

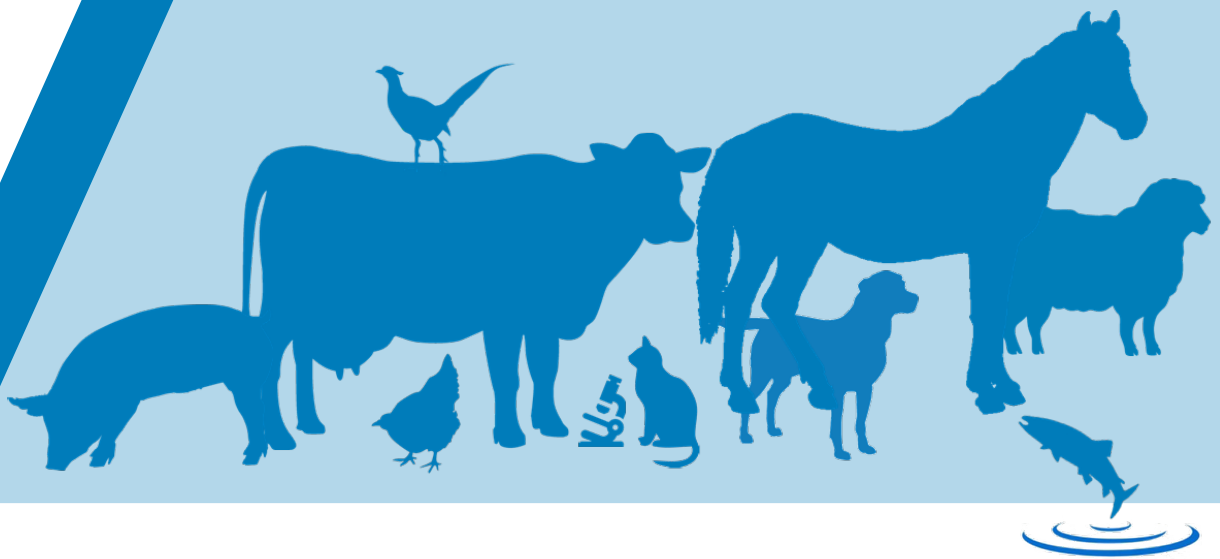


Veterinary
Medicines
Directorate

UK Veterinary Antibiotic Resistance and Sales Surveillance Report

UK-VARSS 2018

Published October 2019





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Foreword

This year, 2019, started with three important publications, the UK's five-year National Action Plan on AMR 2019–24¹, the UK's 20-year Vision for AMR² and the UK One Health Joint report on antibiotic use and antibiotic resistance, 2013–17³; and it's with great pleasure that I introduce the first UK-VARSS report since these publications. Once again, there have been further reductions in UK veterinary antibiotics sales and use. A 53% reduction in sales of antibiotics for food-producing animals over the last four years, coupled with a 68% reduction in sales of highest priority critically important antibiotics in the same period, is a remarkable achievement.



A sales data reporting error affecting the 2016 and 2017 reporting years emerged after the publication of last year's report. The data in the present report, including all the historical trend data, have been updated and the corrected data show that the reductions in antibiotic sales in 2016 and 2017 were markedly greater than originally reported. We have worked closely with the company concerned to satisfy ourselves that the source of this error has been resolved, and we are taking this opportunity to engage all the companies who report sales data to us to review our processes to ensure they are robust.

Year-on-year reductions are continuing although less dramatically between 2018 and 2017, reflecting that reductions are both smaller and harder to achieve as use becomes low. We are now the lowest user of antibiotics amongst EU countries with significant livestock farming and the 5th lowest user overall⁴.

Sales are a proxy for use, and the measure used for EU reporting⁴. However, in the UK we are moving increasingly towards securing usage data. UK farming sectors have been further developing systems for, and reporting on, antibiotic usage. Reporting coverage stands at around 90% of the population or greater for many sectors, with pigs and trout increasing their coverage since last year. These levels are excellent. Cattle still have a way to go before we can be confident that their usage data are representative and we don't yet have usage data for sheep to publish, but these sectors are working towards comprehensive antibiotic usage reporting.

As we emphasise in our UK five-year National Action Plan and 20-year Vision, action on AMR is for everyone. I welcome the formation of the Targets Task Force 2, the farming and veterinary group chaired by the Responsible Use of Medicines in Agriculture Alliance, which will once again develop and publish expected reductions for antibiotic use in animals. The original Task Force has a strong track record of high ambition and an ability to deliver, and I very much look forward to seeing next year their ambitions.

Another important recent initiative involves retailers, manufacturers, processors and food service companies, a diverse but core group of stakeholders who, last year, voluntarily established the

¹ <https://www.gov.uk/government/publications/uk-5-year-action-plan-for-antimicrobial-resistance-2019-to-2024>

² <https://www.gov.uk/government/publications/uk-20-year-vision-for-antimicrobial-resistance>

³ <https://www.gov.uk/government/publications/uk-one-health-report-antibiotic-use-and-antibiotic-resistance-in-animals-and-humans>

⁴ <https://www.ema.europa.eu/en/veterinary-regulatory/overview/antimicrobial-resistance/european-surveillance-veterinary-antimicrobial-consumption-esvac>

Food Industry Initiative on Antimicrobials. This builds on retailers publishing antibiotic use on their supplier farms⁵. The group's vision is to promote and support responsible antimicrobial use and action on AMR. Cooperation and collaboration on AMR as a pre-competitive issue is essential, and the support of this group to existing stakeholder initiatives could, if done in alignment with them, ensure the sustainability of the progress being made.

The primary purpose of reducing antibiotic consumption and improving antibiotic stewardship is to reduce antibiotic resistance. This year, the level of antibiotic resistance measured in the indicator bacteria *E. coli* from poultry examined at slaughter shows further reductions to resistance and represents a marked downward trend. Also, most of the key veterinary pathogens remain susceptible to authorised veterinary antibiotics, including those that have been authorised for many years.

We continue to review the scope and methods of the surveillance we undertake. The intent for next year is to undertake more detailed analysis of susceptibility of a range of animal pathogens, to further refine the companion animals' antibiotic sales data, and to work with public health and food safety colleagues to develop more integrated surveillance. We will also do more to support countries developing surveillance capability, primarily through the recent establishment in the UK of an FAO Reference Centre for AMR.

More also needs to be done to bear down on illegal sales of antibiotics. We now have agreements in place with major internet market-place platform providers to combat illegal on-line sale and capability to block and rapidly remove illegal listings.

More also now needs to be done on improving prevention of infection risks. This will primarily be through improved biosecurity and increased vaccine uptake. We will next year report on vaccine uptake measures.



Professor S. Peter Borriello
Chief Executive Officer

⁵ Asda: http://s7d2.scene7.com/is/content/asdagroceries/Asda.com/7.%20Sites/Environment/ASDA-Antibiotics-report-2018_V7.pdf

Lidl: <https://corporate.lidl.co.uk/sustainability/animal-welfare/antibiotics>

M&S: <https://corporate.marksandspencer.com/documents/plan-a-our-approach/antibiotic-graph-v8-quote-version-alt.pdf>

Tesco: <https://www.tescopl.com/sustainability/downloads/animal-welfare-policy-group/antibiotics/>

Waitrose: https://www.waitrose.com/home/inspiration/about_waitrose/the_waitrose_way/waitrose_animal_welfarecommitments.html

Co-op also collect data, but the results are currently not available on their website.

Highlights

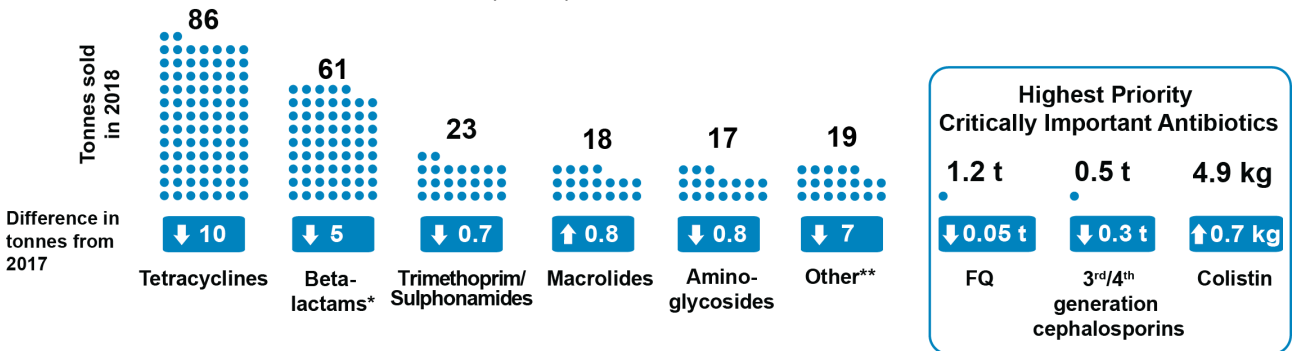
Antibiotic Sales

Total sales in tonnes (all animals)

In 2018 the total quantity of antibiotic active ingredient sold in the UK was 226 tonnes.

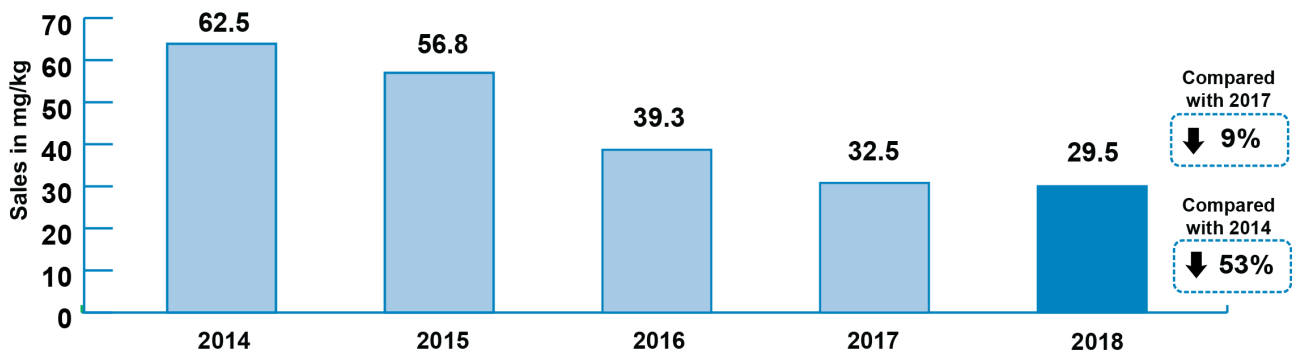
	2014	2015	2016	2017	2018	Compared with 2017	Compared with 2014
Total sales (all animals, tonnes)	448	408	296	248	226	↓ 9%	↓ 49%

Sales of highest priority critically important antibiotics (HP-CIAs) in food-producing animals dropped by a further 0.4 tonnes (18%) from an already low level in 2017; a drop of 3.1 tonnes (66%) since 2014. Overall, tetracyclines remain the most sold antibiotic class (38%), followed by beta-lactams (27%) and trimethoprim/sulphonamides (10%). Sales of HP-CIAs in all animal species represent a small proportion (0.7%) of the overall antibiotic sales.



Overall trends in mg/kg (food-producing animals)

Sales of veterinary antibiotics for use in food-producing animals, adjusted for animal population, were 29.5 mg/kg; a 3 mg/kg (9%) and 33 mg/kg (53%) decrease since 2017 and 2014 respectively.



Sales of HP-CIAs dropped from 0.26 mg/kg from 2017 to 0.21 mg/kg (19%) in 2018.











	2014	2015	2016	2017	2018	Compared with 2014
Fluoroquinolones (mg/kg)	0.35	0.35	0.23	0.15	0.15	↓ 58%
3 rd /4 th generation cephalosporins (mg/kg)	0.19	0.17	0.14	0.11	0.06	↓ 66%
Colistin (mg/kg)	0.12	0.12	0.02	0.0006	0.0007	↓ 99%
Total HP-CIAs (mg/kg)	0.67	0.64	0.38	0.26	0.21	↓ 68%

● = 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 purchased, prescribed and/or administered per sector. The data have been collected and provided to the VMD by the animal industry on a voluntary basis.

Antibiotic usage by food-producing animal species

	Total coverage %*	2018 Total tonnage**	2018 Total per unit***	Compared with 2015 %	Compared with 2016 %	Compared with 2017 %
Pigs 	89	76	110 mg/kg	↓ 60	↓ 40	↓ 16
Turkeys 	90	16	47 mg/kg	↓ 77	↓ 46	↑ 3
Broilers 			12 mg/kg	↓ 55	↓ 27	↑ 26
Ducks 			1.6 mg/kg	↓ 79	↓ 46	↓ 47
Laying hens 	90	3.2	0.63 bird days	—	↓ 13	↑ 11
Gamebirds 	90	9.7	—	—	↓ 52	↓ 25
Salmon 	100	1.0	6.5 mg/kg	—	—	↓ 60
Trout 	90	0.2	13 mg/kg	—	—	↓ 32
Dairy† 	30	4.9	17 mg/kg	↓ 30	↓ 36	↑ 9
Beef † (¥) 	5.5 (4.0)	1.1 (1.0)	21 mg/kg (25 mg/kg)	— 0	— ↓ (2)	— ↓ (6)

Highest Priority Critically Important Antibiotics by food-producing animal species

	Total coverage %*	2018 Total kg**	2018 Total per unit***	Compared with 2015 %	Compared with 2016 %	Compared with 2017 %
Pigs 	89	41	0.06 mg/kg	↓ 94	↓ 78	↓ 39
Meat Poultry 	90	17	0.02 mg/kg	↓ 97	↓ 87	↓ 49
Gamebirds 	90	47	—	—	↓ 27	↓ 5
Dairy 	31	107	0.38 mg/kg	↓ 80	↓ 61	↓ 37
Beef † (¥) 	5.5 (4.0)	14 (10)	0.26 mg/kg (0.27 mg/kg)	— ↓ (73)	— ↓ (66)	— ↓ (49)

* 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 ESVC 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'; † Due to the low proportion of UK cattle in this sample, these figures may not accurately reflect the situation for the whole UK cattle population and caution should also be taken when interpreting trends; ¥ Data from a subset of beef farms where usage data was available for 2015–2018

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

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

Of the highest priority critically important antibiotics, no resistance to 3rd generation cephalosporins was detected in *Salmonella* isolates from broilers, laying hens or turkeys in 2014, 2016 and 2018. Resistance to ciprofloxacin fluctuated at a low level across monitoring years in isolates from broilers, laying hens and turkeys (2%–9% resistance) with the exception of turkey isolates from 2014 (20% resistance).




Resistance in *Escherichia coli* from broilers and turkeys

There was no resistance to colistin in *E. coli* isolates from turkeys or broilers in 2014, 2016 and 2018. Ciprofloxacin-resistance showed a downward trend in turkey isolates between 2014 and 2018 (from 8% to 3%) and fluctuated at a low level over the same period in broiler isolates (between 2% and 4%). No or low resistance to 3rd generation cephalosporins was detected in isolates from turkeys and broilers from 2014, 2016 and 2018.

In 2018, 10.3% of broiler caecal samples yielded *E. coli* with an ESBL and/or AmpC phenotype, for turkey caecal samples this was 3.5%. This was a decrease compared to 2016, when this was 30.1% for broilers and 4.7% for turkeys. No presumptive carbapenemase-producing *E. coli* were detected.

Resistance in *Campylobacter jejuni* from broilers and turkeys

Resistance to erythromycin, a first-line treatment for *Campylobacter* infection in people, remained very low in isolates from broilers and turkeys (1%). A high level of resistance to fluoroquinolones was detected in isolates from broilers (between 41%–48%), whereas in turkeys a decreasing trend was seen (from 35% in 2014 to 31% in 2018).

	<i>E. coli</i> (%)		<i>Salmonella</i> spp. (%)		<i>C. jejuni</i> (%)		
	3 rd /4 th GC	FQ	3 rd /4 th GC	FQ	Ery	FQ	
 Broilers	2014	0	4.4	0	3.6	0	43.6
	2016	0	2.1	0	8.8	0.6	40.6
	2018	0.5/1.6*	4.4	0	6.4	0.6	48.0
 Turkeys	2014	0	8.3	0	20.4	0.6	35.0
	2016	0.4/0.4*	5.8	0	1.8	1.1	34.7
	2018	0	2.8	0	5.3	0.6	31.0
 Layers	2014		0	1.7			
	2016		0	8.8			
	2018		0	3.8			

3rd/4th GC = 3rd and 4th generation cephalosporins; FQ = fluoroquinolones; Ery= erythromycin

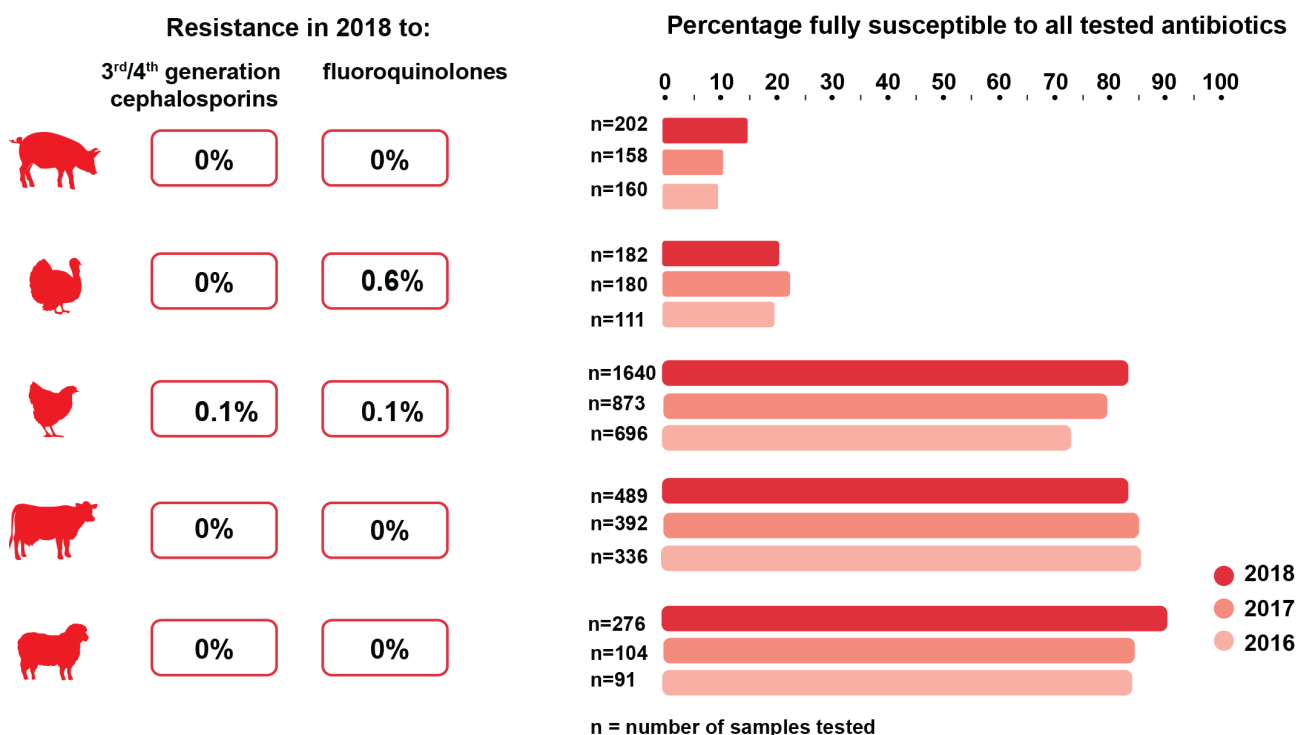
* Resistance to ceftazidime and cefotaxime respectively

Antibiotic Resistance – Clinical Surveillance

Resistance in *Salmonella* spp.

A high percentage of all *Salmonella* isolates tested (76% of 4,414 total isolates) was susceptible to all the antibiotics tested; the results indicate an increasing trend in this susceptible proportion.

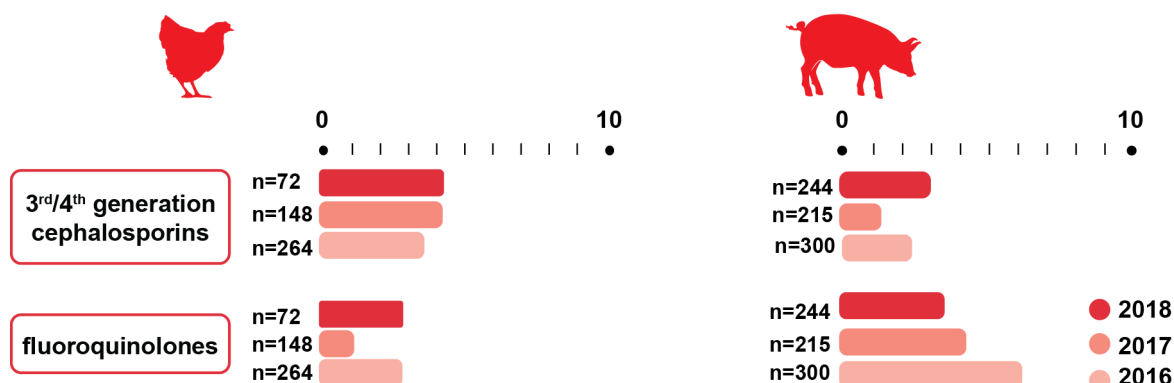
Resistance to 3rd generation cephalosporins was detected in two isolates from chickens, but not in isolates from turkeys, pigs, cattle and sheep. One isolate from turkeys and two isolates from chickens showed resistance to ciprofloxacin (a fluoroquinolone).



Resistance in *Escherichia coli*

Resistance to fluoroquinolones and 3rd generation cephalosporins was low (4%), except in cattle (7% of isolates resistant to fluoroquinolones, 6% resistant to ceftazidime and 12% resistant to cefotaxime; the majority of these isolates were obtained from calves). Resistance to colistin was detected in one isolate from pigs, but not in other major food-producing animal species.

% resistant isolates from poultry and pigs



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. Since then, the UK-VARSS reports present combined data on veterinary antibiotic sales and antibiotic resistance in bacteria from food-producing animals in the UK. Furthermore, the UK-VARSS reports have 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 2018 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 European Union 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 2018, the total quantity of antibiotic active ingredient sold in the UK was 226.2 tonnes, a 21.9 tonne (9%) reduction since 2017. Between 2014 and 2018, there was a 221.7 tonne (49%) reduction. In 2018, sales of veterinary antibiotics, adjusted for animal population, were 29.5 mg/kg, a 3.0 mg/kg (9%) decrease from 2017 and 33.0 mg/kg (53%) decrease from 2014. The year 2014 is referred to in this report as the baseline year as it represents the first full year of the UK Five Year Antimicrobial Resistance Strategy 2013 to 2018 (Department of Health and Social Care and Department for Environment Food & Rural Affairs, 2013).

Tetracyclines remain the most sold class of antibiotics (38% of total sales) and beta-lactams the second (27% of total sales). Since 2017, notable reductions were observed for tetracyclines and macrolides, decreasing by 9.8 tonnes (10%) and 6.7 tonnes (29%), respectively. Excluding tablets, oral products accounted for the majority of antibiotics sold (71%).

Highest Priority Critically Important Antibiotics for human medicine (HP-CIAs) continue to represent a small proportion of total antibiotics sold (0.7% in 2018) and have reduced to 1.6 tonnes; a reduction of 0.4 tonnes (18%) since 2017 and 3.1 tonnes (66%) since 2014.

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 to one decimal place. However, the percentage changes have been calculated using the exact number.

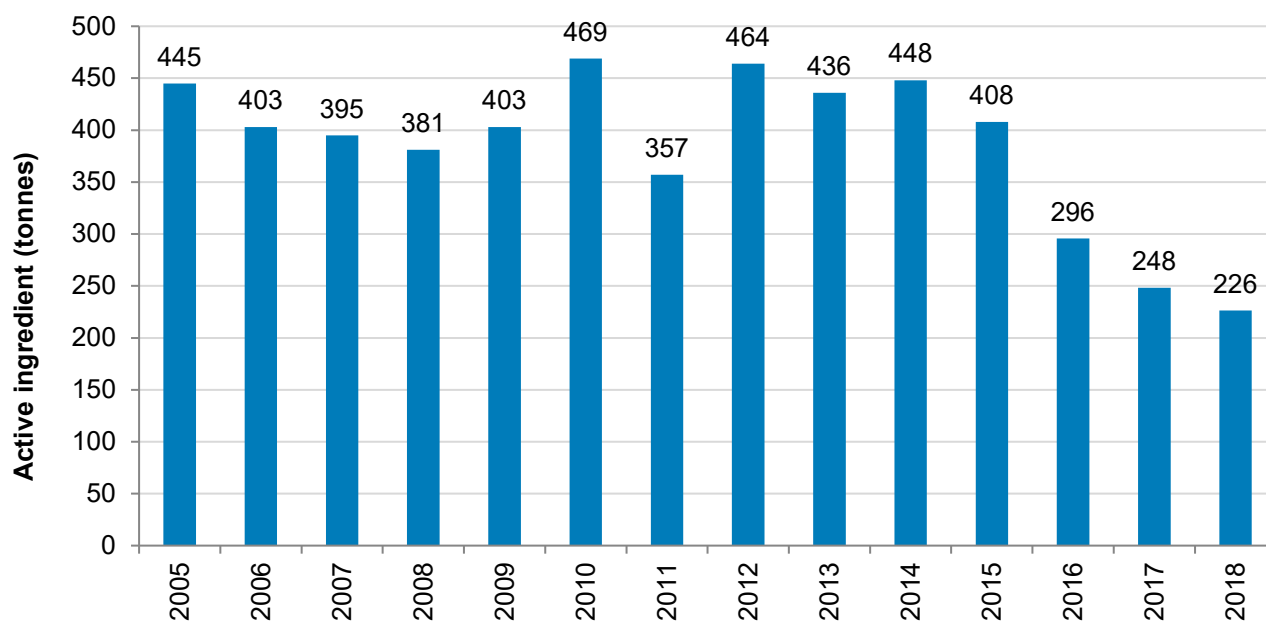
1.3 Results and discussion

1.3.1 Total sales of antibiotics for veterinary use in the UK

Sales data analysed using the 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 2005–2009. Prior to these years, data (covering 1993–2005) 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 are presented in **Figure 1.1**. The total quantity of antibiotic active ingredient sold in 2018 was 226.2 tonnes, a 21.9 tonne (9%) decrease from 2017. This is 42% lower than the ten-year mean for the preceding 2007–2017 period (mean 391.3 tonnes; range 248.2–469.0 tonnes).

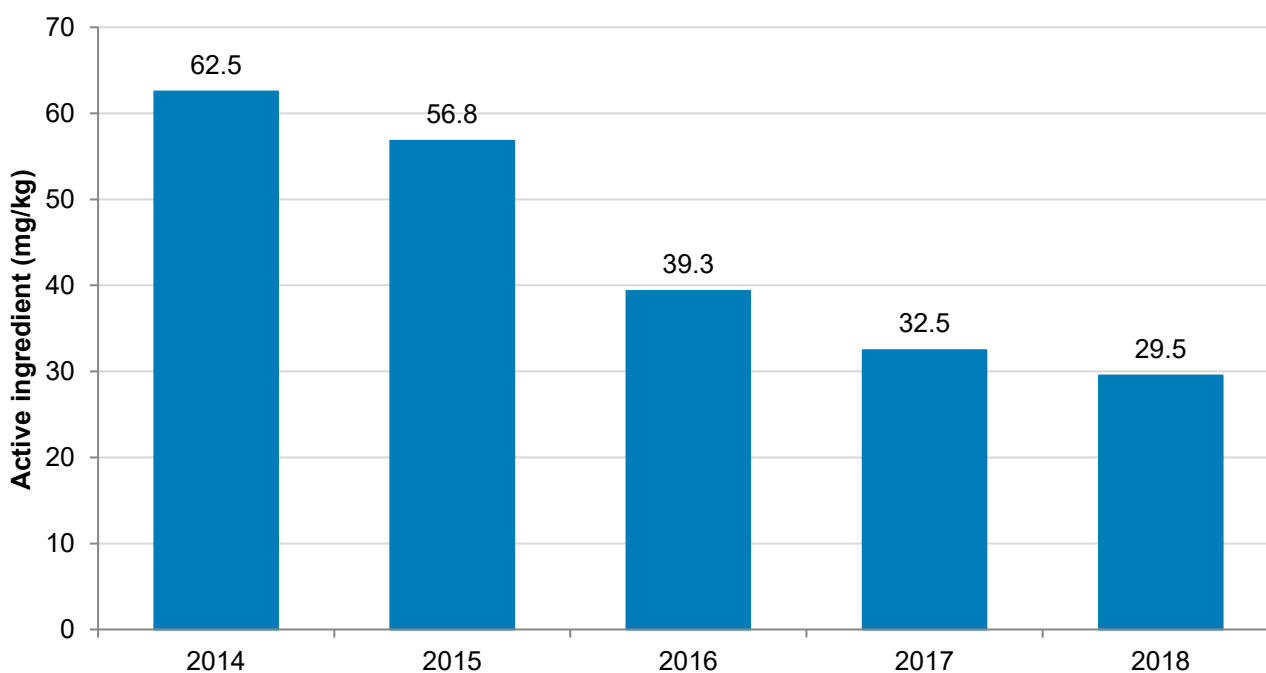
Figure 1.1: Total quantity of antibiotic active ingredient (tonnes) sold in the UK per year using ESVAC methodology; 2005–2018



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 decreased by 3.0 mg/kg (9%) between 2017 and 2018, from 32.5 mg/kg to 29.5 mg/kg (**Figure 1.2**). This is the lowest UK figure reported since ESVAC sales data reporting started in 2005 and a 33.0 mg/kg (53%) reduction since 2014.

Figure 1.2: Active ingredient (mg/kg) of antibiotics sold licenced for use in food-producing animal species; 2014–2018



1.3.3 Total sales of antibiotics by administration route (tonnes)

1.3.3.1 By administration route for all animal species

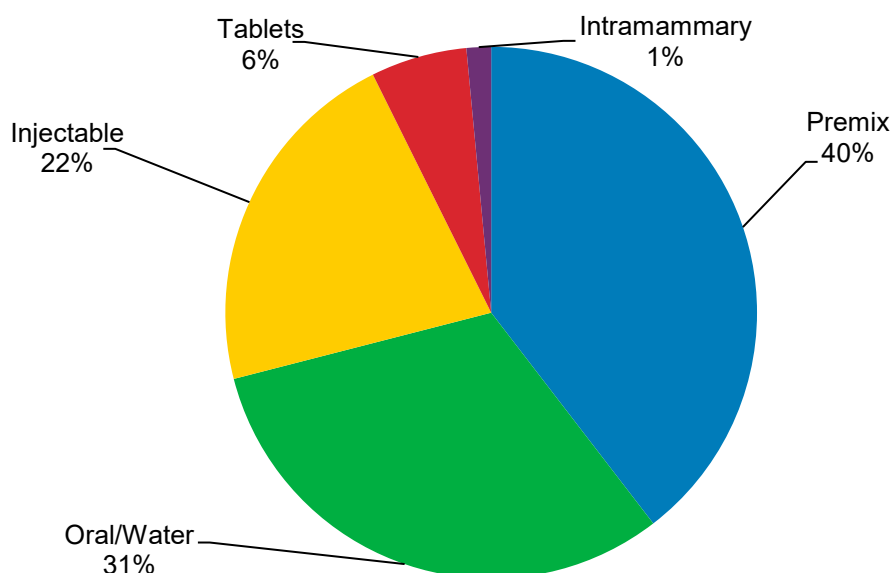
Premix remained the most common administration route, accounting for 89.5 tonnes (40%) of total sold in 2018 (**Table 1.1** and **Figure 1.3**). Oral/water preparations were the second most used administration route, representing 71.1 tonnes (31%) of total sold in 2018. Excluding tablets, sales of oral products (premix and oral/water combined) decreased by 223.9 tonnes (58%) since 2014. Sales of injectable products have fluctuated since 2014 and decreased between 2017 and 2018 by 5.3 tonnes (10%).

Table 1.1: Active ingredient (tonnes) of antibiotic sold for all animal species by route of administration; 2014–2018

Administration route	Active ingredient in tonnes					Trendline
	2014	2015	2016	2017	2018	
Premix	267.2	232.8	147.5	106.5	89.5	
Oral/water*	117.4	109.7	85.0	70.3	71.1	
Injectable	44.5	49.8	45.4	54.3	49.0	
Tablets	15.7	12.6	14.6	14.3	13.2	
Intramammary	3.2	3.3	3.1	2.7	3.4	
Total sales of antibiotics	448.0	408.2	295.6	248.2	226.2	

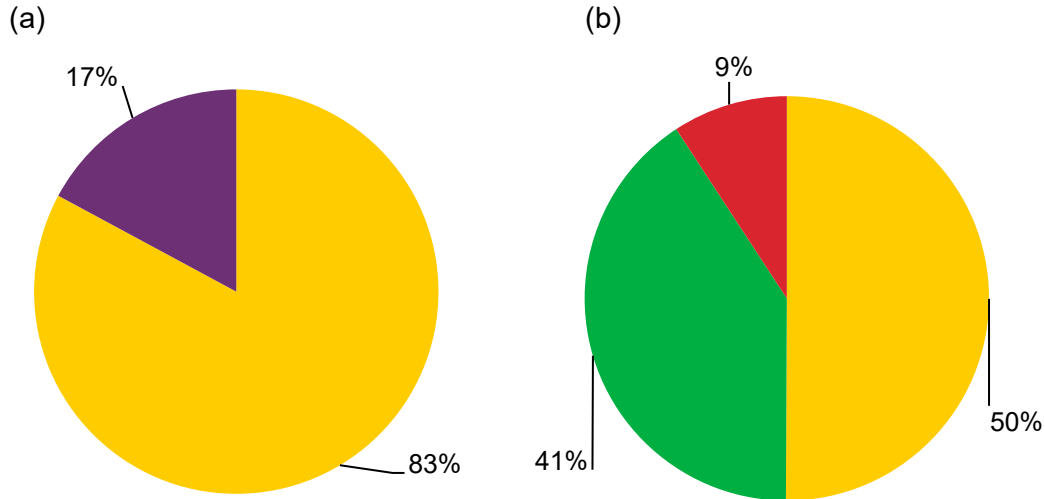
* Excluding tablets, inclusive of bolus preparations.

Figure 1.3: Active ingredient (% of total sales) of antibiotics sold for all animal species by route of administration; 2018



Concerning HP-CIAs, the majority of 3rd and 4th generation cephalosporins and fluoroquinolones in 2018 were for injectable use (83% and 50% respectively; **Figure 1.4**). All colistin was sold in products intended for oral use.

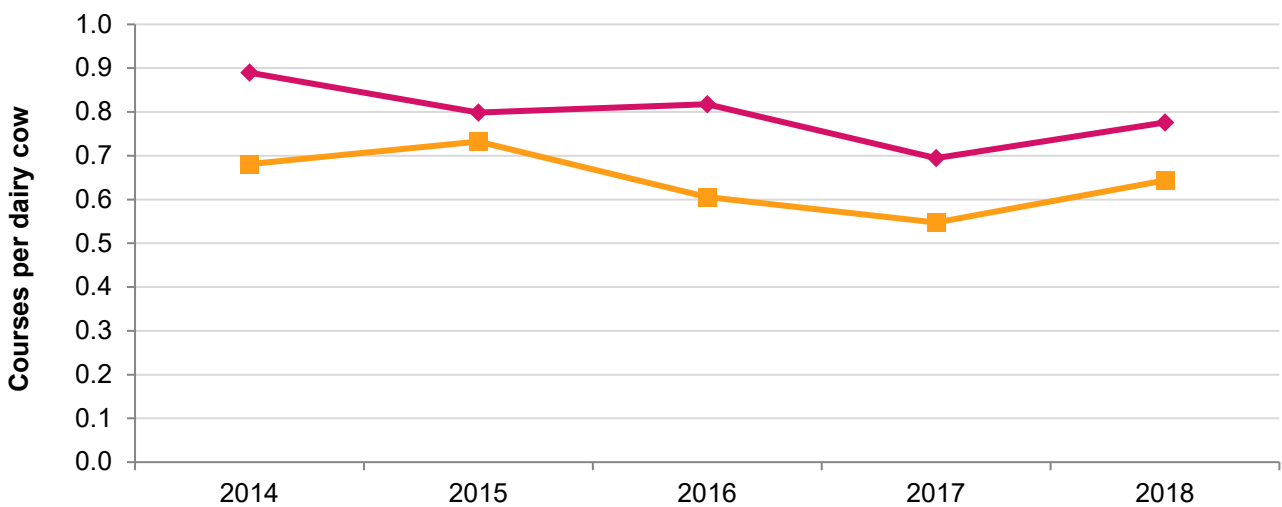
Figure 1.4: Distribution of sales (tonnes) of HP-CIAs for all animal species by the major administration routes (injectables (■), oral/water (■), intramammaries (■), tablets (■)): (a) 3rd and 4th generation cephalosporins and (b) fluoroquinolones; 2018



1.3.3.2 Intramammary antibiotic products

Sales of dry and lactating cow products are measured in 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. This metric harmonises the sales data analysis with the dairy sector specific targets, where DCDvet is used to measure intramammary antibiotic usage. Overall, sales of these products have fluctuated between 2014 and 2018 (**Figure 1.5** and **Table 2.11**).

Figure 1.5: Sales of dry (■) and lactating cow (◆) intramammary products (courses per dairy cow); 2014–2018



1.3.4 Total sales of antibiotics by animal species

The quantities of active ingredient sold between 2014 and 2018, differentiated by the animal species or combination of species for which the products are indicated, are shown in **Table 1.2**.

In 2018, 178.3 tonnes (79%) of total antibiotic sales were attributed to products licenced for food-producing animal species only. This is a 13.5 tonne (7%) reduction since 2017 and a 204.3 tonne (53%) reduction since 2014. Products authorised for use exclusively in pigs and/or poultry accounted for 136.3 tonnes (60% of total sales) and sales continue to decline; a reduction of 9.1 tonnes (6%) since 2017 and 203.4 tonnes (60%) since 2014.

Sales of antibiotics indicated for use in non-food-producing animals reduced by 5.3 tonnes (25%) since 2017 and 16.1 tonnes (50%) since 2014. Horse-only product sales fell by 4.3 tonnes (64%) since 2017 and 13.6 tonnes (85%) since 2014. Sales of products licenced for companion animals only decreased by 1.0 tonne (7%) since 2017, and by 2.5 tonnes (16%) since 2014. 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 category indicated; 2014–2018*

Animal species category	Animal species	Active ingredient in tonnes (% sales)				
		2014	2015	2016	2017	2018
Indicated for food-producing animal species only	Pigs and poultry only	235.9	214.2	127.4	97.3	99.7
	Pigs only	61.4	49.4	39.7	33.0	23.8
	Poultry only*	42.5	38.0	26.5	15.0	12.9
	Cattle only	13.3	14.1	15.2	13.7	12.9
	Fish only	2.4	0.7	1.6	3.4	1.6
	Multiple food-producing animal species**	27.2	29.2	23.4	29.3	27.5
	Total	382.6 (85)	345.6 (85)	233.7 (79)	191.8 (77)	178.3 (79)
Indicated for non-food-producing animal species only	Companion animal only (excluding horse only)	15.9	12.7	14.7	14.4	13.4
	Horse only***	16.0	13.4	14.9	6.7	2.4
	Total	31.8 (7)	26.1 (6)	29.6 (10)	21.1 (9)	15.8 (7)
Indicated for combination of food- and non-food-producing animal species	Total	33.5 (7)	36.3 (9)	32.3 (11)	35.2 (14)	32.1 (14)
Total sales of antibiotics^x		448.0	408.2	295.6	248.2	226.2

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

* 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).

*** 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.

Sales of products licenced for use in both food- and non-food-producing animal species have fluctuated slightly since 2014 and reduced by 3.1 tonnes (9%) between 2017 and 2018.

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.

1.3.5 Sales of antibiotics by antibiotic class

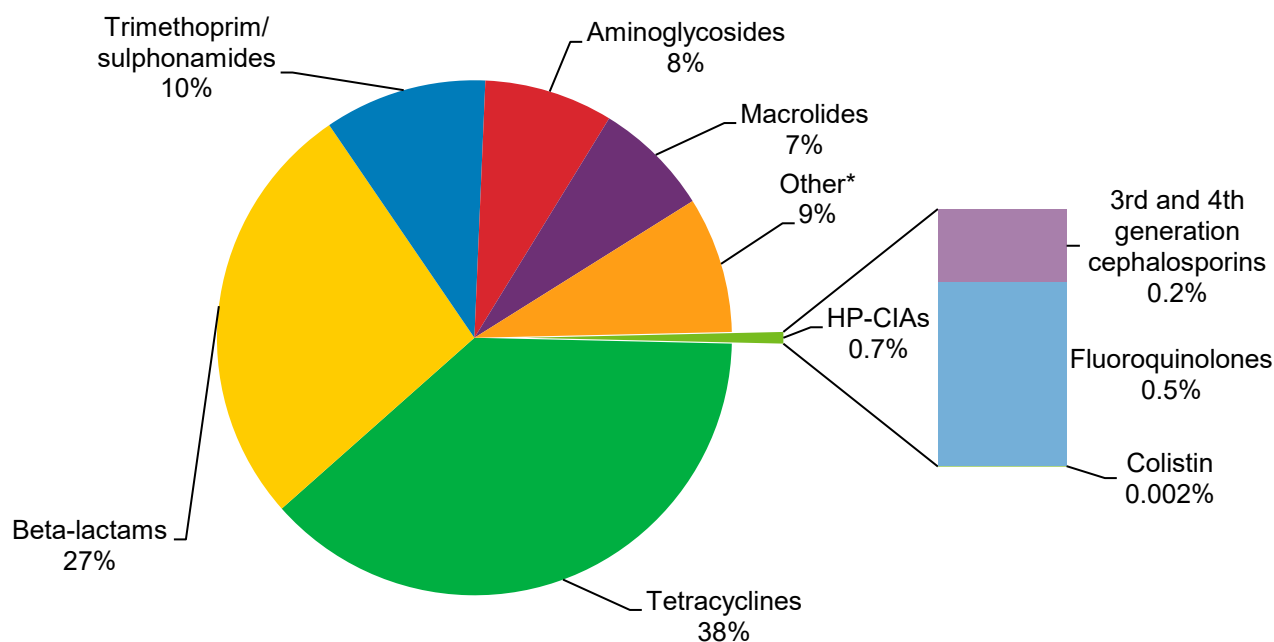
1.3.5.1 For all animal species

The total quantities of antibiotic active ingredient, by antibiotic class, sold between 2014 and 2018 are presented in **Figure 1.6** and **Table 1.3**. 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 38% of total sales in 2018. This class presented the greatest reduction in sales, reducing by 9.8 tonnes (10%) between 2017 and 2018 and 95.4 tonnes (52%) between 2014 and 2018. Beta-lactams were the second most used class in 2018 (accounting for 27% of total sales) and have reduced by 4.7 tonnes (7%) since 2017.

Macrolides represented 7% of total antibiotic sales in 2018 and reduced by 6.7 tonnes (29%) since 2017. Overall, this class has reduced by 33.4 tonnes (67%) since 2014.

Figure 1.6: Active ingredient (% weight) of antibiotics sold for all animal species by antibiotic class; 2018



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

Sales of HP-CIAs were 1.6 tonnes, representing 0.7% of total tonnes of antibiotics in 2018. Sales of these antibiotics have reduced by 0.4 tonnes (18%) since 2017 and 3.1 tonnes (66%) since

2014. Because of the importance of colistin as an HP-CIA, an unexpected increase observed in colistin sales was subjected to close scrutiny. Following from this, one colistin product sold in the UK (which accounted for 2.9 kg and 17.6 kg active ingredient for 2017 and 2018, respectively) was identified by the MAH to be exported as medicated feed and therefore had not been used in the UK. This highlights one of the limitations of antibiotic sales data and the importance of collecting antibiotic usage data, as reported in CHAPTER 2.

Table 1.3: Active ingredient (tonnes or kg) of antibiotics sold for all animal species by antibiotic class; 2014–2018

Antibiotic class	Active ingredient in tonnes (kg)				
	2014	2015	2016	2017	2018
Tetracyclines	181.8	166.3	108.6	96.2	86.4
Beta (β)-lactams	95.1	81.6	70.1	65.9	61.2
1 st /2 nd generation cephalosporins	5.5	4.9	4.8	4.2	4.1
3 rd /4 th generation cephalosporins (kg) [^]	(1,334)	(1,203)	(1,001)	(778)	(467)
Penicillins*	88.3	75.5	64.3	61.0	56.7
Trimethoprim/sulphonamides	70.5	68.3	51.6	23.9	23.2
Trimethoprim	11.6	11.2	8.5	3.9	3.8
Sulphonamides	58.9	57.1	43.1	20.0	19.4
Aminoglycosides	24.0	23.5	14.8	17.5	18.4
Streptomycin	9.4	10.0	8.8	10.6	9.4
Neomycin and framycetin	0.5	0.5	0.6	2.2	3.5
Other aminoglycosides**	14.2	13.0	5.3	4.8	5.5
Macrolides	50.0	38.2	28.7	23.3	16.6
Fluoroquinolones (kg)[^]	(2,593)	(2,532)	(1,729)	(1,210)	(1,160)
Other***	24.2	27.7	20.2	20.1	19.4
Colistin (kg) [^]	(837)	(870)	(128)	(4.2 ⁺)	(4.9 ⁺)
Total sales of antibiotics^x	448.0	408.2	295.6	248.2	226.2

^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 low fluoroquinolones, 3rd and 4th generation cephalosporins and colistin are presented in kg.

⁺ One colistin product (which accounts for 2.9 kg and 17.6 kg active ingredient for 2017 and 2018, 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 2018 analysed by animal species group and antibiotic class are shown in **Table 1.4**.

Table 1.4: Tonnes of antibiotic class sold for each animal species category (% bars of total tonnes for each category); 2018

Animal species category	Antibiotic class	Active ingredient in tonnes with proportion bars
Indicated for food-producing animal species only	Tetracyclines	84.9
	Beta-lactams	40.1
	Aminoglycosides	7.7
	Trimethoprim/sulphonamides	17.4
	Macrolides	15.4
	Fluoroquinolones	0.8
	Other*	12.1
	Colistin	0.005
	Total tonnes for category	178.3
Indicated for non-food-producing animal species only	Tetracyclines	0.4
	Beta-lactams	10.1
	Aminoglycosides	0.2
	Trimethoprim/sulphonamides	2.2
	Macrolides	0.09
	Fluoroquinolones	0.1
	Other*	2.6
	Colistin	0
	Total tonnes for category	15.8
Indicated for combination food- and non-food-producing animal species	Tetracyclines	1.1
	Beta-lactams	11.1
	Aminoglycosides	10.4
	Trimethoprim/sulphonamides	3.5
	Macrolides	1.1
	Fluoroquinolones	0.3
	Other*	4.7
	Colistin	0
	Total tonnes for category	32.1
Total tonnes		226.2

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

Tetracyclines were the most sold antibiotic class in the food-producing species only category, accounting for 84.9 tonnes (48%) of total tonnes for this species category followed by beta-lactams, which accounted for 40.1 tonnes (22%). Fluoroquinolones accounted for a small proportion of sales for this category (0.8 tonnes, 0.4%).

Beta-lactams were the most sold antibiotic class indicated for the non-food-producing species only category, representing 10.1 tonnes (64%) of the total. The 'other' category represented 2.6 tonnes (17%). Trimethoprim/sulphonamides class accounted for 2.2 tonnes (14%) of total tonnes for this species category, where sales were for horses.

Beta-lactams were also the most sold antibiotic class for a combination of food- and non-food producing species, representing 11.1 tonnes (34%) of the total for this animal species category, followed by aminoglycosides, which represented 10.4 tonnes (32%) 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 decreased between 2014 and 2018, with the exception of aminoglycosides (**Figure 1.7**).

Figure 1.7: Active ingredient (mg/kg) of antibiotics by antibiotic class and HP-CIAs, sold for food-producing animal species; 2014–2018



Sales of HP-CIAs for food-producing animal species represented 0.2 mg/kg, a small proportion (0.7%) of the overall antibiotic sales in mg/kg. The sales decreased by 0.05 mg/kg (19%) between 2017 and 2018 and by 0.5 mg/kg (68%) between 2014 and 2018. Between 2017 and 2018, sales of 3rd and 4th generation cephalosporins decreased by 0.04 mg/kg (40%), sales of fluoroquinolones

decreased by 0.007 mg/kg (5%) and sales of colistin experienced a small increase from 0.0006 mg/kg to 0.0007 mg/kg.

1.3.6 Sales of antibiotics for dogs and cats

1.3.6.1 Sales in active ingredient (tonnes)

Quantities of antibiotic active ingredient by antibiotic class sold between 2014 and 2018 for use in dogs and cats combined are presented in **Table 1.5** and **Figure 1.8**. Nearly all sales were for tablet preparations (99% in 2018).

Sales of HP-CIAs were 148.1 kg in 2018, representing 1% of antibiotic active ingredients. This accounts for 9% of total HP-CIA sales for all animal species in 2018 and has reduced by 0.2 kg (0.1%) since 2017 and 63.3 kg (30%) since 2014.

Beta-lactams were the most sold antibiotic class, representing 76% of total sales for dogs and cats in 2018. Sales of products in this class have reduced by 0.6 tonnes (6%) since 2017 and 2.6 tonnes (21%) since 2014. Antibiotic in the 'other' category were the second most sold class in 2018, representing 2.6 tonnes (20%) of total sales.

Table 1.5: Active ingredient (tonnes or kg) of antibiotics by antibiotic class sold for use in dogs and cats; 2014–2018

Antibiotic class	Active ingredient in tonnes (kg)				
	2014	2015	2016	2017	2018
Beta (β)-lactams*	12.7	9.8	10.4	10.8	10.1
3 rd /4 th generation cephalosporins (kg) [^]	(42)	(27)	(42)	(39)	(38)
Other**	0.8	0.8	1.7	2.3	2.6
Imidazole derivatives	0.1	0.08	1.0	1.7	2.0
Lincomycins	0.7	0.7	0.7	0.6	0.7
Tetracyclines	0.9	0.9	0.7	0.9	0.4
Fluoroquinolones (kg)[^]	(169)	(132)	(126)	(109)	(110)
Macrolides	0.1	0.2	0.1	0.1	0.09
Trimethoprim/sulphonamides	1.0	0.9	1.6	0.2	0.0
Total antibiotics^x	15.8	12.7	14.7	14.4	13.3

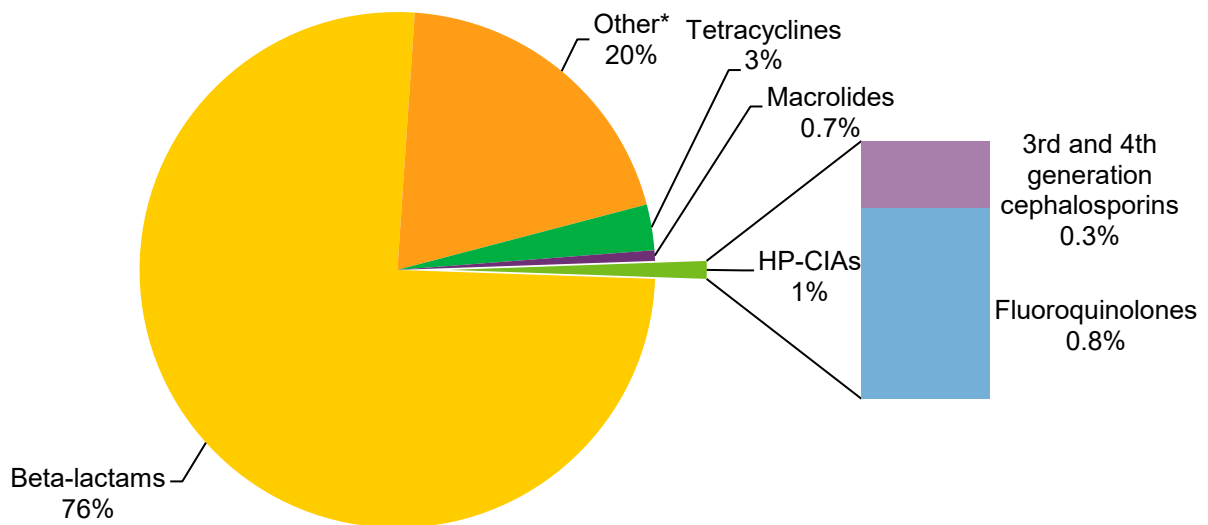
^x The totals were rounded to the nearest integer. This explains any minor discrepancy between the overall total and the classes' totals.

[^] 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 1.8: Active ingredient (% weight) of antibiotics sold for dogs and cats combined by antibiotic class; 2018



* Lincomycins and imidazole derivatives included within this group.

1.3.6.2 Sales in mg/kg

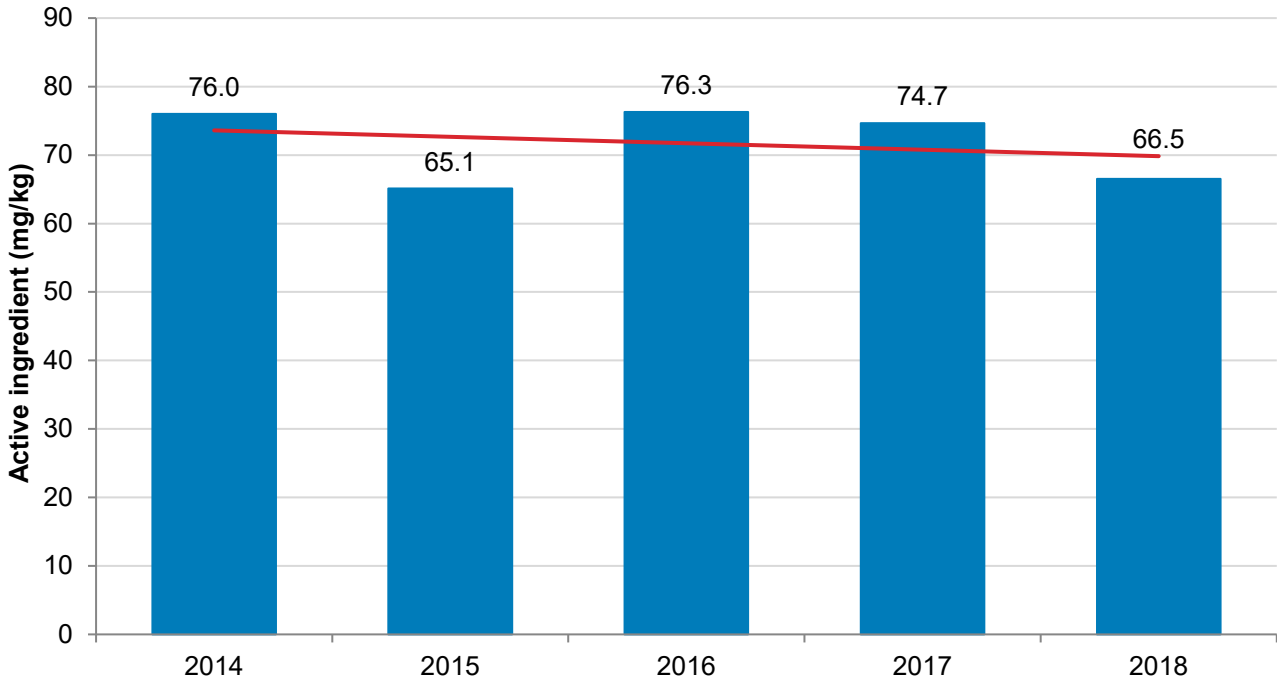
In the UK-VARSS 2017 report, an estimation of antibiotic sales in companion animals adjusted for the animal population was made, using a methodology of grams of active ingredient per head. For the data presented in this section, the ESVAC methodology was used for calculation of active ingredient, analysing 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 as they represented only a small proportion of sales. A combined dog and cat PCU was calculated using population data from the Pet Food Manufacturers' Association⁶ and average cat and dog weights provided by SAVSNET⁷ (see S1.2 of the supplementary material).

Sales of antibiotic products licenced for dogs and cats combined was 66.5 mg/kg in 2018 (**Figure 1.9**). This is an 8.2 mg/kg (11%) reduction since 2017 and a 9.5 mg/kg (12%) reduction since 2014.

⁶ <https://www.pfma.org.uk/statistics>

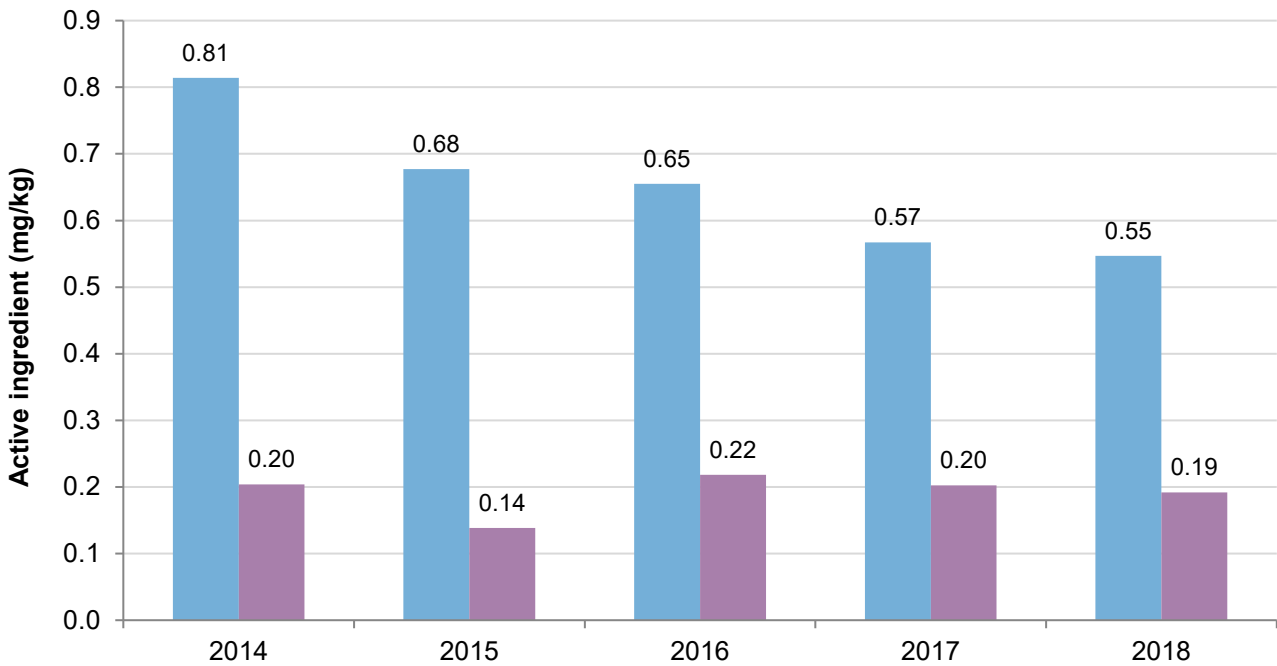
⁷ University of Liverpool, Small Animal Veterinary Surveillance Network (SAVSNET) project, personal communication, August 2019

Figure 1.9: Active ingredient (mg/kg) of antibiotics sold for use in dogs and cats; 2014–2018



Adjusted for cat and dog populations, the sales of HP-CIA products were 0.7 mg/kg in 2018, 1% of overall antibiotic sales in cats and dogs. Sales of 3rd and 4th generation cephalosporins were 0.2 mg/kg in 2018 and have remained stable since 2014. Sales of fluoroquinolones in 2018 were 0.5 mg/kg, having decreased by 0.02 mg/kg (2%) since 2017 and 0.3 mg/kg (33%) since 2014.

Figure 1.10: Active ingredient (mg/kg) of HP-CIAs, sold for dogs and cats combined: fluoroquinolones (■) and 3rd and 4th generation cephalosporins (■); 2014–2018



It should be noted that the combined dog/cat mg/kg metric may not correlate with the number of antibiotic courses administered. In particular, long-acting products and those administered to cats will tend to be under-represented as, in general, less active ingredient is administered per course when compared with short-acting products and those administered to dogs.

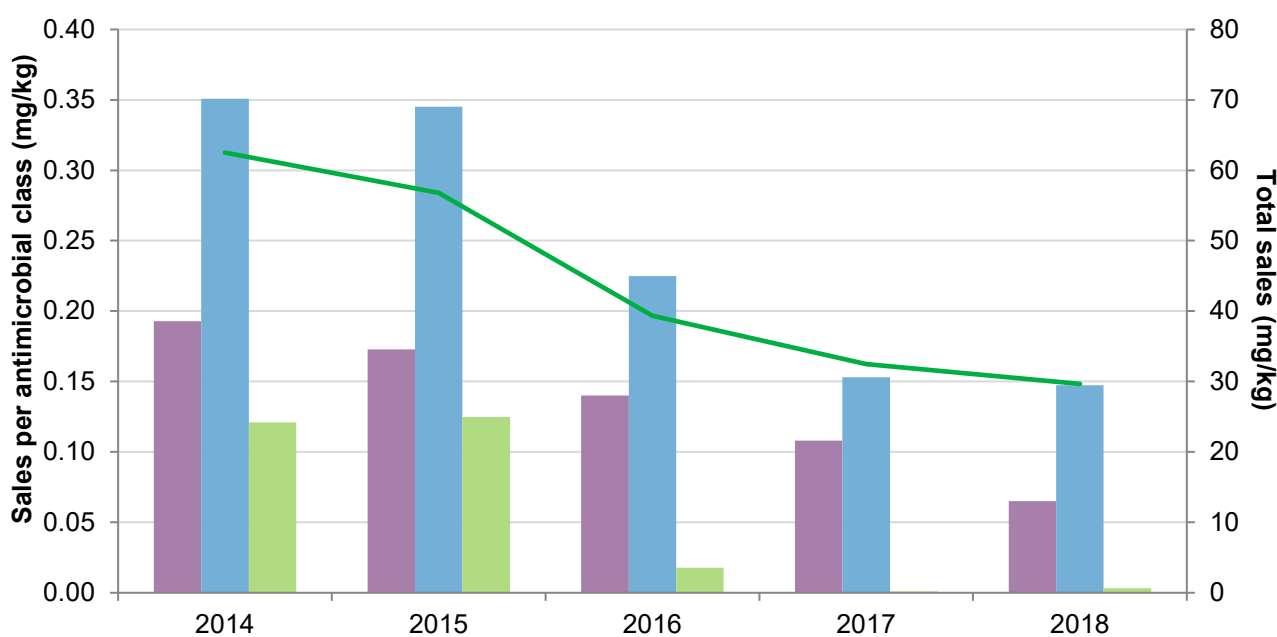
1.3.7 EU harmonised outcome indicators for antibiotic use

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

The primary indicator is “*the overall sales of veterinary antibiotics in milligram of active substance per kilogram of estimated weight at treatment of livestock and of slaughtered animals in a country (mg/PCU)*” (**Figure 1.2**). Secondary indicators are the sales in mg/PCU for 3rd and 4th generation cephalosporins, quinolones (and percentage of fluoroquinolones) and polymyxins (**Figure 1.7**). 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 Chapter 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 2014 (**Figure 1.11**).

Figure 1.11: EU 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; 2014–2018



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 Regulations⁸. 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 this and previous 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

During the 2018 data collection, it was brought to the VMD's attention that sales data for several products were over-reported by one pharmaceutical company in 2016 and 2017. This UK-VARSS 2018 report contains the corrected data and analyses for these years. Sales data within reports for two years prior to this one should no longer be referenced.

⁸ <http://www.legislation.gov.uk/ukxi/2013/2033/contents/made>



CHAPTER 2

Usage of Veterinary Antibiotics by Animal Species

2.1 Summary

The report highlights reductions in total antibiotic usage (when comparing 2017 and 2018) within:

- The pig sector, which have reduced usage by a further 21 mg/kg (16%);
- The duck sector, which have reduced usage by a further 1.5 mg/kg (47%);
- The salmon sector, which have reduced usage by 9.6 mg/kg (60%);
- The trout sector, which have reduced usage by 6.2 mg/kg (32%);
- The gamebird sector, which have reduced usage by a further 3.3 tonnes (25%).

Increases were seen for the following sectors:

- The broiler sector, which increased usage by 2.5 mg/kg (26%);
- The laying hen sector, which increased usage by 0.06 % doses (11%);
- The turkey sector, which increased usage by 1.5 mg/kg (3%).

However, total usage in 2018 was still 27%, 14% and 46% lower than the figures reported in 2016 for broilers, laying hens and turkeys, respectively.

In addition, no HP-CIAs were used in the laying hen, salmon and trout sectors, and further reductions in the use of HP-CIAs were reported in the pig, gamebird, meat poultry, dairy and beef sectors.

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 purchased, 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 will also enable benchmarking, enabling farmers to compare themselves with their peers and encouraging veterinarians and farmers to identify and share good practice.

This chapter describes the progress achieved so far, with updates from the food-producing animal sectors. Note that, for ease of reading, the data have been rounded to the nearest integer, other than for percentages, which have been calculated using the exact number. Methodology is outlined in section 2.4.

2.3 Results

2.3.1 Pigs

2.3.1.1 Antibiotics usage data

Total electronic Medicines Book for Pigs (eMB) recorded antibiotic usage in pigs decreased by 21 mg/kg (16%) from 131 mg/kg in 2017 to 110 mg/kg in 2018. This means that total usage has decreased by 168 mg/kg (60%) since 2015 (**Table 2.1**).

Table 2.1: Usage recorded for active ingredient (mg/kg) of antibiotics in eMB Pigs by antibiotic class; 2015–2018

Antibiotic	Active ingredient in mg/kg (% of total)				% Change 2015–2018
	2015	2016	2017	2018	
Tetracyclines	117.7 (42)	82.4 (45)	55.7 (43)	45.9 (42)	-61
Penicillins	37.0 (13)	27.4 (15)	22.4 (17)	21.5 (19)	-42
Trimethoprim/sulphonamides	66.2 (24)	29.2 (16)	20.8 (16)	18.5 (17)	-72
Macrolides	31.0 (11)	28.8 (16)	16.0 (12)	10.4 (9)	-66
Pleuromutilins	17.3 (6)	7.6 (4)	9.8 (7)	5.1 (5)	-71
Other*	8.6 (3)	7.2 (4)	6.1 (5)	8.8 (8)	+2
Total	278	183	131	110	-60

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

Usage of HP-CIAs in pigs decreased by a further 0.04 mg/kg (39%) between 2017 and 2018, and has now fallen by 0.92 mg/kg (94%) 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 (■); 2015–2018

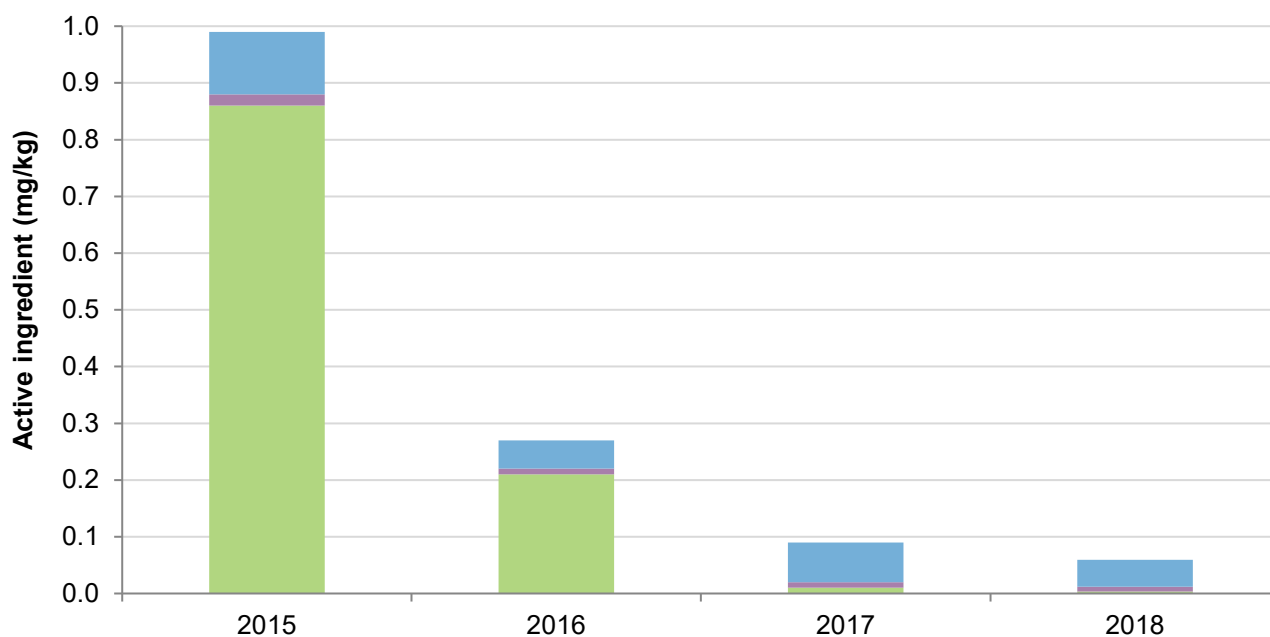
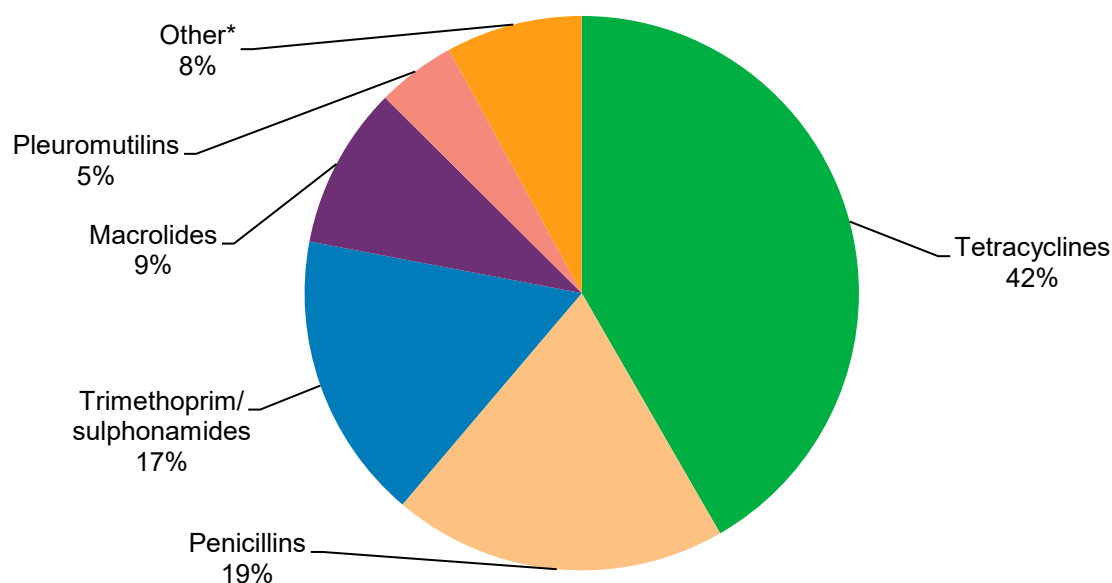


Table 2.2: HP-CIA usage (active ingredient of antibiotics, mg/kg) recorded in eMB Pigs; 2015–18

Antibiotic	Active ingredient in mg/kg				% Change
	2015	2016	2017	2018	2015–2018
Fluoroquinolones	0.11	0.05	0.07	0.05	-55
3 rd /4 th generation cephalosporins	0.02	0.01	0.01	0.01	-54
Colistin	0.86	0.21	0.01	0.004	-99.6
Total	0.98	0.27	0.10	0.06	-94

Tetracyclines represented 42% of antibiotic used, with penicillins, trimethoprim/sulphonamides and macrolides representing a further 45% (**Figure 2.2**). Due to lack of availability of the authorised product, 1.8 and 4.5 tonnes of oral trimethoprim-sulphonamide for pigs was imported under the Special Import Scheme in 2017 and 2018, respectively. This is not included in the sales data in CHAPTER 1.

In-feed is still the most common route of administration, although relative use has decreased from 78% in 2017 to 72% in 2018. Correspondingly, in-water now accounts for 24% active ingredient used (compared with 19% in 2017) and injectables 4% (compared with 3% last year) (data not shown).

Figure 2.2: Antibiotic active ingredients by class (%) reported in eMB Pigs; 2018

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

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

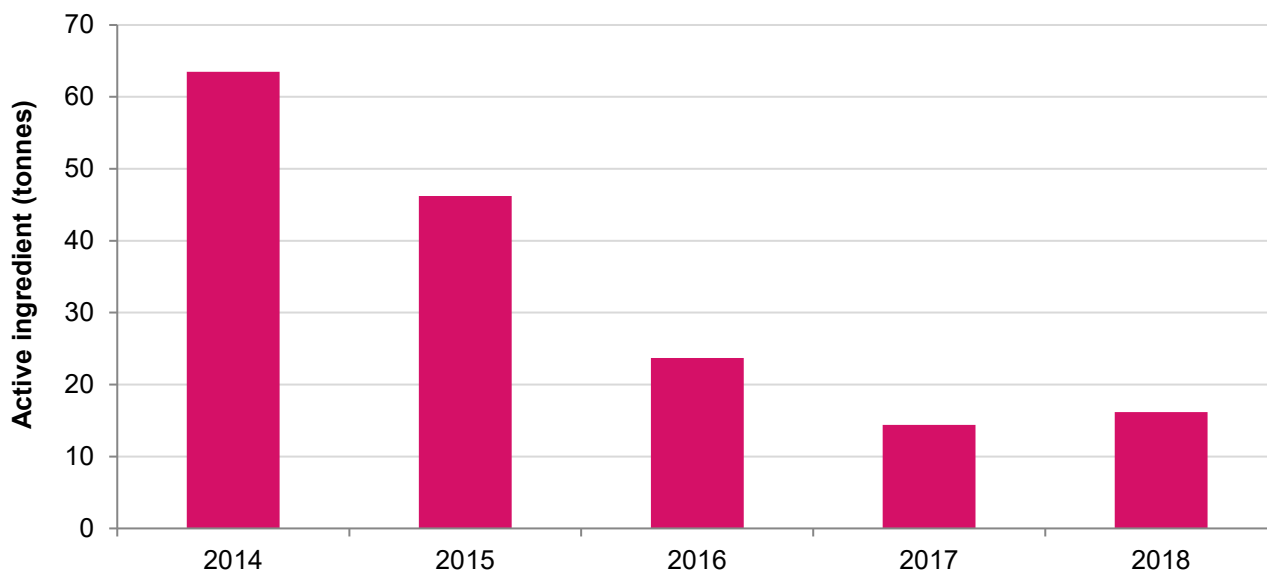
“The further reductions in both total antibiotic use and the use of HP-CIAs by the pig sector is testament to the great efforts and commitment of pig producers and their veterinarians to champion responsible antibiotic use. Factors contributing to this success include improved industry biosecurity and the new benchmarking tool within the eMB which allows producers to benchmark their antibiotic usage against other producers with similar production systems. This has enabled producers to understand their own patterns of antibiotic use and, alongside their veterinarians, make informed decisions around animal treatments. The sector is now well on the way to achieving the challenging target set by the pig sector of reaching 99 mg/kg by 2020. As we approach this target, it is important that producers continue to work with their veterinarians to ensure further reductions don’t compromise animal health or welfare.”

2.3.2 Meat poultry

2.3.2.1 Antibiotic usage data

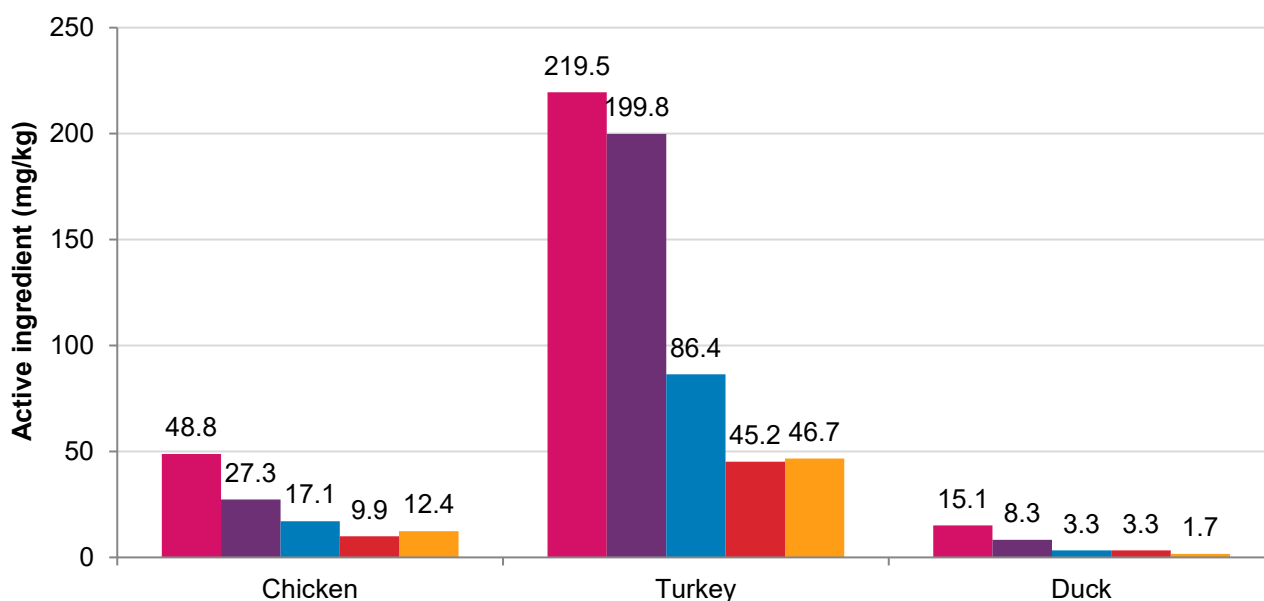
In 2018, the British Poultry Council (BPC) reported the use of 16.2 tonnes of active ingredient; a 1.8 tonne (12%) increase from 2017, although usage has decreased by 47.3 tonnes (75%) since 2014 (**Figure 2.3**).

Figure 2.3: Active ingredient (tonnes) of antibiotics used by all members of BPC Antibiotic Stewardship; 2014–2018



When considering the size of the animal population, between 2017 and 2018 usage in the chicken sector increased by 2.5 mg/kg (26%), usage in the turkey sector increased by 1.5 mg/kg (3%) and usage in the duck sector decreased by 1.5 mg/kg (47%). Since 2014, the chicken sector has reduced antibiotic usage by 36.4 mg/kg (75%), the turkey sector has reduced by 172.8 mg/kg (78%) and the duck sector has reduced by 13.4 mg/kg (88%) (**Figure 2.4**).

Figure 2.4: Active ingredient (mg/kg) of antibiotics used by all members of BPC Antibiotic Stewardship by species (chicken, turkey and duck); 2014 (■), 2015 (■), 2016 (■), 2017 (■) and 2018 (■)



In 2018, 79% of active ingredient classes used comprised penicillins and tetracyclines. However, between 2017 and 2018, penicillin use increased by 2.0 tonnes (25%) whereas tetracycline use decreased by 0.8 tonnes (24%) (**Table 2.3** and **Figure 2.5**). This reduction in tetracyclines is part of an on-going trend since 2015 (**Table 2.3**).

Table 2.3: Active ingredient (tonnes) of antibiotics used by all members of BPC Antibiotic Stewardship by antibiotic class; 2014–2018

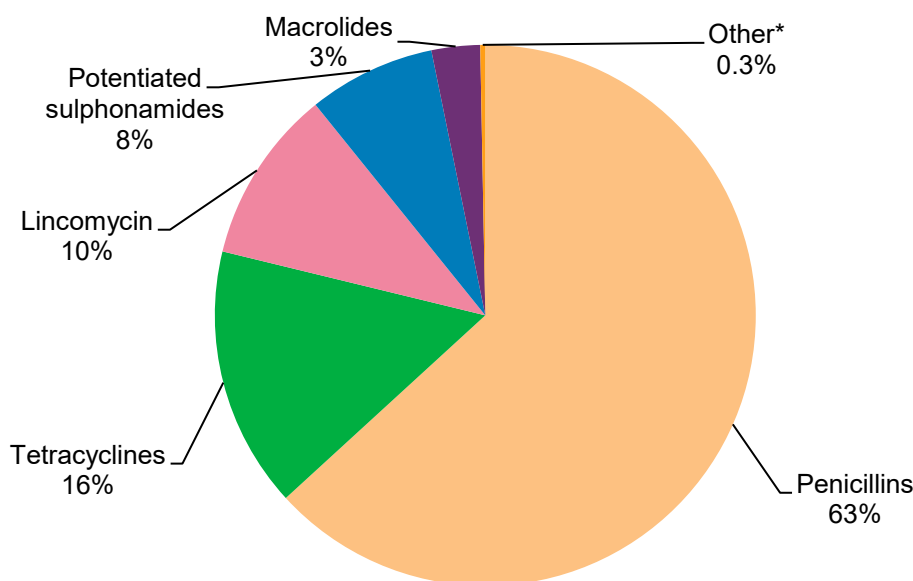
Antibiotic	Active ingredient in tonnes (% of total)					% Change 2014–2018
	2014	2015	2016	2017	2018	
Penicillins*	19.8 (31)	14.1 (30)	10.6 (45)	8.2 (57)	10.2 (63)	-49
Tetracyclines	30.6 (48)	23.9 (52)	9.0 (38)	3.3 (23)	2.5 (16)	-92
Lincomycins	7.1 (11)	4.8 (10)	1.4 (6)	1.2 (8)	1.7 (10)	-76
Potentiated sulphonamides	1.2 (2)	1.0 (2)	1.6 (7)	0.9 (6)	1.2 (8)	+7
Macrolides	2.7 (4)	1.1 (2)	0.5 (2)	0.6 (4)	0.5 (3)	-83
Other**, including:	2.1 (3)	1.4 (3)	0.6 (2)	0.2 (1)	0.1 (0.3)	-98
Fluoroquinolones [^] (kg)	1,131 (2)	540 (1)	122 (0.5)	38 (0.3)	17.3 (0.1)	
Colistin [^] (kg)	121 (0.2)	40 (0.1)	8 (0.03)	0 (0)	0 (0)	
Total	64	46	24	14	16	-75

* Amoxicillin and phenoxymethylpenicillin.

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

[^] Highest priority critically important antibiotics.

Figure 2.5: Antibiotic active ingredient by class (%) used by members of BPC Antibiotic Stewardship; 2018



* 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 2018. Fluoroquinolones were not used by the duck sector and only used in very small quantities by the broiler sector (325 g active ingredient). Between 2017 and 2018, the turkey sector reduced the use of fluoroquinolones by 0.18 mg/kg (46%) to 0.2 mg/kg, which is a reduction of 7.3 mg/kg (97%) since 2014. Overall, the poultry meat sector used 0.016 mg/kg HP-CIAs in 2018, a 49% drop between 2017 and 2018 and a 99% drop since 2014.

2.3.2.2 Statement from British Poultry Council

“BPC Antibiotic Stewardship’s four pillars of data collection, rapid on-farm diagnostics, sharing best practice and understanding patterns of resistance are delivering excellence in bird health and welfare. The poultry meat sector continues to monitor and review on-farm management practices and promote responsible antibiotic use throughout the supply chain. The latest data from 2018 show slight increases in antibiotic usage for the chicken and turkey sectors, although the levels are still 27% below those seen in 2016 for chickens and 46% below 2016 levels for turkeys. BPC Antibiotic Stewardship has carried out a farm-level review into reasons for antibiotic treatment in 2018 and found that there was an increase in seasonal bacterial infections requiring treatment to maintain bird health and welfare. The duck sector reduced usage by a further 47% in 2018 to 1.7 mg/kg and members of the BPC Antibiotic Stewardship are below the government endorsed RUMA species specific targets of 25 mg/PCU for chicken and 50 mg/PCU for turkey.”

2.3.3 Laying hens

2.3.3.1 Antibiotic usage data

A total of 3.2 tonnes of antibiotic active ingredient were used by the laying hen industry in 2018. This represents 0.63 actual bird days treated/100 bird days at risk, an 11% increase from 2017 but 13% lower than the figure reported in 2016 (**Table 2.4**).

Tetracyclines and pleuromutilins accounted for 80% of total use. Over the last two years, tetracyclines increased by 0.087 bird days (30%) whereas pleuromutilins decreased by 0.152 bird days (54%). No HP-CIAs were used in 2018, in keeping with 2017 (Table 2.4. and Figure 2.6).

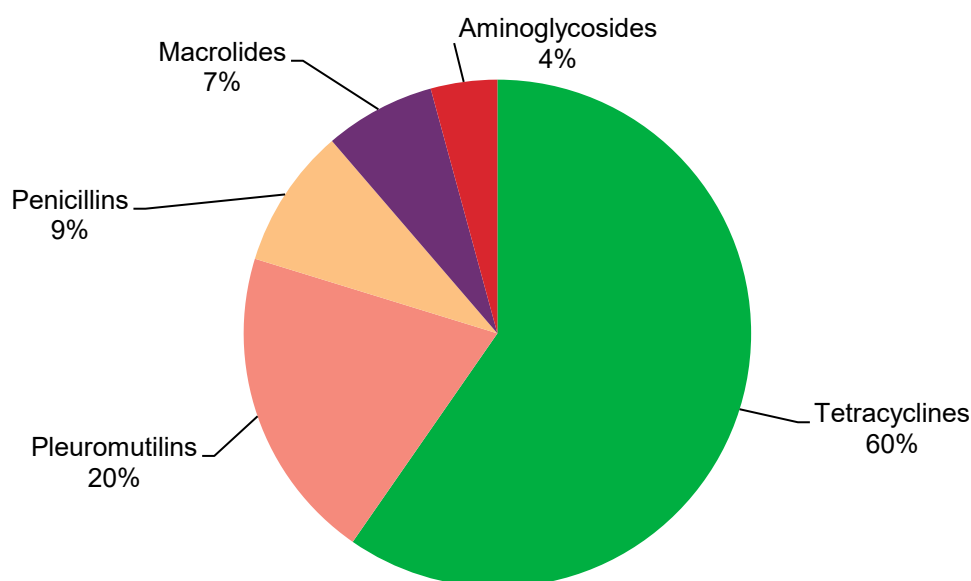
Table 2.4: Active ingredient (bird days and %) of antibiotics used by members of the BEIC Lion Code; 2016–2018

Antibiotic	Bird days (% of total)			% Change 2016–2018
	2016	2017	2018	
Tetracyclines	0.293 (40)	0.314 (55)	0.380 (60)	+30
Pleuromutilins	0.280 (38)	0.168 (29)	0.128 (20)	-54
Penicillins	0.060 (8)	0.056 (10)	0.053 (8)	-11
Macrolides	0.049 (7)	0.022 (4)	0.045 (7)	-8
Aminoglycosides	0.018 (2)	0.011 (2)	0.027 (4)	+48
Other*, includes:	0.030 (4)	0 (0)	0 (0)	-100
Fluoroquinolones [^]	0.002 (0.3)	0 (0)	0 (0)	
Colistin [^]	0.028 (4)	0 (0)	0 (0)	
Total	0.73	0.57	0.63	-13

* Includes fluoroquinolones and colistin.

[^] Highest priority critically important antibiotics.

Figure 2.6: Antibiotic bird days by class (%) used by members of the BEIC Lion Scheme; 2018



2.3.3.2 Statement from the British Egg Industry Council (BEIC)

“The usage data presented for 2018 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 no HP-CIAs were used in 2018, which is again in line with the target to keep their use below 0.05% bird days treated. The total “bird days/ 100 bird days at risk” figure for 2018 was 13% below the figure reported in 2016, but 11% higher than in 2017. Year-to-year fluctuation is unsurprising given the very low level of use in laying hens and given the need to treat in order to maintain bird health and welfare. Our antibiotic

use recording system has been expanded this year to collect data on the indications of each treatment. We hope this will help farmers and veterinarians better understand the main needs for medication and help them reduce the need for medication.”

2.3.4 Gamebirds

2.3.4.1 Antibiotic usage data

In 2018, 9.7 tonnes of active ingredient were reported through the Game Farmers' Association (GFA) data collection programme. This represents a reduction of 3.3 tonnes (25%) between 2017 and 2018, and a reduction of 10.5 tonnes (52%) since 2016 (**Figure 2.7** and **Table 2.5**).

Tetracyclines and pleuromutilins represented 85% of antibiotics used in 2018. Within the HP-CIAs, colistin was once again not used in 2018 and fluoroquinolone use (available for in-water use only) reduced by 3 kg (5.0%).

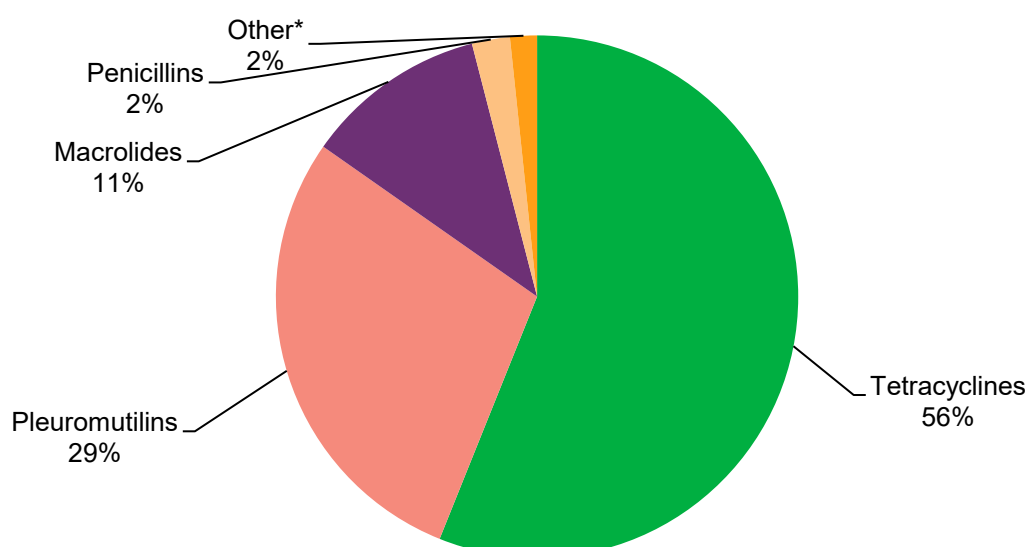
Table 2.5: Active ingredient (tonnes) of antibiotics used by the gamebird industry, recorded by GFA; 2016–2018

Antibiotic class	Active ingredient in tonnes (% of total)			% Change 2016–2018
	2016	2017	2018	
Tetracyclines	14.4 (72)	8.2 (63)	5.5 (56)	-62
Pleuromutilins	3.7 (18)	3.6 (27)	2.8 (29)	-24
Penicillins	1.2 (6)	0.8 (6)	1.1 (11)	-12
Macrolides	0.6 (3)	0.3 (2)	0.2 (2)	-63
Other*:	0.2 (1)	0.1 (0.7)	0.2 (2)	-28
Fluoroquinolones [^] (kg)	64 (0.3)	50 (0.4)	47 (0.5)	
Colistin [^] (kg)	0.6 (0.003)	0 (0)	0 (0)	
Total	20	13	9.7	-52

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

[^] Highest priority critically important antibiotics.

Figure 2.7: Antibiotic active ingredient by class (%) used by the gamebird industry; 2018



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

Analysis of usage data by route of administration shows that in-feed medication accounted for 46% antibiotic use, and this has reduced by 2.5 tonnes (35%) since 2017 and 10.4 tonnes (70%) since 2016. In-water medication reduced by 0.8 tonnes (14%) since 2017, to the same levels seen in 2016.

2.3.4.2 Statement from the Game Farmers' Association

“The reductions demonstrated in 2018 reflect a further year of good engagement by the gamebird sector, and the industry has halved antibiotic use since our voluntary campaign was rolled out in 2016. In particular, the reduction in in-feed use reflects a continuing focus on treating actual disease outbreaks rather than feeding medicated rations ‘just in case’. However, the gamebird sector will not stop here, and are continuing to push for further antibiotic reductions.”

2.3.5 Cattle

2.3.5.1 Dairy usage

The dairy data for 2018 cover 2,978 farms and represent 30% of UK dairy cattle. This is a larger sample than last year, with relatively higher coverage in Wales and Scotland (**Table 2.6**). The mean herd size within the sample is 226 dairy breed animals over 2 years of age, which is 30% higher than the overall UK mean. Because of these differences in the sample population of farms between years, caution should be taken when interpreting trends. In addition, antibiotic usage in this convenience sample may not be representative of the whole UK dairy population.

In this sample of dairy farms, 4.9 tonnes of antibiotic active ingredient were used, which represents 17 mg/kg. Sales of 3rd and 4th generation cephalosporins continued to fall and there was no colistin use in 2018. Overall, HP-CIAs accounted for 2% of antibiotic active ingredient used, a reduction from 4% in 2017.

Table 2.6: Comparison of national coverage of adult dairy cows (over 2 years of age) included in the FarmVet Systems sample; 2017–2018

	% coverage	
	2017	2018
England	30	31
Northern Ireland	33	33
Wales	12	31
Scotland	17	20
UK	26	30

* 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). Note the percentages are slightly lower than those reported last year, when only cows >2 years of age with offspring from national records were considered in the calculation.

As in previous years, penicillins/1st generation cephalosporins, aminoglycosides and tetracyclines were the most commonly used antibiotic classes (**Table 2.7** and **Figure 2.8**). The highest volume of active ingredient was administered by injection (66%) or orally (19%).

Table 2.7: Active ingredient (mg/kg) of antibiotics used by the dairy farms in the FarmVet Systems sample; 2015–2018

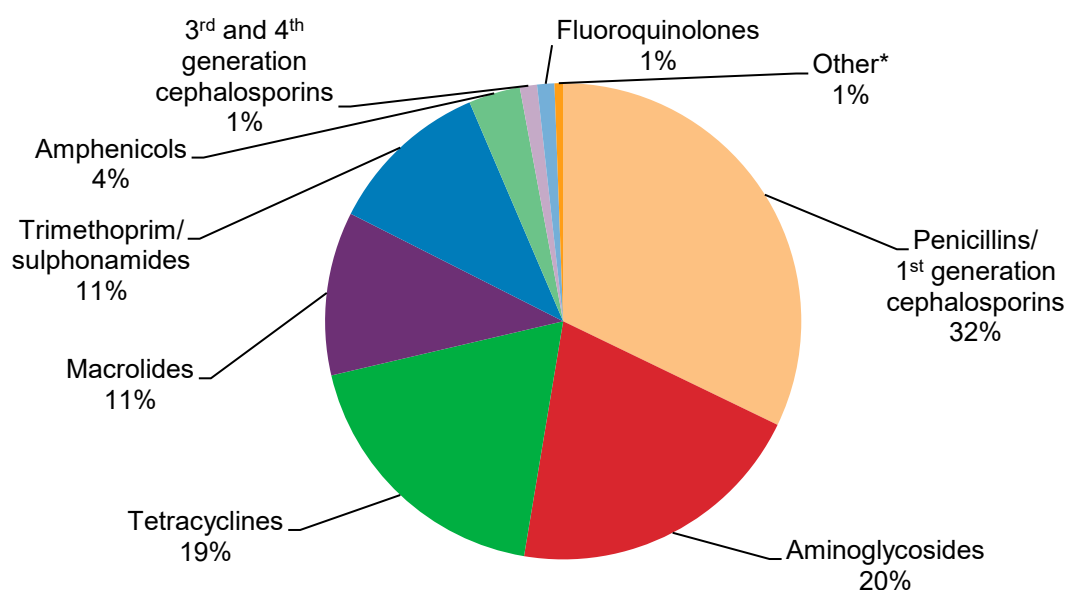
Antibiotic	Active ingredient in mg/kg (%)		% Change 2017–2018
	2017 ⁺	2018	
Penicillins/1 st generation cephalosporins	5.1 (32)	5.5 (32)	+8
Aminoglycosides	3.1 (20)	3.5 (20)	+13
Tetracyclines	2.8 (18)	3.2 (19)	+14
Macrolides	1.9 (12)	1.9 (11)	-2
Trimethoprim/sulphonamides	1.6 (10)	1.9 (11)	+20
Amphenicols	0.5 (3)	0.6 (4)	+19
3 rd /4 th generation cephalosporins [^]	0.4 (3)	0.2 (1)	-50
Fluoroquinolones [^]	0.2 (1)	0.2 (1)	-2
Other*, including: Colistin [^]	0.2 (1) 0.007 (0.04)	0.1 (0.6) 0 (0)	-12 -100
Total	16	17	+9

+ The figures reported this year differ slightly from the previous report due to corrections provided by FarmVet systems for oral and intramammary products. This has had the effect of reducing the total mg/kg figure from 17 to 16 mg/kg.

[^] Highest priority critically important antibiotics.

* Including aminocoumarins, lincosamides and polymyxins.

The mg/kg figure is 9% higher than the 2017 figure reported, and this primarily relates to an increase in active ingredient used in injectable and oral products. However, the number of courses administered for these products (using the ESVAC DCDvet methodology) decreased by 8% (data not shown). This is likely to be related to the reduction in HP-CIAs (in particular 3rd and 4th generation cephalosporins) and alternative products being chosen (such as penicillins/1st generation cephalosporins, aminoglycosides, tetracyclines and trimethoprim-sulphonamide combinations) which have a higher amount of active ingredient per treatment course.

Figure 2.8: Antibiotic active ingredient by class (%) used by the dairy farms in the FarmVet Systems sample; 2018

* Including aminocoumarins and lincosamides.

2.3.5.2 Beef usage

The beef data for 2018 cover 3,458 farms in Great Britain and represent 7.5% of the slaughter animals for GB and 5.5% for the UK. It is therefore a much smaller sample than for dairy, increasing the likelihood that the results are not representative of the beef population in the UK. In addition, farms in England are over-represented, largely because far fewer farms were excluded from the sample due to the presence of sheep (**Table 2.8**).

Table 2.8: Comparison of national coverage of the beef Population Correction Unit (PCU) included in the FarmVet Systems sample; 2018* and % farms excluded due to the presence of sheep

	% Coverage	% Farms excluded due to presence of sheep
England	9	40
Wales	5	65
Scotland	4	68

* 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).

The usage data showed that 1.1 tonnes of antibiotic active ingredient were used in this sample of farms, which represents 21 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 (**Table 2.9** and **Figure 2.9**). The highest volume of active ingredient was administered by injection (71%) or orally (24%).

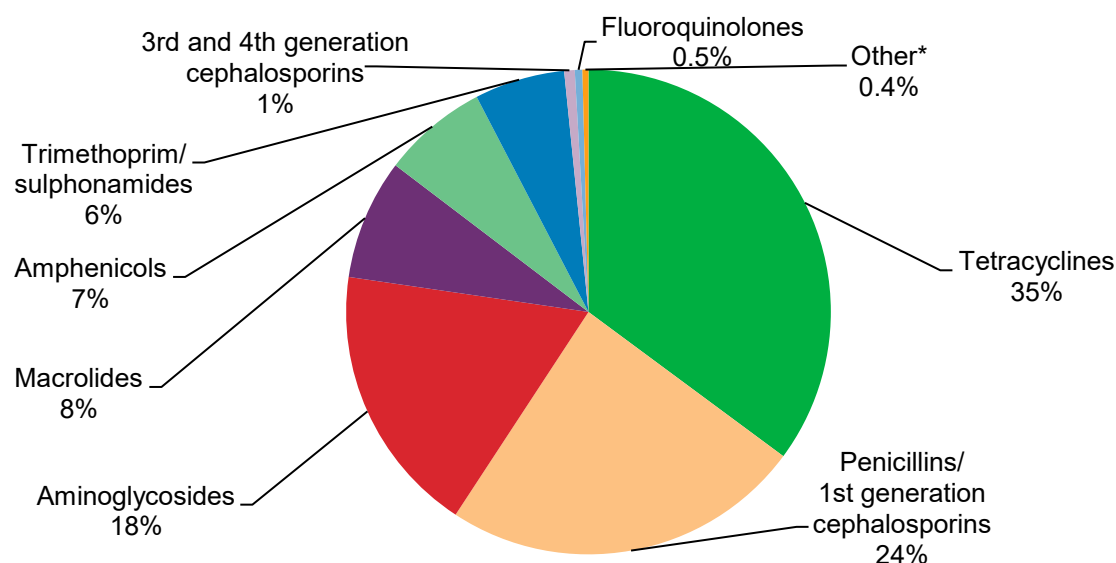
Table 2.9: Active ingredient (mg/kg) of antibiotics used by the beef farms in the FarmVet Systems sample; 2018

Antibiotic	mg/kg (%)
Tetracyclines	7.3 (35)
Penicillins plus 1 st generation cephalosporins	5.0 (24)
Aminoglycosides	3.8 (18)
Macrolides	1.7 (8)
Amphenicols	1.5 (7)
Trimethoprim/sulphonamides	1.3 (6)
3 rd and 4 th generation cephalosporins [^]	0.2 (0.7)
Fluoroquinolones [^]	0.1 (0.5)
Other [*]	0.1 (0.4)
Colistin [^]	0 (0)
Total	21

[^] Highest priority critically important antibiotics.

^{*} Including aminocoumarins and lincosamides.

Figure 2.9: Antibiotic active ingredient by class (%) used by the beef farms in the FarmVet Systems sample; 2018



* Including aminocoumarins and lincosamides.

The overall figure (21 mg/kg) was higher than the figure reported in 2017 (19 mg/kg). However, caution should be exercised with this comparison as representativeness for both years was unknown.

To understand possible trends, antibiotic usage was compared for the 2,350 GB farms (representing 4% UK coverage) where antibiotic usage data was available for 2015, 2016, 2017 and 2018. When looking at this sample, the use of HP-CIAs reduced by 0.7 mg/kg (73%) between 2015 and 2018, whereas overall use remained fairly stable during this period (**Table 2.10**). However, the number of courses administered (analysed using the ESVAC DCDvet methodology) reduced by 5% between 2015 and 2018 (data not shown) which, as with dairy, again reflects the movement away from HP-CIAs towards products with a higher amount of antibiotic active ingredient per course.

Table 2.10: Total antibiotic usage and use of HP-CIAs (mg/kg) in a subset of 2,350 beef farms in the FarmVet Systems sample; 2015–2018

Category	Active ingredient in mg/kg				% Change
	2015	2016	2017	2018	2015–2018
Total antibiotic use	25	26	27	25	0
3 rd and 4 th generation cephalosporins	0.6	0.4	0.3	0.2	-73
Fluoroquinolones	0.4	0.4	0.2	0.1	-72
Colistin	0	0	0	0	0
Total HP-CIAs	1.0	0.8	0.5	0.3	-73

The total antibiotic usage figure is higher in this smaller subset of farms than the full 2018 sample (25 mg/kg versus 21 mg/kg). This may reflect some of the differences in the make-up of the farms included in these samples. BCMS analysis suggests that smallholders (defined as farms with ≤ 10 births and ≤ 10 animals moving on to the farm) are under-represented, as these represent 20% and 16% in the full and smaller sub-set of farms respectively, compared with 33% for all GB beef farms

(calculated by making the same assumptions, i.e. with a beef farm defined as having <15 calves born to dairy dams, but without excluding farms which contain sheep).

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 is close to being met, with a 53% reduction in cattle injectable HP-CIAs since 2015.

Table 2.11: Sales (mg/kg) of injectable HP-CIAs with a licenced indication for cattle and of intramammary tubes (course doses, DCDvet), using methodology defined by ESVAC; 2015–2018

Category	2015	2016	2017	2018	(target) 2020	% Change 2015–2018
Injectable HP-CIA products licenced for cattle (mg/kg)	1.075	0.922 ⁺	0.704	0.502	0.461	-46%
Intramammary HP-CIA products (DCDvet)	0.332 ⁺	0.236	0.174	0.120	0.166	-64%
Intramammary tubes – lactating cow (DCDvet)	0.808 ⁺	0.818	0.694	0.776	0.727	-4%
Intramammary tubes – dry cow (DCDvet)	0.732 ⁺	0.605	0.547	0.644	0.586	-12%

+ Baseline year for targets.

For the dairy sector, there are also targets to reduce intramammary HP-CIAs by 50% by 2020 and reduce dry cow intramammary use and lactating cow intramammary use by 20% and 10%, from a 2015 baseline. The sector has exceeded the target on intramammary HP-CIA use, with a 64% reduction since 2015. However, the total use of lactating cow and dry cow intramammary products need to reduce by a further 6% and 9% respectively over the next two years for these particular targets to be reached.

The reductions in HP-CIA use demonstrated by the sales data are slightly lower than those indicated by the usage data, again highlighting how the sample of dairy and beef farms included in the usage data may not be fully representative of the whole UK situation.

2.3.5.4 Statement from Cattle Health and Welfare Group (CHAWG)

“The downward trend in the sales of injectable and intramammary HP-CIAs is very encouraging. The sample usage beef and dairy 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 sectors in promoting 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.

During 2018, the CHAWG Antimicrobial Usage sub-group (CHAWG AMU) consulted and agreed on core farm benchmarking metric(s) for the dairy sector and are carrying out the same process for the beef sector. Further details can be found here - <http://beefandlamb.ahdb.org.uk/returns/health->

[and-welfare/cattle-health-and-welfare-group-chawg/](#). Farm benchmarking will allow 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 responsible antibiotic use.

Further work is needed by the cattle sectors in order to achieve the 2020 intramammary antibiotic usage targets and to increase the amount, quality and representativeness of antibiotic usage data.”

2.3.6 Aquaculture

2.3.6.1 Salmon

2.3.6.1.1 Results

One tonne of active ingredient of antibiotics was used, representing 6.5 mg/kg (**Table 2.12**), which is 2.0 tonnes and 9.6 mg/kg (60%) lower than the use reported in 2017. Reductions were particularly seen for oxytetracycline, whereas florfenicol use increased. As in 2017, no HP-CIAs were used.

Table 2.12: Active ingredient (mg/kg) of antibiotics used on Scottish salmon farms; 2017–2018

Antibiotic	Active ingredient in mg/kg (%)		% Change
	2017*	2018	2017–2018
Oxytetracycline	13.8 (86)	3.8 (58)	-73
Florfenicol	2.2 (14)	2.6 (41)	+21
Oxolinic acid	0.1 (0.7)	0.08 (1)	-32
Amoxicillin	0.004 (0.02)	0 (0)	-100
Total	16.1	6.5	-60

* Figures reported here for 2017 are slightly different to those presented last year. This is because confirmed (rather than estimated) production figures have been used for the current report.

2.3.6.1.2 Statement from the Scottish Salmon Producers' Organisation

“Antibiotic use has reduced in 2018 compared with 2017. As highlighted by the sales data, usage in the industry can fluctuate year-on-year and the lower figures seen in 2018 relate to the fact that fewer treatments were needed during the seawater phase. The 2018 figure is close to the ambitious target to keep usage in the salmon industry below 5 mg/kg and reflects the on-going commitment from the sector to focus on preventative medicine and only use antibiotics when absolutely necessary in order to maintain health and welfare.”

2.3.6.2 Trout

2.3.6.2.1 Results

The sample obtained represented c. 90% of the UK trout production and a total of 0.16 tonnes of antibiotic active ingredient was used, representing 13 mg/kg, a 32% reduction on the figure reported in 2017 (**Table 2.13**). Reductions were seen particularly with oxytetracyclines and florfenicol (which reduced by 47% and 50% respectively). The quinolone oxolinic acid is now the most commonly used antibiotic class.

Table 2.13: Active ingredient (mg/kg) of antibiotics used on a sample of trout farms; 2017–2018

Antibiotic	Active ingredient in mg/kg (%)		% Change 2017–2018
	2017	2018	
Oxolinic acid	6.6 (34)	5.8 (45)	-12
Oxytetracycline	7.3 (38)	3.8 (29)	-47
Florfenicol	4.4 (23)	2.2 (17)	-50
Amoxicillin	0.9 (5)	1.2 (9)	+34
Total	19	13	-32

2.3.6.2.2 Statement from the British Trout Association

“The trout sector is committed to monitoring antibiotic usage and focusing on biosecurity and good management practices in order to minimise the use of antibiotics. The data show that usage in this large sample of trout farms has reduced by 32% in 2018 and remains below the sector target to maintain an average use of 20 mg/kg. As highlighted in the sector targets report (Responsible Use of Medicines in Agriculture Alliance, 2017), vaccines are a vitally important tool in preventing disease in trout farms and increasing the use as well as improving the availability of cost-effective authorised vaccines is crucial.”

2.4 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;
- 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 and 89% for 2018;
- 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;
- The data for 2018 were extracted from eMB in May 2019;
- 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 to further improve data accuracy;
- 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 2018. 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 2018. 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 including 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.

Overall, the sample for 2018 represents 30% UK dairy cows and 7.5% beef production in Great Britain. For both the beef and dairy farms, the 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

EU Harmonised Monitoring of Antibiotic Resistance

The EU 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 2018, EU Member States were mandated to carry out the following testing:

- Susceptibility testing of *Escherichia coli* obtained from caecal samples taken from healthy broilers and fattening turkeys 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 broilers and fattening turkeys at slaughter, as well as samples of fresh chicken meat at retail;
- Susceptibility testing of *Salmonella* spp. isolates derived from boot swab/dust samples from broiler, layer and turkey flocks collected on farm under the framework of the National Control Programmes for *Salmonella* spp. in poultry;
- Susceptibility testing of *Salmonella* spp. isolates derived from broiler and fattening turkey neck skin samples taken at slaughter by Food Business Operators;
- Susceptibility testing of *Campylobacter jejuni* obtained from caecal samples taken at slaughter from broilers and fattening turkeys.

The results of the testing of isolates from caecal samples, neck skin samples and poultry flocks are presented in this chapter. The Food Standards Agency (FSA) leads on the testing of chicken meat 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 broilers or turkeys.
- Resistance to cefotaxime and ceftazidime was detected in 1.6% and 0.5%, respectively, of *E. coli* from broilers, but not in isolates from turkeys.
- Resistance to ciprofloxacin was detected in 4.4% and 2.8% of isolates from broilers and turkeys respectively, which is a decline in resistance in turkey isolates since 2014.
- A decline in resistance since 2014 was noted to most antibiotics in isolates from broilers and turkeys, including to ampicillin, chloramphenicol, nalidixic acid, sulphonamides, tetracyclines and trimethoprim.
- In total, 4.0% of broiler caecal samples yielded *E. coli* with an ESBL phenotype and 6.3% *E. coli* with an AmpC phenotype. Of turkey caecal samples, 2.4% yielded *E. coli* with an ESBL phenotype and 1.1% with an AmpC phenotype. For all aspects this is a reduction since 2016.
- Presumptive carbapenemase-producing *E. coli* were not detected.
- All EU harmonised AMR outcome indicators show a four-year trend of decreasing resistance and increasing susceptibility.

Salmonella spp.

- A total of 83.6% of *Salmonella* isolates from broiler flocks were susceptible to all the antibiotics tested. This was 80.8% for layer flock isolates and 20.0% for turkey flock isolates.
- There was no resistance to cefotaxime or ceftazidime in isolates from broiler, layer and turkey flocks.
- Low resistance was detected to ciprofloxacin in *Salmonella* from broiler (6.4%), layer (3.8%) and turkey (5.3%) flocks.
- Two of three *S. Enteritidis* isolates from broiler flocks showed resistance to colistin – *S. Enteritidis* is a group D *Salmonella*, which may show a degree of intrinsic resistance to colistin. No other isolates from broiler, layer and turkey flocks were resistant to colistin.
- There was no resistance to meropenem in *Salmonella* isolates from broiler, layer or turkey flocks. Resistance to gentamicin was detected in isolates from layer (1.9%) and turkey (1.2%) flocks, but not in isolates from broiler flocks.
- Overall, resistance in *Salmonella* spp. isolated from poultry flocks under the National Control Programmes fluctuated between 2014–2018.
- No resistance was detected in FBO broiler isolates to cefotaxime, ceftazidime, ciprofloxacin, colistin, gentamicin or meropenem.
- Two of three FBO turkey isolates were resistant to sulphonamides and tetracyclines and the third one was susceptible to all the antibiotics tested.

Campylobacter jejuni

- Resistance to ciprofloxacin was detected in 48.0% of isolates from broilers and in 31.0% from turkeys.
- Resistance to erythromycin was detected in 0.6% of *C. jejuni* from broilers and in 0.6% of isolates from turkeys.
- Resistance to the six antibiotics tested in *C. jejuni* from broilers has slightly increased compared to previous monitoring years, whereas resistance has either slightly decreased or remained stable in turkey isolates.

3.2 Methods

3.2.1 Sample collection

Caecal samples were taken from healthy broilers and turkeys 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, jointly covering 61% of the UK throughput in 2018. Sample collection was randomised and evenly distributed throughout the year. One caecal sample was collected per epidemiological unit (slaughter batch).

Boot/dust swabs were collected in accordance with EU Regulation (EC) No. 2160/2003 (European Commission, 2003) and the National Control Programmes (NCPs) for layers, broilers and turkeys. Swabs were taken from all flocks included in the NCPs and a randomised sample of the isolates obtained from those swabs was further analysed (unless there were fewer than 170 isolates, in which case all isolates were tested).

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 neck skin 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 and the EFSA manual (European Food Safety Authority et al., 2019b).

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.

For this report, the ECOFF and CBP values applied were taken from the latest EFSA technical specifications (European Food Safety Authority et al., 2019a). Data from 2014 and 2016 were retrospectively updated where applicable. 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.

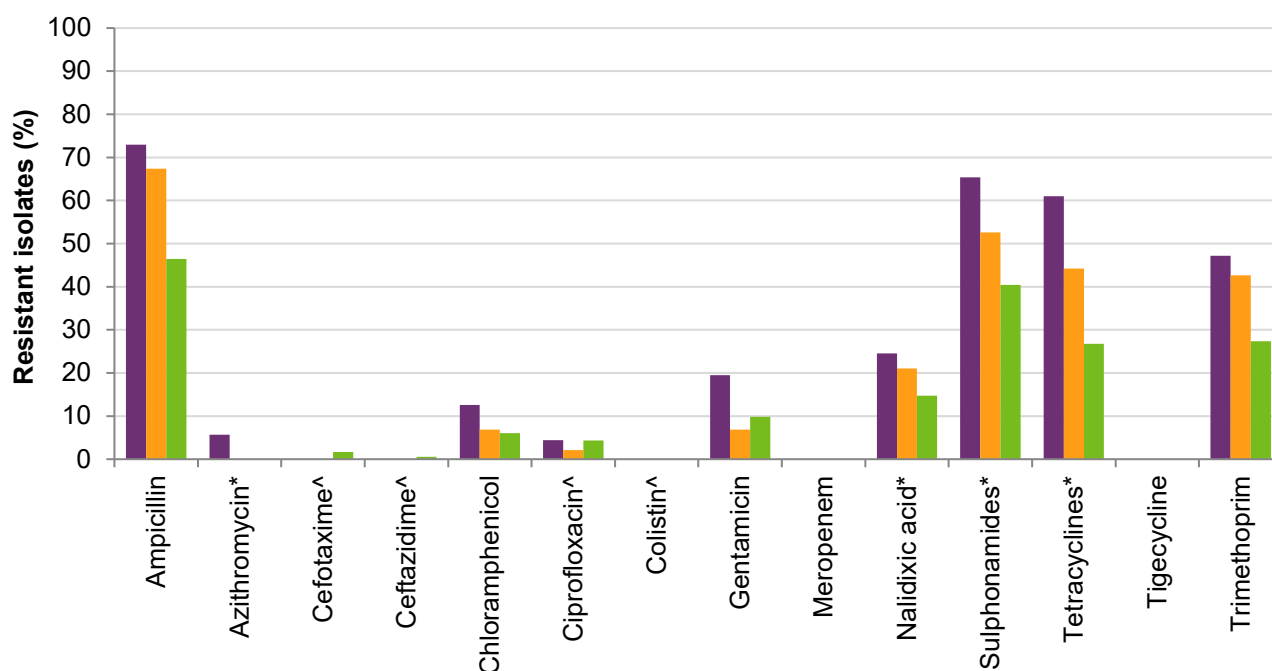
3.3 Results

3.3.1 *Escherichia coli*

3.3.1.1 Broilers

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

Figure 3.1: Percentage resistance (interpreted using EUCAST CBPs) in *E. coli* isolates from broilers at slaughter; 2014 (■; n=159), 2016 (■; n=190) and 2018 (■; n=183)



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

Of the HP-CIAs, resistance to the 3rd generation cephalosporins cefotaxime and ceftazidime was detected in 1.6% and 0.5% of *E. coli*, respectively. Resistance to these antibiotics was not detected in 2014 or 2016. Resistance to ciprofloxacin was observed in 4.4% of *E. coli*, an increase from 2016 but the same level as in 2014. No resistance was detected to colistin.

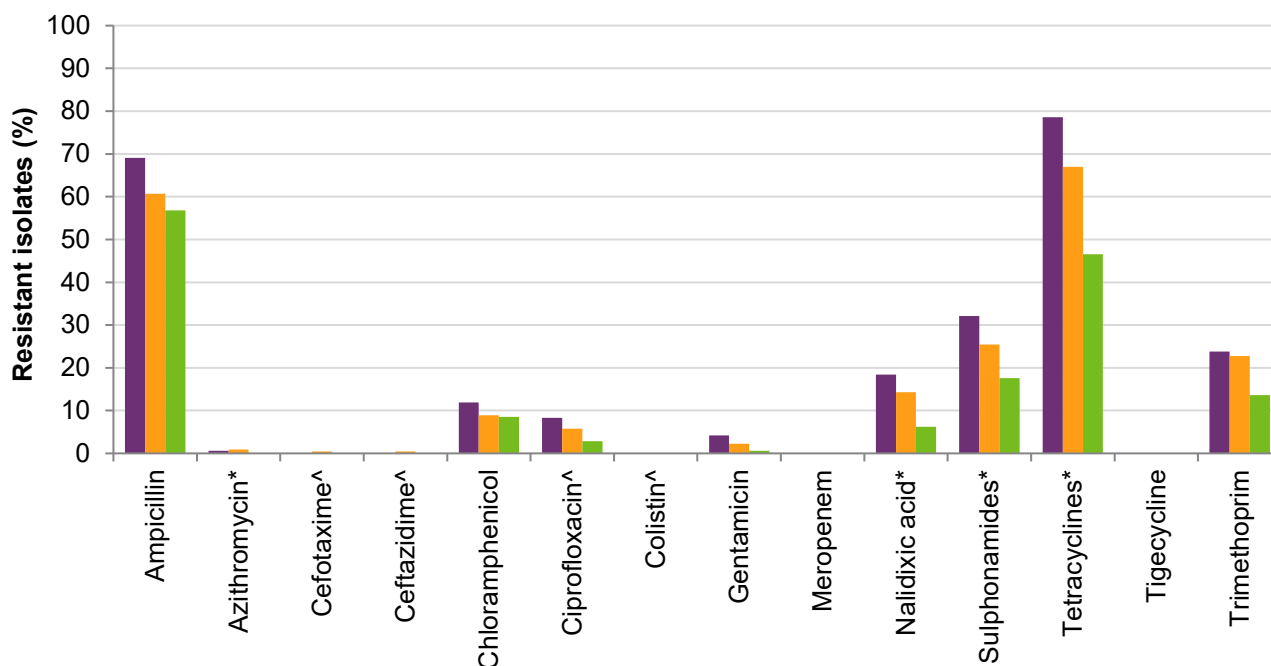
Susceptibility to azithromycin, meropenem and tigecycline has been maintained.

A continued decline in resistance was noted to most antibiotics tested. Resistance to ampicillin or trimethoprim was still high in 2018 at 46.4% and 27.3%, respectively; chloramphenicol and gentamicin resistance was low at 6.0% and 9.8%, respectively. High levels of decreased susceptibility (based on ECOFFs as no CBP value is available) were detected to sulphonamides (40.4%) and to tetracyclines (26.8%). There was a moderate level of decreased susceptibility to nalidixic acid (14.8%).

3.3.1.2 Turkeys

Resistance of *E. coli* isolates from turkey caecal samples is shown in **Figure 3.2**.

Figure 3.2: Percentage resistance (interpreted using EUCAST CBPs) in *E. coli* isolates from healthy turkeys at slaughter; 2014 (■; n=168), 2016 (■; n=224) and 2018 (■; n=176)



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

No resistance was detected to the HP-CIAs cefotaxime, ceftazidime or colistin and only low resistance was observed to ciprofloxacin (2.8%), a further decline from 2014 (8.3%) and 2016 (5.8%).

Susceptibility to meropenem and tigecycline has been maintained.

A continued decline in resistance was noted to most antibiotics. Ampicillin resistance remained high at 56.8%, trimethoprim resistance was moderate at 13.6%, chloramphenicol resistance was low at 8.5% and gentamicin resistance was very low at 0.6%. A high level of decreased susceptibility (based on ECOFFs as no CBP value was available) was detected to tetracycline

(46.6%), a moderate level to sulphonamides (17.6%) and a low level to nalidixic acid (6.3%). No decreased susceptibility was detected to azithromycin, an improvement on previous years (<1%).

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

3.3.2.1 Broilers

An AmpC phenotype *E. coli* (showing decreased susceptibility to cefoxitin, cefotaxime and ceftazidime) was present in 6.3% of caeca samples and 4.0% of samples yielded *E. coli* with an ESBL phenotype (showing synergy with cefotaxime and clavulanate and/or ceftazidime and clavulanate). None of the isolates were positive for both phenotypes (**Table 3.1**). The proportion of caecal samples harbouring ESBL and/or AmpC phenotype *E. coli* has fallen since 2016.

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

Table 3.1: Phenotype in ESBL-/AmpC-producing *E. coli* cultured on selective agars, from caecal samples from healthy broilers at slaughter in the UK; 2016 (n=382) and 2018 (n=302)

Phenotype	Number of isolates		Proportion of caecal samples (%)	
	2016	2018	2016	2018
ESBL	73	12	19.1	4.0
AmpC	40	19	10.5	6.3
ESBL/AmpC	2	0	0.5	0
Carbapenemase	0	0	0	0

All ESBL/AmpC phenotype isolates were resistant to ampicillin, as expected. Of five isolates which showed decreased susceptibility or resistance to ciprofloxacin, two had an ESBL phenotype and three had an AmpC phenotype. Decreased susceptibility to nalidixic acid was observed in all isolates showing decreased susceptibility to ciprofloxacin.

WGS results showed that among the 31 ESBL-/AmpC-producing *E. coli* isolated from broilers, *bla*_{CTX-M-1} (35.5%) was the most common ESBL gene, with *bla*_{SHV-1} (3.2%) the only other ESBL gene identified (see Table S3.2.3 in the supplementary material). The CMY-2 enzyme was the only transferable AmpC enzyme detected and was present in 89.5% of isolates with an AmpC phenotype. In 6.5% of isolates no ESBL/AmpC enzymes were detected, instead mutations in the promoter region associated with upregulation of chromosomal *ampC* expression were present.

The 11 CTX-M-1 isolates were associated with six different multi locus sequence types (MLST), indicating transmission of the plasmid. Sequence type (ST) 57 was assigned most frequently (n=6). The SHV-12 isolate was assigned to ST10. The 17 CMY-2 isolates were assigned to nine STs, including one unknown type, with six isolates belonging to ST2040.

3.3.2.2 Turkeys

An AmpC phenotype *E. coli* (showing decreased susceptibility to cefoxitin, cefotaxime and ceftazidime) was present in 1.1% of the turkey caecal samples and in 2.4% of the samples an ESBL phenotype *E. coli* (showing synergy with cefotaxime and clavulanate and/or ceftazidime and clavulanate) was detected. None of the isolates showed both an AmpC and ESBL phenotype

(Table 3.2). There was a reduction in the proportion of turkey caecal samples yielding AmpC or ESBL *E. coli* since 2016.

One caecal sample yielded *E. coli* which were resistant to cefotaxime, did not show synergy with clavulanate and had a ceftaxime MIC at the microbiological breakpoint.

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

Table 3.2: Phenotype in ESBL-/AmpC-producing *E. coli* cultured on selective agars, from caecal samples from healthy fattening turkeys at slaughter in the UK; 2016 (n=362) and 2018 (n=373)

Phenotype	Number of isolates		Proportion of isolates (%)		Proportion of caecal samples (%)	
	2016	2018	2016	2018	2016	2018
ESBL	12	9	70.6	69.2	3.3	2.4
AmpC	5	4	29.4	30.8	1.4	1.1
ESBL/AmpC	0	0	0	0	0	0
Carbapenemase	0	0	0	0	0	0

Of the 13 *E. coli* which had an AmpC or an ESBL phenotype, all were resistant to ampicillin, as expected. Four isolates which showed decreased susceptibility or resistance to ciprofloxacin had an ESBL phenotype; three of these showed decreased susceptibility to nalidixic acid.

WGS results showed that among 14 ESBL/AmpC producing *E. coli* from turkeys (one isolate had an AmpC genotype but not phenotype), 64.3% harboured CTX-M enzymes, the only ESBL gene type detected (see Table S3.2.5 of the supplementary material). *bla*_{CTX-M-1} was the most common allele (35.7%), followed by *bla*_{CTX-M-14} (21.4%) and *bla*_{CTX-M-15} (7.1%). As a proportion of the total caecal samples, 1.3% were positive for *bla*_{CTX-M-1} *E. coli*. No plasmid mediated transferrable AmpC enzymes were recovered, instead mutations in the *ampC* promoter region causing overexpression of the gene were present.

The five isolates harbouring an *ampC* mutation were assigned to two STs, with four isolates being ST1730. An isolate harbouring the CTX-M-15 gene was assigned to a novel ST, as was one of the three CTX-M-14 isolates; the other two isolates were assigned to ST93. The CTX-M-1 isolates were assigned to four unique STs, with ST10 isolates being recovered twice.

3.3.3 *Salmonella* spp.

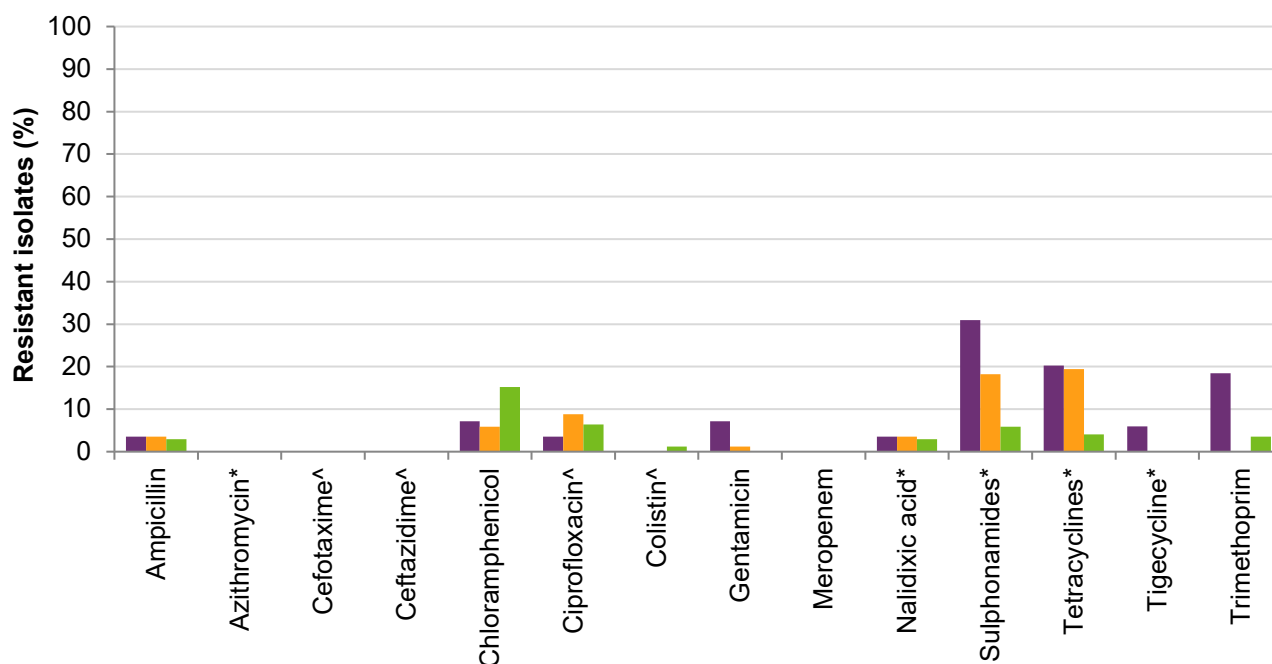
3.3.3.1 Broilers

3.3.3.1.1 Isolates from National Control Programme for *Salmonella*

Of the *Salmonella* isolates from broiler flocks 83.6% were susceptible (based on ECOFFs) to the full panel of antibiotics tested, an improvement from 2016 (67.6%).

No resistance was detected to the HP-CIAs cefotaxime or ceftazidime, but low resistance was detected to colistin (1.2%) and ciprofloxacin (6.4%) (Figure 3.3). The two isolates showing resistance to colistin were *S. Enteritidis*, a group D *Salmonella*, which may show a degree of intrinsic resistance to colistin.

Figure 3.3: Percentage resistance (interpreted using EUCAST CBPs) in *Salmonella* isolates from broiler flock NCP samples; 2014 (■; n=168), 2016 (■; n=170) and 2018 (■; n=171)



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

Resistance was not detected to gentamicin or meropenem. Moderate resistance was detected to chloramphenicol (15.2%), and low resistance to ampicillin (2.9%) and trimethoprim (3.5%). No decreased susceptibility (based on ECOFFs as no CBP value was available) was detected to azithromycin, but decreased susceptibility was detected to nalidixic acid (2.9%) and tetracyclines (4.1%). For most antibiotics, resistance levels were similar or lower compared to 2014 and 2016.

Resistance to ciprofloxacin was detected in 11 *Salmonella* isolates, nine of which were the incomplete serovar 13,23:i:-. Resistance to ciprofloxacin without decreased susceptibility to nalidixic acid was present in six isolates; this phenotype can indicate the presence of transferable fluoroquinolone resistance genes. The remaining five isolates showed resistance or decreased susceptibility to both ciprofloxacin and nalidixic acid, a phenotype typically seen with DNA gyrase mutations conferring quinolone/fluoroquinolone resistance.

Ampicillin resistance was detected in single isolates of *S. Derby*, *S. Kottbus* and 13,23:i:- and in two isolates of *S. Mbandaka*. Decreased susceptibility to sulphonamides was detected in 5.8% of isolates; five *Salmonella* isolates (three *S. Kedougou* and two *S. Ohio*) were also resistant to trimethoprim. Four per cent of isolates showed decreased susceptibility to tetracyclines including *S. Ohio* (n=5) and single isolates of *S. Derby* and *S. Kottbus*.

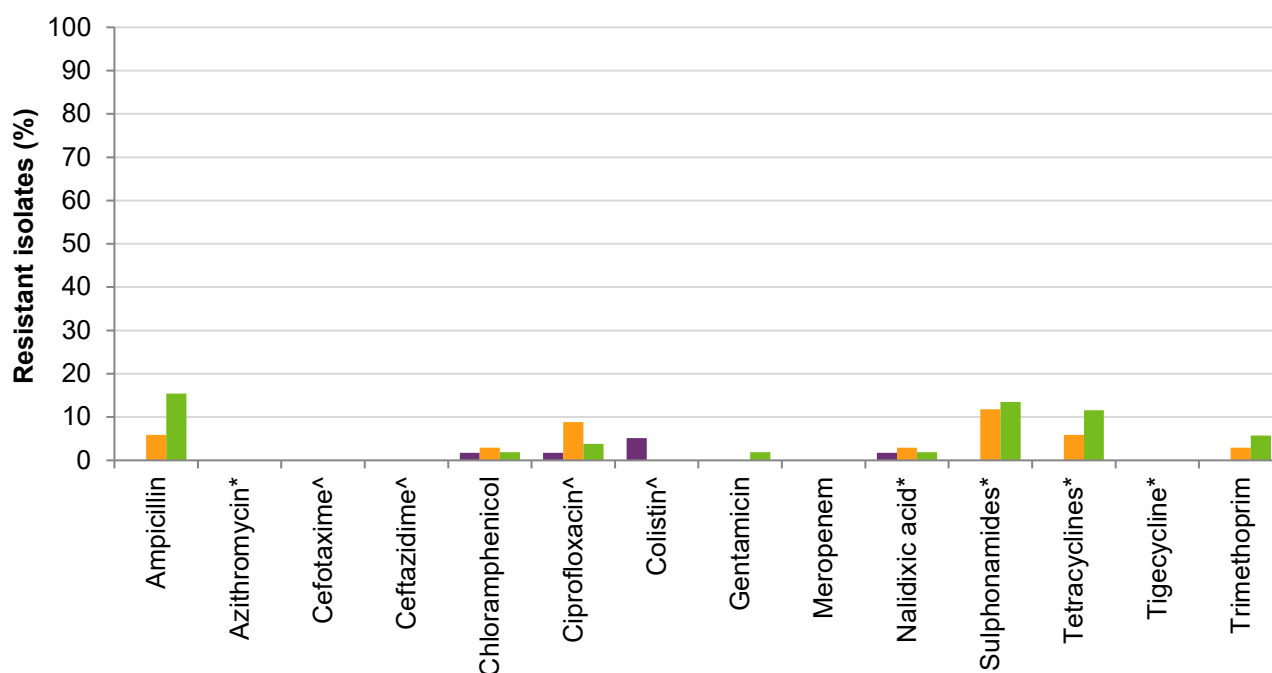
3.3.3.1.2 Isolates from FBO neck skin samples

In *Salmonella* isolates from FBO neck skin samples, no resistance was detected to the HP-CIAs cefotaxime, ceftazidime, ciprofloxacin or colistin (see Table S3.3.4 of the supplementary material). Four isolates showed resistance to chloramphenicol and one isolate resistance to trimethoprim. A single isolate of *S. Kedougou* showed decreased susceptibility (based on ECOFF) to trimethoprim and sulphonamides.

3.3.3.2 Laying hens

Susceptibility (based on ECOFFs) to all the antibiotics tested was shown by 80.8% of isolates, a slight decrease from the percentage seen in 2016 (85.3%). No resistance was detected to the HP-CIAs cefotaxime, ceftazidime and colistin (**Figure 3.4**).

Figure 3.4: Percentage resistance (interpreted using EUCAST CBPs) in *Salmonella* isolates from layer flock NCP samples; 2014 (■; n=58), 2016 (■; n=34) and 2018 (■; n=52)



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

Resistance to ciprofloxacin (3.8%) was detected in two isolates, both belonging to the incomplete serovar 13,23:i:-. Resistance to ciprofloxacin without decreased susceptibility to nalidixic acid was present in one of the isolates; this phenotype can indicate the presence of transferable fluoroquinolone resistance genes. The remaining isolate showed resistance or decreased susceptibility to both ciprofloxacin and nalidixic acid, a phenotype typically seen with DNA gyrase mutations conferring quinolone/fluoroquinolone resistance.

No resistance was detected to meropenem and no decreased susceptibility (based on ECOFFs as no CBP value was available) was detected to azithromycin or tigecycline. Moderate resistance was observed to ampicillin (15.4%) and low resistance to chloramphenicol (1.9%), gentamicin (1.9%) and trimethoprim (5.8%). A low level of decreased susceptibility was observed to nalidixic acid (1.9%) and a moderate level to tetracyclines (11.5%) and sulphonamides (13.5%). Resistance levels fluctuated across the three biennial surveys.

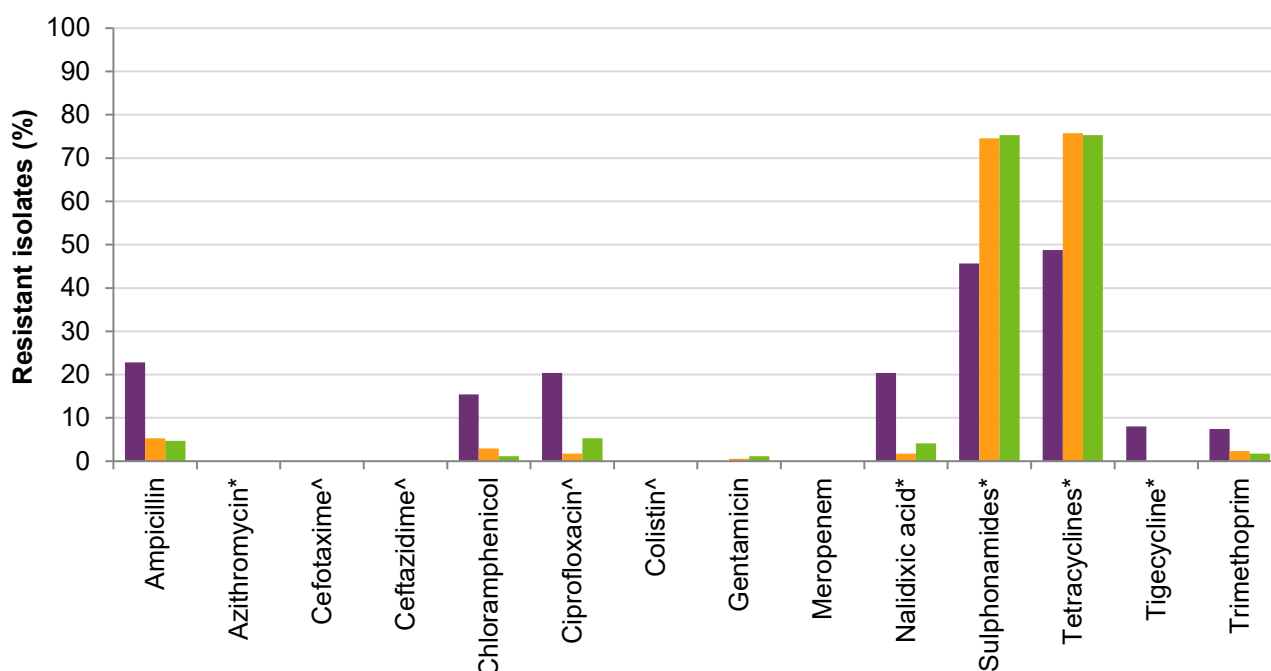
Four *S. Enteritidis* and three *S. Typhimurium* isolates were susceptible to all the antibiotics tested (based on ECOFFs). Four monophasic *S. Typhimurium* isolates showed decreased susceptibility to ampicillin, sulphonamides and tetracyclines (three of four isolates showed decreased susceptibility to tetracycline), with most isolates therefore showing the typical susceptibility pattern associated with monophasic *S. Typhimurium*. Two isolates of *S. Rissen* showed decreased susceptibility to ampicillin, sulphonamides, tetracyclines and trimethoprim.

3.3.3.3 Turkeys

3.3.3.3.1 Isolates from National Control Programme (NCP) for *Salmonella*

Susceptibility to the full panel of antibiotics tested was shown by 20.0% of the NCP *Salmonella* isolates (based on ECOFFs). Resistance was not detected to the HP-CIAs cefotaxime, ceftazidime or colistin, nor to meropenem (see **Figure 3.5**). Low resistance was observed to the HP-CIA ciprofloxacin (5.3%), ampicillin (4.7%), chloramphenicol (1.2%), gentamicin (1.2%) and trimethoprim (1.8%).

Figure 3.5: Percentage resistance (interpreted using EUCAST CBPs) in *Salmonella* isolates from turkey flock NCP samples; 2014 (■; n=162), 2016 (■; n=169) and 2018 (■; n=170)



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

A low level of decreased susceptibility (based on ECOFFs as no CBP value was available) was observed to nalidixic acid (4.1%), and a high proportion of isolates had decreased susceptibility to tetracyclines (75.3%) and/or sulphonamides (75.3%), which was similar to 2016 findings. Resistance levels fluctuated across the three biennial surveys, but for most antibiotics tested resistance was lower in 2016/2018 than 2014.

Five *S. Typhimurium* isolates showed decreased susceptibility to sulphonamides and tetracyclines, with two isolates also showing decreased susceptibility to both ciprofloxacin and ampicillin. The latter two isolates did not show decreased susceptibility to nalidixic acid, a phenotype suggestive of transferable fluoroquinolone resistance.

Resistance to ciprofloxacin was detected in 5.3% of *Salmonella* isolates, six of which were *S. Senftenberg*. All isolates except the two *S. Typhimurium* isolates referred to above showed decreased susceptibility to both ciprofloxacin and nalidixic acid, a phenotype typically seen with DNA gyrase mutations conferring quinolone/fluoroquinolone resistance.

Trimethoprim resistance was observed in three isolates, all *S. Derby* or presumptive *S. Derby*. A single isolate of *S. Derby* was resistant to gentamicin.

3.3.3.3.2 Isolates from FBO neck skin samples

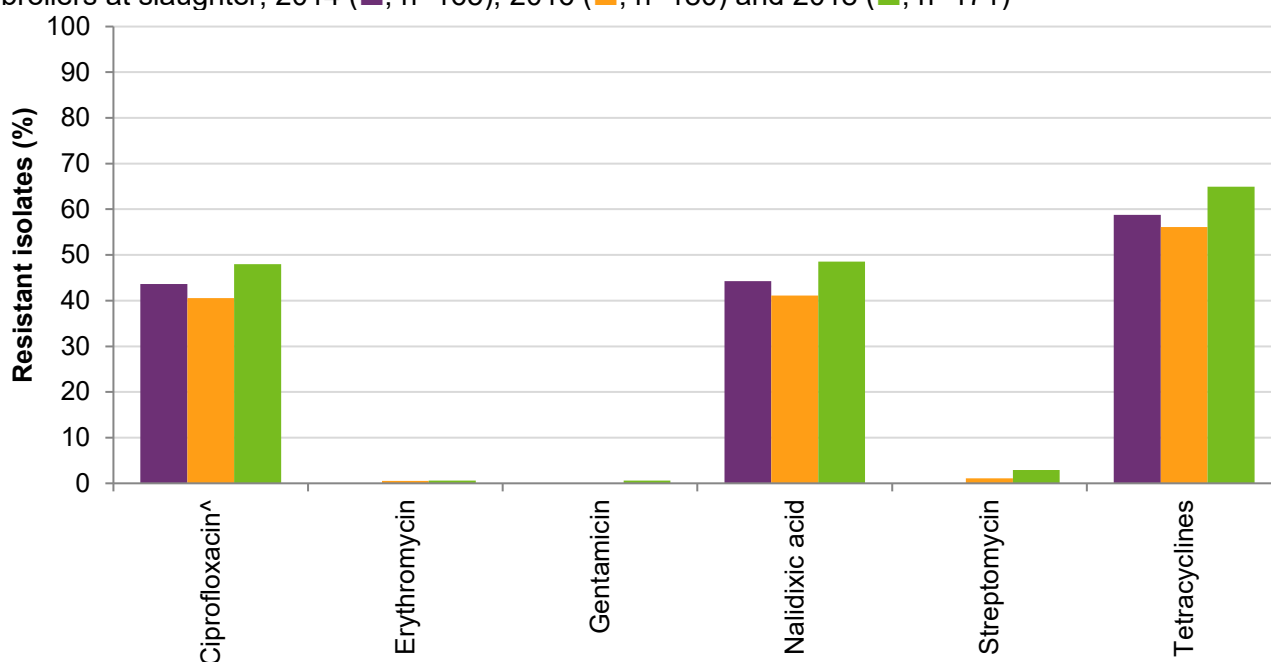
Three FBO turkey isolates were investigated. One *S. Derby* and one incomplete serovar (rough strain) with the antigenic formula O rough:f,g:- showed decreased susceptibility to sulphonamides and tetracyclines but were susceptible to the remaining antibiotics tested. The remaining isolate (*S. Derby*) was susceptible to all the antibiotics tested.

3.3.4 *Campylobacter jejuni*

3.3.4.1 Broilers

The proportion of isolates resistant to ciprofloxacin was 48.0%, an increase from 2016 (40.6%) (**Figure 3.6**). All isolates showing resistance to ciprofloxacin also showed resistance to nalidixic acid; a single isolate showed resistance to nalidixic acid but was susceptible to ciprofloxacin. Most isolates resistant to ciprofloxacin were also resistant to tetracyclines.

Figure 3.6: Percentage resistance (interpreted using EUCAST CBPs) in *C. jejuni* isolates from broilers at slaughter; 2014 (■; n=165), 2016 (■; n=180) and 2018 (■; n=171)



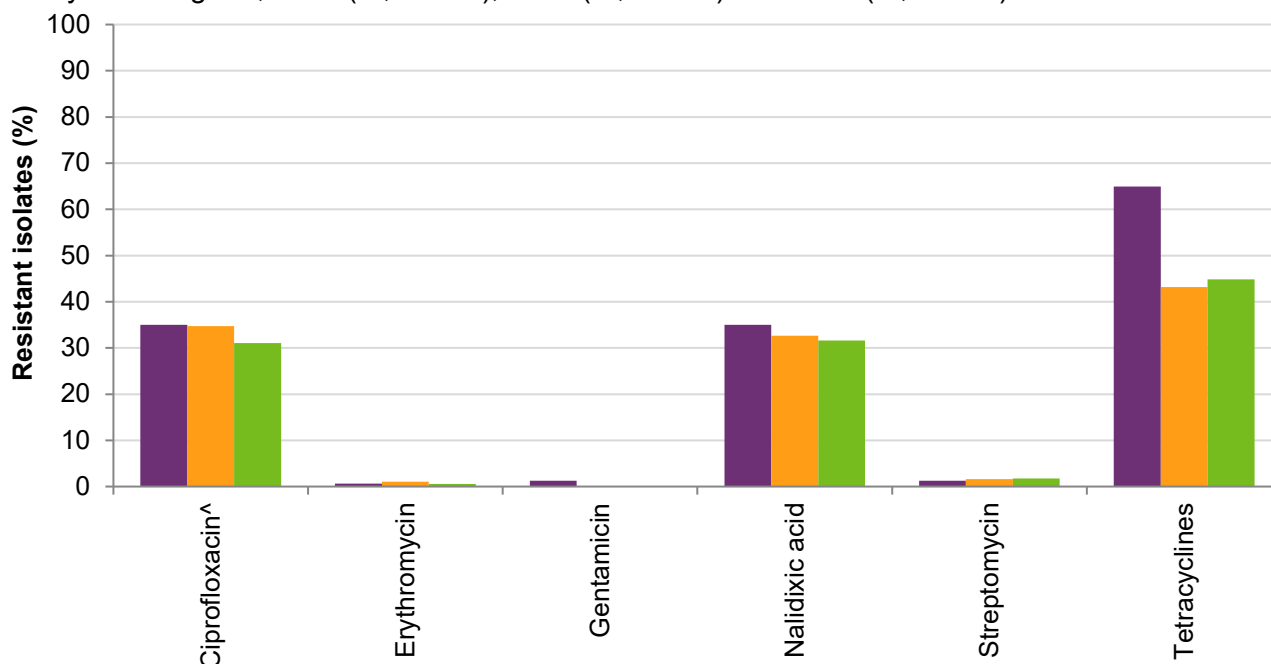
[^] HP-CIA

One isolate (0.6%) was resistant to erythromycin (low level resistance with MIC of 8 mg/l) and susceptible to ciprofloxacin. Resistance to gentamicin was detected in one isolate (0.6%) and resistance to streptomycin was low (2.9%). A high proportion of resistant isolates was detected to tetracycline (64.9%) and to nalidixic acid (48.5%). Overall, resistance has risen slightly over the last six years.

3.3.4.2 Turkeys

Resistance to ciprofloxacin was exhibited by 31.0% of isolates, a decrease from 2016 (34.7%) (**Figure 3.7**). Almost all (53/54) isolates resistant to ciprofloxacin also showed resistance to nalidixic acid; two isolates showed resistance to nalidixic acid but were susceptible to ciprofloxacin. Most (49/54) isolates which were resistant to ciprofloxacin were also resistant to tetracyclines.

Figure 3.7: Percentage resistance (interpreted using EUCAST CBPs) in *C. jejuni* isolates from turkeys at slaughter; 2014 (■; n=157), 2016 (■; n=190) and 2018 (■; n=174)



[^] HP-CIA

One isolate was resistant to erythromycin with a MIC of 128 mg/l; this isolate was susceptible to ciprofloxacin. All isolates were susceptible to gentamicin, 1.7% showed resistance to streptomycin. Tetracycline resistance was observed in 44.8% of isolates.

3.3.5 EU 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:

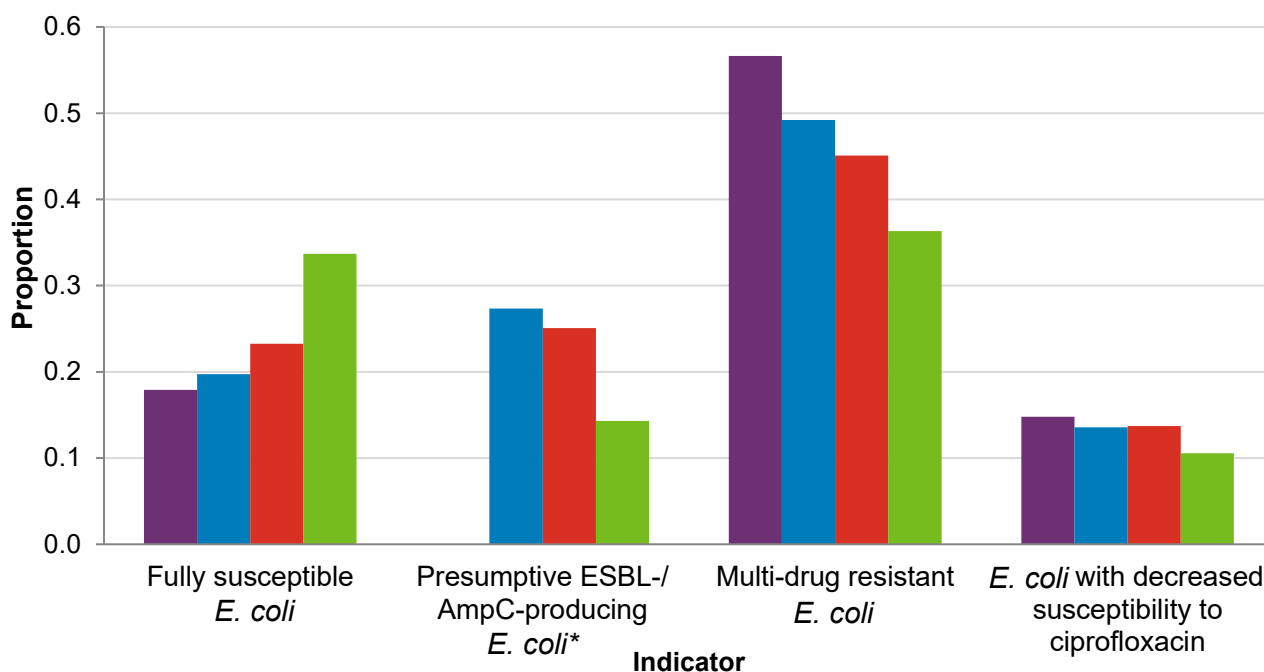
- Proportion of indicator *E. coli* isolates from the four animal species, weighted by PCU, showing decreased susceptibility to at least three antibiotics from different classes from the predefined panel of antibiotics (multi-drug resistant);
- Proportion of indicator *E. coli* isolates from the four 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 indicators show a four-year trend of decreasing resistance and increasing susceptibility (**Figure 3.8**). The proportion of fully susceptible *E. coli* (the primary indicator) has almost doubled (88% increase) and multi-drug resistant *E. coli* (a secondary indicator) decreased by a third (36% decrease).

The other secondary indicators also showed an increase in susceptibility levels. The proportion of samples identified as positive for presumptive ESBL-/AmpC-producing *E. coli* nearly halved (48% decrease) and the proportion of *E. coli* isolates that showed decreased susceptibility to ciprofloxacin decreased by more than a quarter (28% decrease).

Figure 3.8: Harmonised AMR outcome indicators; 2014/15 (■), 2015/16 (■), 2016/17 (■) and 2017/18 (■)



* 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 carcasses or other diagnostic samples submitted by private veterinary surgeons to APHA veterinary laboratories in England and Wales. When a potential bacterial pathogen is identified, antibiotic susceptibility testing is performed to provide the practitioner with 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 1989¹. 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.

¹ <http://www.legislation.gov.uk/ukxi/1989/285/made>

4.1 Summary

The resistance levels observed in many veterinary bacteria showed limited change over the monitoring period covered by this report (2016–2018).

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*, *B. trehalosi*, *H. somni*, *A. pleuropneumoniae*) in 2018 were susceptible to enrofloxacin and florfenicol. The proportion of swine dysentery isolates showing resistance to tiamulin is low and although penicillin resistance was detected in a single *S. suis* from pigs, penicillin resistance in bovine mastitis streptococci (*S. dysgalactiae* and *S. uberis*) was not detected. A large increase in resistance to tetracyclines was however observed in *M. haemolytica* from both cattle and sheep in 2017 and 2018, compared to 2016.

For 3rd generation cephalosporins and fluoroquinolones (HP-CIAs), cefotaxime resistance in diagnostic *E. coli* isolates from neonatal calves and lambs in 2018 was 11% and 2% respectively, whilst cefpodoxime resistance in *E. coli* in the same year was 3% in neonatal piglets and 4% in chickens. Although some fluctuation has occurred, these figures have remained relatively unchanged over the period 2016–2018. Enrofloxacin resistance in diagnostic *E. coli* isolates from neonatal calves, lambs and piglets in 2018 was 4%, 1% and 8% respectively, representing declines on preceding years, whilst enrofloxacin was 3% in chickens. Colistin resistance was detected in one *E. coli* isolate (0.5%) from pigs in 2018; but not any other *E. coli*.

There was a marked decline in 2016 in resistance to several antibiotics in diagnostic *E. coli* isolates from chickens, coinciding with a reduction in antibiotic use in broilers. Levels of resistance observed in 2017 and 2018 were generally similar to those recorded in 2016, although an exception to this general trend was resistance to doxycycline, which has increased.

Livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) ST398 was not recovered from food-producing animals in Scotland or Wales but was isolated from a turkey sample in England and from four pig samples in Northern Ireland in 2018.

The proportion of fully sensitive *S. Typhimurium* increased by 20% to 54.4%.

Resistance to 3rd generation cephalosporins and to fluoroquinolones (HP-CIAs) was very low in *Salmonella* spp. Resistance to ciprofloxacin was 0.1%, one single isolate (an *S. Mbandaka* from a broiler chicken) was resistant to ceftazidime and cefotaxime.

Highly ciprofloxacin resistant *S. Kentucky* and multi-drug resistant *S. Infantis* were detected in a by-product of unknown origin and a dog, respectively. These resistant strains are epidemic in parts of Europe but are only sporadically detected in England and Wales. They have previously been associated with contaminated raw pet food for pets.

4.2 Methods

4.2.1 Sample sources

Bacterial isolates were 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 and for all of the bacterial organism/antibiotic combinations which may require testing. In these cases, a uniform cut-off point of 13 mm zone size diameter has been used to discriminate between sensitive and resistant 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, 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.

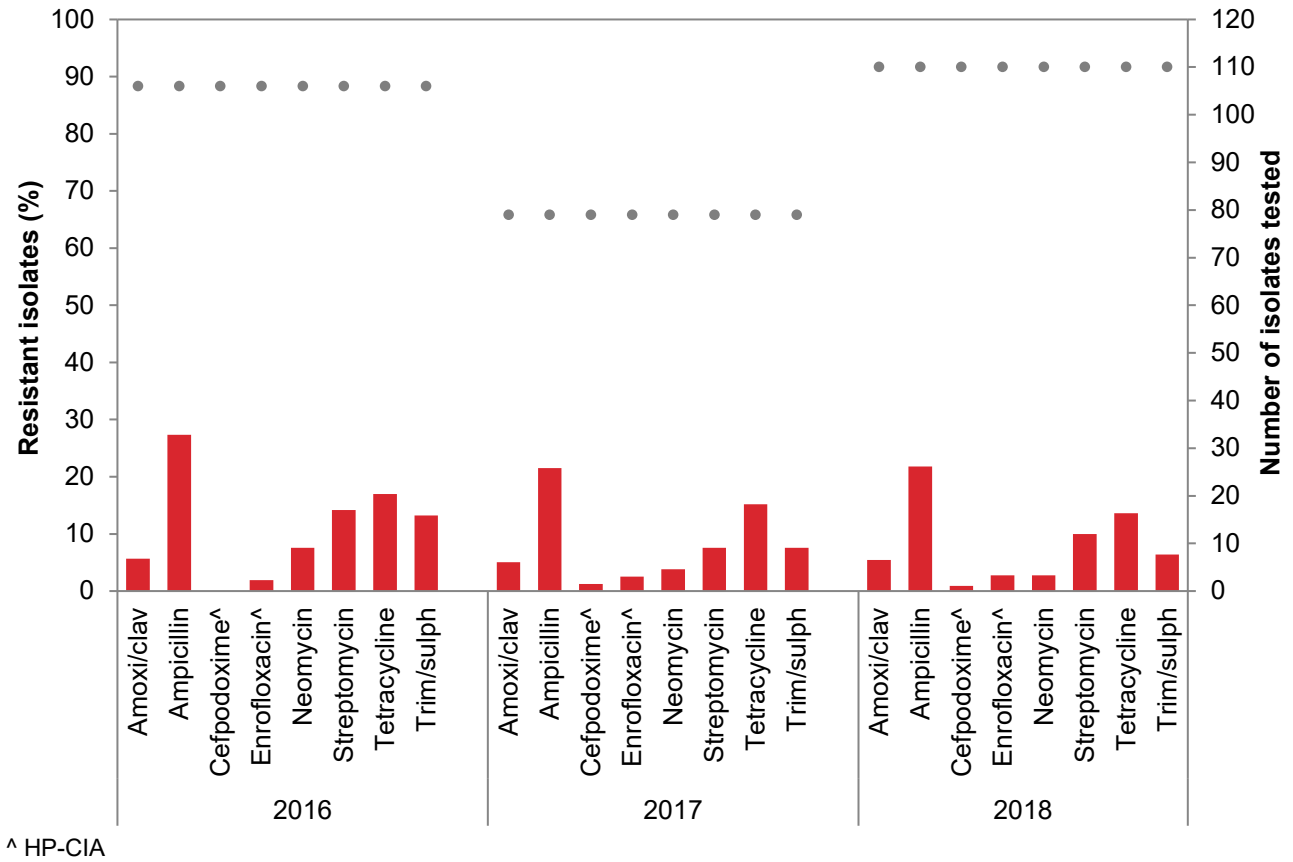
4.3.1.1 *Escherichia coli*

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. These isolates therefore represent those strains that are present in the environment of adult dairy cattle, particularly cattle sheds and cubicle houses, and are probably mainly of faecal origin.

The total number and percentage of *E. coli* isolates from mastitis infections resistant to different antibiotics are presented in **Figure 4.1** (and Table S4.2.1 of the supplementary material). Resistance in *E. coli* from bovine mastitis showed only limited annual fluctuations for most antibiotics, including to enrofloxacin (between 2–3% in 2016–2018). It is noteworthy that the percentage of isolates resistant to cefpodoxime in mastitis *E. coli* and coliform isolates (0.9%) was lower than the percentage resistance to ceftazidime or cefotaxime observed in *E. coli* and coliform isolates from calves (3.3–11.3%) (**Figure 4.9** and Table S4.7.9 of the supplementary material).

As in previous reporting years, the highest level of resistance was observed to ampicillin (21.8%) followed by tetracycline (13.6%), streptomycin (10.0%) and trimethoprim/sulphonamide (6.4%).

Figure 4.1: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from mastitis infections of cattle in England and Wales; 2016–2018

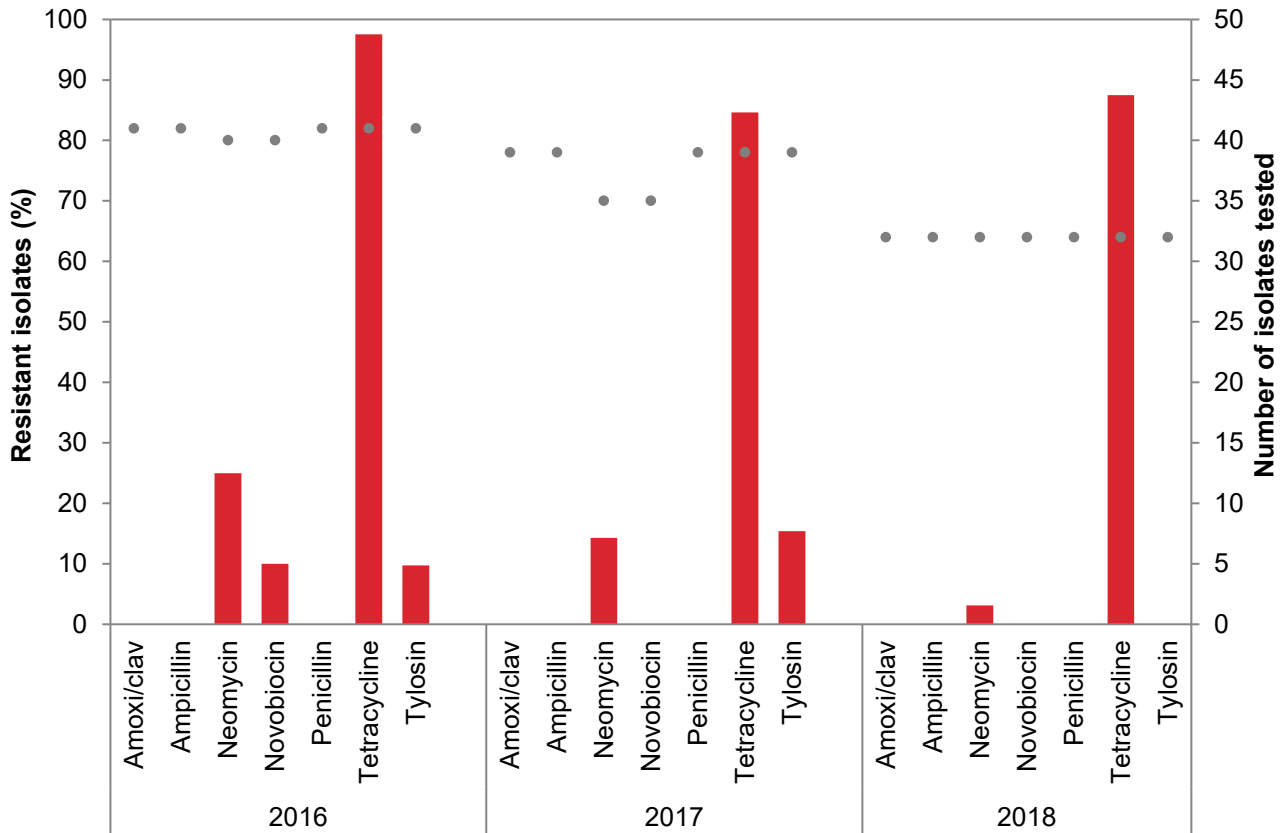


4.3.1.2 *Streptococcus dysgalactiae*

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).

Resistance to tetracycline is common, but resistance to other antibiotics is lower or absent (Figure 4.2 and Table S4.2.3 of the supplementary material). No resistance was detected to amoxicillin/clavulanate, ampicillin or penicillin over the period 2016–2018. In 2016–2017, 9.8–15.4% of isolates were resistant to the macrolide tylosin; no resistance was detected in 2018. These results have not been confirmed by determination of the MIC, but macrolide resistance has been reported in *S. dysgalactiae* isolates from bovine mastitis from other parts of the world. Resistance to neomycin is to be expected in *S. dysgalactiae* because streptococci show a degree of intrinsic resistance to aminoglycosides, but has shown a decline over the period 2016–2018.

Figure 4.2: Number of isolates tested (●) and percentage (■) of resistant isolates of *Streptococcus dysgalactiae* from mastitis infections of cattle; 2016–2018



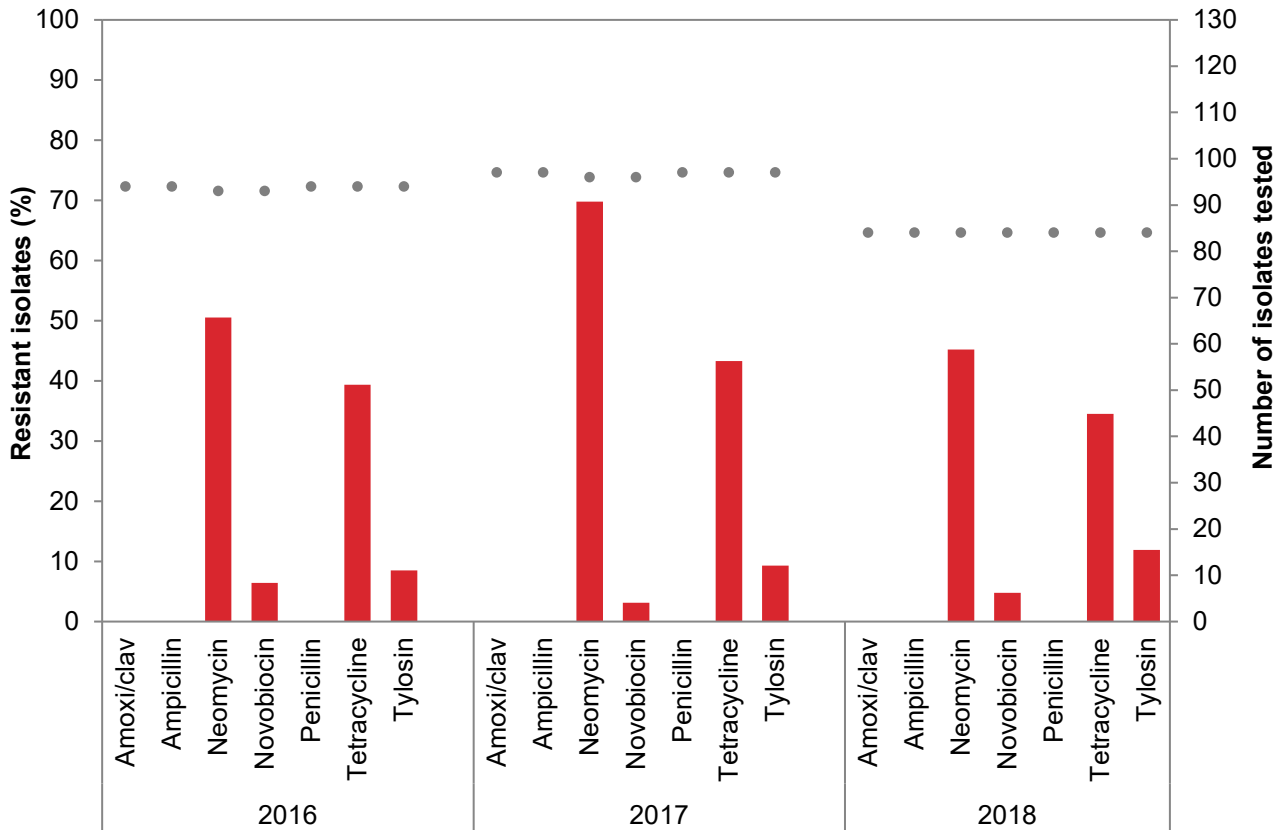
4.3.1.3 *Streptococcus uberis*

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, penicillin or amoxicillin/clavulanate was detected in *S. uberis* over the period 2016–2018 (Table S4.2.3 of the supplementary material). *S. uberis* isolates from bovine mastitis with reduced susceptibility to penicillin have been reported in France (Haenni et al., 2010) and a single isolate of *S. uberis* was previously reported in 2013 from England and Wales with penicillin/ampicillin resistance.

Between 2016 and 2018, 8.5–11.9% of *S. uberis* isolates were resistant to tylosin. Resistance can be mediated by the induction of a plasmid-encoded enzyme which methylates the 20S ribosomal RNA sub-unit and prevents binding of the macrolide to the ribosome and so disrupts protein synthesis. However, the exact mechanism of resistance has not been determined for the isolates recorded here. Resistance to tetracyclines was also detected in *S. uberis* isolates in 2016–2018, ranging from 34.5% to 43.3%.

Figure 4.3: Number of isolates tested (●) and percentage (■) of resistant isolates of *Streptococcus uberis* from mastitis infections of cattle; 2016–2018



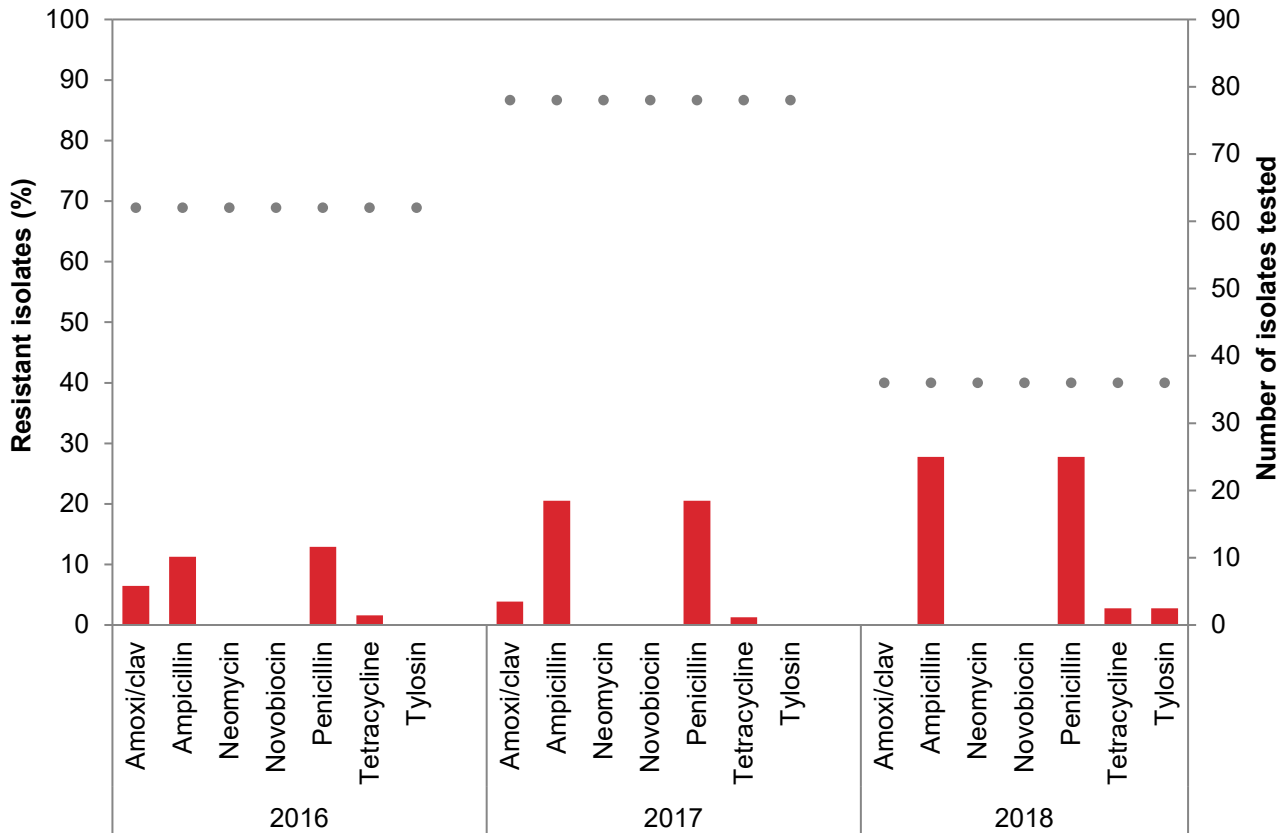
4.3.1.4 *Staphylococcus aureus*

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 was mostly low or absent (**Figure 4.4**). Resistance to penicillin fluctuated between 12.9% and 27.8% over the monitoring period and the underlying cause of this variation is not known. Penicillin resistance in bovine *S. aureus* is thought to occur mainly via the production of beta-lactamases that degrade both penicillin and ampicillin. The genes encoding beta-lactamases can be located on plasmids and often on transposons and may be readily transferable by conjugation.

Those resistant to amoxicillin/clavulanate are currently screened for susceptibility to ceftiofur in order to detect *mecA* and *mecC* MRSA. No MRSA isolates were detected during 2016–2018. Amoxicillin/clavulanate resistance decreased from 6.5% to 0% over this period. Resistance to neomycin and novobiocin was not detected. Tylosin (macrolide) resistance was detected infrequently (0–2.8%). Resistance to tetracycline has remained below 3% (Table S4.2.3 of the supplementary material).

Figure 4.4: Number of isolates tested (●) and percentage (■) of resistant isolates of *Staphylococcus aureus* from mastitis infections in cattle; 2016–2018



4.3.1.5 Other mastitis pathogens

Klebsiella pneumoniae isolates, the majority of which originate from bovine mastitis cases, are frequently resistant to ampicillin. In 2018 there were 11 mastitis isolates, all of which were resistant to ampicillin, reflecting the known intrinsic resistance; most isolates were susceptible to all other antibiotics tested (e.g. cefpodoxime, enrofloxacin, amoxicillin/clavulanic acid).

Pseudomonas aeruginosa are commonly resistant to a range of antibiotics. In total, five isolates were recovered which were all only susceptible to ceftazidime, enrofloxacin and streptomycin, and two of four isolates tested were susceptible to neomycin.

Streptococcus agalactiae was not recovered from bovine mastitis over the period 2016–2018.

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

4.3.2 Respiratory pathogens

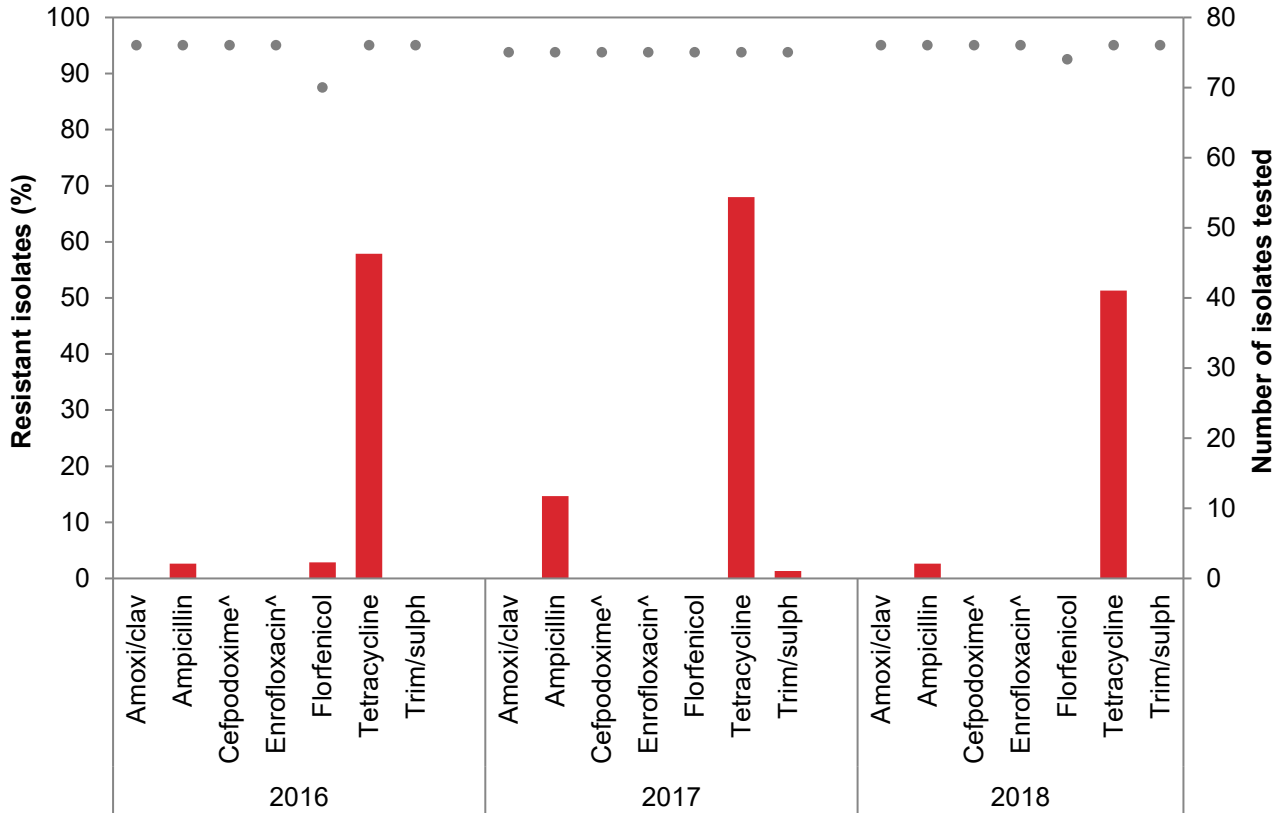
4.3.2.1 *Pasteurella multocida*

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.

No resistance to enrofloxacin or cefpodoxime was detected in isolates from pig, cattle or sheep in 2016–2018. Resistance to trimethoprim/sulphonamides or florfenicol was found in low numbers of

bovine isolates over the period 2016–2018, while resistance to ampicillin or tetracyclines was detected in larger numbers of isolates (**Figure 4.5** and Table S4.3.1 of the supplementary material). A low number of isolates of *P. multocida* was examined from sheep and resistance was observed to ampicillin and tetracyclines (Table S4.5.1 of the supplementary material).

Figure 4.5: Number of isolates tested (●) and percentage (■) of resistant isolates of *Pasteurella multocida* isolates from respiratory infections of cattle; 2016–2018



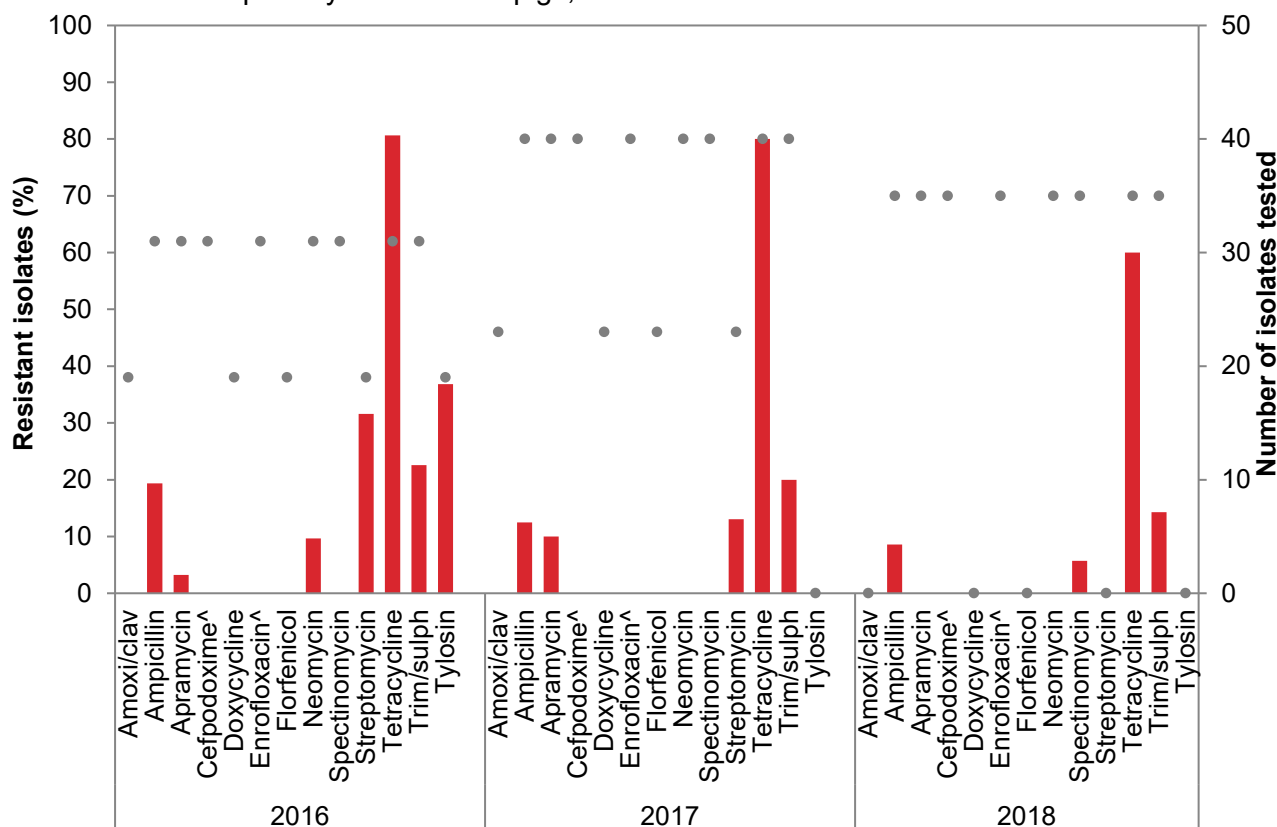
[^] HP-CIA

There was tetracycline, ampicillin or trimethoprim/sulphonamide resistance in *P. multocida* from pigs, with tetracycline resistance most prevalent, although tetracycline resistant isolates, where tested, were susceptible to doxycycline (**Figure 4.6** and Table S4.4.1 of the supplementary material). This may reflect the resistance mechanism involved as some genes confer resistance to tetracyclines but not to doxycycline.

4.3.2.2 *Histophilus somni*

H. somni (formerly known as *Haemophilus somnus*) is a cause of pneumonia in calves. All isolates tested in 2016–2018 were susceptible to the panel of antibiotics listed in Table S4.3.1. of the supplementary material; with the exception of a single isolate in 2017 which was resistant to tetracyclines.

Figure 4.6: Number of isolates tested (●) and percentage (■) of resistant isolates of *Pasteurella multocida* from respiratory infections of pigs; 2016–2018



[^] HP-CIA

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.

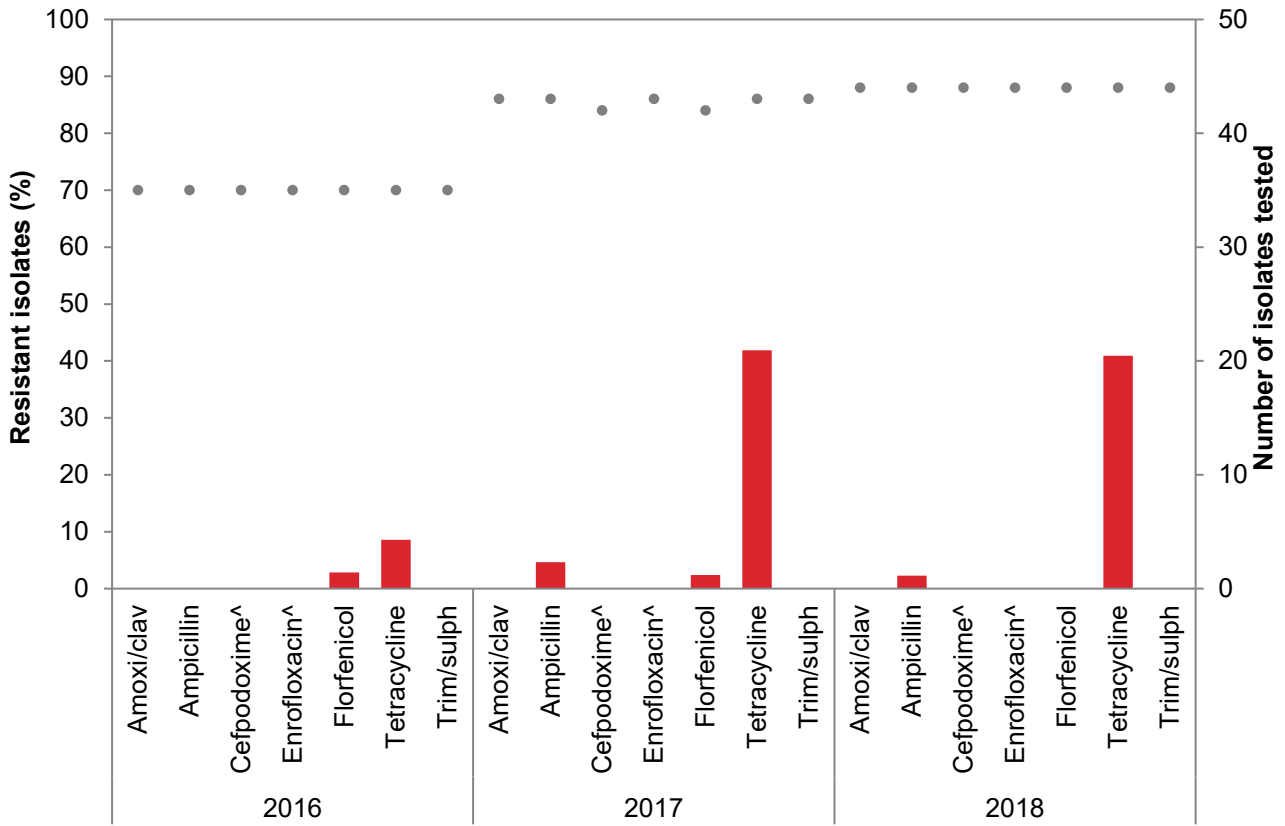
No resistance was detected to cefpodoxime or enrofloxacin in isolates from cattle in 2018 (Figure 4.7 and Table S4.3.1 of the supplementary material). Low resistance to ampicillin (2.3%) was detected in these isolates. Bovine isolates showed high resistance to tetracyclines during 2016–2018 (between 44.2–50.0%).

No resistance was detected in the ovine isolates from 2016–2018 to cefpodoxime or enrofloxacin. Ovine isolates showed a decrease in resistance to tetracyclines during this time period (from 57.1% in 2016 to 46.9% in 2018); low numbers of isolates were resistant to either florfenicol or ampicillin during 2016–2018 (Table S4.5.1 of the supplementary material).

4.3.2.4 Other respiratory pathogens

Although *Bibersteinia (Pasteurella) trehalosi* isolates from sheep were generally susceptible, resistance was detected to tetracycline or florfenicol in single isolates recovered 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; 2016–2018



^ HP-CIA

Data on the less frequently isolated ovine respiratory pathogen *Trueperella (Arcanobacterium) pyogenes* can be found in Table S4.5.1 of the supplementary material. Resistance to tetracyclines and trimethoprim/sulphonamide was detected in isolates of *T. pyogenes* from cattle, sheep and pigs; low numbers of isolates from cattle, sheep and pigs were resistant to macrolides.

Actinobacillus pleuropneumoniae is a cause of pneumonia in pigs. Over the period 2016–2018, resistance was not detected to florfenicol or enrofloxacin. Resistance was detected to ampicillin, apramycin, neomycin, spectinomycin and/or trimethoprim/sulphonamide in isolates recovered in 2018. In 2016/2017, resistance was also detected to doxycycline, streptomycin, tetracycline and/or tylosin (Table S4.4.1 of the supplementary material). Levels of resistance to apramycin, spectinomycin and other aminoglycosides detected in the disc diffusion test may reflect the rather high MICs that have been described for *A. pleuropneumoniae* for some aminoglycoside compounds (Leman et al., 1986).

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

4.3.3 Other animal pathogens

Brachyspira hyodysenteriae is a 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.

The tiamulin MIC for selected *B. hyodysenteriae* isolates tested by broth microdilution over the period 2010–2018 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. A single isolate of 13 tested had a tiamulin MIC of 4 mg/l in 2018; all other isolates had MICs below 1 mg/ml.

Staphylococcus aureus causes a number of infections in poultry and game birds, including septicaemia, yolk sac infection, arthritis and osteomyelitis. Resistance to most of the antibiotics tested was detected in isolates of *S. aureus* from chickens, turkeys or other avian species in 2016 and/or 2017, though resistance to trimethoprim/sulphonamides or lincomycin was not observed (Table S4.6.4 of the supplementary material). In 2018, two isolates were recovered from chickens and both were susceptible to all the antibiotics tested.

Streptococcus dysgalactiae is the major cause of infectious arthritis in young lambs and is probably carried on the mucous membranes of a small proportion of sheep. Low numbers of isolates were resistant to cefalexin in 2017/2018 (Table S4.6.5 of the supplementary material). Levels of resistance to tetracyclines in ovine isolates of *S. dysgalactiae* were high and similar to those recorded for bovine isolates, but there was no resistance to ampicillin.

Staphylococcus 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 antibiotics tested, 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 methicillin resistance can occur relatively frequently in some species of coagulase-negative staphylococci.

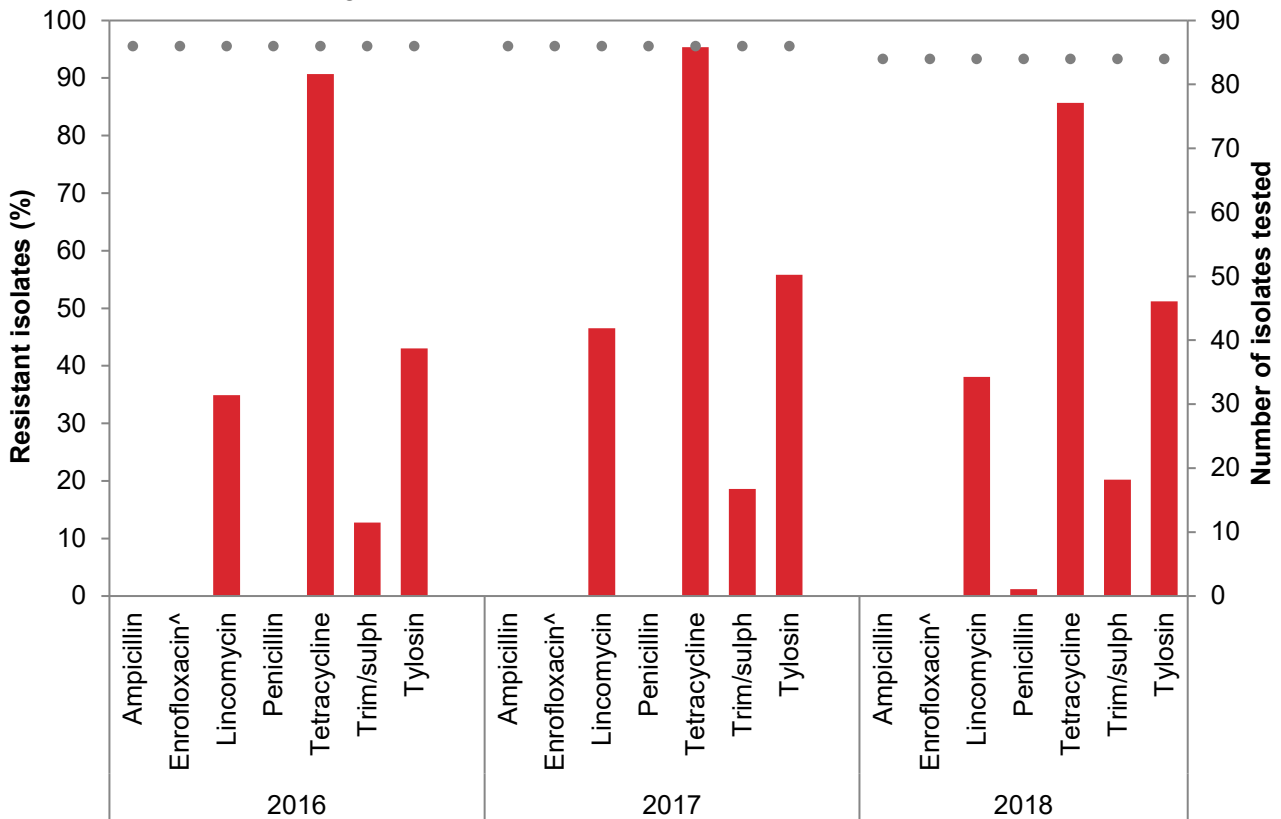
4.3.4 Zoonotic pathogens

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 and ampicillin are often recommended for treatment of *S. suis* in pigs. No resistance to these antibiotics was detected in 2016–2018, with the exception of a single isolate (type 5) from 2018 which was resistant to penicillin (**Figure 4.8** and Table S4.6.2 of the supplementary material). The isolate was recovered from the stomach contents of an aborted piglet from one of a group of 50 sows which had aborted. The penicillin MIC of 0.75 mg/l was determined by e-test, confirming resistance.

Isolates resistant to tetracyclines, trimethoprim/sulphonamide, tylosin or lincomycin were all detected. The resistance to tetracycline, which is not commonly used for the treatment of this disease in pigs, could be due to exposure in asymptomatic pigs following oral administration of tetracycline for the treatment of a different condition. Further details are presented in Table S4.6.2 of the supplementary material.

Figure 4.8: Number of isolates tested (●) and percentage (■) of resistant isolates of *Streptococcus suis* from pigs; 2016–2018



[^] 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 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 **Table 4.1**. These reports should not be interpreted as a prediction of prevalence in the animal population, as samples have been collected through differing methods of passive surveillance in animals which are affected with clinical disease. Results may therefore not be representative of the wider, healthy population.

LA-MRSA was not recovered in 2018 from food-producing animals in Scotland or Wales, but it was detected in a turkey sample from England and in four pig samples from Northern Ireland, all submitted for clinical diagnosis.

Table 4.1: Findings of LA-MRSA in the UK by government laboratories; 2013–2018

Country	Clonal complex	Year	Species	Source of the sample
England and Wales	CC398	2013	Poultry	Clinical investigation
	CC398	2014	Pig	Clinical investigation
	CC398	2015	Pig	Research project
	CC398	2016	Turkey	Clinical investigation
	CC398	2016	Beef cattle	Clinical investigation
	CC398	2016	Pig	Other investigation
	CC398	2017	Pig	Clinical investigation
	CC398	2018	Turkey	Clinical investigation
Northern Ireland	CC398	2014	Pig	Clinical investigation
	CC30	2015	Pig	Clinical investigation
	CC398	2015	Dairy cattle	Clinical investigation
	CC398	2015	Pig (n=2)	Clinical investigation
	CC398	2016	Pig (n=2)	Clinical investigation
	CC398	2017	Pig (n=3)	Clinical investigation
	CC398	2018	Pig (n=4)	Clinical investigation
Scotland	CC398	2017	Pheasant	Clinical investigation

4.3.4.3 Other zoonotic pathogens

Corynebacterium pseudotuberculosis, the cause of caseous lymphadenitis in sheep, has been reported as an uncommon zoonosis. However, corynebacteria may be an emerging cause of zoonoses, particularly in people with intercurrent immunosuppressive disease, such as HIV infection. Resistance was not detected in 2017, although only low numbers of isolates were available for susceptibility testing and no isolates were obtained in 2018. 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 is widely distributed in nature and occurs as a commensal or pathogen of a very wide range of vertebrates and invertebrates. 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 has been isolated (from pigs, sheep and chickens) and the main resistance detected has been to tetracycline and trimethoprim/sulphonamide. All isolates were susceptible to penicillin/ampicillin (see Table S4.6.3 of the supplementary material for information on resistance in *E. rhusiopathiae* isolated from pigs), which is the usual treatment for human infection.

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 bovine isolates were isolated (data not shown). Cefalexin-resistance was observed in both bovine and ovine isolates, reflecting the intrinsic resistance of *Listeria* spp. to this antibiotic. Isolates were otherwise sensitive, apart from low numbers of isolates from sheep in 2016 which were resistant to tetracycline (Table S4.6.5 for details on *L. monocytogenes* recovered from sheep infections). *Listeria ivanovii* were recovered from sheep in 2016 and 2017 and were susceptible to the panel of antibiotics reported (data not shown), but no *L. ivanovii* were recovered from sheep in 2018.

Six isolates of *Klebsiella pneumoniae* were recovered from avian species in 2018, all were resistant to ampicillin, reflecting the known intrinsic resistance to ampicillin (data not shown).

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). The majority of isolates reported in this section were recovered from faeces or intestinal contents.

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–S4.7.15 of the supplementary material.

Collated data for the major food-producing animal species tested are shown in **Table 4.2**. In general, the level of resistance to HP-CIAs in *E. coli* isolates was low to moderate during 2016–2018 (2.1–13.2%).

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 4.2: Number of resistant and number of tested (% resistant) *Escherichia coli* isolates from cattle, pigs, sheep, broilers and turkeys (all ages, combined); 2016–2018

Antibiotic	Number of resistant/tested isolates (% resistant)		
	2016	2017	2018
Amikacin	4/467 (0.9%)	0/266 (0.0%)	1/280 (0.4%)
Amoxicillin/clavulanate	221/1123 (19.7%)	149/694 (21.5%)	137/484 (28.3%)
Ampicillin	683/1200 (56.9%)	420/810 (51.9%)	450/788 (57.1%)
Apramycin	68/1135 (6.0%)	39/756 (5.2%)	49/737 (6.6%)
Cefotaxime [^]	62/469 (13.2%)	32/267 (12.0%)	27/282 (9.6%)
Cefpodoxime [^]	7/314 (2.2%)	8/377 (2.1%)	10/316 (3.2%)
Ceftazidime [^]	41/469 (8.7%)	18/267 (6.7%)	12/282 (4.3%)
Chloramphenicol	200/467 (42.8%)	104/266 (39.1%)	108/280 (38.6%)
Doxycycline	165/538 (30.7%)	151/323 (46.7%)	25/79 (31.6%)
Enrofloxacin [^]	78/1200 (6.5%)	48/810 (5.9%)	32/788 (4.1%)
Florfenicol	164/792 (20.7%)	88/479 (18.4%)	86/329 (26.1%)
Neomycin	249/1100 (22.6%)	134/695 (19.3%)	114/679 (16.8%)
Spectinomycin	423/1135 (37.3%)	233/756 (30.8%)	267/737 (36.2%)
Streptomycin	394/743 (53.0%)	198/429 (46.2%)	149/282 (52.8%)
Tetracycline	727/1200 (60.6%)	463/810 (57.2%)	447/788 (56.7%)
Trimethoprim/sulphonamide	461/1200 (38.4%)	271/810 (33.5%)	293/788 (37.2%)

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.

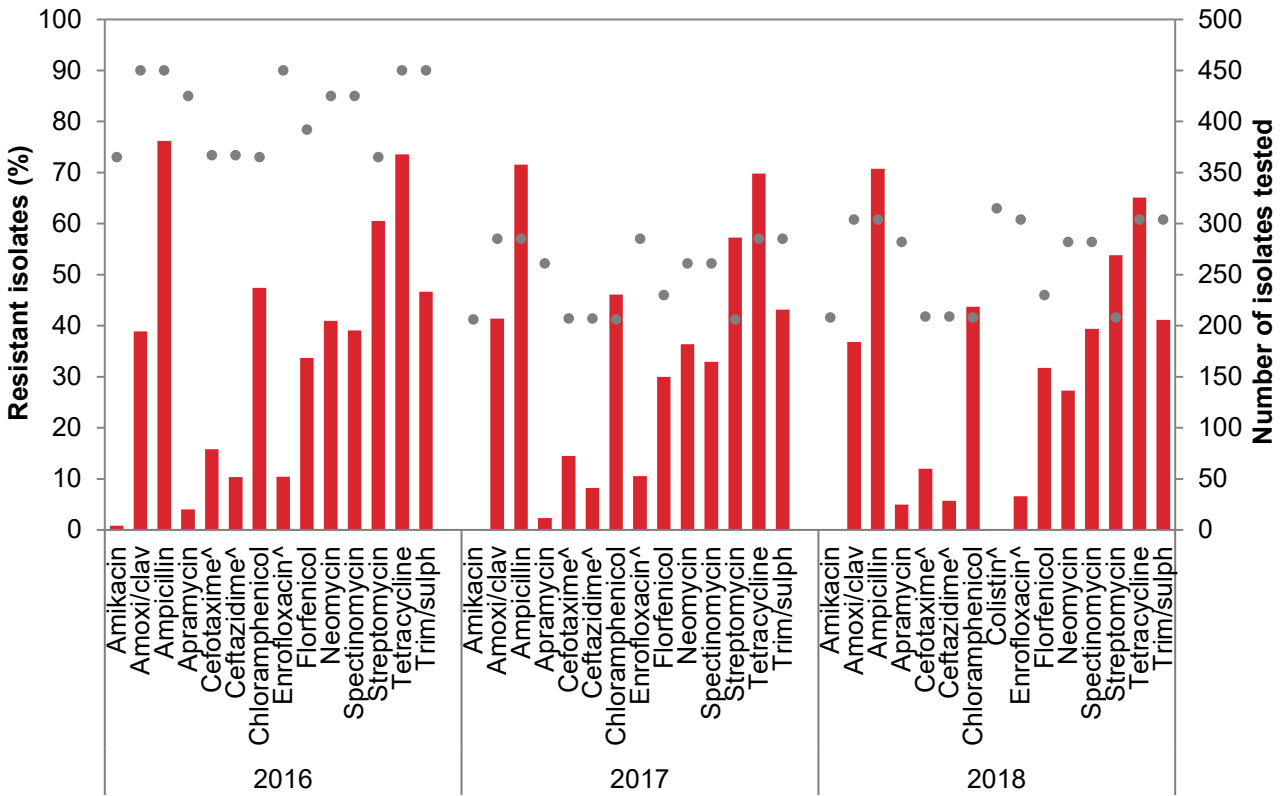
[^] HP-CIA

4.3.5.1 Cattle

The total number and proportion of resistant *E. coli* isolates (all age groups) are shown in **Figure 4.9**. Resistance to 3rd generation cephalosporins (cefotaxime, ceftazidime or cefpodoxime) detected in *E. coli*/coliforms in animals will include resistance mediated by both ESBL- and AmpC-resistance mechanisms. The higher prevalence of resistance to cefotaxime versus ceftazidime observed, for example, in neonatal calves (**Figure 4.10**), is likely to reflect the occurrence of those ESBL enzymes which are cefotaximases, rather than ceftazidimases. In *E. coli* from neonatal calves there was a decline in resistance to 3rd generation cephalosporins, enrofloxacin and neomycin between 2016–2018.

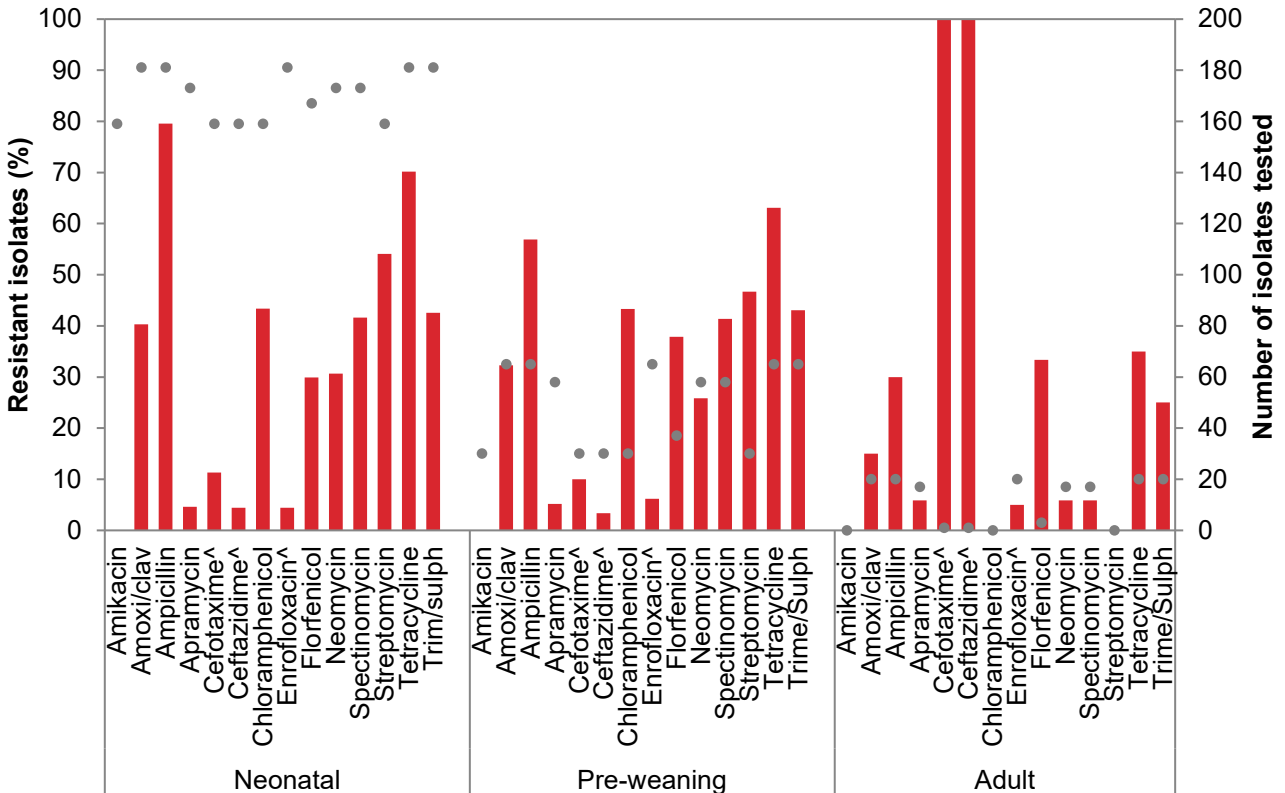
Resistance to enrofloxacin was lower (6.6%) in 2018 than in 2016/2017 (10–11%) and found across all ages. The relatively high frequency at which *E. coli*/coliform isolates resistant to ampicillin are recovered from young calves may reflect the use of dry cow intramammary infusions containing aminopenicillins 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 78–80% over the period 2016–2018 in neonatal calves, it declined from 85.5% to 56.9% in older, pre-weaning calves.

Figure 4.9: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from cattle (all ages); 2016–2018



^ HP-CIA

Figure 4.10: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from cattle (by age category); 2018

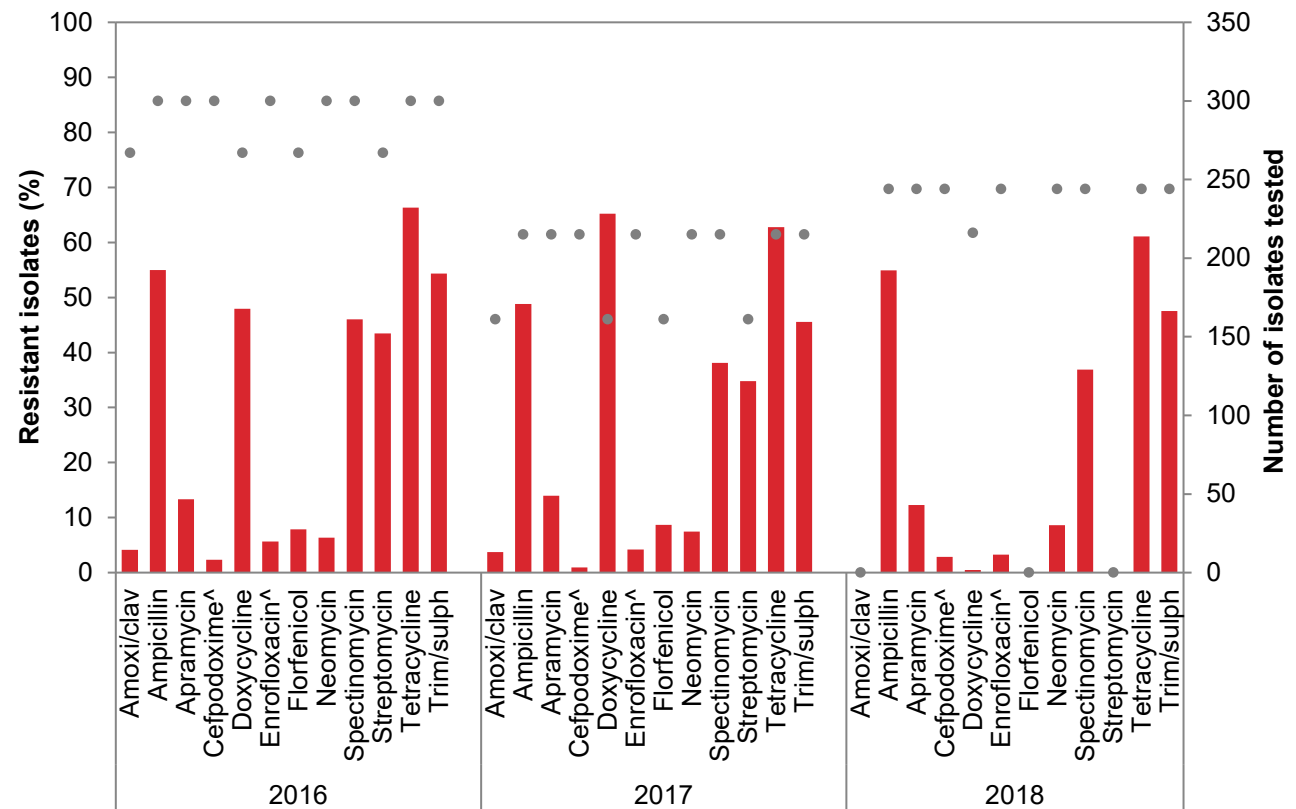


^ HP-CIA

4.3.5.2 Pigs

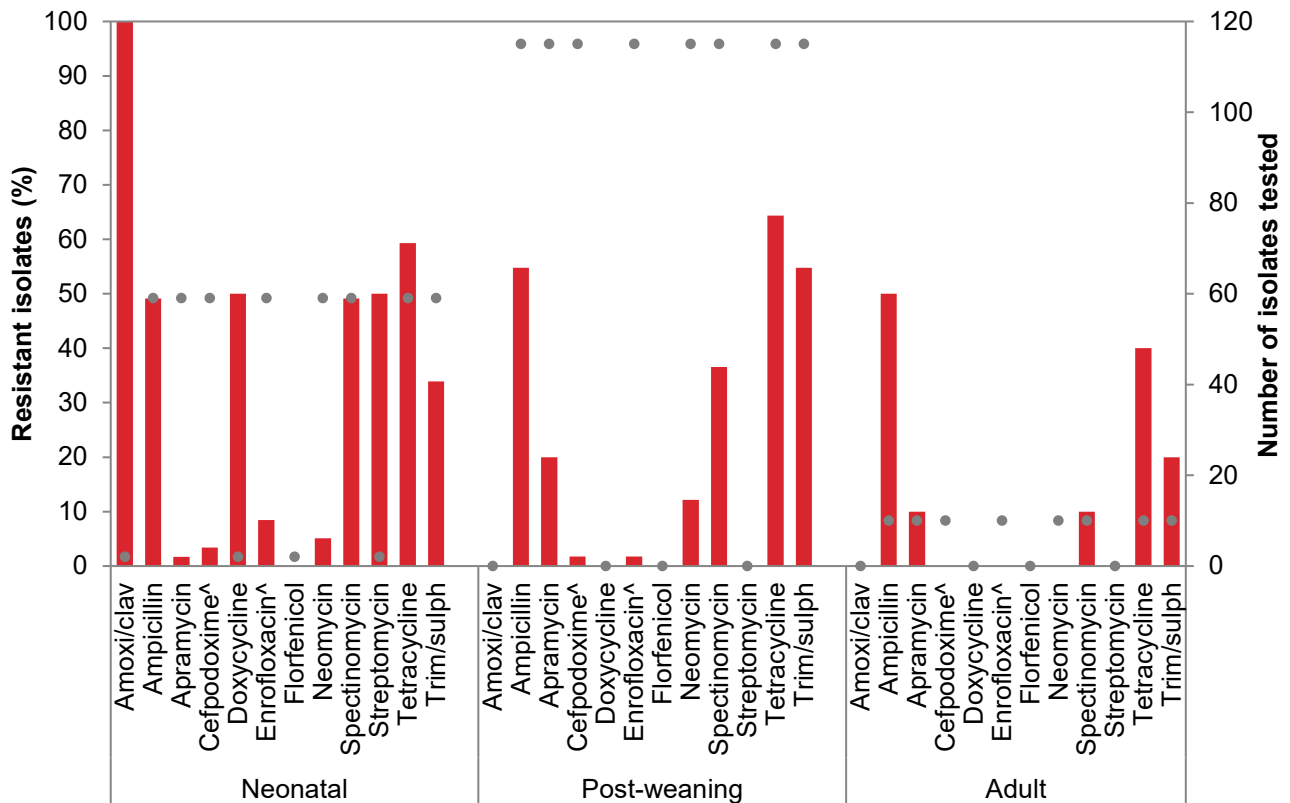
The total number and proportion of resistant isolates from pigs are shown in **Figure 4.11**. Cefpodoxime resistance in *E. coli*/coliform isolates was detected in neonatal and post-weaning piglets at low levels of 1–3% in 2016–2018 (**Figure 4.12**), as was enrofloxacin resistance: 2–15% in neonatal and post-weaning animals. Apramycin resistance was 1–3% in neonatal pigs during this period but was much higher at 20–23% in *E. coli* from pigs post-weaning. This may reflect the use of apramycin to control post-weaning diarrhoea. Resistance to neomycin or florfenicol 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. Resistance to tetracycline and trimethoprim/sulphonamides was relatively high and showed small fluctuations over the period in post-weaning pigs, but resistance to each of these compounds declined in neonatal pigs. The apparent trend of declining multiple drug resistance in neonatal and post-weaning pigs may have been affected by changes in the range of antibiotics tested in different years.

Figure 4.11: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from pigs (all ages); 2016–2018



[^] HP-CIA

Figure 4.12: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from pigs by age category; 2018



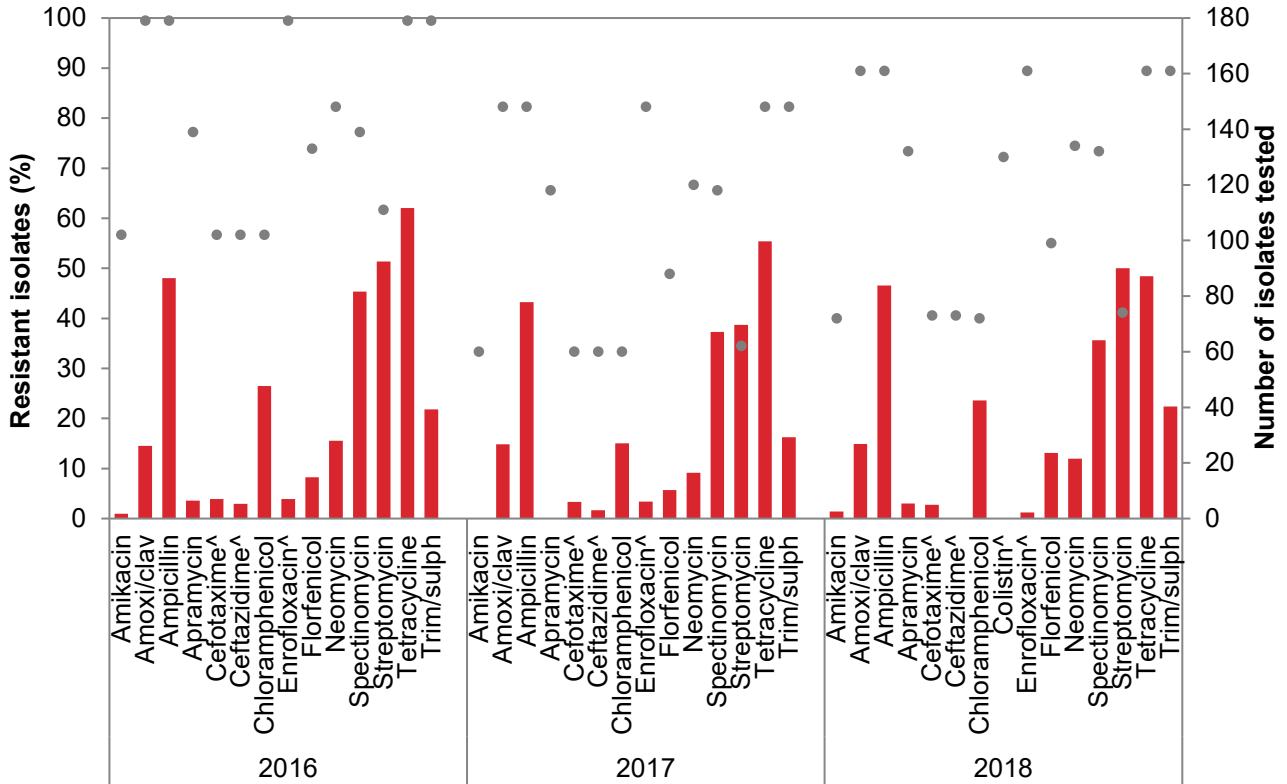
[^] HP-CIA

4.3.5.3 Sheep

Lower levels of resistance to several antibiotics, including enrofloxacin and trimethoprim/sulphonamides, were generally observed in sheep than in pigs and cattle (**Figure 4.13**). Decreasing levels of resistance to the antibiotics ampicillin, tetracyclines and enrofloxacin were observed in neonatal lambs over the period 2016–2018. For all of the antibiotics reported, the levels of resistance in neonatal lambs were lower than those reported for neonatal calves. 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 (**Figure 4.14**).

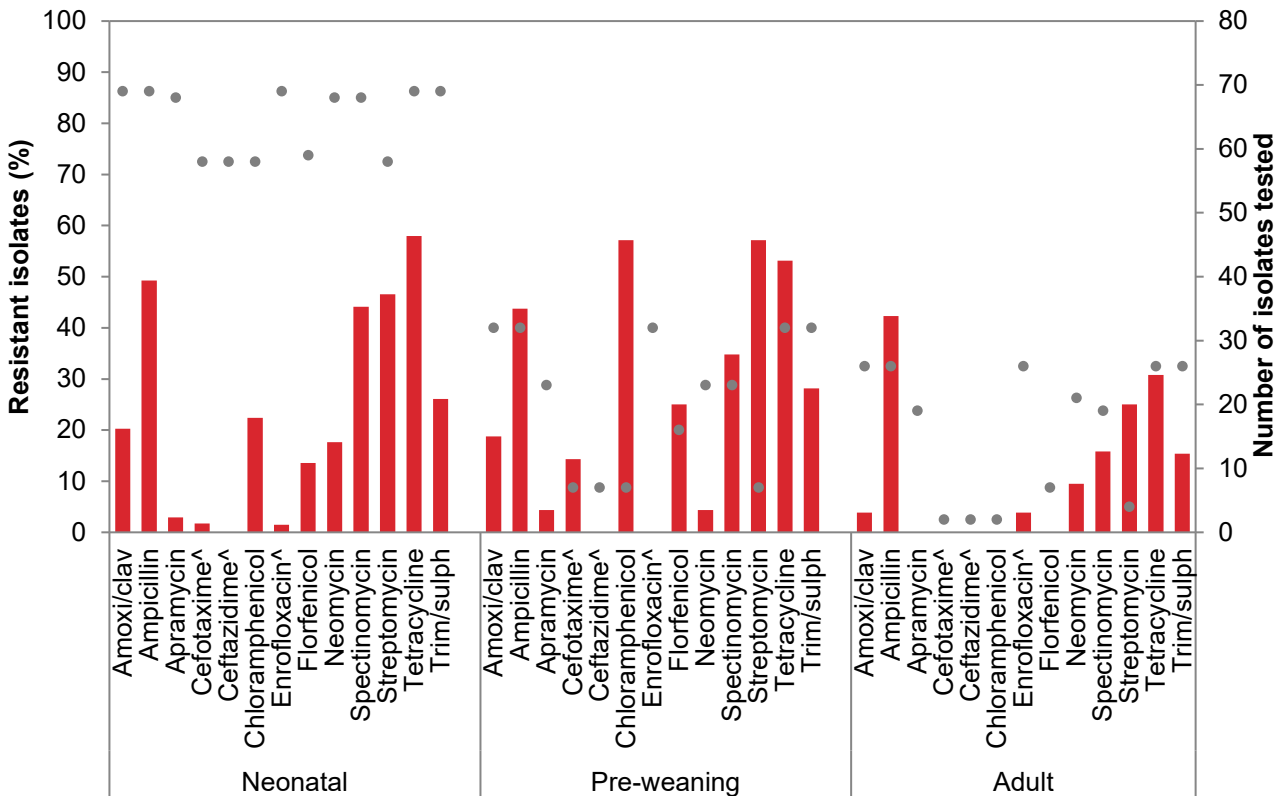
Considering the figures for 2016 and 2018, *E. coli*/coliforms from neonatal calves, neonatal pigs and neonatal lambs have all shown a decline in resistance to enrofloxacin.

Figure 4.13: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from sheep (all ages); 2016–2018



[^] HP-CIA

Figure 4.14: Number of isolates tested (●) and percentage (■) of resistant isolates of *Escherichia coli* from sheep (by age category); 2018



[^] HP-CIA

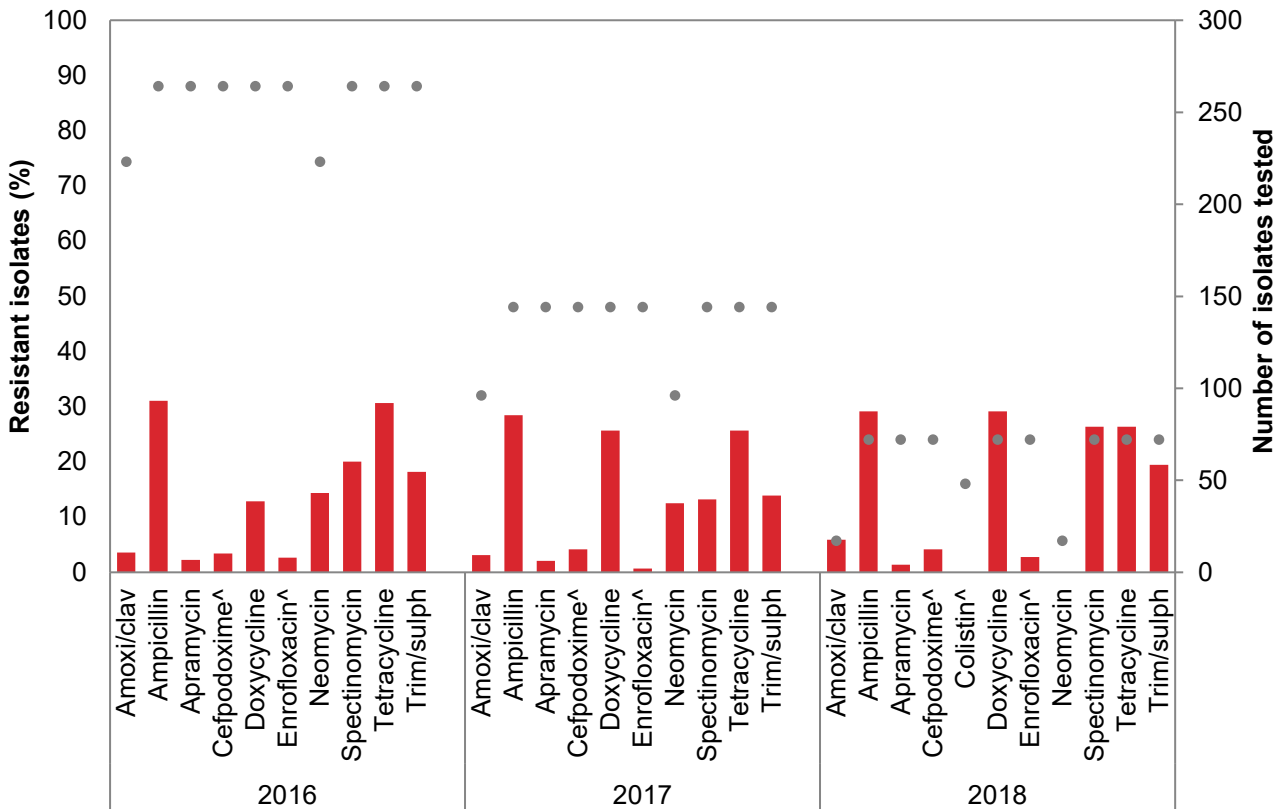
4.3.5.4 Chickens and turkeys

Cefpodoxime resistance ranged from 3% to 4% in *E. coli*/coliforms from chickens in 2016–2018, representing a decline since 2015 when 11% resistance was recorded (Figure 4.15 and Table S4.7.5 of the supplementary material). Usage of 3rd generation cephalosporins has not been permitted in poultry by the BPC 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 cephalosporins.

Levels of resistance detected to the fluoroquinolone enrofloxacin in *E. coli*/coliforms from chickens over the period 2015–2018 declined from 17% to 1–3%, temporally coincident with recent industry initiatives to reduce use of fluoroquinolones in broilers.

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; 2016–2018



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

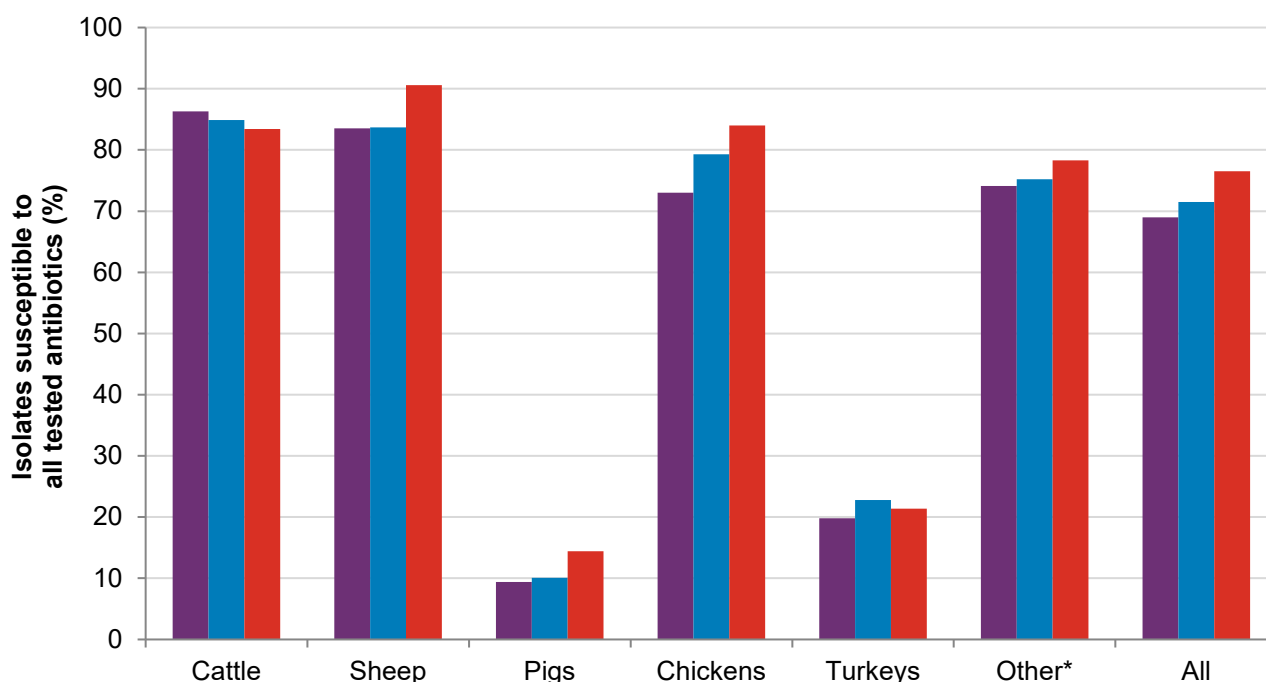
particular importance, since these antibiotics are most commonly used for the treatment of human salmonellosis, when treatment is required. However, it should be noted that most cases of non-typhoidal *Salmonella* infection in humans are non-invasive, limited to the gastro-intestinal tract and do not require antibiotic treatment. Where resistance to 3rd generation cephalosporins and fluoroquinolones is detected in a food-producing animal(s), attempts are made to visit the farms in order to explain the significance of the findings and provide appropriate advice on control.

The number of cultures received from a farm varies enormously, especially in the case of those received from poultry premises. Some poultry companies have a continuous monitoring programme and large numbers of *Salmonella* isolates may be received from a particular company relating to one premises. Thus, in that situation, the numbers of isolates of a particular serotype and their antibiotic susceptibility may not reflect the prevalence in the animal population as a whole but rather the intensity of the monitoring programme on a farm or group of farms. Therefore, to better indicate the prevalence of resistance, only the first isolate from each incident has usually been tested. More detailed results can be found in section S4.8 of the supplementary material.

4.3.6.1 All *Salmonella*

Of the 4,414 *Salmonella* isolates tested in 2018, 3,376 (76.5%) were sensitive to all of the antibiotics tested (**Figure 4.16**). This is similar to the situation in 2017 (71.2%).

Figure 4.16: Percentage of *Salmonella* spp. isolates susceptible to all tested antibiotics, from different sources and animal species; in 2016 (■), 2017 (■) and 2018 (■)



* 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 2018 was 0.1%; one single isolate (*S. Mbandaka* from a broiler chicken) was resistant to ceftazidime and cefotaxime. Ciprofloxacin, cefotaxime or ceftazidime resistance was not detected in *S. Enteritidis* from animals in 2018. No cefotaxime or ceftazidime resistance was detected in *S. Typhimurium* from animals in 2018. These findings are important since these serovars are of particular public health importance.

Tetracycline resistance was most common in *Salmonella* isolates from pigs and turkeys in 2018. This was also the situation for resistance to sulphonamides and streptomycin. Findings were similar in 2017.

Resistance to apramycin in all *Salmonella* serovars was 0.9% in 2018, similar to the level observed in 2017 of 1.4%. *Salmonella* isolates from pigs, where resistance was 14.4% in 2018, 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 2018, 19.6% of *Salmonella* 4,12:i:- isolates (n=46) and 31.6% of *Salmonella* 4,5,12:i:- isolates (n=38) from pigs were resistant to apramycin. Of all *Salmonella* isolates, 1.1% were resistant to gentamicin. No resistance was detected to the aminoglycoside amikacin.

The highest prevalence of resistance to nalidixic acid in 2018 was in *Salmonella* isolates from the environment, feed, turkeys, other avian species and dogs. The high proportion of nalidixic acid resistant isolates in the environment and feed categories represents a difference from 2013–2016 when resistance to nalidixic acid was mostly observed in *Salmonella* from turkeys and “other avian species”. In turkeys, 9/9 *S. Senftenberg* isolates, 1/1 *S. 4,12:z:-* isolates and 1/1 *S. Orion* var 15+ (Binza) isolates were resistant to nalidixic acid in 2018. The situation in turkeys was similar in 2013–2017, with nalidixic acid resistance frequently detected in these serotypes. In broilers, resistance to nalidixic acid was found in *S. 13,23:i:-*, *S. Kedougou* and *S. Montevideo*. Ciprofloxacin resistance occurred in 0.5% of *Salmonella* isolates (1/9 *S. Senftenberg* isolates) from turkeys (n=182) and the ciprofloxacin-resistant isolate was also resistant to nalidixic acid. The other ciprofloxacin-resistant isolates detected in 2018 originated from dogs (*S. Typhimurium*; 1/27 resistant), feed and related samples (*S. Kentucky*; 1/4 resistant, *S. 13,23:1:-*; 1/48 resistant), and the environment (*S. Enteritidis*; 1/1 resistant). Two isolates *S. 13,23:i:-* from broilers were also resistant to ciprofloxacin.

4.3.6.2 *Salmonella* by animal species

The percentage of fully susceptible *Salmonella* isolates from pigs fluctuated between 2014 and 2018 but remained below 20% (**Figure 4.16**). The increase in the proportion of fully susceptible isolates from turkeys noted in 2017 has been maintained, and there has been a big increase in the proportion of fully susceptible isolates from chickens (64% to 84%). The high level of fully susceptible isolates from cattle and sheep has been maintained.

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

Cattle – No resistance was observed to ceftazidime, cefotaxime or ciprofloxacin. The highest level of resistance was to streptomycin (13.9%), sulphonamide compounds (13.9%), tetracycline (11.5%), ampicillin (9.2%) and chloramphenicol (6.5%).

Pigs – No resistance was observed to ceftazidime, cefotaxime or ciprofloxacin. A large proportion was resistant to sulphonamides (79.7%), tetracycline (74.8%), ampicillin (72.3%) and streptomycin (71.3%). These levels of resistance fluctuated over the period 2016–2018. Resistance to chloramphenicol was 51.5%, and to neomycin was 11.9%.

Sheep – There was no resistance to ceftazidime, cefotaxime or ciprofloxacin. The highest level of resistance was to streptomycin (7.6%), sulphonamides (7.2%), tetracycline (6.9%) and ampicillin (6.5%). A decrease in the levels of resistance to these antibiotics was seen compared with 2017.

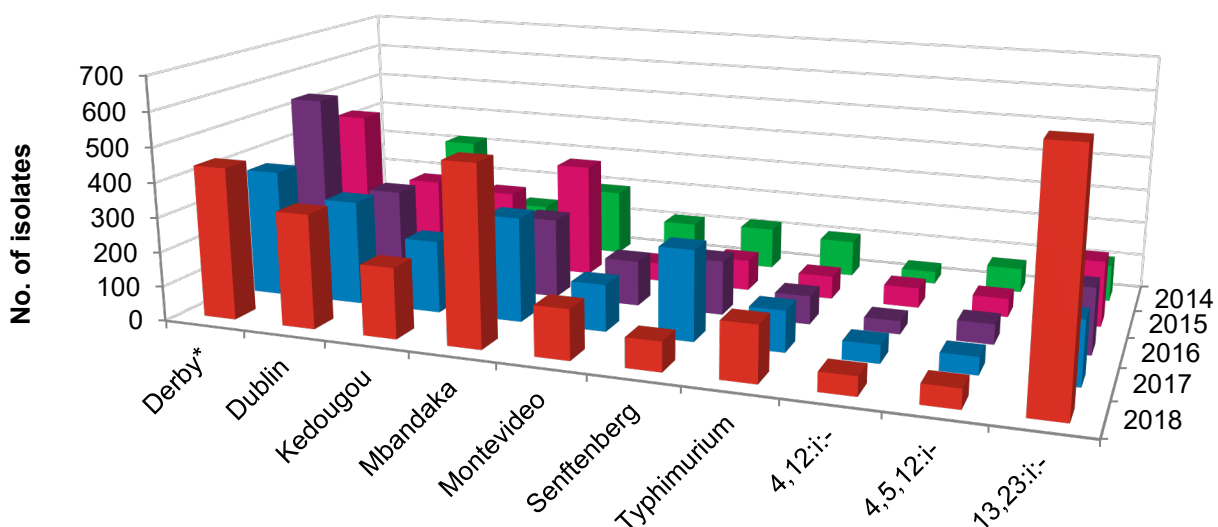
Chickens – Resistance to 3rd generation cephalosporins or fluoroquinolones (ciprofloxacin) was very low (0.1% of the isolates). The highest levels of resistance were seen to sulphonamides (11.3%) and tetracycline (7.8%), which were lower than the previous year. Similar to previous years, gentamicin resistance was present in a very low number of isolates (0.5%).

Turkeys – The low level of ciprofloxacin resistance (0.6%) was similar to the previous year, and no resistance to 3rd generation cephalosporins was detected. The highest level of resistance was to streptomycin (71.8%), sulphonamides (69.6%) and tetracycline (69.1%). These levels were higher than those reported in 2017.

4.3.6.3 Top ten *Salmonella* serovars isolated in 2014–2018

Some serovars can have characteristic patterns of resistance, so knowledge of the most frequently isolated serovars can be of benefit when considering trends in resistance. The ‘top ten’ serovars of non-typhoidal *Salmonella* isolates recovered from cattle, pigs, sheep, chickens and turkeys in Great Britain in 2014–2018 are presented in **Figure 4.17**. *S. Derby*, *S. Dublin* and *S. Mbandaka* are generally the most consistently isolated serovars year-on-year, but in 2018 the most frequent isolated serovar was 13,23:i:- (n=681), followed by Mbandaka (n=514) and (presumptive) Derby (n=439). Details on the number of commonly recovered serovars in Scotland and Northern Ireland are provided separately in Table 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 2018, with corresponding data for previous years



* Data includes presumptive *S. Derby*

4.3.6.4 *Salmonella* Dublin

Of the 320 *Salmonella* Dublin cultures tested during 2018, 96.2% were susceptible to all 16 antibiotics tested (**Table 4.3**). This percentage has shown only slight fluctuations over the period 2006–2018 and the majority of isolates remain susceptible; this has been the situation since

surveillance began in 1971. Most *S. Dublin* isolates (89.0 %) originated from cattle in 2018, in keeping with previous years. Isolates from species other than cattle in 2018, comprised 12 isolates from sheep, 10 from dogs, one from an alpaca, one from a cat and 11 from animal feed.

Table 4.3: Resistance in *Salmonella* Dublin: percentage of resistant isolates; 2014–2018

Antibiotic	Percentage of resistant isolates				
	2014 (n=286)	2015 (n=226)	2016 (n=245)	2017 (n=272)	2018 (n=320)
Ampicillin	0.7	1.8	0.4	0	0
Chloramphenicol	0	0.4	0.4	0	0.3
Furazolidone	0.3	0	0	0	0
Nalidixic acid	0	2.2	1.2	0	2.2
Neomycin	0.3	2.2	0	0	0.3
Streptomycin	2.4	4	1.6	0	0.3
Sulphonamide compounds	0.7	0	0	0	0.3
Tetracycline	0.3	0.4	0.4	0	0.3
Trimethoprim/sulfamethoxazole	0.7	0	0	0	0

4.3.6.5 *Salmonella* Typhimurium

Eight definitive or undefined types were most frequent (445 of 504 isolates) and were examined for susceptibility (**Figure 4.18**). The proportion of *S. Typhimurium* sensitive to the 16 antibiotics included in the panel rose considerably in 2018 (54.4%, compared with 34.2% in 2017). This is likely to be related to an increase in *S. Typhimurium* isolation from sheep, in particular of an RDNC ('Reacts Does Not Conform') strain that is sensitive to the panel of antibiotics.

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; 2018

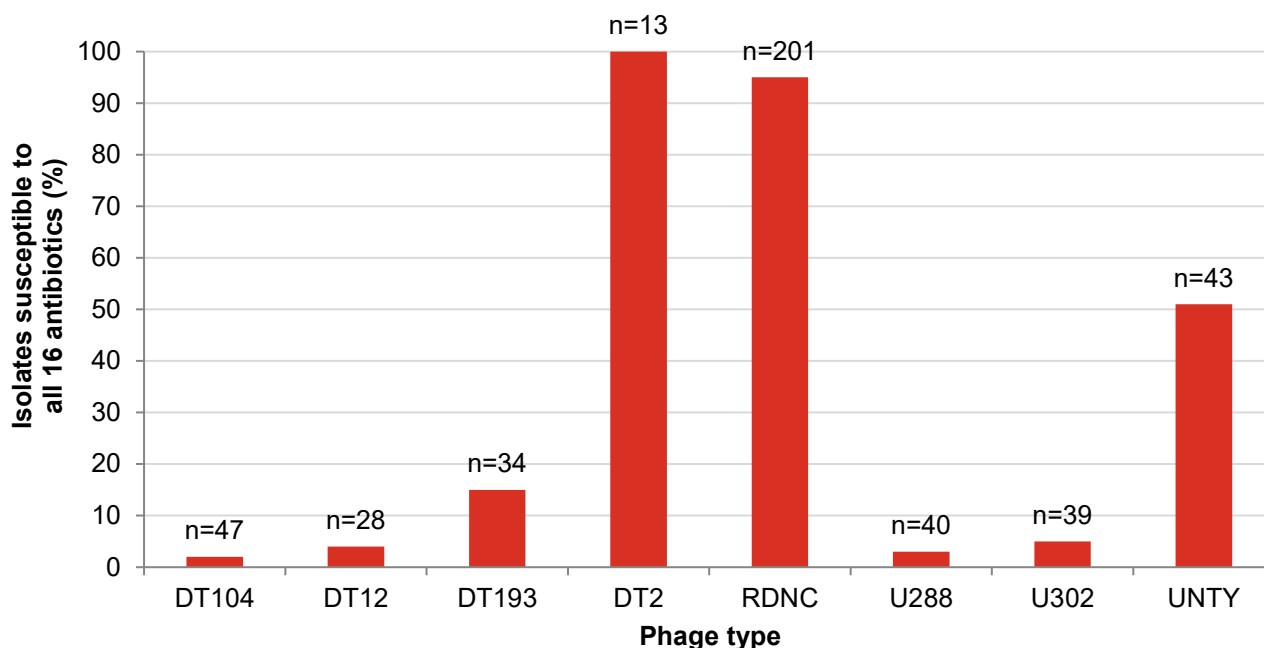
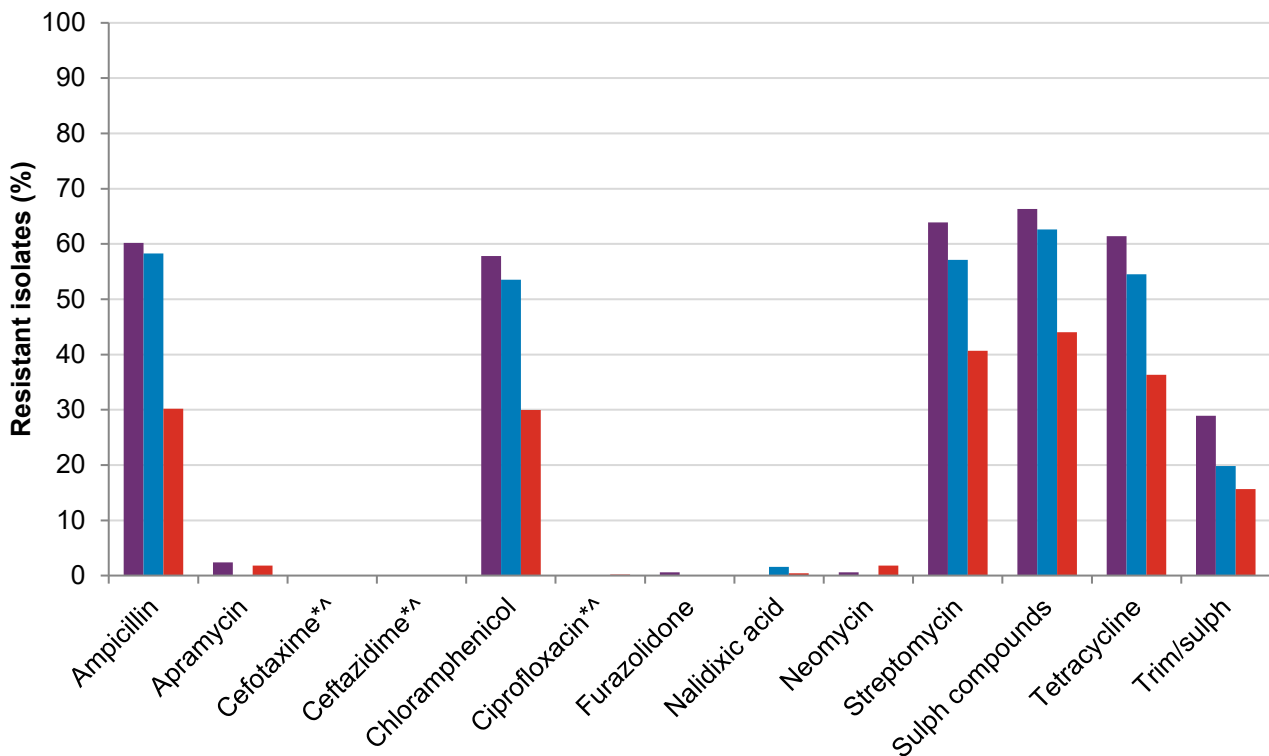


Figure 4.19 (and Table S4.8.8 of the supplementary material) present an overview of percentage of resistance in *S. Typhimurium* to the antibiotics tested in 2016–2018. The generally high level of resistance of *S. Typhimurium* isolates observed in recent years has partly been a reflection of the contribution of DT104 and its variants DT104B and U302 which have comprised more than a quarter of isolates in some years in the previous decade. Only one of 47 DT104 isolates was sensitive to all of the antibiotics tested in 2018. All remaining DT104 and 37/39 U302 isolates were resistant to at least one of the 16 antibiotics (there were no isolates of DT104B recovered in 2018). The proportion of *S. Typhimurium* isolates comprising DT104 and its variants, which had shown a general decline in 2007–2014, has shown a recent resurgence. The resurgence of pentavalent (AmCSSuT) *S. Typhimurium* DT104 continued in 2018. The typical pentavalent resistance pattern was the most common resistance pattern seen in *S. Typhimurium* DT104 isolates, occurring in 82.9% of isolates. This was mainly due to an increased number of incidents of this clone in cattle and sheep from 2017.

Figure 4.19: *Salmonella Typhimurium*: percentage of resistant isolates in 2016 (■; n=166), 2017 (■; n=187) and 2018 (■; n=504)



^ HP-CIA; * no data available for 2016 and 2017

None of the 47 DT104 isolates were resistant to nalidixic acid or trimethoprim/sulphamethoxazole. No isolates of DT104 were recovered from turkeys in 2012 to 2018. DT104 isolates from turkeys, when detected, have commonly shown nalidixic acid resistance in previous years.

Salmonella Typhimurium U288 and DT193 from pigs accounted for 7.3% and 4.2% of the total numbers of *S. Typhimurium* isolates respectively; only one of the U288 and DT193 isolates from pigs was fully susceptible in 2018.

Considering all definitive types of *S. Typhimurium*, resistance to trimethoprim/sulphamethoxazole has fluctuated markedly in recent years (between 27% and 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 trimethoprim/sulfamethoxazole. The definitive and undefined phage types of *S. Typhimurium* resistant to trimethoprim/sulfamethoxazole and recovered from pigs in 2018 included contributions primarily from isolates of two phage types DT193 and U288. AmCSSuTTm was the most common resistance pattern observed in both DT193 isolates (14 isolates) and U288 isolates (22 isolates) from pigs.

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

One *S. Typhimurium* isolate from a dog was resistant to ciprofloxacin in 2018, whilst no amikacin resistant isolates were recovered in 2018. No isolates were resistant to ceftazidime and cefotaxime. One isolate from a cat and one from a dog were resistant to nalidixic acid.

4.3.6.6 Monophasic *Salmonella* Serotypes

Eighty-eight isolates of *Salmonella* 4,12:i:- were tested, belonging to definitive phage types DT120 (n=7), DT193 (n=70), DT2 (n=2), DT32 (n=1) and undefined phage type U311 (n=1); seven isolates were not typable. Most isolates were from pigs (52.3%) with feed and related samples being the next most common source of origin (12.5%). The most common pattern of resistance observed was AmSSuT, which occurred in 36/70 of DT193 isolates, in 2/7 DT120 isolates, 1/1 U311 isolates and in 1/7 of the isolates which were not typable with phages. Considering the DT193 isolates, 51/70 had the AmSSuT resistance pattern alone or with one or more additional resistances.

A total of 79 isolates of *Salmonella* 4,5,12:i:- were tested, including phage types DT193 (n=72), DT12 (n=1) and U311 (n=2); four isolates were untypable. The most common resistance pattern in DT193 isolates was AmSSuT, occurring in 52.8% of isolates. Most isolates of monophasic *Salmonella* 4,5,12:i:- DT193 were from pigs (48.1%).

For aminoglycosides other than streptomycin, apramycin resistance was detected in 19.6% and neomycin resistance in 17.4% of 4,12:i:- from pigs (n=46). Apramycin resistance was detected in 31.6% and neomycin resistance in 26.3% of 4,5,12:i:- from pigs (n=38). Resistance to apramycin was also observed in 6.7% of 4,5,12:i:- isolates from feed or feed constituents (n=15). Resistance to the aminoglycosides apramycin and neomycin was therefore detected in monophasic *S. Typhimurium* isolates from both pigs and feed in 2018. In 2017, neomycin resistance was detected in 4,5,12:i:- isolates from feed, and it was detected in both 4,12:i:- and 4,5,12:i:- isolates from pigs.

4.3.6.7 *Salmonella* other than Dublin or Typhimurium

Of the 3,589 isolates of serotypes other than *S. Dublin* and *S. Typhimurium* tested, 77.7% were sensitive to all the antibiotics in the panel, an increase on the figure recorded in 2017, when 71.2% were fully sensitive (**Figure 4.20**). Forty-eight isolates (1.3% of the total) were *S. Enteritidis*, of which 44 (91.7%) were fully susceptible. Two isolates, a phage type 13a from feed and a PT8 from a snake, were resistant to nalidixic acid.

Neomycin resistant *Salmonella* isolates originated mainly from chicken (1,630 isolates; 1.1% resistant) pigs (123 isolates; 14.6% resistant), feed or feed constituents (826 isolates; 1.1% resistant), and ducks (336 isolates; 3.9% resistant). In ducks, *S. Indiana* was the main serotype

showing resistance to neomycin (101 isolates; 11.9% resistant); the *S. Indiana* isolates from ducks were also frequently resistant to furazolidone (101 isolates; 19.8% resistant) and this was similar to the situation observed in 2017.

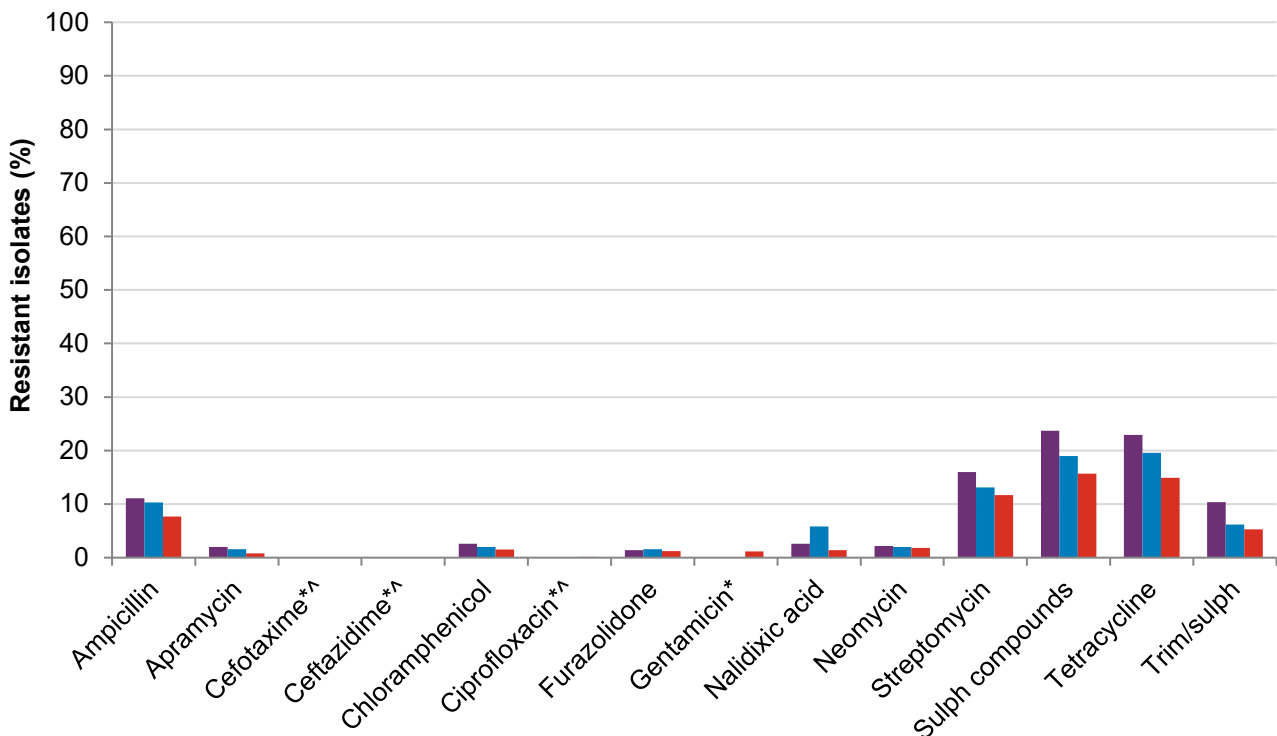
For isolates from turkeys in 2018 (n=137), 70.4% were resistant to streptomycin, 68.2% to sulphonamides and 67.6% to tetracyclines; similar to the equivalent figures for pigs in 2018 (respectively 62.6%, 68.3% and 70.7%), but higher than those for chickens (respectively 5.7%, 11.2% and 7.7%) or cattle (11.6% for the three antibiotics). In 2018, the proportion of *Salmonella* isolates originating from feed (23.0%) was similar to 2017 (26.8%); the proportion of fully susceptible isolates from feed increased slightly from 75.4% to 78.2%.

The number of *S. Enteritidis* isolations was lower in 2018 (n=48) than 2017 (n=102). The increase in 2017 was mainly due to an outbreak of *S. Enteritidis* PT8 that occurred in turkeys. This strain is resistant to nalidixic acid. Only two isolates from 2018 were resistant to nalidixic acid, and they were not related to the 2017 outbreak strain.

One isolate of ciprofloxacin-resistant *S. Kentucky* was retrieved from an animal by-product of unknown origin. This is likely to be the epidemic *S. Kentucky* clone that is circulating in certain areas, including continental Europe, but it is rarely isolated in the UK. It is likely that this isolate originated from contaminated imported meat.

Furazolidone and nalidixic acid resistant *S. Infantis* was isolated from a dog in 2018. These resistances are associated with a multidrug resistant (MDR) *S. Infantis* clone that is common in poultry, in particular in Eastern Europe. This strain has been isolated previously from raw pet food, and it is likely to be related to contaminated imported poultry meat.

Figure 4.20: *Salmonella* other than Dublin and Typhimurium, percentage of isolates resistant to antibiotics tested; 2016 (■; n=1,986), 2017 (■; n=2,652) and 2018 (■; n=3,589)



^ HP-CIA; * no data available for 2016 and 2017

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Annex C: Data background and limitations

Antibiotic sales data

- Sales data do not permit accurate analysis of antibiotic consumption by animal species or production category. Some formulations of antibiotics are authorised with indications for use in more than one species, e.g. pigs and poultry. It is not possible to ascertain from sales data in which species the product was used.
- A given quantity of antibiotic may represent many doses in small animals or few doses in large animals. It is not possible to predict the number of doses represented by the quantity sold.
- Changes in quantities of veterinary antibiotics sold should be considered in parallel with changes in the UK animal population over the corresponding time period. The populations of animal species are an important denominator and may vary quite markedly from year to year depending on market conditions for animal derived food. Similarly variations in the size of the animals being treated should be taken into consideration as larger animals will require a larger relative quantity of antibiotics over a treatment period.
- To try and address the variation in animal populations and demographics, over time and between countries, the ESVAC project has developed a Population Correction Unit (PCU), a calculation that estimates the weight of the animal (or group of animals) receiving an antibiotic at the most likely time of administration. This unit is now used across EU Member States and is currently the best approximation of consumption. We have used this form of analysis in this report.
- Sales data in general over-estimate use, as not all antibiotics sold will be used. There is natural wastage resulting from pack sizes that do not meet dose need, and from drug expiry. In addition, a product could be sold one year and used, for example, the next year.
- Some products may be sold to UK feed mills for inclusion in feed which is then exported outside of the UK; currently there is no method for separating these sales from the total UK sales data, resulting in an over-estimate of use in UK feed.
- Some products may be imported into the UK on a Special Import Certificate; currently there is no method for including these data in the total UK sales data, resulting in an under-estimate of use in the UK.
- Medication sold for use in humans may be used in animals under certain circumstances, according to the prescribing Cascade; figures on such use are not included in the data presented. Further information on Cascade prescribing can be found in section S1.4 of the supplementary material.

Resistance data, EU AMR harmonised monitoring scheme

- The sampling size and strategy are designed to provide a sample which is representative of the wider population for each combination of bacteria and animal species.
- The organisms for which the legislation outlines monitoring provisions, such as *Salmonella* spp. and *E. coli*, are of direct relevance to human health. Additionally, the panel of antibiotics against which these organisms must be tested has been selected based on relevance to human health and includes antibiotics, such as 3rd and 4th generation cephalosporins and fluoroquinolones that are defined by the World Health Organization (WHO) as the HP-CIAs.
- The legislation and accompanying technical specifications provide a standardised and harmonised sampling methodology which produce comparable and robust susceptibility

data for a representative proportion of food-producing animals and food products across the EU. However, animal species are monitored on alternating years, therefore not providing annual data.

- The legislation provides a harmonised set (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 Market Authorisation Holders of manufactured antibiotics to provide the Veterinary Medicines Directorate with total annual sales data for each antibiotic product sold within the UK. Data were collected, verified and analysed to calculate the total weight, in tonnes, of each active ingredient sold for each antibiotic. Antibiotic sales data are collected as a proxy for antibiotic use.

Periodic Safety Update Reports (PSURs)

Sales figures submitted by MAHs in PSURs, for the purpose of Pharmacovigilance, were used to validate sales data published in this report. Where a PSUR had been returned to the VMD Pharmacovigilance team in the 2018 calendar year, reported sales were compared to those returned to the AMR team and any discrepancies were queried.

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

Defra Statistics division

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

CEFAS

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

TRACES

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

Annex E: Glossary of terms

Active ingredient	The part of an antibiotic medicine that acts against the bacterial infection. Alternatively called 'active substance'.
AMEG	Antimicrobial Advice <i>ad hoc</i> Expert Group; AMEG is an <i>ad hoc</i> group established by the European Medicines Agency jointly under the Committee for Medicinal Products for Veterinary Use (CVMP) and the Committee for Medicinal Products for Human Use (CHMP). The AMEG was set up to provide guidance on the impact on public health and animal health of the use of antibiotics in animals, and on the measures to manage the possible risk to humans.
ATCvet	Anatomical Therapeutic Chemical classification system for veterinary medicinal products
AHDB	Agriculture and Horticulture Development Board
Antibiotic	A large group of antibacterial substances capable of destroying or inhibiting the growth of bacteria, used for treatment or prevention of bacterial infections.
Antimicrobial	Naturally occurring, semi-synthetic or synthetic substances that exhibit antimicrobial activity (kill or inhibit the growth of micro-organisms). Used for treatment or prevention of infections. Antimicrobials include antibacterials (antibiotics), antivirals, antifungals and antiprotozoals.
Antibiotic/antimicrobial resistance	The ability of a bacterium/micro-organism to grow or survive in the presence of an antibiotic 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; 3 rd and 4 th generation cephalosporins and colistin.

Defra	Department for Environment, Food and Rural Affairs
ECOFF	Epidemiological cut-off value: represents the point at which bacteria have developed a higher level of resistance to an antibiotic than the background level of resistance that exists naturally for that bacterial species. A 'resistant' (or 'non-susceptible') ECOFF does not necessarily imply a level of resistance which would correspond with clinical treatment failure.
EMA	European Medicines Agency
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
Food-producing animal (species)	Animals used for food production including (but not limited to): cattle, sheep, pigs, poultry, salmon, trout and bees.
Injectable product	A product which is administered to animals via injection.
Intramammary product	A product which is administered into the udder.
Medicated feeding stuff	Feeding stuffs that contain a veterinary medicine and that are intended for feeding to animals without further processing.
MIC	Minimum Inhibitory Concentration: the lowest concentration of an antibiotic that inhibits visible growth of a bacterium after overnight incubation.
Non-food-producing animal (species)	Animals not reared for food. These are mainly companion animals including (but not limited to): dogs, cats, horses, small mammals, rabbits and birds.
PHWC	Pig Health and Welfare Council
Oral/water product	A product that is administered to animals orally. In this report this includes boluses, topdressings, powders, dissolvable powders, solutions.
Population Correction Unit (PCU)	This is a technical unit of measurement which is used to represent the estimated weight at treatment of livestock and slaughtered animals. It takes into account a country's animal population over a year, along with the estimated weight of each particular species at the time of treatment with antibiotics. 1 PCU = 1 kg of different categories of livestock and slaughtered animals.
Premix	Veterinary medicinal products intended for incorporation into medicated feeding stuffs.
Prodrug	Ingredient that after administration is metabolized (i.e. converted within the body) into the pharmacologically active drug.
PSUR	Periodic Safety Update Report. Pharmacovigilance documents submitted by marketing authorisation holders (MAHs) at defined time points post-authorisation. These documents are intended to provide

a safety update resulting in an evaluation of impact of the reports on the risk-benefit of a medicinal product.

TRACES

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

VMD

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

WHO

World Health Organization

Annex F: Contributors

Compiled by the Veterinary Medicines Directorate

Contributing Pharmaceutical Companies and Other Marketing Authorisation Holders

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

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