UK Veterinary Antibiotic Resistance and Sales Surveillance Report

UK-VARSS 2019

Published November 2020

Authors

Veterinary Medicines Directorate
- Dr Fraser Broadfoot MRCVS
- Dr Kitty Healey MRCVS
- Ms Daisy Neale
- Ms Alexandra Pickering
- Ms Sara Sabzikari

Animal and Plant Health Agency
- Dr Muna Anjum
- Dr Francesca Martelli
- Dr Chris Teale MRCVS

Published on 18th November 2020

Contents

Foreword

I reflected last year that while use of antibiotics in UK livestock continued to drop, the magnitude of reductions was decreasing as further reduction becomes harder to achieve. Now, following year-on-year reductions in antibiotic sales in livestock which led to over 50% reduction in sales since 2014, we are seeing this level off with a small increase of 1.5 mg/kg in sales of antibiotics in food-producing animals in 2019. Despite this, UK antibiotic sales in 2019 represent the second lowest level since reporting began, second only to 2018. Based on most recently available data we are still the lowest user of antibiotics amongst European countries with significant livestock farming and the 5th lowest user overall[1].

It is pleasing to see that use of Highest Priority Critically Important Antibiotics remains very low and continues to fall, helping to protect their effectiveness in human health (and in animal health, if no other antibiotic will work). This move to less potent antibiotics may in part explain the small increase in total antibiotic use.

The veterinary profession and livestock sectors have kept up the momentum of delivering against the targets they set and published in 2017, which have played a hugely important part of the change we've seen towards responsible use of antibiotics. While some sectors, cattle and sheep in particular, are still working on improving coverage of usage data, coverage is at least 90% for all the poultry and fish sectors, and the pig sector.

Improving antibiotic usage data, and being less reliant on sales data, is a key part of the success story the UK has seen over recent years. It provides data for farmers and vets which is sufficiently tailored to flag up where change is needed, but it also helps to understand where decreases – or increases – have happened, and for which antibiotics and routes of administration. As the annual report carries increasingly more antibiotic use information, the name of the report will change next year to reflect this.

Accurate usage collection also helps to review the data in context, for example looking at the increase of use of some antibiotics during a year when there have been a number of known disease challenges. This will become increasingly important as the join up with initiatives to reduce disease – and therefore the need to use antibiotics – gather pace.

The goal of reducing antibiotic consumption and improving stewardship is to reduce antibiotic resistance. This year, antibiotic resistance overall in *E. coli* from healthy pigs at slaughter is reported at lower levels compared to 5 years ago. Based on most recently available data, the UK has had one of the most statistically significant increases in levels of fully susceptible *E. coli,* and also one of the lowest prevalences of ESBL-/AmpC- *E. coli* in key livestock sectors amongst European countries[2].

---

[1] https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-31-european-countries-2018-trends-2010-2018-tenth-esvac-report_en.pdf
[2] https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2020.6007

Most of the key veterinary pathogens remain susceptible to authorised antibiotics, including those that have been available for many years. It is our intent to enhance this programme of work and undertake a more detailed analysis of antibiotic susceptibility in a range of animal pathogens, expanding the scope of current surveillance activities.

Professor S. Peter Borriello
Chief Executive Officer
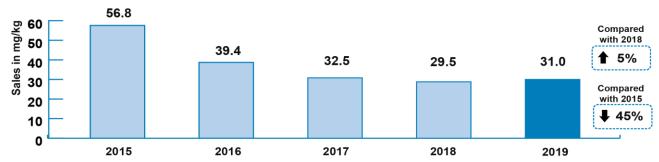
Highlights

Antibiotic Sales

Sales for food-producing animals (mg/kg)

Sales of veterinary antibiotics for use in food-producing animals, adjusted for animal population, were 31.0 mg/kg; a 1.5 mg/kg (5%) increase since 2018, however, there was an overall 25.8 mg/kg (45%) decrease since 2015.

Sales of Highest Priority Critically Important Antibiotics (HP-CIAs) in food-producing animals dropped from 0.21 mg/kg in 2018 to 0.17 mg/kg (21%) in 2019.
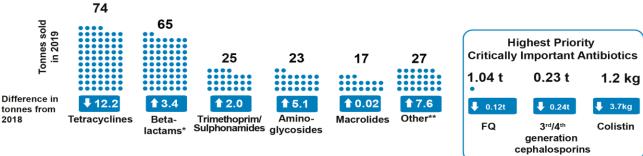
	2015	2016	2017	2018	2019	Compared with 2015
Fluoroquinolones (mg/kg)	0.35	0.23	0.16	0.15	0.13	↓ 61%
3rd/4th generation cephalosporins (mg/kg)	0.17	0.14	0.11	0.06	0.03	↓ 82%
Colistin (mg/kg)	0.12	0.02	0.0006	0.0007	0.0002	↓ 99.9%
Total HP-CIAs (mg/kg)	0.64	0.38	0.26	0.21	0.17	↓ 74%

Sales for all animals (tonnes)

In 2019, the total quantity of antibiotic active ingredient sold in the UK was 232.2 tonnes.

	2015	2016	2017	2018	2019	Compared with 2015	Compared with 2018
Total sales (all animals, tonnes)	408	296	248	226	232	↓ 43%	↑ 3%

Sales of HP-CIAs dropped by a further 0.36 tonnes (22%) from an already low level in 2018; a drop of 3.3 tonnes (72%) since 2015. Overall, tetracyclines remain the most sold antibiotic class (32%), followed by beta-lactams (28%). Sales of HP-CIAs in all animal species represent a small proportion (0.5%) of overall antibiotic sales.

● = 1 tonne; t = tonnes; FQ = fluoroquinolones; * Includes 3rd and 4th generation cephalosporins; ** Includes amphenicols, lincomycins, pleuromutilins, steroidal antibiotics and polymyxins (including colistin).

Antibiotic Usage

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

Antibiotic usage by food-producing animal species

	Total coverage %*	2019 Total tonnage**	2019 Total per unit***	Longer term change****	1 year change
Pigs	95	84.0	110 mg/kg	↓ 168 mg/kg	0 mg/kg
Turkeys			42 mg/kg	↓ 177 mg/kg	↓ 4.7 mg/kg
Broilers	90	19.7	17 mg/kg	↓ 31.3 mg/kg	↑ 5.0 mg/kg
Ducks			1.6 mg/kg	↓ 13.5 mg/kg	↓ 0.10 mg/kg
Laying hens	90	4.8	0.68 % bird days	↑ 0.02 % bird days	↑ 0.13 % bird days
Gamebirds	90	10.4	—	↓ 9.8 tonnes	↑ 0.64 tonnes
Salmon	100	2.8	13.5 mg/kg	↓ 2.6 mg/kg	↑ 6.8 mg/kg
Trout	90	0.13	9.8 mg/kg	↓ 10.0 mg/kg	↓ 3.0 mg/kg

Highest Priority Critically Important Antibiotics by food-producing animal species

	Total coverage %*	2019 Total kg**	2019 Total per unit***	Longer term change****	1 year change
Pigs	95	32	0.04 mg/kg	↓ 0.94 mg/kg	↓ 0.02 mg/kg
Meat Poultry	90	14	0.01 mg/kg	↓ 1.2 mg/kg	↓ 0.01 mg/kg
Gamebirds	90	58	—	↓ 6.6 kg	↑ 11.0 kg

* Represents the % animals covered by the data, except gamebirds which represents an estimate of the total % antibiotics sales
** Relates to the weight of antibiotic active ingredient, using ESVAC methodology
*** mg/kg relates to the amount of active ingredient standardised by kg biomass and calculated using ESVAC methodology, % doses refers to 'actual daily bird-doses/100 bird-days at risk'
**** This represents the change from when antibiotic usage was first published, which was 2015 for pigs, 2014 for meat poultry, 2016 for laying hens, 2016 for gamebirds and 2017 for salmon and trout.

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

Resistance in *Salmonella* spp. from pigs

None of the *Salmonella* isolates tested were resistant to the HP-CIAs cefotaxime, ceftazidime or ciprofloxacin. Two *Salmonella* isolates from pigs were resistant to colistin, however, neither isolate had known transferable colistin resistance genes identified.

Resistance in *Escherichia coli* from pigs
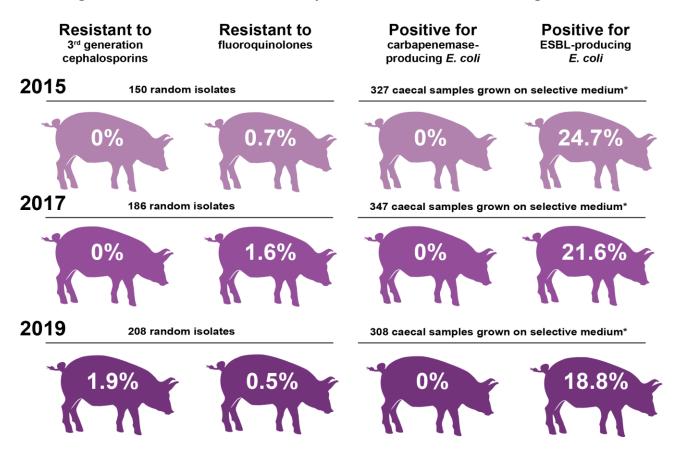
There was no resistance to colistin in *E. coli* from pigs in 2015, 2017 and 2019. Resistance to cefotaxime and ceftazidime was detected in 1.4% and 1.0% respectively, of *E. coli* from pigs in 2019, which was not detected in 2017 or 2015. Very low resistance to ciprofloxacin was detected in isolates from pigs in 2015, 2017 and 2019.

Resistance to other antibiotics tested in the panel was either not detected or has overall declined since 2015.

In 2019, 18.8% of pig caecal samples yielded *E. coli* with an ESBL- and/or AmpC- phenotype, down from 21.6% in 2017 and 24.7% in 2015. No presumptive carbapenemase-producing *E. coli* were detected.

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

Testing carried out on *E. coli* collected as part of the harmonised monitoring scheme

	Resistant to 3rd generation cephalosporins	Resistant to fluoroquinolones	Positive for carbapenemase-producing *E. coli*	Positive for ESBL-producing *E. coli*
2015	150 random isolates		327 caecal samples grown on selective medium*	
	0%	0.7%	0%	24.7%
2017	186 random isolates		347 caecal samples grown on selective medium*	
	0%	1.6%	0%	21.6%
2019	208 random isolates		308 caecal samples grown on selective medium*	
	1.9%	0.5%	0%	18.8%

*To note that 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 4533 isolates) were susceptible to all the antibiotics tested, a similar situation to previous years.
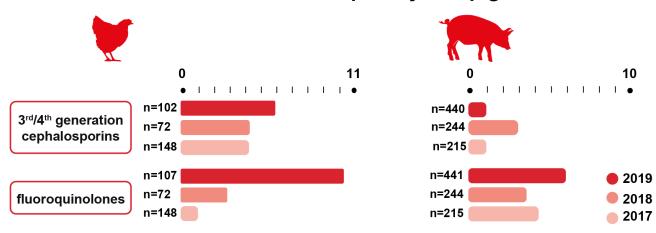
Resistance to 3rd generation cephalosporins was detected in two isolates from environmental samples related to the monitoring of animal by-products, but not in livestock isolates. Nine isolates from turkeys were resistant to ciprofloxacin (a fluoroquinolone).

Resistance in 2019 to:

	3rd/4th generation cephalosporins	fluoroquinolones
(pig)	0%	0%
(turkey)	0%	3.3%
(chicken)	0%	0%
(cattle)	0%	0%
(sheep)	0%	0%

Percentage fully susceptible to all tested antibiotics

0 10 20 30 40 50 60 70 80 90 100

n=206
n=202
n=158

n=270
n=182
n=180

n=1708
n=1640
n=873

n=464
n=489
n=392

n=82
n=276
n=104

● 2019
● 2018
● 2017

n = number of samples tested

Resistance in *Escherichia coli*

Resistance to fluoroquinolones and 3rd generation cephalosporins was low (<5%), except in cattle (7% of isolates resistant to fluoroquinolones, 5% resistant to ceftazidime and 12% resistant to cefotaxime; the majority of these isolates were obtained from calves) and in chickens (11% of isolates resistant to fluoroquinolones). No colistin resistance was detected in any species.

% resistant isolates from poultry and pigs

(chicken) 0 ——— 11

3rd/4th generation cephalosporins	n=102	
	n=72	
	n=148	
fluoroquinolones	n=107	
	n=72	
	n=148	

(pig) 0 ——— 10

n=440	
n=244	
n=215	
n=441	
n=244	
n=215	

● 2019
● 2018
● 2017

Introduction

The first report on sales figures for antibiotic veterinary medicinal products, collated and published by the Veterinary Medicines Directorate (VMD), covered 1993–1998. The figures were provided voluntarily by the veterinary pharmaceutical companies marketing these products. From 2005, sales data were collected as a statutory requirement (Veterinary Medicines Regulations) and in 2013 the first Veterinary Antibiotic Resistance and Sales Surveillance (VARSS) report of the United Kingdom was published. The UK-VARSS report presents combined data on veterinary antibiotic sales and antibiotic resistance in bacteria from food-producing animals in the UK. Furthermore, the UK-VARSS report has increasingly included data on usage by animal production sector, which are, on a voluntary basis, provided to the VMD by these sectors.

The antibiotic sales data from 2005 to 2019 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 livestock 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 *Escherichia 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 harmonised antibiotic resistance monitoring scheme are presented in **CHAPTER 3.** Results from the scanning surveillance 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 UK-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

1.1   Summary

In 2019, the total quantity of antibiotic active ingredient sold in the UK was 232.2 tonnes, a 5.9 tonne (3%) increase since 2018, but still a 176.0 tonne (43%) decrease since 2015.

In 2019, sales of veterinary antibiotics for food-producing animals, adjusted for animal population were 31.0 mg/kg, a 1.5 mg/kg (5%) increase from 2018. However, this is still a 25.8 mg/kg (45%) decrease from 2015. The year 2015 is referred to in this report as the baseline year. This is because the 2015 sales data were used as the baseline for the first targets set in the key livestock sectors, published in 2017 (Responsible Use of Medicines in Agriculture Alliance, 2017).

Tetracyclines remain the most sold class of antibiotics (32% of total sales) and beta-lactams the second (28% of total sales). Since 2018, notable reductions were observed for tetracyclines, decreasing by 12.2 tonnes (14%). Orally administered products (including premix and excluding tablets) accounted for the majority of antibiotics sold (74%).

Highest Priority Critically Important Antibiotics (HP-CIAs) for human medicine continue to represent a small proportion of total antibiotics sold (0.5% in 2019) and have reduced to 1.3 tonnes; a reduction of 0.36 tonnes (22%) since 2018 and 3.3 tonnes (72%) since 2015.

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, imports or exports of veterinary antibiotics, but they serve as the best currently available approximation of the quantity of antibiotics administered to all animal species within the UK (further details on data limitations can be found in Annex C).

Note that, for ease of reading, the data have been rounded. However, the percentage changes have been calculated using the exact number.

1.3   Results and discussion

1.3.1   Total sales of antibiotics for veterinary use in the UK

Sales data analysed using the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) methodology are available from 2005; the ESVAC project was launched in September 2009 and the first report published aggregated sales data for the years from 2005 to 2009. Prior to these years, data (covering from 1993 to 2005) were analysed using the UK-VARSS methodology, further details of which can be found in section S1.1.

Total annual sales of antibiotic active ingredient for veterinary use in the UK from 2005 to 2019 are presented in **Figure 1.1**. The total quantity of antibiotic active ingredient sold in 2019 was 232.2 tonnes, a 5.9 tonne (3%) increase since 2018. This is 62.4 tonnes (21%) lower than the four year
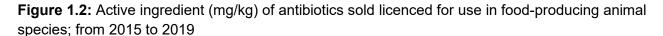
mean for the time period from 2015 to 2018 (mean 294.6 tonnes; range from 226.3 to 408.2 tonnes).
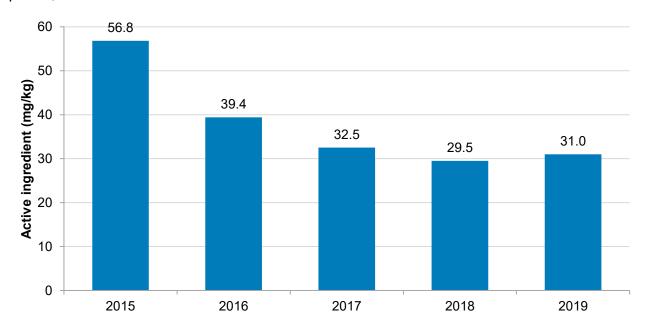
Figure 1.1: Total quantity of antibiotic active ingredient (tonnes) sold in the UK per year using ESVAC methodology; from 2005 to 2019

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

The sales of antibiotic veterinary medicinal products licensed for food-producing animal species increased by 1.5 mg/kg (5%) between 2018 and 2019, from 29.5 mg/kg to 31.0 mg/kg (**Figure 1.2**). However, this is still a 25.8 mg/kg (45%) reduction since 2015.

Figure 1.2: Active ingredient (mg/kg) of antibiotics sold licenced for use in food-producing animal species; from 2015 to 2019

1.3.3 Total sales of antibiotics by administration route (tonnes)

1.3.3.1 By administration route for all animal species
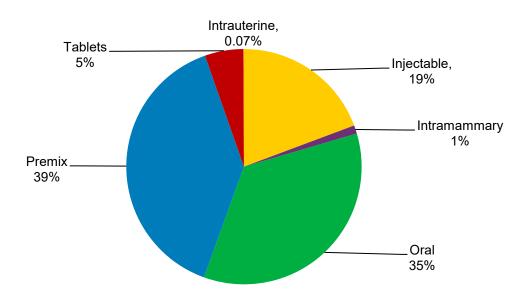
Premix remained the most common administration route, accounting for 90.9 tonnes of active ingredient, 39% of total sales in 2019 (**Table 1.1** and **Figure 1.3**). Oral/water preparations were the second most used administration route, representing 81.2 tonnes, 35% of total sales in 2019. Excluding tablets, sales of oral products (premix and oral/water combined) decreased by 170.3 tonnes (50%) since 2015. Sales of injectable products have fluctuated since 2015, however sales have continually declined since 2017, decreasing between 2018 and 2019 by 4.2 tonnes (8%).

**Table 1.1:** Active ingredient (tonnes) of antibiotic sold for all animal species by route of administration; from 2015 to 2019

Administration Route	2015	2016	2017	2018	2019
Premix	232.7	147.5	106.5	89.5	90.9
Oral/water*	109.7	85.1	70.4	71.1	81.2
Injectable	49.8	45.4	54.3	49.0	44.9
Intramammary	3.2	2.9	2.6	3.2	2.7
Tablets	12.6	14.6	14.3	13.2	12.3
Intrauterine	0.17	0.16	0.18	0.18	0.17
Total	**408.2**	**295.6**	**248.2**	**226.3**	**232.2**

* Excluding tablets, inclusive of bolus preparations.
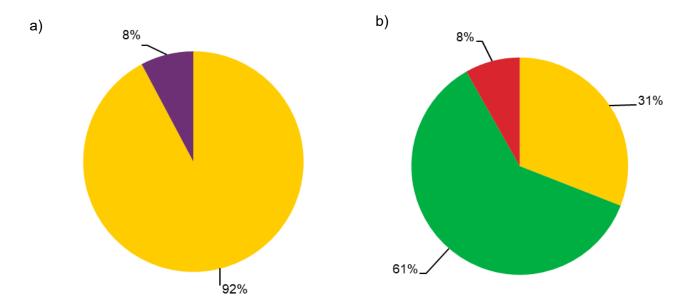
Figure 1.3: Active ingredient (% of total sales) of antibiotics sold for all animal species by route of administration; 2019

Concerning HP-CIAs, the majority of 3rd and 4th generation cephalosporins in 2019 were for injectable use (92%) (**Figure 1.4**). The proportion of 3rd and 4th generation cephalosporins sold as intramammary products has decreased from 17% in 2018 to 8% in 2019. Although overall fluoroquinolone use has decreased, the amount of fluoroquinolones sold for oral use has

increased. Oral fluoroquinolone products now represent 61% of fluoroquinolone sales compared with 41% in 2018.

Figure 1.4: 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; 2019

a)

8%

92%

b)

8%

31%

61%
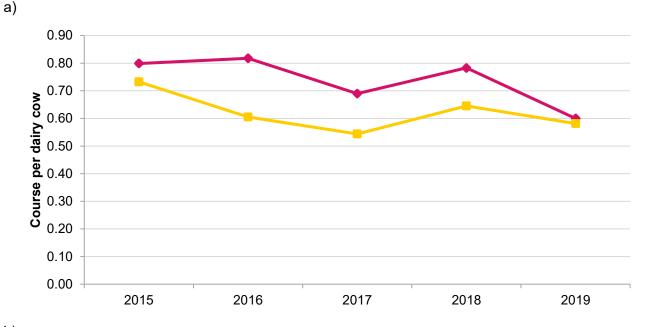
1.3.3.2   Intramammary antibiotic products
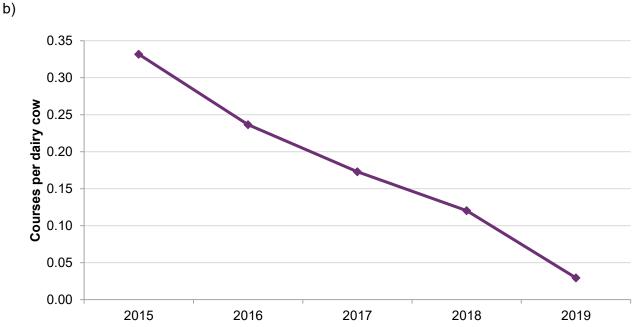
Sales of dry and lactating cow products are measured using the ESVAC defined course dose methodology (DCDvet). The DCDvet represents the average number of courses per dairy cow using a standard course dose of four tubes per dry cow and three tubes for most lactating cow treatments.

Between 2015 and 2018, sales of intramammary products fluctuated. However, between 2018 and 2019, sales of dry and lactating cow products in course doses have decreased by 10% and 23% course doses respectively. Since 2015, this represents a 21% course dose decrease for dry cow products, and a 25% course dose decrease for lactating cow products.

Regarding sales of HP-CIA intramammary products, sales in course doses decreased by 76% since 2018 and 91% since 2015.

Figure 1.5: Sales of a) dry (■) and lactating cow (♦) intramammary products (courses per dairy cow); from 2015 to 2019, b) HP-CIA sales of dry and lactating intramammary products combined

a)

b)

1.3.4 Total sales of antibiotics by animal species

The quantities of active ingredient sold between 2015 and 2019, differentiated by the animal species or combination of species for which the products are indicated, are shown in **Table 1.2**.

In 2019, 179.3 tonnes (77%) of total antibiotic sales were attributed to products licenced for food-producing animal species only. This is a 0.86 tonne (0.5%) increase since 2018 but it is still a 166.3 tonne (48%) reduction since 2015. Sales of antibiotics indicated for use in non-food-producing animals reduced by 1.2 tonnes (7%) since 2018 and 11.5 tonnes (44%) since 2015, whereas antibiotics indicated for a combination of food- and non-food producing species increased

by 6.2 tonnes (19%) since 2018 and 1.8 tonnes (5%) since 2015. A more detailed analysis of companion animal sales data can be found in **Section 1.3.6.**

Table 1.2: Active ingredient (tonnes and % of total sales) of antibiotics sold for the animal species categories: a) food-producing animal species only, b) non-food-producing animal species only and c) combination of food- and non-food-producing animal species; from 2015 to 2019. (Note that totals were rounded to the nearest integer. This explains the minor discrepancies between the sum of individual species categories and the totals presented.)

a)

Animal species	2015	2016	2017	2018	2019
Pigs and poultry only	214.2	127.4	97.3	99.7	96.4
Pigs only	49.4	39.7	33.0	23.8	28.5
Poultry only*	38.0	26.5	15.0	12.9	14.9
Cattle only	14.1	15.3	13.7	13.0	12.0
Fish only	0.71	1.6	3.4	1.6	3.1
Multiple food-producing animal species**	29.2	23.4	29.3	27.5	24.4
Total	**345.6 (85)**	**233.8 (79)**	**191.9 (77)**	**178.4 (79)**	**179.3 (77)**

* Includes products authorised for use in 'ducks' in combination with other poultry 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 (to prevent double counting).

b)

Animal species	2015	2016	2017	2018	2019
Companion animal only (excluding horse only)	12.7	14.7	14.4	13.4	12.5
Horse only***	13.4	14.9	6.7	2.4	2.1
Total	**26.1 (6)**	**29.6 (10)**	**21.1 (9)**	**15.8 (7)**	**14.6 (6)**

*** In the UK, horses are primarily a companion or sport animal, and not raised for food. For this reason, horses have been classified as 'non-food-producing animals' when reporting tonnage of active ingredient.

c)

Animal species	2015	2016	2017	2018	2019
Total for combination of food- and non-food-producing animal species	**36.5 (9)**	**32.3 (11)**	**35.3 (14)**	**32.1 (14)**	**38.3 (17)**

Where antibiotic usage data are available per species or sector and represent a high proportion of the industry (e.g. pigs, meat poultry, laying hens, gamebirds, trout and salmon, see **Chapter 2**), these can be extrapolated and compared with the antibiotic sales of products authorised for those species. This analysis shows that these figures are comparable and follow the same trend.
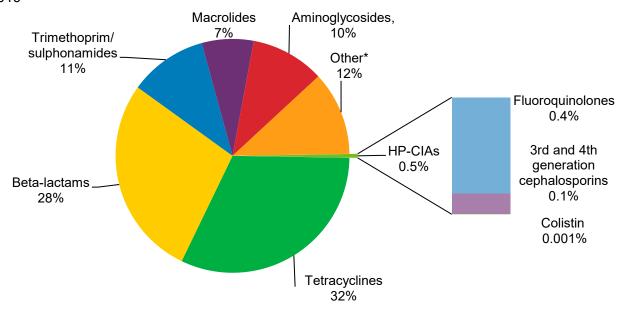
Chapter 1

1.3.5   Sales of antibiotics by antibiotic class

1.3.5.1   For all animal species

The total quantities of antibiotic active ingredient, by antibiotic class, sold between 2015 and 2019 are presented in **Figure 1.6** and **Table 1.3:** Active ingredient (tonnes or kg) of antibiotics sold for all animal species by antibiotic class; from 2015 to 2019. Details of these antibiotic classes and active ingredients can be found in section S1.3 of the supplementary material.

Tetracyclines remain the most sold antibiotic class, accounting for 32% of total sales in 2019. This class has also shown the greatest reduction in sales, reducing by 12.2 tonnes (14%) between 2018 and 2019 and 92.1 tonnes (55%) between 2015 and 2019. Beta-lactams were the second most sold class in 2019 (accounting for 28% of total sales). Beta-lactams sales increased by 3.4 tonnes (6%) from 2018. Excluding tetracyclines and HP-CIAs, all classes of antibiotics increased in sales between 2018 and 2019, with the largest increases occurring in the classes "other" (7.6 tonne increase) and aminoglycosides (5.1 tonne increase). Pleuromutilin sales increased by 6.7 tonnes since 2018, accounting for the majority of the increase seen in the 'other' category.

Figure 1.6: Active ingredient (% weight) of antibiotics sold for all animal species by antibiotic class; 2019

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

Sales of HP-CIAs were 1.3 tonnes, representing 0.5% of total tonnes of antibiotics in 2019. Sales of these antibiotics have reduced by 0.36 tonnes (22%) since 2018 and 3.3 tonnes (72%) since 2015. There was 10.0kg of colistin sold in 2019, however upon further investigation of this figure, the pharmaceutical company confirmed that 8.8kg was exported and therefore had not been sold for use in the UK. A similar situation was observed in 2018 by the same pharmaceutical company. This highlights one of the limitations of antibiotic sales data and the importance of collecting antibiotic usage data, as reported in **Chapter 2**. The remaining 1.2kg of colistin was sold for use within the UK, which is a 3.7kg (76%) decrease since 2018 and an 873.7kg (99.9%) decrease since 2015.

Table 1.3: Active ingredient (tonnes or kg) of antibiotics sold for all animal species by antibiotic class; from 2015 to 2019

Antibiotic class	2015	2016	2017	2018	2019
Tetracyclines	**166.3**	**108.6**	**96.2**	**86.4**	**74.2**
Beta (ß)-lactams	**81.6**	**70.1**	**65.9**	**61.3**	**64.7**
1st/2nd generation cephalosporins	4.9	4.8	4.2	4.1	3.9
3rd/4th generation cephalosporins (kg)^	(1,203)	(1,002)	(779)	(467)	(227)
Penicillins*	75.4	64.2	60.9	56.6	60.4
Trimethoprim/sulphonamides	**68.3**	**51.6**	**23.9**	**23.2**	**25.1**
Trimethoprim	11.2	8.5	3.9	3.8	4.2
Sulphonamides	57.1	43.1	20.0	19.4	21.0
Aminoglycosides	**23.5**	**14.8**	**17.5**	**18.4**	**23.5**
Streptomycin	10.0	8.8	10.6	9.4	10.3
Neomycin and framycetin	0.51	0.61	2.2	3.5	7.0
Other aminoglycosides**	13.0	5.3	4.8	5.5	6.2
Macrolides	**38.2**	**28.7**	**23.3**	**16.6**	**16.7**
Fluoroquinolones (kg)^	**(2,532)**	**(1,729)**	**(1,226)**	**(1,160)**	**(1042)**
Other*	**27.7**	**20.2**	**20.1**	**19.4**	**27.0**
Pleuromutilins	16.4	11.0	10.8	9.1	15.8
Colistin (kg)^	(870)	(128)	(4.2+)	(4.9+)	(1.2)
Total sales of antibioticsˣ	**408.2**	**295.6**	**248.2**	**226.3**	**232.2**

ˣ The totals were rounded to the nearest integer. This explains the minor discrepancy between the overall total and the classes' totals.
^ Because of the heightened interest in HP-CIA classes, and lower amounts sold, the sales of fluoroquinolones, 3rd and 4th generation cephalosporins and colistin are presented in kg.
+ One colistin product (which accounts for 2.9kg, 17.6kg and 8.8kg active ingredient for 2017, 2018 and 2019 respectively) was excluded as the MAH identified that this was exported as medicated feed and therefore not used in the UK.
* Benzylpenicillin, benzathine penicillin, phenoxymethylpenicillin, procaine penicillin, amoxicillin (including in combination with clavulanic acid), ampicillin, cloxacillin, nafcillin.
** Apramycin, gentamicin, kanamycin, spectinomycin and paromomycin.
*** Amphenicols, lincomycins, pleuromutilins, polymyxins (including colistin), steroidal antibiotics and imidazole derivatives.

1.3.5.2   For animal species groups

The quantities of antibiotic active ingredient sold in 2019 analysed by animal species group and antibiotic class are shown in **Table 1.4:** Tonnes of antibiotic class sold for the animal species categories: a) food-producing animal species only, b) non-food-producing animal species only and c) combination of food- and non-food-producing animal species, 2019.

Table 1.4: Tonnes of antibiotic class sold for the animal species categories: a) food-producing animal species only, b) non-food-producing animal species only and c) combination of food- and non-food-producing animal species, 2019

a)

Antibiotic class for food-producing animal species only	2019
Tetracyclines	72.8
Beta-lactams	41.7
Trimethoprim/sulphonamides	20.2
Other*	16.3
Macrolides	15.4
Aminoglycosides	12.3
Fluoroquinolones	0.60
Colistin	0.0012
Total	**179.3**

b)
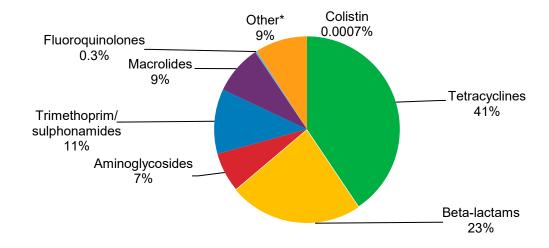
Antibiotic class for non-food-producing animal species only	2019
Beta-lactams	9.5
Other*	2.6
Trimethoprim/sulphonamides	2.0
Tetracyclines	0.24
Aminoglycosides	0.15
Fluoroquinolones	0.10
Macrolides	0.05
Colistin	0.00
Total	**14.6**
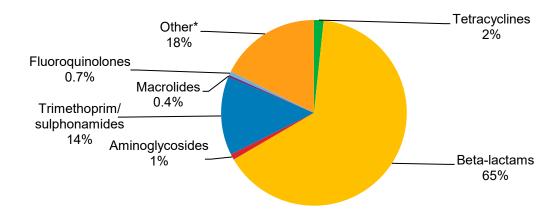
c)
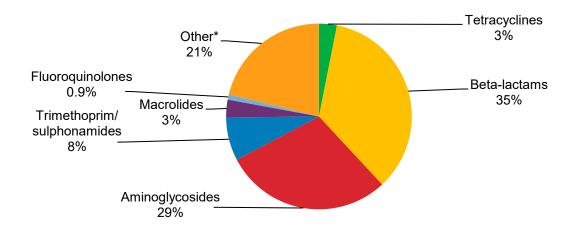
Antibiotic class for combination of food- and non-food-producing animal species	2019
Beta-lactams	13.5
Aminoglycosides	11.0
Other*	8.2
Trimethoprim/sulphonamides	2.9
Macrolides	1.2
Tetracyclines	1.2
Fluoroquinolones	0.35
Colistin	0.00
Total sales of antibiotics	**38.3**

*Amphenicols, lincomycins, pleuromutilins, steroidal antibiotics and imidazole derivatives.

Figure 1.7: Active ingredient (% weight) of antibiotics sold per animal species category by antibiotic class; 2019 a) food-producing animal species, b) non-food-producing animal species and c) combination of food- and non-food producing animal species

Other*
9%

Colistin
0.0007%

Fluoroquinolones
0.3%

Macrolides
9%

Tetracyclines
41%

Trimethoprim/
sulphonamides
11%

Aminoglycosides
7%

Beta-lactams
23%

Other*
18%

Tetracyclines
2%

Fluoroquinolones
0.7%

Macrolides
0.4%

Trimethoprim/
sulphonamides
14%

Aminoglycosides
1%

Beta-lactams
65%

Other*
21%

Tetracyclines
3%

Fluoroquinolones
0.9%

Beta-lactams
35%

Macrolides
3%

Trimethoprim/
sulphonamides
8%

Aminoglycosides
29%

* Amphenicols, lincomycins, pleuromutilins, polymyxins, steroidal antibiotics and imidazole derivatives

a)

Tetracyclines were the most sold antibiotic class in the food-producing species only category, accounting for 72.8 tonnes (41%) of total tonnes for this species category. However, tetracycline use has dropped by 12.1 tonnes (14%) between 2018 and 2019. The second most sold antibiotic class for this category is beta-lactams, which accounted for 41.7 tonnes (23%). Fluoroquinolones accounted for 0.60 tonnes of sales for this category (0.3%).
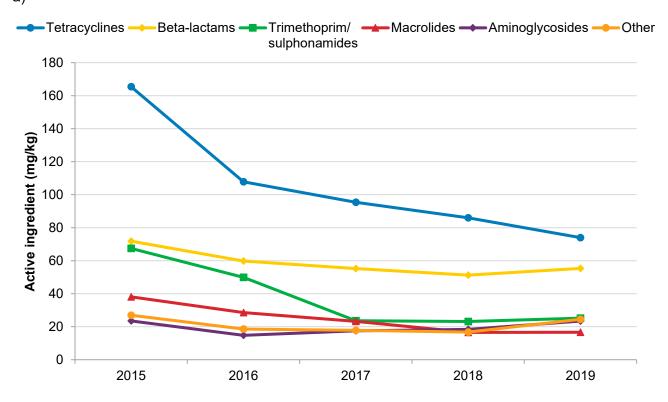
Beta-lactams were the most sold antibiotic class indicated for the non-food-producing species only category, representing 9.5 tonnes (65%) of the total. The 'other' category represented 2.6 tonnes (18%). Trimethoprim/sulphonamides class accounted for 2.0 tonnes (14%) of total tonnes for this species category.
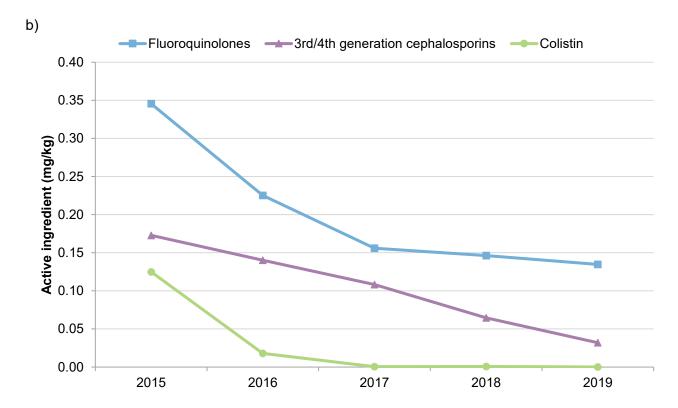
Beta-lactams were also the most sold antibiotic class for a combination of food- and non-food producing species, representing 13.5 tonnes (35%) of the total for this animal species category, followed by aminoglycosides, which represented 11.0 tonnes (29%) of these sales.

1.3.5.3 For food-producing animal species (mg/kg)

Sales of all classes of antibiotic for food-producing animal species increased between 2018 and 2019, with the exception of tetracyclines and all HP-CIAs.

Figure 1.8: Active ingredient (mg/kg) of antibiotics by a) antibiotic class and b) HP-CIAs, sold for food-producing animal species; from 2015 to 2019

a)

b)

Sales of HP-CIAs for food-producing animal species represented 0.17 mg/kg, a small proportion (0.5%) of the overall antibiotic sales in mg/kg. These sales decreased by 0.04 mg/kg (21%) between 2018 and 2019 and by 0.48 mg/kg (74%) between 2015 and 2019. Between 2018 and 2019, sales of 3rd and 4th generation cephalosporins decreased by 0.03 mg/kg (51%), sales of fluoroquinolones decreased by 0.01 mg/kg (8%) and sales of colistin for use in the UK decreased by 0.0005 mg/kg to 0.0002 mg/kg.

1.3.6   Sales of antibiotics for dogs and cats

1.3.6.1   Sales in active ingredient (tonnes)

For the data presented in this section, the ESVAC methodology was used for calculation of active ingredient, analysing sales data of all products (including tablets) licenced for dogs only, cats only and products licenced for a combination of dogs and cats. Products licenced for multiple companion animal species (rabbits, exotics and horses in combination with dogs and cats) were not included in the analysis and represent only a small proportion of sales.

Quantities of antibiotic active ingredient by antibiotic class sold between 2014 and 2019 for use in dogs and cats combined are presented in **Figure 1.5** and **Figure 1.9.** The year 2014 has been chosen as a baseline because this represents the first year where antibiotic sales data has been stored electronically by the VMD. Nearly all sales were for tablet preparations (99% in 2019).

Sales of HP-CIAs were 131.7kg in 2019, representing 1% of antibiotic active ingredients. This accounts for 10% of total HP-CIA sales for all animal species in 2019 and has reduced by 17.5kg (12%) since 2018 and 81.0kg (38%) since 2014.
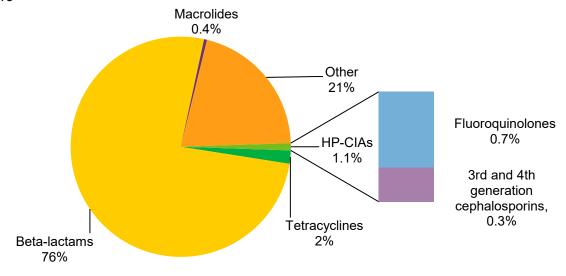
Beta-lactams were the most sold antibiotic class, representing 76% of total sales for dogs and cats in 2019. Sales of products in this class have reduced by 0.64 tonnes (6%) since 2018 and 3.3 tonnes (26%) since 2014. Antibiotics in the 'other' category were the second most sold class in 2019, representing 2.6 tonnes (21%) of total sales.

Table 1.5: Active ingredient (tonnes or kg) of antibiotics by antibiotic class sold for use in dogs and cats; from 2014 to 2019

Antibiotic class	2014	2015	2016	2017	2018	2019
Beta (ß)-lactams*	**12.7**	**9.8**	**10.4**	**10.8**	**10.1**	**9.5**
3rd/4th generation cephalosporins (kg)^	(44)	(27)	(43)	(40)	(40)	(41)
Other**	**0.82**	**0.75**	**1.7**	**2.3**	**2.6**	**2.6**
Imidazole derivatives	0.08	0.08	0.97	1.7	2.0	2.0
Lincomycins	0.75	0.67	0.70	0.62	0.65	0.60
Tetracyclines	**0.90**	**0.94**	**0.75**	**0.85**	**0.38**	**0.24**
Fluoroquinolones (kg)^	**(169)**	**(132)**	**(126)**	**(109)**	**(110)**	**(91)**
Macrolides	**0.14**	**0.15**	**0.14**	**0.11**	**0.09**	**0.05**
Trimethoprim/sulphonamides	**1.02**	**0.88**	**1.6**	**0.25**	**0.00**	**0.00**
Total antibiotics×	**15.8**	**12.7**	**14.7**	**14.4**	**13.3**	**12.4**

× The totals were rounded to the nearest integer. This explains any minor discrepancy between the overall total and the classes' totals.
^ Because of the heightened interest in HP-CIA classes and lower amounts sold, sales of fluoroquinolones and 3rd and 4th generation cephalosporins are presented in kg.
* Benzylpenicillin, benzathine penicillin, phenoxymethylpenicillin, procaine penicillin, amoxicillin (including in combination with clavulanic acid), ampicillin, cloxacillin, nafcillin.
** Lincomycins and imidazole derivatives included within this group.

Figure 1.9: Active ingredient (% weight) of antibiotics sold for dogs and cats combined by antibiotic class; 2019

* Lincomycins and imidazole derivatives included within this group.

1.3.6.2 Sales in mg/kg

In order to calculate the mg/kg for dogs and cats, a combined dog and cat weight of animal at risk (in kg) was calculated using population data from the Pet Food Manufacturers' Association[3] and average cat and dog weights provided by SAVSNET[4] (see S1.2 of the supplementary material). Sales of antibiotic products licenced for dogs and cats combined is shown in **Figure 1.10** and sales of HP-CIA products are shown in **Figure 1.11**.

Figure 1.10: Active ingredient (mg/kg) of antibiotics sold for use in dogs and cats; from 2014 to 2019
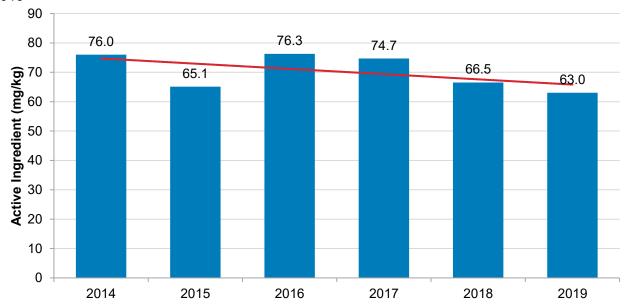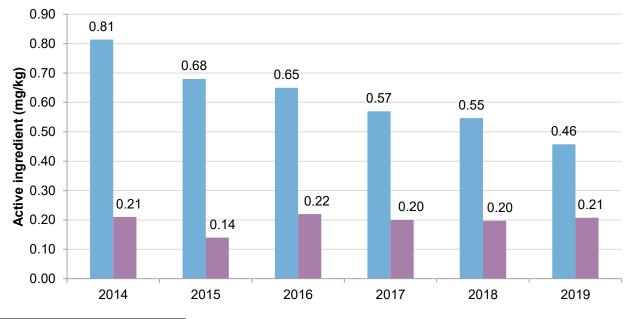

Figure 1.11: Active ingredient (mg/kg) of HP-CIAs, sold for dogs and cats combined: fluoroquinolones (▪) and 3rd and 4th generation cephalosporins (▪); from 2014 to 2019

---

[3] https://www.pfma.org.uk/statistics

[4] University of Liverpool, Small Animal Veterinary Surveillance Network (SAVSNET) project, personal communication, 2020

Adjusted for dog and cat populations, sales of antibiotic products licenced for dogs and cats combined was 63.0 mg/kg in 2019. This is a 3.5 mg/kg (5%) reduction since 2018, and a 13.0 mg/kg (17%) reduction since 2014.

The sales of HP-CIA products were 0.67 mg/kg in 2019, 1% of overall antibiotic sales in cats and dogs. Sales of 3rd and 4th generation cephalosporins were 0.21 mg/kg in 2019 which is an increase of 0.01 mg/kg (5%) since 2018 however, a decrease of 0.002 mg/kg (1%) since 2014. Sales of fluoroquinolones in 2019 were 0.46 mg/kg, having decreased by 0.09 mg/kg (16%) since 2018 and 0.35 mg/kg (43%) since 2014.
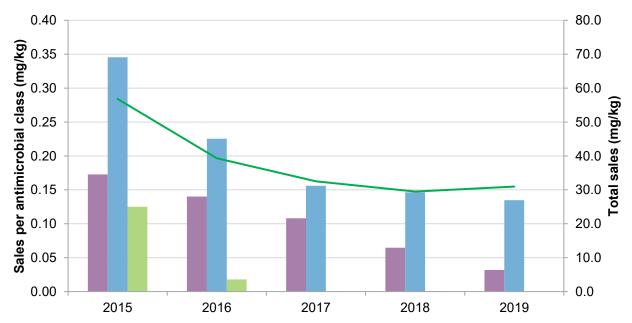
1.3.7   Harmonised outcome indicators for antibiotic use

In 2017, the European Centre for Disease Prevention and Control (ECDC), European Food Safety Authority (EFSA) and the European Medicines Agency (EMA) published a set of harmonised outcome indicators for comparable monitoring of key indicators for antibiotic consumption in food-producing animals. (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 1.7**). In the UK all quinolones sold for use in food-producing animals are fluoroquinolones (although the quinolone oxolinic acid is imported for the fish sector; see **Section 2.3.5.4**), and colistin is the only polymyxin sold for use in food-producing animals. The data show that all indicators have decreased since 2015 (**Figure 1.12**).

Figure 1.12: Harmonised primary (total sales of veterinary antibiotics in mg/kg (—)) and secondary (sales in mg/kg for 3rd and 4th generation cephalosporins (■), quinolones (■) and polymyxins (■)) outcome indicators for antibiotic consumption in food-producing animal species in the UK; from 2015 to 2019
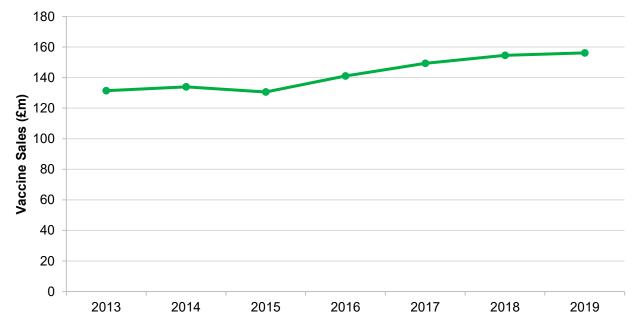
1.3.8 Sales of vaccines for all animal species

The data in this section have been provided by NOAH (National Office of Animal Health)[5].

Figure 1.13 presents the sales of vaccines reported by NOAH member companies and have been independently verified. The data ranges between 2013 and 2019 for vaccines that include products for all animal species, including companion animals, livestock, equines and fish.

Whist the trend in **Figure 1.13** should not be compared with the decline in volumes of antibiotics sold, these data show an increase in the value of the vaccine market over the last six years. Importantly it is not possible to determine whether the monetary value correlates with actual units of vaccine sold as different products have different prices.

An increase in the uptake of animal vaccines is an ambition in the UK's five-year national action plan to help minimise infection and protect animal health (Department of Health and Social Care and Department for Environment Food & Rural Affairs, 2019).

Figure 1.13: Sales of vaccines (in £m) in all animal species, between 2013 and 2019 (note that figures have not been adjusted for inflation)

[5] https://www.noah.co.uk/

1.4   Methods

Data collection and validation

Pharmaceutical companies supplied annual sales of all authorised veterinary antibiotics to the VMD in accordance with the Veterinary Medicines Regulations[6]. Upon receipt, data were collated and validated. Product data entries were compared to those submitted in previous years. If there are large discrepancies between data provided in successive years, data validity is investigated and queried with the pharmaceutical company. Sales data contained in returned Periodic Safety Update Reports (PSURs) for antibiotic veterinary medicinal products were also compared to the sales data returned by the pharmaceutical companies, and any discrepancies investigated (further details can be found in Annex D).

Tonnes of active ingredient

The weight of antibiotic active ingredient sold is a 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. 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, 2018).

Since UK-VARSS 2015 (published in 2016), sales data have been reported using ESVAC methodology. Further details on historical methodology for the calculation of quantity of active ingredient (as well as mg/PCU, see below) can be found in section S1.1 of the supplementary material. Note that data presented in mg/kg for food-producing animals (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 ATCvet Classification System for veterinary medicinal products shown in Table S1.1.2 of the supplementary material (World Health Organization, 2018). Sales of dermatological preparations and preparations for sensory organs (described as 'other' route of administration in the UK-VARSS reports) are not included in calculations. Sales of these products have remained stable and account for no more than 3 tonnes of active ingredient (Table S1.1.3 of the supplementary material).

Population Correction Unit

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, 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 the sales section of this UK-VARSS report, all references to mg/kg for food-producing animals equate to mg/PCU.**

Corrections for historical data

There have been minor retrospective changes in the sales data prior to 2019 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.

---

[6] http://www.legislation.gov.uk/uksi/2013/2033/contents/made

CHAPTER 2

Usage of Veterinary Antibiotics by Animal Species

Chapter 2

2.1   Summary

The key trends are as follows:

- **Pigs** - total usage remained stable between 2018 and 2019 at 110 mg/kg, but this is still 60% below the figure reported in 2015. Highest Priority Critically Important Antibiotics (HP-CIAs) remain very low and continue to fall.
- **Broilers** – total usage increased by 5.0 mg/kg between 2018 and 2019 to 17.4 mg/kg but has still reduced by 64% since 2014. No HP-CIAs were used in 2019.
- **Turkeys** – total usage reduced by 4.7 mg/kg between 2018 and 2019 to 42.0 mg/kg and has reduced by 81% since 2014. Further reductions in HP-CIA use were also seen in 2019.
- **Ducks** – total usage reduced by 0.10 mg/kg between 2018 and 2019 to 1.6 mg/kg and has reduced by 89% since 2014. No HP-CIAs were used in 2019.
- **Laying hens** – total usage increased by 0.13 % bird days to 0.68 % bird days and has increased 3% since 2016. No HP-CIAs were used in 2019.
- **Gamebirds** – total usage increased by 0.64 tonnes between 2018 and 2019 to 10.4 tonnes but has still reduced by 49% since 2016. HP-CIA usage increased by 11kg to 58kg but has reduced by 10% since 2016 (note that gamebird usage does not take population changes into account).
- **Cattle** – In a sample of farms representing 34% UK dairy cattle, HP-CIA use has reduced by 0.73 mg/kg (87%) to 0.11 mg/kg since 2017, and in a sample representing 5.6% GB beef production, HP-CIA use has reduced by 0.86 mg/kg (96%) to 0.04 mg/kg over the same period. While these convenience samples may not be representative, the reduction trend for HP-CIAs is consistent with the sales data which also show a 63% reduction in the sales of injectable HP-CIAs used in cattle and an 82% reduction in the sales of intramammary HP-CIAs since 2017.
- **Salmon** – total usage increased by 6.8 mg/kg to 13.5 mg/kg, which is still 16% lower than the figure reported in 2017.
- **Trout** – total usage decreased by 3.0 mg/kg to 9.8 mg/kg and has decreased by 50% since 2017.

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 food-producing animal sectors to develop, facilitate and coordinate antibiotic usage data collection systems.

Antibiotic usage refers to the amount of antibiotics prescribed and/or administered. 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 better any correlation between changing antibiotic use and antibiotic resistance. Data collection systems also enable benchmarking, allowing 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 food-producing animal sectors. Methodology is outlined in **Section 2.4**.

2.3   Results

2.3.1   Pigs

2.3.1.1   Antibiotic usage data

The electronic Medicines Book for Pigs (eMB) recorded total antibiotic usage in pigs as 110 mg/kg in 2019. This is the same as 2018 but still represents a decrease of 168 mg/kg since 2015 (**Table 2.1**).

Table 2.1: Usage recorded for active ingredient (mg/kg) of antibiotics in eMB Pigs by antibiotic class; from 2015 to 2019

Antibiotic	2015	2016	2017	2018	2019	Change 2015 to 2019
Tetracyclines	117.7	82.4	55.7	45.9	42.2	-64%
Penicillins	37.0	27.4	22.4	21.5	20.3	-45%
Trimethoprim/sulphonamides	66.2	29.2	20.8	18.5	18.0	-73%
Macrolides	31.0	28.8	16.0	10.4	9.0	-71%
Pleuromutilins	17.3	7.6	9.8	5.1	10.5	-39%
Other*	8.6	7.2	6.1	8.8	10.6	+23%
Total	**278**	**183**	**131**	**110**	**110**	**-60%**

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

Usage of HP-CIAs in pigs decreased by a further 0.02 mg/kg between 2018 and 2019 and has now fallen by 0.94 mg/kg since 2015 (**Figure 2.1** and **Table 2.2**).

Figure 2.1: HP-CIA usage recorded for active ingredient (mg/kg) of antibiotics in eMB Pigs: colistin (■), 3rd and 4th generation cephalosporins (■) and fluoroquinolones (■); from 2015 to 2019
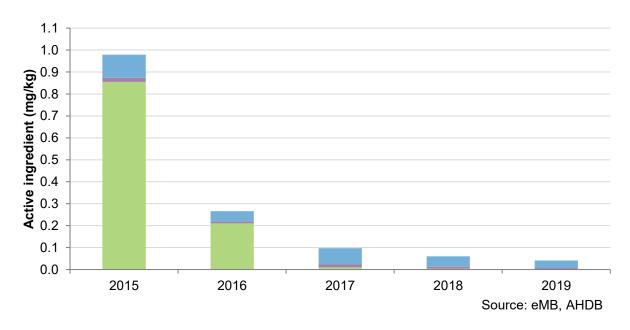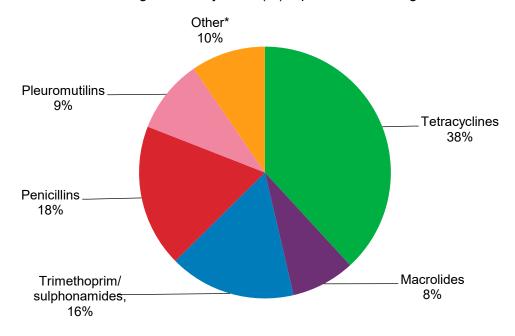

Source: eMB, AHDB

Table 2.2: HP-CIA usage recorded for active ingredient (mg/kg) of antibiotics in eMB Pigs, from 2015 to 2019

Antibiotic	2015	2016	2017	2018	2019	Change 2015 to 2019
Fluoroquinolones	0.11	0.05	0.07	0.05	0.03	-67%
3rd/4th generation cephalosporins	0.02	0.01	0.01	0.01	0.01	-70%
Colistin	0.86	0.21	0.01	0.004	0.002	-99.8%
Total	**0.98**	**0.27**	**0.10**	**0.06**	**0.04**	**-96%**

Tetracyclines represented 38% of antibiotic used, with penicillins, trimethoprim/sulphonamides and macrolides representing a further 42% (**Figure 2.2**).
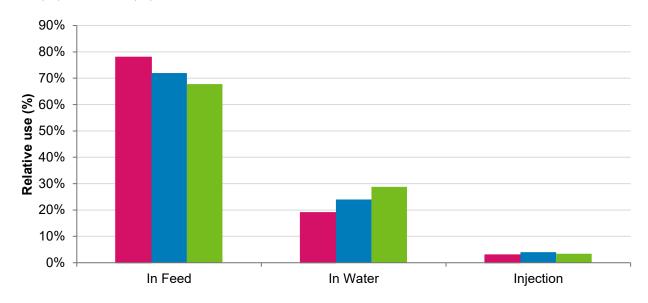
Figure 2.2: Antibiotic active ingredients by class (%) reported in eMB Pigs; 2019

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

In-feed is still the most common route of administration, although use relative to other routes of administration has decreased from 78% in 2017 to 68% in 2019. Correspondingly, in-water antibiotics now account for 29% active ingredient used (compared with 19% in 2017) (**Figure 2.3**).

Figure 2.3: Relative percentage usage of in-feed, in-water and injectable antibiotics, 2017 (■), 2018 (■) and 2019 (■)

2.3.1.2 Statement from Pig Health and Welfare Council (PHWC) Antimicrobial Usage Subgroup
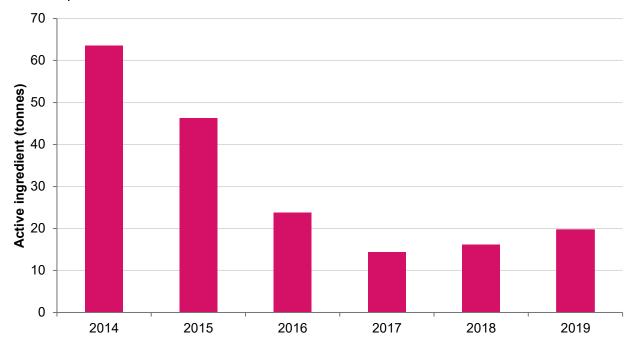
"Following a 60% reduction in antibiotic usage in pigs from 2016 to 2018, usage remained stable in 2019 (at 110 mg/kg). While most antibiotic classes, and the use of antibiotics in-feed, reduced in 2019, there was an increase in the use of pleuromutilins which is related to a spike in swine dysentery cases. Swine dysentery is a bacterial disease and, alongside a number of actions that can prevent disease spread and control infection, treatment with antibiotics is sometimes both responsible and necessary to safeguard pig health and welfare. The continued reduction in Highest Priority Critically Important Antibiotics is encouraging and in line with the Pig Veterinary Society prescribing principles that these should only be used as an absolute last resort. It is vital that veterinarians are able to target specific antibiotic treatments to control disease issues when these arise on pig farms; the use of diagnostic tests and antimicrobial sensitivity testing is encouraged. Pig vets and farmers remain committed to antibiotic stewardship and disease prevention, and their efforts have reduced outbreaks of swine dysentery in the first six months of 2020 and will help the pig industry achieve further antibiotic reductions, alongside improvements in pig health and welfare. The pig sector is now very close to achieving the 2020 Targets Task Force (TTF1) target of a 64% reduction (99 mg/kg) set in 2016 and is currently formulating ambitious new targets to take it through to 2024."

2.3.2 Meat poultry

2.3.2.1 Antibiotic usage data

In 2019, the British Poultry Council (BPC) reported the use of 19.7 tonnes of active ingredient; a 3.5 tonnes increase since 2017, although usage has decreased by 43.8 tonnes since 2014 (**Figure 2.4**).

Figure 2.4: Active ingredient (tonnes) of antibiotics used by all members of BPC Antibiotic Stewardship; from 2014 to 2019

When considering the size of the animal population, between 2018 and 2019 antibiotic usage in the chicken sector increased by 5.0 mg/kg to 17.4 mg/kg, which is 7.6 mg/kg higher than the usage in 2017. However, it is still 31.4 mg/kg (64%) lower than 2014. Antibiotic usage in the turkey sector decreased by 4.7 mg/kg to 42.0 mg/kg and has reduced by 177.5 mg/kg (81%) since 2014, whereas in the duck sector usage has decreased by a further 0.10 mg/kg to 1.6 mg/kg and has reduced by 13.5 mg/kg (89%) since 2014. For both the chicken and turkey sectors, usage remains below the sector targets of 25 mg/kg and 50 mg/kg respectively (**Figure 2.5**, **Figure 2.6**).

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 (■), 2018 (■) and 2019 (■)
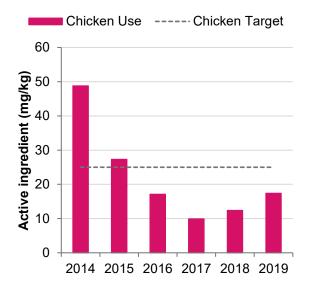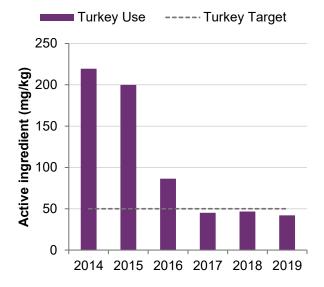
Chapter 2
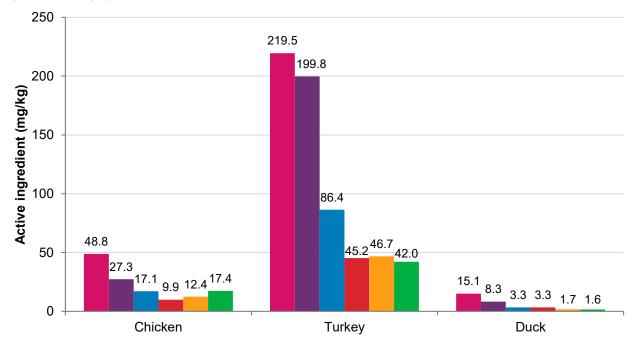
Figure 2.6: Active ingredient (mg/kg) of antibiotics used by all members of BPC Antibiotic Stewardship by species (chicken and turkey) from 2014 to 2019 compared with the sector specific target

In 2019, 85% of active ingredient classes used comprised penicillins and tetracyclines, which increased by 2.5 tonnes and 1.4 tonnes respectively between 2018 and 2019. However, during this period macrolides, lincomycins and potentiated sulphonamides reduced by 0.41 tonnes, 0.14 tonnes and 0.09 tonnes respectively. (**Table 2.3** and **Figure 2.7**).

Table 2.3: Active ingredient (tonnes) of antibiotics used by all members of BPC Antibiotic Stewardship by antibiotic class; from 2014 to 2019
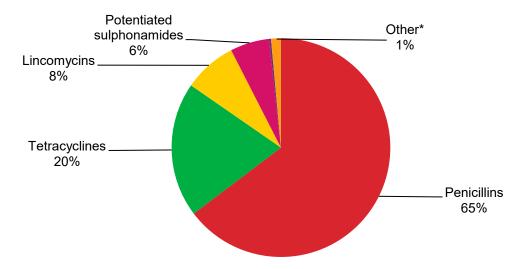
Antibiotic	2014	2015	2016	2017	2018	2019	Change 2014 to 2019
Penicillins*	19.8	14.1	10.6	8.2	10.2	12.7	-36%
Tetracyclines	30.6	23.9	9.0	3.3	2.5	3.9	-87%
Lincomycins	7.1	4.8	1.4	1.2	1.7	1.5	-78%
Potentiated sulphonamides	1.2	1.0	1.6	0.94	1.2	1.1	-1%
Macrolides	2.7	1.1	0.53	0.56	0.47	0.06	-98%
Other** including:	2.1	1.4	0.60	0.17	0.05	0.28	-86%
Fluoroquinolones^ (kg)	1,131	540	122	38	17.3	14.4	-99%
Colistin^ (kg)	121	40	8	0	0	0	-100%
Total	**63.5**	**46.2**	**23.7**	**14.4**	**16.2**	**19.7**	**-69%**

* Amoxicillin and phenoxymethylpenicillin.
** Aminoglycosides, pleuromutilins, fluoroquinolones, colistin and products under the cascade.
^ Highest Priority Critically Important Antibiotics.

Figure 2.7: Antibiotic active ingredient by class (%) used by members of BPC Antibiotic Stewardship; 2019

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

Colistin and 3rd and 4th generation cephalosporins were once again not used by the meat poultry sectors in 2019. Fluoroquinolones were also not used by the duck sector or broiler sector in 2019. Between 2018 and 2019, the turkey sector also reduced the use of fluoroquinolones by 0.09 mg/kg to 0.11 mg/kg, a reduction of 7.5 mg/kg since 2014.

2.3.2.2   Statement from British Poultry Council

"BPC Antibiotic Stewardship continues to ensure the sustainable and responsible use of antibiotics and deliver excellence in bird health and welfare. Clinical governance means that Highest Priority Critically Important Antibiotics are used only as a last resort, and this is highlighted by the ongoing reductions in fluoroquinolones to just 0.01 mg/kg overall in 2019. The turkey and duck sectors reduced their total antibiotic use in 2019, although disease challenges in the broiler sector meant that antibiotic usage increased overall. We are investigating the reason(s) behind this increase, and maintaining our focus on sharing best practice and the 3 Rs i.e. Replacing antibiotics (looking at alternatives where available), Reducing disease and the need to treat and Refining control strategies, supported by the principles of animal husbandry, hygiene and stockmanship."

2.3.3   Laying Hens
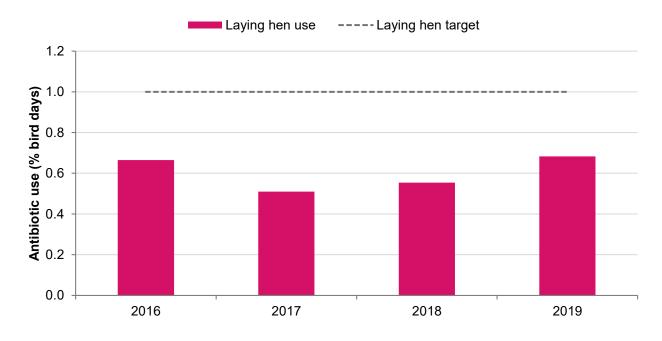
2.3.3.1   Antibiotic usage data

A total of 4.8 tonnes of antibiotic active ingredient were used by the laying hen industry in 2019. This represents 0.68 actual bird days treated/100 bird days at risk (% bird days), an increase of 0.13 and 0.02 since 2018 and 2016 respectively but below the sector target of 1% (**Table 2.4, Figure 2.8**). The methodology for this metric is explained in Section 2.4.

Table 2.4: Antibiotic use (% bird days) by members of the BEIC Lion Code; from 2016 to 2019 (please note the figures from 2016, 2017 and 2018 are different to those published last year, which is due to some corrections that BEIC have made to the number of bird days at risk):

Antibiotic	2016	2017	2018	2019	Change 2016 to 2019
Tetracyclines	0.26	0.28	0.33	0.41	+57%
Pleuromutilins	0.25	0.15	0.11	0.12	-51%
Macrolides	0.04	0.02	0.04	0.06	+40%
Penicillins	0.06	0.05	0.05	0.05	-15%
Aminoglycosides	0.02	0.01	0.02	0.04	+100%
Other* includes:	0.03	0	0	0.003	
Fluoroquinolones^	0.001	0.001	0	0	-91%
Colistin^	0.03	0	0	0	
Total	**0.67**	**0.51**	**0.55**	**0.68**	**+3%**

* Includes fluoroquinolones and colistin.
^ Highest Priority Critically Important Antibiotics.
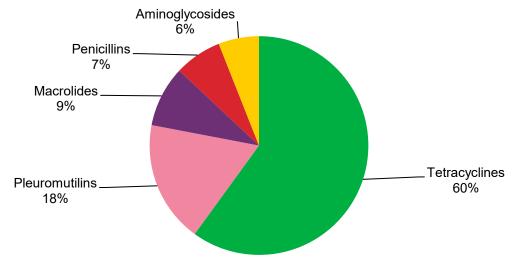
Figure 2.8: Antibiotic use (% bird days) by members of the BEIC Lion Code; from 2016 to 2019 alongside the sector target

Tetracyclines and pleuromutilins accounted for 78% of total use. Since 2016, tetracyclines have increased by 0.15 % bird days and pleuromutilins have decreased by 0.13 % bird days. For the second year running there were no HP-CIAs used by the laying hen sector in 2019 (**Figure 2.9**).

Figure 2.9: Antibiotic use (% bird days) by class (%) used by members of the BEIC Lion Scheme; 2019

2.3.3.2   Statement from the British Egg Industry Council (BEIC)

"The usage data presented for 2019 show that the members of the BEIC Lion Scheme, which represent over 90% of the industry, have once again met the sector target for percentage bird days treated to remain below 1%. It is also encouraging to see that once again no HP-CIAs were used in 2019, which is in line with the target to keep their use below 0.05% bird days treated. However, the total "bird days/100 bird days at risk" figure for 2019 was higher than in the previous three years. The reason for treatment data was recorded in >86% of cases in 2019 and this showed that there was a higher incidence of enteritis. We will be working with farmers and veterinarians to better understand the reason for this increase and using this reason for treatment data to prioritise research and interventions to reduce disease and the subsequent need for medication. There will be a new version of the Lion Code of Practice published in 2020, which will require medicines training through the Lion passport. This will cover areas relevant to reducing the need to medicate, including biosecurity and medicine use. It will also require an annual review of a "Veterinary Health and Welfare Plan", which will consider antibiotic use and management changes to prevent and control disease, including, where appropriate the use of licensed and autogenous vaccines, the use of non-antimicrobial feed additives, or other interventions."

2.3.4   Gamebirds

2.3.4.1   Antibiotic usage data

Antibiotic usage data from the gamebird sector doesn't correct by gamebird population and is therefore presented in tonnes of active ingredient. In 2019, 10.4 tonnes of active ingredient were reported through the Game Farmers' Association (GFA) data collection programme. This represents an increase in 0.64 tonnes between 2018 and 2019, but still a reduction of 9.8 tonnes since 2016 (**Table 2.5**).

Tetracyclines and pleuromutilins represented 79% of antibiotics used in 2019 (**Figure 2.10**). Within the HP-CIAs, there was an 11kg increase in fluoroquinolone use between 2018 and 2019, although overall HP-CIA has reduced by 6.6kg since 2016.
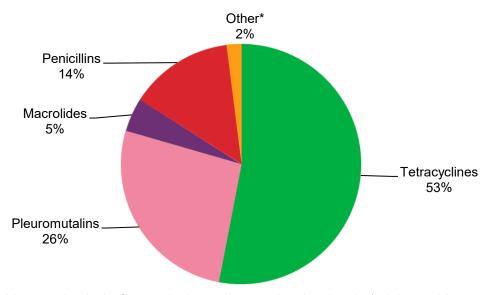
Analysis of usage data by route of administration shows that in-feed medication accounted for 41% antibiotic use, and this has reduced by 0.26 tonnes since 2018 and 10.7 tonnes since 2016. By contrast, in-water medication has increased by 0.86 tonnes since 2016.

Table 2.5: Active ingredient (tonnes) of antibiotics used by the gamebird industry, recorded by GFA; from 2016 to 2019

Antibiotic class	2016	2017	2018	2019	Change 2016 to 2019
Tetracyclines	14.4	8.2	5.5	5.5	-62%
Pleuromutilins	3.7	3.6	2.8	2.7	-25%
Penicillins	1.2	0.83	1.1	1.5	-17%
Macrolides	0.62	0.33	0.23	0.47	-24%
Other*:	0.22	0.10	0.16	0.20	-9%
Fluoroquinolones^ (kg)	64	50	47	58	-9%
Colistin^ (kg)	0.60	0	0	0	-100%
Total	**20.2**	**13.0**	**9.7**	**10.4**	**-49%**

* Aminoglycosides, amphenicols, colistin, fluoroquinolones, lincomycins, trimethoprim/sulphonamides.
^ Highest Priority Critically Important Antibiotics.

Figure 2.10: Antibiotic active ingredient by class (%) used by the gamebird industry; 2019

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

2.3.4.2   Statement from the Game Farmers' Association

"The 2019 results for the gamebird sector show overall antibiotic use at similar levels to the year before. However, this was in the context of a very wet summer, just when gamebirds were being released, and that increased stress-related diseases markedly and thus the need to treat sick birds, notably with soluble antibiotics, which consequently rose slightly. This included a slight rise in fluoroquinolone use and, in 2020 we issued guidance and a governance process to ensure that HP-CIAs are only used as a last resort, backed up where possible and appropriate by diagnostic and sensitivity testing.

During 2019, The Game and Wildlife Conservation Trust also published data showing the number of gamebirds released continuing to rise at an average of 2.4% a year, implying an overall increase since our base year (2016) of 7.4%. In light of these factors, 2019 represented a further year of progress in limiting antibiotic use by the gamebird sector, which remains fully committed to seeking further reductions so far as good animal welfare allows."

2.3.5   Cattle

2.3.5.1   Dairy usage

The dairy sector antibiotic usage data for 2019 cover 3,410 farms (which is 15% higher than last year) and represents 34% of UK dairy cattle. The mean herd size within the sample is 216 dairy breed animals over 2 years of age, 4% smaller than last year's sample and 31% higher than the overall UK mean. When looking at farms in Great Britain, 30% of farms in the 2019 sample were not present in the 2018 sample. In order to better interpret trends, it was therefore decided to re-analyse the 2017 and 2018 datasets using the current VetImpress dataset, which includes 84% and 93% respectively of the farms in the 2019 dataset. It should be noted, however, that antibiotic usage and the trends demonstrated in this convenience sample may not be representative of the whole UK dairy population.

Table 2.6: Comparison of national coverage (% coverage*) of adult dairy cows (over 2 years of age) included in the FarmVet Systems sample; 2019

Country	2019
England	34
Northern Ireland	36
Wales	35
Scotland	32
UK	**34**

* Calculated by comparing the number of dairy cattle >2 years of age in the sample with national records of number of dairy cows >2 years of age (with and without offspring).

In this sample of dairy farms, 7.1 tonnes of antibiotic active ingredient were used, which represents 22.5 mg/kg. This is higher than the 17 mg/kg reported last year. However, when looking at the more comparable 2017 and 2018 dataset, this shows that total use is actually very similar to previous years (21.9 and 22.8 for 2017 and 2018 respectively) (**Table 2.7**).
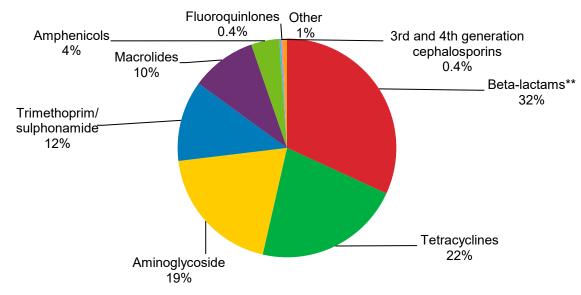
However, within this sample there has been a clear shift in use away from the Highest Priority Critically Important Antibiotics (HP-CIAs) for human use, with 3rd and 4th generation cephalosporins and fluoroquinolones falling by 0.48 mg/kg and 0.25 mg/kg respectively over the last two years. HP-CIAs now account for 0.5% of total use, down from 3.8% in 2017. Macrolides have also seen a reduction of 0.83 mg/kg over the same period. By contrast, other non-HP-CIA products, have increased by 0.51 mg/kg, 0.36 mg/kg, 0.62 mg/kg and 0.66 mg/kg for trimethoprim-sulphonamides, aminoglycosides, tetracyclines and penicillins/1st generation cephalosporins respectively. The products which have increased have a higher amount of active ingredient per course than the products which have reduced and this "product switching" away from HP-CIAs and macrolides is responsible for the slight increase in total mg/kg.

Table 2.7: Active ingredient (mg/kg) of antibiotics used by the dairy farms in the FarmVet Systems sample; from 2017 to 2019

Antibiotic	2017	2018	2019	Change 2017 to 2019
Penicillins/1st generation cephalosporins	6.5	6.8	7.2	+10%
Tetracyclines	4.3	5.2	4.9	+15%
Aminoglycosides	4.0	4.4	4.4	+9%
Trimethoprim/sulphonamides	2.2	2.5	2.7	+23%
Macrolides	3.0	2.6	2.2	-28%
Amphenicols	0.91	0.87	0.94	+4%
Fluoroquinolones^	0.30	0.17	0.06	-81%
3rd/4th generation cephalosporins^	0.54	0.24	0.05	-90%
Other* including:	0.17	0.15	0.14	-16%
Colistin^	0.005	0	0	-100%
Total	**21.9**	**22.8**	**22.5**	**+3%**

^ Highest Priority Critically Important Antibiotics.
* Including aminocoumarins, lincosamides and polymyxins.

Figure 2.11: Antibiotic active ingredient by class (%) used by the dairy farms in the FarmVet Systems sample; 2019

* Including aminocoumarins and lincosamides; ** Not including 3rd and 4th generation cephalosporins

When looking at usage by route of administration then 71% and 18% of the weight of active ingredient used is attributable to the injectable and oral routes of administration (**Table 2.8**).

Table 2.8: Active ingredient in mg/kg (course doses) of antibiotics used by the dairy farms in the FarmVet Systems sample for injectable and oral products, from 2017 to 2019

Administration route	2017	2018	2019	Change 2017 to 2019
Injectable	15.6 (0.58)	15.8 (0.55)	16.0 (0.54)	+3% (-7%)
Oral	3.7 (0.024)	3.8 (0.025)	3.9 (0.027)	+7% (+13%)

While these volumes of active ingredient (in mg/kg) increased for injectable and oral products over the last two years (by 0.43 mg/kg and 0.27 mg/kg respectively), the number of course doses for injectables have decreased by 0.04 (7%) (**Table 2.8**). This can be explained by the fact that, as explained earlier, the injectable products which have fallen (macrolides, 3rd and 4th generation cephalosporins and fluoroquinolones) have a lower amount of active ingredient per course than the injectable products which have increased (penicillins/1st generation cephalosporins, tetracyclines, aminoglycosides and trimethoprim/sulphonamides). For example:

- Consider ten 100kg calves have pneumonia, with a bacterial component that is sensitive to marbofloxacin (a fluoroquinolone, an HP-CIA) and amoxicillin (an aminopencillin, not an HP-CIA).
- Injectable marbofloxacin is commonly administered at a dose rate of 2 mg/kg/day in a single daily injection for 3 to 5 days. If we assume 3 days of treatment were needed, each calf would receive 600mg active ingredient in total, resulting in 6000mg being administered in total.
- An alternative short acting amoxicillin product is licensed at a dose rate of 7 mg/kg for up to 5 days. Again, if we assume 3 days of treatment were needed each calf would receive 2100mg, resulting in 21,000mg being administered in total, 3.5 times more active ingredient.

However, despite this, moving away from HP-CIAs and using them as a last resort only when necessary, is an example of responsible antibiotic use as it should help to preserve their efficacy as a last resort antibiotic for serious infections in people.

2.3.5.2   Beef usage

The beef data for 2019 cover 4,188 farms in Great Britain (compared with 3,458 in 2018) and represents 9.6% of the slaughter animals for GB. While it is larger than the full 2018 sample, it is 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, farms in England are over-represented, largely because far fewer farms were excluded from the sample due to the presence of sheep (**Table 2.9**). These are excluded because it is not possible to determine for which species products licensed for cattle and sheep have been used.

Table 2.9: Comparison of national coverage of the beef Population Correction Unit (PCU) included in the FarmVet Systems sample; 2019* and % farms excluded due to the presence of sheep
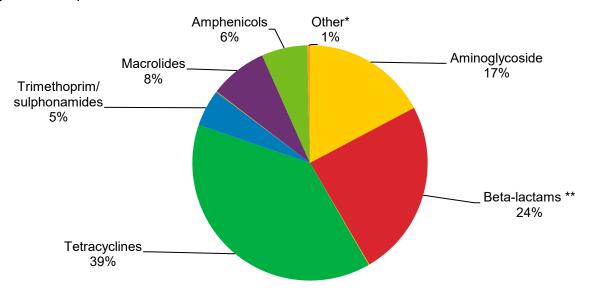
Country	% Coverage	% Farms excluded due to presence of sheep
England	10	44
Wales	6	64
Scotland	9	66

* Calculated by comparing PCU for the sample with PCU per country, using data from BCMS and making the same assumptions (i.e. with a beef farm defined as having <15 calves born to dairy dams).

Chapter 2

The usage data showed that 1.7 tonnes of antibiotic active ingredient were used in this sample of farms, which represents 24.4 mg/kg. HP-CIAs represented 1% of antibiotics administered, with no colistin use reported.

Tetracyclines, penicillins/1st generation cephalosporins and aminoglycosides were the most commonly used antibiotic classes (**Figure 2.12**) and HP-CIAs accounted for 0.2% of antibiotic active ingredient used. The highest volume of active ingredient was administered by injection (73%).

Figure 2.12: Antibiotic active ingredient by class (%) used by the beef farms in the FarmVet Systems sample; 2019

* Including aminocoumarins and lincosamides; ** Not including 3rd and 4th generation cephalosporins

The overall figure (24.4 mg/kg) was higher than the figure reported in 2018 (21 mg/kg). However, caution should be exercised with this comparison as, while the 2019 sample does include 65% of the farms included in the 2018 sample, there are also 1391 additional farms that were not included in the 2018 sample.

To understand possible trends, antibiotic usage was compared for the 2,265 GB farms (representing 5.6% GB coverage) where antibiotic usage data was available for 2015, 2016, 2017, 2018 and 2019. When looking at this sample, the overall usage is higher for 2019 than the full sample (28.2 mg/kg versus 24.4 mg/kg), which may reflect differences in the make-up of the farms between these samples. However, the total use reduced by 7.8 mg/kg and the use of HP-CIAs reduced by 1.5 mg/kg in these farms between 2015 and 2019 (**Table 2.10**). As highlighted earlier, due to the fact that this is a relatively small convenience sample, the trends observed here may not reflect the national situation.

Table 2.10: Total antibiotic usage and use of HP-CIAs (active ingredient in mg/kg) in a sample of 2,265 beef farms; from 2015 to 2019

Category	2015	2016	2017	2018	2019	Change 2015 to 2019
Total antibiotic use	36.0	35.5	35.4	34.4	28.2	-22%
3rd and 4th generation cephalosporins	0.86	0.70	0.46	0.20	0.01	-99%
Fluoroquinolones	0.69	0.61	0.44	0.28	0.03	-96%
Colistin	0	0	0	0	0	0
Total HP-CIAs	1.5	1.3	0.89	0.47	0.04	-97%

2.3.5.3　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 2016 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. **Table 2.11** shows that this target has been exceeded, with a 72% reduction in cattle injectable HP-CIAs since the baseline year of 2016.

Table 2.11: 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; from 2015 to 2019

Category	2015	2016	2017	2018	2019	(Target) 2020	Change 2015 to 2019
Injectable HP-CIA products licenced for cattle (mg/kg)	1.1	0.92*	0.70	0.50	0.26	**0.46**	-77%
Intramammary HP-CIA products	0.33*	0.24	0.17	0.12	0.03	**0.17**	-91%
Intramammary tubes – lactating cow	0.80*	0.82	0.69	0.78	0.60	**0.73**	-25%
Intramammary tubes – dry cow	0.73*	0.61	0.54	0.64	0.58	**0.59**	-21%

* Baseline year for targets.

For the dairy sector, there are also targets to reduce intramammary HP-CIAs by 50% by 2020 and reduce lactating cow intramammary use and dry cow intramammary use by 10% and 20%, from a 2015 baseline. The sector has exceeded these targets, with a 91% reduction in intramammary HP-CIA use as well as a 25% reduction in lactating cow therapy sales and a 21% reduction in dry cow therapy sales since the baseline year of 2015.

2.3.5.4   Statement from Cattle Health and Welfare Group (CHAWG)

"Once again, the downward trend in the sales of injectable and intramammary HP-CIAs is very encouraging. The cattle survey data suggests that this has been achieved alongside a reduction in the number of antibiotic courses administered. This is testament to the work of the cattle sector in promoting disease prevention strategies alongside responsible antibiotic use, and has also been greatly helped by the strengthened Red Tractor requirement, which was introduced in June 2018 and requires that HP-CIAs are only used as a last resort, alongside antibiotic sensitivity and/or diagnostic testing. The reductions in the sales of intramammary antibiotics (for both dry and lactating cow therapy) also reflect industry initiatives, including those to promote selective dry cow therapy. During 2019, the CHAWG Antimicrobial Usage sub-group (CHAWG AMU) consulted and agreed on core farm benchmarking metric(s) for the beef sector as well additional metrics for benchmarking dairy and beef youngstock. Further details can be found here – www.chawg.org.uk. Farm benchmarking allows farms to understand their antibiotic use, and how this is changing over time and relative to the industry, as well as help guide the veterinarian-farmer discussions around disease prevention and responsible antibiotic use. Further work is needed by the cattle sector to improve the collection and collation of antibiotic usage data, and the industry is confident that the launch of the Medicine Hub for cattle and sheep in 2020 by AHDB will greatly help to bring these data together."

2.3.6   Aquaculture

2.3.6.1   Salmon

2.3.6.1.1 Results

In 2019, 2.8 tonnes of active ingredient of antibiotics were used, representing 13.5 mg/kg (**Table 2.12**), which is 6.8 mg/kg higher than the use reported in 2018, but 2.6 mg/kg lower than usage reported in 2017. Under the new AMEG advice published in January 2020, the quinolone oxolinic acid is now considered an HP-CIA, although this was not the case in 2019.

Table 2.12: Active ingredient in mg/kg of antibiotics used on Scottish salmon farms; from 2017 to 2019

Antibiotic	2017	2018	2019	Change 2017 to 2019
Oxytetracycline	13.8	3.9	10.2	-26%
Florfenicol	2.2	2.7	3.3	+51%
Oxolinic acid	0.12	0.08	0.02	-79%
Amoxicillin	0.004	0	0	-100%
Total	**16.1**	**6.7**	**13.5**	**-16%**

2.3.6.1.2 Statement from the Scottish Salmon Producers' Organisation

"Antibiotic use has increased in 2019 compared with 2018, but use remains lower than in 2017. As highlighted by recent use figures and historical sales data, usage in the sector can fluctuate year-on-year. This is due to a number of factors, notably challenging environmental conditions and

differences between use in the freshwater and marine stages of production. The 2019 figure is above the ambitious target set by the sector, to keep usage in the salmon industry below 5 mg/kg. The sector remains committed to focus on preventative medicine and only use antibiotics when absolutely necessary in order to maintain fish health and welfare."

2.3.6.2   Trout

2.3.6.2.1 Results

The sample obtained represented approximately 90% of the UK trout production and a total of 0.13 tonnes of antibiotic active ingredient was used, representing 9.8 mg/kg, a 3.0 and 10.0 mg/kg reduction on the figure reported in 2018 and 2017 respectively (**Table 2.13**). Under the new AMEG advice published in January 2020, the quinolone oxolinic acid is now considered an HP-CIA, although this was not the case in 2019.

Table 2.13: Active ingredient in mg/kg of antibiotics used on a sample of trout farms; from 2017 to 2019

Antibiotic	2017	2018	2019	Change 2017 to 2019
Oxytetracycline	7.6	3.8	5.2	-32%
Oxolinic acid	7.0	5.8	2.5	-64%
Florfenicol	4.4	2.2	1.9	-56%
Amoxicillin	0.78	1.1	0.23	-71%
Total	**19.8**	**12.8**	**9.8**	**-50%**

2.3.6.2.2 Statement from the British Trout Association

"The data show that usage in this large sample of trout farms has reduced again in 2019 and remains below the sector target of using less than 20 mg/kg. This reflects the commitment of the trout sector to focus on biosecurity and good management practices, including widespread vaccination, in order to minimise the use of antibiotics. It is also partly linked to a shift in the market towards larger fish. There is no prophylactic use in the trout sector and so antibiotics are only used when needed to treat disease as outlined in the Veterinary Health Plan. Oxolinic acid has also reduced, but remains vital for the treatment of specific diseases in the trout sector, in particular Enteric Redmouth (*Yersinia. ruckeri*)."

2.3.7   Companion Animals

2.3.7.1   Horses

In the equine sector, a new study has been published exploring the use of Highest Priority Critically Important Antibiotics (HP-CIAs)[7].

---

[7] Use of Protected Antimicrobials in UK Equine Practice, Allen S, Brodbelt D, Slater J, Verheyen K, BEVA Congress Sept 2020, Clinical Research Abstract.

This study focused on three HP-CIA classes, namely the 3rd and 4th generation cephalosporins and fluoroquinolones, which are collectively labelled 'protected' by the British Equine Veterinary Association. These 'protected' antibiotics should only be used as a last resort where there are no alternatives and ideally be guided by culture and sensitivity testing.

Anonymised electronic patient records (EPR) for all equids attended by five UK equine veterinary practices between 14th October 2016 and 13th October 2017 were collected via the bespoke data-capture system Equine VetCompass™. Out of 28,994 equids for which EPR were obtained, 5,524 (19%) were prescribed at least one antibiotic course during the study period and 8.2% of courses included a 'protected' antibiotic.

Highest priority CIAs were prescribed as first-line therapy for 378 courses (66% of courses where highest priority CIAs used, 95% CI 62.1-70.0%). Culture and sensitivity testing informed antibiotic choice in only 19% of courses including a 'protected' antibiotic. Integumentary and respiratory disorders were the respective primary indication for antibiotic use in 25% and 19% of courses including a 'protected' antibiotic. The study also identified that 'protected' antibiotic use was more common in youngstock, thoroughbreds, racehorses and hospitalised patients.

While data were only available from a small convenience sample of veterinary practices, it provides some interesting observations and further work is needed to understand drivers for HP-CIA use in horses, particularly in those identified at increased risk.

2.3.7.2   Dogs and Cats

In a newly published study, which was funded by the VMD (VM0520), data from Electronic Health Records, collected by SAVSNET, were analysed from 173 UK veterinary practices covering 155,732 unwell dogs and 111,139 unwell cats between 2014 and 2016[8].

The results showed that, in dogs, systemic antibiotics were prescribed during 26% of these consultations and systemic HP-CIAs during 1.4%, whereas for cats, systemic antibiotics were prescribed during 33% of these consultations and systemic HP-CIAs during 17%.

In dogs the most commonly prescribed HP-CIA was fluoroquinolones (0.9% consultations) whereas in cats it was 3rd generation cephalosporins (16%). In both dogs and cats, HP-CIAs were less likely to be prescribed if animals were vaccinated and more likely to be prescribed if animals were insured. In both dogs and cats the highest prescription odds were for animals with a respiratory complaint.

Industry guidance for dogs and cats recommends that HP-CIAs should only be used when first-line antibiotics are inappropriate or ineffective[9], and this should ideally be guided by culture and sensitivity. However, these results demonstrate frequent prescription of HP-CIAs, especially in cats, and also provide some interesting risk factors for the prescription of HP-CIAs, although more work is still needed to better understand prescribing behaviours.

---

[8] Singleton DA, Pinchbeck GL, Radford AD, Arsevska E, Dawson S, Jones PH, et al. Factors Associated with Prescription of Antimicrobial Drugs for Dogs and Cats, United Kingdom, 2014–2016. Emerg Infect Dis. 2020;26(8):1778-1791. https://dx.doi.org/10.3201/eid2608.191786
[9] https://www.bsava.com/Resources/Veterinary-resources/PROTECT-ME

Chapter 2

2.4   Methods

Pigs

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 2016.

The scope and limitations of the data (as provided by AHDB-Pork) are presented below:
- These data are national, aggregated figures for antibiotic usage calculated from individual unit data held in the eMB for pig farms across the UK;
- eMB uptake to date has been voluntary (although since 2017 at the request of industry, data entry into eMB has been required by the Red Tractor and Quality Meat Scotland assurance schemes), and this sample may not be representative for the whole of the UK;
- In terms of UK pig production, the eMB data covers 56% for 2015, 62% for 2016, 87% for 2017, 89% for 2018 and 95% for 2019;
- The data are inputted by producers and, although clear outliers have been identified and queried, AHDB 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;
- The data for 2019 were extracted from eMB on 19 May 2020 and these figures will now be fixed as the reference levels for 2019. Data in Method of Administration, Breakdown by Product and Class and Breakdown by class tabs was extracted from eMB on 21 August 2020 based on the same criteria used during May, but some corrections to data entries have amended the figures slightly;
- The eMB database and the calculations within it are subject to a series of quality assurance checks to ensure national aggregated figures are as accurate as possible. As a result of this process, the eMB system is continuing to develop and work to further improve data accuracy is ongoing;
- The calculations used for the eMB data are in-line with the methods used by the ESVAC project, to allow comparisons to be made with European counterparts.

Meat poultry

The British Poultry Council (BPC) provided antibiotic usage data for the poultry meat (chicken, turkey and duck) sectors. 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 both 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 standardised estimated weights at time of treatment (chickens: 1.0 kg as derived by ESVAC; turkeys: 6.5 kg as derived by ESVAC; ducks: 1.75 kg as derived by BPC based on ESVAC principles).

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

Laying hens

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 then reported to the BEIC on a quarterly basis. The BEIC collated 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 methodology. Denominator data are available from monthly records of the total number of birds in the scheme, averaged over the year.

The data published here as 'actual daily bird days/100 bird days at risk' represent the average number of days treatment administered per chicken over a 100-day period. Note that a 'mg/kg' figure has not been included, as ESVAC methodology does not include a standardised method for laying hens.

Gamebirds

The Game Farmers' Association (GFA) coordinated a comprehensive, voluntary data collection exercise to measure the use of antibiotics throughout the sector for 2019. This involved the collection of in-feed medication records from game feed producers (which supply 95% of game farmers and rearers) and prescribing records from specialist gamebird vets (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 2019. GFA aggregated the results and provided them to the VMD, who then used ESVAC methodology to calculate the amount of antibiotic active ingredient administered by the game sector. Note that a 'mg/kg' figure has not been included, as ESVAC methodology does not include a standardised method for gamebirds.

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 has been delivered to a farm keeping cattle.

In this analysis, farms were considered dairy if they had greater than or equal to 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.
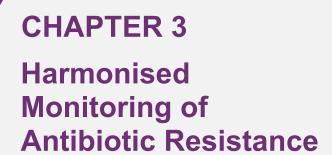
Farms which had fewer than 15 calves born to dairy dams were considered beef. In addition, farms were removed if Radar GB Census Survey data indicated the presence of sheep or if data showed 'sheep-only' products had been used on the farm. This is because it is not possible to easily distinguish usage between sheep and beef cattle from practice management data. Note that it was only possible to carry out this sheep analysis for farms from 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 the mg/kg using ESVAC methodology. Note that living cattle present on the farm are not included in the ESVAC beef denominator. This is different to the equivalent metric for dairy herds, sheep flocks and pig herds, where breeding populations on farms are part of the denominator.

VMD converted the aggregate usage data into amount of antibiotic 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 licenced for 'multi-species' – including cattle – may have been used in other species kept on the farm.

Aquaculture

The trout data were collected from the main veterinary practices dealing with trout in England and Scotland and represent c. 90% 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 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 not in the weight denominator, leading to a potential overestimate of the mg/kg. 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 that may require treatment.

CHAPTER 3

Harmonised Monitoring of Antibiotic Resistance

In 2019, the UK was a Member State in the European Union (EU) and this report presents the data collected and analysed at this time, in accordance with EU legislation.

The harmonised monitoring of antibiotic resistance is a programme set out in the Commission Implementing Decision 2013/652/EU (European Commission, 2013), which mandates all EU Member States to monitor and report antibiotic resistance in zoonotic and commensal bacteria from healthy food-producing animals and food products at retail.

An overview of the sampling plan, by year, is summarised in Table S3.1.1 of the supplementary material. The sampling size and strategy are designed to provide a sample which is representative of the wider population for each combination of bacteria and animal species.

In 2019, EU Member States were mandated to carry out the following testing:

- Susceptibility testing of *Escherichia coli* obtained from caecal samples taken from healthy pigs at slaughter;
- Testing for the presence of Extended-Spectrum Beta-Lactamase (ESBL)-, AmpC Beta-Lactamase (AmpC)-, or carbapenemase-producing *E. coli* in caecal contents from pigs at slaughter, as well as samples of fresh pork and beef at retail;
- Susceptibility testing of *Salmonella* spp. isolates derived from pig carcase samples taken at slaughter by Food Business Operators.

The results of the testing of isolates from caecal samples and carcase samples are presented in this chapter. The Food Standards Agency (FSA) leads on the testing of pork and beef samples and presents the results in their own reports (https://www.food.gov.uk/research/foodborne-diseases/eu-harmonised-survey-of-antimicrobial-resistance-amr-on-retail-meats-pork-and-beefchicken-0).

3.1   Summary

Escherichia coli

- There was no resistance to colistin or meropenem in *E. coli* from pigs.
- Resistance to cefotaxime and ceftazidime was detected in 1.4% and 1.0%, respectively, of *E. coli* from pigs, but was not detected in 2017 or 2015.
- Resistance to ciprofloxacin was detected in 0.5% of *E. coli* isolates from pigs and also detected at very low levels in 2017 and 2015.
- Resistance to azithromycin, chloramphenicol, nalidixic acid, sulphonamides and tetracyclines was reported at lowest levels since 2015.
- An overall decline in resistance since 2015 was noted to ampicillin and trimethoprim.
- In total, 15% of pig caecal samples yielded *E. coli* with an ESBL- phenotype and 3.6% of *E. coli* with an AmpC- phenotype.
- Presumptive carbapenemase-producing *E. coli* were not detected.
- All harmonised outcome indicators were consistent with the previous year.

Salmonella spp.

- Four of the nine *Salmonella* isolates were susceptible to the full panel of antimicrobials tested.
- None of the *Salmonella* isolates tested were resistant to the HP-CIAs cefotaxime, ceftazidime or ciprofloxacin.
- While two isolates (serovars *S*. Dublin and *S*. Bovismorbificans) were resistant to colistin, neither isolate had known transferable colistin resistance genes present.

3.2   Methods

In 2019, the UK was a Member State in the EU and the methods for sample collection and testing used are in accordance with EU legislation, as required at that time.

3.2.1   Sample collection

Caecal samples were taken from healthy pigs at slaughter, in accordance with Decision 2013/652/EU (European Commission, 2013), by Food Standards Agency (FSA) personnel. The sampling plan was randomised, stratified and weighted by slaughter throughput. Samples were collected from the biggest slaughterhouses, covering over 60% of the UK throughput in 2019. Sample collection was randomised and evenly distributed throughout the year. One caecal sample was collected per epidemiological unit (pig holding).

Under the requirements of Commission Regulation (EC) No. 2073/2005 (European Commission, 2005) on microbiological criteria for foodstuffs (process hygiene criteria only) Food Business Operators (FBOs) collect pig carcase samples which are submitted to private laboratories for bacteriological culture. Any *Salmonella* isolate should then be submitted to the Animal and Plant Health Agency (APHA) for serotyping and susceptibility testing.

3.2.2   Antibiotic susceptibility testing (AST)

AST 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. Standardised broth microdilution was used to determine the minimum inhibition concentration (MIC) against a panel of antibiotics in accordance with Decision 2013/652/EU.

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 for isolation of ESBL- or AmpC-producing *E. coli* and chromID OXA-48 and chromID CARBA agars for isolation of carbapenemase-producing *E. coli*.

Whole genome sequencing (WGS) 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.

3.2.3   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 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 human treatment failure when using the antibiotic in question to treat a human 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 'decreased susceptibility' (or 'resistant') result based on ECOFFs does not necessarily imply a level of resistance which would correspond with clinical treatment failure.
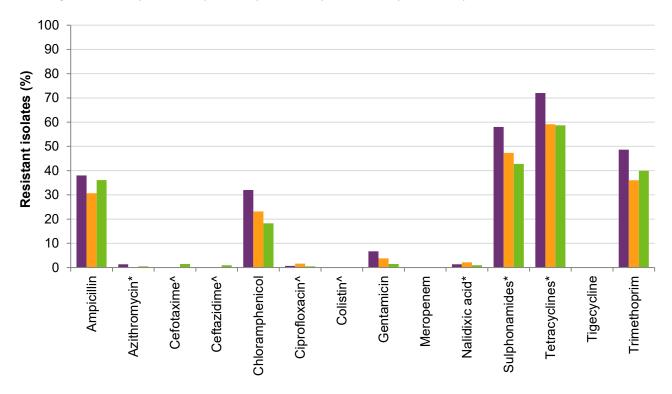
Results interpreted using both human CBPs and ECOFFs are provided in full in sections S3.2, S3.3 and S3.4 of the supplementary material.

3.3 Results

3.3.1 *Escherichia coli*

Resistance of *Escherichia coli* isolates from pig caecal samples is shown in **Figure 3.1**.

Figure 3.1: Percentage resistance (interpreted using EUCAST CBPs) in *E. coli* isolates from pigs at slaughter; 2015 (■; n=150), 2017 (■; n=186) and 2019 (■; n=208)

^ HP-CIA; * Interpreted using EUCAST ECOFF values as no CBP value is available.

Of the HP-CIAs, resistance to the indicator 3rd generation cephalosporins cefotaxime and ceftazidime was detected in 1.4% and 1.0% of *E. coli*, respectively.

Resistance to these antibiotics was not detected in 2017 or 2015. Because of the importance of 3rd and 4th generation cephalosporins as HP-CIAs, this result was further scrutinised. Interpreted using EUCAST CBPs, four isolates (1.9%) showed clinical resistance (with an ESBL- phenotype) to the indicator cephalosporins cefotaxime and/or ceftazidime. One additional isolate did not show clinical resistance, instead, this isolate is considered susceptible to cefotaxime but has decreased susceptibility to ceftazidime.

Of the other HP-CIAs, resistance to ciprofloxacin was detected in one isolate (0.5%). Colistin resistance was not detected in *E. coli* from pigs in 2019.

Susceptibility to meropenem and tigecycline has been maintained. One *E. coli* isolate (0.5%) had resistance to azithromycin (based on ECOFFs as no CBP value is available).

High levels of decreased susceptibility were detected to tetracyclines (59%) and sulphonamides (43%), the lowest levels reported since 2015. High levels of resistance were also detected to

trimethoprim (40%) and ampicillin (36%), representing an overall decline since 2015. Resistance levels to chloramphenicol were moderate in 2019 (18%). Resistance to gentamicin and nalidixic acid was low in 2019 at 1.4% and 1.0%, respectively.

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

An ESBL- phenotype *E. coli* (showing synergy with cefotaxime and clavulanate and/or ceftazidime and clavulanate) was present in 15% of caecal samples and 3.6% of samples yielded *E. coli* with an AmpC- phenotype (showing decreased susceptibility to cefoxitin, cefotaxime and ceftazidime). None of the isolates were positive for both phenotypes. The figures obtained in 2019 for AmpC- and ESBL- phenotype *E. coli* show a slight decline from those obtained in 2017.

No presumptive carbapenemase-producing *E. coli* isolates were detected.

Table 3.1: Phenotype in ESBL-/AmpC-producing *E. coli* cultured on selective agars, from caecal samples from healthy pigs at slaughter in the UK for a) 2017 (n=347) and b) 2019 (n=308)

a)   2017

Phenotype	Number of isolates	Proportion of isolates (%)	Proportion of caecal samples (%)
ESBL	52	69	15
AmpC	19	25	5.5
ESBL/AmpC	4	5.3	1.2
Carbapenemase	0	0	0

b) 2019

Phenotype	Number of isolates	Proportion of isolates (%)	Proportion of caecal samples (%)
ESBL	47	81	15
AmpC	11	19	3.6
ESBL/AmpC	0	0	0
Carbapenemase	0	0	0

All ESBL-/AmpC- phenotype isolates were resistant to ampicillin, as expected. Sixteen isolates showed decreased susceptibility or resistance to ciprofloxacin. Eight isolates also showed decreased susceptibility to nalidixic acid (see section S3.2.4 of the supplementary material for further details).

WGS results showed that $bla_{CTX-M-1}$ was the most common ESBL- gene identified (52%) and was found in 10% of the caecal samples tested. A number of isolates also harboured other variants including $bla_{CTX-M-15}$ (16%), $bla_{CTX-M-14}$ (7%), $bla_{CTX-M-55}$ (2%), $bla_{CTX-M-65}$ (2%) and bla_{SHV-12} (2%) (Table S3.2.2 of the supplementary material). The CMY-2 enzyme was the only transferable AmpC- enzyme detected and was present in three isolates (27%) with an AmpC- phenotype. In 14% of the isolates, no ESBL-/AmpC- enzymes were detected, only mutations associated with upregulation of chromosomal *ampC* expression.

The $bla_{CTX-M-1}$ isolates were associated with eighteen different sequence types (ST), with most isolates represented by a single ST indicating isolate diversity, although two or more isolates belonged to ST23, ST88, ST101, and ST117.The isolates harbouring CTX-M-14 and CTX-M-15, globally the most common variants, were usually represented by a single ST.

The three CMY-2 isolates were associated with different STs. Four of the eight upregulated *ampC* isolates belonged to different STs. It was noted that isolates belonging to ST23 and ST88 could harbour CMY-2, CTX-M-1, CTX-M-15 or mutation in the *ampC* promoter region. There was only one isolate harbouring SHV-12, and one with CTX-M-65; these were of distinct STs to others in the ESBL-/AmpC- panel. Although the CTX-M-55 enzyme has only one amino acid variation to the CTX-M-15 enzyme, the ST for this isolate did not match with any CTX-M-15 isolates but did match with one isolate harbouring CTX-M-1.

3.3.3 *Salmonella* spp.

A total of nine *Salmonella* isolates from pig carcase 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.

Four of the nine isolates were susceptible to the panel of antimicrobials tested. Tetracycline resistance was detected in three isolates, with one isolate (a monophasic *S*. Typhimurium) having additional resistance to ampicillin and sulphonamides. None of the *Salmonella* isolates tested were resistant to the HP-CIAs cefotaxime, ceftazidime, ciprofloxacin, or to azithromycin, chloramphenicol, gentamicin, meropenem, nalidixic acid, tigecycline or trimethoprim.

Two isolates (serovars *S*. Dublin and *S*. Bovismorbificans) were resistant to colistin. The *S*. Dublin serovar show a degree of intrinsic resistance to colistin. Whole genome sequencing of the *S*. Bovismorbificans revealed that chromosomal mutations conferring colistin resistance were present. Neither isolate had known transferable colistin resistance genes detected.

Results interpreted using both CBP and ECOFF values are presented in Table S3.3.1 of the supplementary material.

3.3.4 Harmonised AMR outcome indicators

In 2017, the ECDC, EFSA and EMA recommended harmonised outcome indicators for presenting data on antibiotic resistance in food-producing animal species (European Centre for Disease Prevention and Control et al., 2017). These comprise one primary and three secondary indicators.

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:
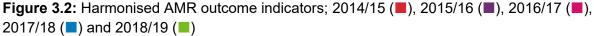
- Proportion of indicator *E. coli* isolates from the four animal species, weighted by PCU, showing decreased susceptibility to at least three antibiotics from different classes from the predefined panel of antibiotics (multi-drug resistant);
- Proportion of indicator *E. coli* isolates from the four animal species, weighted by PCU, showing decreased susceptibility to ciprofloxacin;
- Proportion of samples identified as positive for 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.
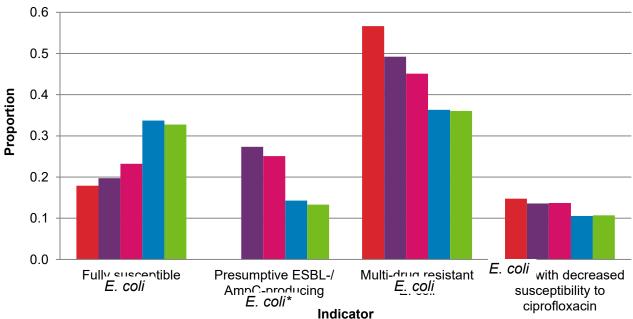
Because of the alternating sampling schedule, these indicators cannot be given for one calendar year, but are calculated based on any two consecutive calendar years to ensure data are available for all animal species covered by the indicator.

All indicator levels in the 2018/2019 period are consistent with the previous period. The other secondary indicators show similar susceptibility levels to the preceding period. Since the 2015/2016 period (data not available for 2014/2015), the proportion of samples identified as ESBL-/AmpC-producing *E. coli* have reduced by 51%. The proportion of samples showing decreased susceptibility to ciprofloxacin decreased by 27% since the 2014/2015 period (**Figure 3.2**).

The increased proportion of fully susceptible *E. coli* (the primary indicator) has been sustained and is an 83% increase compared with the 2014/2015 period. There has also been no meaningful change in the proportion of multi-drug resistant *E. coli* (a secondary indicator) since the previous period.

The other secondary indicators show similar susceptibility levels to the preceding period. Since the 2015/2016 period (data not available for 2014/2015), the proportion of samples identified as ESBL/AmpC-producing *E. coli* have reduced by 51%. The proportion of samples showing decreased susceptibility to ciprofloxacin decreased by 27% since the 2014/2015 period.

Figure 3.2: Harmonised AMR outcome indicators; 2014/15 (■), 2015/16 (■), 2016/17 (■), 2017/18 (■) and 2018/19 (■)

* Data not available for 2014/15.

CHAPTER 4
Clinical Surveillance of Antibiotic Resistance

Clinical surveillance is a programme of passive surveillance which evaluates antibiotic resistance in bacteria of relevance to animal health, isolated from carcases 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 relevant information for treatment. Similar programmes are conducted by Scottish (SRUC Veterinary Services) and Northern Irish (Agri-Food Biosciences Institute, AFBI-NI) laboratories. This chapter for the majority reports the APHA methods and results.

The primary aim of the 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[4]. 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 and to the Veterinary Medicines Directorate (VMD) 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]http://www.legislation.gov.uk/uksi/1989/285/made

4.1   Summary

Overall, the resistance levels observed in many veterinary bacteria showed limited change over the monitoring period from 2017 to 2019.

Many veterinary pathogens, especially respiratory pathogens, remain susceptible to authorised veterinary antibiotics, including those compounds which have been authorised for many years. The majority of isolates of the main respiratory pathogens in sheep, cattle and pigs (*P. multocida, M. haemolytica*, *H. somni, A. pleuropneumoniae*) in the reporting period from 2017 to 2019 were susceptible to enrofloxacin and florfenicol, with the exception of one *P. multocida* isolate resistant to enrofloxacin in 2019 and single *M. haemolytica* isolates resistant to florfenicol in 2017 and 2018.

Penicillin resistance was detected in a single isolate of *S. suis* between 2017 and 2019 but not detected in bovine mastitis streptococci (*S. dysgalactiae* and *S. uberis*) during the monitoring period. Swine dysentery isolates showing clinical resistance to tiamulin were not detected in 2019.

For 3rd generation cephalosporins and fluoroquinolones (HP-CIAs), cefotaxime resistance in diagnostic *E. coli* isolates from neonatal calves in 2019 was 7.6%. Cefotaxime and ceftazidime resistance was not detected in neonatal lambs. Cefpodoxime resistance in *E. coli* in the same year was 1.1% in neonatal piglets and 5.9% in chickens. Although some fluctuation has occurred, these figures have remained relatively unchanged over the period between 2017 and 2019. *E. coli* from neonatal calves, piglets and lambs had all shown a decline in resistance to enrofloxacin in 2018, but there was no further decline in resistance in 2019. An increase in resistance to enrofloxacin to 11% was noted in diagnostic *E. coli* from chickens in 2019 from 2.8% in 2018.

Levels of resistance to tetracycline and doxycycline have increased in *E. coli* from chickens in 2019, compared to levels observed between 2017 and 2018 (from 26% to 29%).

Livestock-associated meticillin-resistant *Staphylococcus aureus* (LA-MRSA) ST398 was not recovered from food-producing animals in England, Wales or Scotland but was isolated from four pig samples in Northern Ireland in 2019.

The proportion of fully sensitive *S*. Typhimurium declined to 49% but these levels are higher than those in 2017 (34%). Resistance to 3rd generation cephalosporins and to fluoroquinolones (HP-CIAs) was very low in *Salmonella* spp. A single *S*. Enteritidis isolate was resistant to ciprofloxacin in 2019. Two *S*. Infantis isolates, obtained from environmental samples related to monitoring of animal by-products, were resistant to cefotaxime. These strains were also resistant to nine and ten (respectively) other antimicrobials included in the panel. Cephalosporin resistance in *S*. Infantis isolates has not been reported in UK livestock.

4.2 Methods

4.2.1 Sample sources

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

For *Salmonella* spp., any laboratory isolating these from animals (for species specified in the UK Zoonoses Order) 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.

4.2.2 Susceptibility testing methodology

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

Isolates were classed as either sensitive or resistant; intermediate isolates (meaning not susceptible to a standard dose but susceptible to an increased dose) were included under the resistant category. 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.

Published breakpoints are not available for all animal species 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 isolates. 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 several organism-antibiotic combinations (Table S4.1.1 of the supplementary material). However, where most isolates of a particular organism are highly resistant or fully susceptible to an antibiotic, breakpoint issues may affect only a low number of isolates.

Breakpoints used to interpret the results from the antimicrobial susceptibility testing are reviewed on a regular basis. Data presented in this report and the supplementary material are retrospectively updated when required to reflect any changes to the interpretative criteria and ensure consistency and comparability of the data.

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 in this chapter cannot be extrapolated to the general livestock population.**

4.3 Results and discussion

Susceptibility was determined for certain antibiotics not authorised for use in any food-producing animal species (e.g. cefpodoxime, chloramphenicol, amikacin) or not authorised for particular animal species (e.g. tetracycline and trimethoprim in sheep). This is to provide a full picture of resistance emergence and/or as a surrogate (e.g. tetracycline, chlortetracycline and oxytetracycline are all equivalent for resistance testing purposes: testing one provides the answer for all three – however, tetracycline is used for testing as BSAC validation data are available for this compound).

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 consistently, results are presented in the supplementary material only.

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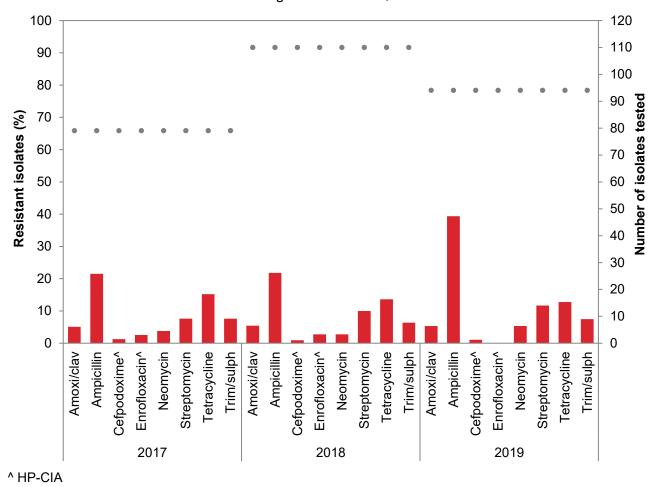
Mastitis is complex and the patterns of resistance observed vary with time and between farms. The data presented are aggregated at a national level and therefore have limited ability to inform treatment protocols. However, they do highlight that acquired resistance does occur in England and Wales and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

4.3.1.1 *Escherichia coli*

E. coli and other coliforms are one of the three main causes of bovine mastitis. 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.

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). Resistance in *E. coli* from bovine mastitis showed only limited annual fluctuations for most antimicrobials, with the occurrence of resistance tending to be relatively stable, apart from ampicillin where resistance increased from 22% in 2017 and 2018 to 39% in 2019. It is noteworthy that the percentage of isolates (1.1%) resistant to cefpodoxime in mastitis *E. coli*/coliform isolates was much lower than the percentage resistance to ceftazidime (2.5%) or cefotaxime (7.6%) observed in *E. coli*/coliform isolates from neonatal calves in 2019 and this is similar to the situation in previous years (**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 in England and Wales; from 2017 to 2019

^ HP-CIA
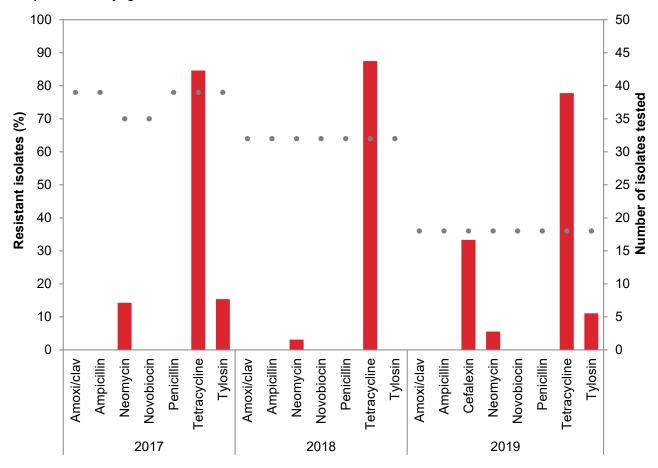
4.3.1.2   *Streptococcus dysgalactiae*

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

Tetracycline resistance, recorded in between 78% and 88% of isolates in this period, is recognised as being common in *S. dysgalactiae*. No resistance to ampicillin or penicillin was detected in *S. dysgalactiae* between 2017 and 2019. 15% and 11% of isolates of *S. dysgalactiae* were resistant to the macrolide tylosin in 2017 and 2019 respectively; resistance to this compound was not detected in 2018. The resistant results in 2017 and 2019 were not confirmed by determination of the minimum inhibitory concentration (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.

Figure 4.2: Number of isolates tested (●) and percentage (■) of resistant isolates of *Streptococcus dysgalactiae* from mastitis infections of cattle; from 2017 to 2019
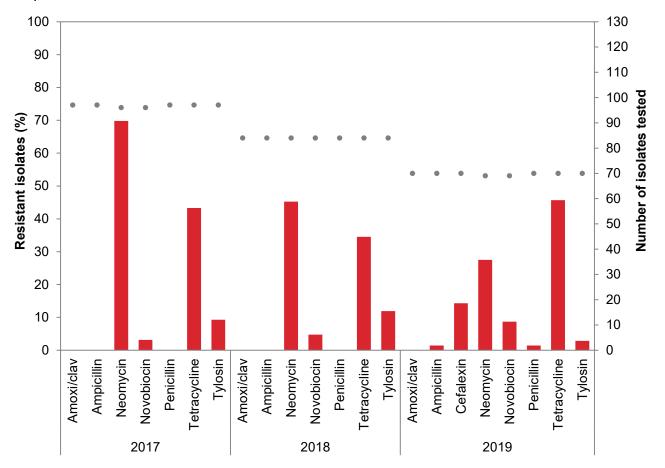
4.3.1.3   *Streptococcus uberis*

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

The total number and percentage of *S. uberis* isolates from mastitis infections resistant to different antibiotics are presented in **Figure 4.3**. No resistance to ampicillin or penicillin was detected in *S. uberis* in 2017 or 2018 but was detected in 1.4% of isolates in 2019. *S. uberis* isolates from bovine mastitis with reduced susceptibility to penicillin have been reported in France (Haenni *et al*. 2010). The percentage of *S. uberis* isolates resistant to tylosin declined from 12% in 2018 to 2.9% in 2019. 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. Resistance to neomycin is to be expected in *S. uberis* because streptococci show a degree of intrinsic resistance to aminoglycosides. Resistance to tetracyclines was also detected in *S. uberis* isolates between 2017 and 2019, with 35% to 46% of isolates resistant.

Figure 4.3: Number of isolates tested (●) and percentage (■) of resistant isolates of *Streptococcus uberis* from mastitis infections of cattle; from 2017 to 2019
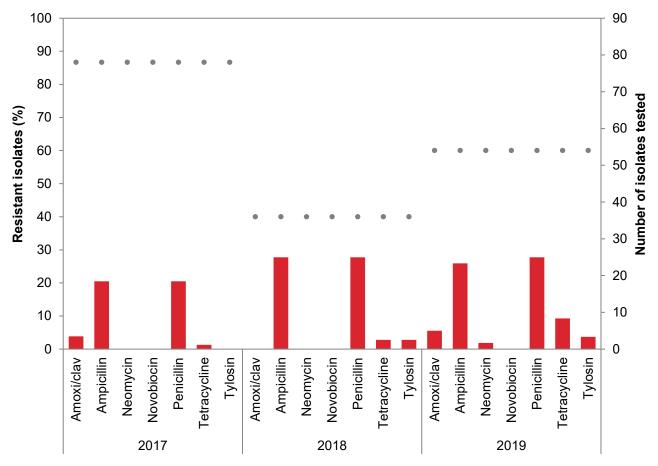
4.3.1.4   *Staphylococcus aureus*

S. aureus is normally resident on the skin and mucous membranes of cattle and is a common cause of mastitis. It is not generally regarded as zoonotic and although both *mecA* MRSA and *mecC* MRSA have been detected in cattle (Garcia-Alvarez et al., 2011, Vanderhaeghen et al., 2010), the possible role of cattle as a source of human infection has not been well-defined.

Resistance to penicillin fluctuated between 21% and 28% over the monitoring period. Penicillin resistance in bovine *S. aureus* from England and Wales occurs most frequently via the production of beta-lactamases. The genes encoding beta-lactamases can be located on plasmids and often on transposons and may be readily transferable by conjugation.

Those resistant to amoxicillin/clavulanate are currently screened for susceptibility to cefoxitin in order to detect *mecA* and *mecC* MRSA. No MRSA isolates were detected from bovine mastitis between 2017 and 2019 at APHA. Amoxicillin/clavulanate resistance fluctuated between 0% and 6% over the reporting period. Aminoglycoside resistance was rarely detected with only a single *S. aureus* isolate displaying neomycin resistance between 2017 and 2019. Tylosin (a macrolide) resistance was recorded in low numbers (between 0% and 3.7%) of isolates. Resistance to tetracycline has remained at or below 9.3% over the monitoring period.

Figure 4.4: Number of isolates tested (●) and percentage (■) of resistant isolates of *Staphylococcus aureus* from mastitis infections in cattle; from 2017 to 2019

4.3.1.5   Other mastitis pathogens

Klebsiella pneumoniae - the majority of *K. pneumoniae* originate from bovine mastitis cases and were frequently resistant to ampicillin. This reflects the intrinsic resistance to ampicillin shown by this organism; most isolates were susceptible to the other antimicrobials reported.

Pseudomonas aeruginosa - commonly resistant to a range of antimicrobials and isolates from bovine mastitis proved no exception in this regard. A low number of isolates was available for testing.

Streptococcus agalactiae - not recovered from bovine mastitis between 2017 and 2019.

Trueperella (Arcanobacterium) pyogenes - isolates from bovine mastitis were susceptible to penicillins, though commonly showed resistance to tetracyclines.

See Table S4.2.4 of the supplementary material for further details.

Chapter 4

4.3.2   Respiratory pathogens
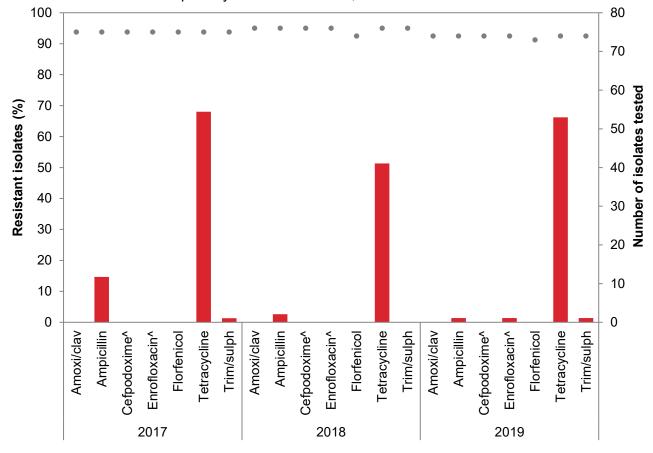
4.3.2.1   *Pasteurella multocida*

P. multocida primarily causes 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 to trimethoprim/sulphonamides, ampicillin or enrofloxacin was found in low numbers of bovine isolates over the monitoring period, with single isolates showing resistance to each compound in 2019. In 2017, a single *P. multocida* isolate was recorded from cattle showing resistance to ampicillin, sulphonamides and tetracyclines. Resistance to both trimethoprim/sulphonamides and tetracyclines was also detected in a single *P. multocida* isolate from cattle in 2019. A low number of isolates of *P. multocida* were examined from sheep and resistance was observed to either ampicillin or tetracyclines in low numbers of isolates between 2017 and 2019.

The tetracycline breakpoint adopted for respiratory pathogens is a BSAC legacy breakpoint for *Pasteurella multocida* and is under review as it now lies below the ECOFF for tetracycline which has been suggested for *P. multocida*.
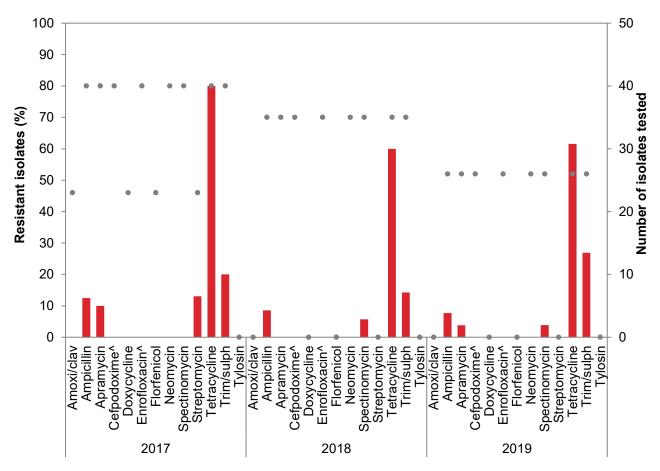
Figure 4.5: Number of isolates tested (●) and percentage (■) of resistant isolates of *Pasteurella multocida* isolates from respiratory infections of cattle; from 2017 to 2019

^ HP-CIA

Tetracycline, ampicillin or trimethoprim/sulphonamide resistance were all observed in *P. multocida* from pigs (**Figure 4.6**), with tetracycline resistance most prevalent, although tetracycline resistant isolates, where tested, were susceptible to doxycycline. This may reflect the resistance mechanism involved as some genes confer resistance to tetracyclines but not to doxycycline, although the breakpoints used may also be a factor. Resistance to both tetracyclines and trimethoprim/sulphonamides was observed in 4 out of 26 (15%) of *P. multocida* from pigs.

There was no resistance detected in *P. multocida* to florfenicol in any of the domestic species in 2017 to 2019, though isolates from pigs were not tested against florfenicol in 2018 and 2019.

Figure 4.6: Number of isolates tested (●) and percentage (■) of resistant isolates of *Pasteurella multocida* from respiratory infections of pigs; from 2017 to 2019

^ HP-CIA

4.3.2.2 *Histophilus somni*

H. somni (formerly known as *Haemophilus somnus*) is a cause of pneumonia and thrombo-embolic meningo-encephalitis in calves. All isolates tested between 2017 and 2019 were susceptible to the panel of antibiotics tested with the exception of a single isolate in 2017 which was resistant to tetracyclines and a single isolate in 2019 which was resistant to ampicillin.
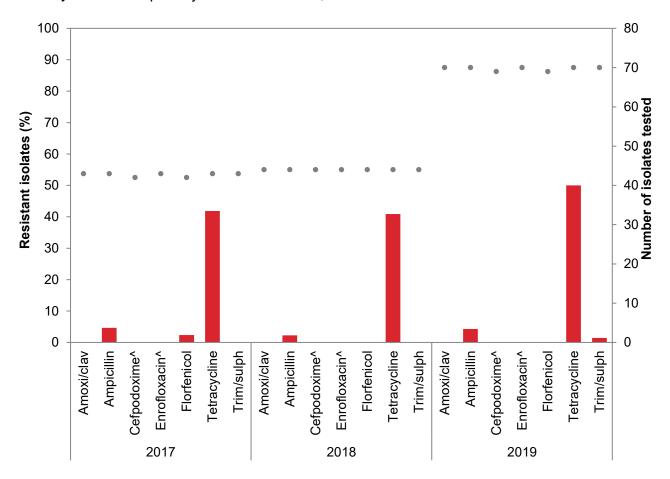
4.3.2.3   *Mannheimia haemolytica*

M. 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 was detected to enrofloxacin in isolates from cattle between 2017 and 2019 (**Figure 4.7** and Table S4.3.1 of the supplementary material). In cattle, low resistance to either ampicillin or trimethoprim/sulphonamides was detected. Bovine isolates showed high resistance to tetracyclines between 2017 and 2019 (between 41% and 50%) and this reflects the low legacy BSAC breakpoint used. A single isolate resistant to florfenicol was detected in cattle in 2017.

No resistance was detected in the ovine isolates between 2017 and 2019 to enrofloxacin. The prevalence of resistance to tetracyclines was high (54% in 2019) in ovine *M. haemolytica* isolates and this reflects the low legacy BSAC breakpoint used. A single isolate resistant to florfenicol was detected in sheep in 2018 (Table S4.5.1 of the supplementary material).

Figure 4.7: Number of isolates tested (●) and percentage (■) of resistant isolates of *Mannheimia haemolytica* from respiratory infections of cattle; from 2017 to 2019

^ HP-CIA

4.3.2.4   Other respiratory pathogens

Bibersteinia trehalosi – *B. trehalosi* isolates from sheep were generally susceptible, with no resistance detected to tetracyclines, ampicillin, trimethoprim/sulphonamides, enrofloxacin or florfenicol in 2019 (data not shown).

Trueperella (Arcanobacterium) pyogenes - Data on this less frequently isolated ovine respiratory pathogen can be found in Table S4.5.1 of the supplementary material. Resistance to tetracyclines and trimethoprim/sulphonamides was detected in isolates of *T. pyogenes* from respiratory and other infections of cattle (excluding mastitis cases), sheep and pigs. Low numbers of isolates from pigs were resistant to macrolides and/or lincosamides.

Actinobacillus pleuropneumoniae – *A*. *pleuropneumoniae* is a cause of pneumonia in pigs. Over the period 2017 to 2019, resistance was not detected to enrofloxacin. Resistance was detected to ampicillin, tetracyclines, trimethoprim/sulphonamides and tylosin. Levels of resistance to apramycin, spectinomycin and other aminoglycosides detected in the disc diffusion test probably reflect the rather high MICs that have been described for *A. pleuropneumoniae* in the scientific literature for some aminoglycoside compounds (Leman *et al*. 1986).

Glaesserella (Haemophilus) parasuis - There were two *G. parasuis* isolates recovered in 2019 and these were susceptible to the panel of antibiotics tested. Between 2017 and 2018 resistance was detected in some *G. parasuis* isolates to tetracyclines, trimethoprim/sulphonamides and macrolides.

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

4.3.3   Other animal pathogens

Brachyspira hyodysenteriae - *B. hyodysenteriae* is the cause 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 treatment of swine dysentery, and since resistance arises through mutation, reliance on ongoing medication without addressing other aspects of disease control, such as hygiene and herd husbandry (for example all-in, all-out management or periodic depopulation) carries the attendant risk that mutational resistance may arise.

Tiamulin is an important antibiotic used for the treatment of swine dysentery. Because of the importance of this disease and the significance of resistance to tiamulin, all available isolates of *B. hyodysenteriae* are tested for tiamulin susceptibility each year. A breakpoint of resistance >4 mg/l tiamulin has been suggested for MIC determination by agar dilution (Rønne and Szancer, 1990, Duinhof *et al*. 2008), whilst for broth microdilution the suggested clinical breakpoint is one dilution lower at >2 mg/l tiamulin. An epidemiological cut-off value of wild type $\leq$ 0.25 has been suggested for broth dilution MIC determination of tiamulin versus *B. hyodysenteriae* (Pringle et al. 2012).

The tiamulin MIC for selected *B. hyodysenteriae* isolates tested by broth microdilution over the period 2010 to 2019 are shown in Table S4.6.1 of the supplementary material. 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. No *B. hyodysenteriae* isolates of 45 tested in 2019 had a tiamulin MIC > 0.5 mg/l.

Staphylococcus aureus - *S. aureus* causes a number of infections in poultry and game birds, including septicaemia, yolk sac infection, arthritis and osteomyelitis. Low numbers of isolates were available and resistance to penicillin/ampicillin, tetracyclines, lincosamides, macrolides or trimethoprim/sulphonamides was detected in isolates of *S. aureus* from chickens, turkeys or other avian species in one or more years. *S. aureus* causes mastitis and tick pyaemia as well as other infections in sheep. *S. aureus* isolates from sheep were susceptible to penicillin but 20% of isolates were resistant to tetracyclines, assumed to reflect usage of this compound in this species.

Streptococcus dysgalactiae - *S. dysgalactiae* is the major cause of infectious arthritis in young lambs and is thought to be carried on the mucous membranes of a small proportion of sheep. Levels of resistance to tetracyclines in ovine isolates of *S. dysgalactiae* were high (between 74% and 94%) and similar to those recorded for bovine (mastitis) isolates. No resistance to ampicillin or penicillin was detected in ovine *S. dysgalactiae* isolates, though low numbers of isolates were reportedly resistant to cephalexin or tylosin between 2017 and 2019.
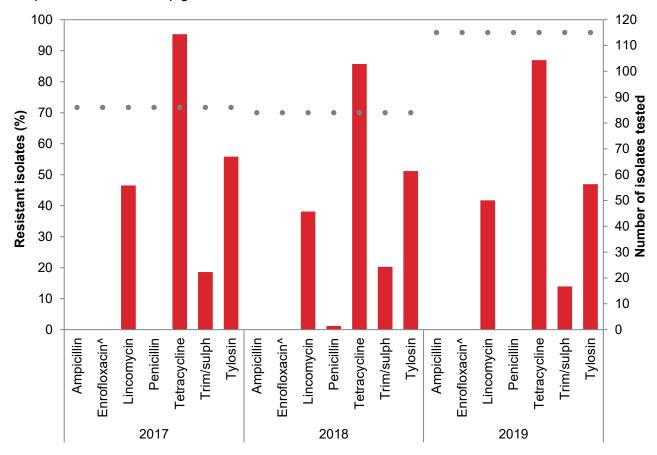
Staphylococcus xylosus – *S. xylosus* is a coagulase-negative *Staphylococcus* which has been reported to cause dermatitis in sheep and mastitis in cattle. A single isolate from chickens in 2017 was susceptible to the antimicrobials reported, whereas two isolates from cattle and one from sheep in 2018 were resistant to ampicillin with the bovine isolates also resistant to amoxicillin/clavulanate though susceptible to cefalexin. The isolates were not characterised further, though meticillin resistance can occur relatively frequently in some species of coagulase-negative staphylococci. In 2019, single isolates from pigs and cattle were susceptible to the panel of antibiotics tested, whereas isolates from chickens were more resistant, with resistance to tetracyclines, ampicillin, macrolides and lincosamides detected.

4.3.4 Zoonotic pathogens

4.3.4.1 *Streptococcus suis*

S. suis is a pathogen of pigs that can cause pneumonia, meningitis and arthritis. In rare cases, it can also infect man. Penicillin resistance was detected in a single isolate of *S. suis* during the period 2017 to 2019 (**Figure 4.8**).The penicillin resistant *S. suis* isolate was detected in 2018, speciation was confirmed by 16S sequencing and it was further typed as *S. suis* type 5.The isolate was recovered from the foetal stomach contents of an aborted piglet from one of a group of 50 sows which had aborted. The penicillin MIC was determined by e-test and found to be 0.75 mg/l, confirming resistance. Considering the other *S. suis* isolates tested over the monitoring period, isolates resistant to tetracyclines, trimethoprim/sulphonamide, tylosin and lincomycin were all recorded.

Figure 4.8: Number of isolates tested (●) and percentage (■) of resistant isolates of *Streptococcus suis* from pigs; from 2017 to 2019

^ HP-CIA

4.3.4.2 Livestock Associated-MRSA (LA-MRSA)

LA-MRSA are 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 and is an opportunist pathogen. Usually this is a local skin infection, but occasionally it can cause diseases such as pneumonia or bacteraemia. 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 S4.6.6 of the supplementary material. 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.

LA-MRSA was not recovered in 2019 from food-producing animals in England, Wales or Scotland, but it was detected in four pig samples from Northern Ireland all submitted for clinical diagnosis.

4.3.4.3 Other zoonotic pathogens

Corynebacterium pseudotuberculosis – *C. pseudotuberculosis* the cause of caseous lymphadenitis in sheep, is a zoonosis though it rarely infects man. Resistance was detected to tetracyclines and trimethoprim/sulphonamides in 2019 with only low numbers of isolates available for susceptibility testing and none in 2018 (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.

Erysipelothrix rhusiopathiae – *E. 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 have been tested and the main resistance detected has been to tetracyclines and trimethoprim/sulphonamides in pigs, sheep, turkeys and chickens. All isolates, irrespective of the species from which they were isolated, were susceptible to penicillin/ampicillin, which is the usual treatment for infection with this organism.

Listeria spp. – *Listeria* 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 *Listeria monocytogenes* 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 compound. Isolates from cattle and sheep were otherwise sensitive to the panel of compounds tested over the period 2017 to 2019; prior to 2017 low numbers of ovine *L. monocytogenes* were reported as tetracycline resistant. *Listeria ivanovii* was recovered from sheep in 2017 and 2019 and (with the exception of cephalexin) was susceptible to the panel of antimicrobials reported (data not shown).

Klebsiella pneumoniae - A limited number of isolates of *K. pneumoniae* have been recovered from avian species; the isolates were all resistant to ampicillin reflecting intrinsic resistance to ampicillin of this organism. Resistance to tetracyclines and trimethoprim/sulphonamides was frequent in avian *K. pneumoniae*.

Yersinia enterocolitica – was reported in 2017 from ruminants and was susceptible to the antibiotics tested. There were no isolates of *Yersinia pseudotuberculosis* reported in the period 2017 to 2019.

4.3.5 *Escherichia coli*

E. coli is an important potential zoonotic. *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 4.3.1.1**). Collated 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 to S4.7.15 of the supplementary material.

Collated data for the major food-producing animal species tested are shown in **Table 4.1**. In general, the level of resistance to HP-CIAs in *E. coli* isolates was low to moderate during 2017 to 2019 (between 1.8% and 12%).

For cattle, pigs and sheep the data are also analysed for each species by the age categories of neonatal, pre- or post-weaning and adult (see **Figure 4.10**, **Figure 4.12** and **Figure 4.14**, respectively). Resistance is usually less prevalent in older animals, including those older animals which are slaughtered for meat. 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 the summary table and figures for animals of all ages may reflect, to a significant degree, the proportions of each age-class which have contributed to the total. Similar considerations can apply to the contribution of different animal production types, for example laying hens and broiler chickens. These considerations should be borne in mind when interpreting the summary figures. The totals in this section exclude the *E. coli* isolates from bovine mastitis which can be found in **Section 4.3.1.1**.

Table 4.1: Number of resistant and number of tested (% resistant) *Escherichia coli* isolates from cattle, pigs, sheep, broilers and turkeys (all ages, combined); from 2017 to 2019

Antibiotic	2017	2018	2019
Amikacin	0/266 (0.0%)	1/280 (0.4%)	0/220 (0.0%)
Amoxicillin/clavulanate	149/694 (21.5%)	137/484 (28.3%)	97/474 (20.5%)
Ampicillin	420/810 (51.9%)	450/788 (57.1%)	564/998 (56.5%)
Apramycin	39/756 (5.2%)	49/737 (6.6%)	70/949 (7.4%)
Cefotaxime^	32/267 (12.0%)	27/282 (9.6%)	17/225 (7.6%)
Cefpodoxime^	8/377 (2.1%)	10/316 (3.2%)	10/547 (1.8%)
Ceftazidime^	18/267 (6.7%)	12/282 (4.3%)	7/225 (3.1%)
Chloramphenicol	104/266 (39.1%)	108/280 (38.6%)	63/220 (28.6%)
Doxycycline	151/323 (46.7%)	25/79 (31.6%)	48/108 (44.4%)
Enrofloxacin^	48/810 (5.9%)	32/788 (4.1%)	63/998 (6.3%)
Florfenicol	88/479 (18.4%)	86/329 (26.1%)	56/266 (21.1%)
Neomycin	134/695 (19.3%)	114/679 (16.8%)	151/868 (17.4%)
Spectinomycin	233/756 (30.8%)	267/737 (36.2%)	296/949 (31.2%)
Streptomycin	198/429 (46.2%)	149/282 (52.8%)	114/222 (51.4%)
Tetracycline	463/810 (57.2%)	447/788 (56.7%)	587/998 (58.8%)
Trimethoprim/sulphonamide	271/810 (33.5%)	293/788 (37.2%)	381/998 (38.2%)

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.
^ HP-CIA

4.3.5.1   Cattle
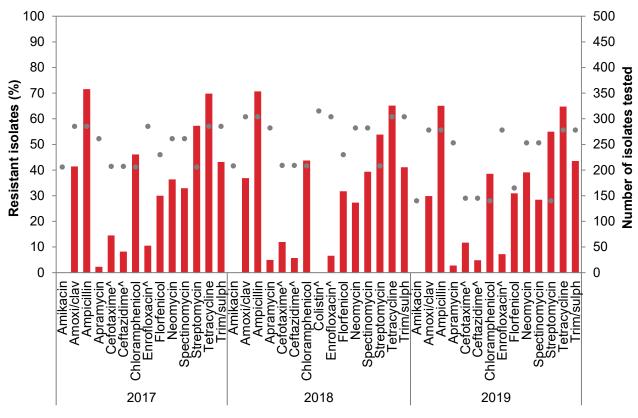
The total number and proportion of resistant *E. coli* isolates (all age groups) are shown in **Figure 4.9**. The resistance to 3rd generation cephalosporins (cefotaxime, ceftazidime or cefpodoxime) detected in *E. coli* in animals will include resistance mediated by both ESBL- and AmpC- resistance mechanisms. The higher prevalence of resistance to cefotaxime versus ceftazidime observed, for example, in neonatal calves (**Figure 4.10**), is likely to reflect the occurrence of those ESBL- enzymes which are cefotaximases, rather than ceftazidimases. A decline in resistance in *E. coli* from neonatal calves to 3rd generation cephalosporins was noted over the period 2017 to 2019.

The relatively high frequency at which *E. coli*/coliform isolates resistant to ampicillin are recovered from young calves (77% to 80% over the period 2017 to 2019) may reflect the use of dry cow intramammary infusions containing aminopenicillins 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. Although ampicillin resistance remained consistently high at 77% to 80% over the period 2017 to 2019 in neonatal calves it fluctuated between 57% and 71% in older, pre-weaned calves.

Resistance to apramycin was low in *E. coli* from both neonatal calves (1.7% to 4.6%) and in older calves, pre-weaning (4.3% to 7.9%), whilst neomycin resistance (31% to 46%) and spectinomycin resistance (33% to 42%) were higher in *E. coli* from neonatal calves. The available formulations differ for these aminoglycoside compounds, with neomycin, for example, available in some intramammary tubes for mastitis as well as in oral formulations, whereas apramycin is not available in intramammary preparations. Amikacin is not authorised for treatment of animals but was included in some of the panels to detect the possible occurrence of 16S rRNA methyltransferase enzymes which confer resistance to all aminoglycosides except streptomycin; amikacin resistance was not detected in *E. coli* from cattle in 2017 to 2019.
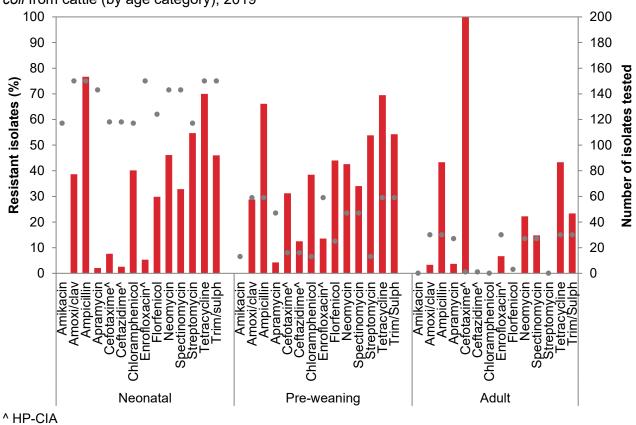
Resistance to enrofloxacin was 4.4% to 9.2% in *E. coli* from neonatal calves and 6.2% to 19% in older calves pre-weaning, with florfenicol resistance at 27% to 30% in neonatal calves and 38% to 45% in older calves. These changes probably reflect patterns of usage in the different age groups of calves, related to the occurrence of pneumonia in the different age classes. Tetracycline and trimethoprim/sulphonamide resistance was high in *E. coli* from neonatal and older calves, reflecting widespread usage in previous decades.

Figure 4.9: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from cattle (all ages); from 2017 to 2019

^ HP-CIA

Figure 4.10: Number of isolates tested (●) and percentage (■) of resistant isolates *of Escherichia coli* from cattle (by age category); 2019

^ HP-CIA
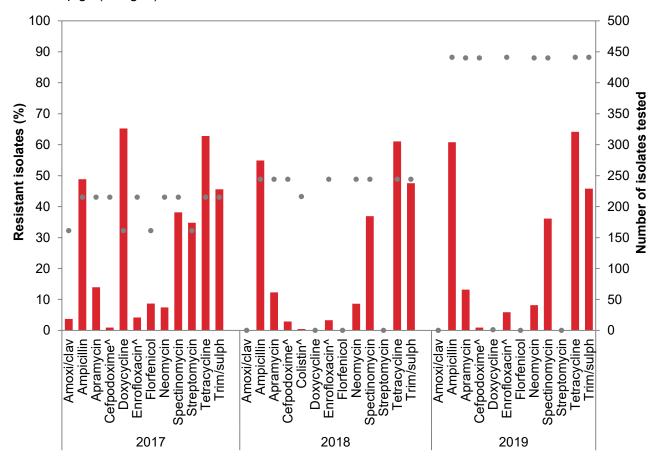
4.3.5.2   Pigs

The total number and proportion of resistant isolates from pigs are shown in **Figure 4.11**. Cefpodoxime resistance in *E. coli*/coliform isolates was detected in neonatal and post-weaning piglets at low levels of 1.1% to 3.4% between 2017 and 2019 (**Figure 4.12**). Ampicillin resistance increased both in neonatal pigs (45% in 2017 and 61% in 2019) and in pigs after weaning (51% in 2017 and 67% in 2019).

Apramycin resistance was 1.7% to 2.5% in neonatal pigs during this period but was much higher at 20% to 23% in *E. coli* from pigs post-weaning. This is assumed to reflect the use of apramycin in treating post-weaning diarrhoea in pigs. Resistance to neomycin was also in most years higher in *E. coli* from post-weaning pigs compared to neonatal pigs, again, probably reflecting patterns of usage, though the difference was less marked. Spectinomycin resistance was higher in *E. coli* from neonatal piglets than in pigs after weaning, where resistance was constant at 37% to 39%.
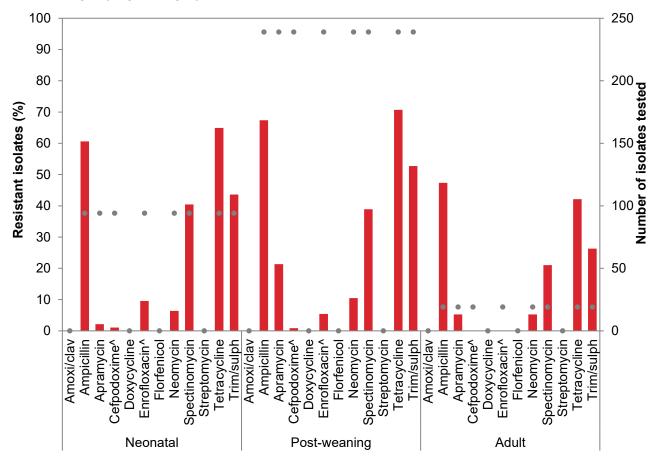
Resistance to tetracyclines and trimethoprim/sulphonamides was relatively high and showed small fluctuations over the period in post-weaning pigs, with slightly lower levels of resistance to each of these compounds observed in neonatal pigs. The apparent trend of declining multiple drug resistance in neonatal and post-weaning pigs is artefactual and influenced by changes in the different panels of antimicrobials tested in different years.

Figure 4.11: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from pigs (all ages); from 2017 to 2019

^ HP-CIA

Figure 4.12: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from pigs by age category; 2019

^ HP-CIA

4.3.5.3   Sheep

There has been a decline in resistance to ampicillin and tetracyclines observed in *E. coli* from neonatal lambs over the period 2017 to 2019. For most antimicrobials reported in 2019, the levels of resistance in *E. coli* from neonatal lambs were lower than those reported for neonatal calves, with the exception of enrofloxacin where resistance was similar in both calves (5.3%) and lambs (4.8%) and spectinomycin where resistance in lambs (40%) exceeded that in calves (33%). The sample size for pre-weaning and adult sheep of approximately 30 isolates was low and is likely to have been a factor in the variation in the occurrence of resistance observed in different years. Cefotaxime/ceftazidime resistance was not detected in *E. coli* from neonatal lambs, contrasting with the detection of cefotaxime resistance in 7.6% of *E. coli* from neonatal calves; there are greatly differing patterns of intramammary antimicrobial usage in these species.

Figure 4.13: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from sheep (all ages); from 2017 to 2019

^ HP-CIA
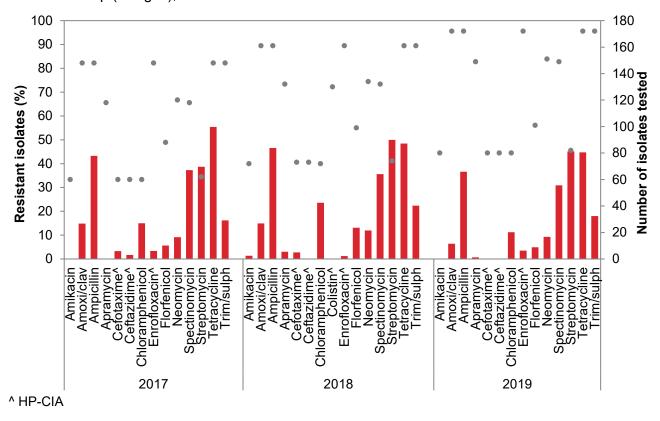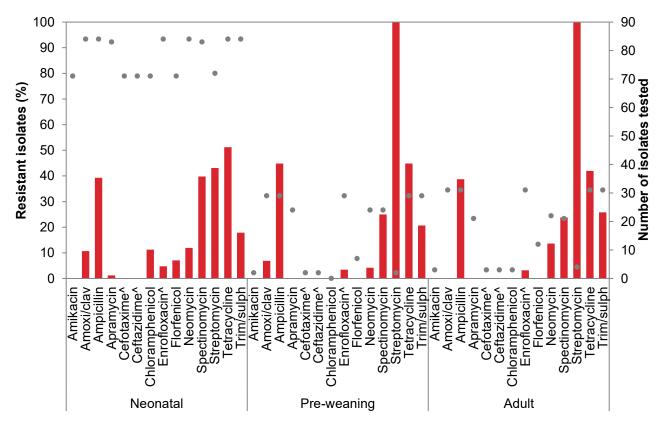
Figure 4.14: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from sheep (by age category); 2019

^ HP-CIA

4.3.5.4   Chickens and turkeys

Cefpodoxime resistance ranged from 4.2% to 5.9% in *E. coli*/coliforms from chickens between 2017 and 2019 representing a decline since 2015 when 11% resistance was recorded (**Figure 4.15**). Usage of 3rd generation cephalosporins has not been permitted in poultry since 2012. However, other beta-lactam compounds, for example ampicillin, can also exert a degree of selective pressure for 3rd generation cephalosporin resistance, though this has been shown to be lower than that exerted by the 3rd generation cephalosporin compounds.
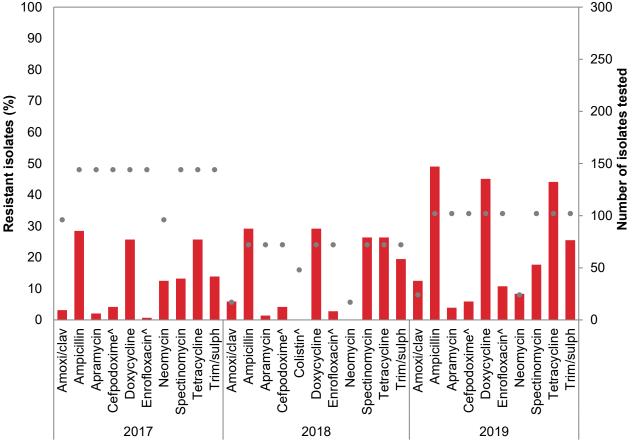
Tetracycline and doxycycline resistance increased in *E. coli*/coliforms from chickens in 2019 (44% and 45%, respectively), compared to levels observed between 2017 and 2018 (26% to 29%). Levels of resistance detected to the fluoroquinolone enrofloxacin in *E. coli*/coliforms from chickens over the reporting period 2015 to 2018 declined from 17% to low levels, temporally coincident with recent industry initiatives to reduce use of fluoroquinolones in broilers. However, an increase in resistance to enrofloxacin to 11% was noted in diagnostic *E. coli*/coliforms from chickens in 2019.

Resistance in *E. coli* isolates from turkeys is shown in Table S4.7.6 of the supplementary material.

Figure 4.15: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from chickens; from 2017 to 2019

^ HP-CIA

4.3.6 *Salmonella* spp.
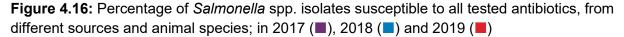
Due to the relevance of *Salmonella* as a zoonotic pathogen, and the importance of the serovar, and even phage type, of an isolate when investigating potential epidemiological links between animal and human cases, results are presented by individual serovar/phage type in this section. Regarding the antimicrobials referred to in this report, resistance to 3rd generation cephalosporins and fluoroquinolones is considered of most importance, since these antimicrobials are particularly relevant for the treatment of human salmonellosis, where this 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 may not require treatment with antimicrobials.
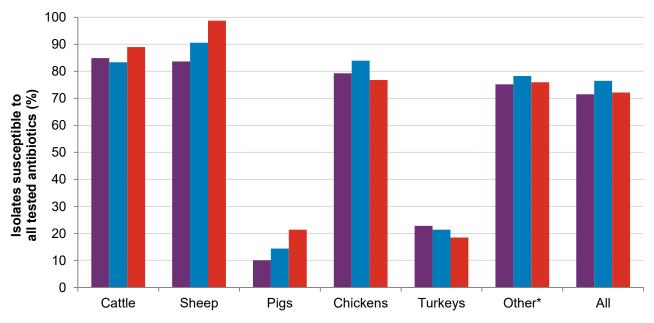
Where resistance to 3rd generation cephalosporins and fluoroquinolones is detected in a food-producing animal(s), attempts are made to visit the farms in order to explain the significance of the findings and provide appropriate advice on control.

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. Full datasets can be found in section S4.8 of the supplementary material.

4.3.6.1 All *Salmonella*

Of the 4533 *Salmonella* isolates tested in 2019, 3273 (72%) were sensitive to all of the antimicrobials tested (**Figure 4.16**). This is similar to the situation in 2018, when 4413 isolates were tested and 3376 (77%) were sensitive to all of the antimicrobials tested.

Figure 4.16: Percentage of *Salmonella* spp. isolates susceptible to all tested antibiotics, from different sources and animal species; in 2017 (■), 2018 (■) and 2019 (■)

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

The percentage of *Salmonella* isolates that were resistant to ciprofloxacin in 2019 was 0.4%. One single *S.* Enteritidis isolate (a PT12 from quail) was resistant to ciprofloxacin in 2019. Two *S.* Infantis isolates, obtained from environmental samples related to monitoring of animal by-products, were resistant to cefotaxime. These strains were also resistant to nine and ten (respectively) other antimicrobials included in the panel. Multidrug resistant clones of *S.* Infantis have been reported in central Europe since 2012. These clones have subsequently acquired further antimicrobial resistance to 3rd generation cephalosporins, also reported in other countries, in particular from Italy and the USA. Cephalosporin resistance in *S.* Infantis isolates from livestock has never been reported in the UK. Cefotaxime or ceftazidime resistance was not detected in *S.* Enteritidis from animals in 2019. No cefotaxime or ceftazidime resistance was detected in *S.* Typhimurium from animals in 2019. These findings are important since these serovars are of particular public health importance.

The number of *S.* Enteritidis isolations was higher in 2019 (n=132) when compared to 2018 (n=48). In 2019, the increase was mainly due to the identification of *S.* Enteritidis PT8 in laying hens on five separate holdings which were potentially linked by the use of common packing centres. This strain is sensitive to all sixteen antimicrobials tested.

Tetracycline resistance was most commonly found in *Salmonella* isolates originating from pigs and turkeys in 2019. This was also the situation for resistance to sulphonamides and streptomycin. Findings were similar in 2018.

Resistance to apramycin in all *Salmonella* serovars was 1.2% in 2019, similar to previously reported levels. *Salmonella* isolates from pigs, where resistance was 20% in 2019, 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 2019, 39.7% of *Salmonella* 4,12:i:- isolates (n=58) and 37.5% of *Salmonella* 4,5,12:i:- isolates (n=40) from pigs were resistant to apramycin. 1.2% of all *Salmonella* isolates were resistant to gentamicin. No resistance was detected to amikacin.

The highest prevalence of resistance to nalidixic acid in 2019 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 in 2019 is different to the period 2013 to 2016 when resistance was mostly observed in *Salmonella* from turkeys and "other avian species". In turkeys, 52 out of 53 *S.* Senftenberg isolates and one out of one *S.* 3,19:-:- isolates were resistant to nalidixic acid in 2019. The situation in turkeys was similar in 2013 to 2018, with nalidixic acid resistance frequently detected in this serotype. In broilers, resistance to nalidixic acid was found in *S.* 13,23:i:-, *S.* Indiana, *S.* Senftenberg and *S.* Montevideo. Ciprofloxacin resistance occurred in 17% of *Salmonella* isolates (nine out of 53 *S.* Senftenberg isolates) from turkeys (n=270) and the ciprofloxacin-resistant isolates were also resistant to nalidixic acid. The other ciprofloxacin-resistant isolates detected in 2018 originated from dog (*S.* O Rough:r:1,5 [one out of one resistant]), feed and related samples (*S.* Orion [four out of five resistant]), quail (one out of one resistant),and the environment (*S.* Newport [one out of two resistant]).

4.3.6.2   *Salmonella* by animal species

Considering all *Salmonella* isolates from pigs, the percentage of fully susceptible isolates fluctuated since 2012 and is reported at 21% in 2019 (**Figure 4.16**). Between 2018 and 2019, there has been a decline in the proportion of fully susceptible isolates from turkeys noted (21% to 19%)

and in chickens (84% to 77%). In 2019, the high level of fully susceptible isolates from cattle and sheep has been maintained (89% and 99% respectively).

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 to S4.8.6 of the supplementary material. A summary is given below.

Cattle – No resistance was observed to ceftazidime, cefotaxime or ciprofloxacin. The highest level of resistance was to tetracycline (9.9%), streptomycin (8.8%), sulphonamide compounds (8.4%), ampicillin (8.0%) and chloramphenicol (6.5%).

Pigs – No resistance was observed to ceftazidime, cefotaxime or ciprofloxacin. A large proportion were resistant to sulphonamide compounds (76%), ampicillin (69%), tetracycline (68%) and streptomycin (66%), however these proportions are lower compared to 2018. Resistance to chloramphenicol was 53% and to neomycin was 19%.

Sheep – There was no resistance to ceftazidime, cefotaxime or ciprofloxacin. Resistance was only recorded for streptomycin (1.2%) and sulphonamide compounds (1.2%). A decrease in the levels of resistance to these antibiotics was seen compared with 2018.
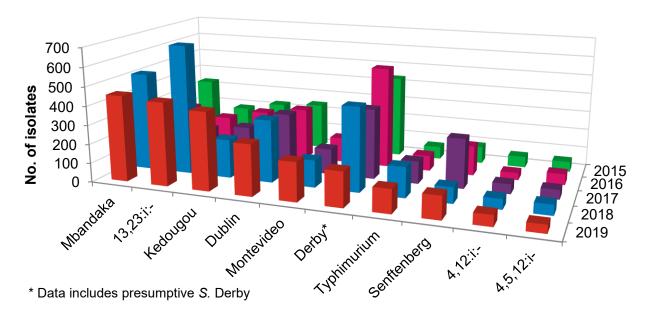
Chickens – There was no resistance to ceftazidime, cefotaxime or ciprofloxacin. The highest levels of resistance were to sulphonamide compounds (18%), tetracyclines (16%) and trimethoprim/sulphonamides (13%). Similar to previous years, gentamicin resistance was present in a very low number of isolates (0.1%).

Turkeys – There was a low level of ciprofloxacin resistance (3.3%) however this is an increase from levels in 2018 (0.6%). No resistance to 3rd generation cephalosporins was detected. The highest level of resistance was to sulphonamide compounds (57%), tetracycline (54%) and streptomycin (47%).

4.3.6.3   Top ten *Salmonella* serovars isolated between 2015 and 2019

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 between 2015 and 2019 are presented in **Figure 4.17**. Prior to 2018, *S*. Derby, *S. Dublin* and *S.* Mbandaka were the most consistently isolated serovars year-on-year, however in 2018 the most frequently isolated serovar was 13,23:i:- (n=681). In 2019 the most consistently isolated serovar was *S*. Mbandaka (n=451), followed by 13,23:i:- (n=436) and *S*. Kedougou (n=409). *S*. Indiana (n=101) and *S*. Ohio (n=76) were also isolated in 2019 (data not presented). Details of commonly recovered serovars in Northern Ireland and Scotland are provided in Tables S4.8.10 and S4.8.11 of the supplementary material.

Figure 4.17: Top ten most commonly isolated *Salmonella* serovars from livestock in Great Britain in 2019, with corresponding data for previous years

* Data includes presumptive *S.* Derby

4.3.6.4 *Salmonella* Dublin

Of the 269 *Salmonella* Dublin cultures tested during 2019, 99.6% were susceptible to all 16 antimicrobials (**Table 4.2**). The percentage of *S.* Dublin isolates sensitive to all 16 antimicrobials has shown only slight fluctuations over the period 2006 to 2019 and most isolates remain susceptible; this has been the situation since surveillance began in 1971. Most *S.* Dublin isolates (88%) originated from cattle in 2019 and this was similar to the situation recorded in previous years. *S.* Dublin isolates from species other than cattle in 2019, comprised fourteen isolates from animal feed, nine isolates from dogs, five from sheep, and single isolates from a chicken, cat, horse, another mammalian species and an environmental sample.

Table 4.2: Resistance in *Salmonella* Dublin: percentage of resistant isolates; from 2015 to 2019

Antibiotic	2015 (n=226)	2016 (n=245)	2017 (n=272)	2018 (n=320)	2019 (n=269)
Ampicillin	1.8	0.4	0	0	0
Chloramphenicol	0.4	0.4	0	0.3	0.4
Furazolidone	0	0	0	0	0
Nalidixic acid	2.2	1.2	0	2.2	0
Neomycin	2.2	0	0	0.3	0
Streptomycin	4	1.6	0	0.3	0.4
Sulphonamide compounds	0	0	0	0.3	0.7
Tetracycline	0.4	0.4	0	0.3	0.4
Trimethoprim/ sulfamethoxazole	0	0	0	0	0.4

4.3.6.5 *Salmonella* Typhimurium

254 *Salmonella* Typhimurium isolates were tested in 2019. The eight most frequent definitive or undefined types were examined for susceptibility (**Figure 4.18**). 49% of *S*. Typhimurium isolates were sensitive to all antimicrobials tested, a decrease from 2018 figures (54%), but greater than levels reported in 2017 (34%).

Figure 4.18: Percentage of fully susceptible isolates of *S*. Typhimurium (and number tested) of eight most frequent definitive or undefined types subjected to susceptibility testing at APHA; 2019
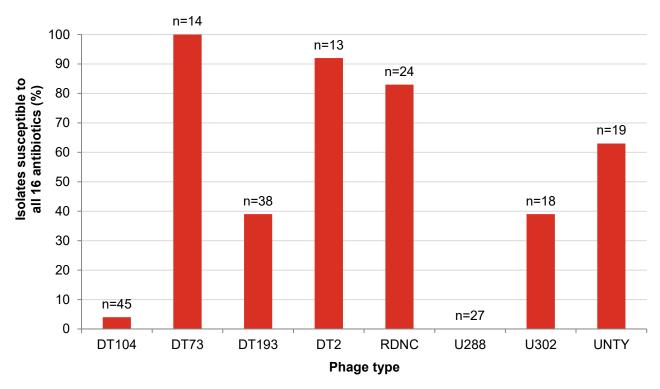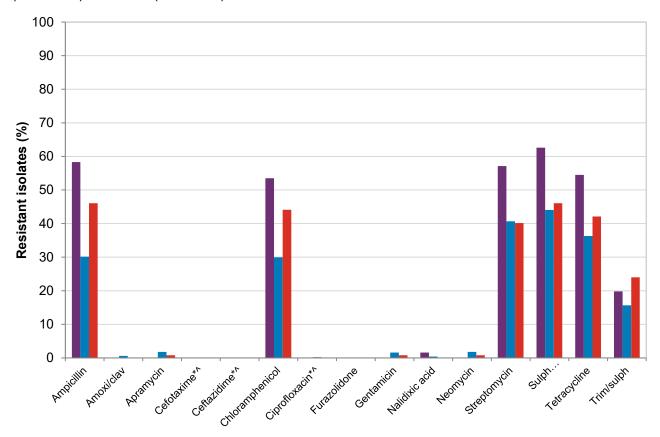
Figure 4.19 (and Table S4.8.8 of the supplementary material) presents an overview of percentage resistance in *S*. Typhimurium to the antibiotics tested between 2017 and 2019. The generally high level of resistance of *S*. Typhimurium isolates observed in recent years has partly been a reflection of 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.

Two out of 45 DT104 isolates were sensitive to all antimicrobials tested in 2019. All remaining DT104 isolates, 11 out of 18 U302 isolates and four out of four DT104B isolates were resistant to at least one of the 16 antimicrobials tested.

The proportion of *S.* Typhimurium isolates comprising DT104 and its variants, which had shown a general decline in the period 2007 to 2014, has shown a resurgence since 2017. This resurgence was mainly due to an increased number of incidents in cattle and sheep from 2017. In 2019, incidents of this *Salmonella* phenotype were still identified, but at lower levels than 2017. The typical pentavalent resistance pattern AmCSSuT was the most common resistance pattern seen in *S*. Typhimurium DT104 and DT104B, occurring in 92% (n=49) of isolates in 2019.

Figure 4.19: *Salmonella* Typhimurium: percentage of resistant isolates in 2017 (■; n=187), 2018 (■; n=504) and 2019 (■; n=254)

^ HP-CIA; * no data available for 2017

Zero out of 49 DT104 and DT104B isolates were resistant to nalidixic acid or sulphamethoxazole/trimethoprim. No isolates of DT104 were recovered from turkeys in 2012 to 2019. DT104 isolates from turkeys, when detected, have commonly shown nalidixic acid resistance in previous years.

Salmonella Typhimurium U288 and DT193 from pigs accounted for 11% and 7% of the total numbers of *S*. Typhimurium isolates respectively; none of the U288 and DT193 isolates from pigs were fully susceptible in 2019.

Considering all definitive types of *S*. Typhimurium, resistance to sulphamethoxazole/trimethoprim has fluctuated markedly in recent years (range between 16% to 45%). It has been predominantly isolates from pigs that have accounted for these fluctuations. A high proportion of many definitive types of *S*. Typhimurium isolated from pigs are resistant to sulphamethoxazole/trimethoprim. The definitive and undefined phage types of *S*. Typhimurium resistant to sulphamethoxazole/trimethoprim and recovered from pigs in 2019 included contributions primarily from isolates of two phage types, DT193 and U288. AmCSSuTTm was the most common resistance pattern observed in both DT193 isolates (nine isolates) and U288 isolates (21 isolates) from pigs.

After a peak in apramycin resistance in *S*. Typhimurium in 2011 and 2012, resistance has fluctuated between 0% and 2%.

No *S*. Typhimurium isolates in 2019 were resistant to ciprofloxacin, amikacin, ceftazidime, cefotaxime or nalidixic acid.

4.3.6.6   Monophasic *Salmonella* Serotypes

124 isolates of *Salmonella* 4,12:i:- were tested, belonging to definitive phage types DT120 (n=3), DT193 (n=102), DT2 (n=2), and undefined phage types U302 (n=1) and U323 (n=1); eleven isolates were not typable and for four isolates a phage type could not be determined. Most isolates were from pigs (48%) followed by feed and related samples (22%). The most common pattern of resistance observed was AmSSuT, which occurred in 37 out of 102 of DT193 isolates, one out of three DT120 isolates, one out of one U302 isolates, in two out of eleven of the isolates which were not typable with phages and two out of four of the isolates for which a PT could not be determined. Considering the DT193 isolates, 69 out of 102 had the AmSSuT resistance pattern alone or with one or more additional resistances.

A total of 86 isolates of *Salmonella* 4,5,12:i:- were tested, including phage types DT193 (n=81), four isolates that were untypable and one isolate for which no phage type could be determined. The most common resistance pattern in DT193 isolates was AmSSuT, occurring in 33% of isolates. Most isolates of monophasic *Salmonella* 4,5,12:i:- DT193 were from pigs (44%).

For aminoglycosides other than streptomycin, resistance to apramycin and neomycin was detected in monophasic *S.* Typhimurium isolates from both pigs and feed in 2019. Apramycin resistance was detected in 40% and neomycin resistance in 28% of 4,12:i:- from pigs (n=58). Resistance to neomycin and apramycin was observed in 3.7% of 4,12:i:- isolates from feed or feed constituents (n=27). Apramycin resistance was detected in 38% and neomycin resistance in 53% of 4,5,12:i:- from pigs (n=40). Resistance to apramycin was also observed in 5.3% of 4,5,12:i:- isolates from feed or feed constituents (n=19).
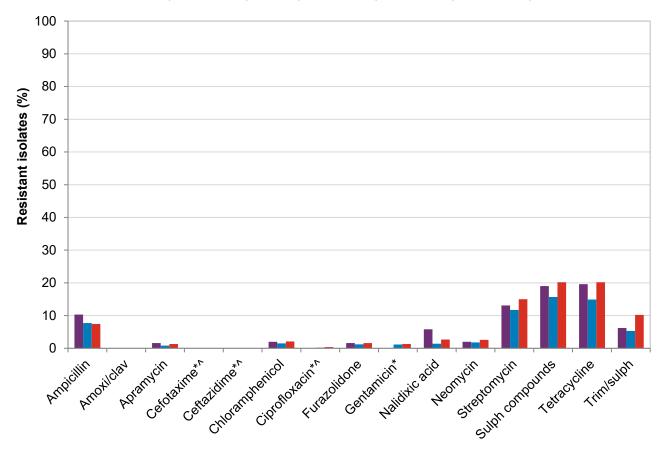
4.3.6.7   *Salmonella* other than Dublin or Typhimurium

Of the 4010 isolates of serotypes other than *S.* Dublin and *S.* Typhimurium tested, 72% were sensitive to all of the antimicrobials in the panel (**Figure 4.20**), a slight decrease on the figure recorded in 2018, when 78% were fully sensitive. 132 isolates (3.9%) were *S.* Enteritidis, 118 out of 132 (89%) of which were fully susceptible. Ten isolates were resistant to nalidixic acid: four phage type 13a isolates (one isolate from laying hens and three from equines), three phage type 3a from feed, one PT1 from feed and single PT12 isolates from quails and horses.

Neomycin resistant *Salmonella* isolates originated mainly from chicken (n=1695, 0.2% resistant), pigs (n=148; 26% resistant), feed or feed constituents (n=971; 1.3% resistant), and ducks (n=297; 6.4% resistant). In ducks, *S.* Indiana was the main serotype showing resistance to neomycin (17 out of 96 isolates resistant; 18% resistant); the *S.* Indiana isolates from ducks were also frequently resistant to furazolidone (36 out of 96 isolates; 38% resistant) and this was similar to the situation observed in 2018.

For isolates from turkeys in 2019 (n=270), 47% were resistant to streptomycin, 57% to sulphonamides and 54% to tetracyclines; similar to the equivalent figures for pigs in 2019 (respectively 63%, 67% and 66%), but higher than those for chickens (respectively 8.6%, 18% and 16%) or cattle (5.6%, 4.5% and 9.0% respectively). In 2019, the proportion of *Salmonella* isolates originating from feed (24%) was similar to 2018 (23%); the proportion of fully susceptible isolates from feed decreased slightly from 78% to 75%.

Figure 4.20: *Salmonella* other than Dublin and Typhimurium, percentage of isolates resistant to antibiotics tested; 2017 (■; n=2,652), 2018 (■; n=3,589) and 2019 (■; n=4,010)

^ HP-CIA; * no data available for 2017

References

Anjum, M. F., Duggett, N. A., Abuoun, M*., et al.* (2016). Colistin resistance in *Salmonella* and *Escherichia coli* isolates from a pig farm in Great Britain. *Journal of Antimicrobial Chemotherapy* 71(8): 2306-13.

Department of Health and Social Care & Department for Environment Food & Rural Affairs (2019). Tackling Antimicrobial Resistance 2019-2024 - The UK's five-year national action plan. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/784894/UK_AMR_5_year_national_action_plan.pdf.

Duggett, N. A., Sayers, E., Abuoun, M*., et al.* (2017). Occurrence and characterization of mcr-1-harbouring *Escherichia coli* isolated from pigs in Great Britain from 2013 to 2015. *Journal of Antimicrobial Chemotherapy* 72(3): 691-5.

Duinhof, T. F., Dierikx, C. M., Koene, M. G. J*., et al.* (2008). Multiresistentie bij *Brachyspira hyodysenteriae* - isolaten op een varkensvermeerderingsbedrijf in Nederland. *Tijdschrift voor Diergeneeskunde* 133(14-15): 604-8.

European Centre for Disease Prevention and Control, European Food Safety Authority Panel on Biological Hazards & European Medicines Agency Committee for Medicinal Products for Veterinary Use (2017). ECDC, EFSA and EMA Joint Scientific Opinion on a list of outcome indicators as regards surveillance of antimicrobial resistance and antimicrobial consumption in humans and food-producing animals. *EFSA Journal* 15(10): 5017.

European Commission (2003). Regulation (EC) No 2160/2003 of the European Parliament and of the Council of 17 November 2003 on the control of salmonella and other specified food-borne zoonotic agents. *Official Journal of the European Union* 46(L325).

European Commission (2005). COMMISSION REGULATION (EC) No 2073/2005 of 15 November 2005 on microbiological criteria for foodstuffs. *Official Journal of the European Union* 48(L338).

European Commission (2013). Commission Implementing Decision of 12 November 2013 on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria (2013/652/EU). *Official Journal of the European Union,* 56(L303).

European Medicines Agency (2011). European Surveillance of Veterinary Antimicrobial Consumption. Trends in the sales of veterinary antimicrobial agents in nine European countries (2005-2009). (EMA/238630/2011) Available from: https://www.ema.europa.eu/veterinary-regulatory/overview/antimicrobial-resistance/european-surveillance-veterinary-antimicrobial-consumption-esvac.

European Medicines Agency (2020). European Surveillance of Veterinary Antimicrobial Consumption. Sales of veterinary antimicrobial agents in 31 European countries in 2018. (EMA/24309/2020) Available from: https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-31-european-countries-2018-trends-2010-2018-tenth-esvac-report_en.pdf

Garcia-Alvarez, L., Holden, M. T., Lindsay, H*., et al.* (2011). Meticillin-resistant *Staphylococcus aureus* with a novel *mecA* homologue in human and bovine populations in the UK and Denmark: a descriptive study. *The Lancet Infectious Diseases* 11(8): 595-603.

Haenni, M., Galofaro, L., Ythier, M.*, et al.* (2010). Penicillin-binding protein gene alterations in *Streptococcus uberis* isolates presenting decreased susceptibility to penicillin. *Antimicrobial Agents and Chemotherapy* 54(3): 1140-5.

Leman, A. D., Straw, B., Glock, R. D.*, et al.* (1986). *Diseases of Swine,* Ames, Iowa, USA, Iowa State University Press.

Responsible Use of Medicines in Agriculture Alliance (2017). Targets Task Force Report 2017. Available from: https://www.ruma.org.uk/wp-content/uploads/2017/10/RUMA-Targets-Task-Force-Report-2017-FINAL.pdf.

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

Vanderhaeghen, W., Cerpentier, T., Adriaensen, C.*, et al.* (2010). Methicillin-resistant *Staphylococcus aureus* (MRSA) ST398 associated with clinical and subclinical mastitis in Belgian cows. *Veterinary Microbiology* 144(1-2): 166-71.

World Health Organization (2020) WHO Collaborating Centre for Drug Statistics Methodology - ATCvet Index 2020. www.whocc.no/atcvet/atcvet_index/.

Annexes

Annex A: List of figures

Annex B: List of tables

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, 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 (EUCAST) 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 for 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.

▪ It should be noted that when using selective culture methods, the occurrence of ESBL-, AmpC- or carbapenemase-producing *E. coli* 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 most 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.

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 surveillance performed on chickens includes a range of types of bird (layers, broilers, breeders and others) as well as both commercial and backyard flocks. The occurrence of resistance can be influenced by a number of factors, including the types of chickens examined, degree of epidemic spread of certain bacterial clones that may be resistant, the emergence, dissemination and transfer of resistance determinants between and amongst bacteria as well as by the selective pressure exerted by the use of antibiotics.

▪ 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, but that it was not tested for. This is especially true of commensal organisms.

- Criteria for the susceptibility testing of some veterinary pathogens are not well-established; this document presents the data which have been collected and acknowledges their limitations and shortcomings. Resistances of particular importance or significance are wherever possible subject to confirmatory testing. The disc diffusion test can be regarded as a screening test, enabling the rapid testing of large numbers of isolates in a cost-effective way and providing a timely result for veterinarians which can assist them in the selection of antimicrobial chemotherapy.

- 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 Marketing 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 2019 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 *ad hoc* Expert Group; AMEG is an *ad hoc* 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 at a concentration 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; 3rd and 4th 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

Annex F: Contributors

Compiled by the Veterinary Medicines Directorate

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

Contributors of other statistics:

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