
England	65	32	229
Northern Ireland	22	45	170
Wales	9	20	225
Scotland	4	12	261

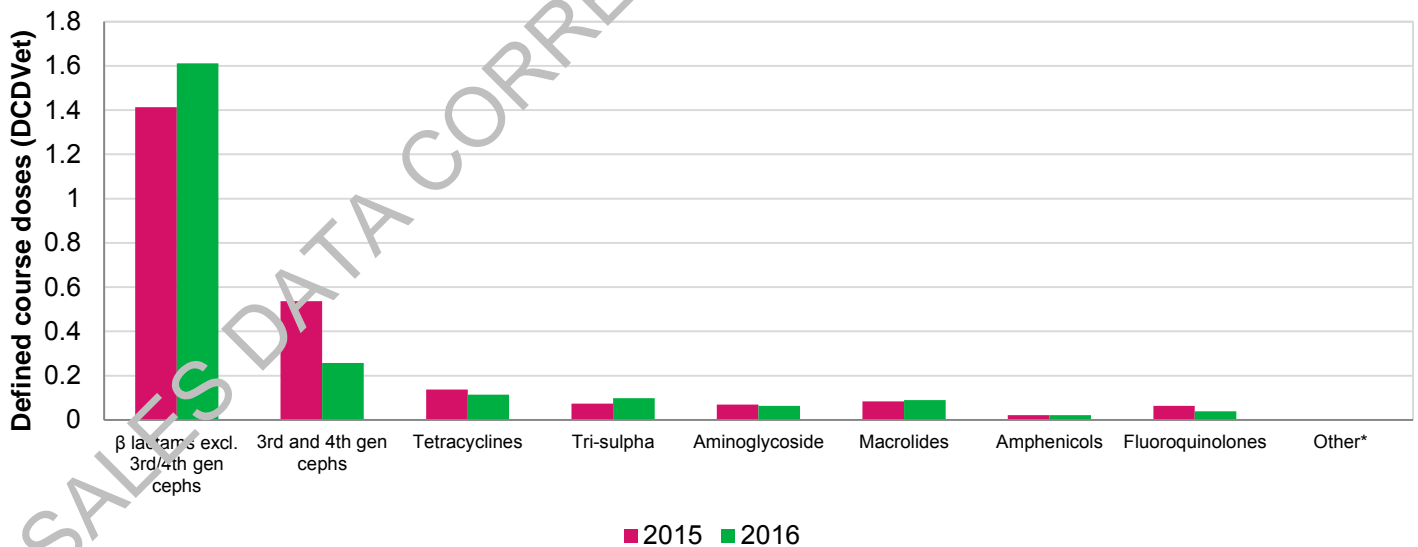
* calculated by comparing the number of dairy cattle over 2 years of age in the sample with national records.

The usage for these dairy farms was 24.0 mg/kg and 26.2 mg/kg in 2015 and 2016 respectively. However, the number of courses administered (measured using the ESVAC defined course doses (DCDVet) methodology) has reduced from 2.4 to 2.3 (Table 2.5).

There are two key reasons for this discrepancy between mg/kg and DCDVet:

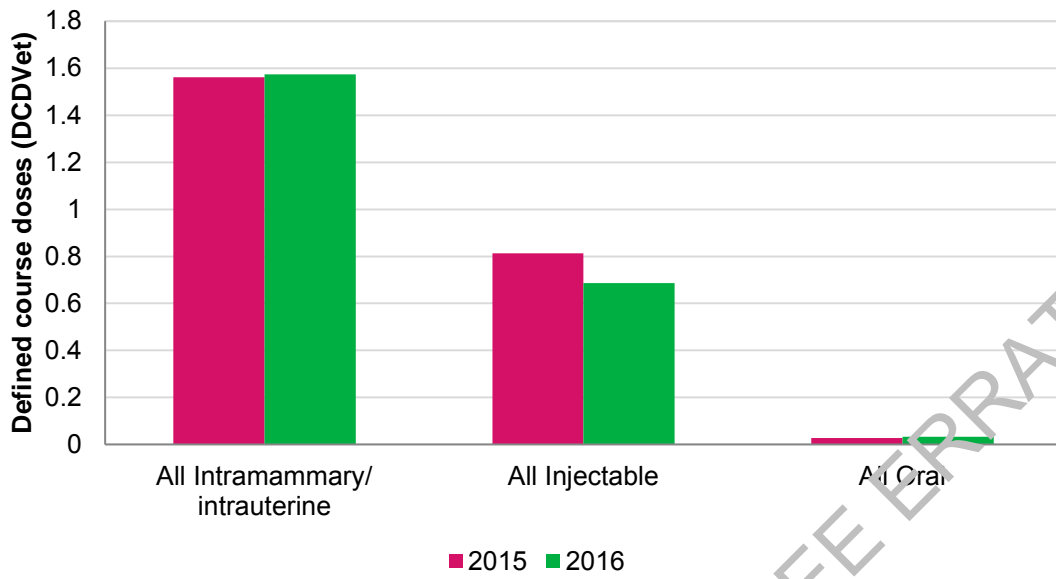
1. There has been a switch away from HP-CIAs to non HP-CIAs (in particular other β -lactams) which have a higher amount of active ingredient per course than HP-CIAs (Fig 2.11). This explains, for example, why the DCDVet for injectable courses has decreased by 15% (Fig 2.12), but the mg/kg for injectables has increased by 6% (Table 2.5).

Figure 2.11. Number of defined course doses (DCDVet) administered by active ingredient



2. There has been an increase in the use of oral preparations (Fig. 2.12), which was also observed in the 2016 sales data. On average, oral antibiotics for cattle have a higher amount of antibiotics per dose than injectables. This explains why, in 2016, oral antibiotics accounted for 1.4% of the antibiotic courses but represented 17% of the active ingredient given (derived from Table 2.5).

Figure 2.12. Number of defined course doses (DCDVet) administered by route of administration



HP-CIAs have reduced from 1.91 mg/kg to 0.96 mg/kg (50%), with reductions for both 3rd and 4th generation cephalosporins and fluoroquinolones (Fig. 2.13), and for injectable and intramammary use (Figure 2.14).

Figure 2.13. Number of defined course doses (DCDVet) of Highest Priority Critically Important Antibiotics by active ingredient

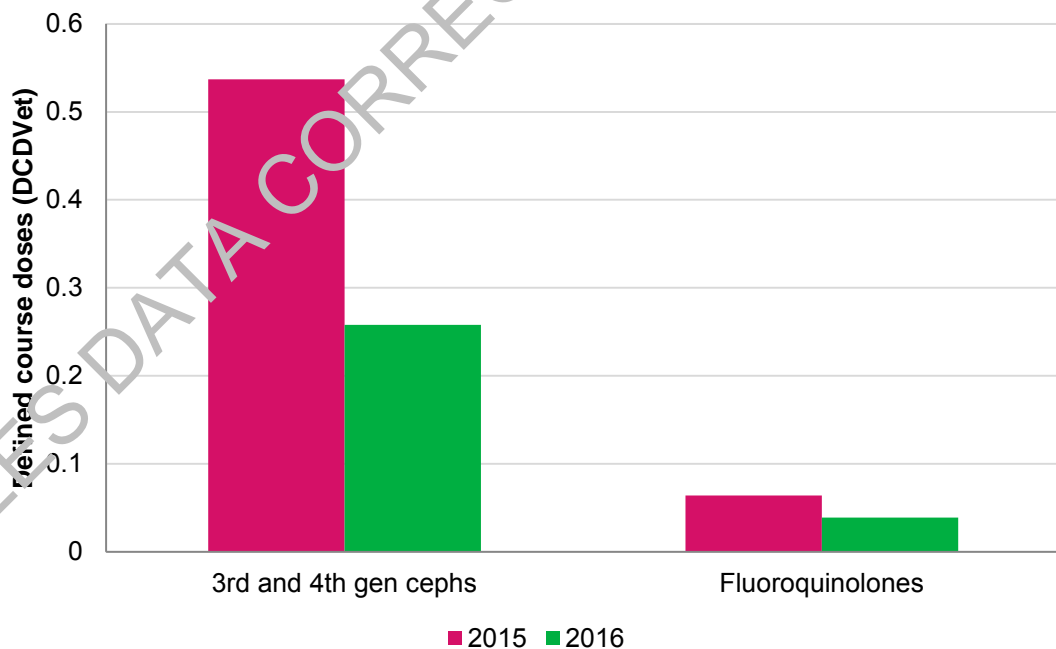
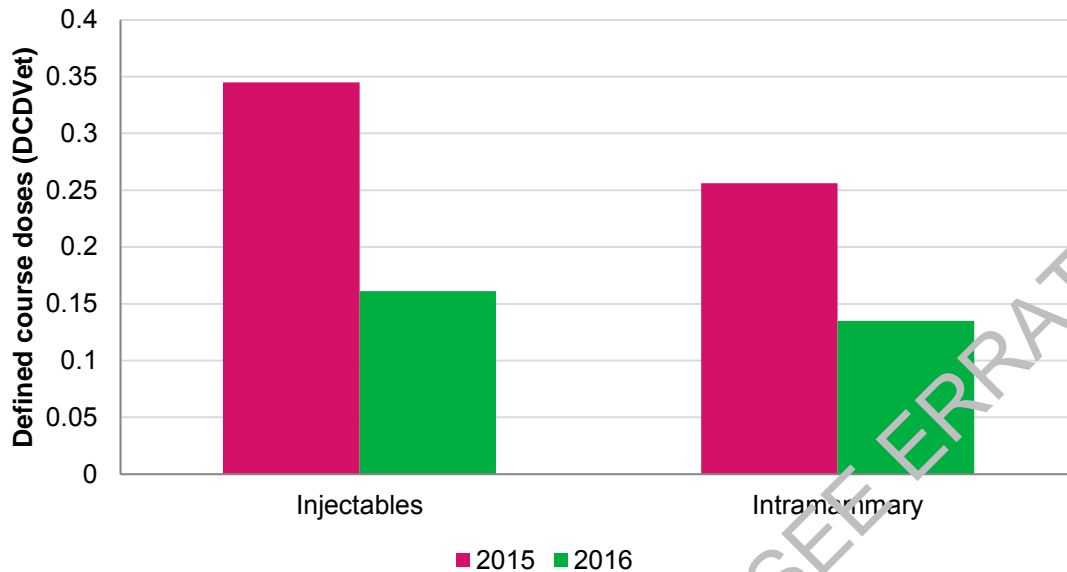


Figure 2.14. Number of defined course doses (DCDVet) of Highest Priority Critically Important Antibiotics by route of administration



In this sample of farms, the usage of intramammary HP-CIA was 23% lower in 2015 than the national sales data (0.256 course doses versus 0.332 course doses). There was also a greater level of reduction in course doses of intramammary HP-CIAs in 2016 (47% for this sample versus 7% for national sales data). This suggests that this sample includes veterinary practices that work with farmers who use less intramammary HP-CIAs, and have also been more proactive in moving their farms away from these products.

By contrast, in 2015, the usage of HP-CIA injectables in this sample is higher than the sales data would suggest. For example, in 2015, national sales for all injectable products including cattle in the license were 1.08 mg/kg (data not shown), whereas in this sample the usage was 1.68 mg/kg. Between 2015 and 2016, however, farms from the sample reduced their use of injectable HP-CIAs more than was demonstrated in the sales data (51% versus 9% reduction in mg/kg). For this reason, the usage of HP-CIA injectables is more similar in 2016 (0.97 mg/kg for national sales versus 0.83 mg/kg for the sample data). Note that some HP-CIA injectables licensed for cattle do include other species on their license (in particular pigs). However, industry feedback suggests that 75-80% of these products are used in cattle.

Other limitations for sales data that should be taken into consideration when making these comparisons are presented in Annex A.

Table 2.5. Tonnes of active ingredient, mg/kg and defined course doses (DCDVet) by active ingredient and route of administration

		Tonnes		Mg/kg		DCDVet	
		2015	2016	2015	2016	2015	2016
Classes of antibiotics	β-lactams excl. 3rd/4th gen cephs	1.96	2.48	7.24	9.07	1.413	1.612
	Tetracyclines	1.22	1.31	4.51	4.78	0.137	0.144
	Aminoglycoside	1.06	0.98	3.92	3.59	0.070	0.063
	Macrolides	0.88	1.12	3.24	4.09	0.084	0.090
	Tri-sulpha	0.58	0.74	2.14	2.72	0.073	0.098
	3rd and 4th gen cephs	0.37	0.17	1.36	0.62	0.536	0.258
	Amphenicols	0.24	0.23	0.87	0.84	0.022	0.021
	Fluoroquinolones	0.15	0.09	0.54	0.33	0.064	0.039
	Other* (includes colistin)	0.05 (0.0015)	0.05 (0.0028)	0.19 (0.005)	0.19 (0.011)	0.003 (0.00023)	0.001 (0.00042)
	All Products Total	6.49	7.18	24.01	26.22	2.402	2.290
Administration Route	All Intramammary/ intrauterine	1.00	1.05	3.71	3.83	1.561	1.574
	All Injectable	4.57	4.89	16.92	17.88	0.813	0.687
	All Oral	0.91	1.23	3.37	4.50	0.028	0.033
	HP-CIA Injectables	0.45	0.23	1.68	0.83	0.345	0.161
	HP-CIA Intramammary	0.06	0.03	0.229	0.123	0.256	0.135
	HP-CIA Oral	0.0015	0.0028	0.0057	0.0101	0.0003	0.0005
	HP-CIA Total	0.52	0.26	1.91	0.96	0.60	0.30

* includes polymyxins and lincomycins

2.8 Companion Animals

The VMD has funded studies investigating antibiotic use in companion animals and these are summarised below.

The first study looked into systemic antibiotic prescriptions between 2012-2014 for 963,463 dogs and 594,812 cats from 374 veterinary practices (Buckland et al., 2016). These data were extracted from practice management systems by VetCompass, which is managed by the Royal Veterinary College.

The results showed that, overall, 25% of dogs and 21% of cats received at least one antibiotic over the 2 year period. The total quantity of antibiotics used within the study population was estimated to be 1,473 kg for dogs and 58 kg for cats. The most frequently prescribed antibiotics were penicillin types (53.88% in dogs, 46.37% in cats) and cephalosporins (17.15% in dogs, 32.25% in cats). Highest Priority Critically Important Antibiotics (HP-CIAs) accounted for 6.17% of dog and 34.4% of cat prescriptions. Fluoroquinolones and third generation cephalosporins were the most frequently prescribed HP-CIA class in dogs (4.84% prescriptions) and cats (30.2% prescriptions), respectively.

A second study looked at antibiotic prescription patterns between 2014 and 2016, for 413,780 dogs and 200,541 cats recorded from 457 veterinary premises in the UK (Singleton, et al., 2017). These data were extracted from Practice Management Systems by the Small Animal Veterinary Surveillance Network (SAVSNET) system, which is managed by the University of Liverpool.

As a percentage of total recorded consultations (including routine consultations such as vaccinations), antibiotic prescription was recorded in 18.8% of dog and 17.5% of cat consultations. As a percentage of total recorded animals by species, 28.4% of dogs and 23.3% of cats were prescribed an antibiotic at least once during the two-year period. Between 2014 and 2016, the study demonstrated a reduction in the frequency with which veterinary surgeons decided to prescribe an antibiotic for both dogs and cats, this being particularly apparent for systemically administered (route of administration oral or injectable) antibiotics in both species.

Prescription was most common for pruritus in dogs (51% of pruritus consultations) and trauma in cats (53.5% of trauma consultations). Interestingly, premises, which frequently prescribed antibiotics to dogs, tended to also frequently prescribe antibiotics to cats. The most frequently prescribed antibiotics were clavulanic acid potentiated amoxicillin in dogs (28.6% of antibiotic prescriptions) and cefovecin, a third generation cephalosporin, in cats (36.2% of antibiotic prescriptions). Prescription of HP-CIAs represented 5.4% of dog and 39.2% of cat antibiotic prescriptions respectively.

CHAPTER 3

EU Harmonised Monitoring of Antibiotic Resistance

SALES DATA CORRECTIONS - SEE ERRATUM

Chapter 3: EU Harmonised Monitoring of Antibiotic Resistance

3.1 Summary

E. coli from broilers and turkeys

- With the exception of a single *E. coli* isolate from fattening turkeys which showed microbiological resistance to cefotaxime and ceftazidime, resistance to cefotaxime, ceftazidime, meropenem, colistin or tigecycline was not detected in indicator *E. coli* isolates recovered from the caecal contents of randomly-selected healthy broilers or turkeys at slaughter.
- Resistance to fluoroquinolones (ciprofloxacin), a class of high priority-critically important antibiotics in human medicine, was observed in 21.6% and 15.6% of the indicator *E. coli* isolates recovered from caecal contents of healthy broilers and fattening turkeys at slaughter, respectively.
- Both in broiler and turkey *E. coli* isolates, high or very high levels of resistance were identified for ampicillin, sulfamethoxazole and tetracycline. These compounds are commonly used therapeutically in animals and have been for many years.
- Resistance levels were generally higher among *E. coli* isolates from broilers than isolates from fattening turkeys with the exception of resistance to tetracycline, chloramphenicol, cefotaxime and ceftazidime which was higher in *E. coli* isolates from turkeys.
- Resistance levels in *E. coli* isolates from broilers and turkeys showed a decline for most when compared with 2014 data. This decline was particularly marked for tetracycline and ampicillin in *E. coli* isolates from both animal populations and for gentamicin in broiler isolates.

Salmonella from laying hens, broilers and turkeys

- Resistance to meropenem, cefotaxime, ceftazidime, tigecycline or colistin was not detected in *Salmonella* isolates.
- Resistance to ciprofloxacin was detected in a relatively low level (2%-9%) in all the animal species and it was generally associated with the presence of certain serovars such as the incomplete *Salmonella* serovar 13:23:i:-, *S. Kentucky*, *S. Infantis* in broilers, *S. Newport* and *S. Derby* in turkeys and *S. Kentucky* in laying hens. The occurrence of fluoroquinolone resistance in a limited number of serovars is suggestive of clonal expansion of these serovars in these food production animals.
- Very high levels of resistance to tetracycline (75.7%) and sulfamethoxazole (74.6%) were observed in *Salmonella* isolates from fattening turkeys. Isolates from laying hens displayed

the lowest levels of resistance to these antibiotics (5.7%-11.7%) with moderate levels observed for broiler isolates (19.4%-18.2%).

- Resistance levels to tetracycline and sulfamethoxazole showed an increasing trend in *Salmonella* isolates from turkeys and laying hens.

C. jejuni from broilers and turkeys

- Resistance to ciprofloxacin was observed in a relatively high proportion of *C. jejuni* isolates from broilers (40.6%) and turkeys (34.7%).
- Only one *C. jejuni* isolate from broilers (1/180; 0.6%) and two from turkeys (2/190; 1.1%) were resistance to erythromycin.
- Resistance level to streptomycin and gentamicin in *C. jejuni* isolates from broilers and turkeys was very low or not detected.
- A decreasing trend in the level of resistance was observed for some antibiotics tested. The decline in resistance level was particularly marked for tetracycline in turkeys which decreased from 65% in 2014 to 43.2% in 2016.

3.2 Introduction

The EU harmonised monitoring of antibiotic resistance is a programme set out in the Commission Decision 2013/652/EU, which mandates all EU Member States to monitor and report the antibiotic resistance in zoonotic and commensal bacteria from healthy food-producing animals at slaughter and food products at retail. Member States shall carry out, every 2 years, the sampling, collection and antibiotic susceptibility testing of each combination of bacterial species and type of sample from the different animal populations in accordance with a rotation system. An overview of the sampling plan, by year, is summarised in Table S3.1 of the supplementary material. The sampling size and strategy are designed to provide a sample which is representative of the wider population for each combination of bacteria and animal species.

In 2016, Member States were mandated to carry out the following testing:

- Susceptibility testing of *Escherichia coli* from broiler and turkey caecal samples taken at slaughter.
- Susceptibility testing of *Salmonella* isolates derived from boot swabs/dust samples for each population of laying hens, broilers and fattening turkeys collected on farm under the framework of the National Control Plan (NCP).
- Susceptibility testing of *Salmonella* isolates derived from both broiler and fattening turkey carcass swab samples taken by food business operators.
- Susceptibility testing of *Campylobacter jejuni* isolates gathered from broiler and fattening turkey caecal samples taken at slaughter.
- Testing for the presence of Extended Spectrum β -Lactamase (ESBL-), AmpC-, and carbapenemase-producing *E. coli* in caecal contents from broilers and fattening turkeys at slaughter and samples of fresh broiler meat at retail.

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

- The organisms for which the legislation outlines monitoring provisions, such as *Salmonella* and *E. coli*, are of direct relevance to human health. Additionally, the panel of antibiotics against which these organisms must be tested has been selected based on relevance to human health and includes antibiotics, such as 3rd and 4th generation cephalosporins and fluoroquinolones that are defined by the WHO as the Highest Priority Critically Important Antibiotics (HP-CIA) for human health.
- The legislation and accompanying technical specifications provide a standardised and harmonised sampling methodology which produce comparable and robust susceptibility data for a representative proportion of food producing animals and food products across the EU.
- The legislation provides a harmonised set of epidemiological cut-off values (ECVs) and human clinical break points (CBPs) to interpret susceptibility to antibiotics. This will enable the comparison of animal resistance data with similar data generated by human health, both within the UK and across the EU. Minimum inhibitory concentrations (MICs) are also recorded, and will enable any future changes in ECVs or CBPs to be taken into account.

3.3 Methods

3.3.1 Sample collection

In accordance with Commission Decision 2013/652/EU, 2007/516/EC, and the Microbiological Criteria for Foodstuffs, caecal samples were collected from broilers and turkeys by meat inspectors at slaughterhouses across the UK. A summary of the sample collection and antibiotic susceptibility testing for each bacterial and animal species combination is provided below.

***E. coli* from broilers and turkeys**

Collection of caecal samples from healthy broiler chickens at slaughter was conducted under a UK-wide *Campylobacter* survey funded by the Food Standards Agency. The design of this survey was based on an EU technical specification (EU decision 2007/516/EC) and consisted of a randomised, stratified and weighted sampling strategy based on slaughter throughput. Samples were collected from the biggest slaughterhouses representing more than 85% of the UK throughput. Sample collection was distributed evenly throughout the year. A pool of ten caecal samples per epidemiological unit (i.e. flock) was collected.

Caecal samples from healthy turkeys at slaughter were taken in accordance with Commission Decision 2013/652/EU by Food Standards Agency (FSA) personnel. The sampling plan was randomised, stratified and weighted by slaughter throughput. Samples were collected from the biggest slaughterhouses representing 60% of the UK throughput. Sample collection was randomised and evenly distributed throughout the year. One caecal sample per epidemiological unit (flock) was collected.

Salmonella isolates from laying hens, broilers and turkeys

Salmonella isolates derived from boot/dust swabs were collected in accordance with EU Regulation (EC) No. 2160/2003 and Regulation (EC) No. 200/2012, and the National Control Programme (NCP) for laying hens, broilers and turkeys. Annual official samples were taken as follows:

- Broilers: samples were taken from one flock on 10% of holdings with more than 5,000 birds each year.
- Laying hens: samples were taken from one flock on each holding with more than 1,000 birds.
- Turkeys: samples were taken from one flock on 10% of holdings with at least 500 fattening turkeys.

Salmonella from Food Business Operator's samples

Carcase neck skin samples were collected by food business operators and then submitted to private laboratories for bacteriological culture. Where a sample was found to be positive for *Salmonella* the private laboratory was asked to submit isolates for serotyping and susceptibility testing.

Campylobacter jejuni isolates from broilers and turkeys

Collection of samples from broilers and turkeys at slaughter were conducted as described in 3.3.1.

3.3.2 Antibiotic susceptibility testing

The isolation of bacteria and the antibiotic susceptibility testing was carried out by the national reference laboratory for antibiotic resistance in the UK (Animal and Plant Health Agency, APHA). Broiler caecal samples for *Campylobacter* were tested by the Agri-Food Biosciences Institute (AFBI) for samples collected in Northern Ireland.

Bacterial isolates were cultured and a single colony selected for susceptibility testing against a defined panel of antibiotics using a standardised broth microdilution method. In addition, caecal samples were cultured on MacConkey agar + 1 mg/L cefotaxime to isolate ESBL- and AmpC-producing *E. coli* on CHROM agar to isolate ESBL-producing *E. coli*, and onto chromID CARBA and chromID CXA-48 agars to isolate carbapenemase-producing *E. coli*.

E. coli isolates from samples collected in GB were additionally cultured on MacConkey agar + 2 mg/L colistin.

3.3.3 Interpretation of results

Both EUCAST human clinical break points (CBPs) and EUCAST epidemiological cut-off values (ECVs) were used to determine the susceptibility of the different bacterial population. CBPs relate the laboratory results to the likelihood of clinical treatment success or failure. Therefore, 'resistant' results using CBPs correspond to a likelihood of treatment failure when using the antibiotic in question to treat a clinical infection caused by that bacterial isolate. ECVs 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 for that bacterial species. A 'resistant' (or 'non-susceptible') ECV does not necessarily imply a level of resistance which would correspond with clinical treatment failure.

Susceptibility results included in the main body of this report are interpreted using ECVs. Results interpreted using both human CBPs and ECVs are provided in full in Table S3.3.1, S3.4.1 and S3.5.1 of the supplementary material.

3.4 Results and discussion

3.4.1 *Escherichia coli*

In 2016, a total of 190 and 224 *E. coli* isolates from broiler and turkey caecal samples respectively were collected at slaughter throughout the year and tested for antibiotic resistance. Figure 3.1 and 3.2 show the percentage of *E. coli* isolates resistant to the different antibiotics tested from broilers and turkeys, respectively. For comparative purposes, data from 2014 are included.

Considering the antibiotics critically important to human medicine, no resistance was detected to cefotaxime, ceftazidime, colistin, meropenem or tigecycline in *E. coli* isolates from broilers or turkeys with the exception of a single isolate resistant to cefotaxime and ceftazidime detected in turkeys (0.4%). In 2014, all *E. coli* isolates from broilers and turkeys were fully susceptible to these antibiotics. The level of resistance to ciprofloxacin was 21.6% and 15.6% in broiler and turkey *E. coli* isolates respectively.

A high level of resistance was observed in *E. coli* isolates to tetracycline (44.2% and 67%) and ampicillin (67.4% and 60.7%) from broilers and turkeys respectively. High level of resistance was also observed to sulphonamide (52.6%) and trimethoprim (42.6%) in *E. coli* isolates from broilers although resistance to these antibiotics was lower in isolates from turkeys (25.4% and 22.8%, respectively).

The level of resistance to most of the antibiotics tested was higher in broiler than in turkey *E. coli* isolates, with the exception of tetracycline, chloramphenicol, cefotaxime and ceftazidime which were higher in turkey isolates.

Resistance levels for most antibiotics in *E. coli* isolates from broilers and turkeys showed a decreasing trend when compared with data from 2014.

Figure 3.1. Percentage resistant (interpreted using EUCAST ECVs) in *E. coli* isolates from broilers at slaughter, 2014 and 2016

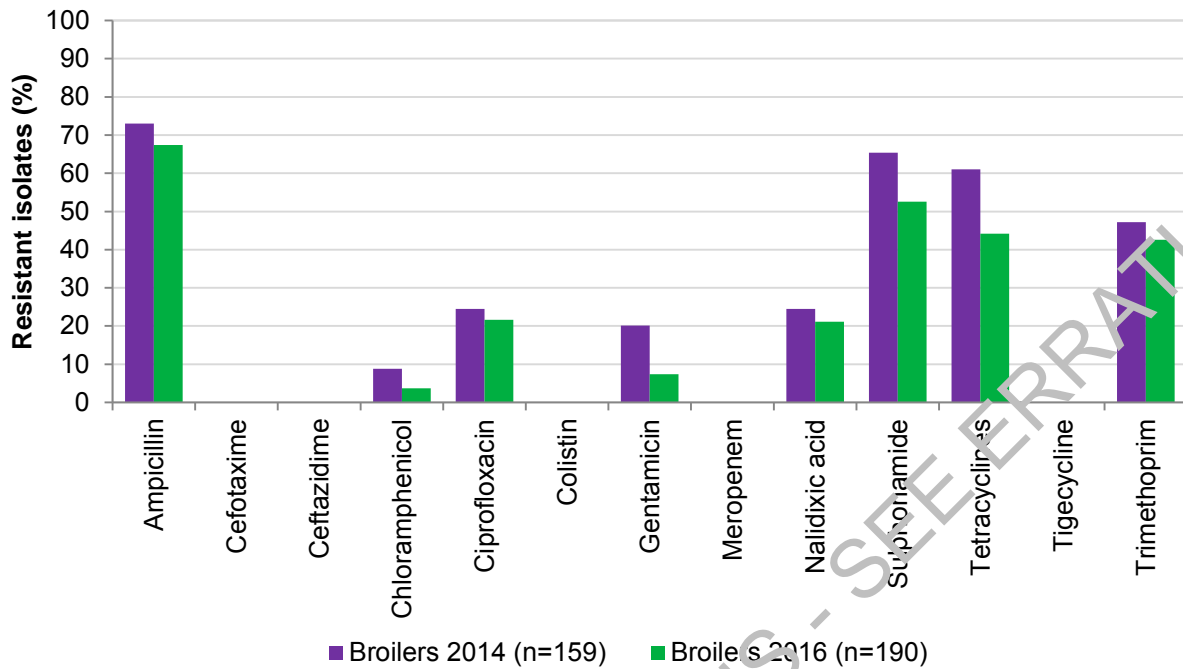
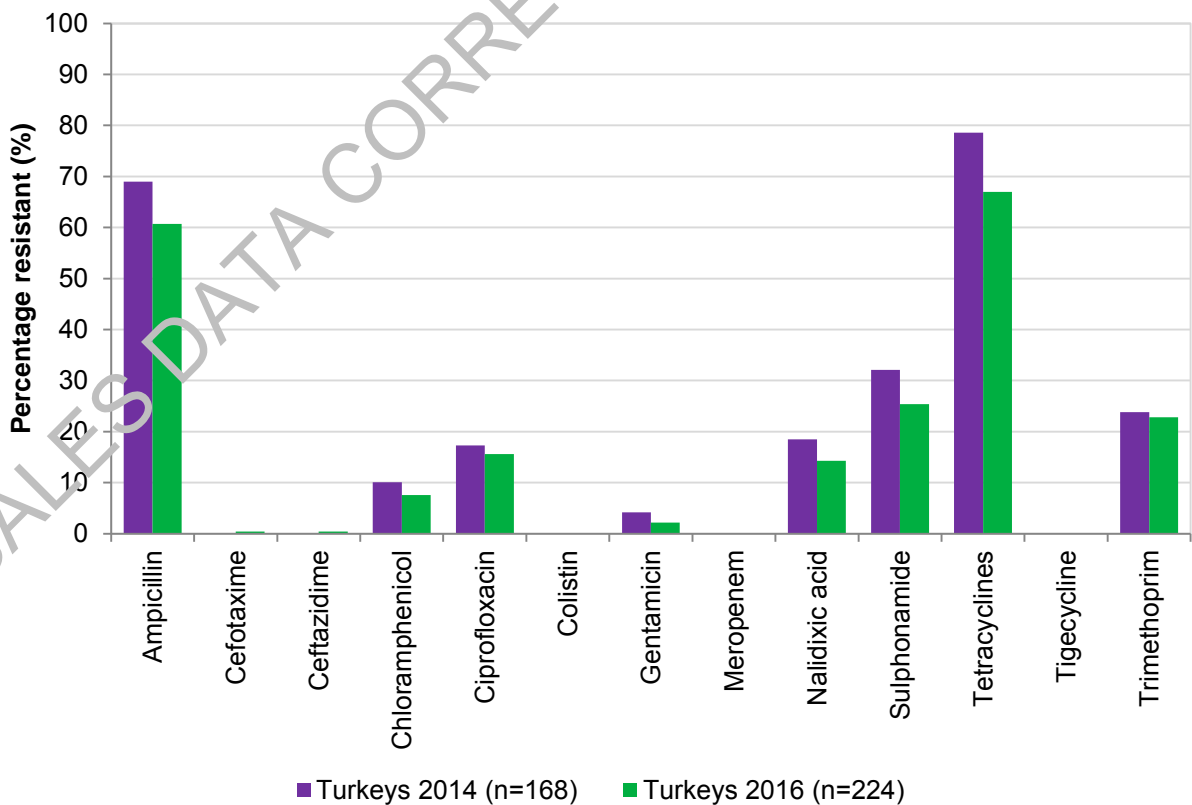


Figure 3.2. Percentage resistant (interpreted using EUCAST ECVs) in *E. coli* isolates from turkeys at slaughter, 2014 and 2016



3.4.2 ESBL-, AmpC- and carbapenemase-producing *E. coli*

A total of 29.6% and 4.7% of the samples tested from broilers and turkeys respectively had a presumptive ESBL-/AmpC-producing *E. coli* (Table 3.1). No presumptive carbapenemase-producing *E. coli* isolates were detected in 382 and 315 samples tested from broilers and turkeys respectively. It should be noted that when using selective culture methods, the occurrence of ESBL-, AmpC- and carbapenemase-producing *E. coli* in broilers and fattening turkeys is assessed with much greater sensitivity than when using non-selective culture methods. The difference is most likely explained by the fact that the population of ESBL-, AmpC- and carbapenemase-producing *E. coli* may be a minority among the *E. coli* populations in the gut flora of these food-producing animals, so the probability of randomly picking a resistance phenotype from a non-selective agar plate is not high for the majority of samples tested. Therefore, these selective methods are not able to quantify the risk which these bacteria may potentially pose to human or animal health. Selective methods are used to detect low number of resistant *E. coli* which may be present as a minor component of the total flora.

Table 3.1. Results of specific testing for ESBL-, AmpC-producing *E. coli* isolates from broiler and turkey caeca following selective culture, 2016

Poultry population	Number of caecal samples tested on selective media	Number (%) of caecal samples tested positive for ESBL-/AmpC-producing <i>E. coli</i> *
Broiler	382	113 (29.6%)**
Turkey	362	17 (4.7%)***

*MacConkey agar containing 1 mg/L of cefotaxime was used as selective medium

** Data from Great Britain

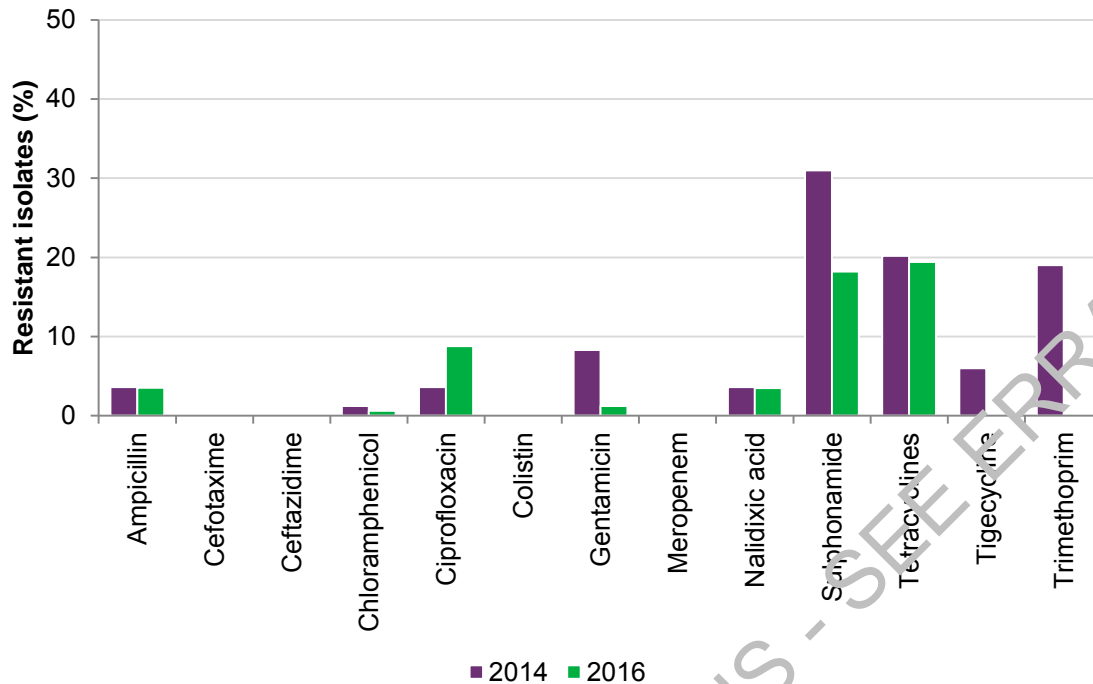
*** Data from the UK

3.4.3 *Salmonella* spp.

Broilers

In 2016, no isolates of *Salmonella* from broilers were resistant to meropenem, cefotaxime, ceftazidime or colistin. Sixty-seven percent (115/170) of *Salmonella* spp. isolates from broilers were fully sensitive to all antibiotics which was comparable to the levels seen in 2014 (64.3%). No isolates of *S. Enteritidis* or *S. Typhimurium* were recovered from broilers. One isolate of monophasic *Salmonella* Typhimurium was tested and showed resistance to ampicillin, sulphonamide, tetracycline and gentamicin. The most prevalent serovars from broilers were *S. Mbandaka* (54 isolates) and *S. Kedougou* (37 isolates). Eighty-eight percent of *S. Mbandaka* isolates (48/54) were susceptible to all of the antibiotics tested, a percentage higher than that observed in 2014 (74.5%). The *S. Kedougou* isolates were commonly resistant to tetracycline (33/37; 89.2%), sulphonamide (31/37; 83.8%) or both (13/37; 35.1%). Nine *Salmonella* isolates (8.8% of the total) were resistant to ciprofloxacin and these comprised mainly *Salmonella* from the serogroup G (*S. 13,23:i:-*) (9), *S. Mbandaka* (2), *S. Indiana* (1), *S. Infantis* (1), *S. Kentucky* (1) and *S. Senftenberg* (1). Forty percent of the ciprofloxacin resistant isolates were also resistant to nalidixic acid.

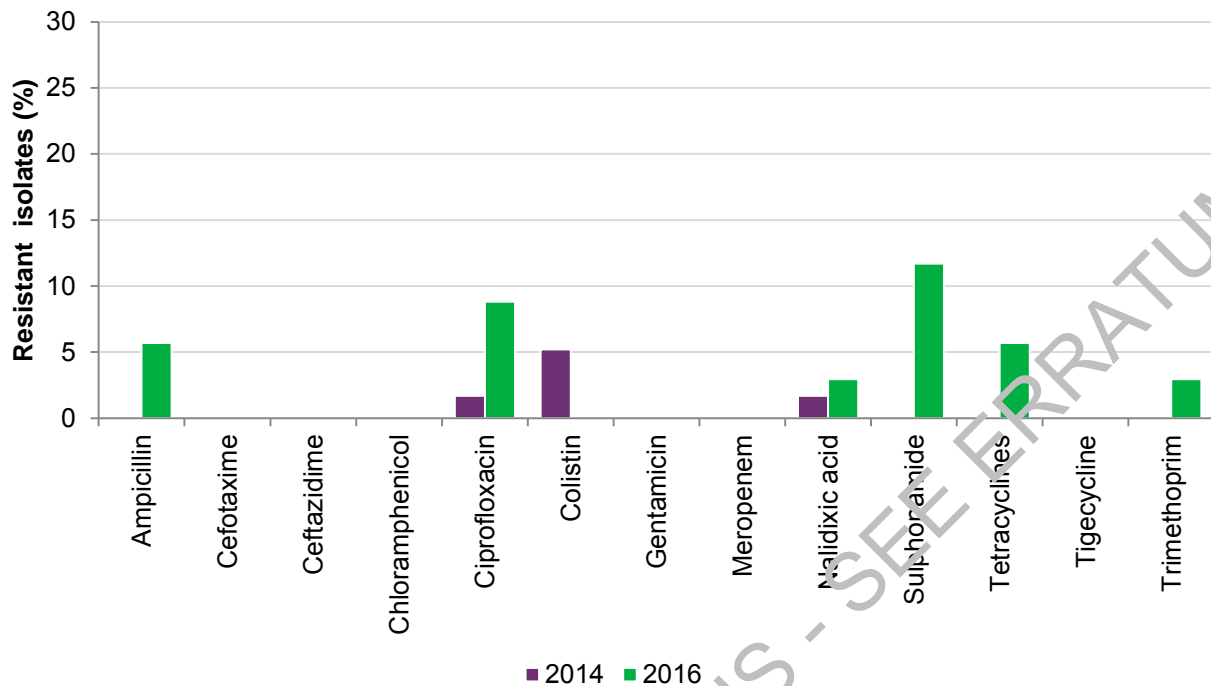
Figure 3.3. Percentage of resistant isolates (interpreted using EUCAST ECVs) in *Salmonella* from broiler NCP samples, 2014 and 2016



Layers

No *Salmonella* isolates recovered from layers in 2016 were resistant to meropenem, cefotaxime, ceftazidime, tigecycline or colistin. Eighty-five percent (29/34; 85.3%) of the *Salmonella* isolates tested were fully sensitive to all antibiotics; this was a slight decrease from the percentage seen in 2014 (93%). Two isolates of *S. Enteritidis* were recovered; both were sensitive to all the antibiotics apart from one which was resistant to sulphonamide. There were two *S. Typhimurium* isolates recovered from layers which were fully susceptible. Only three isolates were resistant to ciprofloxacin; of those, one (*S. Indiana*) was also resistant to nalidixic acid and ampicillin) and one (*S. Kentucky*) was also resistant to sulphonamide, tetracycline and trimethoprim.

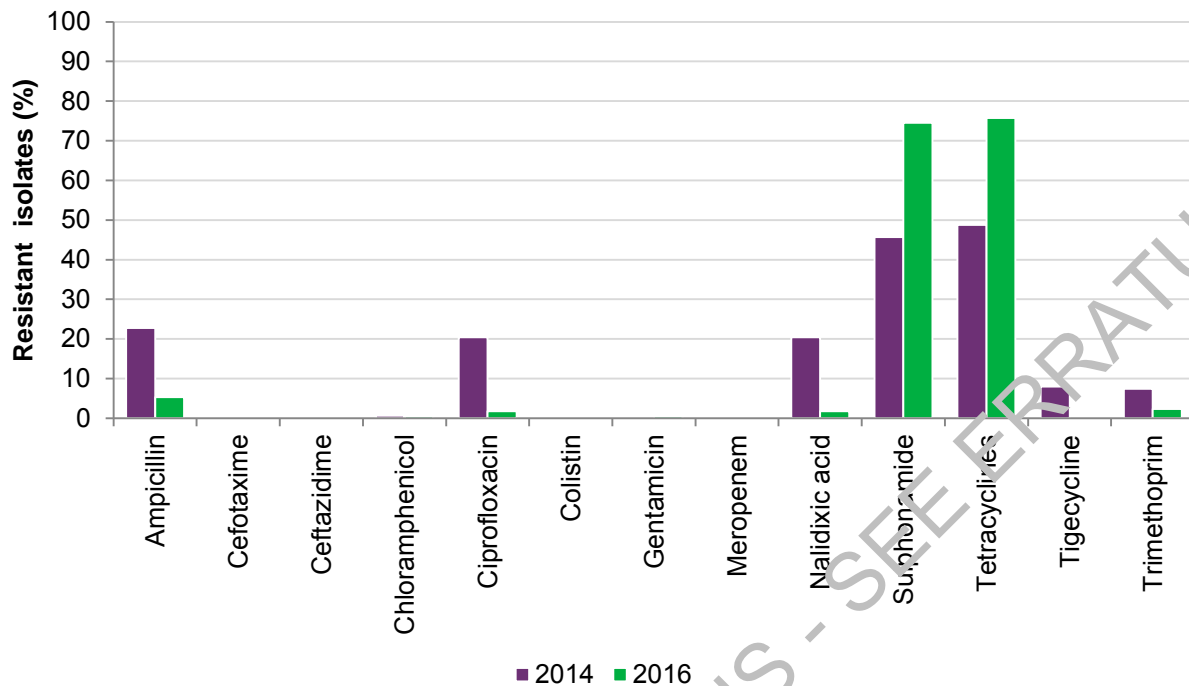
Figure 3.4. Percentage of resistant isolates (interpreted using EUCAST ECVs) in *Salmonella* from laying hen NCP samples, 2014 and 2016



Turkeys

Resistance to meropenem, cefotaxime, ceftazidime, tigecycline or colistin was not detected in *Salmonella* isolates from turkeys in 2016. Twenty-two percent of *Salmonella* isolates (37/169; 21.9%) were fully susceptible to all antibiotics, this was a decrease from the 31% (51/162) of isolates fully sensitive seen in 2014. There were no *S. Enteritidis* isolates recovered from turkeys in 2016. A single isolate of *S. Typhimurium* was recovered and was fully sensitive to all the antibiotics tested. Isolates of the monophasic *Salmonella* 4,5,12:i:- (n=3) and 4,12:i:- (n=1) were recovered from turkeys and all but one were resistant to ampicillin, sulphonamide and tetracyclines, one was resistant to sulphonamide and tetracycline and one was fully susceptible. Resistance to ciprofloxacin was detected in three isolates (8%), belonging to serotypes *S. Newport*, *S. Senftenberg* and *S. Derby*. All of these isolates were also resistant to nalidixic acid. In 2014, resistance to ciprofloxacin was detected in 20% of *Salmonella* from turkeys, mainly associated with *S. Newport*. There were 90 isolates of *S. Derby* isolated and 73 (81%) were resistant to sulphonamides and tetracyclines. All of the 43 isolates of *S. Kedougou* examined were resistant to sulphonamides and tetracyclines.

Figure 3.5. Percentage of resistant isolates (interpreted using EUCAST ECVs) in *Salmonella* isolates from turkey NCP samples, 2014 and 2016



Broiler carcass samples from Food Business Operators

A total of 17 *Salmonella* isolates from broiler carcasses were tested for antimicrobial resistance. As only a small number of isolates were recovered, the results are not likely to be representative and should be interpreted with caution. Low to moderate levels of resistance were observed to sulphonamide (11.8%), tetracycline (5.9%) and trimethoprim (11.8%). Results are presented in Table S3.6.1 of the supplementary material.

3.4.4 *Campylobacter* spp.

In 2016, a total of 180 and 190 *C. jejuni* isolates from broilers and turkeys, respectively, was examined for antibiotic resistance. Results are presented in Figure 3.6 and 3.7 alongside data from 2014 for comparison.

Considering the antibiotics most frequently used for treatment of human campylobacter infections, resistance to ciprofloxacin was observed in 41% (73/180) and 35% (66/190) of *C. jejuni* isolates from broilers and turkeys, respectively. Only one *C. jejuni* isolate from broilers (1/180; 0.6%) and two from turkeys (2/190; 1.1%) were resistance to erythromycin. In 2014, no resistance to erythromycin was observed in *C. jejuni* isolates from broilers and only one isolates from turkeys was resistant to this antibiotic. High levels of resistance were observed to tetracyclines both in broilers (56.1%) and turkeys (43.2%). Level of resistance to streptomycin 2016 in *C. jejuni* isolates from broilers (2/180; 1.1%) and turkeys (3/190; 1.6%) remained low. Resistance to gentamicin was not observed. (Fig. 3.6 and 3.7)

When compared with results from 2014, a decreased trend in the level of resistance was observed for most antibiotics tested. This decreasing trend was particularly high for resistance to tetracycline in turkeys which decreased from 65% in 2014 to 43% in 2016.

Figure 3.6. Percentage resistant (interpreted using EUCAST ECVs) in *Campylobacter jejuni* from broilers at slaughter in 2014 and 2016

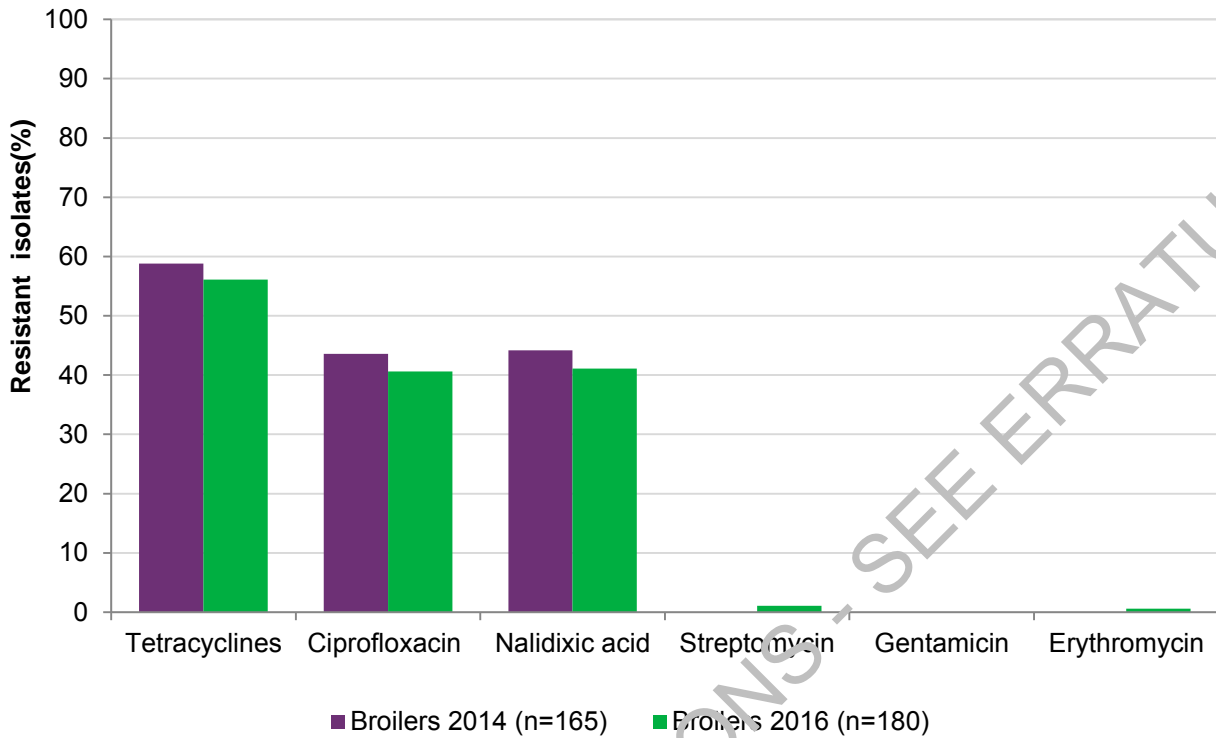
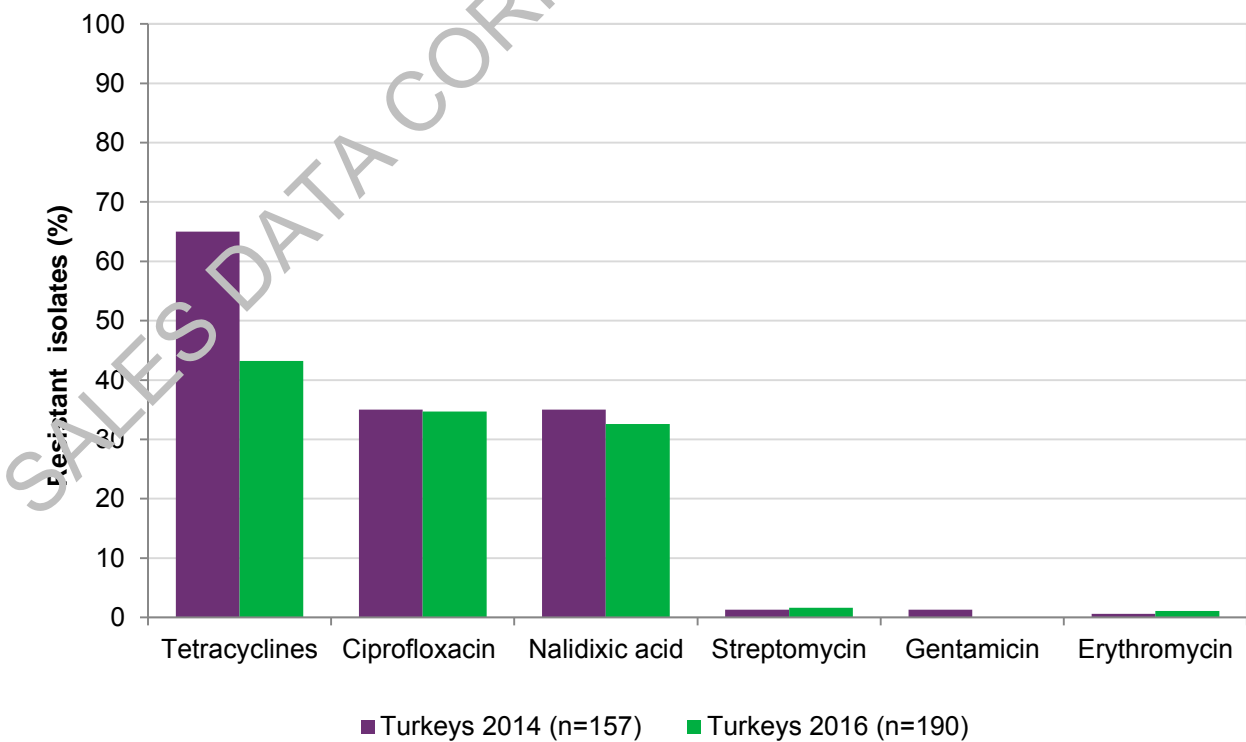


Figure 3.7. Percentage resistant (interpreted using EUCAST ECVs) in *Campylobacter jejuni* from turkeys at slaughter in 2014 and 2016



CHAPTER 4

Clinical Surveillance of Antibiotic Resistance

SALES DATA CORRECTIONS - SEE ERRATUM

Chapter 4: Clinical Surveillance of Antibiotic Resistance

4.1 Summary

- Colistin resistance was not detected in *E. coli* from scanning surveillance.
- A relatively high percentage of all *Salmonella* isolates (69.0%) were susceptible to all the 16 antibiotics tested.
- A very low level of resistance to ciprofloxacin (0.6%) was observed in *Salmonella* isolates tested in 2016 (based on clinical breakpoints).
- Of 166 isolates of *Salmonella* Typhimurium, none were resistant to amikacin, ciprofloxacin, ceftazidime or cefotaxime.
- A very low level of resistance to cefotaxime or ceftazidime was observed in *Salmonella* isolates (0.4%). Resistance to this antibiotic was observed in five isolates of *S. Oslo* from an outbreak of salmonellosis in horses, as well as single isolates of *S. Kedougou* from broilers and *S. Agona* and *S. Ajiobo* from dogs.
- Cefotaxime resistance in diagnostic *E. coli* isolates from neonatal calves and lambs in 2016 was 16% and 3%, respectively, whilst cefpodoxime resistance in *E. coli* in the same year was 3% in neonatal piglets, 3% in chickens and 0% in turkeys.
- Resistance in diagnostic *E. coli* isolates from chickens which has shown an upward trend since 2013, showed a marked decline in 2016 for several antibiotics, coinciding with a reduction in antibiotic use in broilers.
- Penicillin resistance was not detected in *Streptococcus suis* isolates from pigs in the reporting period (2014-2016).
- Most isolates of the main respiratory pathogens in sheep, cattle and pigs were susceptible to enrofloxacin and florfenicol, with the exception of two *Pasteurella multocida* and a single *Mannheimia haemolytica* from cattle which were resistant to florfenicol and a single isolate of *Bibersteinia trehalosi* from sheep which was resistant to enrofloxacin.
- Livestock-associated methicillin-resistant *Staphylococcus aureus* (MRSA) ST398, was detected in samples from pigs, turkeys and a beef cow on different premises.

4.2 Introduction

Clinical surveillance is a programme of passive surveillance which evaluates antibiotic resistance in bacteria of relevance to animal health which have been isolated from diagnostic samples submitted by private veterinary surgeons to APHA veterinary laboratories. The primary aim of this

programme is to provide a diagnostic service for veterinarians. However, it also helps to identify new and emerging patterns of resistance, particularly since treatment failure is a frequent reason for submission of samples. The programme also incorporates results from the susceptibility testing of *Salmonella* isolates recovered from animals and their environment, as part of the UK Zoonoses Order 1989. Any findings that are considered to pose a potential risk to human or animal health are reported to the Defra Antibiotic Resistance Coordination (DARC) group for consideration and management in accordance with the protocols outlined in the VMD AMR Contingency Plan:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/497125/771046_Contingency_planning_guidance.pdf

4.3 Methods

4.3.1 Sample sources and target microorganisms

Bacterial populations are obtained from samples of field cases of clinical disease undergoing investigation by practising veterinary surgeons for diagnostic purposes. Carcasses or other diagnostic samples collected by private veterinary surgeons are sent to APHA veterinary laboratories in England and Wales. When a potential bacterial pathogen is identified, antibacterial susceptibility testing is performed to provide the practitioner with relevant information for treatment. Similar programmes are conducted by Scottish (SAC Veterinary Services) and Northern Irish (Agri-Food Biosciences Institute, AFBI-NI) laboratories. For *Salmonella* isolates, any laboratory isolating *Salmonella* from animals and their environment in Great Britain is required to notify and submit an isolate to Defra-approved laboratory (APHA) for characterisation including antibiotic sensitivity testing.

4.3.2 Susceptibility testing methodology

Susceptibility tests were conducted by the network of APHA Veterinary Investigation Centres. For isolates recovered through the clinical surveillance scheme, the susceptibility testing was performed (unless otherwise stated) using a disc diffusion method on Isosensitest Agar (Oxoid) with appropriate media supplementation, where necessary, for fastidious organisms, following the guidelines described by the British Society for Antibiotic Chemotherapy (BSAC, 2015). Resistance was interpreted using human Clinical Break Points (CBP) as published by BSAC. Isolates were classified 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 (13 mm zone size diameter) has been used to indicate resistance. The disc concentrations and breakpoints used for the different bacteria are presented in Table S4.1 of the supplementary material.

For some bacterial pathogens, very few isolates are recovered in any one year and therefore the prevalence of resistance and any trends need to be interpreted with caution. Due to issues with sampling representativeness, results cannot be extrapolated to the general livestock population.

4.4 Results and discussion

Where more than 20 isolates of any pathogen were recovered in any given year the results are presented graphically in the main body of the report, with additional numerical data available in the supplementary materials. Where fewer than 20 isolates were recovered, results are presented in the supplementary materials only.

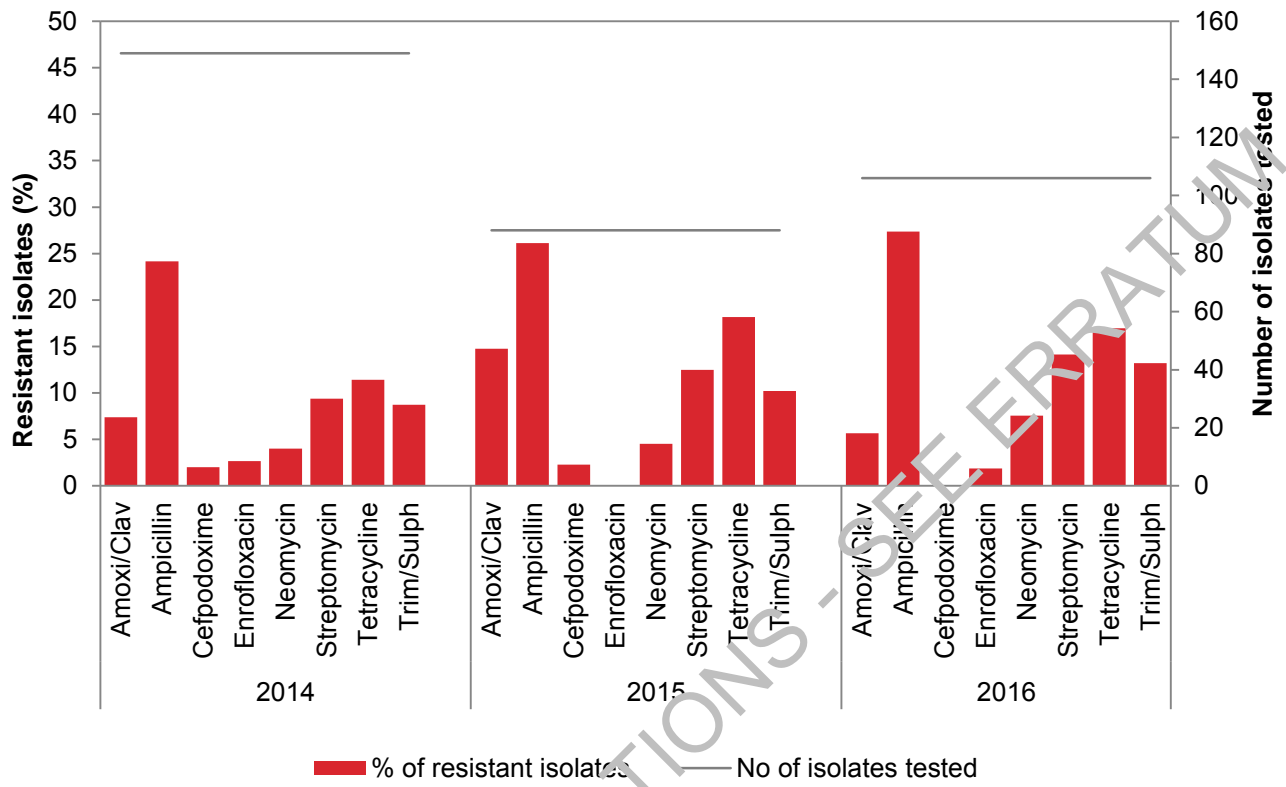
4.4.1 Mastitis pathogens

Similarly to previous reporting years, the most frequently isolated organisms from milk samples in 2016 were *E. coli* (n=106), followed by *S. uberis* (n=94), *S. aureus* (n=62) and *S. dysgalactiae* (n=41). Details on the percentage of resistant isolates from bovine mastitis are presented in Tables S4.2.1 and S4.2.2 of the supplementary material.

Escherichia coli

E. coli and coliforms are one of the three main causes of bovine mastitis (resistance in *E. coli* isolates not associated with mastitis is reported in Table 4.2). Most strains originate from the immediate environment of the cow and it is thought that no special virulence factors are required to infect the mammary gland. These isolates, therefore, represent the normal types that are present in the environment of adult dairy cattle, particularly cattle sheds and cubicle houses and are probably mainly of faecal origin. Total number and percentage of *E. coli* isolates from mastitis infections resistant to different antibiotics are presented in Figure 4.1. Similarly to previous reporting years, the highest level of resistance was observed to ampicillin (27.4%) followed by tetracycline (17%), streptomycin (14%) and trimethoprim/sulfamethoxazole (13%), and those levels of resistance were lower for all antibiotics than those observed in *E. coli* isolates not associated with mastitis.

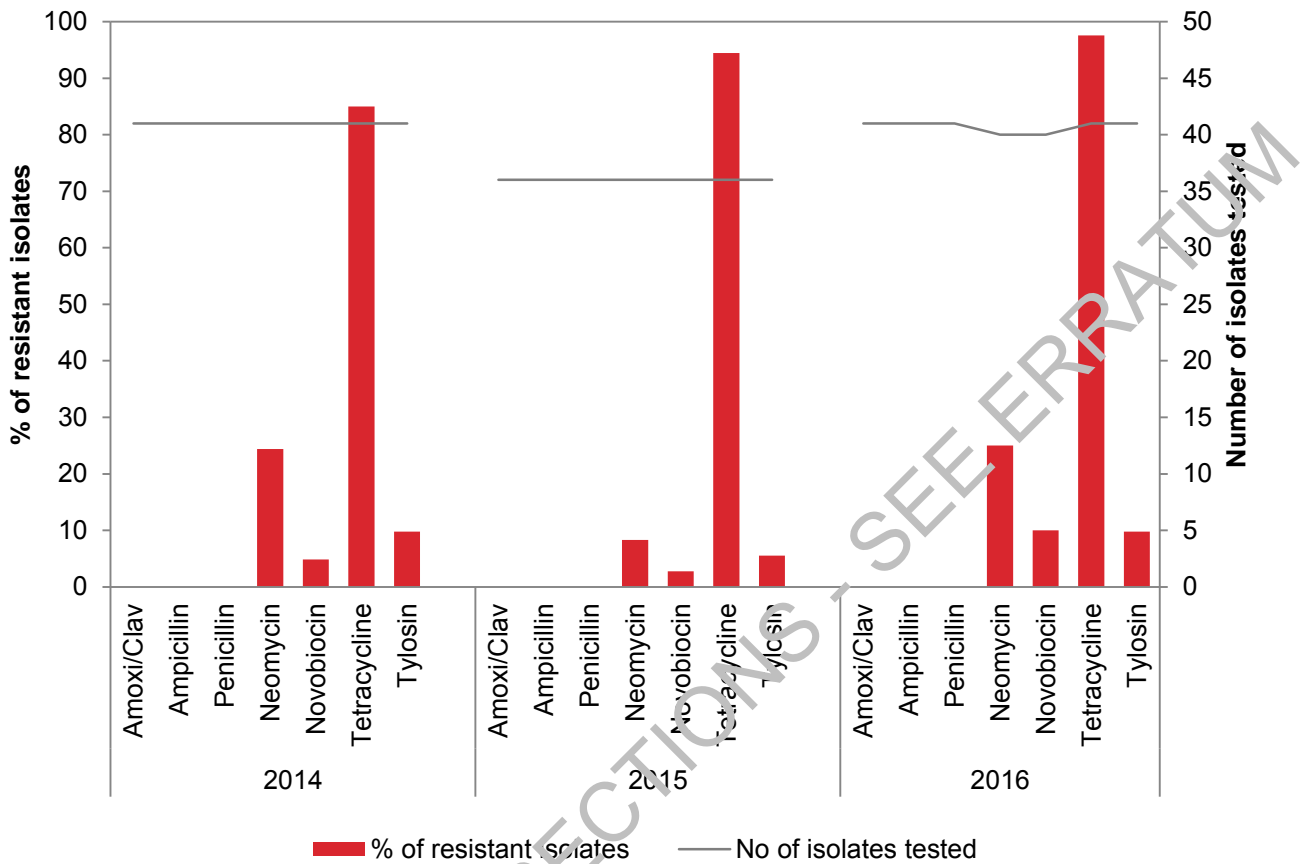
Figure 4.1. Total number and percentage of resistant isolates of *Escherichia coli* from mastitis infections of cattle



Streptococcus dysgalactiae

S. dysgalactiae is a Lancefield Group C streptococcus and a commensal of the mucous membranes of cattle. It is a cause of mastitis and occasionally, it can be responsible for other diseases in other livestock species. It is not considered a zoonosis because Group C streptococci that cause disease in humans constitute a separate population. Total number and percentage of *S. dysgalactiae* isolates from mastitis infections resistant to different antibiotics are presented in Figure 4.2. Resistance to tylosin was reported in 10% of the isolates and macrolide resistance has been reported in *S. dysgalactiae* isolates from bovine mastitis in other parts of the world. Resistance to neomycin (25%) and tetracycline (98%) is recognised as being common in this bacterial species.

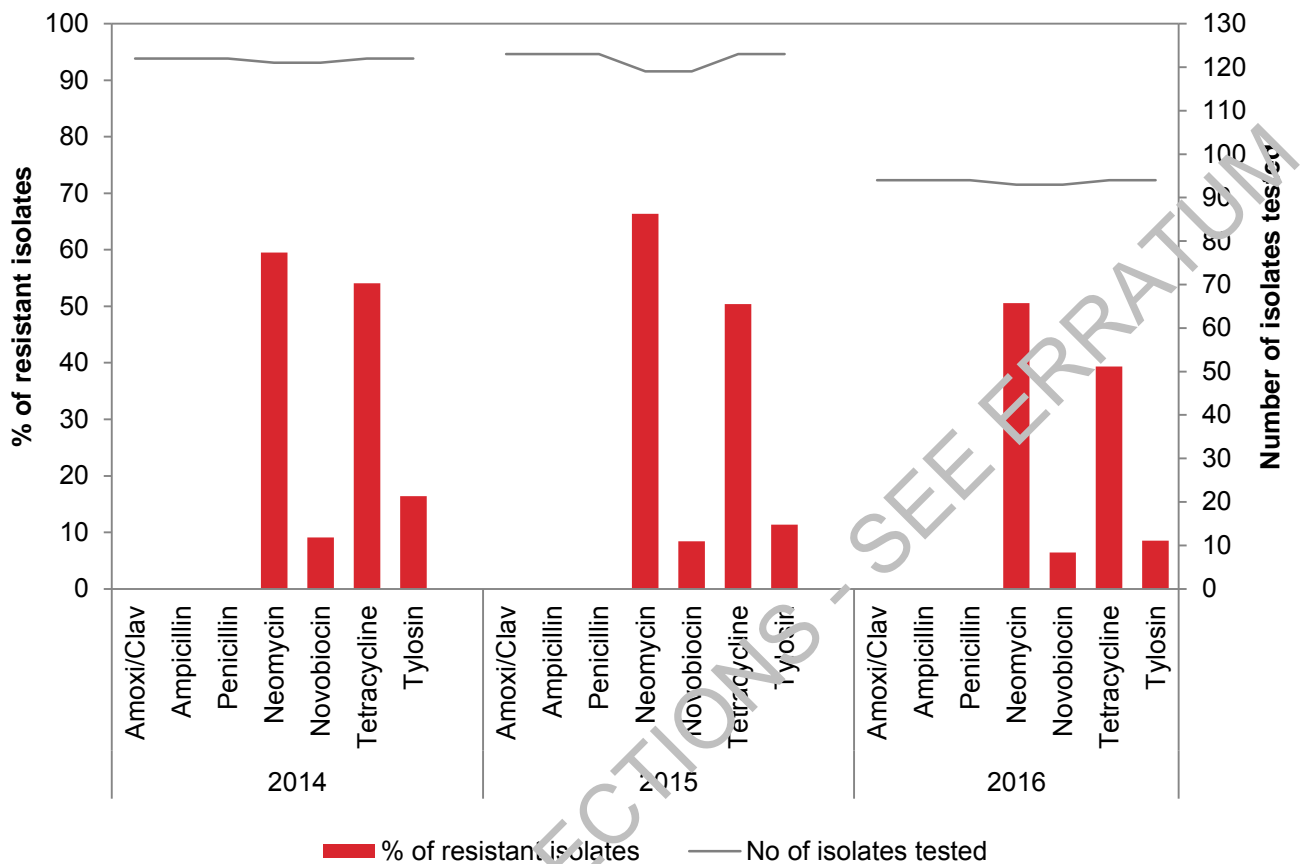
Figure 4.2. Total number and percentage of resistant isolates of *Streptococcus dysgalactiae* from mastitis infections of cattle



Streptococcus uberis

S. 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. Total number and percentage of *S. uberis* isolates from mastitis infections resistant to different antibiotics are presented in Figure 4.3. In the 2014-2016 reporting period, 9-16% of *S. uberis* isolates were resistant to tylosin and between 39% and 54% of the isolates were resistant to tetracycline. The mechanism of resistance is unknown. It is worth noting that none of the authorised intramammary preparations contain tetracycline so this high level of resistance is not likely to be attributable to the use of these preparations. *S. uberis* is ubiquitous in the environment and can exist in the gastrointestinal tract and on the skin of bovines. Without knowledge of the clinical history of each case, it is not possible to assess whether the tetracycline resistance may have been selected for by efforts to treat mastitis with systemic antibiotics or as a result of the bacteria being exposed to systemic or oral antibiotics used in the treatment of other conditions.

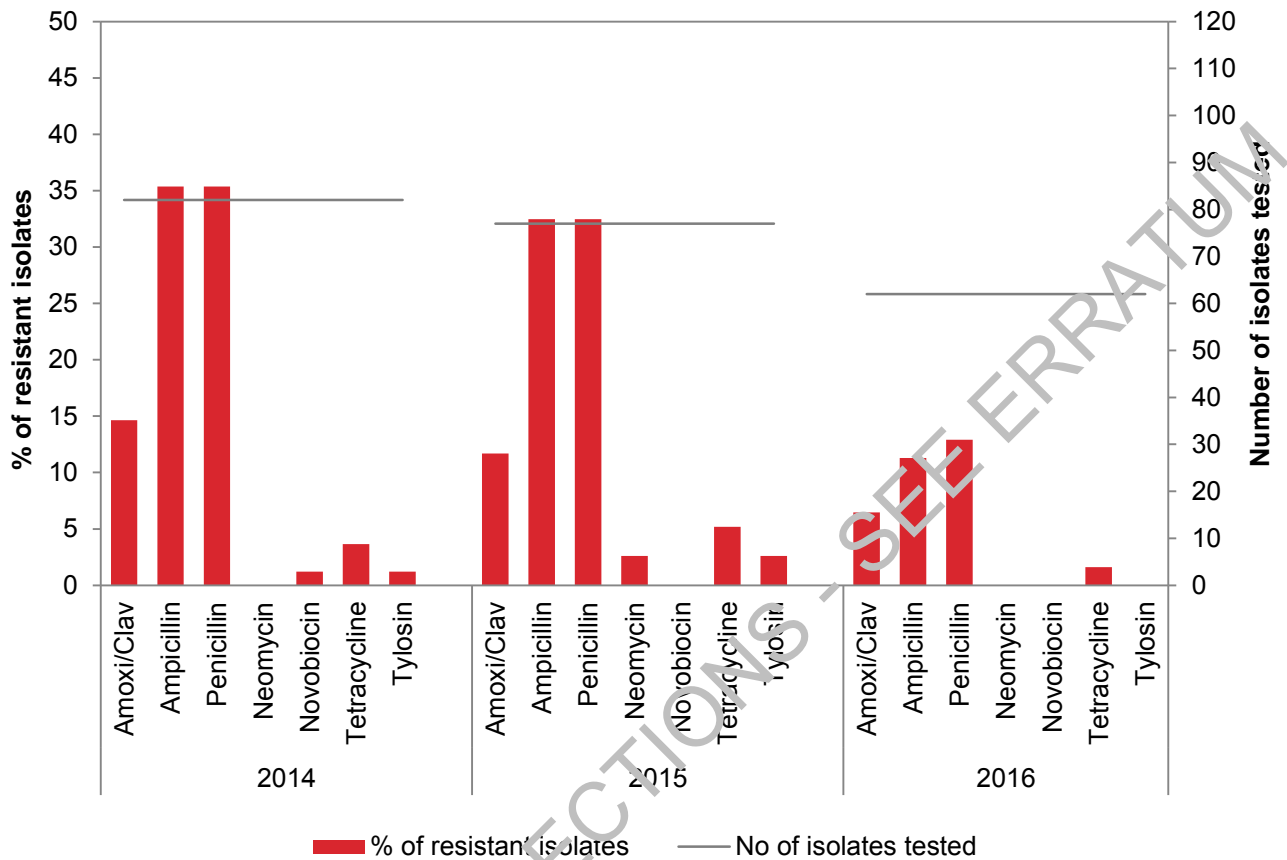
Figure 4.3. Total number and percentage of resistant isolates of *Streptococcus uberis* from mastitis infections of cattle



Staphylococcus aureus

S. 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 a common cause of zoonotic infections, and although both MRSA and a recently-described variant form of MRSA have been detected in cattle (Vanderhaeghen et al., 2010, Garcia-Alvarez 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, generally specific to a host-species. Total number and percentage of *S. aureus* isolates from mastitis infections resistant to different antibiotics are presented in Figure 4.4. Resistance to penicillin and ampicillin declined over the reporting period from 35% to 13%, although the reason for this remains unknown. Resistance to ampicillin and penicillin is significant as many intramammary preparations contain these antibiotics and highlights the need for regular and accurate culture and sensitivity testing as empirical treatment with penicillin may result in treatment failure and prolong disease. Penicillin resistance in bovine *S. aureus* is thought to occur mainly via the production of β -lactamases that degrade both penicillin and ampicillin. The genes encoding β -lactamases can be located on plasmids and often on transposons and may be readily transferable by conjugation. Isolates of *S. aureus* resistant to penicillin or ampicillin are currently screened for susceptibility to ceftiofur in order to detect the variant *mecA* gene (*mecC*) as well as isolates of classical MRSA. No MRSA were detected in cattle over the period 2014-2016. Amoxicillin/clavulanate resistance also declined from 15% to 6% over the reporting period and tetracycline and tylosin resistance was not observed or recorded in low numbers (below 5%).

Figure 4.4. Total number and percentage of resistant isolates of *Staphylococcus aureus* from mastitis infections in cattle



Mastitis is complex and the patterns of resistance observed vary with time and between farms. These data are aggregated at a national level and therefore have a limited ability to inform treatment protocols but they do highlight that acquired resistance does occur in England and Wales and should be considered when vets and farmers develop mastitis control programs for individual farms.

4.4.2 Respiratory pathogens

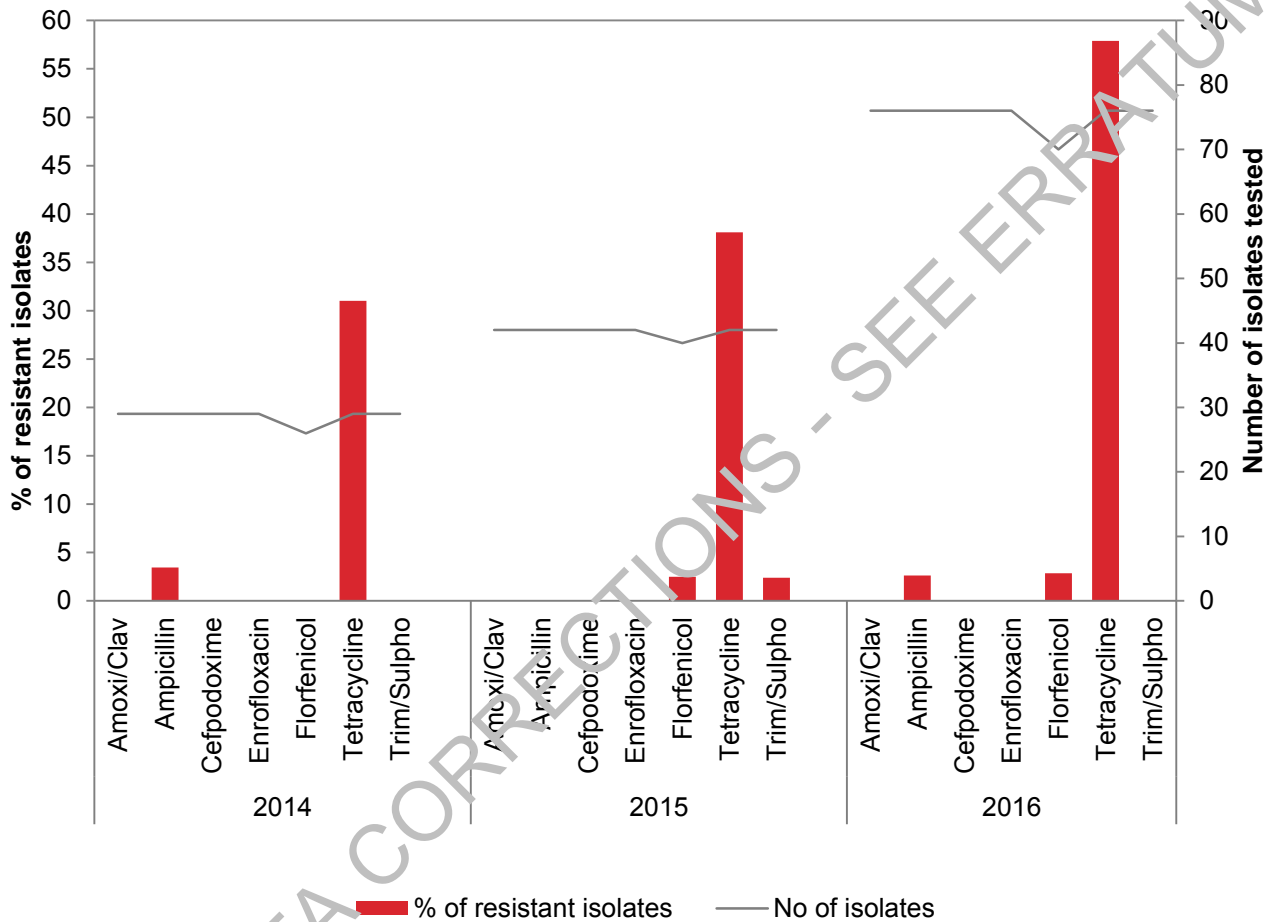
4.4.2.1 Cattle

Pasteurella multocida

P. multocida is a causative agent of respiratory or systemic disease in cattle. Toxigenic strains are responsible for the development of atrophic rhinitis in pigs and strains of the organism can also affect poultry (fowl cholera). It is a rare pathogen of sheep in the UK. 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. Resistance to ampicillin, tetracycline, trimethoprim/sulphonamides and florfenicol was observed in bovine isolates over the reporting period. Resistance to florfenicol was first observed in 2015 and was reported again in 2016. Florfenicol is effective for treating a number of pathogens which contribute to bovine respiratory disease complex; therefore it is a valuable option for the treatment of the bacterial component of respiratory disease in cattle. This finding

combined with an increased percentage of resistant isolates to tetracycline (58%) in 2016 compared to that reported in previous years (31% and 38%) demonstrates that resistance is present and highlights the need to reduce the incidence of respiratory disease in cattle through measures such as improving biosecurity, optimising husbandry and vaccination.

Figure 4.5. Total number and percentage of resistant isolates of *Pasteurella multocida* isolates from respiratory infections of cattle



Histophilus somni

H. somni (formerly known as *Haemophilus somnus*) is a cause of pneumonia in calves. All isolates tested in 2014-2016 were susceptible to the panel of antibiotics tested.

Further details on percentage of resistance for respiratory infections of cattle are included in Table S4.3.1 of the supplementary material.

4.4.2.2 Pigs

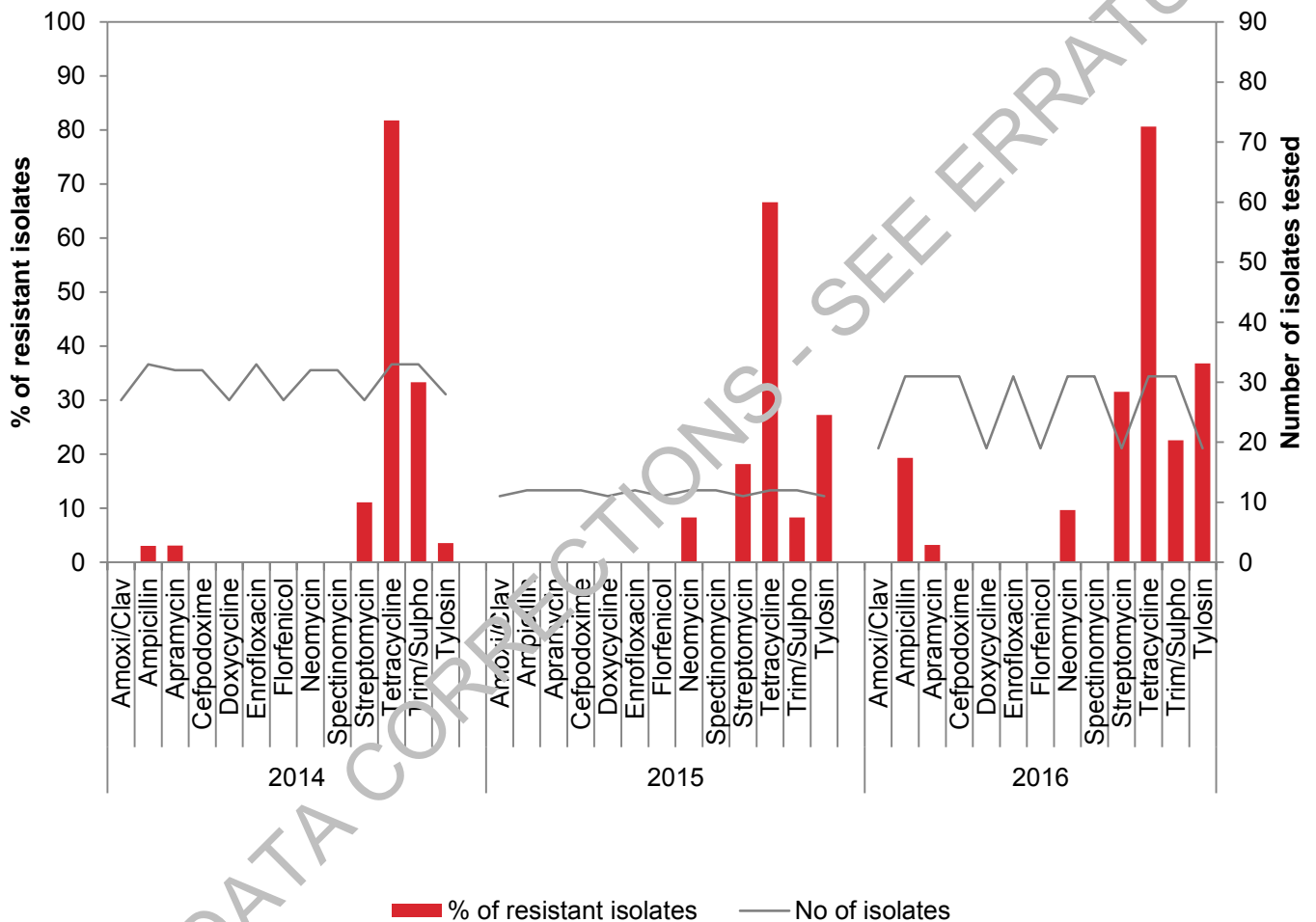
Pasteurella multocida

P. multocida from pigs showed resistance to ampicillin which was observed in 2014 (3%) and increased in 2016 (19%). Tetracycline resistant isolates were frequent (81%) although they were susceptible to doxycycline. Resistance to streptomycin and trimethoprim/sulphonamides was also

observed. An increased percentage of resistant isolates to tylosin was found in 2016 (37%) compared to previous years (27% in 2015 and 3% in 2014) (Figure 4.6).

Further details on percentage of resistance for respiratory infections of pigs are included in Table S4.4.1 of the supplementary material.

Figure 4.6. Total number and percentage of resistant isolates of *Pasterurella multocida* from respiratory infections of pigs



4.4.2.3 Sheep

Mannheimia haemolytica

M. haemolytica is a common cause of respiratory disease in the UK. There is carriage in the upper respiratory tract in healthy animals and ovine *Mannheimia* strains can also occasionally cause mastitis. The number of *M. haemolytica* isolates cultured from sheep was low and therefore any trends need to be interpreted with caution. Antibiotic resistance appears to be rare in these isolates and may reflect the suspected low use of antibiotics in sheep (See Table S4.5.1 of the supplementary material). Data on less frequently isolated ovine respiratory pathogens such as *Biversteinia trehalosi* and *Trueperella pyogenes* can be found in Table S4.5.1 of the supplementary material.

4.4.3 Other animal pathogens

Brachyspira hyodysenteriae

B. 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, carries the attendant risk that mutational resistance may arise.

Tiamulin is an important antibiotic used for the treatment of swine dysentery, and resistant isolates are of particular concern as they may also show resistance to some or all of the other antibiotics currently used for treatment. When resistance occurs to all of the available therapeutic antibiotics, the only practical option may eventually be to depopulate herds, with serious economic implications for the farmer. However, tiamulin-resistance in *B. hyodysenteriae* in conjunction with resistance to other available therapeutic compounds remains extremely uncommon. It should be noted that *B. hyodysenteriae* is not a zoonotic pathogen and tiamulin is not used to treat humans, therefore concerns about resistance in this pathogen are centred on animal health and welfare.

The susceptibility of 54 isolates of *B. hyodysenteriae* isolates tested from between 2010 and 2016 are reported. This includes some “repeat” isolates (i.e. isolates recovered from the same farm premises over a period of time) and two isolates from 2013 taken from the same premises which had a tiamulin MIC > 8 mg/L. A breakpoint of resistance > 4 mg/L tiamulin was used (Rønne and Szancer, 1990), which has also recently been quoted in a Dutch study of swine dysentery in pigs (Duijnhof et al., 2008). None of the three isolates from 2016 were resistant, reflecting the position of no resistance in 2010 and 2011 in 13 and 12 isolates respectively. For the years 2012-15, 3/9, 4/8, 2/4 and 1/4 showed resistance. Because of the importance of this disease and the significance of resistance to tiamulin, all available isolates are tested for tiamulin susceptibility each year. The minimum inhibitory concentration (MIC) values of *B. hyodysenteriae* isolates from pigs to tiamulin are presented in Table S4.6.1 of the supplementary material.

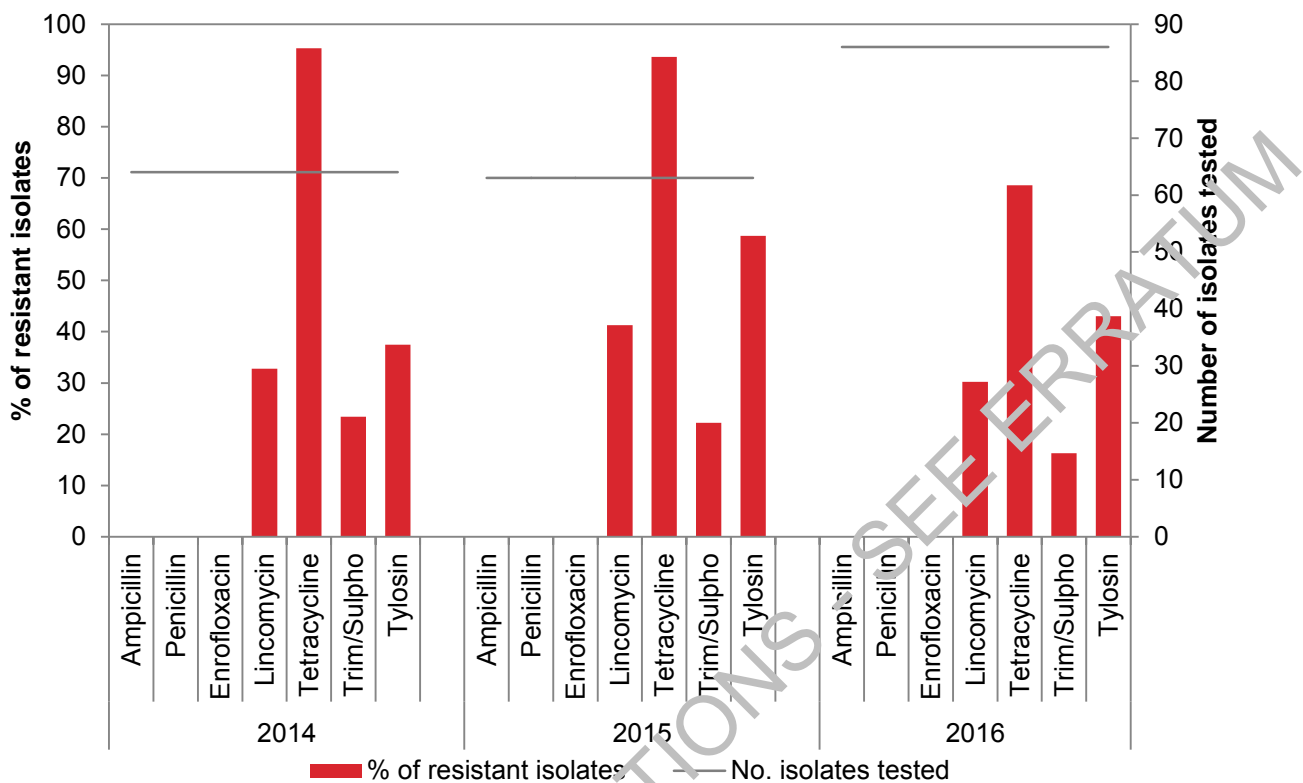
4.4.4 Zoonotic pathogens

Streptococcus suis

S. suis is a pathogen that can cause pneumonia, meningitis and arthritis in pigs. It can also rarely infect man. Between 2014 and 2016, a total of 213 isolates were recovered from pigs via clinical surveillance activities. Similarly to findings from previous years, no resistance to ampicillin or penicillin was observed in *S. suis* in 2016 (Figure 4.7). These antibiotics are often recommended for treatment of *S. suis*, so the absence of resistance is favourable. The findings suggest that treatment with highest priority critically important antibiotics were rarely indicated in these cases.

Each year, a relatively high frequency of resistance to some of the antibiotic agents was demonstrated, with resistance being most common to tetracycline (95%-69%) followed by resistance to tylosin (37%-43%), lincomycin (33%-41%) and trimethoprim-sulfamethoxazole (23%-16%). Tetracycline is not commonly used for the treatment of this disease. *S. suis* can reside in the tonsillar crypts of asymptomatic pigs, therefore the resistance observed may be a result of exposure following oral administration of tetracycline for the treatment of a different condition. Further details are presented in Table S4.6.2 of the supplementary material.

Figure 4.7. Total number and percentage of resistant isolates of *Streptococcus suis* from pigs, 2014-2016



Livestock Associated-MRSA

LA-MRSA was detected for the first time in 2005, and has since spread worldwide, being detected in the UK for the first time in 2013.

LA-MRSA is different from other types of MRSA, such as hospital or community associated strains which are more frequently found in humans. Anyone who has contact with colonised livestock can become colonised with LA-MRSA but prolonged colonisation is more likely in people who have regular, prolonged contact with colonised animals. LA-MRSA usually lives in the nose or on skin but if it is able to get into the body e.g. via a wound it can cause an infection. Usually this is a local skin infection, but occasionally it can cause diseases such as pneumonia or blood stream infections.

Further information for people who work with livestock is available at:

<https://www.gov.uk/government/publications/la-mrsa-information-for-people-who-work-with-livestock>.

A summary of all findings identified by UK government veterinary laboratories is provided in Table 4.1. These reports should not be interpreted as a prediction of prevalence in the animal population, as samples have been collected through differing methods of passive surveillance in animals which are affected with clinical disease. Results may therefore not be representative of the wider, healthy population.

CC398 is the most common LA-MRSA CC group isolated from food-producing animal populations in the UK. All isolates are whole genome sequenced and shared with Public Health England (PHE) to investigate any possible associations with infections in humans.

Table 4.1. Findings of LA-MRSA in the UK by government laboratories, 2013-2016

Country	LA-MRSA Clonal complex	Year	Species	Source of the sample
England and Wales	CC398	2013	Poultry	Clinical investigation
	CC398	2014	Pig	Clinical investigation
	CC398	2015	Pig	Research project
	CC398	2016	Turkey	Clinical investigation
	CC398	2016	Beef cattle	Clinical Investigation
	CC398	2016	Pig	Other Investigation
Northern Ireland	CC398	2014	Pig	Clinical investigation
	CC30	2015	Pig	Clinical investigation
	CC398	2015	Dairy cattle	Clinical investigation
	CC398	2015	Pig	Clinical investigation
	CC398	2015	Pig	Clinical investigation
	CC398	2016	Pig	Clinical investigation
	CC398	2016	Pig	Clinical investigation

4.4.5 *Escherichia coli*

E. coli is an important ubiquitous bacterium with 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 *E. 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 a previous section on mastitis organisms (see Section 4.4.1).

The majority of isolates reported in this section were recovered from faeces or intestinal contents, and includes both pathogenic and commensal strains. Results have been collated for the major food producing animals (Table 4.2), and resistance data analysed to animal species and age category level (Fig.4.8 - 4.15). 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, with 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.

Table 4.2. Number (%) of resistance in all *Escherichia coli* isolates from cattle, pigs, sheep, broilers and turkeys (all ages, combined)

Antibiotic	2014	2015	2016
Amikacin	2/590 (0.3%)	3/524 (0.6%)	4/467 (0.9%)
Amoxi/Clav	314/1045 (30%)	282/1034 (27.3%)	221/1123 (19.7%)
Ampicillin	733/1144 (64.1%)	713/1101 (64.8%)	683/1200 (56.9%)
Apramycin	73/1118 (6.5%)	60/1073 (5.6%)	68/1135 (6%)
Cefotaxime	80/593 (13.5%)	49/526 (9.3%)	62/469 (13.2%)
Cefpodoxime	19/481 (4%)	34/474 (7.2%)	7/314 (2.2%)
Ceftazidime	44/593 (7.4%)	34/526 (6.5%)	41/469 (8.7%)
Chloramphenicol	298/590 (50.5%)	244/524 (46.6%)	200/467 (42.8%)
Doxycycline	157/452 (34.7%)	132/451 (29.3%)	165/538 (30.7%)
Enrofloxacin	93/1144 (8.1%)	118/1101 (10.7%)	73/1200 (6.5%)
Florfenicol	209/764 (27.4%)	174/709 (24.5%)	164/792 (20.7%)
Neomycin	287/1049 (27.4%)	266/1030 (25.8%)	249/1100 (22.6%)
Spectinomycin	441/1118 (39.4%)	462/1073 (43.1%)	423/1135 (37.3%)
Streptomycin	442/742 (59.6%)	445/685 (64.7%)	394/743 (53%)
Tetracycline	779/1144 (68.1%)	708/1101 (64.3%)	727/1200 (60.6%)
Trimetho/Sulpho	442/1144 (38.6%)	420/1101 (38.1%)	461/1200 (38.4%)

Note: A table detailing the full breakdown of proportion of resistance to all antibiotics in all livestock species can be found in section S4.6 of the supplementary material

Data from England and Wales are presented in the main body of the report. Data for Scotland and Northern Ireland are presented in Tables S4.7.1-S4.7.15.

Fluoroquinolones and 3rd/4th generation cephalosporins are considered to be highest priority critically important antibiotics (HP-CIA) for use in people (for more detailed discussion of this classification, please refer to Chapter 1). In general, the level of resistance to these antibiotics in *E. coli* isolates was low.

At the end of 2015 the EMA's Antibiotics Expert Group (AMEG) advised that colistin should also be considered as a HP-CIA. All clinical isolates are tested for resistance using a disc diffusion method; however colistin is a very large molecule which means that conventional disc diffusion is an unreliable method for testing colistin susceptibility. Following the recommendation by AMEG, APHA implemented a pre-diffusion method to test for colistin resistance. This additional step was adopted as standard in 2016 but was not frequently used in 2015; therefore results of colistin susceptibility testing in 2015 are not reported.

Resistance to the third generation cephalosporins (cefotaxime, ceftazidime or cefpodoxime) detected in *E. coli* 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 (Fig. 4.10), may reflect the occurrence of ESBL enzymes which are cefotaximases, rather than ceftazidimases.

The relatively high frequency at which *E. coli* resistant to ampicillin are recovered from young calves may reflect the use of dry cow intramammary infusions in the dam and the transfer of residual antibiotics to calves in colostrum, which may then exert a selective pressure on the intestinal bacterial flora of the neonatal calf.

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 slightly higher prevalence. As in calves, this may reflect the occurrence of ESBL enzymes which are cefotaximases, rather than ceftazidimases.

4.4.5.1 Cattle

Figure 4.8. Total number and percentage of resistant isolates of *Escherichia coli* from cattle (all ages)

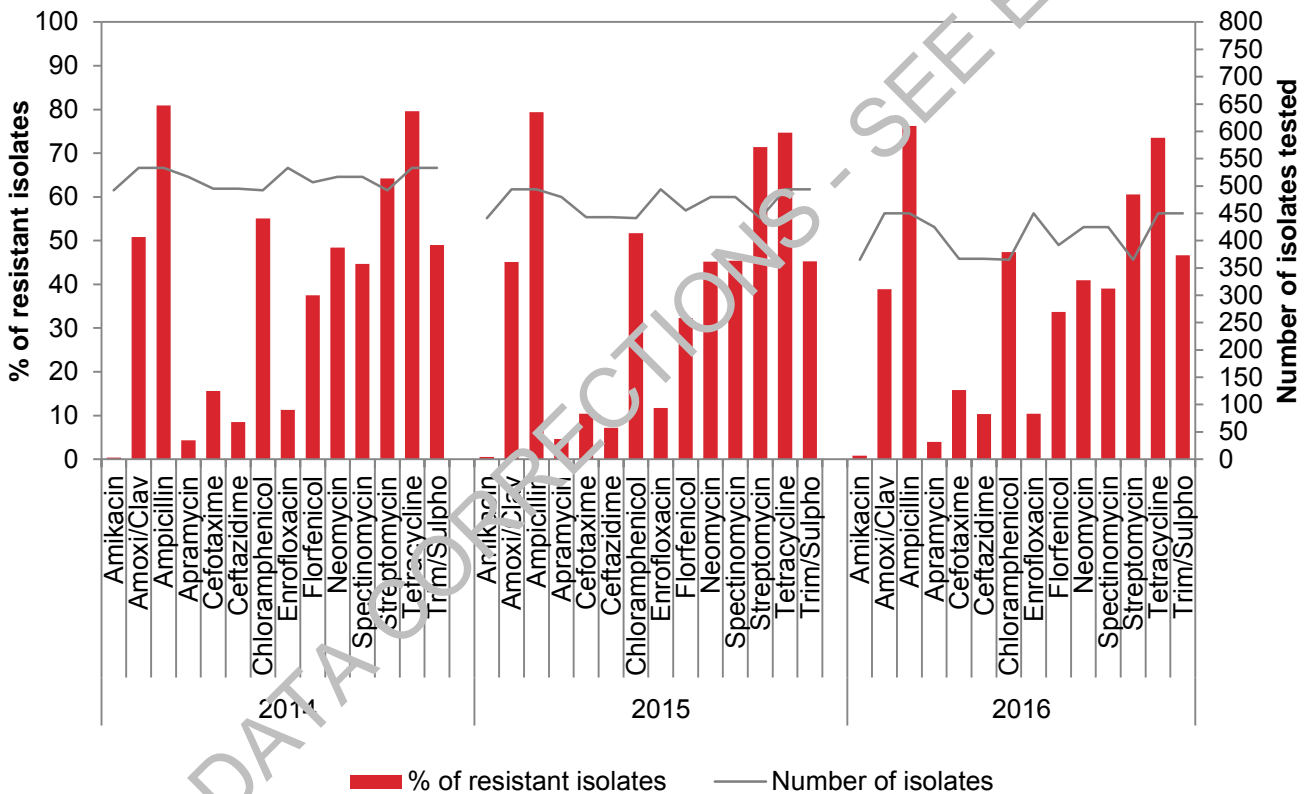
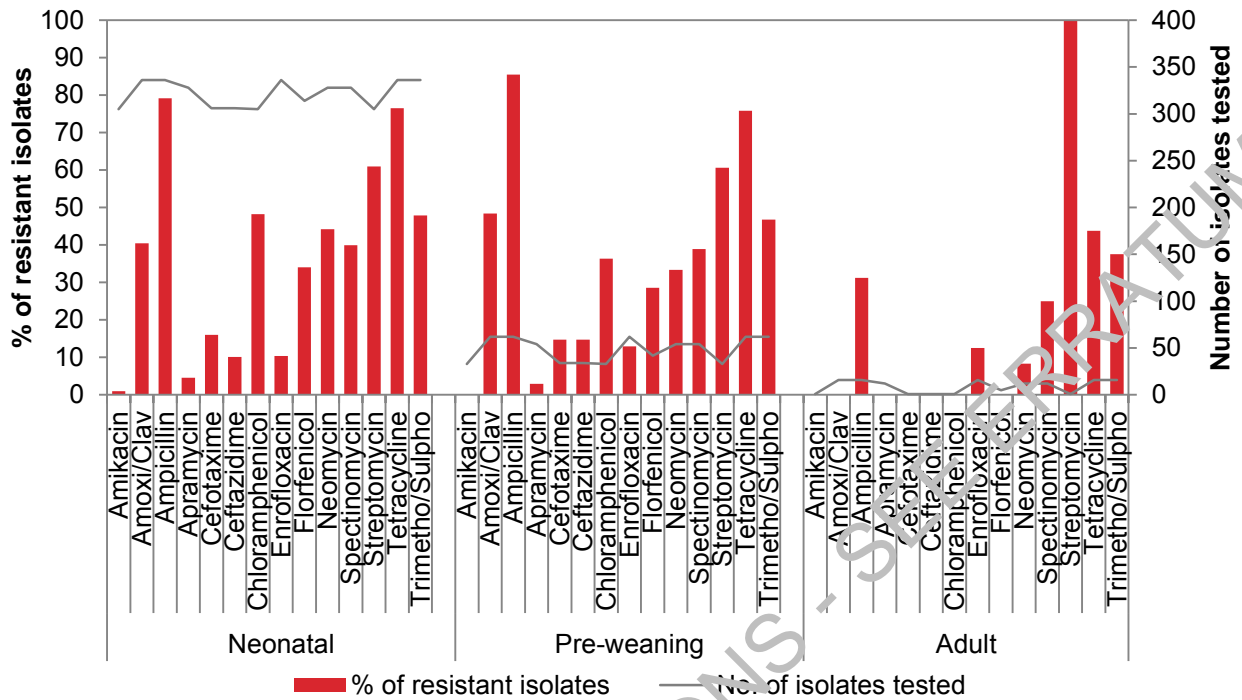


Figure 4.9. Total number and percentage of resistant isolates of *Escherichia coli* from cattle (by age category) in 2016



4.4.5.2 Pigs

Figure 4.10. Total number and percentage of resistant isolates of *Escherichia coli* from pigs (all ages)

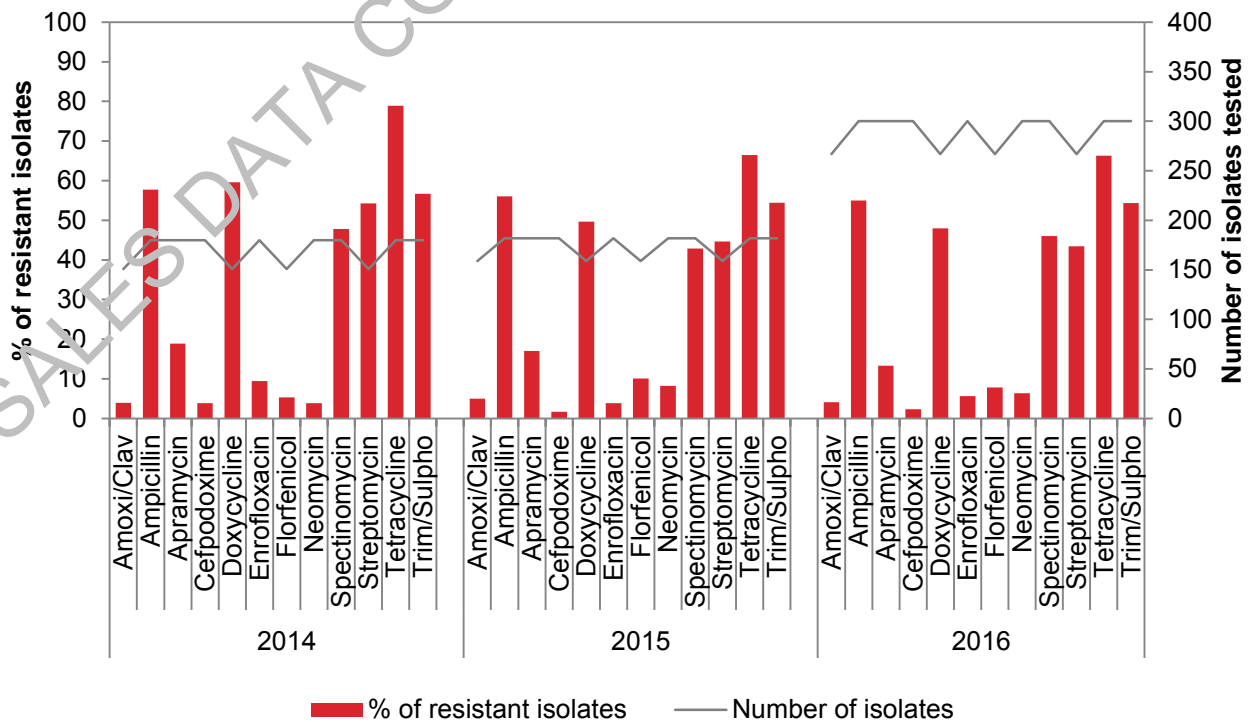
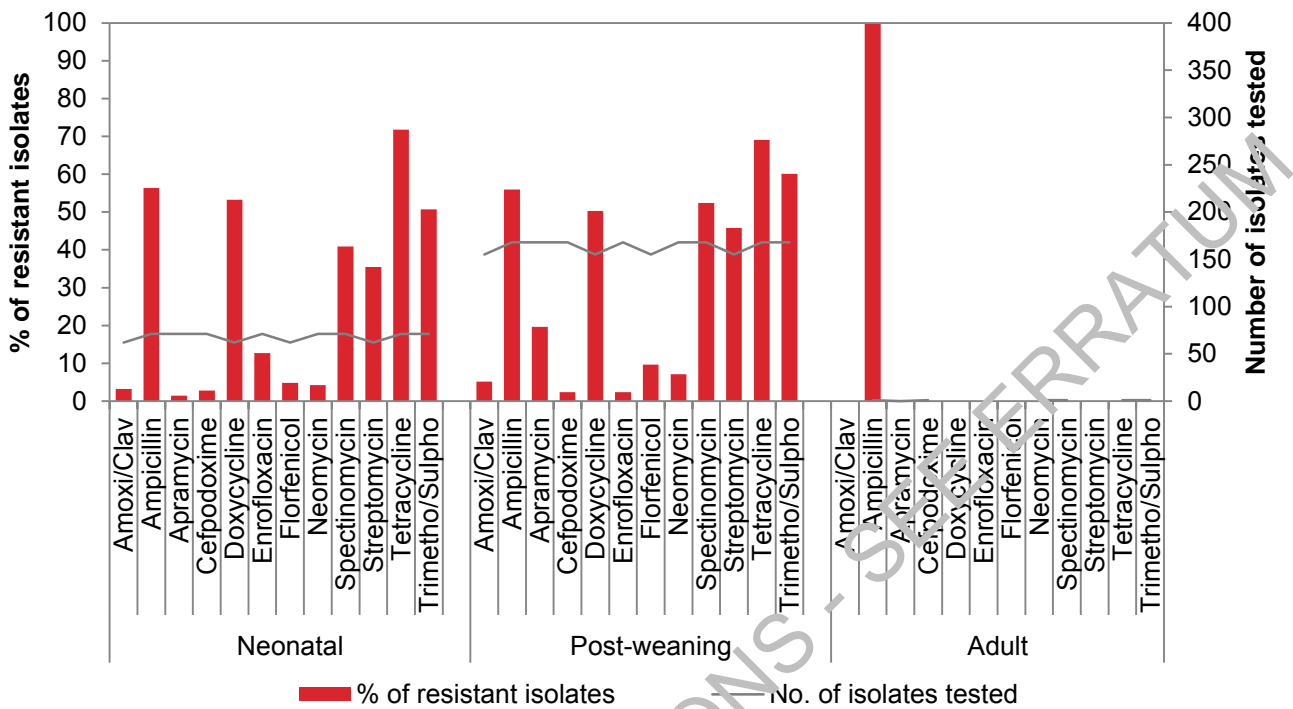


Figure 4.11. Total number and percentage of resistant isolates of *Escherichia coli* from pigs by age category in 2016



4.4.5.3 Sheep

Figure 4.12. Total number and percentage of resistant isolates of *Escherichia coli* from sheep (all ages)

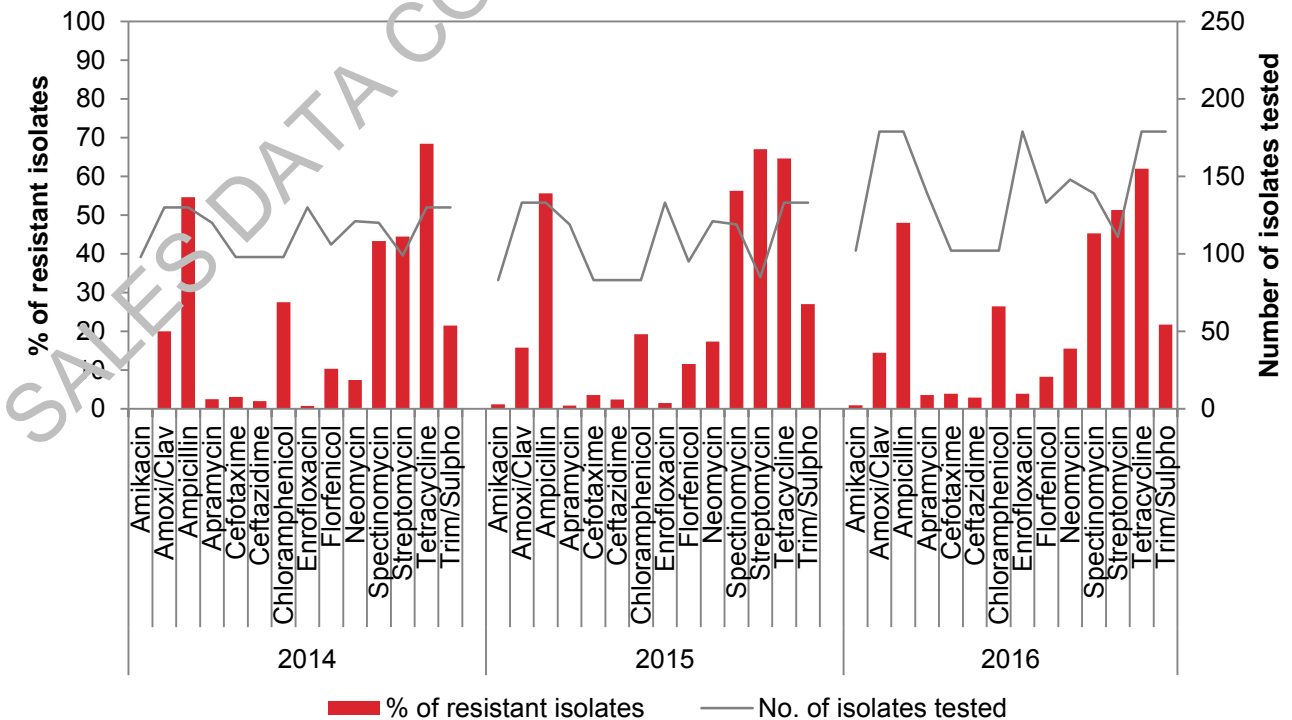
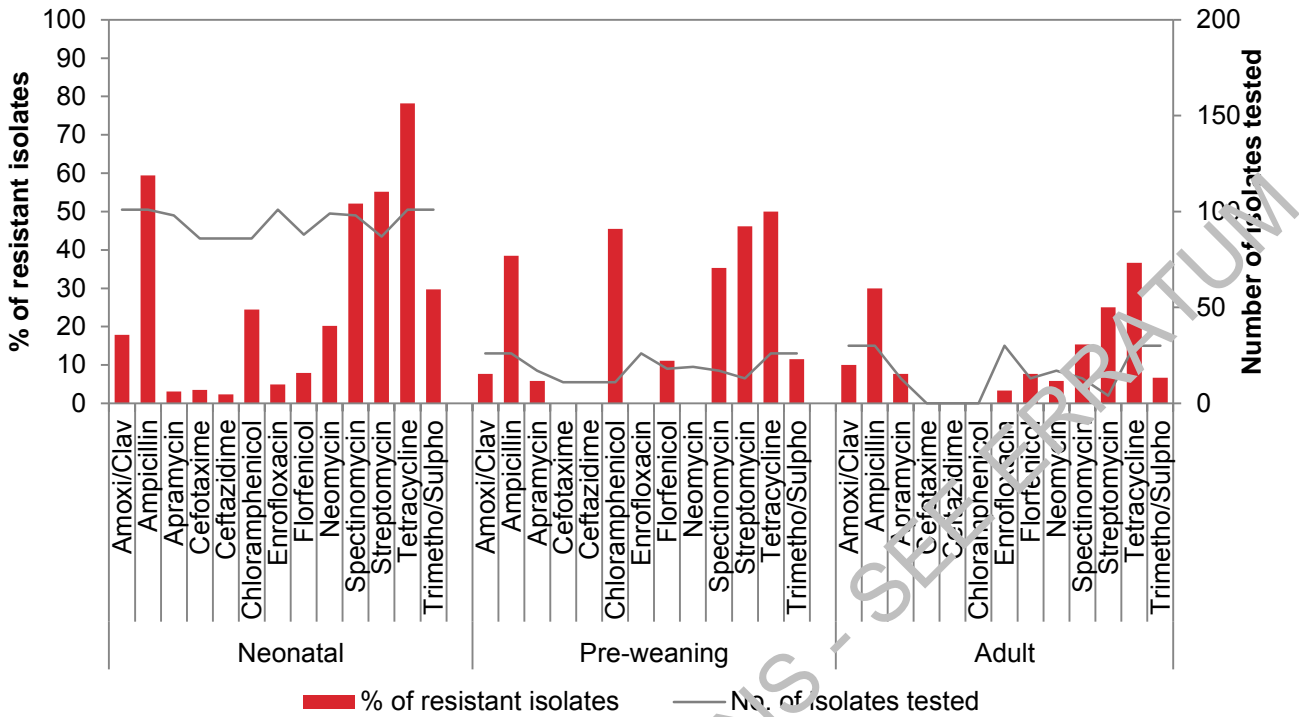
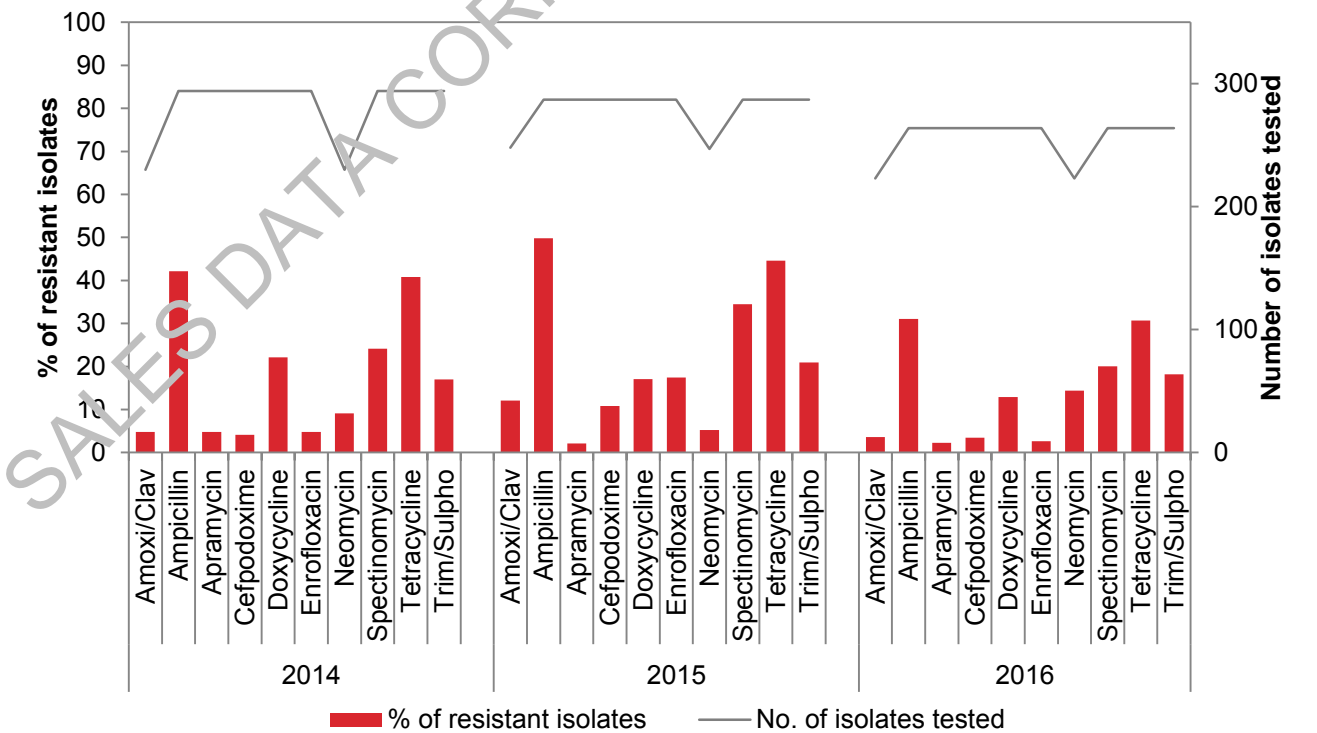


Figure 4.13. Total number and percentage of resistant isolates of *Escherichia coli* from sheep (by age category) in 2016



4.4.5.4 Chickens

Figure 4.14. Total number and percentage of resistant isolates of *Escherichia coli* from chickens



4.4.6 *Salmonella* spp.

The number of cultures received from a farm greatly varied, especially in the case of those received from poultry premises. Some poultry companies have a continuous monitoring programme and 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.

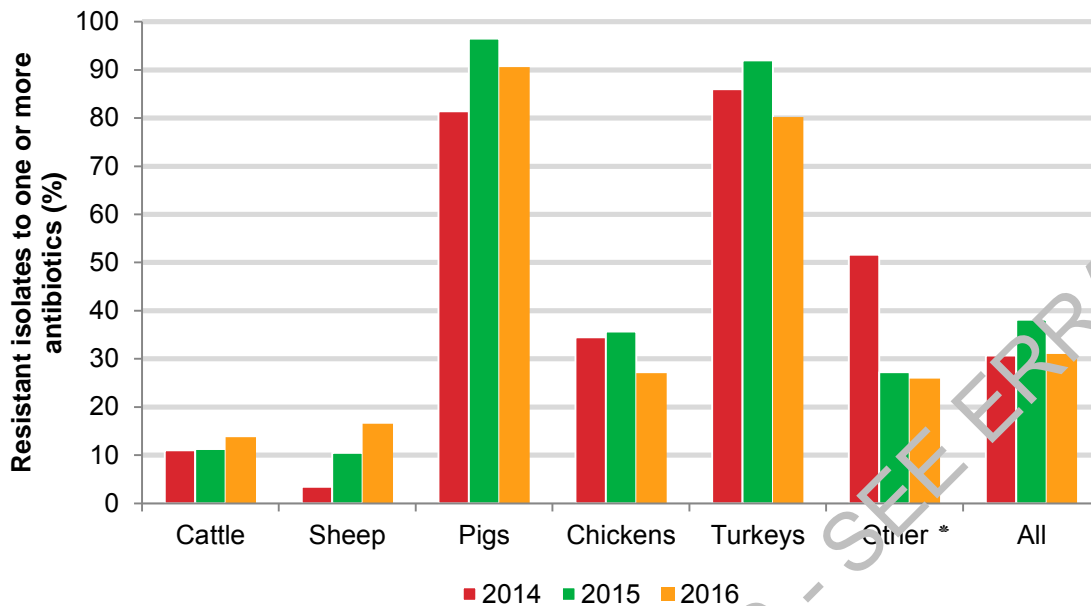
Due to the relevance of *Salmonella* as a zoonotic pathogen, and the importance of the serotype, and even phage type, of an isolate when investigating potential epidemiological links between animal and human case, results will be presented by individual serotypes/phage types in this section. Resistance to third generation cephalosporins and fluoroquinolones in *Salmonella* isolates is of particular importance, since these antibiotics are most commonly used for the treatment of human salmonellosis, where treatment is required. However, it should be noted that, most cases of non-typhoidal *Salmonella* infection in humans are non-invasive, limited to the gastro-intestinal tract and 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.

4.4.6.1 All *Salmonella*

Of the 2,397 *Salmonella* isolates tested in 2016, 1,654 (69.0%) were sensitive to all of the antibiotics tested (Fig. 4.15). This is similar to the situation in 2014, when 69.3% (1,626 of 2,347) were sensitive to all of the antibiotics tested and slightly higher than in 2015 when 61.9% (1,653 of 2,584) were fully susceptible.

Only 0.6% of all *Salmonella* isolates were resistant to ciprofloxacin and 0.4% were resistant to ceftazidime or cefotaxime in 2016. Ciprofloxacin, cefotaxime or ceftazidime resistance was not detected in *S. Typhimurium* in 2016, one of the serotypes of particular public health importance.

Figure 4.15. Percentage of *Salmonella* isolates resistant to one or more antibiotic from different sources and animal species, 2014-2016



*Other: Ducks, horses, dogs, other non-avian species, other avian species, feed and environment

Other noteworthy isolations were the isolation of *S. Kentucky* ST198 with high-level ciprofloxacin resistance (ciprofloxacin MIC \geq 8mg/l) which was detected in boot swabs collected from UK broilers on a single farm. The farm was investigated after depopulation, after thorough cleansing and disinfection had been performed and after re-stocking with the subsequent crop of birds and *S. Kentucky* was not detected at either of these follow-up visits. *S. Oslo* was recovered from horses at an equine premise. Both susceptible and resistant *S. Oslo* were detected and the resistant isolates were resistant to multiple antibiotics including ampicillin, chloramphenicol, streptomycin, sulphonamides, tetracycline, trimethoprim, gentamicin, neomycin, cefotaxime and ceftazidime. Several horses were affected with diarrhoea (one died) and three people and one child visiting or working at the premises also developed mild symptoms of gastro-intestinal disease which resolved within 24-48 hours. A visit was subsequently performed and multidrug-resistant (MDR) *S. Oslo* was detected at a low number of environmental samples on the premises. The ESBL enzyme CTX-M-1 was confirmed in the *S. Oslo* isolate. This enzyme was also detected in *E. coli* on the site, which may have provided a reservoir of resistance genes which were acquired by the *Salmonella*.

4.4.6.2 *Salmonella* by animal species

Considering all *Salmonella* isolates from the different animal species, a decreased trend in the percentage of resistant isolates from pigs, chickens and turkeys was observed. In pigs, the percentage of susceptibility increased from 3.5% in 2015 to 9.4% in 2016, although this figure was still lower than that observed in 2014 (18.6%). In turkeys, the percentage of fully susceptible isolates rose from 12% and 8% in 2014 and 2015, respectively, to 19.8% in 2016. Similarly, an increased percentage of susceptible isolates was recorded for chickens which increased from 49% in 2014 to 72.8% and 74.1% in 2015 and 2016, respectively. Conversely, a decreased trend in susceptibility was observed for cattle (from 89% in 2014 and 2015 to 87% in 2016) and sheep (from 96.6% and 89.5% in 2014 and 2015, respectively, to 83.5% in 2016) although the level of susceptibility in isolates from these two animal species was overall much higher (Fig. 4.15). Data

for the resistance levels for *Salmonella* isolates from the different animal species to the antibiotics tested is presented in full in tables S4.8.2-S4.8.6 of the supplementary material. A summary is given below.

Cattle – Of the 336 *Salmonella* recovered in 2016, the highest level of resistance was to streptomycin (12.2%), sulphonamide compounds (11%), ampicillin (10.7%) and tetracycline (10.4%). A slight increase in the levels of resistance to these antibiotics was seen compared with 2015 and 2014.

Pigs – A large proportion of isolates was resistant to sulphonamide compounds (85.6%), tetracycline (80%), streptomycin (76.9%) and ampicillin (72.5%). These levels of resistance were slightly lower than those reported in 2015 (90.7%, 90.1%, 82.6% and 84.9%, respectively), but still higher than levels observed in 2014 (74.5%, 74.5%, 68.6% and 68.1%, respectively).

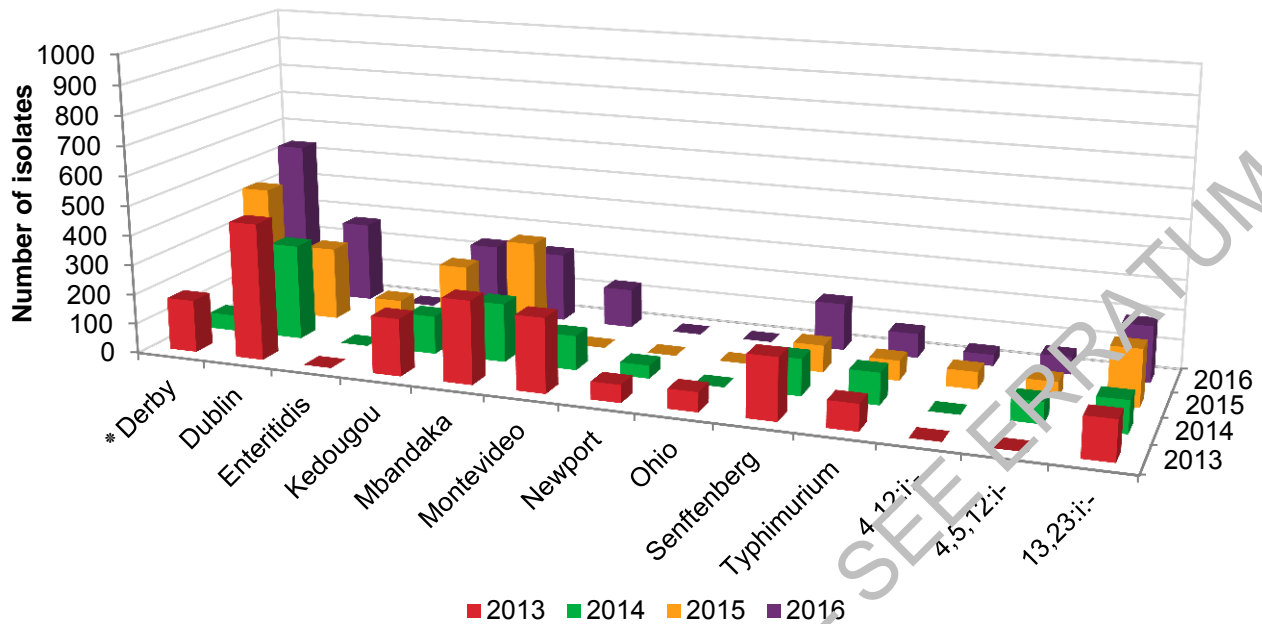
Sheep – Of the 91 *Salmonella* isolates cultured in 2016, the highest level of resistance was observed to streptomycin (15.4%), tetracycline (14.3%), sulphonamide compounds (13.2%) and ampicillin (12.1%). A slight increase in the levels of resistance to these antibiotics was seen compared with 2014 and 2015.

Chickens – Of the 696 isolates tested in 2016, the highest level of resistance was seen to sulphonamide compounds (22.3%) and tetracycline (16.7%), which represented very similar levels to those observed in previous years. Resistance to 3rd generation cephalosporin was only seen in one isolate and resistance to fluoroquinolone (ciprofloxacin) was only seen in 0.9% (six of 696) of the isolates. Similarly to previous years, gentamicin resistance was only present in a very low number of isolates (1%, seven of 696).

Turkeys – Similarly to isolates from other livestock species, the highest level of resistance was to sulphonamide compounds (72.1%), tetracycline (70.3%) and streptomycin (53.2%). These levels were similar or slightly lower to those reported in 2014 and 2015. The level of ciprofloxacin resistance in turkeys (1.8%) was the highest compared to other livestock species although a decreased when compared with 2014 (5.6%) and 2015 (11.2%).

Top ten *Salmonella* serovars isolated in 2014-2016

Some serovars can have characteristic patterns of resistance, so knowledge of the most frequently isolated serovars can be of benefit when considering trends in resistance. The 'top ten' serotypes of non-typhoidal *Salmonella* isolates recovered from cattle, pigs, sheep, chickens and turkeys in Great Britain in 2014-2016 are presented (Fig. 4.16). *S. Dublin* and *S. Mbandaka* are generally the most consistently isolated serovars year-on-year. Further details on the number of commonly recovered serovars in Scotland and Northern Ireland can be found in Table S4.8.10 and S4.8.11 of the supplementary material.

Figure 4.16. Top ten most commonly isolated *Salmonella* serovars from livestock, 2013-2016

*Data from 2016 includes presumptive *S. Derby* (388 isolations)

Tetracycline resistance was most commonly found in *Salmonella* isolates originating from pigs and turkeys in 2016. This was also the situation for resistance to sulphonamides and streptomycin, similar to the findings reported in 2015.

Resistance to apramycin in all *Salmonella* serovars was 1.8% in 2016, similar to the level observed in 2015 (2.4%). The majority of the apramycin resistant isolates were from pigs with 21.9% of the pig isolates resistant to this antibiotic in both monophasic *S. Typhimurium* and *S. Typhimurium* isolates. In 2016, 8.5% of *S. Typhimurium* (n=47), 41.9% of *Salmonella* 4,12:i:- isolates (n=31) and 34.0% of *Salmonella* 4,5,12:i:- isolates (n=53) from pigs were resistant to apramycin. A total of 2.3% of all *Salmonella* isolates were resistant to gentamicin. No resistance was detected to the aminoglycoside amikacin.

Similar to data from 2014 and 2015, the highest prevalence of resistance to nalidixic acid in 2016 was observed in *Salmonella* isolates from dogs, turkeys and other avian species (gamebirds, pet birds, etc). In turkeys, three of five *S. Newport* isolates and all *S. Senftenberg* isolates (n=4) were resistant to nalidixic acid in 2016. The situation in turkeys was similar in 2014 and 2015, with nalidixic acid resistance frequently detected in these serotypes. In broilers, resistance to nalidixic acid was mainly observed in *S. Infantis* (5/5 isolates) with lesser contributions from *S. Indiana*, *S. Kentucky*, *S. Mbandaka*, *S. Newport* and *S. Senftenberg*. Ciprofloxacin resistance occurred in 1.8% of *Salmonella* isolates from turkeys (n=111) and ciprofloxacin-resistant isolates were also resistant to nalidixic acid. All of the ciprofloxacin resistant isolates from turkeys were *S. Newport*. The other ciprofloxacin-resistant isolates detected in 2016 originated from broilers (*S. Kentucky*, 3/4 resistant), dogs (*S. Kentucky*, 2/2 resistant), partridges (*S. Orion* var. 15+, 1/3 resistant), pheasants (*S. Orion*, 2/2 resistant) and reptiles (*S. Give*, 1/1 resistant). Three isolates of the incomplete serovar 13,23:i:- were also identified in broilers which were resistant to ciprofloxacin.

In 2016, resistance to cefotaxime and ceftazidime was detected in *S. Oslo* from horses, in a single isolate of *S. Kedougou* from broilers, as well as in single isolates of *S. Agona* and *S. Ajibobo* from dogs.

4.4.6.3 *Salmonella* Dublin

Of the 245 *Salmonella* Dublin isolates tested during 2016, 96.3% were susceptible to all 16 antibiotics (Table 4.3). The percentage of fully susceptible *S. Dublin* isolates has shown only slight fluctuations over the period 2007-2016 and the majority of isolates remain susceptible. This has been the situation since surveillance began in 1971.

Most *S. Dublin* isolates (90.6%) originated from cattle in 2016 and this was also similar to the situation recorded in previous years. Isolates from species other than cattle were all fully susceptible to the panel of 16 antibiotics in 2016.

Single *S. Dublin* isolates from cattle were resistant to ampicillin or chloramphenicol, whilst a single isolate was resistant to both streptomycin and tetracycline. Resistance to nalidixic acid and streptomycin were the most frequent resistances observed, although it only occurred in 1.2% and 1.6% of the isolates, respectively.

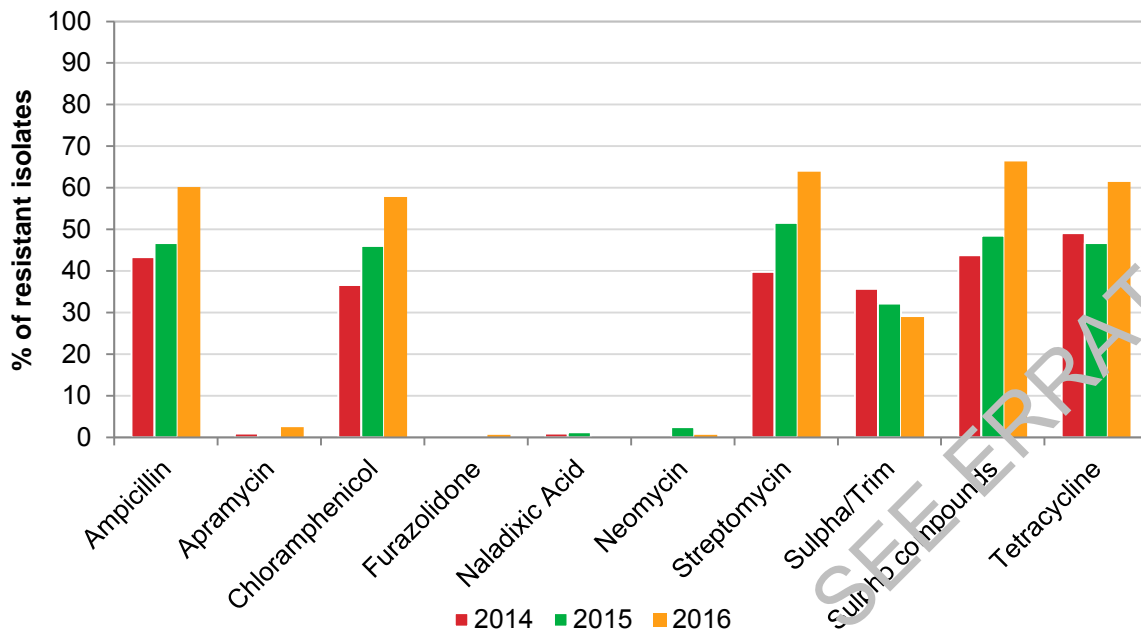
Table 4.3. Resistance in *Salmonella* Dublin: percentage of resistant isolates, 2013-2016

Antibiotic	Percentage of isolates resistant			
	2013 (n=393)	2014 (n=286)	2015 (n=226)	2016 (n=245)
Ampicillin	0.3	0.7	1.8	0.4
Chloramphenicol	0	0	0.4	0.4
Furazolidone	0	0.3	0	0
Nalidixic Acid	1	0	2.2	1.2
Neomycin	0.3	0.3	2.2	0
Streptomycin	1.3	2.4	4	1.6
Sulphamethoxazole/Trimethoprim	0	0.7	0	0
Sulphonamide compounds	0	0.7	0	0
Tetracycline	0	0.3	0.4	0.4

4.4.6.4 *Salmonella* Typhimurium

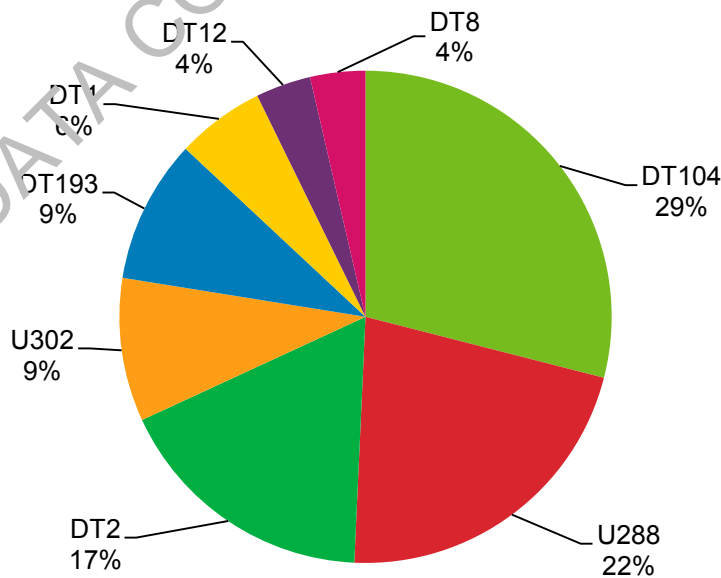
The percentage of *S. Typhimurium* isolates that were sensitive to all of the antibiotics tested was 50.1% (50 of 166), which is a decrease from the figures reported in 2015 (41.8%) and 2014 (44.2%). There were no *S. Typhimurium* isolates resistant to ceftazidime, cefotaxime, ciprofloxacin, nalidixic acid or amikacin. The percentage of resistant *S. Typhimurium* isolates to the panel of antibiotics tested is shown in Figure 4.17.

Figure 4.17. *Salmonella* Typhimurium: percentage of resistant isolates in 2014 (n=224), 2015 (n=165) and 2016 (n=166)



More than one third (38%) of *S. Typhimurium* isolates were of age types DT104 or U302; there were no isolates of DT104B. The percentage of the eight most common definitive and undefined types of *S. Typhimurium* in 2016 is given in Figure 4.18. The proportion of *S. Typhimurium* isolates comprising DT104 and its variants, which had shown a general decline in 2007-2014, has shown a recent resurgence.

Figure 4.18. Percentage of isolates of *Salmonella* Typhimurium of the eight most frequent definitive or undefined types subject to susceptibility testing in 2016



The generally high level of resistance of *S. Typhimurium* isolates observed in recent years has partly been a reflection of the contribution of DT104 and its variants DT104B and U302 which have comprised more than a quarter of isolates in some years in the previous decade, including 2016.

4.4.6.5 Monophasic *Salmonella* Serotypes

Sixty-three isolates of *Salmonella* 4,12:i:- were tested, belonging to phage types DT120 (n=1), DT193 (n=58) and DT41 (n=1); three isolates were either not typable or reacted with phages but did not conform to a recognised phage type. Most isolates were from pigs (49.2%) with feed and related samples being the next most common source of origin (17.5%). The most common pattern of resistance observed was AmSSuT, which occurred in 26/58 of DT193 isolates and in 2/3 of the isolates which were not typable with phages. Considering the DT193 isolates, 42/58 (72.4%) had the AmSSuT resistance pattern alone or with one or more additional resistances.

A total of 87 isolates of *Salmonella* 4,5,12:i:- were tested, including phage and undefined types DT193 (n=80), DT208 (n=4) and U323 (n=1); two isolates were untypable or reacted with phages without conforming to a recognised pattern. The most common resistance pattern in DT193 isolates was AmSSuT, occurring in 53.8% of isolates (43/80). Most isolates of monophasic *Salmonella* 4,5,12:i:- DT193 were from pigs (62.5%).

Considering the aminoglycosides other than streptomycin, apramycin resistance was detected in 41.9% and neomycin resistance in 12.9% of 4,12:i:- from pigs (n=31). Apramycin resistance was detected in 34.0% and neomycin resistance in 9.4% of 4,5,12:i:- from pigs (n=53). Resistance to apramycin was also observed in 9.1% of 4,12:i:- isolates from feed or feed constituents (n=11) and 25% of 4,5,12:i:- from feed or feed constituents (n=8). Neomycin resistance was detected in 4,12:i:- isolates from feed (36.4% of isolates resistant; n=11) and 4,5,12:i:- isolates from feed (25% of isolates resistant; n=8). Resistance to the aminoglycosides apramycin and neomycin was therefore detected in monophasic *S. Typhimurium* isolates from both pigs and feed in 2016. In 2015, neomycin resistance was not detected in monophasic *S. Typhimurium* isolates from feed (n=11), though it was detected in both 4,12:i:- and 4,5,12:i:- isolates from pigs.

4.4.6.6 *Salmonella* other than Dublin or Typhimurium

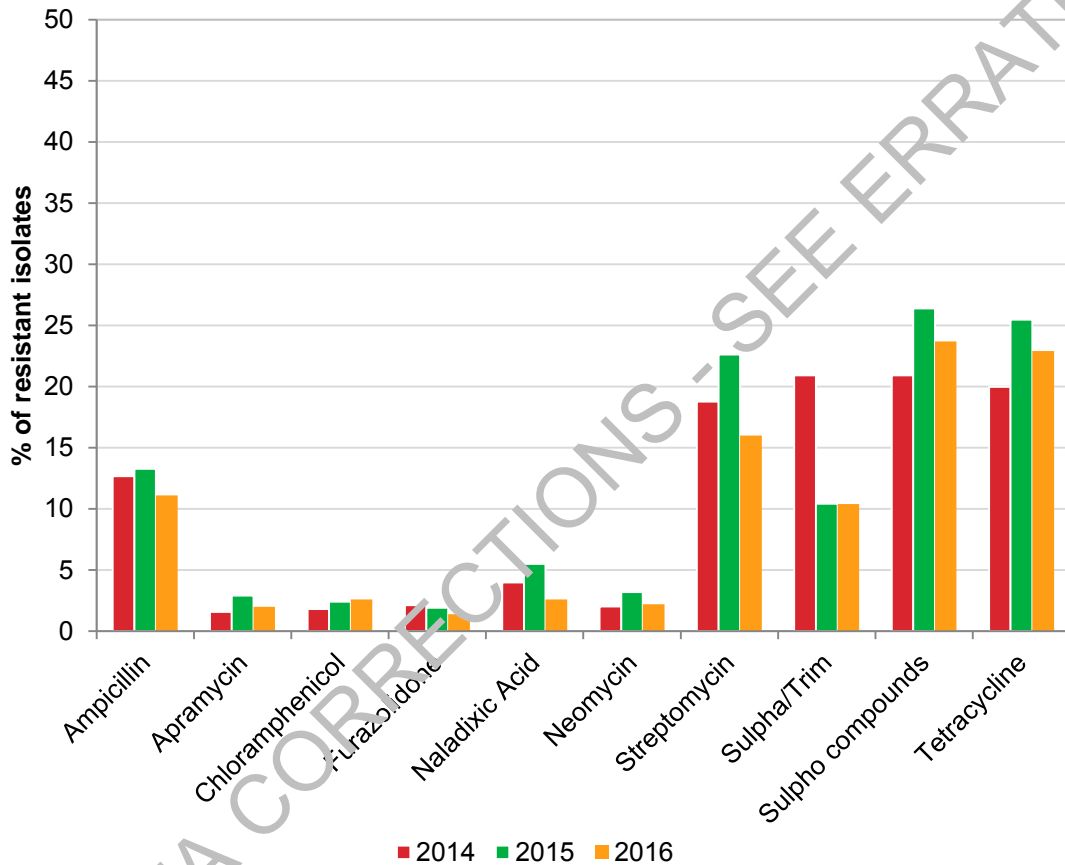
Of the 1,986 isolates of serotypes other than *S. Dublin* and *S. Typhimurium* tested, 68.9% were sensitive to all the antibiotics tested, an increase on the figure recorded in 2015, when 60.2% were fully sensitive. Only 16 isolates (0.8% of the total) were *S. Enteritidis* and considering these *S. Enteritidis* isolates, 15/16 (94%) were fully susceptible, with a single isolate from ducks showing resistance to both streptomycin and sulphonamides. Definitive phage typing information was not available for the isolate from ducks. A single isolate from a snake was sensitive and untypable with phages; otherwise the sensitive *S. Enteritidis* isolates belonged to phage types 11 (n=2), 13a (n=2), 21 (n=1), 4 (n=2), 8 (n=2) and 9a (n=4).

Neomycin resistant *Salmonella* isolates originated mainly from feed or feed constituents (432 isolates; 2.8% resistant), pigs (113 isolates; 8.0% resistant), horses (39 isolates; 12.8% resistant) and ducks (213 isolates; 2.4% resistant). In ducks, *S. Indiana* was the main serotype showing resistance to neomycin (5/73 isolates resistant); the *S. Indiana* isolates from ducks were also frequently resistant to furazolidone (11/73 isolates) and this was similar to the situation observed in 2015.

The apparent increase in the prevalence of resistance to streptomycin, sulphonamides and tetracyclines which was observed following 2009 reflected in part the increased monitoring of turkeys that has occurred since 2010 under the Control of *Salmonella* in Turkeys Order. Considering *Salmonella* isolates other than *S. Typhimurium* and *S. Dublin* from turkeys in 2016 (n=111), 53.2% were resistant to streptomycin, 72.1% to sulphonamides and 70.3% to

tetracyclines; lower than the equivalent figures for pigs in 2016 (73%-80%), but higher than those for chickens (9%-22%) or cattle (13%-16%). In 2016, the proportion of *Salmonella* isolates originating from feed (21.8%) was similar to 2015 (17.9%); the proportion of fully susceptible isolates from feed increased slightly from 68.0% to 73.8%.

Figure 4.19. *Salmonella* other than Dublin and Typhimurium, percentage of isolates resistant to antibiotics tested in 2014 (n=1837), 2015 (n=2198) and 2016 (n=1986)



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Annexes

Annex A: Data limitations

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, e.g. 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 5.

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 2).

Resistance data, clinical surveillance

There are a number of limitations associated with the antibiotic resistance data and they should be borne in mind when interpreting results from the veterinary clinical surveillance. This is a biased population and cannot be considered to accurately reflect the bacterial populations present within the general animal population in the UK:

- Veterinary surgeons have the option to submit samples to private laboratories rather than Government laboratories/Veterinary Investigation Centres. The proportion of samples that Government laboratories tests compared to other laboratories is not known, and therefore we cannot know how representative the samples processed by APHA, SACCVS, and AIBI are of total diagnostic submissions.
- Furthermore, geographical proximity of a farm or veterinary practice to a Government 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.
- Other factors can also influence the submission rate of samples to veterinary diagnostic laboratories. These can include for example the severity of disease, impact on production or the value of the animals involved.
- The levels of resistance demonstrated by the clinical surveillance isolates presented in this report may be higher than those seen in the wider bacterial populations present within animals in England and Wales. This is because samples from diseased animals may 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. APHA does not provide a veterinary diagnostic service for companion animals.
- The veterinary clinical surveillance data detail the number of bacterial isolates that underwent sensitivity testing, but not the numbers of animals for which samples were submitted for examination. Several bacteria may have been cultured from an individual animal or from a group of animals on the same farm. This type of clustering is not accounted for in the report, though since only low numbers of bacteria are usually subjected to susceptibility testing from the same outbreak of disease, its importance is probably limited.
- 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.
- The breakpoints used for determining resistance for isolates recovered under the veterinary clinical surveillance programme in GB 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 approximately 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. Currently, there is insufficient data available to apply animal species specific breakpoints to all organism/antibiotic combinations where these are required.

- Different antibiotic susceptibility testing methodologies are used in England & Wales (APHA), Scotland (SACCVS), and Northern Ireland (AFBI). APHA and SACCVS use BSAC methodology to determine resistance/susceptibility based on human clinical breakpoints, whilst AFBI use CLSI. **In light of the different methodologies and breakpoints used, the amalgamated results of UK wide monitoring should be interpreted with caution.**
- For AST testing done by APHA, in the case of some veterinary drug/bug combinations a BSAC cut-off may not exist. In this case, APHA may have derived a tentative or suggested breakpoint or the historical veterinary breakpoint (zone size cut-off of resistant ≤ 13 mm) may have been used to define resistance. The breakpoints used are set out in S4.1 of the supplementary materials.
- *Escherichia coli* isolates are not collected from routine samples from healthy livestock in Northern Ireland. Only clinical cases submitted for post-mortem investigation when colibacillosis, or similar diseases, will proceed to isolate pathogenic *E. coli*. AMR testing on *E. coli* isolates is mainly performed if samples are coming from less than 2-week old calves and animals with bovine mastitis.
- With regards to *E. coli*, each organisation in the United Kingdom sets their own criteria for testing AMR in *E. coli* from clinically sick animals and these criteria are not uniform. This is pertinent to highlight as the selection of isolates for susceptibility testing based on age or other criteria can influence the result obtained. Bacterial isolates recovered from young animals can often be more resistant than those from older animals and this relates to the fact that antibiotics are in general more frequently administered to young animals than to older animals.

Annex B: Data sources

Marketing Authorisation Holders (MAHs)

It is mandatory for Market Authorisation Holders of manufactured antibiotics to provide the Veterinary Medicines Directorate with total annual sales data for each antibiotic product sold within the UK. Data are collected, verified and analysed to calculate the total weight, in tonnes, of each active ingredient sold for each antibiotic. Antibiotic sales data are collected as a proxy for antibiotic 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 2015 calendar year reported sales were compared to those returned to the AMR team and any discrepancies were queried.

To calculate the Population Correction Unit, data are 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.

Annex C: Glossary of Terms

a.i.	Active Ingredient; the part of an antibiotic medicine that acts against the bacterial infection.
ATCvet	Anatomical Therapeutic Chemical Classification System for veterinary medicinal products
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 large group of antimicrobial substances capable of inhibiting the growth of, or destroying bacteria. Often used synonymously with antibacterials.
Antimicrobial	A general term for any compound with a direct action on micro-organisms used for treatment or prevention of infections. Antimicrobials include antibacterials (antibiotics), antivirals, antifungals and antiprotozoals.
Antibiotic Resistance	The ability of a micro-organism to grow or survive in the presence of an antibiotic 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 <i>Cephalosporium acremonium</i> . 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 colistin.
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 <i>Streptomyces</i> 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.
PSUR	Periodic Safety Update Report. Pharmacovigilance documents submitted by marketing authorisation holders (MAHs) at defined time points post-authorisation. These documents are intended to provide a safety update resulting in an evaluation of impact of the reports on the risk-benefit of a medicinal product.
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 <i>Streptomyces</i> 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.

Annex D: Contributors

Compiled by the Veterinary Medicines Directorate:

Contributing Pharmaceutical Companies and Other Marketing Authorisation Holders

- | | |
|-------------------------------------|----------------------------------|
| • Alfasan Nederland BV | • Krka Dd |
| • Andres Pinaluba, S.A. | • Laboratorios Calier S.A. |
| • Animalcare Limited | • Laboratorios Hipra S.A. |
| • aniMedica GmbH | • Laboratorios Karizmo S.A. |
| • Avimedical | • Laboratorios Maymo S.A. |
| • Bayer Plc | • Laboratorios SYVA S.A.U |
| • Bela-Pharm GmbH & Co. KG | • Laboratorios Welvian, S.L. |
| • Bimeda Chemicals Ltd | • Lavet Pharmaceuticals Ltd |
| • Boehringer Ingelheim Ltd | • Le Vet B.V. |
| • Ceva Animal Health Ltd | • Livisto Int.'I.S.L |
| • Chanelle Animal Health Ltd | • Merial Animal Health Ltd |
| • Continental Farmaceutica SL. | • Miklich Laboratorios S.L |
| • CP Pharma Handelsgesellschaft mbH | • Nimrod Veterinary Products Ltd |
| • Cross Vetpharm Group Ltd | • Norbrook Laboratories Ltd |
| • Dechra Ltd | • Novartis Animal Health UK Ltd |
| • Divasa Farmavic S.A. | • Oropharma N.V. |
| • Dopharma Research B.V. | • Pharmaq Ltd |
| • ECO Animal Health | • Pharmsure International Ltd |
| • Ecuphar N.V. | • Phibro Animal Health SA |
| • Eli Lilly & Company Ltd | • Qalian Ltd |
| • Emdoka bvba | • Richter Pharma |
| • Eurovet Animal Health B.V. | • Sogeval S.A. |
| • Fatro S.P.A. | • SP Veterinaria, S.A. |
| • Forte Healthcare Ltd | • Triveritas Ltd |
| • Forum Products Limited | • Universal Farma S.L |
| • Franklin Pharmaceuticals Ltd | • Univet Ltd |
| • Harkers Ltd | • Vetcare Oy |
| • Huvepharma N.V. | • Vétoquinol UK Ltd |
| • I.C.F. Sri Industria Chimica Fine | • Vetpharma Animal Health S.L |
| • Industria veterinaria S.A. | • Virbac S.A |
| • Intervet UK Ltd | • VMD NV |
| • Kela N.V. | • Zoetis UK Ltd |
| • Kernfarm B.V. | |
-

Contributors of other statistics:

- Defra Statistics Branch Scottish Government
- Department of Agriculture and Rural Development, Northern Ireland
- Centre for Environment Fisheries and Aquaculture Science