



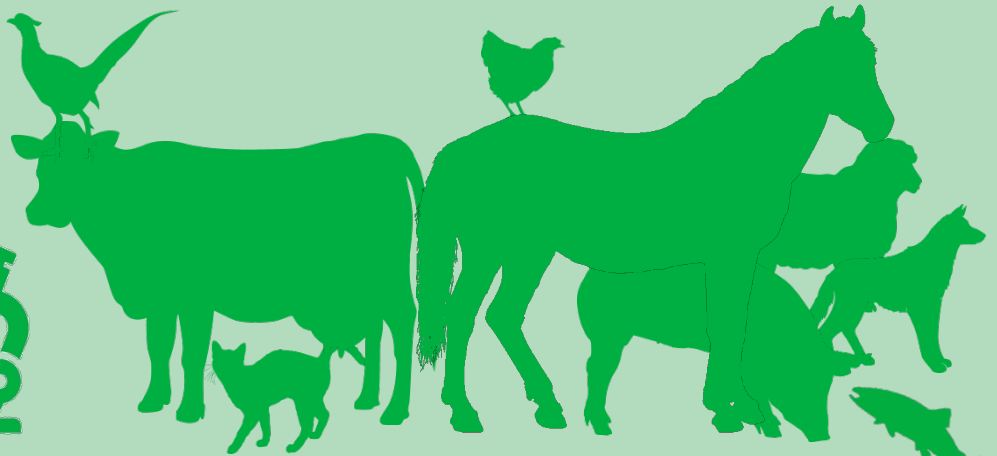
Veterinary
Medicines
Directorate

UK Veterinary Antibiotic Resistance and Sales Surveillance Report

UK-VARSS 2017

Published October 2018

SALES DATA





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SALES DATA CORRECTIONS - SEE ERRATUM

Foreword

This year's VARSS report had a hard act to follow: last year's VARSS-2016¹ was a landmark UK report for antibiotic resistance in animal health in many respects. VARSS-2016 not only saw publication of figures which revealed the lowest recorded UK veterinary antibiotic sales since regular reporting began in 1993, but it also marked the achievement, well ahead of schedule, of our whole-country antibiotic use target of 50 mg/kg. At the same time as VARSS-2016 came out, the agriculture industry published a suite of sector-specific targets focused on reducing antibiotic use in animals through measuring accurate usage, promoting prudent antibiotic use principles and optimising disease management.² This balanced, holistic approach forms the foundation for our action on antibiotic resistance over coming years.



I am delighted that this year's VARSS-2017 report shows more evidence that the goals set by the food-producing animal sectors are taking effect. The report for the first time presents data on the use of antibiotics in the beef, trout and salmon industries, in addition to the meat poultry, pig, dairy, gamebird and laying hens industries. Antibiotic use in animals has fallen sharply once again, and in patterns which reflect the focus on responsible use. The year-on-year trends now starting to come through in the data support what we know anecdotally – that there has been a turning point in attitudes to antibiotics, and this is becoming embedded as standard good practice across the different food-producing animal sectors.

To illustrate, these are some of the highlights this year:

- For the second year running, the lowest level of sales of veterinary antibiotics in the UK (282 tonnes) was recorded since regular recording began in 1993.
- Total sales of veterinary antibiotics, adjusted for animal populations, was 37 mg/kg in 2017. This result signals an additional 18% reduction from 2016 and a 40% reduction since the publication of the UK AMR strategy in 2013.
- Sales of the highest priority critically important antibiotics (HP-CIAs) have dropped a further 29% from already very low levels in 2016, to 0.8% of total sales in 2017.
- Sales of colistin decreased by a further 94% to 0.001 mg/kg (7.1 kg), which is considerably below the 1 mg/kg maximum target recommended by the European Medicines Agency (EMA) to protect public health.
- For those food-producing animal sectors where usage data were available for more than one year (pigs, meat poultry, laying hens, gamebirds and dairy), both total and HP-CIA usage decreased compared to 2016.

Our monitoring of the levels of antibiotic resistance has continued. The focus this year was on resistance monitoring in zoonotic and commensal bacteria from pigs and the data show that resistance to HP-CIAs in indicator *E. coli* from healthy pigs at slaughter was not detected or remained low. Similarly, levels of resistance to most of the antibiotics tested against *E. coli* from chickens, obtained through our clinical surveillance programme, have continued to decrease.

¹ <https://www.gov.uk/government/publications/veterinary-antimicrobial-resistance-and-sales-surveillance-2016>

² <https://www.ruma.org.uk/wp-content/uploads/2017/10/RUMA-Targets-Task-Force-Report-2017-FINAL.pdf>

For the first time, we were able to include a set of harmonised outcome indicators, recommended by the European Centre for Disease Control and Prevention, European Food Safety Authority and EMA, as a tool to monitor progress in the fight against AMR. This set of indicators already shows progress in the right direction with regards to antibiotic use in animal health and resistance in bacteria of importance for public health.

It is worth reflecting that while recent years have seen very significant successes in action on antibiotic resistance in the UK animal health arena, these did not happen overnight or in isolation. The cross-government UK 5 year AMR strategy 2013–2018 and the 2016 AMR Review chaired by Lord O'Neill reflected a strong level of UK ambition with commitment at the highest level to action on AMR in human health, animal health and the environment – collectively 'one-health'. International momentum on AMR has also been strong, with the Inter-Agency Coordination Group and the Tripartite of Food and Agriculture Organization, World Organisation for Animal Health and World Health Organization playing important roles in carrying forward the actions agreed at the United Nations General Assembly High Level meeting on AMR in 2016. AMR truly is a global concern and the importance of national, regional and international action remains as fundamental as ever.

With the present UK AMR strategy concluding this year, 2018 has been a time to take stock of recent achievements and review, evaluate and reflect as we work across government and with stakeholders to finalise the new UK AMR Strategy and Vision due to be published in coming months. The core principles which underpin effective action on AMR have not changed, but the structures and communities that have evolved over the course of the last strategy mean that the next chapter starts with a strong foundation already laid, and we can collectively set our sights high for long term, sustainable change.



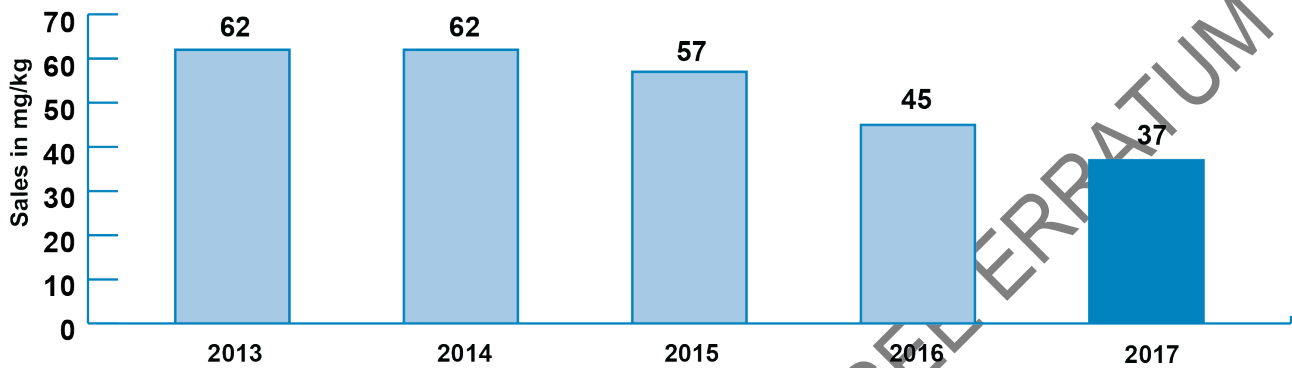
Professor S. Peter Borriello
Chief Executive Officer

Highlights

Antibiotic Sales

Overall trends in mg/kg

In 2017, sales of veterinary antibiotics for use in food-producing animals, adjusted for animal population, were 37 mg/kg; an 8 mg/kg (18%) drop from 2016, and 25 mg/kg (40%) decrease from 2013.

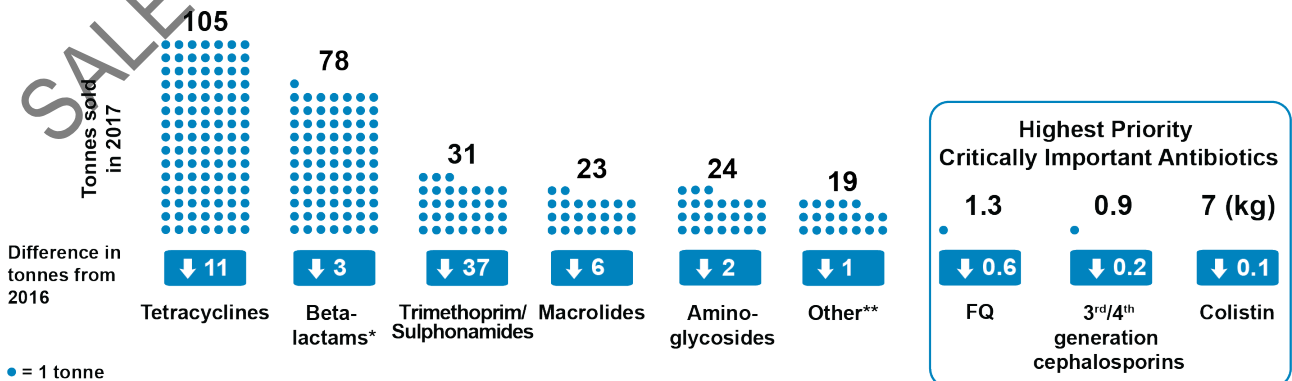


Sales of highest priority critically important antibiotics (HP-CIAs) in food-producing animals dropped by a further 0.86 tonnes (29%) from an already low level in 2016; an overall drop of 2.35 tonnes (52%) between 2013 and 2017.

	2013	2014	2015	2016	2017	Compared with 2016	Compared with 2013
Sales (all antibiotics, mg/kg)	62	62	57	45	37	↓ 18%	↓ 40%
Fluoroquinolones (mg/kg)	0.36	0.35	0.34	0.23	0.16	↓ 30%	↓ 55%
3 rd /4 th generation cephalosporins (mg/kg)	0.18	0.19	0.17	0.15	0.12	↓ 21%	↓ 32%
Colistin (mg/kg)	0.11	0.12	0.12	0.02	0.001	↓ 94%	↓ 99%
Total sales (all animals, tonnes)	436	448	408	338	282	↓ 17%	↓ 35%

Total sales in tonnes of active ingredient by antibiotic class (all animal species)

Overall, tetracyclines remain the most sold antibiotic class (37%), followed by beta-lactams (28%) and trimethoprim/sulphonamides (11%). Sales of HP-CIAs in all animal species represent a small proportion (0.8%) of the overall antibiotic use.



● = 1 tonne

FQ = fluoroquinolones











* Includes 3rd and 4th generation cephalosporins.

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

Antibiotic Usage

Antibiotic usage by food-producing animal species

Antibiotic usage refers to the amount of antibiotics purchased, prescribed and/or administered per sector. The data have been collected and provided to the VMD by the animal industry on a voluntary basis.





		Total coverage %*	2017 Total tonnage	2017 Total per unit**	Compared with 2016 %	HP-CIA usage	Compared with 2016 %
Pigs		87	90	131 mg/kg	↓ 28	0.1 mg/kg	↓ 63
Turkeys		90	14	45 mg/kg	↓ 48	0.03 mg/kg	↓ 75
Broilers				10 mg/kg	↓ 42		
Ducks				3 mg/kg	0		
Laying hens		90	2.2	0.57 % doses	↓ 22	0	↓ 100
Gamebirds		90*	13	—	↓ 36	49.6 kg	↓ 22
Salmon		100	3.0	17 mg/kg	—	0	—
Trout		70	0.2	19 mg/kg	—	0	—
Dairy		31†	4.2	17 mg/kg	↓ 35†	0.6 mg/kg	↓ 28†
Beef		5†	0.9	19 mg/kg	—	0.3 mg/kg	—

* Represents the % animals covered by the data, except gamebirds which represents an estimate of the % total antibiotic sales.

** mg/kg relates to the amount of active ingredient standardised by kg biomass and calculated using ESVAC methodology, % doses refers to the 'actual daily bird-doses/100 bird-days at risk', tonnes and kg relates to the amount of antibiotic active ingredient. More details are provided in the methods sections.

† Due to the small sample size, and the fact that these data are from a convenience sample, results may not be representative of the situation across the UK. In addition, because of the differences in the sample population of farms between years, caution should be taken when interpreting trends.

The usage data from the meat poultry and pig sectors highlight how the reductions achieved in 2017 have built on the reductions reported in previous years.

		2014 (mg/kg)	2015 (mg/kg)	2016 (mg/kg)	2017 (mg/kg)	Compared with 2015 (pigs) or 2014 (meat poultry)
Pigs		—	278	183	131	↓ 53%
Turkeys		220	200	86	45	↓ 79%
Broilers		49	27	17	10	↓ 80%
Ducks		15	8	3	3	↓ 78%

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

Resistance in *Salmonella* from pigs

No resistance to HP-CIAs was detected in *Salmonella* isolates from pigs.

Resistance in *Escherichia coli* from pigs

Similar to 2015, resistance to ciprofloxacin (fluoroquinolone) in indicator *E. coli* from healthy pigs at slaughter was low in 2017 (1.6%, up from 0.7% in 2015) and no resistance was detected to the other HP-CIAs. Resistance to nalidixic acid was up from 1.3% in 2015 to 2.2% in 2017.

Resistance levels to the other eight antibiotics tested were lower compared to 2015.

ESBL-, AmpC- or carbapenemase-producing *Escherichia coli* from pigs

In 2017, 22% (75/347) of caecal samples from the UK yielded presumptive ESBL-/AmpC-producing *E. coli* following selective culture, which was down from 25% in 2015. Of the 347 samples, 15% were ESBL-positive, 5% were AmpC-positive and 1% were positive for both. No presumptive carbapenemase-producing *E. coli* were detected.

Testing carried out on *E. coli* collected as part of the EU Harmonised Monitoring Scheme



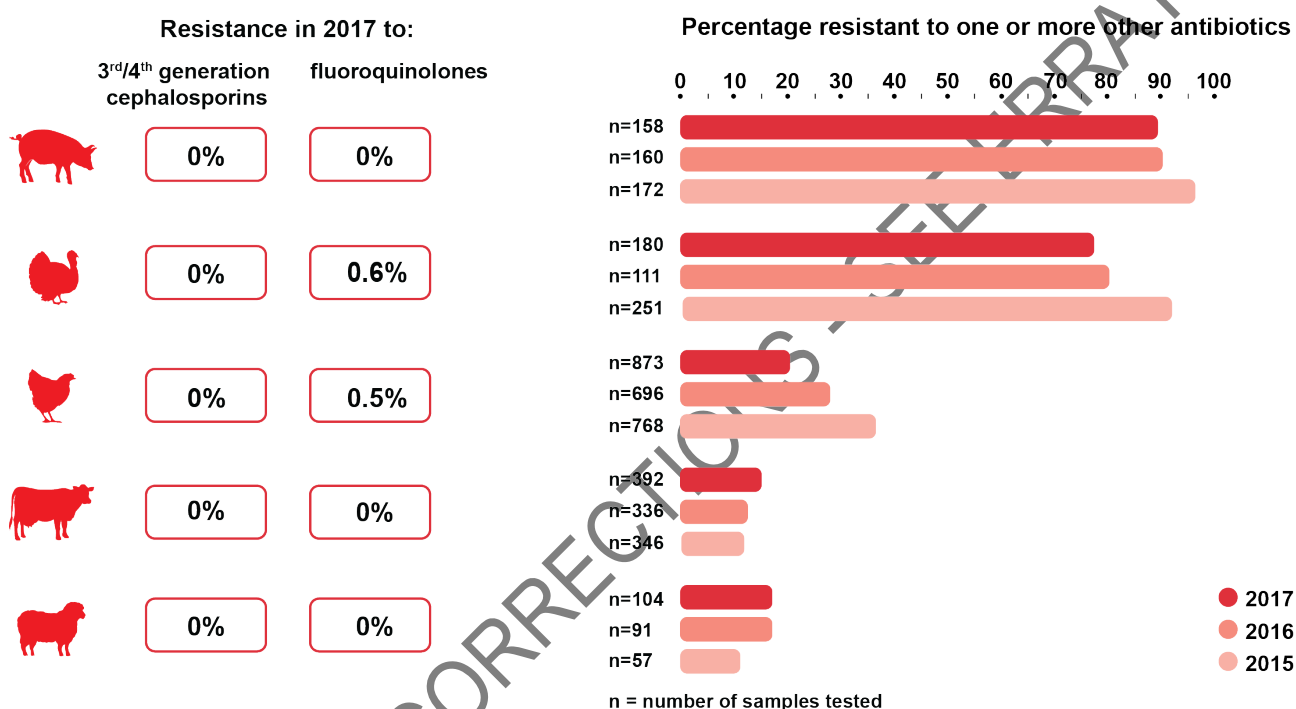
* To note this testing does not identify the type or number of ESBLs present.

Antibiotic Resistance – Clinical Surveillance

Resistance in *Salmonella* spp.

A high percentage of all *Salmonella* isolates tested (72% of 3,111 isolates obtained in total) was susceptible to all antibiotics tested. The results indicate an increasing trend in the proportion of isolates that are susceptible to all antibiotics tested.

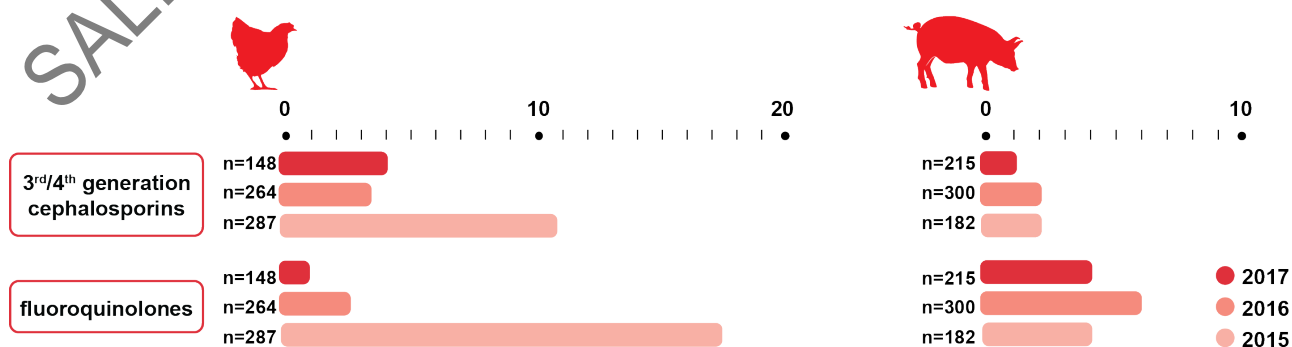
No resistance to cefotaxime or ceftazidime (3rd generation cephalosporins) was detected in 1,707 *Salmonella* isolates from pigs, turkeys, chickens, cattle and sheep tested in 2017. Five isolates obtained from these animal species (0.3%) showed resistance to ciprofloxacin (fluoroquinolone).



Resistance in *Escherichia coli*

Resistance to fluoroquinolones and 3rd generation cephalosporins was low (<4%), except in cattle (11% of isolates resistant to fluoroquinolones, 8% resistant to ceftazidime and 14% resistant to cefotaxime; the vast majority of these isolates were obtained from calves) and turkeys (17% of isolates resistant to fluoroquinolones). No resistance was detected to colistin in any species.

% resistant isolates from poultry and pigs



Introduction

Twenty years ago, the Veterinary Medicines Directorate (VMD) published the first report on sales data of antibiotic veterinary medicinal products (covering 1993–1998), provided voluntarily by the veterinary pharmaceutical companies marketing these products. From 2005, sales data were collected as a statutory requirement (Veterinary Medicines Regulations). In 2013, the first Veterinary Antibiotic Resistance and Sales Surveillance (VARSS) report of the United Kingdom was published, presenting combined data on veterinary antibiotic sales and antibiotic resistance in bacteria obtained from food-producing animals in the UK. The VARSS-2014 report included the first data collected through the European Union (EU) harmonised antibiotic resistance monitoring scheme, as well as data on antibiotic usage in meat poultry. In subsequent years the reports also included usage data for an increasing number of animal production sectors. The current report for the first time includes detailed phenotypic and genotypic data from the specific monitoring for ESBL-/AmpC-producing *Escherichia coli*.

The antibiotic sales data from 2005 to 2017 are presented in CHAPTER 1 and are based on sales of antibiotic veterinary medicinal products authorised for use in animals in the UK. Sales data are generally used as an estimate for antibiotic usage. However, as 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 food-producing animal sectors to develop, facilitate and coordinate antibiotic usage data collection systems; these data are presented in CHAPTER 2.

The VMD collates data from government laboratories on antibiotic resistance in bacteria obtained from food-producing animals, which are collected under the framework of two surveillance schemes. The surveillance activities focus on the occurrence of antibiotic resistance in pathogens that cause infections in animals, zoonotic bacteria, and indicator bacteria such as *E. coli*. Zoonotic bacteria are covered in the surveillance because they can develop resistance in the animal reservoir, which may subsequently compromise treatment outcome when causing human infection. *E. coli* are included due to their ubiquitous nature in animals, food and humans and their ability to readily develop or transfer antibiotic resistance between these reservoirs. Results from the EU harmonised AMR monitoring scheme are presented in CHAPTER 3. Results from the clinical surveillance monitoring scheme are presented in CHAPTER 4.

Details on methodology and results not presented in the report are included in the supplementary material. The supplementary material and previous VARSS reports are available to download at <https://www.gov.uk/government/collections/veterinary-antimicrobial-resistance-and-sales-surveillance>.



CHAPTER 1

Sales of Veterinary Antibiotics

SALES DATA CORRECTIONS - SEE EX

1.1 Summary

Between 2013 and 2017, the total quantity of active ingredient sold decreased by 154 tonnes (35%) to 282 tonnes; the lowest since sales data were first recorded in 1993. Between 2016 and 2017, the decrease constituted 56 tonnes (17%). In 2017, total sales of veterinary antibiotics, adjusted for animal population, were 37 mg/kg, representing an 8 mg/kg (18%) decrease from 2016 and a 25 mg/kg (40%) decrease from 2013.

Tetracyclines remain the most sold antibiotic class (representing 37% of total sales) despite these sales falling by 89 tonnes (46%) since 2013. Beta-lactams are the second most sold class (representing 28% of total sales) and their sales have fallen at a slower rate, by 16 tonnes (17%) since 2013.

The premix route of administration remains the most common, accounting for 38% of all antibiotics sold in 2017, despite a reduction in sales of premixes since 2013 of 157 tonnes (60%) to 107 tonnes in 2017. During the same period, sales of antibiotics for oral/water use have declined by 33 tonnes (30%) to 76 tonnes whereas injectable products have increased by 34 tonnes (73%) to 81 tonnes. For the first time, a higher quantity of antibiotics was sold for administration by the injectable route than by the oral/water route.

Sales of highest priority critically important antibiotics (HP-CIAs) have reduced from an already low level to 2.1 tonnes; a further reduction of 0.86 tonnes (29%) since 2016 and 2.35 tonnes (52%) since 2013.

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 (see section S1.1 in the supplementary material for further details). The data reported in this chapter do not take into account wastage, nor imports under the Special Import Certificate scheme 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 C).

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 were collated and validated. To check correctness and completeness, product data entries were compared to those submitted in previous

years. If large discrepancies were observed between data provided in successive years, data validity was further investigated and queried with the pharmaceutical company. Sales data for antibiotic products returning Periodic Safety Update Reports (PSURs) were also compared to those sales data returned by the pharmaceutical companies, and any discrepancies were investigated (further details can be found in Annex D).

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, taken from the Summary of Product Characteristics (SPC), by the number of units sold as reported by the pharmaceutical companies. 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 European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project (European Medicines Agency, 2017). Using the active ingredient for reporting consumption is considered to be the most accurate.

All sales data published in this chapter have been reported using European methodology since 2016 (2015 data). Further details on historical methodology for the calculation of active ingredient (as well as mg/PCU) can be found in section S1.1 of the supplementary material. Note that data presented in mg/kg (which equals mg/PCU) do not include tablets, as, in line with the ESVAC methodology, these are assumed to be exclusively administered to companion animals.

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** (World Health Organization, 2018). Antibiotics 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 VARSS reports) are not included (sales of these preparations are reported in Table S1.1.3 of the supplementary material). These represent 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
Antibiotics for intestinal use	QA07AA; QA07AB
Antibiotics for intrauterine use	QG01AA; QG01AE; QG01BA; QG01BE; QG51AA; QG51AG
Antibiotics for systemic use	QJ01
Antibiotics for intramammary use	QJ51
Antibiotics for antiprotozoal use (solely sulphonamides)	QP51AG

1.3.3 Population Correction Unit (PCU)

Trends in sales of antibiotics over time are determined by taking into consideration variations in the size and number of the animal population. To achieve this, sales data were analysed using the Population Correction Unit (PCU), a theoretical unit of measure formulated by the EMA and adopted by the countries participating in the ESVAC project 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 ingredient sold per kilogram bodyweight of food-producing animal in the UK 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 section S1.2 of the supplementary material and full technical details on PCU methodology can be found in the 2011 ESVAC report (European Medicines Agency, 2011). **Within this VARSS report, all references to mg/kg equate to mg/PCU.**

1.3.4 Corrections for historical data

There have been minor retrospective changes in the sales data prior to 2017 provided by a number of pharmaceutical companies, as well as updates to product information on the national database. All data and figures within this report have been corrected to account for these.

1.4 Results and discussion

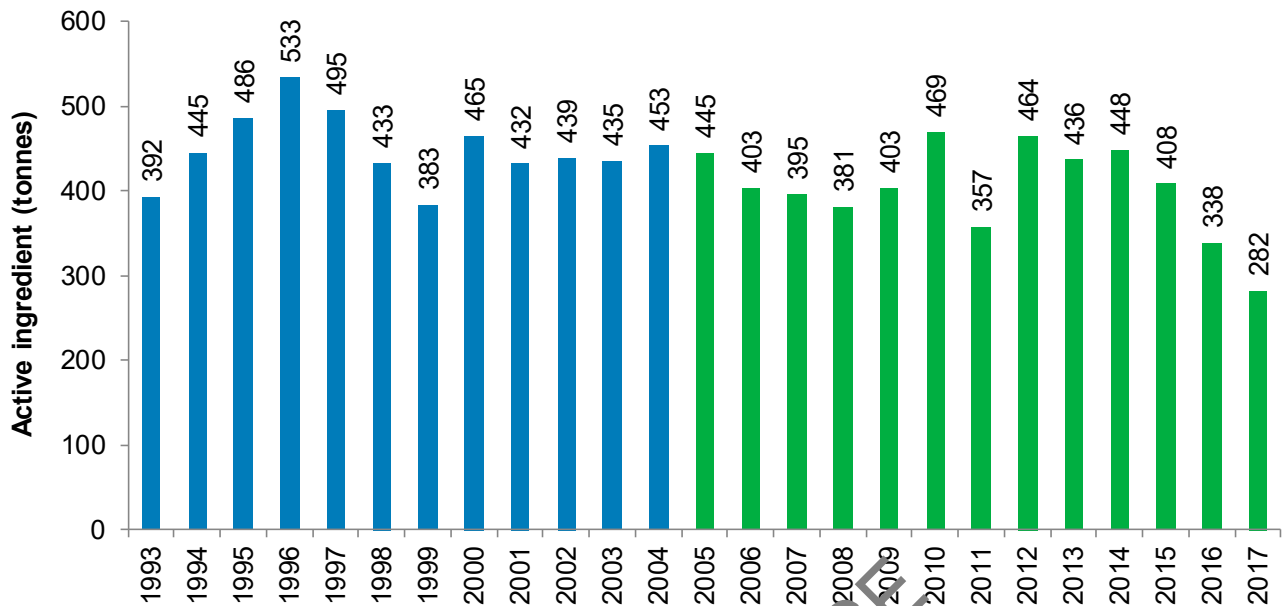
1.4.1 Total sales of antibiotics for veterinary use in the UK (tonnes)

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

It should be noted that the ESVAC methodology produces a higher figure than the UK-VARSS methodology. For further detail on the difference between the ESVAC and UK-VARSS methodology see section S1.1 of the supplementary material.

Total annual sales of antibiotics for veterinary use within the UK between 1993 and 2017 are presented in **Figure 1.1**. The total quantity of active ingredients sold in 2017 was 282 tonnes, which represents a 56 tonnes (17%) reduction from 2016. This is 31% lower than the ten-year mean for the preceding 2006 to 2016 period (mean 409 tonnes; range 357–469 tonnes). It is also the lowest total observed since 1993, when the VMD began recording veterinary antibiotic sales.

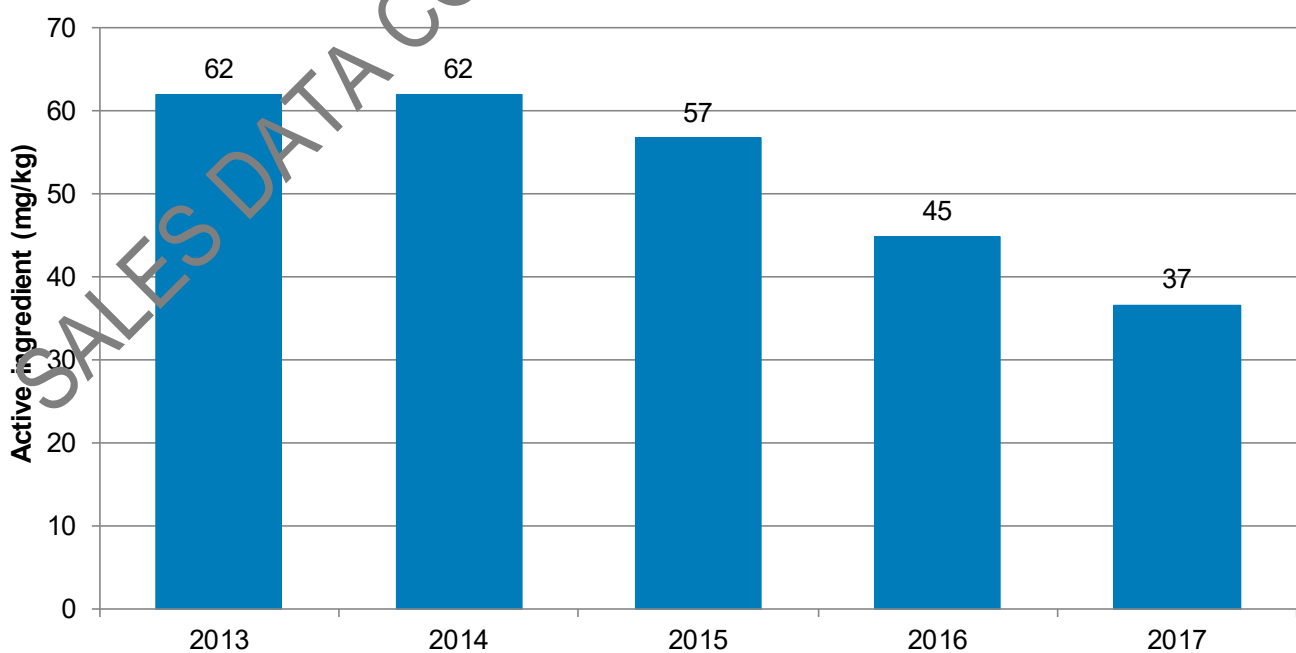
Figure 1.1: Total active ingredient (tonnes) of antibiotics sold in the UK per year using UK-VARSS (■) and ESVAC (■) methodology, 1993–2017



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

The sales of antibiotics licensed for food-producing animal species decreased by 8 mg/kg (18%) between 2016 and 2017, from 45 to 37 mg/kg (Figure 1.2). This is the lowest UK figure reported since ESVAC sales data reporting started in 2005, and sales have decreased by 25 mg/kg (40%) since the publication of the UK AMR Strategy in 2013 (Department of Health and Social Care and Department for Environment Food & Rural Affairs, 2013).

Figure 1.2: Active ingredient (mg/kg) of antibiotics sold licensed for use in all food-producing animal species, 2013–2017



In September 2017, the European Centre for Disease Prevention and Control (ECDC), European Food Safety Authority (EFSA) and EMA published a set of harmonised outcome indicators for comparable monitoring of key indicators for antibiotic consumption in food-producing animals in the EU (European Centre for Disease Prevention and Control et al., 2017).

The primary indicator is “the overall sales of veterinary antibiotics in milligram of active substance per kilogram of estimated weight at treatment of livestock and of slaughtered animals in a country (mg/PCU)” (Figure 1.2). Secondary indicators are the sales in mg/PCU for 3rd and 4th generation cephalosporins, quinolones (and percentage of fluoroquinolones) and polymyxins (Figure 1.5). In the UK all quinolones sold for use in food-producing animals are fluoroquinolones (although a small quantity of the quinolone oxolinic acid is imported for the fish sector), and colistin is the only polymyxin sold for use in food-producing animals. The data show that all indicators have decreased between 2016 and 2017.

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

The quantities of active ingredient sold between 2013 and 2017 are shown in Table 1.2, differentiated by the animal species or combination of animal species for which they are indicated.

Table 1.2: Active ingredient (tonnes and % of total sales) of antibiotics sold for the animal species category indicated, 2013–2017*

Animal species category	Animal species	Active ingredient in tonnes (% sales)				
		2013	2014	2015	2016	2017
Indicated for food-producing animal species only	Pigs and poultry only	217	236	214	127	98
	Pigs only	63	61	49	40	33
	Poultry only*	43	42	38	26	15
	Cattle only	14	13	14	18	16
	Fish only	0.8	2.4	0.7	1.6	3.4
	Multiple food-producing animal species**	30	27	29	32	39
	Total	368 (84)	382 (85)	345 (85)	244 (72)	204 (72)
Indicated for non-food-producing animals species only	Companion animal only (excluding horse only)	14	16	13	16	15
	Horse only	22	16	13	29	12
	Total	36 (8)	32 (7)	26 (6)	45 (13)	27 (10)
Indicated for combination of food- and non-food-producing animal species	Total	32 (7)	34 (7)	36 (9)	49 (15)	51 (18)
Total sales of antibiotics^x		436	448	408	338	282

^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 VARSS-2015, products authorised for use in ‘ducks’ in combination with other poultry species were included in the ‘multiple livestock species’ category. These products are included in the ‘poultry only’ category in this table. This change affects those data reported in previous 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.

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**, horses have been classified as 'non-food-producing animals' when reporting tonnage of active ingredient.

In 2017, 204 tonnes (72%) of total antibiotic sales were attributed to products authorised for food-producing animals only. Products sold exclusively for pigs and/or poultry accounted for 146 tonnes (52%), which is a reduction of 48 tonnes (25%) from 2016 and 177 tonnes (55%) from 2013. Between 2016 and 2017, the sales of antibiotics authorised for horses only decreased by 17 tonnes (58%), following an equivalent increase the year before.

Sales of antibiotics indicated for a combination of food- and non-food-producing animals have increased by 19 tonnes (60%) from 2013. These are largely injectable products, and this increase correlates with the increase in the sales of injectable products highlighted in sections 1.4.5.1 and 1.4.5.3.

Based on figures from the Pet Food Manufacturers' Association, there are 22 million (non-aquatic) pet and companion animals in the UK. Therefore, a rough estimate for total sales of active ingredient (**Table 1.2**) in (non-aquatic) pet and companion animals results in 0.68 g active ingredient/head. For next year's report we intend to perform more detailed analyses.

1.4.4 Total sales of antibiotics by antibiotic class

1.4.4.1 Total sales of antibiotic by antibiotic class for all animal species (tonnes)

The total quantities of active ingredient sold between 2016 and 2017, broken down by antibiotic class, are presented in **Table 1.3** and **Figure 1.3**. Definitions of these classes and the active ingredients that are included within each class can be found in section S1.3 of the supplementary material.

Tetracyclines remained the most sold antibiotic class, despite their use falling by 89 tonnes (46%) since 2013. Beta-lactams were the second most used class (representing 28% of total sales) and these sales decreased by 16 tonnes (17%) since 2013. Trimethoprim/sulphonamides were the third most sold antibiotic class. While sales of these products remained stable between 2013 and 2016, they reduced by 37 tonnes (54%) in 2017 when compared to 2016.

Sales of highest priority critically important antibiotics (HP-CIAs) were 2.1 tonnes, representing 0.8% of antibiotic active ingredient sold. This represents a decrease of 0.86 tonnes (29%) from 2016 and 2.35 tonnes (52%) from 2013, see section 1.4.5.3 for further details.

Table 1.3: Active ingredient (tonnes or kg) of antibiotics sold for all animal species by antibiotic class, 2013–2017

Antibiotic class	Active ingredient in tonnes (kg)				
	2013	2014	2015	2016	2017
Tetracyclines	194	182	166	116	105
Beta (β)-lactams	94	95	81	81	78
1 st and 2 nd generation cephalosporins	4.9	5.4	4.9	4.8	4.2
3 rd and 4 th generation cephalosporins (kg)*	(1,192)	(1,332)	(1,202)	(1,071)	(857)
Penicillins**	88	89	75	75	72
Trimethoprim/sulphonamides	61	71	68	68	31
Trimethoprim	10	12	11	11	5.1
Sulphonamides	51	59	57	57	26
Aminoglycosides	24	24	23	22	24
Streptomycin	11	9.4	10	16	18
Neomycin and framycetin	0.6	0.5	0.5	0.7	2.2
Other aminoglycosides***	12	14	13	5.0	4.4
Macrolides	40	50	38	29	23
Fluoroquinolones (kg)*	(2,562)	(2,593)	(2,532)	(1,786)	(1,267)
Other****	21	24	28	20	19
Colistin (kg)*	(728)	(837)	(870)	(128)	(7.1)
Total sales of antibiotics^x	436	448	408	338	282

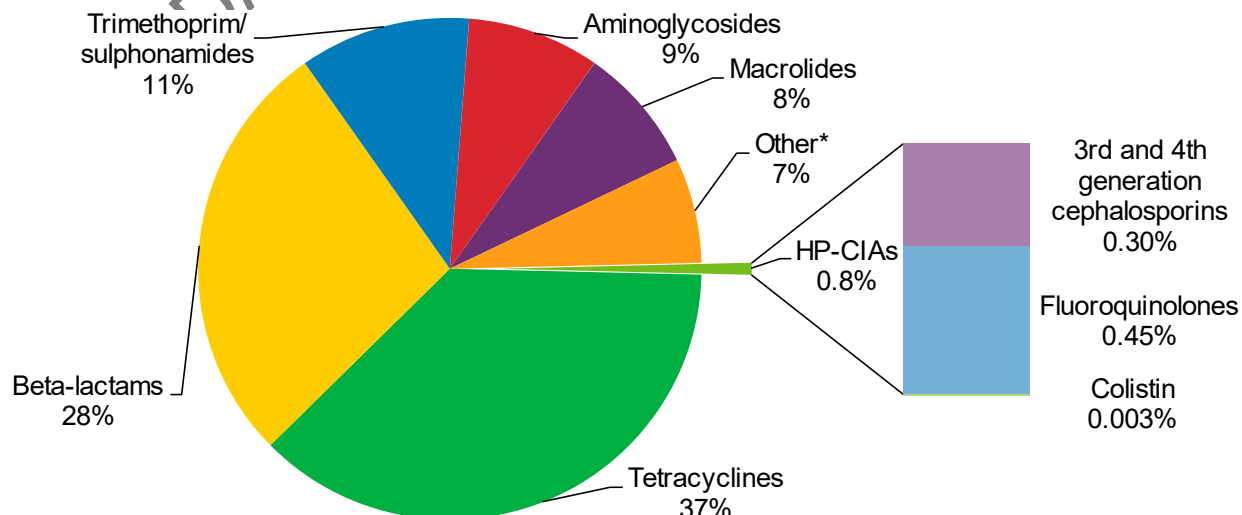
^x The totals were rounded to the nearest integer. This explains the discrepancy between the overall total and the classes' totals.

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

** Benzylpenicillin, benzathine penicillin, phenoxymethylpenicillin, procaine penicillin, amoxicillin (including in combination with clavulanic acid), ampicillin, cloxacillin, nafcillin.

*** Apramycin, gentamicin, kanamycin, spectinomycin.

**** Amphenicols, lincomycins, pleuromutilins, polymyxins and steroidal antibiotics. Colistin is included within this group.

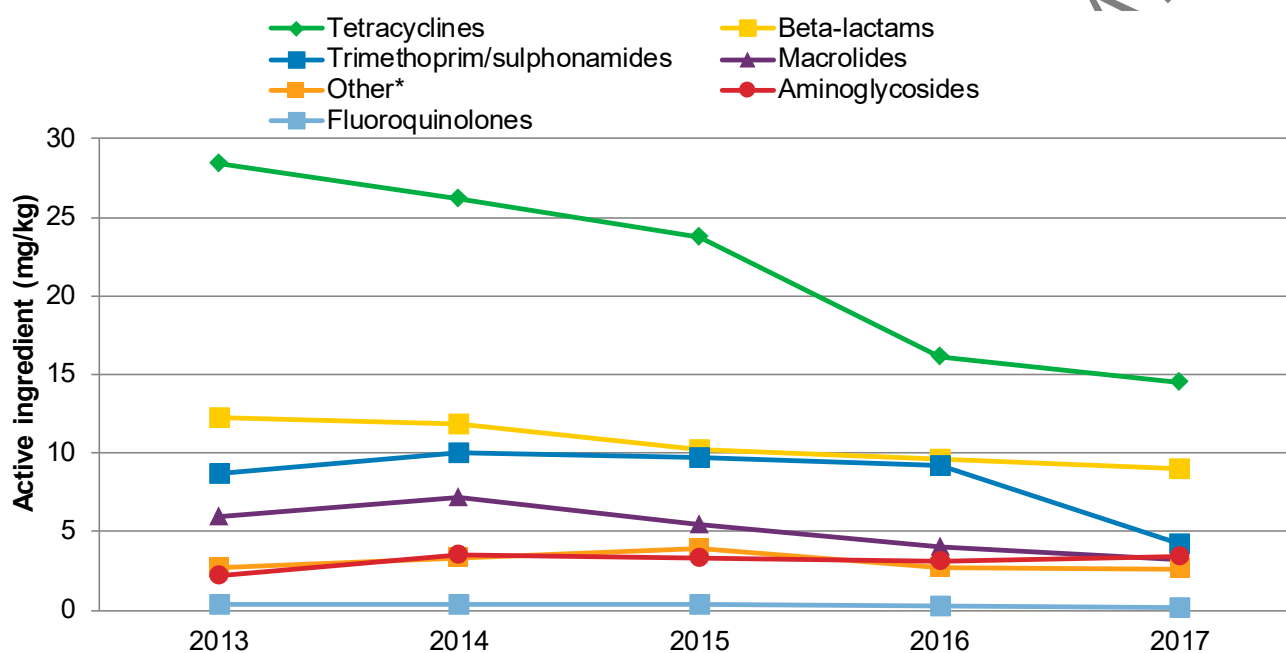
Figure 1.3: Active ingredient (% weight) of antibiotics sold for all animal species by antibiotic class, 2017

* Amphenicols, lincomycin, pleuromutilins, polymyxins (excluding colistin) and steroidal antibiotics.

1.4.4.2 Sales by antibiotic class for food-producing animal species (mg/kg)

Sales of all classes of antibiotic for food-producing animal species decreased between 2013 and 2017, with the exception of aminoglycosides (**Figure 1.4**). Tetracyclines remained the most sold antibiotic class over the last five years despite a 14 mg/kg (49%) decrease over this period; sales of beta-lactams and trimethoprim/sulphonamides decreased by 3.2 mg/kg (26%) and 4.4 mg/kg (51%), respectively.

Figure 1.4: Active ingredient (mg) of antibiotic sold per kg of food-producing animal species by antibiotic class, 2013–2017

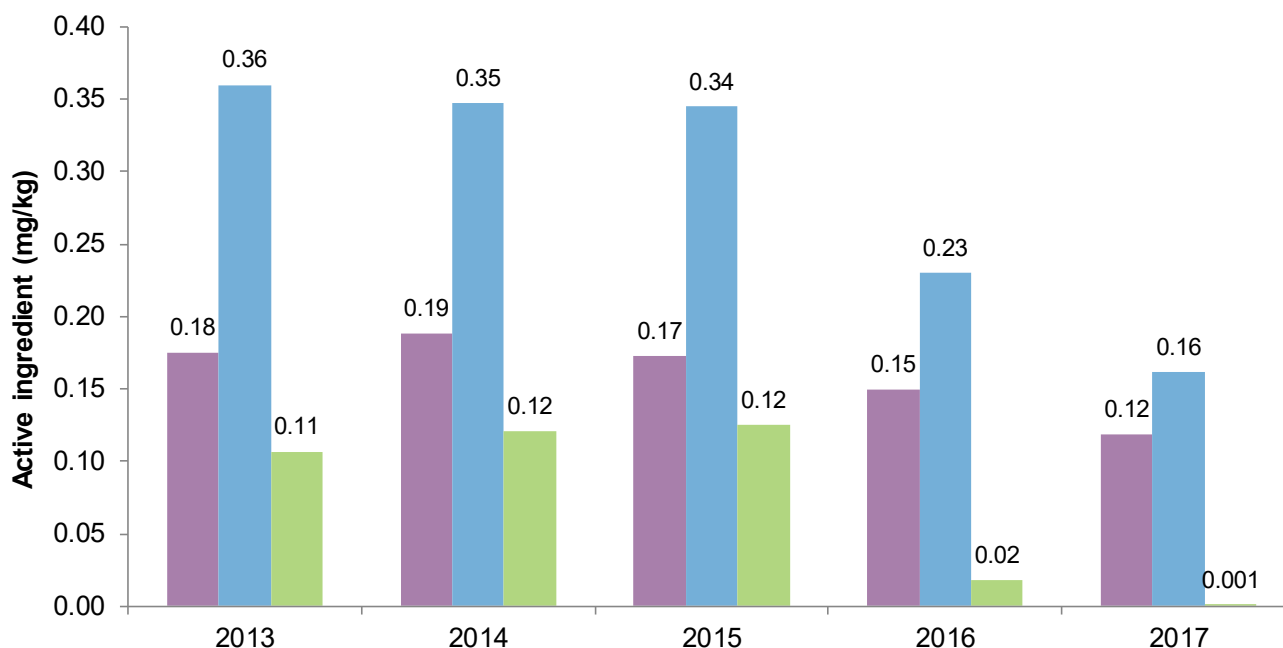


* Amphenicols, lincomycins, pleuromutilins, polymyxins (including colistin) and steroidal antibiotics.

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

In VARSS reports, HP-CIAs are identified according to the categorisation by the Antimicrobial Advice *ad hoc* Expert Group (AMEG) of the EMA, and therefore include fluoroquinolones, 3rd and 4th generation cephalosporins and colistin (European Medicines Agency, 2014, 2016). Sales of HP-CIAs for food-producing animal species represented 0.28 mg/kg, a small proportion (0.8%) of the overall antibiotic sales. The sales decreased by 0.12 mg/kg (30%) between 2016 and 2017 and by 0.36 mg/kg (56%) since 2013 to 0.28 mg/kg in 2017. Between 2016 and 2017, sales of 3rd and 4th generation cephalosporins decreased by 0.03 mg/kg (21%), sales of fluoroquinolones decreased by 0.07 mg/kg (30%) and sales of colistin decreased by 0.017 mg/kg (94%) to very low levels (0.001 mg/kg), see **Figure 1.5**.

Figure 1.5: Active ingredient (mg/kg) of HP-CIAs, sold for food-producing animal species: 3rd and 4th generation cephalosporins (■), fluoroquinolones (■) and colistin (■), 2013–2017



1.4.5 Sales of antibiotics by administration route

1.4.5.1 Total sales of antibiotics by administration route for all animal species

When assessing antibiotic sales by how they are administered, premix remained the most common route in 2017 (38% of active ingredient sold) (Table 1.4). The sales of premix antibiotics decreased by 157 tonnes (60%) since 2013. During the same period, sales of antibiotics for oral/water administration decreased by 33 tonnes (30%) to 76 tonnes and injectable products increased by 34 tonnes (73%) to 81 tonnes. For the first time, sales for products administered by injection were greater than sales of products for administration by oral/water route. These trends may reflect a decline in the practice of group treatment (by the in-feed or in-water routes) and an increase in the treatment of individual animals (by injectable route).

Table 1.4: Active ingredient (tonnes and % of total sales) of antibiotic sold for all animal species by route of administration, 2013–2017

Administration route	Active ingredient in tonnes (% sales)				
	2013	2014	2015	2016	2017
Premix	263 (60)	267 (60)	233 (57)	147 (43)	107 (38)
Injectable	47 (11)	45 (10)	50 (12)	72 (21)	81 (29)
Oral/water*	109 (25)	117 (26)	109 (27)	99 (29)	76 (27)
Tablets	14 (3)	16 (4)	13 (3)	16 (5)	15 (5)
Intramammary	3.2 (0.7)	3.2 (0.7)	3.3 (0.8)	3.8 (1)	3.4 (1)
Total sales of antibiotics	436	448	408	338	282

* Excluding tablets, including bolus preparations.

1.4.5.2 Sales of intramammary antibiotic products

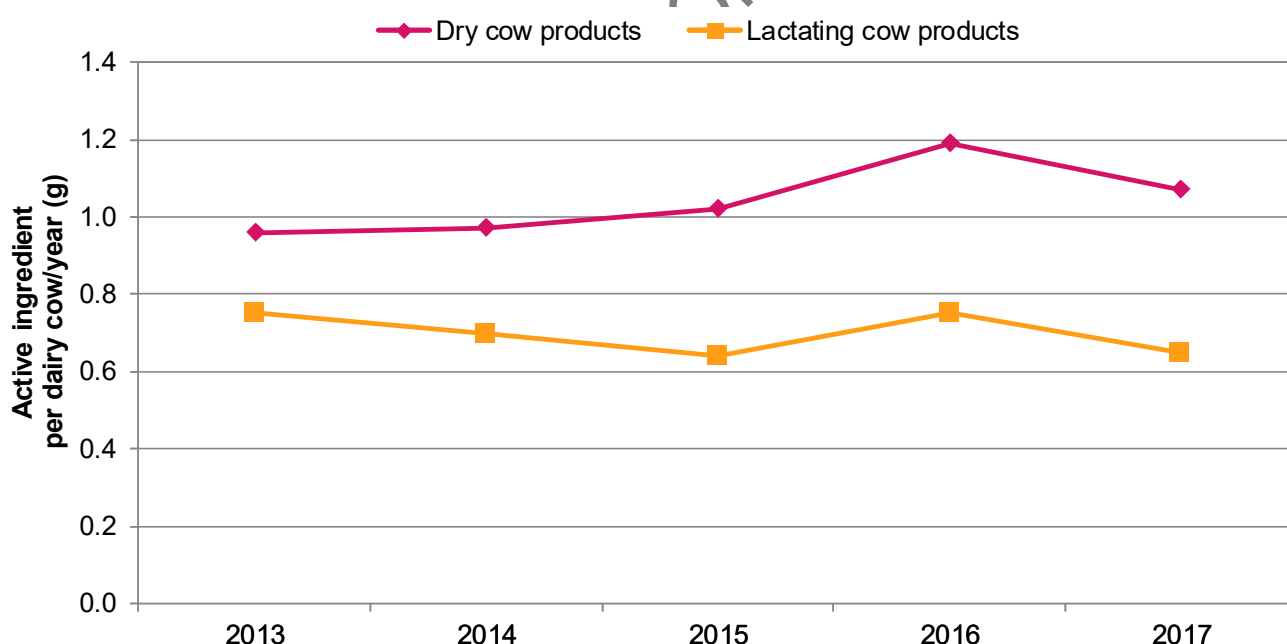
Sales for dry and lactating cow intramammary products both decreased by 0.1 grams per dairy cow, a reduction of 10% and 13%, respectively (**Table 1.5** and **Figure 1.6**). However, the overall sales trend between 2013 and 2017 remains stable.

Table 1.5: Total (kg) and average amount (g per dairy cow*) of active ingredient of intramammary antibiotics sold, 2013–2017

Intramammary	Active ingredient in kg (average in g/cow)				
	2013	2014	2015	2016	2017
Dry cow products	1,716 (0.96)	1,782 (0.97)	1,941 (1.01)	2,267 (1.19)	2,022 (1.07)
Lactating cow products	1,331 (0.75)	1,289 (0.70)	1,209 (0.63)	1,430 (0.75)	1,231 (0.65)
Total sales of antibiotics	3,047 (1.71)	3,072 (1.67)	3,150 (1.64)	3,697 (1.94)	3,253 (1.72)

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

Figure 1.6: Average annual quantity in grams (g) of active ingredient of intramammary antibiotic sold per dairy cow, 2013–2017



An assessment of courses administered can be made based on the ESVAC defined course dose (DCDvet) methodology, where four tubes represent one course for dry cow therapy and, for most products, three tubes represent one course for lactating cow therapy. Based on this assessment, the number of DCDvet decreased from 0.75 to 0.68 courses (9%) for dry cow therapy and from 0.98 to 0.82 courses (16%) for lactating cow therapy (data not shown).

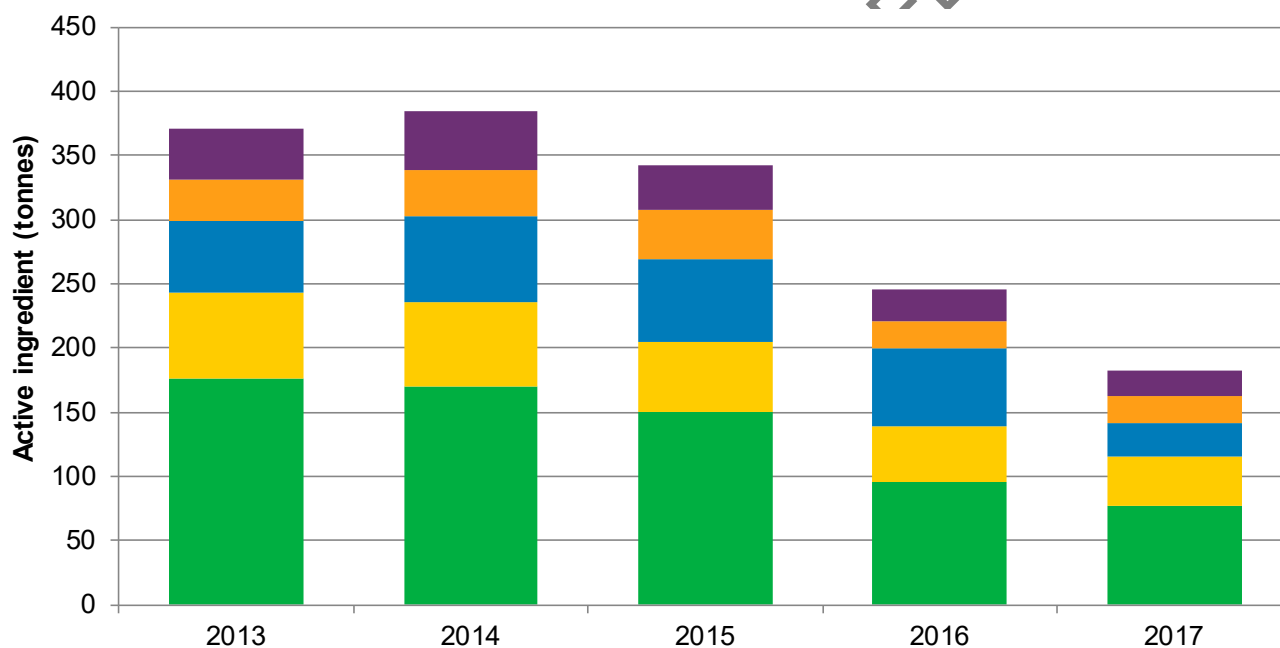
The total amount of active ingredient of HP-CIAs sold for intramammary use decreased by 46 kg (21%) from 217 kg in 2016 to 171 kg in 2017. HP-CIAs represented 5.3% of intramammary active

ingredient sales in 2017, compared with 5.9% in 2016. In terms of courses (based on DCDvet methodology), sales decreased by 29% from 0.3 courses in 2016 (18% of intramammary courses) to 0.2 courses in 2017 (15% of intramammary courses) (data not shown).

1.4.5.3 Sales of active ingredients of antibiotic classes (including HP-CIAs) by administration route

Excluding tablets, sales of oral products (premix and oral/water combined) for all antibiotic classes decreased by 189 tonnes (51%) between 2013 and 2017. Tetracyclines were the most sold antibiotic class in this category and decreased by 99 tonnes (56%) during this period. In 2016, trimethoprim/sulphonamides was the second most sold antibiotic class for oral products; but sales of oral beta-lactam products were higher in 2017 than sales of oral trimethoprim/sulphonamide products (**Figure 1.7**).

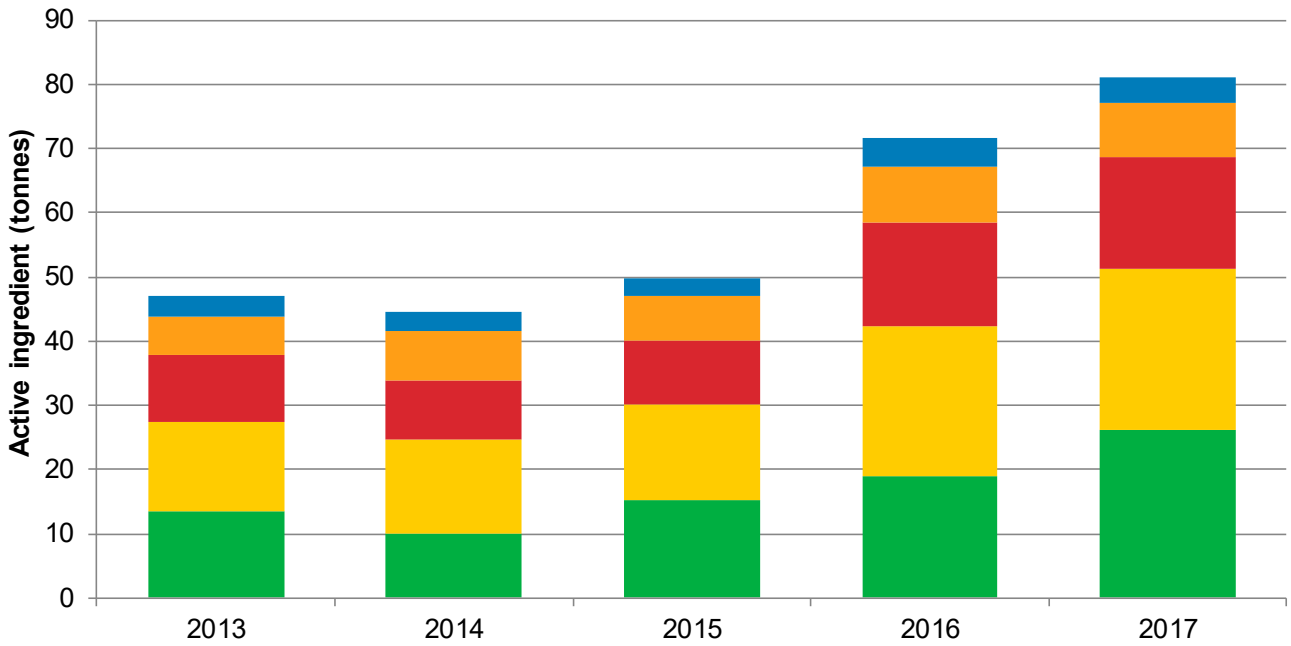
Figure 1.7: Sales of combined premix and oral/water antibiotic products (tonnes of active ingredient) for this administration route, for tetracyclines (■), beta-lactams (■), trimethoprim/sulphonamides (■), other* (■) and macrolides (■), 2013–2017



*Aminoglycosides, fluoroquinolones, amphenicols, lincomycins, pleuromutilins, polymyxins and steroidal antibiotics.

Tetracyclines were the most sold antibiotic class for injectable products, and those sales increased by 13 tonnes (95%) to 26 tonnes between 2013 and 2017. The sales for the second and third most sold classes, beta-lactams and aminoglycosides, increased by 11 tonnes (80%) to 25 tonnes and by 7 tonnes (66%) to 17 tonnes, respectively (**Figure 1.8**).

Figure 1.8: Sales of injectable antibiotics (tonnes of active ingredient) for this administration route, for tetracyclines (■), beta-lactams (■), aminoglycosides (■), other* (■) and trimethoprim/sulphonamides (■), 2013–2017

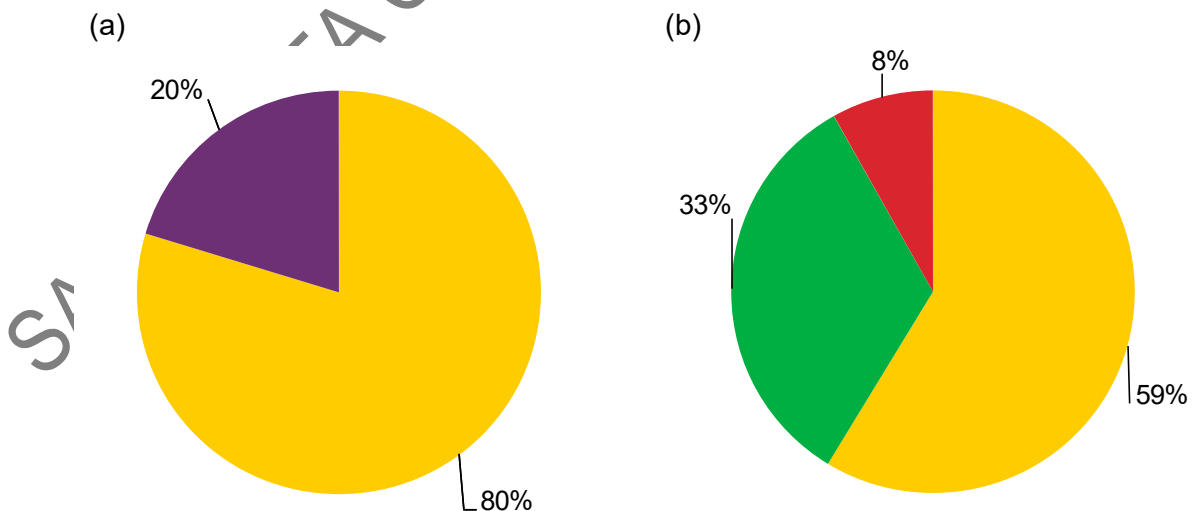


* Macrolides, fluoroquinolones, amphenicols, lincomycins, pleuromutilins, polymyxins and steroidal antibiotics.

The majority of 3rd and 4th generation cephalosporins and fluoroquinolones sold in 2017 were for injectable use (80% and 59%, respectively; **Figure 1.9**).

All sales of colistin in 2017 were for pre-mix and oral/water administration routes.

Figure 1.9: Distribution of sales (tonnes) of HP-CIAs for all animal species by the major administration routes (injectables (■), oral/water (■), intramammaries (■), tablets (■)): (a) 3rd and 4th generation cephalosporins and (b) fluoroquinolones, 2017





CHAPTER 2

Usage of Veterinary Antibiotics by Animal Species

SALES DATA CORRECTIONS - SEE EX

2.1 Summary

Antibiotic usage data from the meat poultry sector were presented for the first time in the VARSS-2014 report, followed by data from the pig, gamebird, laying hen and dairy industries in 2016. This year, usage data are also available for the salmon, trout and beef sectors. The food-producing animal industry is collecting these data on a voluntary basis.

The report highlights further reductions achieved in 2017 compared to 2016 by the pig and poultry sectors, with overall reductions in mg/kg of 28% in pigs, 42% in chickens, 48% in turkeys and 60% in ducks. The gamebird and laying hen sectors also reported reductions of 36% and 22%, respectively.

The salmon and trout industries present their baseline data in this report. Further work is needed to collect accurate usage data from the cattle sector, but results are presented from a convenience sample of 31% of UK dairy farms and 6% of beef farms in Great Britain.

All sectors which reported usage data have demonstrated significant reductions and low or, in some cases, no use of HP-CIAs.

2.2 Introduction

Many antibiotics are authorised for use in multiple animal species, so it is not possible to determine from sales data how much is used per species. The VMD is working in partnership with key food-producing animal sectors to develop, facilitate and coordinate antibiotic usage data collection systems. For the first time, data are presented from the salmon, trout and beef industries.

Antibiotic usage refers to the amount of antibiotics purchased, prescribed and/or administered. The data were obtained from producers (pig, poultry and laying hen industries), feed companies (gamebirds) and veterinary practice sales records (gamebirds, salmon, trout, dairy and beef cattle).

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

This chapter describes the progress achieved so far, with updates from the key food-producing animal sectors. Note that, for ease of reading, the data have been rounded to the nearest integer. However, the data expressed as percentage have been calculated using the exact number.

2.3 Methods

2.3.1 Pig industry

The antibiotic usage data in pigs were 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 farm-level data held in the eMB for participating pig farms across the UK.
- eMB uptake to date has been voluntary and this sample may not be representative for the whole of the UK pig production.
- The eMB data cover 56% UK pig production for 2015, 62% UK pig production for 2016 and 87% UK pig production for 2017.
- The data are inputted by producers and, although clear outliers have been identified and queried, AHDB-Pork 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 1st May 2018.
- The eMB database and the calculations within it have recently been subjected 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 continues to develop and data accuracy continues to improve.

The calculations used for the eMB data are in line with the methodology used for the ESVAC reports to allow comparisons to be made with European counterparts.

2.3.2 Meat poultry industry

The British Poultry Council (BPC) provided antibiotic usage data for the poultry meat (chicken, turkey and duck) sector. BPC runs BPC Antibiotic Stewardship, which covers 90% of UK poultry meat production. This process of data collection started in 2012 and producers are responsible for submitting quarterly (chicken, duck) or annual (turkey and all breeders) antibiotic usage data in the form of an aggregate spreadsheet. BPC then collate the data and report usage by sector in their annual report. This includes the overall annual amount of active ingredient used (in tonnes), which covers 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: 1.0 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.

2.3.3 Laying hen industry

The collection of antibiotic usage data for the laying hen industry is organised by the British Egg Industry Council (BEIC). Sharing these data with BEIC is mandatory through the Lion Scheme, which represents over 90% of the UK laying hen industry. All egg producers, pullet rearers and breeding companies are required to report any use of an antibiotic to their subscriber. This is reported to the BEIC on a quarterly basis. 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 carried out the calculations and validation of the usage by active ingredient using ESVAC principles. The data published here as 'actual daily bird-doses/100 bird-days at risk' represent the average number of doses administered per chicken over a 100-day period and are based on the actual number of doses administered, which is provided directly by the industry to BEIC.

Note that a 'mg/kg' figure has not been included, as ESVAC methodology does not include a standardised method for laying hens.

2.3.4 Gamebird industry

The Game Farmers' Association (GFA) coordinated a comprehensive, voluntary usage data collection exercise to measure the use of antibiotics throughout the sector for 2017. This involved the collection of:

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

Each company was asked to provide a spreadsheet showing the amount of antibiotics used in 2017. GFA aggregated the results and provided them to the VMD, who then used ESVAC methodology to calculate the amount of active ingredient administered by the game sector.

Note that a 'mg/kg' figure has not been included, as ESVAC methodology does not include a standardised method for gamebirds.

2.3.5 Cattle industry

The data from dairy and beef farms presented in this report were taken from FarmVet Systems, a software company which extracts and cleanses sales data from Practice Management Systems and which can determine whether the medicine was 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). For these farms, the average number of dairy breed animals over two years of age was determined for each farm and used to calculate the mg/kg using ESVAC methodology.

Farms which had less than 15 calves born to dairy dams were considered beef. In addition, farms were removed if Rader GB Census Survey data indicated the presence of sheep or if data showed

'sheep-only' products had been used on the farm. This is because it is not possible to easily distinguish usage between sheep and beef cattle from practice management data. Note that it was only possible to carry out this sheep analysis for farms in Great Britain, so no farms in Northern Ireland were included in the beef dataset. For all eligible beef farms, the number of slaughtered cows, steers, bulls, heifers and calves was collected using BCMS movement records and used to calculate usage in mg/kg using ESVAC methodology. Note that living cattle present on a farm are not included in the ESVAC beef denominator. This is different to the same metric for dairy herds, sheep flocks and pig herds, where breeding populations on farms are counted in the denominator.

Overall, the sample for 2017 represents 31% UK dairy cows and 6% beef production in Great Britain. For both the beef and dairy farms, the VMD converted the aggregate usage data into amount of active ingredient using the standard ESVAC methodology. Products that did not include 'cattle' in the target species in the SPC 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 also possible that products licensed for 'multi-species' (including cattle) may also have been used in other species kept on the farm.

2.3.6 Aquaculture

The trout data were collected from the main veterinary practices dealing with trout in England and Scotland and represent 70% of UK trout production. The salmon usage data were collected by the Scottish Salmon Producers' Organisation (SSPO) from all veterinary practices treating salmon in Scotland and therefore represent 100% of Scottish salmon production. The aggregated data were then analysed as mg/kg using ESVAC methodology, where kg represents the weight of slaughtered fish as live weight.

It is important to note that around 30% of trout are reared for restocking waters for angling rather than directly for food production. Antibiotic use on these restocking fish will be captured in the weight of active ingredient, but will not be captured in the 'kg' denominator. It should also be noted that salmon have a three year production cycle, so the tonnes of fish produced in any one year do not fully represent the overall salmon population at risk of treatment.

2.4 Results

2.4.1 Pig industry

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

"The halving of antibiotic usage in the pig sector between 2015 and 2017, which includes a 90% reduction in the use of HP-CIAs, demonstrates how all parts of the pig industry including producers, their representative bodies, veterinarians, feed, pharmaceutical and building companies have come together to recognise and address the challenge posed by increasing antimicrobial resistance. This reduction in antibiotic use has been achieved by pig producers working with their veterinary surgeons and other industry advisors to focus on improving key areas such as disease control, biosecurity, husbandry, cleaning and disinfection and nutrition, enabling producers to have the 'courage to cut' continual use while protecting pig welfare. Importantly, these actions also

contribute to raising the overall health status of the national pig herd. There is still much to do, but these very encouraging results show that the pig sector is well on track to meet its target of reducing usage to 99 mg/kg by 2020.”

2.4.1.2 Antibiotics usage data from eMB Pigs

Total eMB recorded antibiotic usage in pigs decreased by 52 mg/kg (28%) from 183 mg/kg in 2016 to 131 mg/kg in 2017. This means that total usage decreased by 147 mg/kg (53%) over the last two years (**Table 2.1** and **Figure 2.2**). The majority of active ingredient in 2017 was used as a premix (78%), followed by oral (19%) and injection (3%) (data not shown). Tetracyclines represented 43% of antibiotic used, with penicillins, trimethoprim/sulphonamides and macrolides representing a further 45% (**Table 2.1** and **Figure 2.1**).

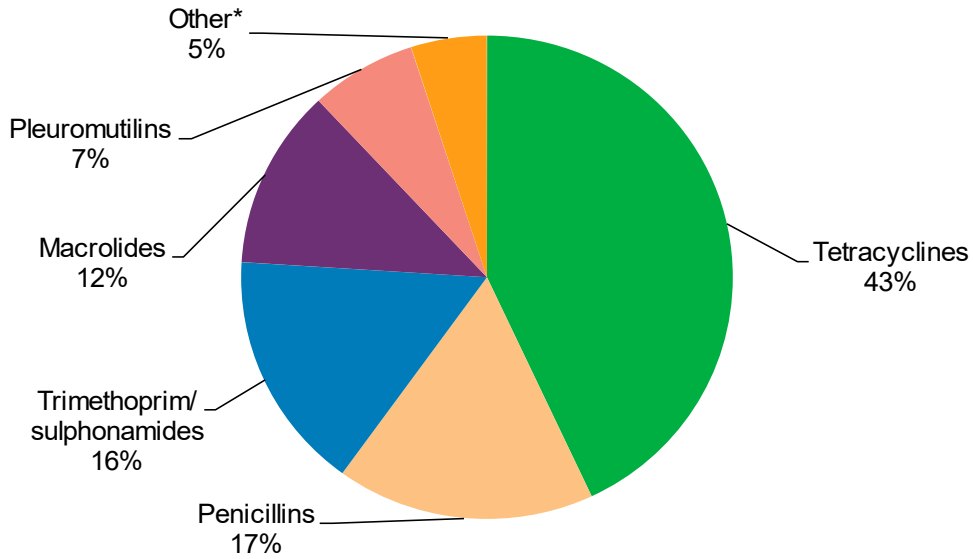
Reductions were seen across all antibiotic classes. However, the biggest falls occurred with trimethoprim/sulphonamides, which decreased by 46 mg/kg (69%) and tetracyclines, which decreased by 62 mg/kg (53%). Penicillins decreased by 15 mg/kg (39%) and now represent the second most used antibiotic class in pigs (**Table 2.1** and **Figure 2.2**).

Table 2.1: Usage recorded for active ingredient (mg/kg) of antibiotics in eMB Pigs by antibiotic class, 2015–2017

Antibiotic	Active ingredient in mg/kg (%)			% Change 2015–2017
	2015	2016	2017	
Tetracyclines	118 (42)	83 (45)	56 (43)	-53
Penicillins	37 (13)	28 (15)	22 (17)	-39
Trimethoprim/sulphonamides	66 (24)	29 (16)	21 (16)	-69
Macrolides	31 (11)	29 (16)	16 (12)	-49
Pleuromutilins	17 (6)	7.6 (4)	9.8 (7)	-44
Other*	8.6 (3)	7.2 (4)	6.1 (5)	-28
Total	278	183	131	-53

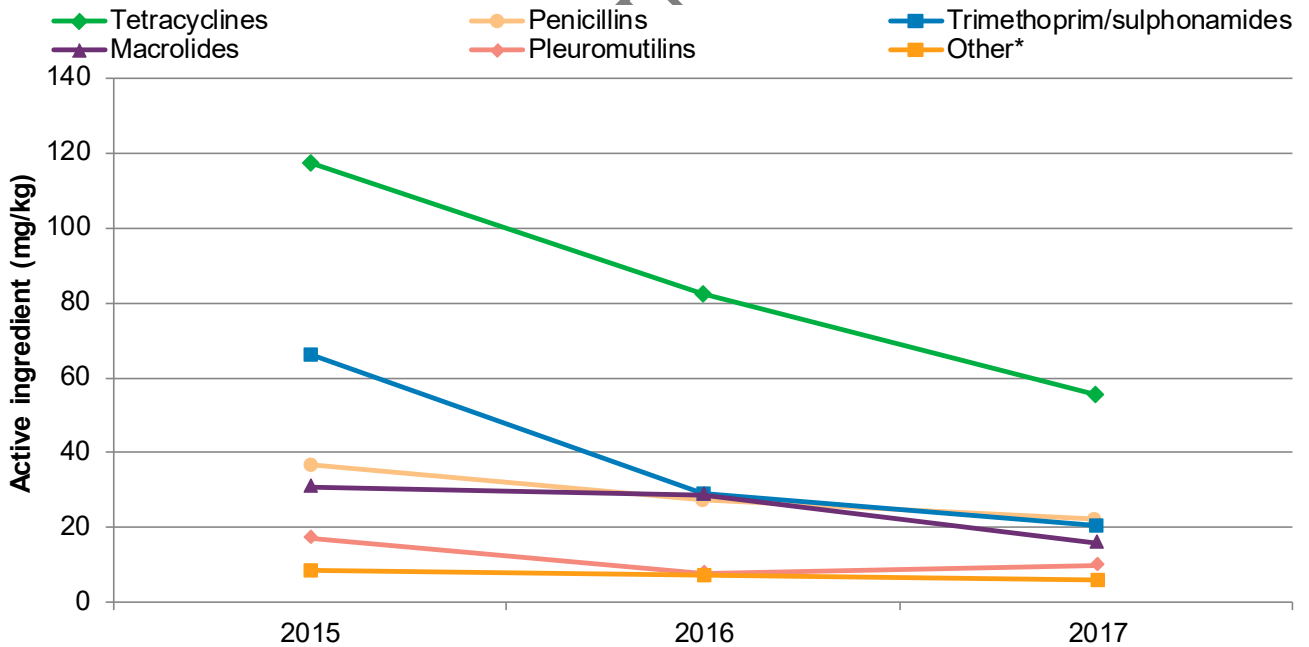
* Aminoglycosides, lincosamides, amphenicols, polymyxins, fluoroquinolones and 3rd and 4th generation cephalosporins.

Figure 2.1: Usage recorded for active ingredient (% mg/kg) of antibiotics in eMB Pigs by antibiotic class, 2017



* Aminoglycosides, lincosamides, amphenicols, polymyxins, fluoroquinolones and 3rd and 4th generation cephalosporins.

Figure 2.2: Usage recorded for active ingredient (mg/kg) of antibiotics in eMB Pigs by antibiotic class, 2015–2017



* Aminoglycosides, lincosamides, amphenicols, polymyxins, fluoroquinolones and 3rd and 4th generation cephalosporins.

Usage of HP-CIAs in pigs decreased by a further 0.17 mg/kg (63%) between 2016 and 2017, and has fallen by 0.88 mg/kg (90%) since 2015: from 0.98 mg/kg to 0.10 mg/kg. Although reductions were seen in all HP-CIA classes, this was driven primarily by a 0.85 mg/kg (99%) reduction in colistin use between 2015 and 2017 (**Figure 2.3** and **Table 2.2**).

Figure 2.3: HP-CIA usage recorded for active ingredient (mg/kg) of antibiotics in eMB Pigs: colistin (■), 3rd and 4th generation cephalosporins (■) and fluoroquinolones (■), 2015–2017

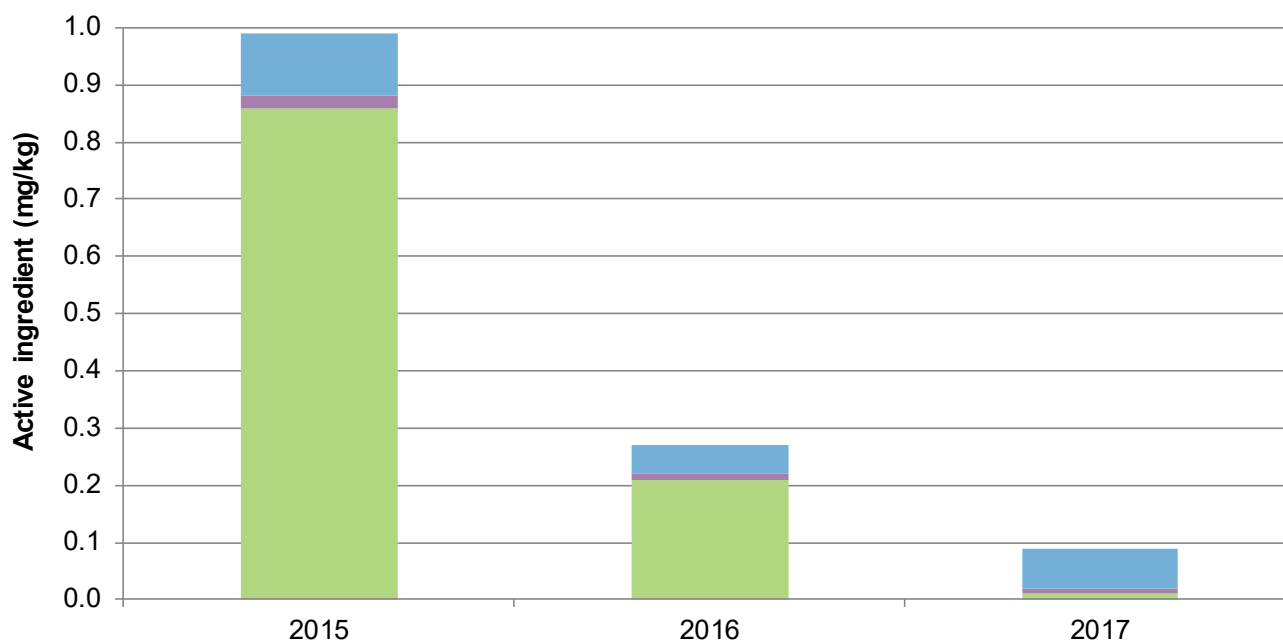


Table 2.2: HP-CIA usage (active ingredient of antibiotics, mg/kg) recorded in eMB Pigs, 2015–2017

Antibiotic	Active ingredient in mg/kg			% Change
	2015	2016	2017	2015–2017
Fluoroquinolones	0.11	0.05	0.07	-30
3 rd and 4 th generation cephalosporins	0.02	0.01	0.01	-26
Colistin	0.86	0.21	0.01	-99
Total	0.98	0.27	0.10	-90

2.4.2 Meat poultry industry

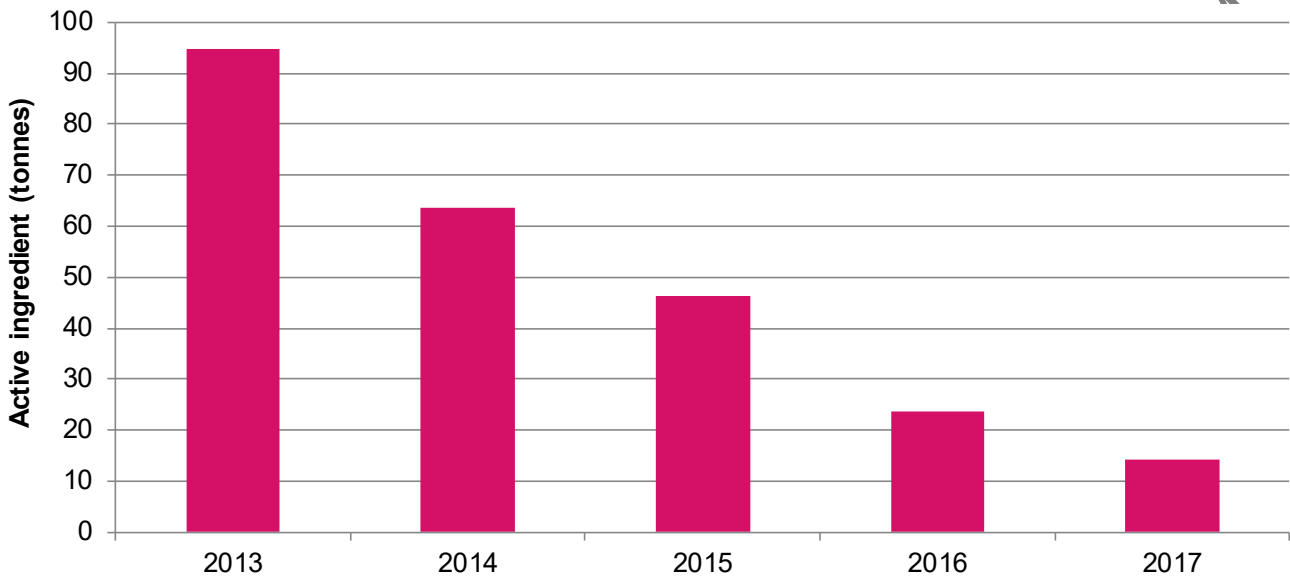
2.4.2.1 Statement from British Poultry Council

“The latest data from 2017 demonstrate further reductions in antibiotic use, both in terms of total use and HP-CIAs. Importantly, the British poultry meat sector have achieved this, through BPC Antibiotic Stewardship, by focusing on delivering excellence in bird health and welfare by monitoring and reviewing on-farm management practices and ensuring responsible use of antibiotics throughout the supply chain. This has only been possible because of openness within the sector to accept change, encourage innovation and share best practice. The sector has stopped the prophylactic use of antibiotics, the use of 3rd and 4th generation cephalosporins (since 2012) and the use of colistin (since 2016). In addition, the reductions in fluoroquinolones are testament to the fact that they can only be used as a last resort after alternative options have been explored.”

2.4.2.2 Antibiotic usage data from British Poultry Council

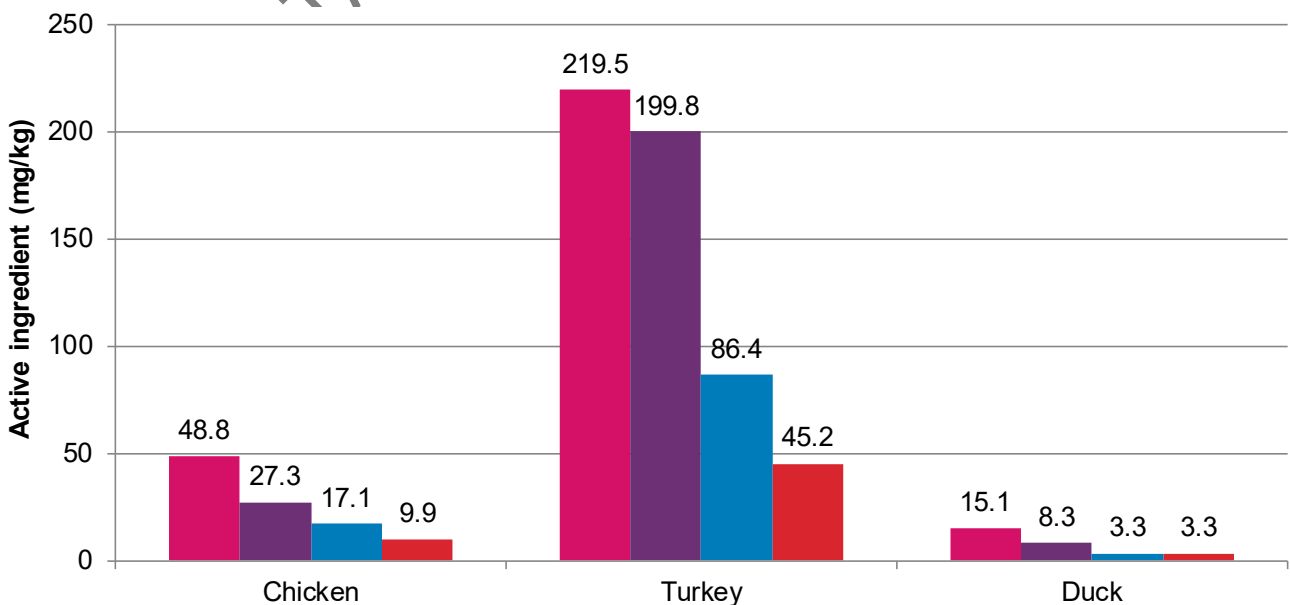
In 2017, the BPC reported the use of 14 tonnes of active ingredient; a 9.3 tonne (39%) reduction from 2016. This also represents a reduction of 80 tonnes (85%) from 2013 and is the lowest recorded value over the six years that BPC has been collecting these data (Figure 2.4).

Figure 2.4: Active ingredient (tonnes) of antibiotics used by all members of BPC Antibiotic Stewardship, 2013–2017



When taking into account the size of the animal population, data by species show that, between 2016 and 2017, usage in the chicken sector reduced by 7.2 mg/kg (42%), usage in the turkey sector reduced by 41 mg/kg (48%) and usage in the duck sector remained stable. This means that, since 2014, the chicken sector reduced usage by 39 mg/kg (80%), the turkey sector reduced usage by 174 mg/kg (79%) and the duck sector reduced usage by 12 mg/kg (78%) (Figure 2.5).

Figure 2.5: Active ingredient (mg/kg) of antibiotics used by all members of BPC Antibiotic Stewardship by species (chicken, turkey and duck), 2014 (■), 2015 (■), 2016 (■), 2017 (■)



In 2017, 80% of active ingredient classes used comprised penicillins and tetracyclines (**Table 2.3** and **Figure 2.6**).

Table 2.3: Active ingredient (tonnes) of antibiotics used by all members of BPC Antibiotic Stewardship by antibiotic class, 2013–2017

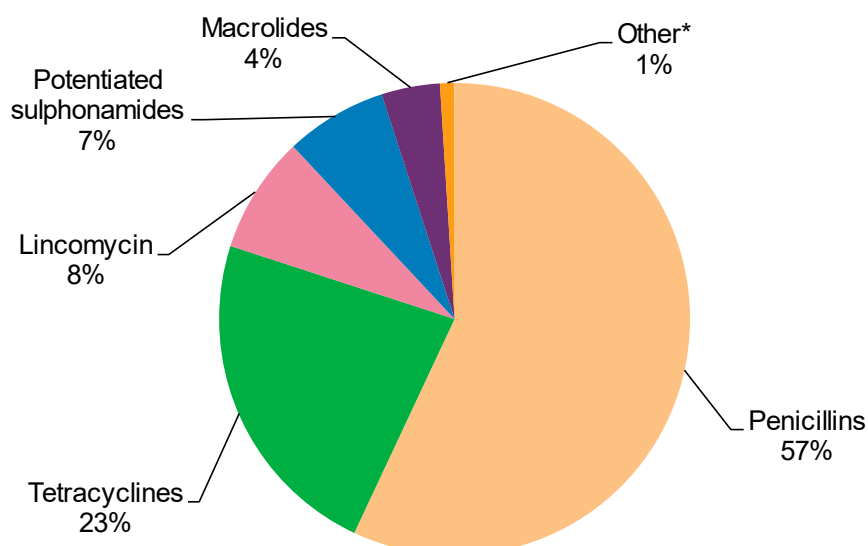
Antibiotic	Active ingredient in tonnes (%)					% Change 2013–2017
	2013	2014	2015	2016	2017	
Penicillins*	31 (33)	20 (31)	14 (30)	11 (45)	8.2 (57)	-73
Tetracyclines	48 (50)	31 (48)	24 (52)	9.0 (38)	3.3 (23)	-94
Lincomycins	7.5 (8)	7.1 (11)	4.8 (10)	1.4 (6)	1.2 (8)	-84
Potentiated sulphonamides	1.4 (1)	1.2 (2)	1.0 (2)	1.6 (7)	0.9 (7)	-36
Macrolides	5.0 (5)	2.7 (4)	1.1 (2)	0.5 (2)	0.6 (4)	-88
Other**, including:	2.1 (2)	2.1 (3)	1.4 (3)	0.6 (3)	0.2 (1)	-90
Fluoroquinolones*** (kg)	741 (0.8)	1131 (2)	540 (1)	122 (0.5)	38 (0.3)	
Colistin*** (kg)	29 (0.03)	121 (0.2)	40 (0.1)	8 (0.03)	0 (0)	
Total	95	64	46	24	14	-85

* Amoxicillin and phenoxymethylpenicillin.

** Aminoglycosides, pleuromutilins, fluoroquinolones, colistin and products under the cascade.

*** Highest priority critically important antibiotics.

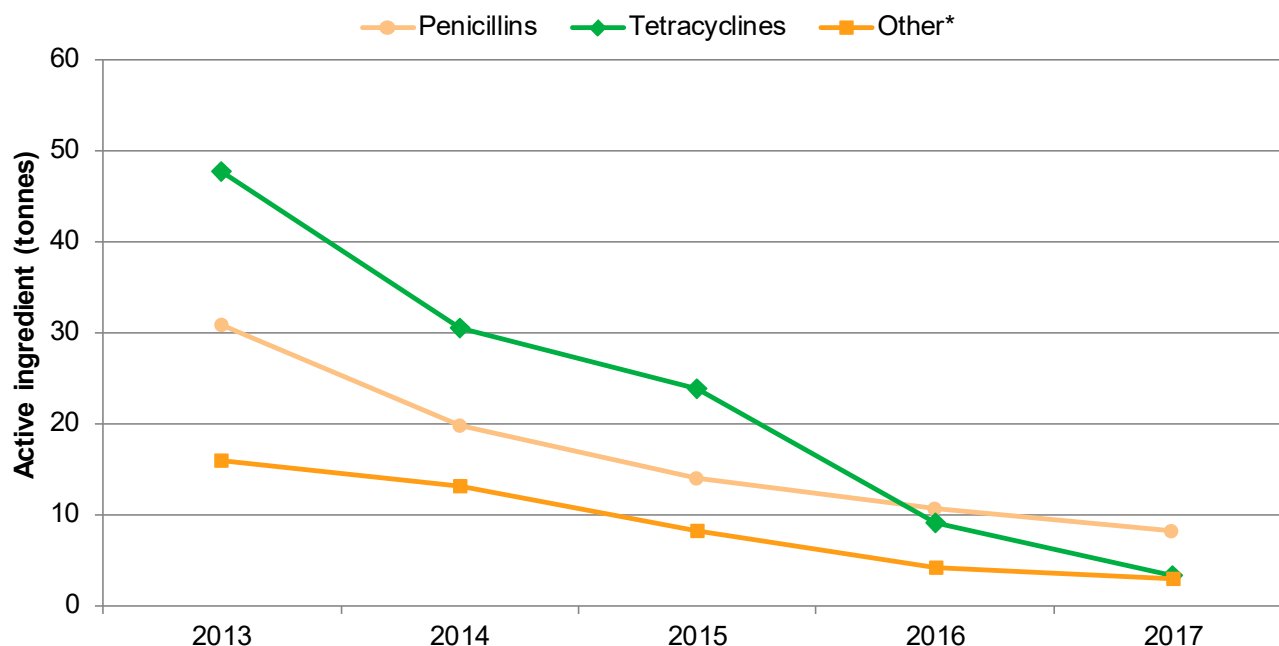
Figure 2.6: Active ingredient (% tonnes) of antibiotic used by all members of BPC Antibiotic Stewardship by antibiotic class, 2017



* Aminoglycosides, pleuromutilins, fluoroquinolones, colistin and products under the cascade.

A marked reduction of 44 tonnes (93%) in use of tetracyclines was reported between 2013 and 2017 (**Figure 2.7**). The reduction in tetracyclines was reported in both the chicken sector, where usage reduced by 95% from 15 mg/kg in 2014 to 0.7 mg/kg in 2017, and the turkey sector, where usage reduced by 87% from 165 mg/kg in 2014 to 22 mg/kg in 2017 (data not shown).

Figure 2.7: Active ingredient (tonnes) of antibiotic used by all members of BPC Antibiotic Stewardship by antibiotic class, 2013–2017



* Lincomycins, potentiated sulphonamides, macrolides, aminoglycosides, pleuromutilins, fluoroquinolones, colistin and products under the cascade.

Colistin and 3rd and 4th generation cephalosporins were not used by the sector in 2017.

Fluoroquinolones were not used by the duck sector and only used in small quantities by the broiler sector. The turkey sector reduced its use of fluoroquinolones by 95% from 7.4 mg/kg in 2014 to 0.4 mg/kg in 2017. Overall, the poultry meat sector used 0.03 mg/kg of HP-CIAs; a 75% drop between 2016 and 2017.

2.4.3 Laying hen industry

2.4.3.1 Statement from the British Egg Industry Council

“The usage data presented for 2017 show that the members of the BEIC Lion Code, which represent over 90% of the industry, have managed to reduce usage from an already low base, and met the sector target for percentage bird days treated to remain below 1%. This has been achieved with a focus on disease prevention, including widespread vaccination. It is also a requirement for all farms to have a written biosecurity and veterinary health plan and, in addition, the Lion Training Passport provides a common training standard on key topics, including welfare and biosecurity. It is encouraging to see that no HP-CIAs were used in 2017, which is again in line with the target to keep their use below 0.05% bird days treated. Colistin and 3rd and 4th generation cephalosporins cannot be used under the BEIC Lion Code. In addition, fluoroquinolones cannot be used in day old chicks and any other use can only be where it has been confirmed no other medication is appropriate in order to maintain bird welfare.”

2.4.3.2 Antibiotic usage data from the British Egg Industry Council

A total of 2.2 tonnes of antibiotic active ingredient were used by the laying hen industry in 2017, a reduction of 0.45 tonnes (17%) from 2016. This represents 0.57 actual daily bird doses/100 bird days at risk (% doses), a reduction of 22% from 2016 (**Table 2.4**).

Reductions were seen for most antibiotic classes, but were particularly marked for macrolides (56%), pleuromutilins (40%) and aminoglycosides (39%). Tetracyclines and pleuromutilins accounted for 84% of total use. No HP-CIAs were used (**Table 2.4** and **Figure 2.8**).

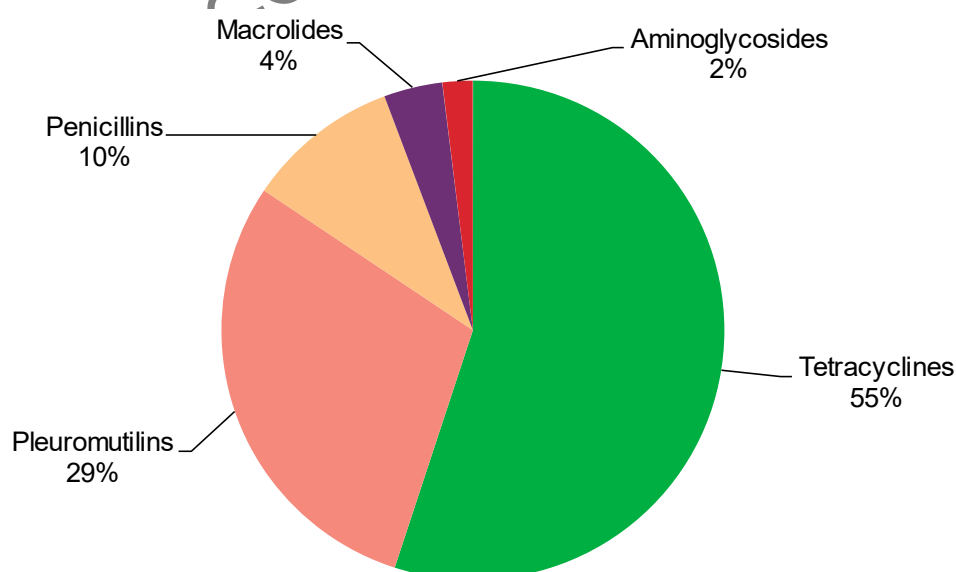
Table 2.4: Active ingredient (bird doses and %) of antibiotics used by members of the BEIC Lion Code, 2016–2017

Antibiotic	Active ingredient in bird doses (%)		% Change 2016–2017
	2016	2017	
Tetracyclines	0.293 (40)	0.314 (55)	7
Pleuromutilins	0.280 (38)	0.168 (29)	-40
Penicillins	0.060 (8)	0.056 (10)	-6
Macrolides	0.049 (7)	0.022 (4)	-56
Aminoglycosides	0.018 (2)	0.011 (2)	-39
Other*, includes:	0.030 (4)	0 (0)	-100
Fluoroquinolones**	0.002 (0.3)	0 (0)	
Colistin**	0.028 (4)	0 (0)	
Total	0.73	0.57	-22

* Includes fluoroquinolones and colistin.

** Highest priority critically important antibiotics.

Figure 2.8: Active ingredient (% bird doses) of antibiotics used by members of the BEIC Lion Code, 2017



2.4.4 Gamebird industry

2.4.4.1 Statement from Game Farmers' Association

"We very much welcome the 36% fall in the amount of antibiotics used in the rearing of pheasants and partridges in the UK in 2017. This has been achieved voluntarily through the hard work of game farmers, game keepers, the veterinary profession and the game feed trade. The use of antibiotics in gamebird rearing is sometimes essential for welfare reasons but administration can be reduced through good biosecurity and correct management, in close liaison with specialist veterinarians. The sector has committed to build on these successes and reduce use by a further 25% between now and 2020."

2.4.4.2 Antibiotic usage data from Game Farmers' Association (GFA)

In 2017, 13 tonnes of active ingredient were reported through the GFA data collection programme. This represents a reduction of 7.2 tonnes (36%) between 2016 and 2017 (**Figure 2.9** and **Table 2.5**).

Tetracyclines and pleuromutilins represented 90% of antibiotics used in 2017 (**Figure 2.9**). Within the HP-CIAs, colistin was not used in 2017 and fluoroquinolone use (available for in-water use only) reduced by 14 kg (22%). While reductions were seen across all antibiotic classes, tetracyclines accounted for 88% (6.3 tonnes) of the overall decrease observed (**Table 2.5**).

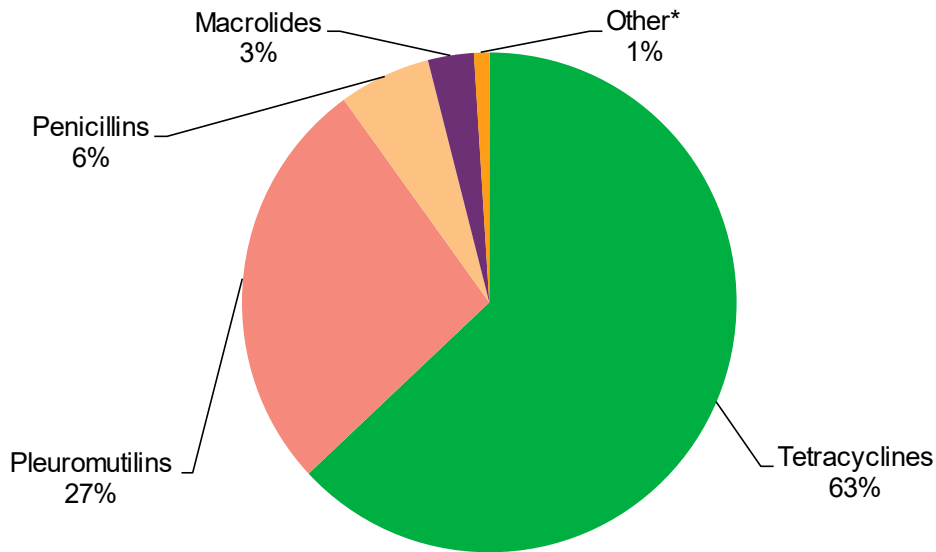
Table 2.5: Active ingredient (tonnes) of antibiotics used by the gamebird industry, recorded by GFA, 2017

Antibiotic class	Active ingredient in tonnes (%)		% Change 2016–2017
	2016	2017	
Tetracyclines	15 (72)	8.2 (63)	-43
Pleuromutilins	3.7 (18)	3.6 (27)	-3
Penicillins	1.2 (5.9)	0.8 (6)	-33
Macrolides	0.6 (3)	0.3 (3)	-50
Other*:	0.2 (1)	0.1 (0.8)	-50
Fluoroquinolones** (kg)	64 (0.3)	50 (0.4)	
Colistin** (kg)	0.6 (0.003)	0 (0)	
Total	20	13	-36

* Aminoglycosides, amphenicols, colistin, fluoroquinolones, lincomycins, trimethoprim/sulphonamides.

** Highest priority critically important antibiotics.

Figure 2.9: Active ingredient (% tonnes) of antibiotics used by the gamebird industry, recorded by GFA, 2017



* Aminoglycosides, amphenicols, colistin, fluoroquinolones, lincomycin, trimethoprim/sulphonamides.

Analysis of usage data by route of administration shows that in-feed medication reduced by 8 tonnes (53%) and accounted for 54% of all antibiotics used (down from 74% in 2016). This was largely due to a 7.2 tonne (61%) reduction of in-feed tetracyclines. During the same period, in-water medication increased by 0.8 tonnes (15%).

2.4.5 Cattle industry

2.4.5.1 Statement from Cattle Health and Welfare Group (CHAWG)

“The sample data presented here, representing a convenience sample of 31% UK dairy cows and 5% UK beef production, 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. The data provide useful information for the industry, but the dairy and beef sectors are committed to increasing the amount, quality and representativeness of the data for both antibiotic usage monitoring and benchmarking.”

Both the dairy usage and cattle sales data demonstrate that the sectors are well on the way to achieving the 2020 targets, with encouraging reductions seen in overall use, use of intramammary tubes and the use of intramammary and injectable HP-CIAs. The dairy and beef sectors are committed to promoting responsible antibiotic use, with a key focus on training and sharing of best practice, herd health planning, disease prevention and reducing the need for antibiotics. In 2018, Red Tractor strengthened its requirements on the use of HP-CIAs for the beef, lamb and dairy sectors, such that they can only be used as a last resort under veterinary direction, alongside sensitivity and/or diagnostic testing. It is therefore expected that this downward trend in the use of HP-CIAs will continue.”

2.4.5.2 Dairy usage

The dairy data for 2017 cover 2,923 farms and represent 31% of all dairy cows in the UK, with relatively higher coverage in England and Northern Ireland than in Wales and Scotland. However,

when compared to the 2015 and 2016 samples, the coverage in Scotland increased, whereas the coverage in Wales and Northern Ireland decreased (**Table 2.6**). The mean herd size within the sample is 204, which is 28% higher than the overall UK mean. This is slightly lower than for the 2015 and 2016 samples, where the mean herd size was 214 and 211 respectively. Because of these differences in the sample population of farms between years, caution should be taken when interpreting trends. In addition, antibiotic usage in this convenience sample may not be representative of the whole UK dairy population.

Table 2.6: Comparison of national coverage of adult dairy cows (over 2 years of age) included in the FarmVet Systems sample, 2015–2017

	% Coverage*		
	2015	2016	2017
England	36	32	34
Northern Ireland	46	45	38
Wales	22	20	14
Scotland	15	12	21
UK	32	34	31

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

As in previous years, penicillins/1st generation cephalosporins, tetracyclines, aminoglycosides and macrolides were the most commonly used antibiotic classes (**Table 2.7** and **Figure 2.10**).

Four tonnes of active ingredient were used in the sample of dairy farms in 2017, which represented 17 mg/kg, a reduction of 29% since 2015. Reductions were seen across all antibiotic classes, with particularly marked decreases in the HP-CIAs, which represented 0.6 mg/kg (4% of active ingredient administered) in 2017. The majority of active ingredient was administered by injection (69%) and the oral route (19%).

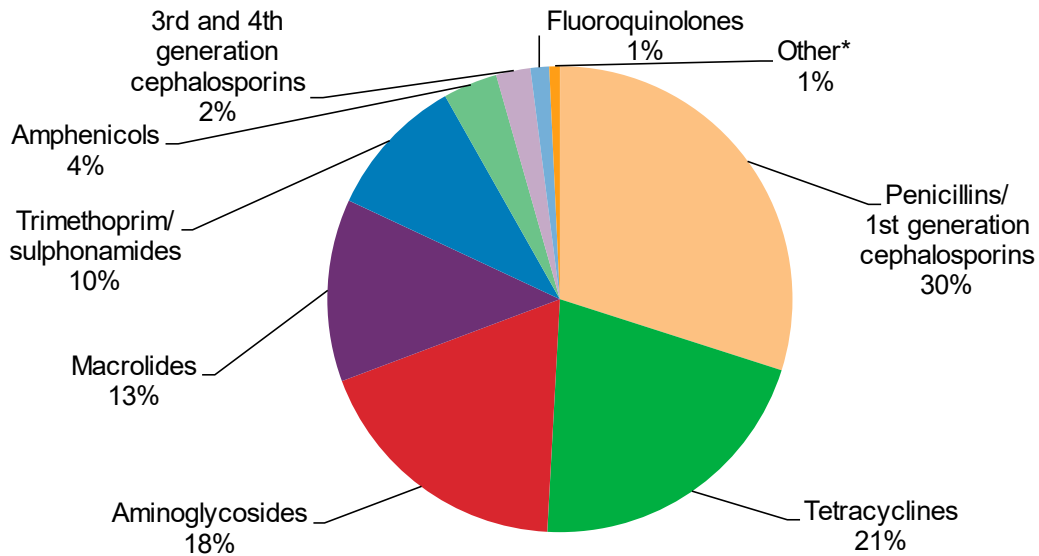
Table 2.7: Active ingredient (mg/kg) of antibiotics used by the dairy farms in the FarmVet Systems sample, 2015–2017

Antibiotic	Active ingredient in mg/kg (%)			% Change
	2015	2016	2017	2015–2017
Penicillins and 1 st generation cephalosporins	7.2 (30)	9.1 (38)	5.0 (30)	-31
Tetracyclines	4.5 (19)	4.8 (20)	3.5 (21)	-23
Aminoglycosides	3.9 (16)	3.6 (15)	3.1 (18)	-22
Macrolides	3.2 (13)	4.1 (17)	2.1 (13)	-35
Trimethoprim/sulphonamides	2.1 (9)	2.7 (11)	1.6 (10)	-23
Amphenicols	0.9 (4)	0.8 (3)	0.6 (4)	-28
3 rd and 4 th generation cephalosporins*	1.4 (6)	0.6 (3)	0.4 (2)	-71
Fluoroquinolones*	0.5 (2)	0.3 (1)	0.2 (1)	-61
Other**, including: Colistin*	0.2 (1) 0.005 (0.02)	0.2 (1) 0.011 (0.04)	0.1 (1) 0.007 (0.04)	-37

Total	24	26	17	-29
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* Highest priority critically important antibiotics.
 ** Aminocoumarins, lincosamides and polymyxins.

Figure 2.10: Active ingredient (% mg/kg) of antibiotics used by the dairy farms in the FarmVet Systems sample, 2017



* Aminocoumarins, lincosamides and polymyxins.

2.4.5.3 Beef usage

The beef data for 2017 cover 2,705 farms in Great Britain, with the majority of these (86%) being in England. The sample overall represents 6% production for GB and 5% for the UK. It is therefore a much smaller sample than for dairy, increasing the likelihood that the results are not representative of the beef population in the UK. In addition, the sample only includes beef farms which do not have any sheep.

The beef sector is made up of many different farm types, including calf rearers, suckler beef and finisher units, and it is not possible to determine usage by farm type from this sample.

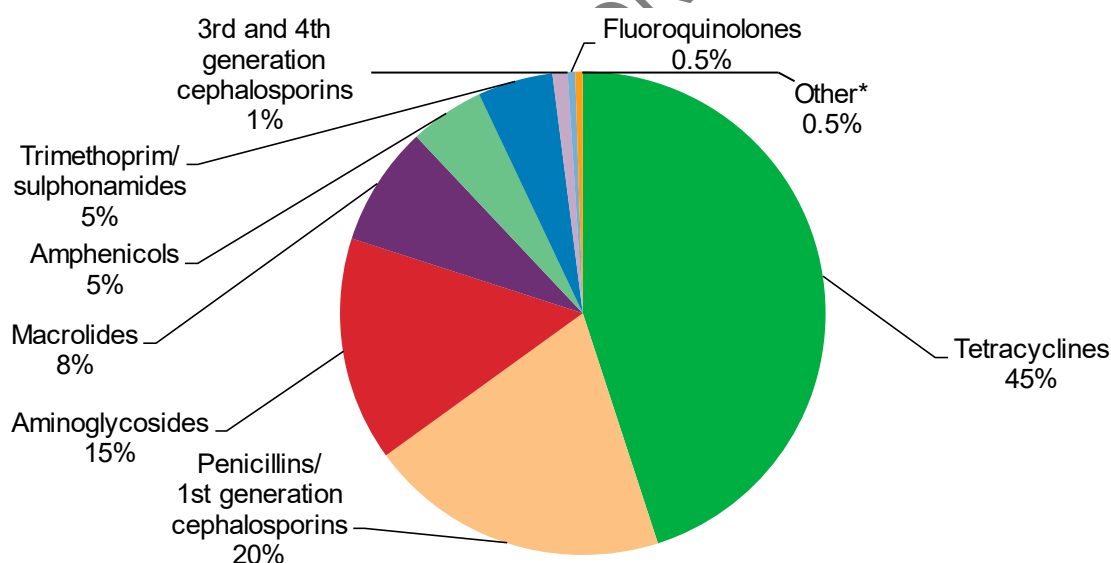
The usage data showed that 0.9 tonnes of active ingredient of antibiotic were used in this sample of beef farms, which represented 19 mg/kg, with tetracyclines, penicillins/1st generation cephalosporins, aminoglycosides and macrolides the most commonly used antibiotic classes (**Table 2.8** and **Figure 2.11**). HP-CIA use was 0.3 mg/kg, representing 1.5% of antibiotic active ingredient administered. The majority of active ingredient was administered by injection (63%) and the oral route (32%).

Table 2.8: Active ingredient (mg/kg) of antibiotics used by the beef farms in the FarmVet Systems sample, 2017

Antibiotic	mg/kg (%)
Tetracyclines	8.7 (45)
Penicillins plus 1 st generation cephalosporins	3.9 (20)
Aminoglycosides	2.9 (15)
Macrolides	1.5 (8)
Amphenicols	1.0 (5)
Trimethoprim/sulphonamides	1.0 (5)
3 rd and 4 th generation cephalosporins*	0.2 (1)
Fluoroquinolones*	0.1 (0.5)
Other** including: Colistin*	0.1 (0.5) 0.006 (0.03)
Total	19

* Highest priority critically important antibiotics.

** Aminocoumarins, lincosamides and polymyxins.

Figure 2.11: Active ingredient (% mg/kg) of antibiotics used by the beef farms in the FarmVet Systems sample, 2017

* Aminocoumarins, lincosamides and polymyxins.

24.5.4 Cattle sales targets

In the sector-specific targets document (Responsible Use of Medicines in Agriculture Alliance, 2017), the dairy and beef sectors made a commitment to reduce the use of injectable HP-CIAs by 50% by 2020 (using 2015 as the baseline). This can be measured by analysing the sales of such products that include cattle in their license. Although some of these products include other species in their license indication, industry feedback suggests that the majority (75%) are used in cattle. For the dairy sector, there are also targets to reduce intramammary HP-CIAs by 50% and dry cow use and lactating cow use by 20% and 10% respectively by 2020, again using 2015 as the

baseline. Good progress is being made towards reaching these targets, especially in reducing the use of HP-CIAs (**Table 2.9**).

Table 2.9: Sales (mg/kg) of injectable HP-CIAs with a licensed indication for cattle and of intramammary tubes (course doses, DCDvet) – using methodology defined by ESVAC, 2015–2017

Category	Sales			Target	% Change
	2015	2016	2017	2020	2015–2017
Injectable HP-CIA products licensed for cattle (mg/kg)	1.075	0.959	0.760	0.538	-29
Intramammary HP-CIA products (DCDvet)	0.332	0.308	0.223	0.166	-33
Intramammary tubes – lactating cow (DCDvet)	0.808	0.977	0.818	0.727	+1
Intramammary tubes – dry cow (DCDvet)	0.732	0.748	0.677	0.586	-8

2.4.6 Aquaculture

2.4.6.1 Salmon

2.4.6.1.1 Statement from the Scottish Salmon Producers' Association

*“The data presented here fulfil our commitment in the sector targets to gather and share information on antibiotic usage for the salmon industry. The salmon sector is committed to only using antibiotics when absolutely necessary in order to maintain health and welfare and practises a high level of preventative medicine; for example all salmon are vaccinated against *Aeromonas salmonicida* (furunculosis) during the freshwater phase. It is also a requirement of membership of SSPO that companies adhere to the Code of Good Practice for Scottish Finfish Aquaculture and, under this, all farms must have a veterinary health plan which covers the responsible use of medicines. The usage in 2017 was above the ambitious target to keep usage in the salmon industry below 5 mg/kg. As highlighted by the sales data, the usage in the industry can fluctuate year-on-year. This occurs as a result of various factors, for example changing water temperature (which strongly influences physiological processes in both fish and fish pathogens). In addition, year-to-year variation in the number of treatments necessary during the freshwater phase of production (where the biomass of fish treated is relatively low) and the seawater phase (where the biomass of fish is relatively high) can impact fluctuations in the overall level of antibiotic used between years.”*

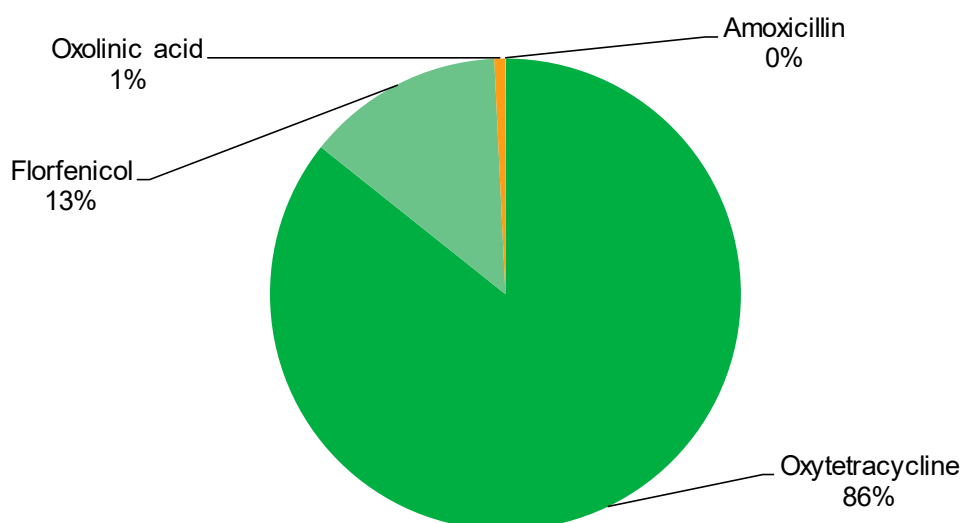
2.4.6.1.2 Results

The sample from which data are obtained represents 100% of Scottish salmon production.

The results show that 3.0 tonnes of active ingredient of antibiotics were used, representing 17 mg/kg (**Table 2.10**). There were only four antibiotic active ingredients used, with oxytetracycline being by far the most common (representing 86% of active ingredient used), and no HP-CIAs were used (**Figure 2.12**). Note that the quinolone oxolinic acid is made available under a Special Import Certificate, and so is not captured in the antibiotic sales data.

Table 2.10: Active ingredient (mg/kg) of antibiotics used on Scottish salmon farms, 2017

Antibiotic	Active ingredient in mg/kg (%)
Oxytetracycline	14.8 (86)
Florfenicol	2.3 (13)
Oxolinic acid	0.1 (0.7)
Amoxicillin	0.004 (0.02)
Total	17

Figure 2.12: Active ingredient (% mg/kg) of antibiotics used on Scottish salmon farms, 2017

2.4.6.2 Trout

2.4.6.2.1 Statement from the British Trout Association

“The trout sector is committed to monitoring antibiotic usage and focusing on biosecurity and good management practices in order to minimise the use of antibiotics. The data presented here show that usage in this sample of trout farms is just below the sector target to maintain an average use of 20 mg/kg. As highlighted in the sector targets report (Responsible Use of Medicines in Agriculture Alliance, 2017), vaccines are a vitally important tool in preventing disease in trout farms and increasing the use as well as improving the availability of cost-effective authorised vaccines is crucial.”

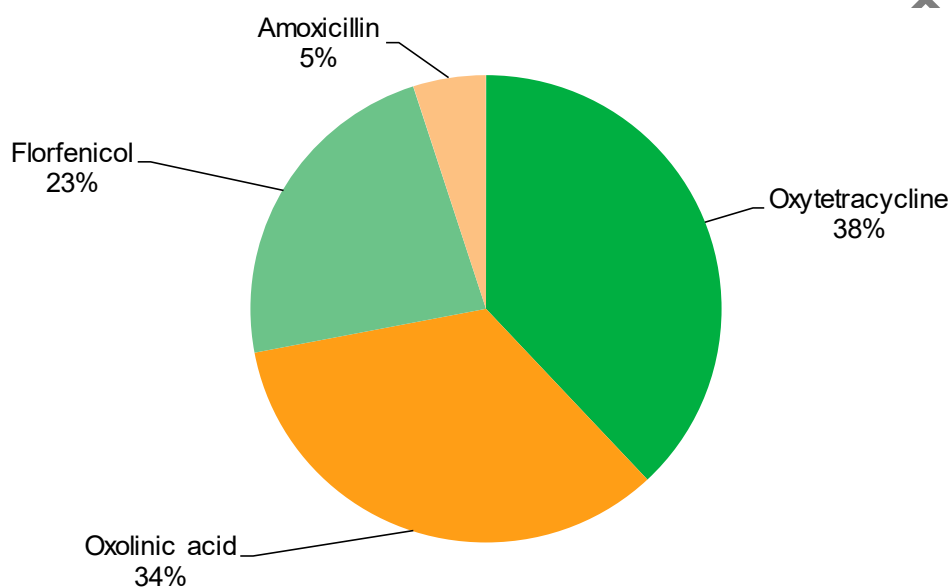
2.4.6.2.2 Results

The sample obtained represented around 70% of the UK trout production, with around 90% of the English trout sector (5,100 tonnes fish production) and 60% of the Scottish trout sector (5,023 tonnes fish production).

The results show that 0.19 tonnes of antibiotic was used on the sample of trout farms, representing 19 mg/kg (**Table 2.11**). Only four antibiotic active ingredients were used, with oxytetracycline (38%) and oxolinic acid (34%) the most common, and no HP-CIAs were used (**Figure 2.13**). Note that the quinolone oxolinic acid is made available under a Special Import Certificate, and so is not captured in the antibiotic sales data.

Table 2.11: Active ingredient (mg/kg) of antibiotics used on the sample of trout farms, 2017

Antibiotic	Active ingredient in mg/kg (%)
Oxytetracycline	7.3 (38)
Oxolinic acid	6.6 (34)
Florfenicol	4.4 (23)
Amoxicillin	0.9 (5)
Total	19

Figure 2.13: Active ingredient (% mg/kg) of antibiotics used on the sample of trout farms, 2017

SALES DATA CORRE



CHAPTER 3

EU Harmonised Monitoring of Antibiotic Resistance

SALES DATA CORRECTIONS - SEE ER/

3.1 Summary

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 pigs at slaughter. Resistance to ciprofloxacin and nalidixic acid was observed in 1.6% and 2.2% of the isolates, respectively. Resistance to tetracycline, sulphonamide, trimethoprim, ampicillin, chloramphenicol and gentamicin decreased when compared to the levels detected in 2015.

Seventy-five (22%) presumptive ESBL-/AmpC-producing *E. coli* isolates were recovered from 347 caecal samples tested on selective media. The majority displayed an ESBL-phenotype (69%), with CTX-M ESBL being the most common type. No presumptive carbapenemase-producing *E. coli* isolates were detected in the 347 caecal samples.

None of the four *Salmonella* isolates tested under this monitoring scheme were resistant to meropenem, cefotaxime, ceftazidime, colistin or tigecycline. Two isolates were resistant to ampicillin and two were resistant to tetracycline.

3.2 Introduction

The EU harmonised monitoring of antibiotic resistance is a programme set out in the Commission Implementing Decision 2013/652/EU, which mandates all EU Member States to monitor and report antibiotic resistance in zoonotic and commensal bacteria from healthy food-producing animals at slaughter and food products at retail. An overview of the sampling plan, by year, is summarised in Table S3.1.1 of the supplementary material.

In 2017, EU Member States were mandated to carry out the following testing:

- Susceptibility testing of *Escherichia coli* from pig caecal samples taken at slaughter.
- Susceptibility testing of *Salmonella* spp. isolates derived from pig carcass swab samples.
- Testing for the presence of Extended-Spectrum Beta-Lactamase (ESBL-), AmpC-, or carbapenemase-producing *E. coli* in caecal contents from pigs at slaughter and samples of fresh pig and bovine meat at retail.

3.3 Methods

3.3.1 Sample collection

Caecal samples were taken from healthy pigs at slaughter, 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, jointly covering 71% of the UK throughput in 2017. Sample collection was randomised and evenly distributed throughout the year. A maximum of one caecal sample per epidemiological unit (pig holding) was collected.

Under the requirements of European Commission regulation 2073/2005 on microbiological criteria for foodstuff (process hygiene criteria only) food business operators collected carcass swabs which

were 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 to the Animal and Plant Health Agency (APHA) for serotyping and susceptibility testing.

3.3.2 Antibiotic susceptibility testing

Isolation of bacteria and antibiotic susceptibility testing was carried out by the national reference laboratories (NRLs).

Bacterial isolates (*E. coli* and *Salmonella* spp.) were cultured and a single colony selected for susceptibility testing against a panel of antibiotics, defined in Decision 2013/652/EU, using a standardised broth microdilution method to determine the MIC. *E. coli* isolates from samples collected in England, Wales and Scotland were additionally cultured on MacConkey agar + 2 mg/L colistin.

In addition, caecal samples were cultured for ESBL-/AmpC-/carbapenemase-producing *E. coli* following the procedures outlined in Decision 2013/652/EU. This included a pre-enrichment step followed by inoculation of samples onto MacConkey agar plates supplemented with 1 mg/L cefotaxime and incubated at 44°C for isolation of ESBL- or AmpC-producing *E. coli*, onto CHROM agar for isolation of ESBL-producing *E. coli*, and onto chromID CARBA and chromID OXA-48 agars for isolation of carbapenemase-producing *E. coli*.

Whole genome sequencing and *in silico* bioinformatic tools were used to detect the antibiotic resistance determinants for the ESBL-/AmpC-phenotypes identified. The isolates were sequenced using the Illumina NextSeq platform followed by quality control steps and mapping of the raw reads to a database of antibiotic resistance genes, using the APHA SeqFinder pipeline (Anjum et al., 2016, Duggett et al., 2017). The sequence of isolates negative for all known ESBL-, AmpC- and carbapenemase-encoding genes were investigated for promoter mutations in *ampC*, which is compatible with increased expression of the chromosomal *ampC*, using the APHA SeqFinder pipeline.

3.3.3 Interpretation of results

Both the European Committee on Antimicrobial Susceptibility Testing (EUCAST) human clinical breakpoints (CBPs) and EUCAST epidemiological cut-off values (ECOFFs) were used to assess susceptibility and resistance of the bacterial isolates. 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. ECOFFs 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 population. A 'resistant' (or 'non-susceptible') ECOFF does not necessarily imply a level of resistance which would correspond with clinical treatment failure.

Results interpreted using both human CBPs and ECOFFs are provided in full in Tables S3.2.1 and S3.3.1 of the supplementary material.

3.4 Results and discussion

3.4.1 *Escherichia coli*

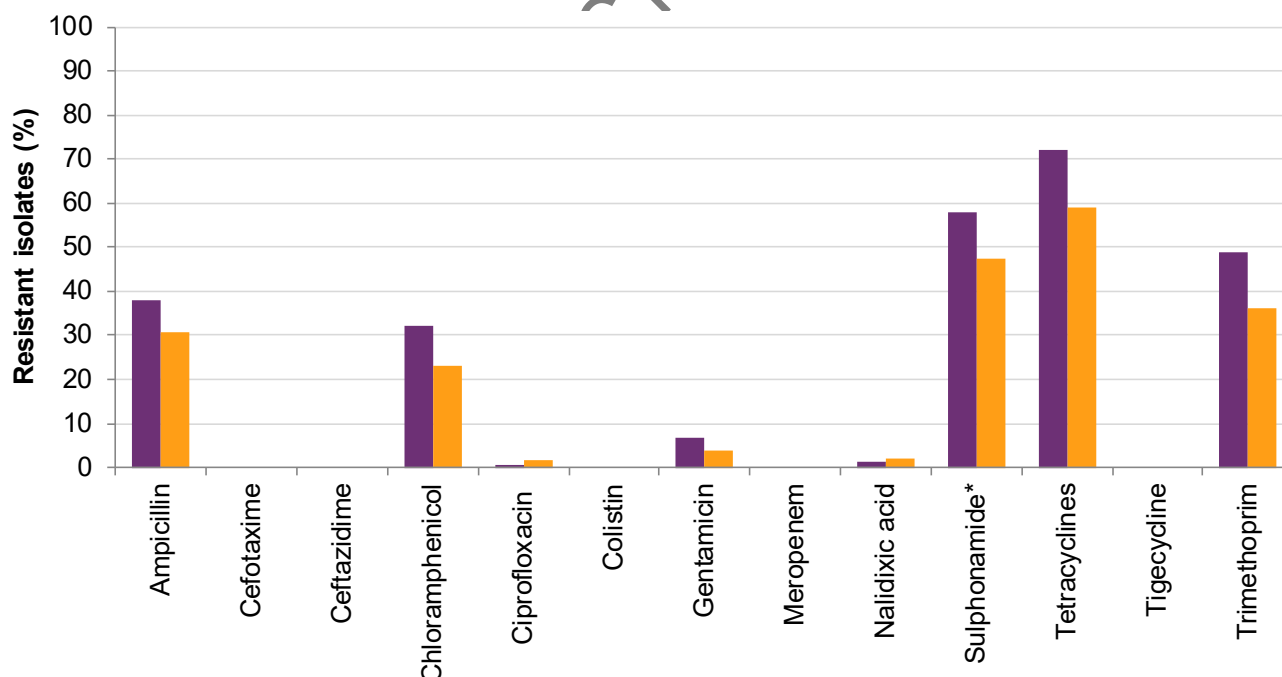
In 2017, 186 *Escherichia coli* isolates from pig caecal samples were collected at slaughter and tested for antibiotic resistance. **Figure 3.1** shows the percentage of *E. coli* isolates resistant to the antibiotics tested. For comparative purposes, data from 2015 are also included.

With regard to highest priority critically important antibiotics to human medicine, resistance was not detected to cefotaxime, ceftazidime or colistin in *E. coli* isolates from pigs. No resistance was detected to meropenem or tigecycline. In 2015, all *E. coli* isolates from pigs were also fully susceptible to these antibiotics. The level of resistance to ciprofloxacin (1.6%) increased from that reported in 2015 (0.7%).

A high to very high level of resistance was observed in *E. coli* isolates to tetracycline (59%), sulphonamide (47%, based on ECOFF as no BCP value is available), trimethoprim (36%), ampicillin (31%) and chloramphenicol (23%). Low level of resistance was detected to gentamicin (3.8%) and nalidixic acid (2.2%).

With the exception of ciprofloxacin and nalidixic acid, levels of resistance to all antibiotics in *E. coli* isolates from pigs were lower in 2017 when compared to data from 2015.

Figure 3.1: Percentage resistance (interpreted using EUCAST CBPs) in *E. coli* isolates from healthy pigs at slaughter, 2015 (■; n=150) and 2017 (■; n=186)



* Interpreted using EUCAST ECOFF values as no CBP value is available.

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

The EU AMR harmonised monitoring scheme also requires a minimum of 300 caecal samples to be collected from healthy pigs at slaughter for monitoring for ESBL-, AmpC- or carbapenemase-

producing *E. coli*. In total, 347 caecal samples were collected throughout the UK and tested on selective media. A total of 75 (22%) caecal samples yielded presumptive ESBL-/AmpC-producing *E. coli*. No presumptive carbapenemase-producing *E. coli* isolates were detected.

It should be noted that when using selective culture methods, the occurrence of ESBL-, AmpC- or carbapenemase-producing *E. coli* in pigs 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- or 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 low 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 numbers of resistant *E. coli* which may be present as a minor component of the total flora.

The majority of isolates displayed an ESBL-phenotype (69%) and 19 of the 75 isolates (25%) displayed AmpC-phenotype; four isolates (5%) displayed both phenotypes (Table 3.1).

Table 3.1: 3rd generation cephalosporin-resistance phenotype in ESBL-/AmpC-producing *E. coli* from caecal samples (n=347) from healthy pigs at slaughter in the UK, 2017

Phenotype	Number of isolates	Proportion of isolates (%)	Proportion of caecal samples (%)
ESBL	52	69	15
AmpC	19	25	5
ESBL/AmpC	4	5	1
Carbapenemase	0	0	0

Three isolates showed decreased susceptibility to ertapenem (interpreted using ECOFFs), probably due to increased OmpA activity; decreased susceptibility to imipenem and meropenem was not detected (Table 3.2). A large proportion of the isolates displaying decreased susceptibility to cefotaxime also displayed decreased susceptibility to trimethoprim, sulphonamides and tetracyclines (72–77%). A smaller proportion of isolates showed decreased susceptibility to chloramphenicol and ciprofloxacin (23%), with few isolates (1–11%) showing decreased susceptibility to gentamicin, nalidixic acid, azithromycin and tigecycline.

CTX-M was the most common type among the 75 ESBL-/AmpC-producing *E. coli* from pigs, with seven different allelic variants identified (Table S3.2.2 of the supplementary material). The most common variant was CTX-M-1 (43%), but a number of isolates also harboured other variants including CTX-M-15 (11%), CTX-M-14 (7%) and CTX-M-55 (5%). CTX-M-1 *E. coli* was found in 9% of the caecal samples tested.

The CMY-2 enzyme was the only transferable AmpC enzyme detected and was present in 16% of the isolates; while SHV-12 was detected in 3% of the isolates (Table S3.2.2 of the supplementary material). In 13% of the isolates no ESBL/AmpC enzymes were detected but only mutations associated with upregulation of chromosomal *ampC* expression. Two isolates contained both CTX-M-1 and CMY-2.

The 32 isolates producing CTX-M-1 belonged to 22 different sequence types (ST) with most isolates represented by a single ST, including one unknown ST (Table S3.2.2 of the supplementary

material). A single isolate harbouring CTX-M-1 belonged to ST131; strains belonging to this sequence type, but carrying CTX-M-15, have been associated with pathogenicity in humans. All ten upregulated *ampC* isolates belonged to a different ST, as did the two SHV-12 isolates.

Table 3.2: Decreased susceptibility in ESBL-/AmpC-producing *E. coli* from caecal samples from healthy pigs at slaughter in the UK, 2017

Antibiotic	Number of isolates with decreased susceptibility*	Proportion of isolates (%)	Proportion of caecal samples (%)
Ampicillin	75	100	22
Azithromycin	4	5	1
Cefepime	67	89	19
Cefotaxime	75	100	22
Cefoxitin	23	31	7
Ceftazidime	74	99	21
Chloramphenicol	17	23	5
Ciprofloxacin	17	23	5
Colistin	0	0	0
Ertapenem	3	4	1
Gentamicin	8	11	2
Imipenem	0	0	0
Meropenem	0	0	0
Nalidixic acid	8	11	2
Sulfonamide	58	77	17
Tetracycline	54	72	16
Tigecycline	1	1	0
Trimethoprim	55	73	16

* Interpreted using EUCAST ECOFFs.

3.4.3 *Salmonella* spp.

A total of four *Salmonella* isolates from pig carcass samples from Food Business Operators were tested for antibiotic resistance. As only a small number of isolates was recovered, the results are not likely to be representative and should be interpreted with caution. Two isolates were resistant to tetracyclines and two to ampicillin. None of the *Salmonella* isolates tested were resistant to the HP-OAs cefotaxime, ceftazidime, ciprofloxacin or colistin, or to meropenem, nalidixic acid or tigecycline. Results interpreted using both CBP and ECOFF values are presented in Table S3.3.1 of the supplementary material.

3.4.4 EU harmonised AMR outcome indicators

In 2017, ECDC, EFSA and EMA recommended harmonised outcome indicators for presenting data on antimicrobial resistance in food-producing animal species (European Centre for Disease Prevention and Control et al., 2017).

Primary indicator:

- Proportion of indicator *E. coli* isolates from broilers, fattening turkeys, fattening pigs and calves (as collected in the framework of Decision 2013/652/EU) fully susceptible to the entire panel of antibiotics defined in the Decision, weighted by the size (expressed in PCU) of the four animal populations.

Secondary indicators:

- Proportion of indicator *E. coli* isolates from the four animal species, weighted by PCU, showing decreased susceptibility to at least three antibiotics from different classes from the predefined panel of antibiotics ('multiple resistant');
- Proportion of indicator *E. coli* isolates from the four animal species, weighted by PCU, showing decreased susceptibility to ciprofloxacin;
- Proportion of samples identified as presumptive ESBL-/AmpC-producing indicator *E. coli* under the specific monitoring for ESBL-/AmpC-/carbapenemase-producing indicator *E. coli* from the four animal species, weighted by PCU.

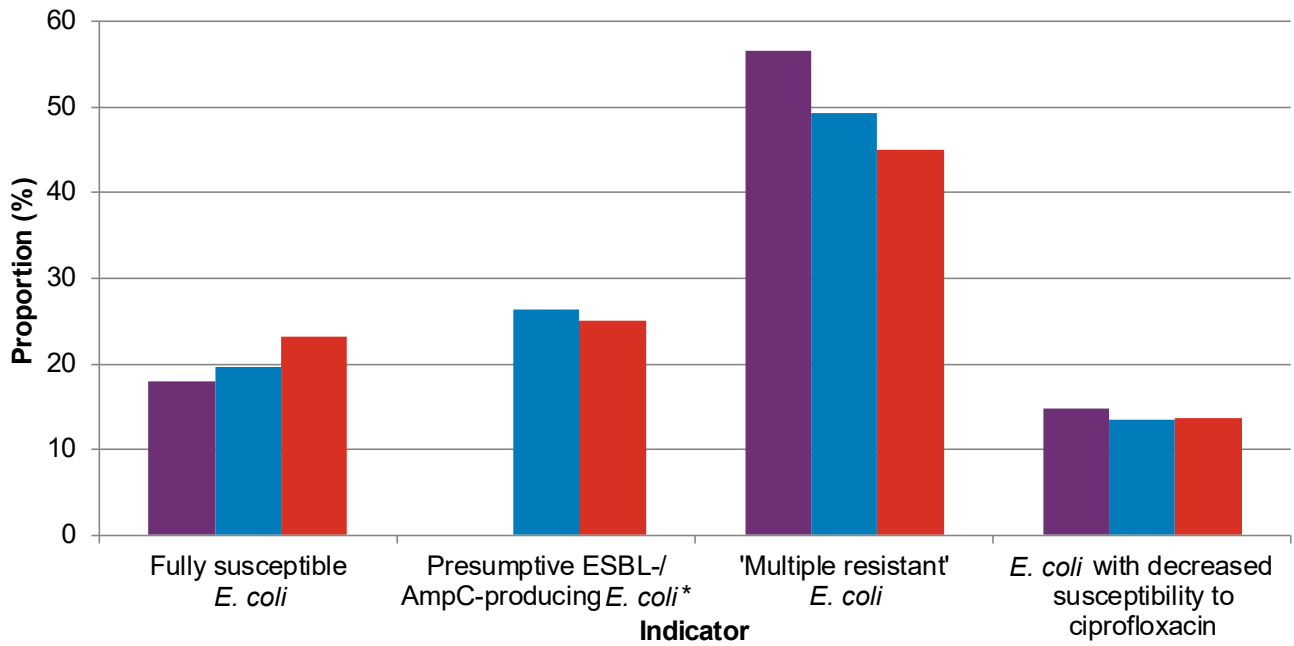
Because of the alternating sampling schedule, these indicators cannot be given for one calendar year, but are calculated based on any two consecutive calendar years to ensure data are available for all animal species covered by the indicator.

The primary indicator of full susceptibility showed an increase of 30% between 2014/2015 and 2016/2017, from 17.9% to 23.2%, indicating an increase in the level of antibiotic susceptibility in relation to the population of food-producing animal species (**Figure 3.2**).

The secondary indicators also showed an increase in susceptibility levels (**Figure 3.2**). The proportion of *E. coli* isolates that showed decreased susceptibility to at least three antibiotics, decreased by 20% (from 56.7% in 2014/2015 to 45.1% in 2016/2017). The proportion of *E. coli* isolates that showed decreased susceptibility to ciprofloxacin decreased by 7% (from 14.8% to 13.7%), and the proportion of samples identified as positive for presumptive ESBL-/AmpC-producing *E. coli* decreased by 5% between 2015/2016 (26.3%) and 2016/2017 (25.1%).

Figure 3.2: ECDC, EFSA and EMA recommended harmonised outcome indicators on AMR, interpreted using ECOFFs: primary (proportion of fully susceptible *E. coli* isolates) and secondary (proportion of presumptive ESBL-/AmpC-producing *E. coli* isolates; proportion of 'multiple resistant')

E. coli isolates; proportion of *E. coli* isolates showing decreased susceptibility to ciprofloxacin), 2014/15 (■), 2015/16 (■) and 2016/17 (■)



* Data not available for 2014/15.

SALES DATA CORRECTIONS -



CHAPTER 4

Clinical Surveillance of Antibiotic Resistance

SALES DATA CORRECTIONS - SEE EXHIBIT

4.1 Summary

Taken overall, the resistance levels of many veterinary bacteria have not changed greatly over the period covered by this report (2015–2017). The number of isolates that are resistant to four or more antibiotics has also remained relatively unchanged for many organisms over this period.

Most isolates of the main respiratory pathogens in sheep, cattle and pigs were susceptible to enrofloxacin and florfenicol (the antibiotics available for treatment), with the exception of a single *M. haemolytica* from cattle which was resistant to florfenicol. Penicillin resistance (using BSAC human CBPs) was not detected in *Streptococcus suis* isolates from pigs over the period 2015–2017 or in *S. dysgalactiae* or *S. uberis* from bovine mastitis. Livestock-associated methicillin-resistant *S. aureus* (LA-MRSA) CC398 was recovered in five instances (four in pig and one in pheasant) in the UK in 2017.

Considering those antibiotics and pathogens of particular importance and interest in human medicine, cefotaxime-resistance in diagnostic *E. coli* isolates from neonatal calves and neonatal lambs in 2017 was 12% and 3.6%, respectively (interpreted using BSAC human CBPs). Cefpodoxime-resistance in *E. coli* in the same year was 2.5% in neonatal piglets, 4.2% in chickens and not detected in turkeys. Resistance in *E. coli* from scanning surveillance of chickens which has previously shown an upward trend since 2013, contrastingly showed a marked decline between 2016 and 2017 for several antibiotics, coinciding with a reduction in antibiotic use in broilers. An exception to this general trend was resistance to doxycycline, which increased. An increase in doxycycline resistance was also noted in *E. coli* from scanning surveillance of neonatal and post-weaning pigs. Colistin-resistance was not detected in *E. coli* from scanning surveillance.

Of the *Salmonella* spp. isolates tested, 0.3% were resistant (using BSAC human CBPs) to ciprofloxacin; 72% of *Salmonella* spp. isolates were susceptible to all 16 antibiotic drugs tested. Of 187 *S. Typhimurium* isolates tested, none were resistant to amikacin, or ciprofloxacin, while a single *S. Typhimurium* DT1 isolate from a cat was resistant to ceftazidime and cefotaxime. Pentavalent (AmCSSuT) *S. Typhimurium* DT104 was isolated, mainly due to an increased number of incidents of this clone in cattle in 2017 compared to 2016. The number of *S. Enteritidis* isolates tested was higher in 2017 (n=102) compared to 2016 (n=16), mainly due to an outbreak of *S. Enteritidis* phage type (PT 8) that occurred in turkeys in 2017. This strain is commonly resistant to nalidixic acid. *S. Infantis* isolates resistant to four or more antibiotics were isolated from three poultry farms; follow-up investigations indicated successful elimination from these premises after cleaning and disinfection. Multiply resistant *S. Infantis* is rare in the UK but is commonly detected in some parts of Europe.

4.2 Introduction

Clinical surveillance is a programme of passive surveillance which evaluates antibiotic resistance in bacteria of relevance to animal health isolated from carcasses or other diagnostic samples submitted by private veterinary surgeons to APHA veterinary laboratories in England and Wales. When a potential bacterial pathogen is identified, antibiotic susceptibility testing is performed to provide the practitioner with the relevant information for treatment. Similar programmes are

conducted by Scottish (SRUC Veterinary Services) and Northern Irish (Agri-Food Biosciences Institute, AFBI-NI) 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* spp. 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/576403/1095349-v1_contingency_external.pdf.

4.3 Methods

4.3.1 Sample sources and target microorganisms

Bacterial populations were obtained from samples of field cases of clinical disease undergoing investigation by practising veterinary surgeons for diagnostic purposes.

For *Salmonella* spp. isolates, any laboratory isolating *Salmonella* spp. from animals and their environment in Great Britain is required to notify and submit an isolate to a Defra-approved laboratory for characterisation including antibiotic sensitivity testing.

A network of APHA veterinary laboratories performed the susceptibility tests reported in 2017. The laboratories are situated throughout England and Wales with one laboratory located in Scotland.

4.3.2 Susceptibility testing methodology

The susceptibility tests described in this chapter were performed (unless otherwise stated) using a disc diffusion technique on Isosensitest Agar (Oxoid) with appropriate media supplementation where necessary for fastidious organisms. The disc concentrations used were as stated in Table S4.1.1 of the supplementary material and a semi-confluent inoculum was used in the test procedure. The method used was that formerly recommended by the British Society for Antimicrobial Chemotherapy (BSAC). Where published human breakpoints were available from BSAC, these were used for the interpretation of the veterinary antibiotic susceptibility results.

Isolates were classed as either sensitive or resistant; intermediate isolates under the BSAC guidelines were considered to be resistant. The disc diffusion breakpoints used are given in Table S4.1.1 of the supplementary material which also provides the MIC corresponding to that zone diameter breakpoint where this is known or has been estimated from APHA data on file.

For some veterinary antibiotic and organism combinations, there are no published breakpoints available using either the BSAC method or other methods. Published breakpoints are therefore not available for all animal species and for all of the bacterial organism/antibiotic combinations which may require testing. In these cases, a uniform cut-off point of 13 mm zone size diameter has been

used to discriminate between sensitive and resistant strains; an intermediate category of susceptibility has not been recorded. This breakpoint is the historical APHA veterinary breakpoint and although it has been used for a considerable number of years, published validation data are not available for a number of organism-antibiotic combinations (Table S4.1.1 of the supplementary material). However, where the majority of isolates of a particular organism are highly resistant or fully susceptible to an antibiotic, breakpoint issues may affect a low number of isolates.

The panels of antibiotics which may be tested at a particular APHA laboratory can show slight variation, dependent on the circumstances of the case and the requirements of the veterinary surgeon administering treatment.

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

Certain antibiotics included in the results in this chapter are not authorised for use in food-producing animal species (e.g. cefpodoxime, chloramphenicol, amikacin), or not authorised for use in the animal species for which susceptibility results are reported (e.g. tetracycline and trimethoprim in sheep). These antibiotics are however included in the test panels to monitor emergence or risk of resistance to those antibiotics in bacteria in man, or because no breakpoints are available for the antibiotic for which testing ideally should be taking place (e.g. tetracycline instead of oxytetracycline).

When more than 20 isolates of any pathogen are 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 material. When fewer than 20 isolates are recovered, results are presented in the supplementary material only.

4.4.1 Mastitis pathogens

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

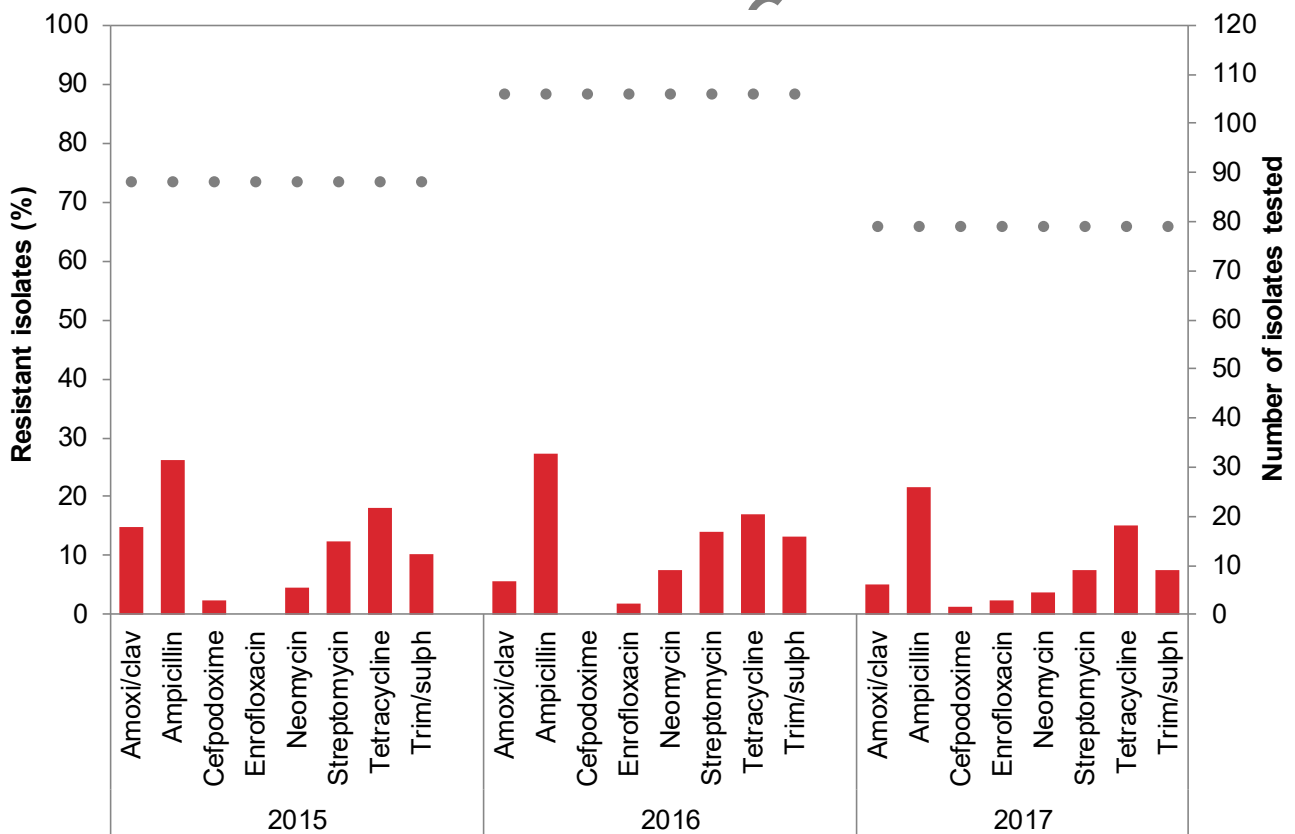
Similar to previous reporting years, the most frequently isolated organisms from milk samples were *Streptococcus uberis* (n=97), *Escherichia coli* (n=79), *Staphylococcus aureus* (n=78) and *Streptococcus dysgalactiae* (n=39). *Klebsiella pneumoniae* isolates, the majority of which originate from bovine mastitis cases, were frequently resistant to ampicillin. This reflects the intrinsic resistance to ampicillin shown by this organism. *Pseudomonas aeruginosa* isolates are commonly resistant to a range of antibiotics and isolates from bovine mastitis are no exception in this regard.

4.4.1.1 *Escherichia coli*

E. coli and other coliforms are one of the three main causes of bovine mastitis (resistance in *E. coli* isolates not associated with mastitis is reported in section 4.4.5.1). Most *E. coli* 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.

The total number and percentage of *E. coli* isolates from mastitis infections resistant to different antibiotics are presented in **Figure 4.1** and Table S4.2.1 of the supplementary material. As in previous reporting years, the highest level of resistance (based on BSAC human CBPs and veterinary zone size breakpoints) was observed to ampicillin (22%) followed by tetracycline (15%), streptomycin (8%) and trimethoprim/ sulfamethoxazole (8%). The percentage of isolates resistant to cefpodoxime in mastitis *E. coli* and coliform isolates (1%) was much lower than the percentage resistance to ceftazidime or cefotaxime observed in *E. coli* and coliform isolates from calves (7–22% in 2017; **Figure 4.9** and Table S4.7.9 of the supplementary material).

Figure 4.1: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from mastitis infections of cattle, 2015–2017

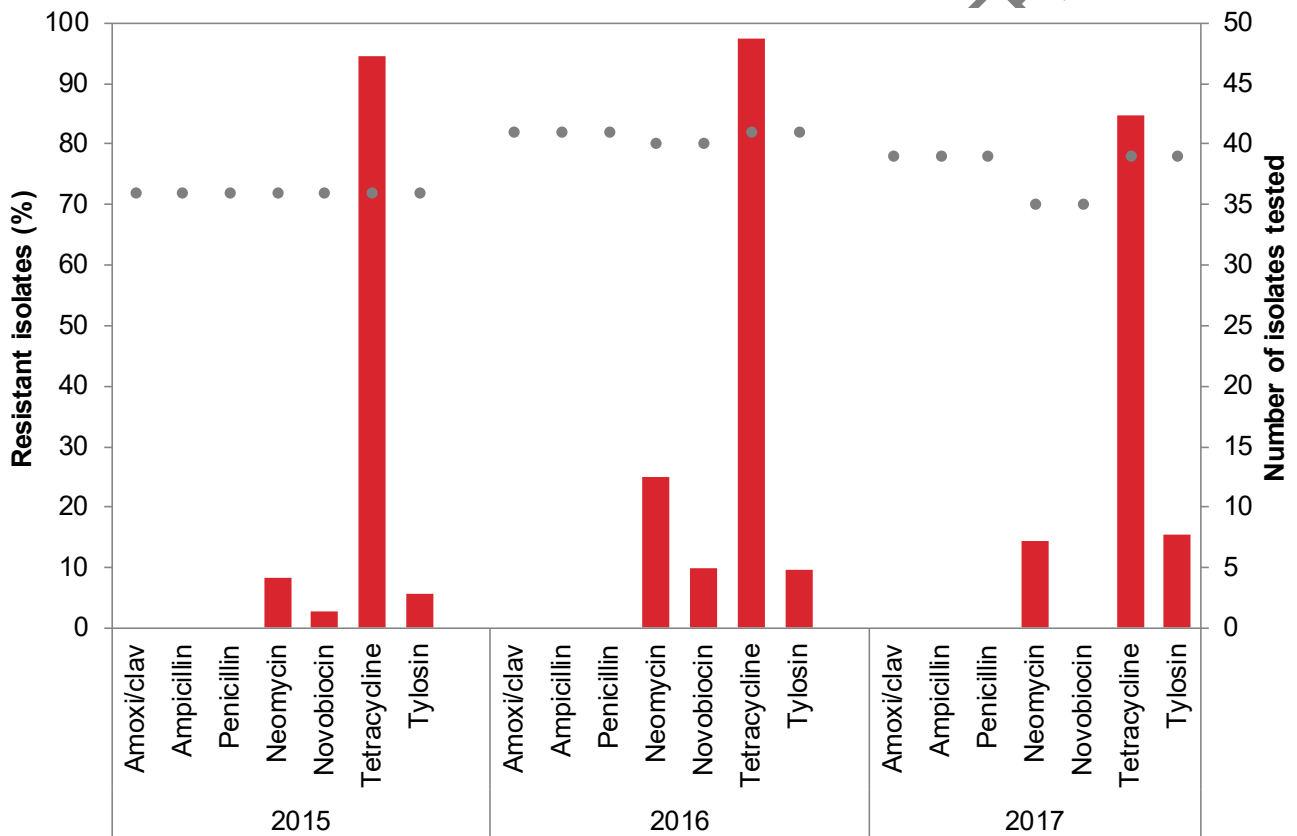


4.4.1.2 *Streptococcus dysgalactiae*

Streptococcus dysgalactiae is a commensal of the mucous membranes of cattle; it is a cause of mastitis and occasionally other diseases in cattle. It is not considered a zoonosis; Group C streptococci that can cause disease in humans constitute a separate population.

The total number of *S. dysgalactiae* cultured from mastitis infections and percentage isolates resistant to different antibiotics are presented in **Figure 4.2**. No resistance (using BSAC human CBPs and historical AHVLA veterinary breakpoints) to ampicillin, penicillin or amoxicillin/clavulanate was detected in *S. dysgalactiae* over the period 2015–2017, but 6–15% of isolates of *S. dysgalactiae* recorded each year were resistant to the macrolide tylosin (Table S4.2.2 of the supplementary material). These results have not been confirmed by determination of the MIC, but macrolide resistance has been reported in *S. dysgalactiae* isolates from bovine mastitis from other parts of the world. Resistance to neomycin is to be expected in *S. dysgalactiae* because streptococci show a degree of intrinsic resistance to aminoglycosides. Tetracycline resistance, recorded in between 85% and 98% of isolates in this period, is also recognised as being common in this species.

Figure 4.2: Number of isolates tested (●) and percentage (■) of resistant isolates of *Streptococcus dysgalactiae* from mastitis infections of cattle, 2015–2017



4.4.1.3 *Streptococcus uberis*

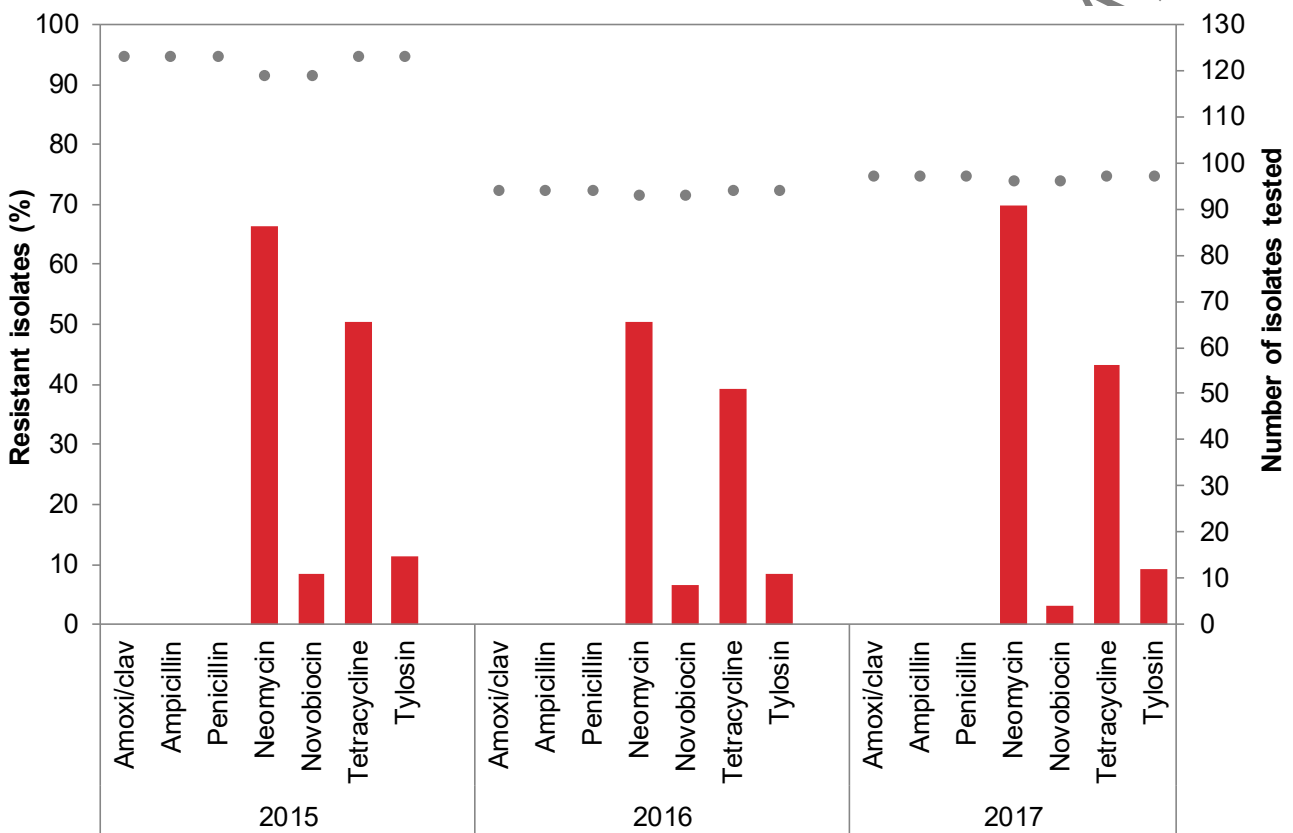
Streptococcus uberis is widely distributed in the environment and a normal commensal resident of the bovine vagina, tonsil and skin. It is a common cause of mastitis and not regarded as zoonotic.

The total number and percentage of *S. uberis* isolates from mastitis infections resistant to different antibiotics are presented in **Figure 4.3**. No resistance (using BSAC human CBPs and historical AHVLA veterinary breakpoints) to ampicillin, penicillin or amoxicillin/clavulanate was detected in *S. uberis* over the period 2015–2017 (Table S4.2.2 of the supplementary material). *S. uberis* isolates from bovine mastitis with reduced susceptibility to penicillin have been reported in France

(Haenni et al., 2010) and a single isolate of *S. uberis* was previously reported in 2013 from England and Wales with penicillin/ampicillin resistance.

Between 2015 and 2017, 9–11% of *S. uberis* isolates were resistant to tylosin. Resistance can be mediated by the induction of a plasmid-encoded enzyme which methylates the 20S ribosomal RNA sub-unit and prevents binding of the macrolide to the ribosome and so disrupts protein synthesis. However, the exact mechanism of resistance has not been elucidated in the isolates recorded here. Resistance to tetracycline was also detected in *S. uberis* isolates between 2015 and 2017, ranging from 39% to 50%.

Figure 4.3: Number of isolates tested (●) and percentage (■) of resistant isolates of *Streptococcus uberis* from mastitis infections of cattle, 2015–2017



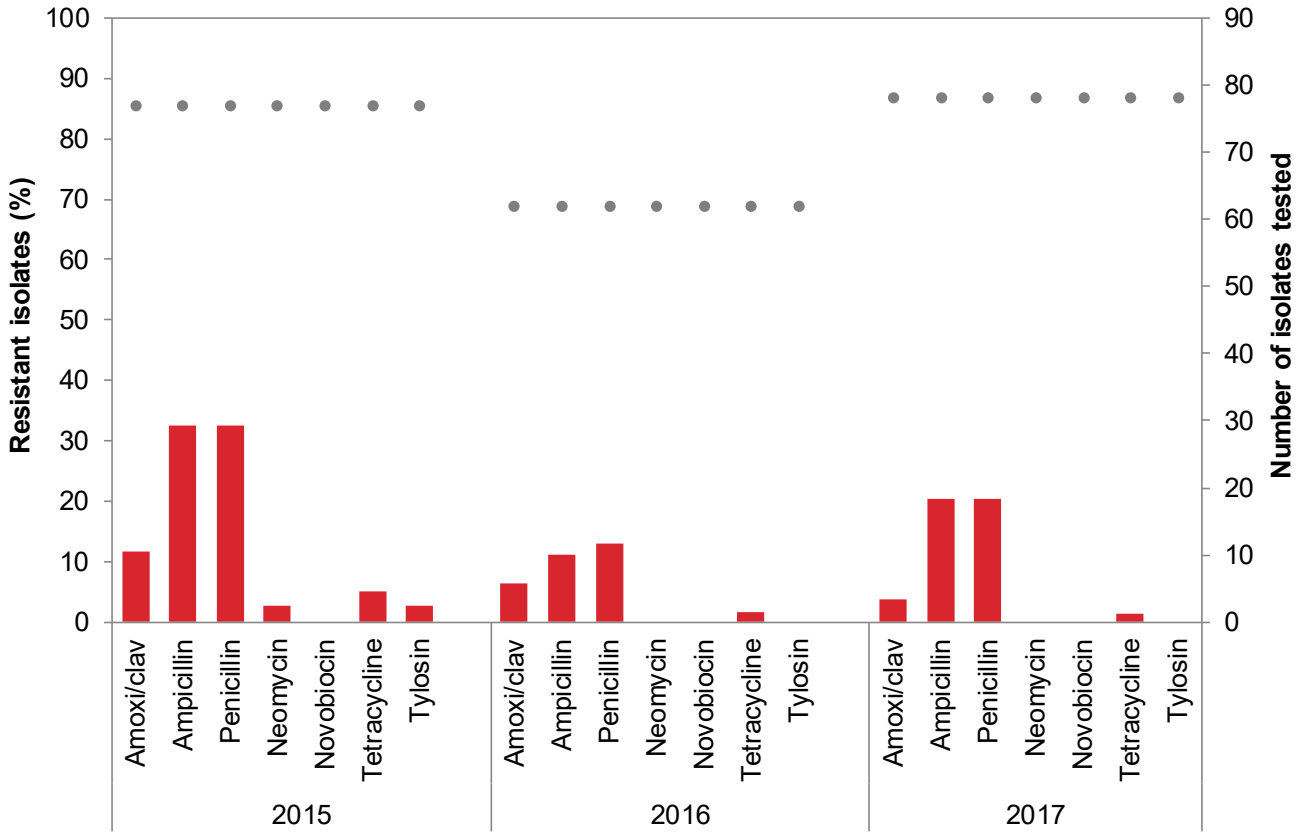
4.4.1.4 Staphylococcus aureus

Staphylococcus aureus is normally resident on the skin and mucous membranes of cattle and is a common cause of mastitis.

The total number and percentage of *S. aureus* isolates from mastitis infections resistant to different antibiotics are presented in **Figure 4.4**. Resistance (using BSAC human CBPs and historical AHVLA veterinary breakpoints) to penicillin and ampicillin fluctuated between 11% and 33% over 2015–2017 and the underlying cause of this variation is unknown. Penicillin resistance in bovine *S. aureus* is thought to occur mainly via the production of beta-lactamases that degrade both penicillin and ampicillin. The genes encoding beta-lactamases can be located on plasmids and often on transposons and may be readily transferable by conjugation. *S. aureus* isolates from bovine mastitis resistant to amoxicillin/clavulanate are currently screened for susceptibility to ceftiofur in order to detect *mecA* and *mecC* MRSA. No MRSA isolates were detected from bovine

mastitis between 2015 and 2017. Amoxicillin/clavulanate resistance decreased from 12% to 4% over this period. Resistance to neomycin and novobiocin was not detected in 2016 and 2017. Tylosin (macrolide) resistance was recorded in low numbers (0–3%) of isolates. Resistance to tetracycline has remained at or below 5% (Table S4.2.2 from the supplementary material).

Figure 4.4: Number of isolates tested (●) and percentage (■) of resistant isolates of *Staphylococcus aureus* from mastitis infections in cattle, 2015–2017



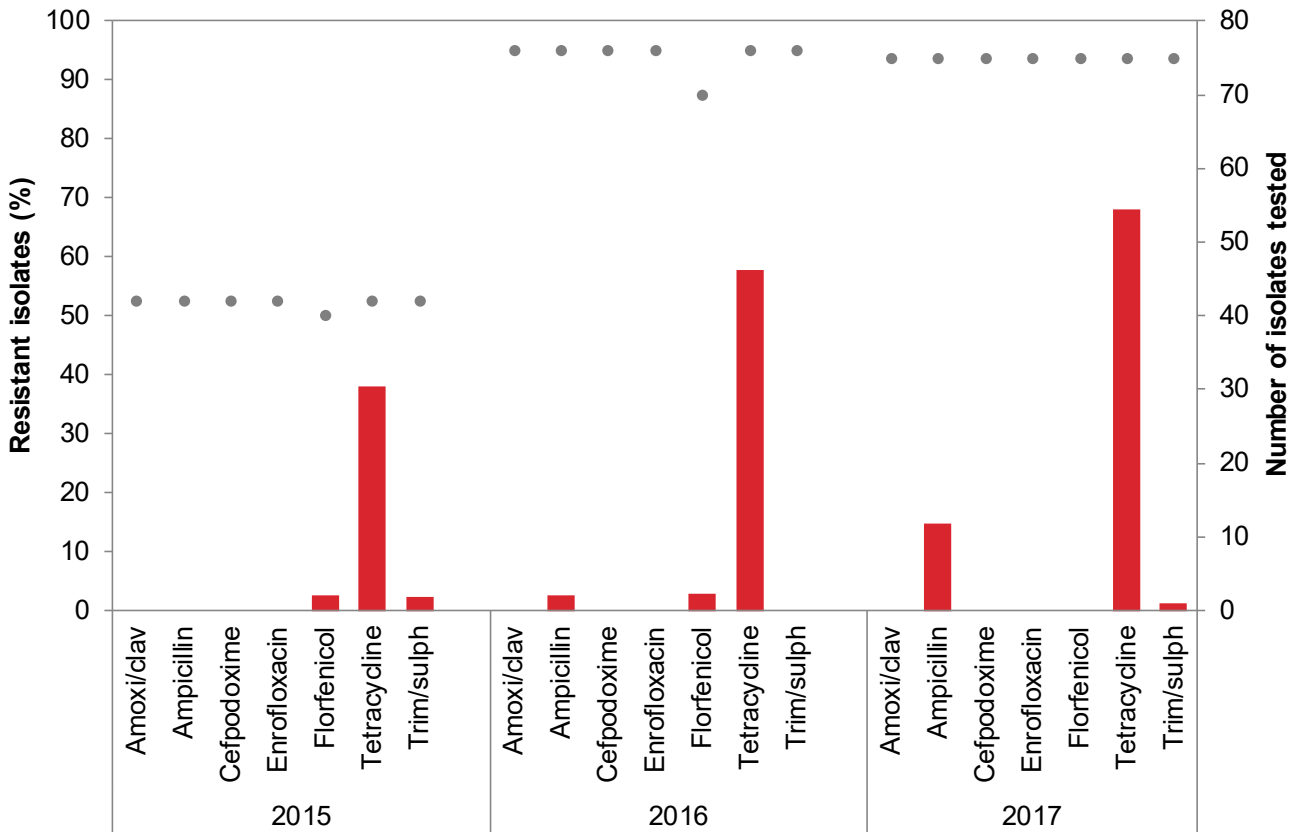
4.4.2 Respiratory pathogens

4.4.2.1 *Pasteurella multocida*

Pasteurella multocida causes primarily respiratory disease in cattle in the UK. Toxigenic strains are responsible for the development of atrophic rhinitis in pigs; strains of the organism can also affect poultry (fowl cholera). It is a rare pathogen of sheep in the UK.

Resistance (using BSAC human CBPs and historical AHVLA veterinary breakpoints) to ampicillin, tetracycline, trimethoprim/sulphonamide and florfenicol was found in bovine isolates from 2015 to 2017 (Figure 4.5 and Table S4.3.1 of the supplementary material). Resistance to ampicillin was not detected in 2015 but rose to 15% in 2017 and resistance to tetracycline rose from 38% to 68% in the same period. Resistance to florfenicol and trimethoprim/sulphonamide fluctuated between 0% and 3%.

Figure 4.5: Number of isolates tested (●) and percentage (■) of resistant isolates of *Pasteurella multocida* isolates from respiratory infections of cattle, 2015–2017



There was no resistance to enrofloxacin or cefpodoxime detected in *P. multocida* isolated from pig, cattle or sheep in 2017.

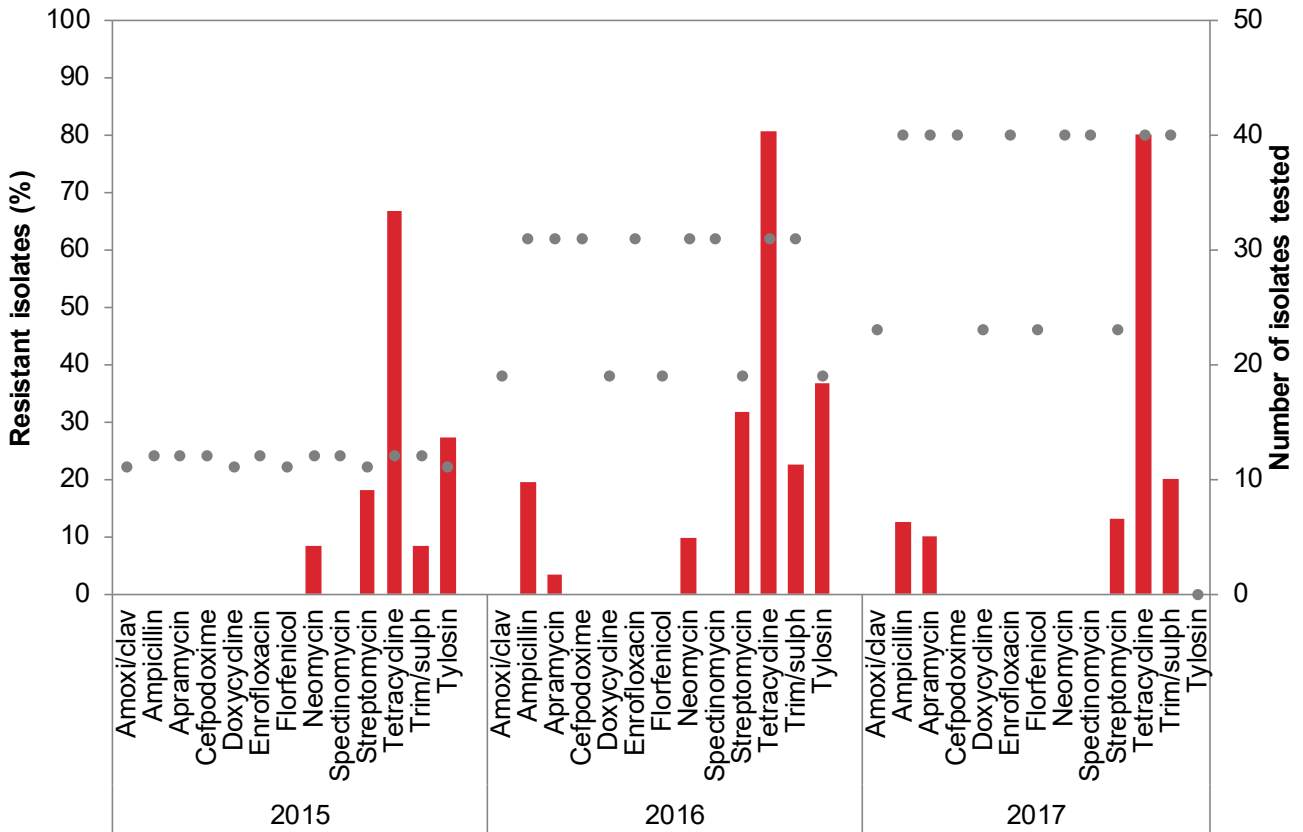
In isolates from pigs, ampicillin resistance was not observed in 2015 but was detected in both 2016 (19%) and 2017 (13%; **Figure 4.6** and Table S4.4.1 of the supplementary material). Tetracycline resistance was frequent in *P. multocida* from pigs (67–81%), although isolates were susceptible to doxycycline. This may reflect the resistance mechanism involved as some genes confer resistance to tetracycline but not to doxycycline, but might equally relate to breakpoint considerations.

Resistance to trimethoprim/sulphonamide, which was detected in cattle but not detected in isolates from sheep, was observed in isolates from pigs, varying between 8% and 23% during 2015–2017.

A low number of isolates of *P. multocida* were examined from sheep and resistance was observed to ampicillin and tetracycline (Table S4.5.1 of the supplementary material).

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Figure 4.6: Number of isolates tested (●) and percentage (■) of resistant isolates of *Pasteurella multocida* from respiratory infections of pigs, 2015–2017



4.4.2.2 Histophilus somni

Histophilus somni (formerly known as *Haemophilus somnus*) is a cause of pneumonia in calves. All isolates tested in 2015 and 2016 were susceptible (using BSAC human CBPs and historical AHVLA veterinary breakpoints) to the panel of antibiotics listed in Table S4.3.1 of the supplementary material; a single isolate in 2017 was resistant to tetracycline.

4.4.2.3 Mannheimia haemolytica

Mannheimia haemolytica is a common cause of respiratory disease in both cattle and sheep in the UK although different serotypes predominantly affect each species. There is carriage in the upper respiratory tract in healthy animals and ovine *Mannheimia* strains can also cause mastitis. *M. haemolytica* has also been more rarely recorded as causing mastitis in cattle.

No resistance (using BSAC human CBPs and historical AHVLA veterinary breakpoints) was detected to cefpodoxime or enrofloxacin in *M. haemolytica* isolated from cattle in 2017 (Table S4.3.1 of the supplementary material). Resistance to ampicillin (5%), florfenicol (2%) and tetracycline (42%) was detected in these isolates.

No resistance was detected in the ovine isolates from 2015–2017 to cefpodoxime, enrofloxacin or florfenicol. Ovine isolates showed a marked change in the prevalence of resistance to tetracycline from 3% and 4% in 2015 and 2016, to 48% in 2017; low numbers of isolates were resistant to either trimethoprim/sulphonamide (0–3%) or ampicillin (0–1%) over the period 2015–2017 (Table S4.5.1 of the supplementary material).

4.4.2.4 Other respiratory pathogens

Although *Bibersteinia (Pasteurella) trehalosi* isolates from sheep were generally susceptible, resistance (using BSAC human CBPs and historical AHVLA veterinary breakpoints) was detected to tetracycline and trimethoprim/sulphonamide in isolates recovered in 2015–2017 and a single isolate was resistant to enrofloxacin in 2016 (Table S4.5.1 of the supplementary material). Data on less frequently isolated ovine respiratory pathogens such as *Trueperella (Arcanobacterium) pyogenes* can be found in Table S4.5.1 of the supplementary material.

Actinobacillus pleuropneumoniae is a cause of pneumonia in pigs. Levels of resistance to apramycin, spectinomycin and other aminoglycosides detected in the disc diffusion test may reflect the rather high minimal inhibitory concentrations that have been described for *A. pleuropneumoniae* in the scientific literature for some aminoglycoside compounds (Leman et al., 1986). Over the period 2015–2017, resistance (using BSAC human CBPs and historical AHVLA veterinary breakpoints) was detected to ampicillin, doxycycline, tetracycline, trimethoprim/sulphonamide and tylosin (Table S4.4.1 of the supplementary material). Resistance to doxycycline occurred at a lower prevalence than resistance to tetracycline in 2017. This may again reflect the resistance mechanism involved as some genes confer resistance to tetracycline but not to doxycycline, but might equally relate to breakpoint considerations.

Resistance to tetracycline and trimethoprim/sulphonamide was detected in isolates of *T. pyogenes* from cattle, sheep and pigs; some isolates from pigs were also resistant to macrolides/lincosamides.

Further details on percentage of resistance for respiratory infections of cattle are included in Table S4.3.1 of the supplementary material. Further details on percentage of resistance for respiratory infections of pigs are included in Table S4.4.1 of the supplementary material.

4.4.3 Other animal pathogens

Brachyspira hyodysenteriae is the causative organism of swine dysentery, an enteric disease of pigs, resulting in serious ill-thrift in its chronic form. A limited range of antibiotics is available for the treatment of swine dysentery. Since tiamulin is an important antibiotic used for the treatment of swine dysentery, all available isolates of *B. hyodysenteriae* are tested for tiamulin susceptibility each year. This includes some 'repeat' isolates (i.e. isolates recovered from the same farm premises over a period of time) and two isolates are included from 2013 from the same premises which had a tiamulin MIC >8 mg/l.

The MIC values of *B. hyodysenteriae* isolates from pigs to tiamulin are presented in Table S4.6.1 of the supplementary material. There was an increase in the proportion of isolates with a tiamulin MIC >4 mg/l in 2012, 2013 and 2014, although the number of isolates tested each year is low. In 2015, 1/5 *B. hyodysenteriae* isolates tested was resistant to tiamulin. In 2016 three *B. hyodysenteriae* isolates were examined and all had tiamulin MICs <4 mg/l of tiamulin (breakpoint suggested for MIC determination by agar dilution (Rønne and Szancer, 1990, Duinhof et al., 2008)). In 2017, eight isolates were tested and all were susceptible to tiamulin with a MIC <2 mg/l of tiamulin (breakpoint suggested for broth microdilution).

Staphylococcus aureus causes a number of infections in poultry and game birds, including septicaemia, yolk sac infection, arthritis and osteomyelitis. Resistance to most of the antibiotics

tested was detected in isolates of *S. aureus* from chickens, turkeys and other avian species in one or more years, though resistance to trimethoprim/sulphonamides was not observed (Table S4.6.4 of the supplementary material).

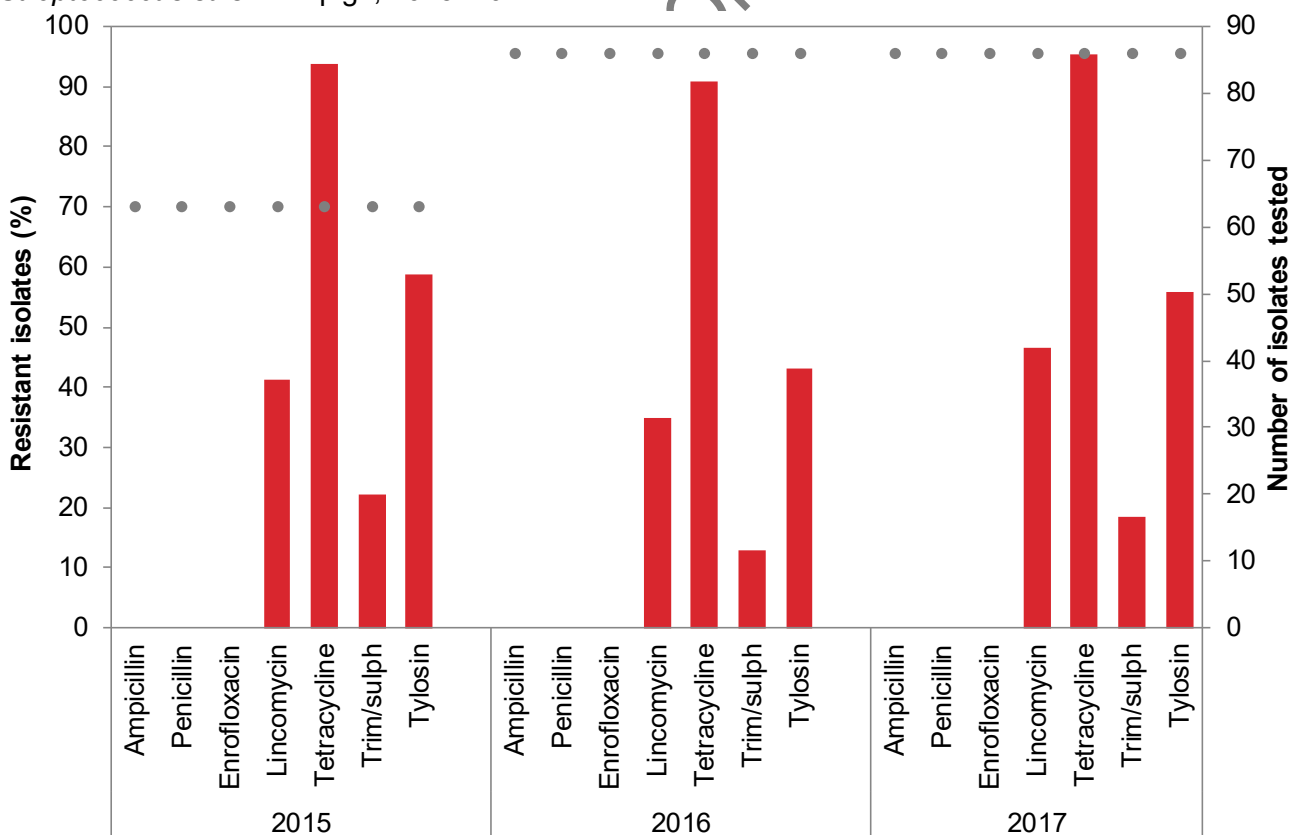
Streptococcus dysgalactiae is the major cause of infectious arthritis in young lambs and is probably carried on the mucous membranes of a small proportion of sheep. The degree of relatedness between ovine and bovine strains of *S. dysgalactiae* is not known. Levels of resistance to tetracyclines in ovine isolates of *S. dysgalactiae* were high and similar to those recorded for bovine isolates. There was no resistance to ampicillin detected in ovine *S. dysgalactiae* isolates, though two isolates were reportedly resistant to cefalexin (Table S4.6.5 of the supplementary material).

4.4.4 Zoonotic pathogens

4.4.4.1 *Streptococcus suis*

Streptococcus suis is a pathogen of pigs that can cause pneumonia, meningitis and arthritis. In rare cases, it can also infect man. Penicillin and ampicillin are often recommended for treatment of *S. suis* in pigs, but no resistance to these antibiotics was detected in 2015–2017. Considering the other antibiotics tested, isolates resistant to tetracycline (91–95%), tylosin (43–59%), lincomycin (35–47%) and trimethoprim/sulphonamide (13–22%) were detected (Figure 4.7).

Figure 4.7: Number of isolates tested (●) and percentage (■) of resistant isolates of *Streptococcus suis* from pigs, 2015–2017



Tetracycline is not commonly used for the treatment of this disease in pigs. *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. The

findings suggest that treatment with the HP-CIA enrofloxacin (a fluoroquinolone) was rarely indicated in these cases as no resistance to this antibiotic was detected. Further details are presented in Table S4.6.2 of the supplementary material.

4.4.4.2 Livestock Associated-MRSA

Livestock-associated methicillin-resistant *Staphylococcus aureus* (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 humans 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>.

Since the first discovery in 2005, LA-MRSA was found to be prevalent in livestock around the world. It was detected in the UK for the first time in 2013, and sporadic cases are detected annually. Clonal Complex (CC) 398 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.

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.

In 2017, LA-MRSA CC398 was detected in England in young pigs with skin lesions, from which *Staphylococcus hyicus* was also recovered and considered to be the primary pathogen. In Scotland, LA-MRSA CC398 was recovered from a diagnostic sample from a pheasant and in Northern Ireland from three samples from pigs.

Table 4.1: Findings of LA-MRSA in the UK by government laboratories, 2013-2017

Country	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
	CC398	2017	Pig	Clinical 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
	CC398	2017	Pig	Clinical investigation
	CC398	2017	Pig	Clinical investigation
	CC398	2017	Pig	Clinical investigation
Scotland	CC398	2017	Pheasant	Clinical investigation

4.4.4.3 Other zoonotic pathogens

Erysipelothrix rhusiopathiae is widely distributed in nature and occurs as a commensal or pathogen of a very wide range of vertebrate and invertebrate species. The main reservoir amongst the domestic species is probably pigs, though infection of both birds and rodents is said to be common. A low number of isolates of this organism were tested and the main resistance detected was to tetracycline and trimethoprim/sulphonamide in pigs, sheep and chickens. All isolates, irrespective of the species from which they were isolated, were susceptible to penicillin/ampicillin (data not shown; Table S4.6.3 of the supplementary material for information on resistance in *E. rhusiopathiae* isolated from pigs), which is the usual treatment for humans infected with this organism.

Listeria spp. are widely distributed in the environment and can be isolated from soil, decaying vegetation and poorly fermented silage. Asymptomatic faecal carriage occurs in man and in many species of animal. Only low numbers of bovine isolates were tested (data not shown). Cefalexin-resistance was observed in both bovine and ovine isolates, reflecting the intrinsic resistance of *Listeria* spp. to this antibiotic. Isolates were otherwise sensitive, apart from low numbers of isolates from cattle and sheep which were resistant to tetracycline (Table S4.6.5 for details on *L. monocytogenes* recovered from sheep infections). *Listeria ivanovii* was recovered from sheep in 2015 and 2017 and was largely susceptible (data not shown).

A limited number of isolates of *Klebsiella pneumoniae* have been recovered from avian species; the isolates were resistant to ampicillin reflecting intrinsic resistance (data not shown). A low

number of isolates of *Yersinia pseudotuberculosis* from sheep were examined and these were fully susceptible to the panel of antibiotics. *Yersinia enterocolitica* was reported in 2017 and was also susceptible (data not shown).

Corynebacterium pseudotuberculosis, the cause of caseous lymphadenitis in sheep, has been reported as a zoonosis though it rarely infects man. However, corynebacteria may be an emerging zoonosis particularly in humans with intercurrent immunosuppressive disease, such as HIV infection. Resistance was not detected although only low numbers of isolates were available for susceptibility testing (data not shown). Irrespective of in vitro susceptibility, treatment of clinical cases of this infection in sheep is often difficult because of the difficulties in delivering sufficient antibiotic to the typical “onion-ring” abscesses that occur.

4.4.5 *Escherichia coli*

Escherichia coli is an important ubiquitous bacterium with zoonotic potential. *E. coli* is a commensal organism in animals and humans and has the capacity to function as a reservoir of transferable resistance determinants. The *E. coli* and coliforms presumptively identified as *E. coli* referred to in the tables in this report will include some *E. coli* strains which are pathogenic for animals as well as commensal strains.

This section includes all isolates of *E. coli* and coliform bacteria presumptively identified as *E. coli*, with the exception of isolates recovered from milk which are included in the section on mastitis organisms (see section 4.4.1.1). The majority of isolates reported in this section were recovered from faeces or intestinal contents. Data from England and Wales are presented in the main body of the report. Due to differences in methodology, data for Scotland and Northern Ireland are presented in Tables S4.7.1–S4.7.15 of the supplementary materials.

Collated data for the major food-producing animal species tested are shown in **Table 4.2**. In general, the level of resistance (based on BSAC human CBPs) to HP-CIAs in *E. coli* isolates was low during 2015–2017 (2–13%). The optimal situation is that resistance occurring in bacteria from animals to these particular compounds remains low, particularly where resistance occurs in a bacterial species which has direct or indirect public health relevance. The figures for young animals represent the age group in which most resistance is usually detected; resistance is usually less prevalent in older animals, including those older animals which are slaughtered for meat.

No resistance to amikacin was detected in *E. coli* isolated from cattle, pigs, sheep, turkeys and broilers in 2017, which reflects that this is not authorised for use in these species. Although the context in which the isolates were obtained means that the data should be interpreted with caution, there appeared to be a decrease in resistance to most antibiotics tested when looking at the collated figures from the major food-producing animal species. The exception is resistance to doxycycline, which showed an increase.

For cattle, pigs and sheep the data are also analysed by the age categories of neonatal, pre- or post-weaning and adult for each species (see **Figure 4.9**, **Figure 4.11** and **Figure 4.13**, respectively). The large differences in the prevalence of resistance commonly observed in cattle, pigs and sheep of different ages mean that the level of resistance shown in these summary tables for animals of all ages may reflect, to a significant degree, the proportions of each age-class of animal which have contributed to the total. Similar considerations can apply to the contribution of different animal production types, for example layer and broiler chickens. These considerations

should be borne in mind when interpreting these summary figures. The totals in this section exclude the *E. coli* isolates from bovine mastitis which can be found in section 4.4.1.1.

Table 4.2: Number of resistant and number of tested (% resistant) *Escherichia coli* isolates from cattle, pigs, sheep, broilers and turkeys (all ages, combined), 2015–2017

Antibiotic	Number of resistant/tested isolates (% resistant)		
	2015	2016	2017
Amikacin	3/524 (0.6)	4/467 (0.9)	0/266 (0)
Amoxicillin/clavulanate	282/1034 (27)	221/1123 (20)	149/694 (22)
Ampicillin	713/1101 (65)	683/1200 (57)	420/810 (52)
Apramycin	60/1073 (6)	68/1135 (6)	39/756 (5)
Cefotaxime	49/526 (9)	62/469 (13)	32/267 (12)
Cefpodoxime	34/474 (7)	7/314 (2)	8/377 (2)
Ceftazidime	34/526 (6)	41/469 (9)	18/267 (7)
Chloramphenicol	244/524 (47)	200/467 (43)	104/266 (39)
Doxycycline	132/451 (29)	165/538 (31)	151/323 (47)
Enrofloxacin	118/1101 (11)	78/1200 (7)	48/810 (6)
Florfenicol	174/709 (25)	164/792 (21)	88/479 (18)
Neomycin	266/1030 (26)	249/1100 (23)	134/695 (19)
Spectinomycin	462/1073 (43)	423/1135 (37)	233/756 (31)
Streptomycin	443/685 (65)	394/743 (53)	198/429 (46)
Tetracycline	708/1101 (64)	727/1200 (61)	463/810 (57)
Trimethoprim/sulphonamide	420/1101 (38)	461/1200 (38)	271/810 (34)

Note: tables detailing the full breakdown of proportion of resistance to all antibiotics in all livestock species can be found in section S4.7 of the supplementary material.

4.4.5.1 Cattle

The total number and proportion of resistant isolates from cattle (all ages) are shown in **Figure 4.8**. Resistance (using BSAC human CBPs) to 3rd generation cephalosporins (cefotaxime, ceftazidime or cefpodoxime) detected in *E. coli*/coliforms in animals will include resistance mediated by both ESBL- and AmpC- resistance mechanisms. The higher prevalence of resistance to cefotaxime versus ceftazidime observed, for example, in neonatal calves (**Figure 4.9**), is likely to reflect the occurrence of those ESBL enzymes which are cefotaximases, rather than ceftazidimases. The relatively high frequency at which *E. coli*/coliform isolates resistant to ampicillin (using BSAC human CBR) are recovered from young calves may reflect the use of dry cow intramammary infusions containing amino-penicillins in the dam and transfer of residual antibiotics to calves in colostrum, which may then exert a selective pressure on the intestinal bacterial flora of the neonatal calf.

Figure 4.8: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from cattle (all ages), 2015–2017

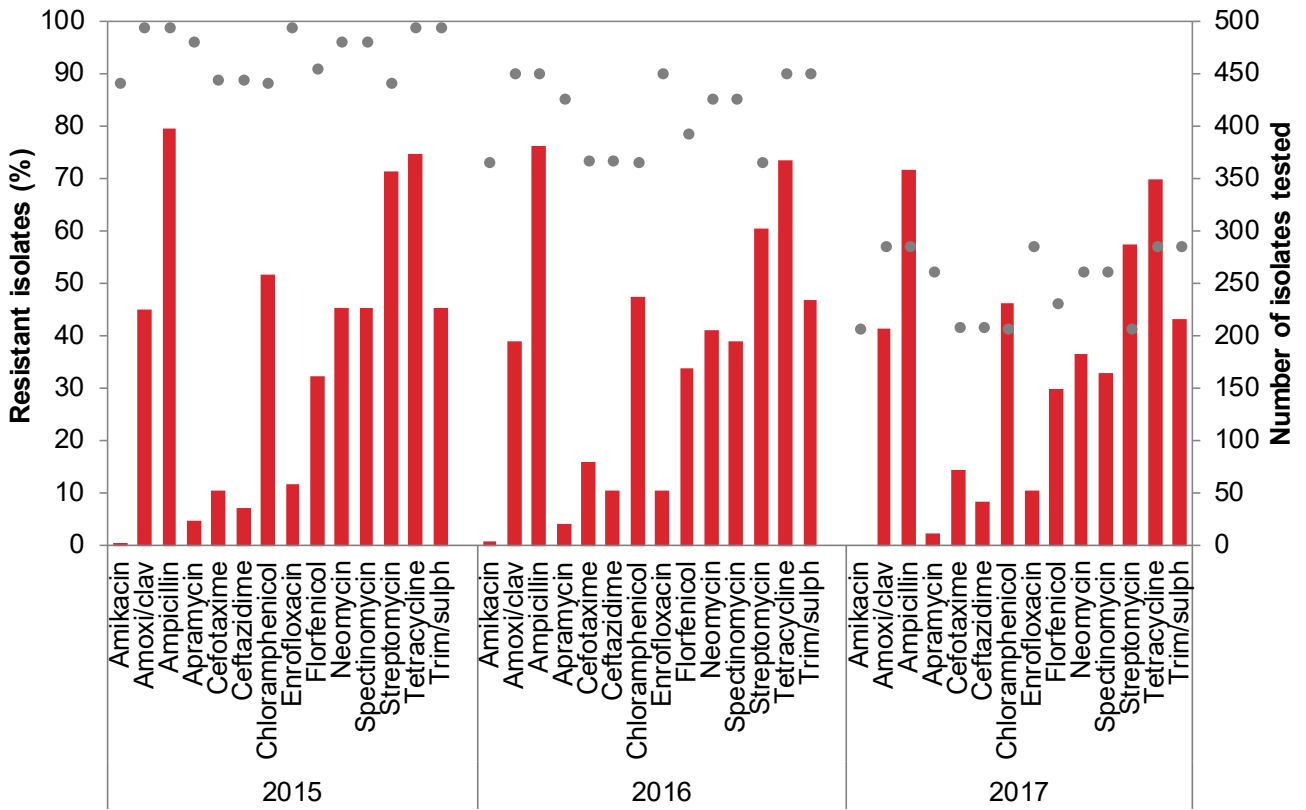
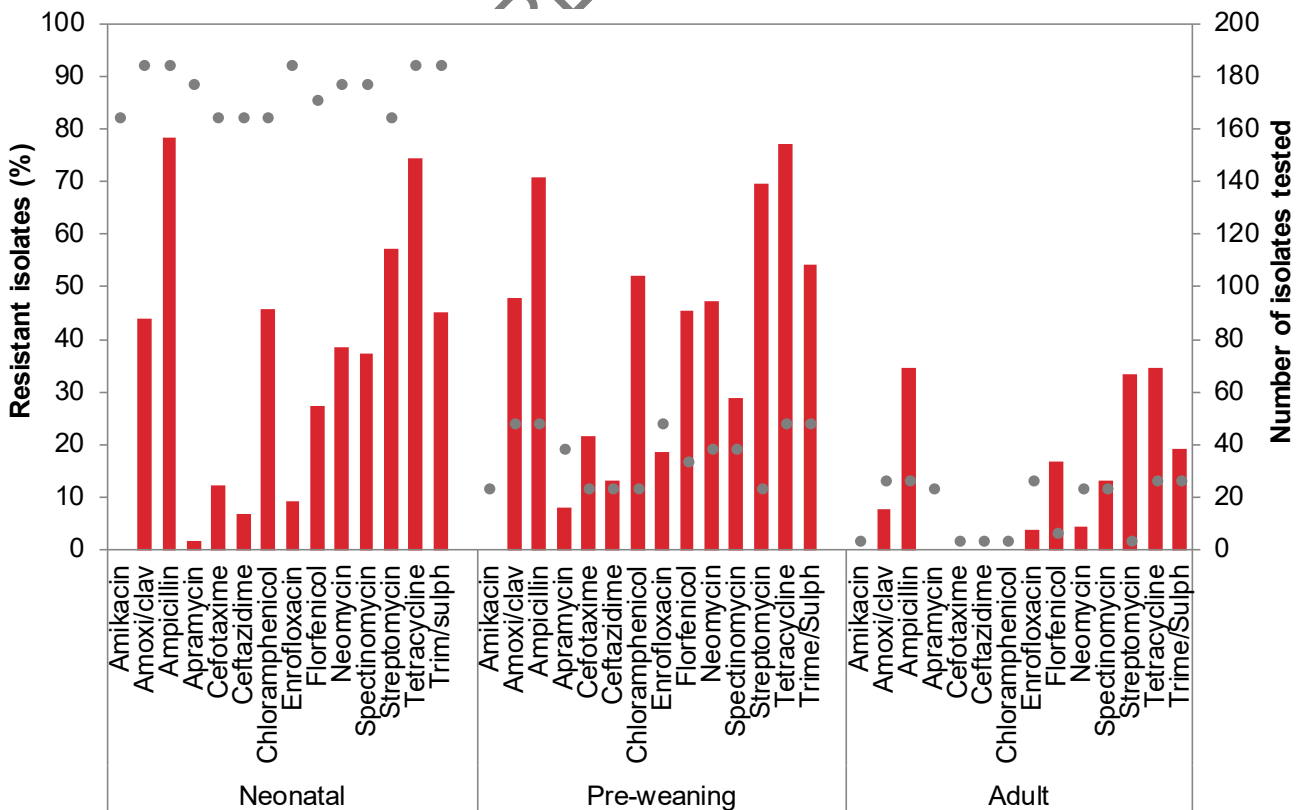


Figure 4.9: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from cattle (by age category), 2017



4.4.5.2 Pigs

The total number and proportion of resistant isolates from pigs are shown in **Figure 4.10**. Cefpodoxime resistance in *E. coli*/coliform isolates from pigs was detected in neonatal and post-weaning piglets at low levels of 0–3% in 2015–2017 (**Figure 4.11**). Apramycin resistance (using APHA historical zone size breakpoint) was 0–3% in neonatal pigs during this period, but was much higher at 20–26% in *E. coli* from pigs post-weaning. This is assumed to reflect the use of apramycin in controlling post-weaning diarrhoea in pigs. Resistance to neomycin or florfenicol (using APHA historical zone size breakpoint) was also higher in *E. coli* from post-weaning pigs compared to neonatal pigs, again, probably reflecting patterns of usage, though the difference was less marked. Resistance (using AHVLA historical veterinary breakpoint) to doxycycline increased in *E. coli* from neonatal and post-weaning pigs over the period, whilst tetracycline resistance (using APHA historical zone size breakpoint) was relatively high and stable over the period (post-weaning pigs) or showed a decline (neonatal pigs). The reasons for this observed resistance trend are not known, but might reflect breakpoint issues or changes in the underlying genetic basis of resistance, since certain genes *tet(B)* and *tet(E)* confer resistance to both tetracyclines and doxycycline in Gram-negative bacteria, whilst others, for example *tet(A)*, are not protective against doxycycline (Rice and Bonomo, 1996).

Figure 4.10: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from pigs (all ages), 2015–2017

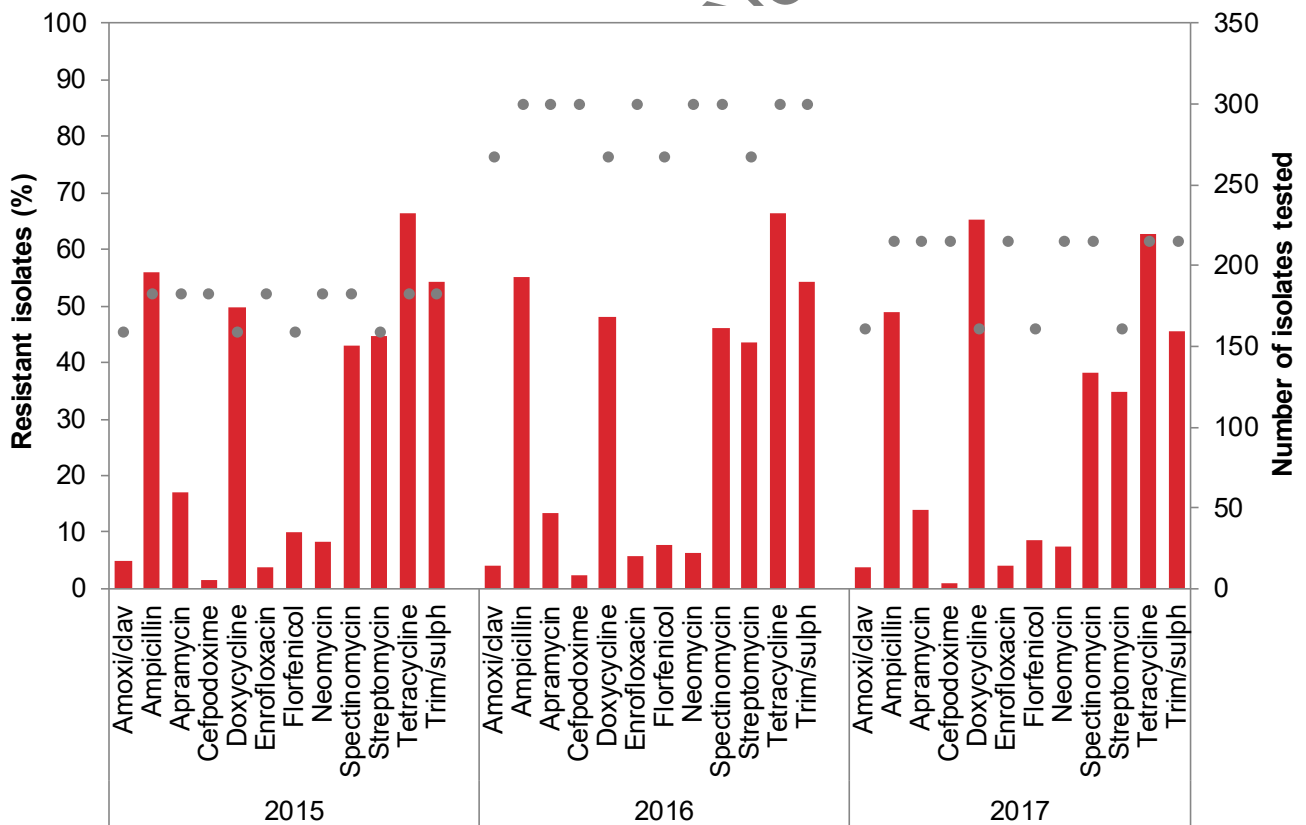
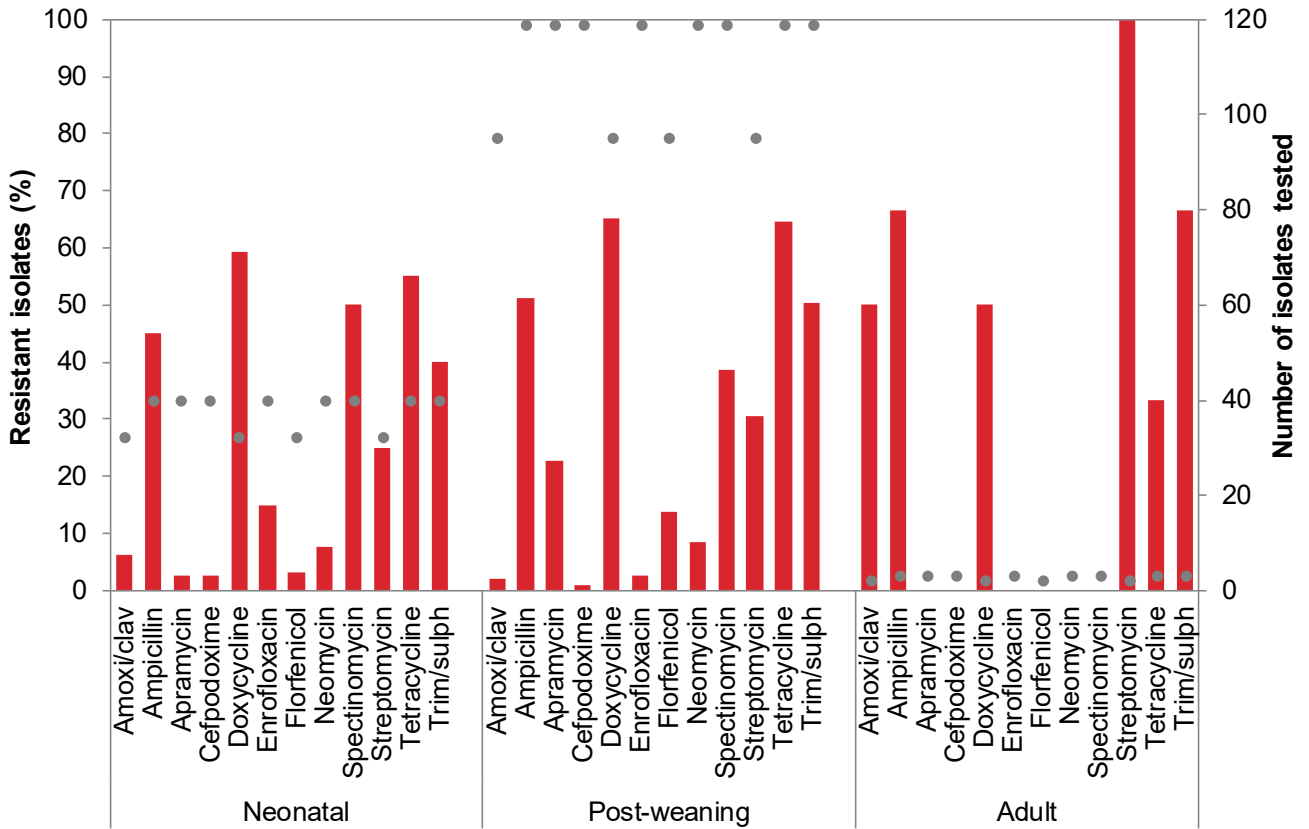


Figure 4.11: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from pigs by age category, 2017



4.4.5.3 Sheep

Lower levels of resistance to several antibiotics, including enrofloxacin and trimethoprim/sulphonamides, were generally observed in sheep than in pigs and cattle (**Figure 4.12**). Cefotaxime and ceftazidime resistance were detected in neonatal lambs, the former at a slightly higher prevalence; as in calves, this probably reflects the occurrence of ESBL enzymes which are cefotaximases, rather than ceftazidimases (**Figure 4.13**).

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Figure 4.12: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from sheep (all ages), 2015–2017

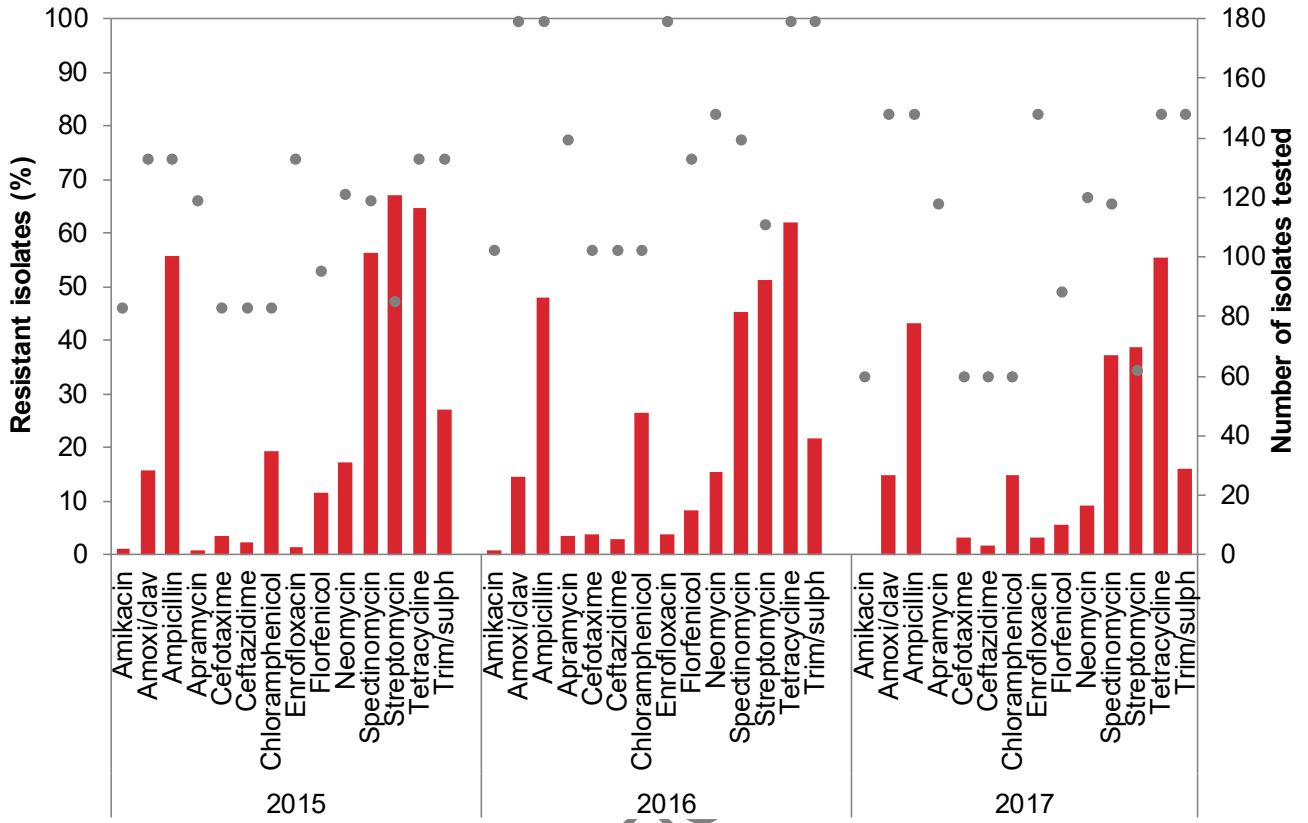
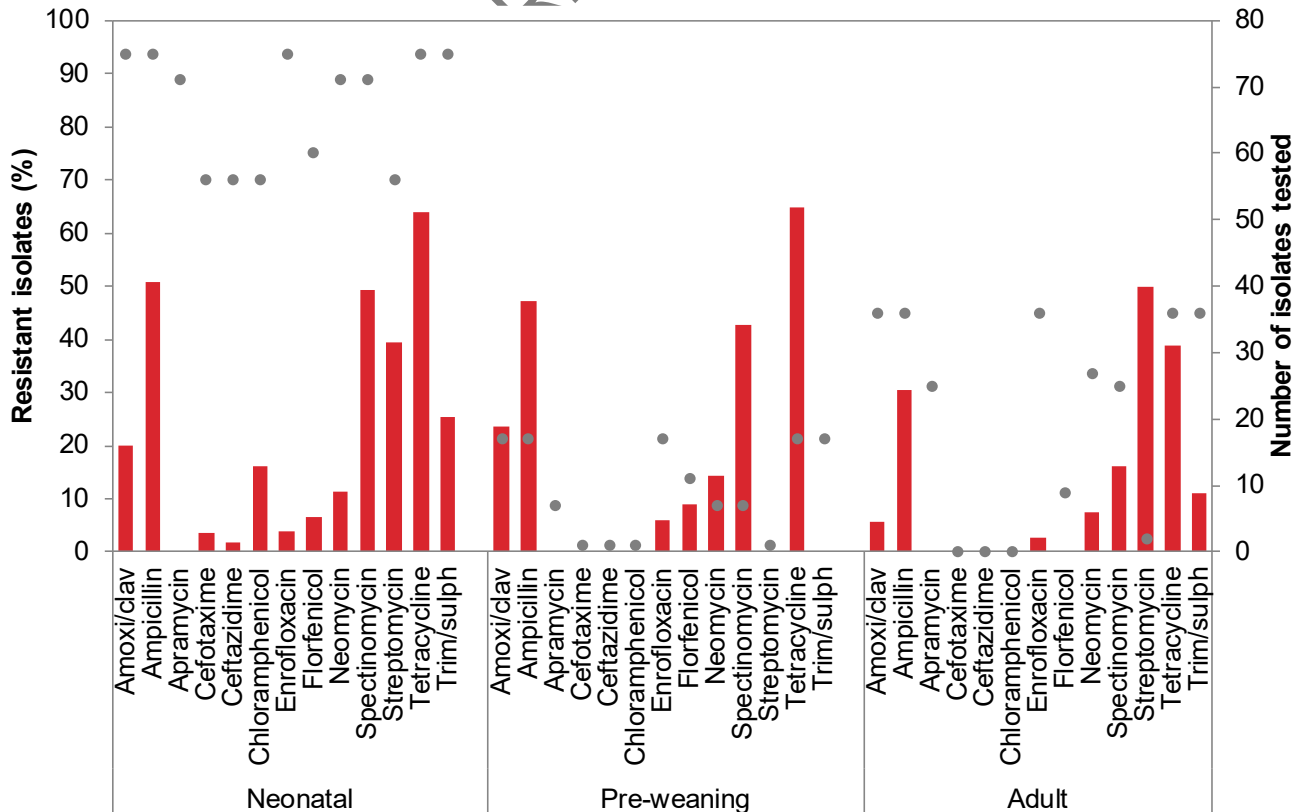


Figure 4.13: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from sheep (by age category), 2017



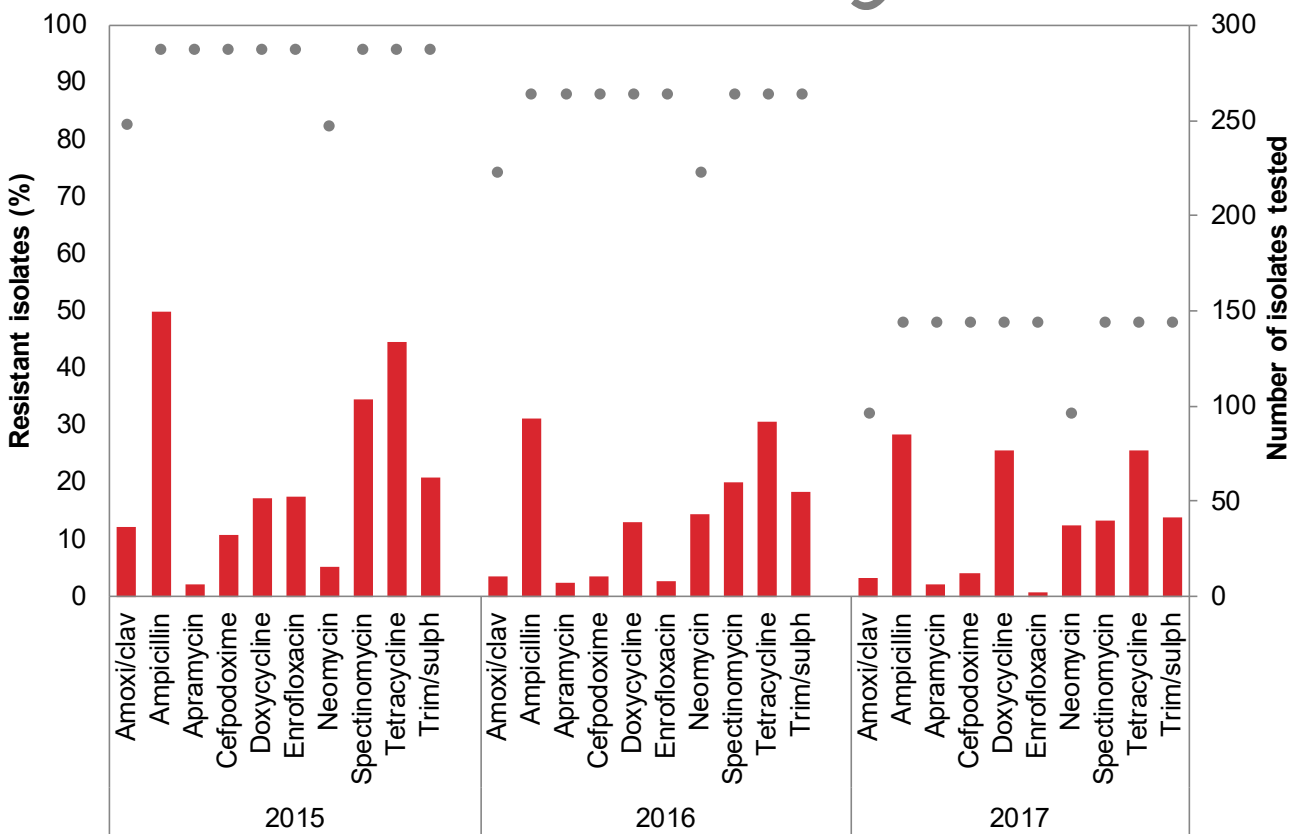
4.4.5.4 Chickens and turkeys

Cefpodoxime resistance ranged from 11% to 3% in *E. coli*/coliforms from chickens in 2015–2017 (Figure 4.14 and Table S4.7.5 of the supplementary material) and showed similar fluctuations in 2013–2014, suggesting perhaps bias in the sample or possibly clonal spread, since usage of 3rd generation cephalosporins has voluntarily been banned by BPC in poultry since 2012.

Cefpodoxime resistance was not detected in turkeys over the same period, although fewer isolates were examined from turkeys than from chickens (Table S4.7.6 of the supplementary material).

Levels of resistance (based on APHA historical zone size breakpoint) detected to the fluoroquinolone enrofloxacin in *E. coli*/coliforms from chickens over the reporting period 2015–2017 declined from 17% to 1%, temporally coincident with recent industry initiatives to reduce use of fluoroquinolones in broilers. These figures contrast with 9% to 10% resistance over the sampling period in *E. coli*/coliforms from neonatal calves, 3% to 15% in neonatal pigs (with an increasing trend) and 2% to 5% in neonatal lambs; only a few *E. coli* isolates were tested from turkeys.

Figure 4.14: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from chickens, 2015–2017



4.4.6 *Salmonella* spp.

Due to the relevance of *Salmonella* as a zoonotic pathogen, and the importance of the serovar and even phage type of an isolate when investigating potential epidemiological links between animal and human cases, results are presented by individual serovar/phage type in this section.

Resistance to 3rd generation cephalosporins and fluoroquinolones in *Salmonella* isolates is of

particular importance, since these antibiotics are most commonly used for the treatment of human salmonellosis, when 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 3rd generation cephalosporins and fluoroquinolones is detected in a food-producing animal(s), attempts are made to visit the farms in order to explain the significance of the findings and provide appropriate advice on control.

The number of cultures received from a farm varies enormously, 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 relating to one premises. Thus, 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 better indicate the prevalence of resistance, only the first isolate from each incident has usually been tested since the start of 1996. More detailed results can be found in S4.8 of the supplementary material.

4.4.6.1 All *Salmonella*

Of the 3,111 *Salmonella* isolates tested in total in 2017, 2,224 (72%) were sensitive to all of the antibiotics tested (based on disk zone size and BSAC human clinical breakpoints). This is similar to the situation in 2016, when 2,397 isolates were tested and 1,654 (69%) were sensitive to all of the antibiotics tested.

Similar to 2016, tetracycline resistance was most commonly found in *Salmonella* isolates originating from pigs and turkeys in 2017. This was also the situation for resistance to sulphonamides and streptomycin.

The resistance level to apramycin in all *Salmonella* serovars was 1.4% in 2017, similar to the level observed in 2016 (1.8%). *Salmonella* isolates from pigs, where apramycin-resistance was 23% in 2017, contributed most to the overall apramycin-resistance figure; in pigs, apramycin-resistance was observed in both monophasic *S. Typhimurium* variants 4,12:i:- and 4,5,12:i:-. In 2017, 24% of *Salmonella* 4,12:i:- isolates and 47% of *Salmonella* 4,5,12:i:- isolates from pigs were resistant to apramycin. Of all *Salmonella* isolates, 1.4% were resistant to gentamicin. No resistance was detected to the aminoglycoside amikacin.

The highest prevalence of resistance to nalidixic acid in 2017 was observed in *Salmonella* isolates from the environment, feed, turkeys and dogs. The high proportion of nalidixic acid resistant isolates in the environment and feed categories represents a difference from 2013–2016 when resistance to nalidixic acid was mostly observed in *Salmonella* isolates from turkeys and 'other avian species'. In turkeys, 17/17 *S. Enteritidis* isolates, 1/1 *S. Indiana* isolates and 15/15 *S. Senftenberg* isolates were resistant to nalidixic acid in 2017. The situation in turkeys was similar in 2013–2016, with nalidixic acid resistance frequently detected in these serotypes. In broilers, resistance to nalidixic acid was accounted for mainly by resistance in *S. Infantis* (8/8 isolates) with lesser contributions from *S. 13,23:i:-*, *S. 4,12:i:-* and *S. Mbandaka*. Ciprofloxacin resistance occurred in 0.3% of *Salmonella* isolates (1/17 *S. Enteritidis* isolates) from turkeys (n=180) and the ciprofloxacin-resistant isolate was also resistant to nalidixic acid. The other ciprofloxacin-resistant isolates detected in 2017 originated from dogs (*S. Kentucky*; 1/1 resistant), feed (*S. Kentucky*; 1/7 resistant), and the environment (*S. Enteritidis*; 1/1 resistant). *S. Infantis* and *S. Kentucky* with

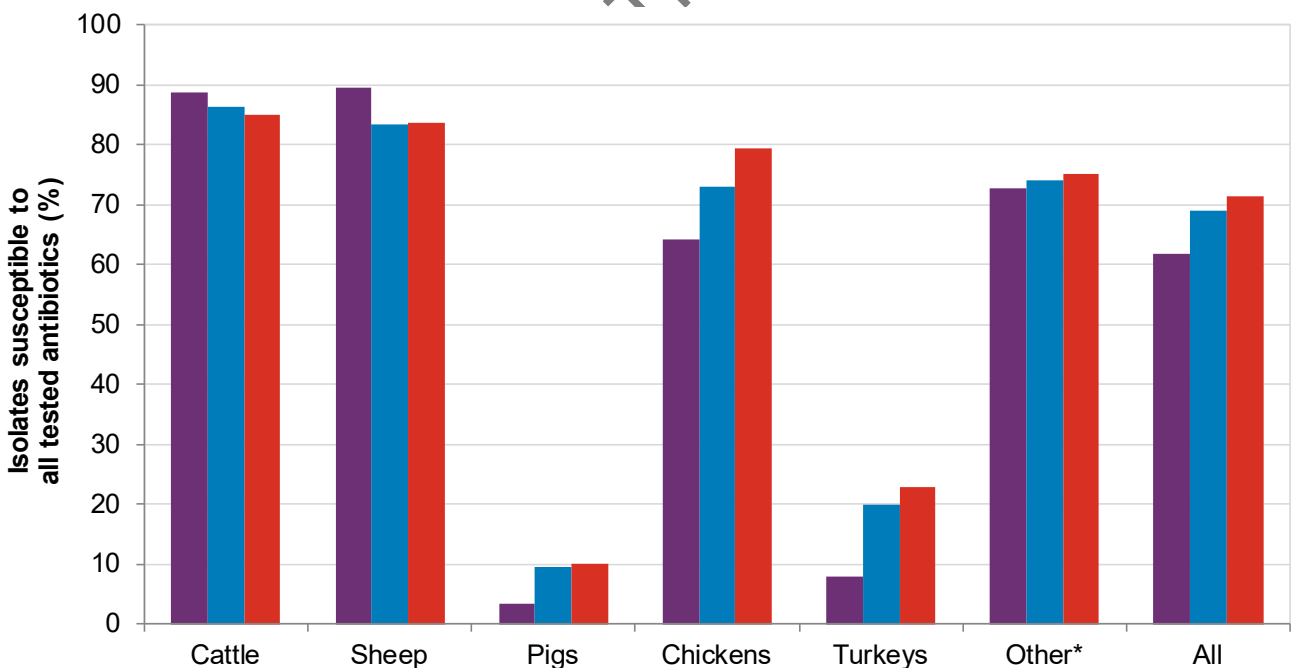
resistance to ciprofloxacin and at least three more antibiotics were detected in dogs. This is of interest because these serovar and resistance combinations are infrequent in the UK. The detection of these serovars in raw pet food in 2017 suggests the probable route of incursion for dogs, since raw pet food may contain raw meat sourced from outside the UK. Eight isolates (four from layer chicken and four from broilers) of the incomplete serovar 13,23:i:- were also resistant to ciprofloxacin. Resistance to cefotaxime and ceftazidime was detected in 2017 in a single *S. Typhimurium* from a cat.

4.4.6.2 *Salmonella* by animal species

Considering all *Salmonella* isolates from pigs, the percentage of fully susceptible isolates rose from 4% in 2015 to 9% in 2016 and 10% in 2017 (**Figure 4.15**). In turkeys, the percentage of fully susceptible isolates rose from 8% in 2015 to 23% in 2017, in chickens the percentage changed from 64% in 2015 to 79% in 2017. Conversely, a decreasing trend in susceptibility was observed for cattle (from 89% in 2015 to 85% in 2017) and sheep (from 90% in 2015 to 84% in 2017) although the level of susceptibility in isolates from these two animal species was overall much higher.

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.

Figure 4.15: Percentage of *Salmonella* spp. isolates susceptible to all tested antibiotics, from different sources and animal species, in 2015 (■), 2016 (■) and 2017 (■)



* Ducks, horses, dogs, other non-avian species, other avian species, feed and farm environment.

Cattle – Of the 392 *Salmonella* recovered in 2017, the highest level of resistance was to streptomycin (15%), sulphonamide compounds (15%), ampicillin (14%), tetracycline (14%) and chloramphenicol (11%). An increase in the levels of resistance to these antibiotics was seen compared with 2016.

Pigs – A large proportion of the 158 isolates tested in 2017 was resistant to sulphonamide compounds (88%), tetracycline (79%), ampicillin (79%) and streptomycin (78%). These levels of resistance fluctuated over the period 2015–2017. Resistance to neomycin was 20% in 2017, up from 6% in 2016.

Sheep – Of the 104 *Salmonella* isolates cultured in 2017, the highest level of resistance was observed to streptomycin, tetracycline, sulphonamide compounds and ampicillin (all 16%). An increase in the levels of resistance to these antibiotics was seen compared with 2016.

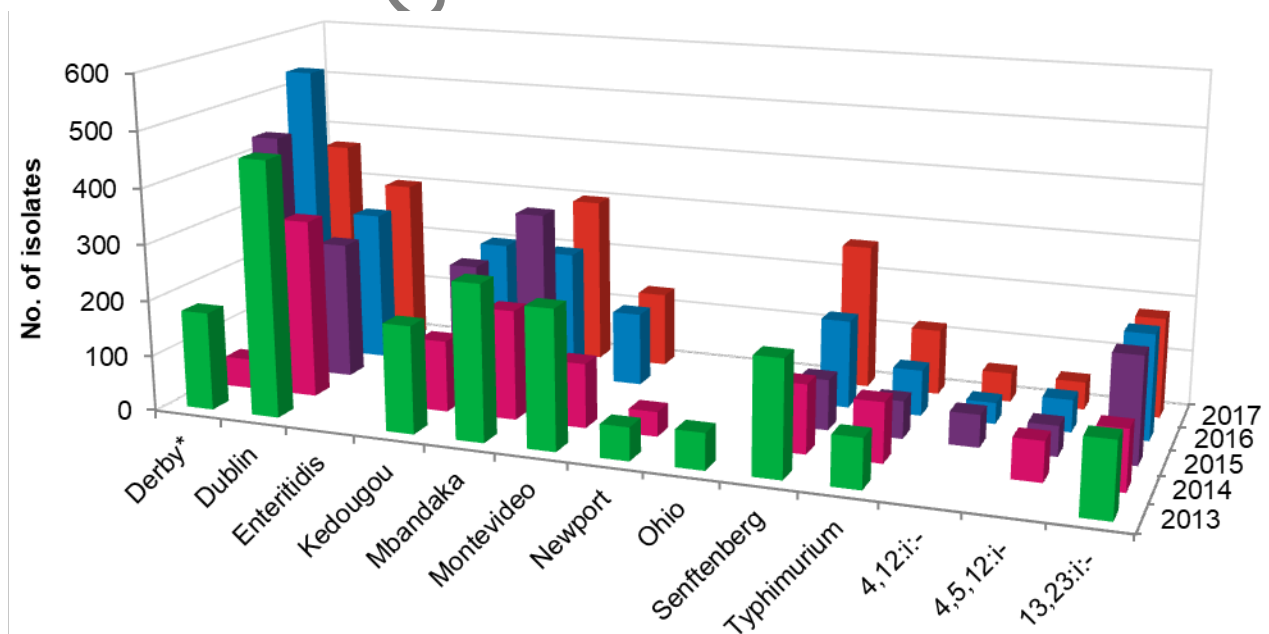
Chickens – In 2017, 873 isolates from chickens were tested for susceptibility. The highest levels of resistance were seen to tetracycline (11%) and sulphonamide compounds (15%), which were lower than the previous year. No resistance to 3rd generation cephalosporins was seen and resistance to fluoroquinolones (ciprofloxacin) was seen in 0.5% of the isolates. Similarly to previous years, gentamicin resistance was present in a very low number of isolates (0.1%).

Turkeys – Reflecting the resistance levels in isolates from other livestock species, the highest level of resistance in 180 isolates from turkeys was to sulphonamide compounds (57%), tetracycline (57%) and streptomycin (45%). These levels were lower than those reported in 2016. The level of ciprofloxacin resistance in turkeys (0.6%) decreased compared to the previous year.

4.4.6.3 Top ten *Salmonella* serovars isolated in 2013–2017

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’ serovars of non-typhoidal *Salmonella* isolates recovered from cattle, pigs, sheep, chickens and turkeys in Great Britain in 2013–2017 are presented in **Figure 4.16**. *S. Derby*, *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, 2013–2017



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

4.4.6.4 *Salmonella* Dublin

Of the 272 *Salmonella* Dublin cultures tested during 2017, 100% were susceptible to all 16 antibiotics. The percentage of *S. Dublin* isolates sensitive to all 16 antibiotics showed only slight fluctuations over the period 2006–2017 and the majority of isolates remained susceptible; this has been the situation since surveillance began in 1971. Most *S. Dublin* isolates (93%) originated from cattle in 2017 and this was similar to the situation recorded in previous years. *S. Dublin* isolates from species other than cattle in 2017 comprised eight isolates from sheep, nine from dogs, two from chickens, one from a ferret and one from animal feed (Table S4.8.7 of the supplementary material).

Table 4.3: Resistance in *Salmonella* Dublin: percentage of resistant isolates, 2013–2017

Antibiotic	Percentage of resistant isolates				
	2013 (n=393)	2014 (n=286)	2015 (n=226)	2016 (n=245)	2017 (n=272)
Ampicillin	0.3	0.7	1.8	0.4	0
Chloramphenicol	0	0	0.4	0.4	0
Furazolidone	0	0.3	0	0	0
Nalidixic acid	1	0	2.2	1.2	0
Neomycin	0.3	0.3	2.2	0	0
Streptomycin	1.3	2.4	4	1.6	0
Sulphonamide compounds	0	0.7	0	0	0
Tetracycline	0	0.3	0.4	0.4	0
Trimethoprim/sulphamethoxazole	0	0.7	0	0	0

4.4.6.5 *Salmonella* Typhimurium

The number of isolates of *Salmonella* Typhimurium tested in 2017 was 187. The eight most frequent definitive or undefined types subjected to susceptibility testing at APHA are given in **Figure 4.17**. Approximately one third (36%) of *S. Typhimurium* isolates were phage types DT104 or U302; there were no isolates of DT104B. The percentage of the eight most common definitive and undefined types of *S. Typhimurium* sensitive to all 16 antibiotics in 2016 is given in **Figure 4.18**. The percentage of *S. Typhimurium* isolates that were sensitive to all of the antibiotics tested was 34%, which is an increase from the 2016 figures (30%), but still lower than figures reported in 2015 (42%) and 2014 (44%).

Figure 4.19 and Table S4.8.8 of the supplementary material present an overview of percentage of resistance in *S. Typhimurium* to the antibiotics tested in 2015–2017. 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 2017. There was only one of the 59 DT104 isolates which was sensitive to all of the antibiotics tested in 2017. All remaining DT104 and U302 isolates were resistant to at least one of the 16 antibiotics tested (there were no isolates of DT104B examined in 2017). 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. The typical pentavalent resistance pattern AmCSSuT was the most common

resistance pattern seen in *S. Typhimurium* DT104 isolates, occurring in 86% of isolates. Three further isolates had this pentavalent resistance pattern with additional resistance to nalidixic acid. Only these three DT104 isolates were resistant to nalidixic acid and no isolates were resistant to trimethoprim/sulphamethoxazole. No isolates of DT104 were recovered from turkeys in 2012 to 2017 and DT104 isolates from turkeys, when detected, commonly showed nalidixic acid resistance in the preceding years. In 2017, nalidixic acid resistance in *S. Typhimurium* DT104 was only found in isolates obtained from cattle (6%).

Figure 4.17: Number of isolates of *Salmonella* Typhimurium of the eight most frequent definitive or undefined types subjected to susceptibility testing at APHA, 2017

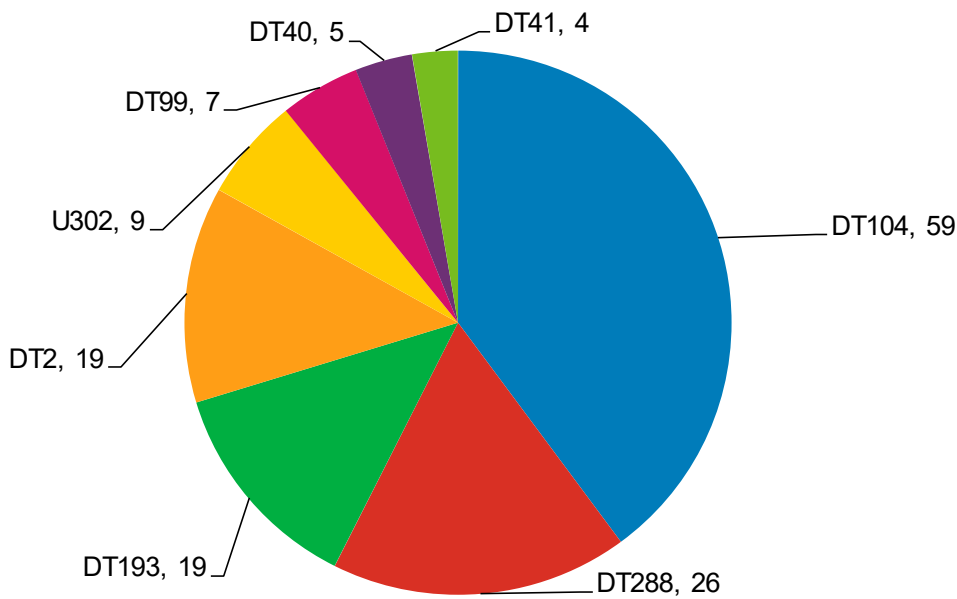


Figure 4.18: Percentage of fully susceptible isolates of *S. Typhimurium* of eight most frequent definitive or undefined types subjected to susceptibility testing at APHA, 2017

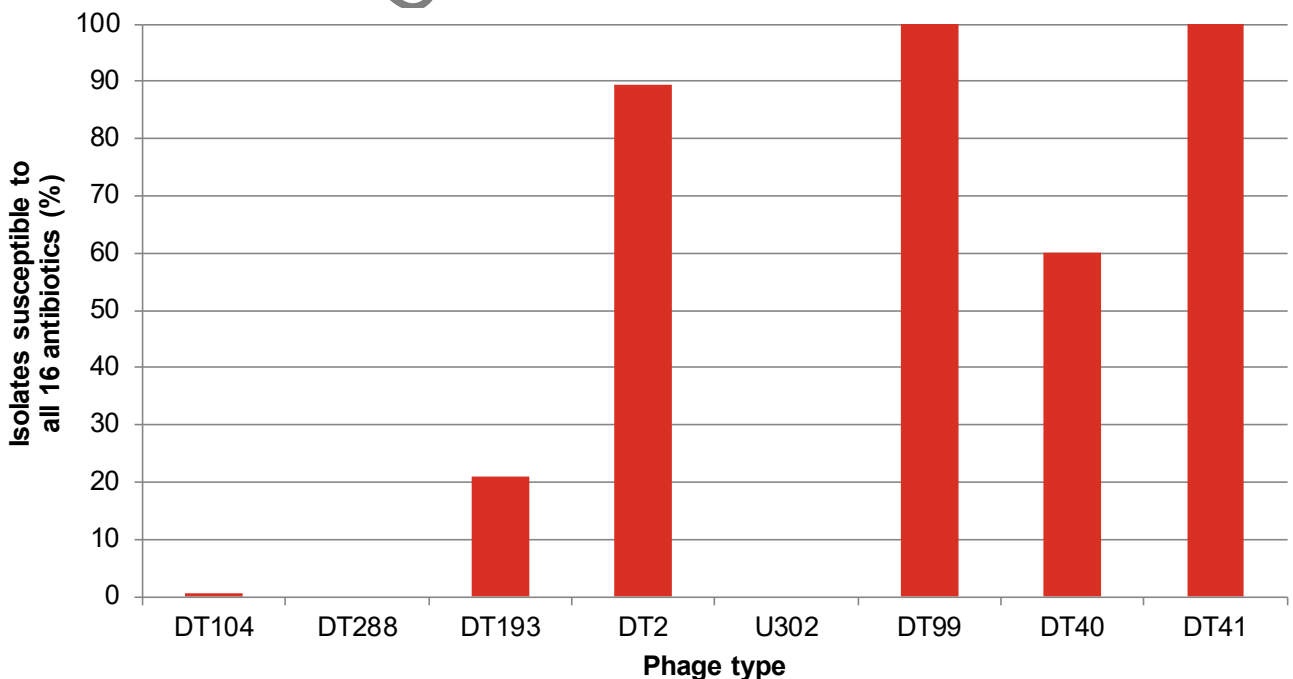
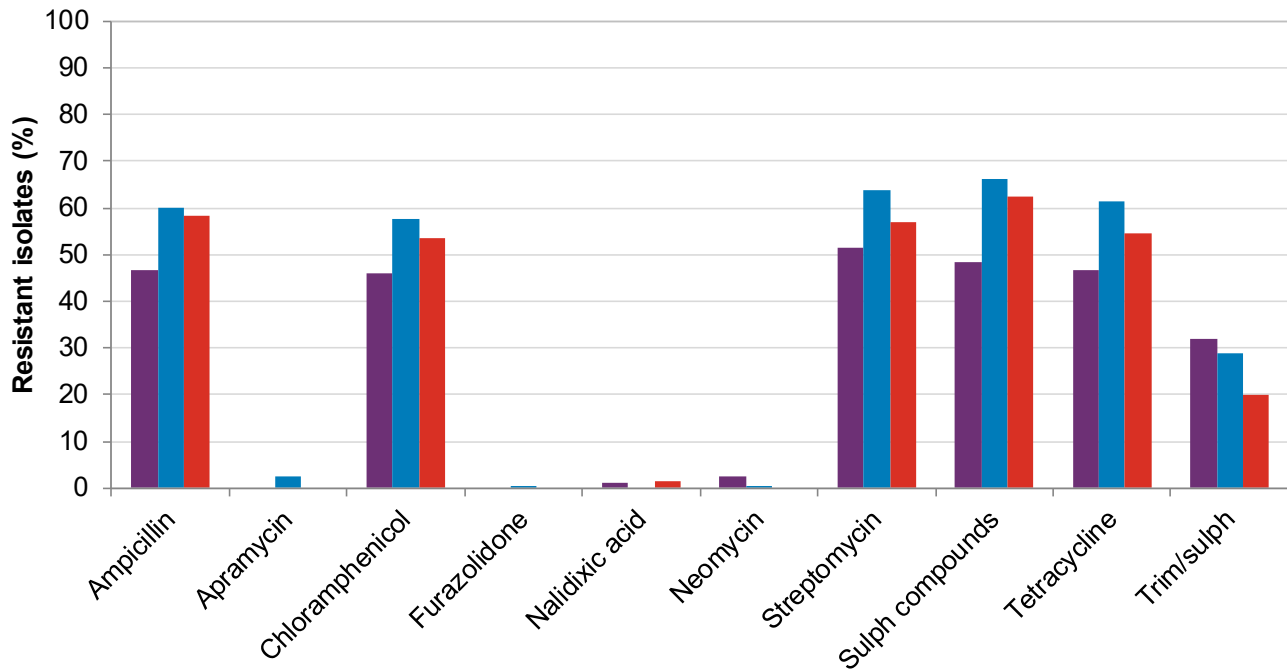


Figure 4.19: *Salmonella* Typhimurium: percentage of resistant isolates in 2015 (■; n=165), 2016 (■; n=166) and 2017 (■; n=187)



Salmonella Typhimurium U288 and DT193 from pigs accounted for 14% and 41% of the total numbers of *S. Typhimurium* isolates respectively; none of the U288 and DT193 isolates from pigs were fully susceptible in 2017.

Considering all definitive types of *S. Typhimurium*, resistance to trimethoprim/sulphamethoxazole has decreased markedly in recent years. The prevalence of resistance to trimethoprim/sulphamethoxazole was 45% in 2013, 36% in 2014, 32% in 2015, 29% in 2016 and 20% in 2017. It was predominantly isolates from pigs that accounted for trimethoprim/sulphamethoxazole resistance; a high proportion of many definitive types of *S. Typhimurium* isolated from pigs are resistant to trimethoprim/sulphamethoxazole. The definitive and undefined phage types of *S. Typhimurium* resistant to trimethoprim/sulphamethoxazole and recovered from pigs in 2017 included contributions primarily from isolates of two phage types DT193 and U288. AmCSSuTTm was the most common resistance pattern observed in both DT193 isolates (n=4) and U288 isolates (n=16) from pigs.

In 2013, apramycin resistance was 2% in *S. Typhimurium*; it was 0.9% in 2014, not detected in 2015, 2% in 2016 and not detected in 2017.

There were no *S. Typhimurium* isolates resistant to ciprofloxacin or amikacin recovered in 2017. One single DT1 isolate from a cat was resistant to ceftazidime and cefotaxime. Two cattle isolates and one feed isolate were resistant to nalidixic acid.

Resistance to four or more antibiotics was detected in definitive and undefined phage types DT104, DT193, U302 from cattle, in phage type DT104 from chickens, in types DT104, and U302 from sheep, in types DT193, U288 and U311 from pigs, in phage type 1 from a cat, and in phage types DT36 and DT40 from pheasants. Of the 15 different definitive and undefined phage types detected, five (namely DT12, DT12a, DT41, DT46a, DT8), several of which are mainly associated with wildlife, were fully susceptible to all of the antibiotics in the test panel.

4.4.6.6 Monophasic *Salmonella* Serotypes

Ninety-one isolates of *Salmonella* 4,12:i:-, belonging to definitive phage types DT120 (n=1), DT193 (n=74), and undefined phage types U208 (n=1) and U311 (n=4), were tested. Eleven isolates were either not typable or reacted with phages but did not conform to a recognised phage type. Most isolates were from pigs (49%) with feed and related samples being the next most common source of origin (17%). The most common pattern of resistance observed was AmSSuT, which occurred in 45% of DT193 isolates, 100% U311 isolates and 100% of the isolates which were not typable with phages. Considering the DT193 isolates, 62% had the AmSSuT resistance pattern alone or with one or more additional resistances.

A total of 76 isolates of *Salmonella* 4,5,12:i:- were tested, including phage types DT193 (n=70), DT104 (n=1) and U40 (n=1); four isolates were untypable. The most common resistance pattern in DT193 isolates was AmSSuT, occurring in 40% of isolates. Most isolates of monophasic *Salmonella* 4,5,12:i:- DT193 were from pigs (67%).

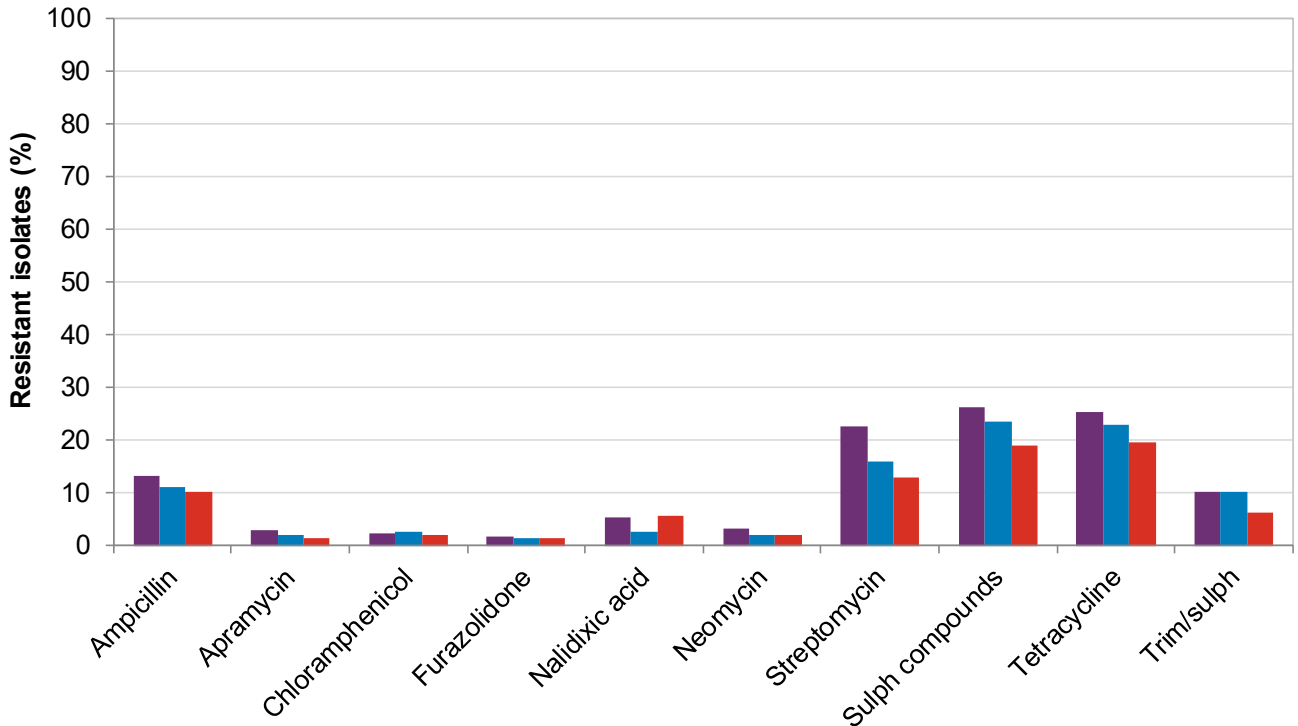
Considering the aminoglycosides other than streptomycin, apramycin resistance was detected in 24% and neomycin resistance in 16% of 4,12:i:- from pigs (n=45). Apramycin resistance was detected in 47% and neomycin resistance in 44% of 4,5,12:i:- from pigs (n=55). Resistance to apramycin was also observed in 14% and neomycin resistance in 71% of 4,5,12:i:- isolates from feed or feed constituents (n=7). Resistance to the aminoglycosides apramycin and neomycin was therefore detected in monophasic *S. Typhimurium* isolates from both pigs and feed in 2017. In 2016, neomycin resistance was detected in monophasic *Typhimurium* isolates from feed, and it was detected in both 4,12:i:- and 4,5,12:i:- isolates from pigs.

4.4.6.7 *Salmonella* other than Dublin or Typhimurium

Of the 2,652 isolates of serotypes other than *S. Dublin* and *S. Typhimurium* tested, 71% were sensitive to all antibiotics in the panel, similar to the figure recorded in 2016, when 69% were fully sensitive (Table S4.8.9 of the supplementary material). One hundred and two isolates (4% of the total) were *S. Enteritidis* and considering these *S. Enteritidis* isolates, 62% were fully susceptible. Thirty-nine isolates were resistant to at least one antibiotic, and 38 isolates were resistant to nalidixic acid. Twenty isolates were untypable with phages or reacted with phages but did not conform to a recognised phage type, and of these 12 were resistant to nalidixic acid. The nalidixic acid resistant *S. Enteritidis* isolates with definitive and undefined phage types detected belonged to phage types 13a (n=4), 20a (n=5), 3 (n=4), 4 (n=4) and 8 (n=9).

Neomycin-resistant *Salmonella* isolates originated mainly from pigs (119 isolates; 26% resistant), feed or feed constituents (710 isolates; 2% resistant), and ducks (303 isolates; 1% resistant). In ducks, *S. Indiana* was the main serotype showing resistance to neomycin (100 isolates; 4% resistant); the *S. Indiana* isolates from ducks were also frequently resistant to furazolidone (100 isolates; 6% resistant) and this was similar to the situation observed in 2016.

Figure 4.20: *Salmonella* other than Dublin and Typhimurium, percentage of isolates resistant to antibiotics tested in 2015 (■; n=2,198), 2016 (■; n=1,986) and 2017 (■; n=2,652)



Considering *Salmonella* isolates other than Typhimurium and Dublin from turkeys in 2017 (n=180), 45% were resistant to streptomycin, 57% to sulphonamide and 57% to tetracycline; lower than the equivalent figures for pigs in 2017 (respectively 82%, 86% and 82%), but higher than those for chickens (respectively 8%, 15% and 11%) or cattle (15% for the three antibiotics). In 2017, the proportion of *Salmonella* isolates originating from feed (27%) was higher than in 2016 (22%); the proportion of fully susceptible isolates from feed remained stable, 74% and 75% in 2016 and 2017, respectively.

SALES DATA CORRECTION

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SALES DATA CORRECTIONS - SEE ERRATUM

Annex C: Data background and limitations

Antibiotic sales data

- 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 animal 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. In addition, a product could be sold one year and used, for example, the next year.
- 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.
- Some products may be imported into the UK on a Special Import Certificate; currently there is no method for including these data in the total UK sales data, resulting in an under-estimate of use in the UK.
- 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 section S1.4 of the supplementary material.

Resistance data, EU AMR harmonised monitoring scheme

- 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.
- The organisms for which the legislation outlines monitoring provisions, such as *Salmonella* spp. 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 World Health Organization (WHO) as the HP-CIAs.
- 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. However, animal species are monitored on alternating years, therefore not providing annual data.

- The legislation provides a harmonised set of epidemiological cut-off values (ECOFFs) 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 ECOFFs or CBPs to be taken into account.

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 programme. 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 test compared to other laboratories is not known, and therefore we cannot know how representative the samples processed by APHA, SRUC Veterinary Services and AFBI 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. 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 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 and Wales (APHA), Scotland (SRUC Veterinary Services), and Northern Ireland (AFBI). APHA and SRUC Veterinary Services 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 antibiotic susceptibility testing done by APHA, in the case of some veterinary drug-bug combinations a BSAC CBP value 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 material.
- *E. coli* isolates are not collected from routine samples from healthy livestock in Northern Ireland. Only clinical cases submitted for post-mortem investigation of 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 UK 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 D: Sources for reporting of sales data

To enable calculation of sold quantities of active ingredient of antibiotics, data were supplied by:

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 were 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 data published in this report. Where a PSUR had been returned to the VMD Pharmacovigilance team in the 2017 calendar year, reported sales were compared to those returned to the AMR team and any discrepancies were queried.

To enable calculation of the Population Correction Unit, data were supplied by:

Defra Statistics division

The live weights of animals slaughtered for food are calculated by Defra. The population numbers of food-producing animals were supplied by Defra via the 'Agriculture in the UK' report.

CEFAS

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

TRACES

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

Annex E: Glossary of terms

Active ingredient	The part of an antibiotic medicine that acts against the bacterial infection. Alternatively called 'active substance'.
AMEG	Antimicrobial Advice <i>ad hoc</i> Expert Group; AMEG is an <i>ad hoc</i> group established by the European Medicines Agency jointly under the Committee for Medicinal Products for Veterinary Use (CVMP) and the Committee for Medicinal Products for Human Use (CHMP). The AMEG was set up to provide guidance on the impact on public health and animal health of the use of antibiotics in animals, and on the measures to manage the possible risk to humans.
ATCvet	Anatomical Therapeutic Chemical classification system for veterinary medicinal products
AHDB	Agriculture and Horticulture Development Board
Antibiotic	A large group of antibacterial substances capable of destroying or inhibiting the growth of bacteria, used for treatment or prevention of bacterial infections.
Antimicrobial	Naturally occurring, semi-synthetic or synthetic substances that exhibit antimicrobial activity (kill or inhibit the growth of micro-organisms). Used for treatment or prevention of infections. Antimicrobials include antibacterials (antibiotics), antivirals, antifungals and antiprotozoals.
Antibiotic/antimicrobial resistance	The ability of a bacterium/micro-organism to grow or survive in the presence of an antibiotic that is usually sufficient to inhibit or kill bacteria/micro-organisms of the same species.
BPC	British Poultry Council
CBP	Clinical Break Point: relates the laboratory results to the likelihood of clinical treatment success or failure.
CHAWG	Cattle Health and Welfare Group
Critically Important Antibiotics	These are antibiotic classes, which are the sole or one of limited available therapies, to treat serious bacterial infections in people and are used to treat infections caused by bacteria that may be transmitted to humans from non-human sources or, bacteria that may acquire resistance genes from non-human sources (WHO definition).
HP-CIAs	Highest Priority Critically Important Antibiotics. In this report the classification according to the AMEG has been used; therefore the following classes of antibiotics are included under HP-CIAs: fluoroquinolones; 3 rd and 4 th generation cephalosporins and colistin.

Defra	Department for Environment, Food and Rural Affairs
ECOFF	Epidemiological cut-off value: represents 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') ECOFF does not necessarily imply a level of resistance which would correspond with clinical treatment failure.
EMA	European Medicines Agency
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
Food-producing animal (species)	Animals used for food production including (but not limited to): 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.
Medicated feeding stuff	Feeding stuffs that contain a veterinary medicine and that are intended for feeding to animals without further processing.
MIC	Minimum Inhibitory Concentration: the lowest concentration of an antibiotic that inhibits visible growth of a bacterium after overnight incubation.
Non-food-producing animal (species)	Animals not reared for food. These are mainly companion animals including (but not limited to): dogs, cats, horses, small mammals, rabbits and birds.
PHWC	Pig Health and Welfare Council
Oral/water product	A product that is administered to animals orally. In this report this includes boluses, topdressings, powders, dissolvable powders, solutions.
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. It takes into account a country's animal population over a year, along with the estimated weight of each particular species at the time of treatment with antibiotics. 1 PCU = 1 kg of different categories of livestock and slaughtered animals.
Premix	Veterinary medicinal products intended for incorporation into medicated feeding stuffs.
Prodrug	Ingredient that after administration is metabolized (i.e. converted within the body) into the pharmacologically active drug.
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.

TRACES

The 'TRAdE Control and Expert System' (TRACES) is the European Commission's online management tool for all sanitary requirements on intra-EU trade and importation of animals, semen and embryo, food, feed and plants.

VMD

Veterinary Medicines Directorate, an Executive Agency of the Department for Environment, Food and Rural Affairs (Defra).

WHO

World Health Organization

SALES DATA CORRECTIONS - SEE ERRATUM

Annex F: Contributors

Compiled by the Veterinary Medicines Directorate

Contributing Pharmaceutical Companies and Other Marketing Authorisation Holders

- Alfamed
 - Alfasan Nederland B.V.
 - Andres Pinaluba S.A.
 - Animalcare Limited
 - aniMedica GmbH
 - Avimedical
 - Bayer Plc
 - Bela-Pharm GmbH & Co. KG
 - Bimeda Chemicals Ltd
 - Boehringer Ingelheim Ltd
 - Ceva Animal Health Ltd
 - Chanelle Animal Health Ltd
 - Cross Vetpharm Group Ltd
 - Dechra Ltd
 - Divasa Farmavic S.A.
 - Dopharma Research B.V.
 - ECO Animal Health
 - Ecuphar N.V.
 - Eli Lilly & Company Ltd
 - Elanco Europe Ltd
 - Emdoka bvba
 - Eurovet Animal Health B.V.
 - Fatro S.P.A.
 - Forte Healthcare Ltd
 - Forum Products Limited
 - Franklin Pharmaceuticals Ltd
 - Harkers Ltd
 - HCS bvba
 - Huvepharma N.V.
 - I.C.F. Sri Industria Chimica Fine Industrial Veterinaria S.A.
 - Intervet UK Ltd
 - Kela N.V.
 - Kernfarm B.V.
 - Krka Dd
 - Laboratorios Calier S.A.
 - Laboratorios Hipra S.A.
 - Laboratorios Karizoo S.A.
 - Laboratorios Maymo S.A.
 - Laboratorios SYVA S.A.U
 - Lavet Pharmaceuticals Ltd
 - Le Vet B.V.
 - Livisto Int'l S.L
 - Merial Animal Health Ltd
 - Nimrod Veterinary Products Ltd
 - Norbrook Laboratories Ltd
 - Oropharma N.V.
 - Pharmaq Ltd
 - Pharmsure International Ltd
 - Phibro Animal Health S.A.
 - Qalian Ltd
 - Richter Pharma
 - SP Veterinaria S.A.
 - Triveritas Ltd
 - Univet Ltd
 - Vetcare Oy
 - Vétoquinol UK Ltd
 - Vetpharma Animal Health S.L.
 - Virbac S.A.
 - VMD N.V.
 - Zoetis UK Ltd
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Contributors of other statistics:

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