Veterinary Medicines Directorate

UK Veterinary Antibiotic Resistance and Sales Surveillance Report

UK-VARSS 2022

Published November 2023
Updated March 2024

Suggested citation: UK-VARSS (2023). *Veterinary Antibiotic Resistance and Sales Surveillance Report (UK-VARSS 2022)*. New Haw, Addlestone: Veterinary Medicines Directorate.

This publication is available online. Any enquiries or correspondence regarding this publication should be sent to us at: postmaster@vmd.gov.uk.

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Acknowledgements

This report is issued by the VMD. The veterinary antibiotic resistance and sales data monitoring programmes are commissioned and funded by the VMD. Data for the sales section are produced by the VMD. Data for the antibiotic resistance section are produced and collated by the APHA, Catherine Couzens (Agri-Food Biosciences Institute) and Geoff Foster (SRUC Veterinary Services). We are grateful to the vets and farmers for providing, and following parties for collecting and sharing usage data with the VMD: Agriculture and Horticulture Development Board Pork (pigs and ruminants), British Poultry Council (meat poultry), British Egg Industry Council (laying hens), Game Farmers' Association/British Veterinary Poultry Association gamebird subcommittee/ Agricultural Industries Confederation (gamebirds), British Trout Association (trout) and Salmon Scotland (salmon). We would also like to thank Starcross laboratory for providing the Minimum Inhibitory Concentration (MIC). We would like to thank Lily Simpkins of the VMD for her support and contribution to the production of this report. **Published on 1st November 2023. Updated on 13th March 2024.**

Contents

Foreword

As we publish this year's UK- VARSS report, the current five year UK National Action Plan (NAP) for AMR is drawing to a close. While next year's UK-VARSS will report the final year of data within the current NAP cycle, this year's report is significant as it is the last dataset that we consider as we finalise our plans for the next five year NAP. Our focus during the present 2019-2024 NAP has been to continue the reduction of unnecessary use of antibiotics in the animal health sector, maintaining and building on the dramatic early gains achieved a number of years ago. We have seen focused and collaborative action across the animal health and veterinary sectors become established and mature, in many cases, and this is reflected in the antimicrobial consumption trends in this report.

At the time of initial publication, this UK-VARSS report incorporated chapter 1 on antibiotic sales, chapter 2 on antibiotic use, and chapter 3 on harmonised monitoring of antibiotic resistance. Chapter 4, which reports the results from the clinical surveillance programme, was delayed but was published on 13th March 2024.

The 2022 reporting year has given us a new milestone figure of a 59% decrease, since 2014, in UK-wide sales of veterinary antibiotics intended for food-producing animals. This new figure was achieved following a 9% decrease in nationwide sales of antibiotics in 2022.

Alongside reducing overall use, vets and the agriculture sectors have continued to ensure highest priority critically important antibiotics (HP-CIAs) for humans are protected: these continue to account for less than half a percent of overall usage.

Reductions in antibiotic use reported by farmers and vets have correspondingly been seen in most animal sectors. While the pig industry remains the highest-using sector, their results are notable for the significant and year-on-year reductions that they have been achieving for antibiotic use. This is reflective of the energy and commitment shown by the pig sector in addressing AMR. Also of note is the sharp decline (by 57%) in the salmon sector's usage after a peak was seen last year. However, this year the trout sector has reported an increase in use, which contrasts strikingly with the low and declining trend seen in previous years. This increase has been investigated by the British Trout Association who report that this has been due to a specific disease outbreak of *Aeromonas salmonicida* on a small number of production sites and expect usage to fall back below industry targets next year.

The results in the salmon and trout sectors over recent years highlight that these sectors are particularly prone to fluctuations in their yearly antimicrobial use trends, because a small number of disease outbreaks can have a large impact on the individual sector's usage. This is particularly marked because their baseline usage is low. On each occasion, usage spikes have been attributable to treatment of diagnosed disease. This shows that the importance of usage data collection is not confined to tracking trends, but it also allows for signals arising from the data to be followed up, understood, and for changes to be instigated if they are needed.

We do not yet have nationally representative antibiotic usage data for ruminants. There are committed teams working very hard within the ruminant sectors to encourage and support

vet and farmer reporting of cattle and sheep antibiotic usage data to the centralised data collection system, Medicine Hub. The ruminant sectors are working on a number of excellent antibiotic stewardship initiatives, and we look forward to being able to evidence the impact of these with usage data trends once the Medicine Hub becomes sufficiently populated.

Turning to antimicrobial resistance monitoring, our key indicators for resistance show trends of decreasing resistance in the indicator bacteria *E. coli*, presenting a positive picture for AMR trends in the UK for 2022. These overall downward trends in resistance accompany the overall downward trends in UK veterinary antibiotic consumption.

Ciprofloxacin resistance in *Campylobacter jejuni* in broilers remains high. This resistance is relevant to human health because fluoroquinolones are one of the antibiotic classes used in certain human *Campylobacter* infections which need antibiotic treatment. This isn't a new finding (or unique to the UK), and the poultry sectors here have worked hard to implement policies which discourage persistence of this resistance: there has been very low use of fluoroquinolones in chickens and turkeys in recent years and there was no use of fluoroquinolones in grower farms in 2022. However, it serves as a reminder that prevention of the emergence of resistance, where possible, should be our goal, as not all resistance can be easily managed through actions after the event.

In recognition of the One Health principle that antimicrobial resistance in one sector can impact on other sectors, we expanded our surveillance programme in 2022 to include three new bacterial species: *Enteroccocus faecalis*, *Enterococcus faecium* and *Campylobacter coli*. This expansion gives a more complete picture of antimicrobial resistance in animals, and its relevance to human health.

On the other side of the coin, and as use of antibiotics in animals continues to reduce, our need to understand the influence of other drivers, including non-animal AMR sources, and transmission routes on our surveillance results is becoming more pressing: increasingly, resistance is being detected in animals that cannot be explained by veterinary antibiotic usage alone.

One Health, fully integrated, surveillance initiatives are therefore crucial to understanding and mitigating the risk of AMR. Our shared need for knowledge gaps to be filled include transmission from people to animals as well as animals to people, both direct and through the environment. The PATH-SAFE programme has made some large advances in this area, and the National Biosurveillance Network initiative has the potential to build on that as we embed cross-disciplinary working to better understand and mitigate AMR risks.

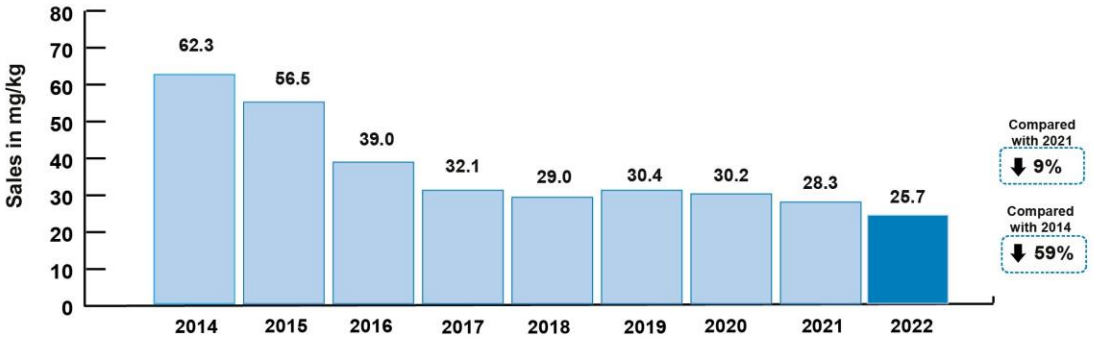
AMR remains a national challenge and a global challenge. AMR is coming into sharp international focus as momentum builds towards the United Nation's High Level Meeting on AMR next year. We look forward to continuing to drive progress over the next twelve months as we finalise our new National AMR Action Plan and prepare for the international discussions at the UN General Assembly, keeping at the forefront our shared responsibility to ensure that we keep antibiotics working.

Dr Kitty Healey BVSc PhD MRCVS
Head of Surveillance Division, Head of Antimicrobial Resistance

Antibiotic sales

Sales for food-producing animals (mg/kg)

Sales of veterinary antibiotics for use in food-producing animals, adjusted for animal population, were 25.7 mg/kg in 2022; this is a 9% (2.6mg/kg) decrease since 2021 and an overall 59% (36.6mg/kg) decrease since 2014. This represents the lowest sales ever recorded.



Sales of Highest Priority Important Antibiotics (HP-CIAs) in food-producing animals remain at very low levels at 0.12mg/kg in 2022 and account for less than 0.5% of total sales.

	2014	2021	2022	Compared with 2014
Total HP-CIAs	0.67	0.12	0.12	⬇ 82%
Fluoroquinolones	0.35	0.10	0.10	⬇ 72%
3rd/4th generation cephalasporins	0.19	0.02	0.02	⬇ 90%
Colistin	0.12	0.00	0.00	⬇ 100%

Sales of antibiotics for all animals (tonnes)

In 2022 the total quantity of antibiotic active ingredient sold in the UK was 193 tonnes, the lowest sales to date.

	2014	2015	2016	2017	2018	2019	2020	2021	2022	Compared with 2014
Total sales (all animals tonnes)	447	406	293	246	223	229	227	212	193	⬇ 57%

Tetracyclines remain the most sold antibiotic class (32%), followed by penicillins (28%).

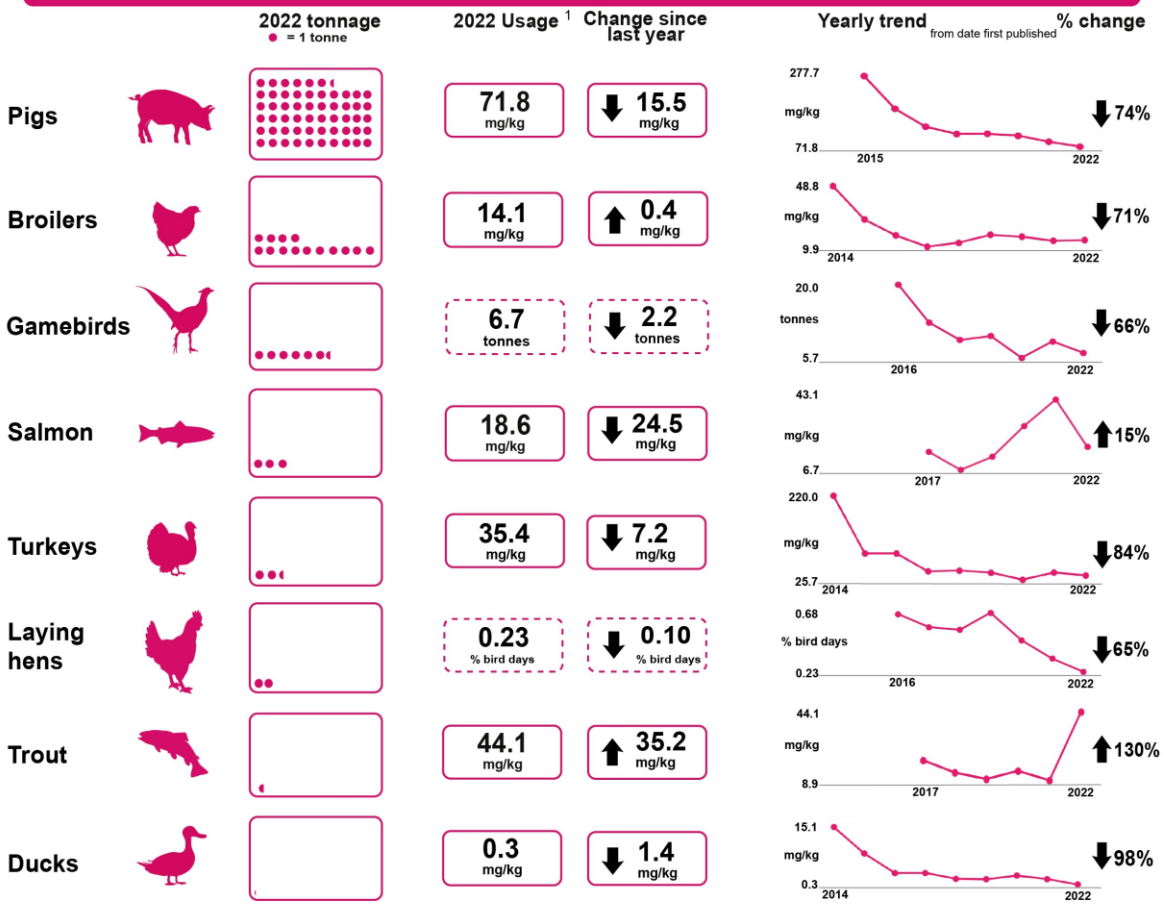
Sales of HP-CIAs for all animals (tonnes)

Sales of HP-CIAs for 2022 was 0.91 tonnes representing a small increase of 0.01 tonnes since 2021 but a reduction of 81% (3.9 tonnes) since 2014. Sales of HP-CIAs continue to represent a small proportion (less than 0.5%) of total veterinary antibiotic sales.

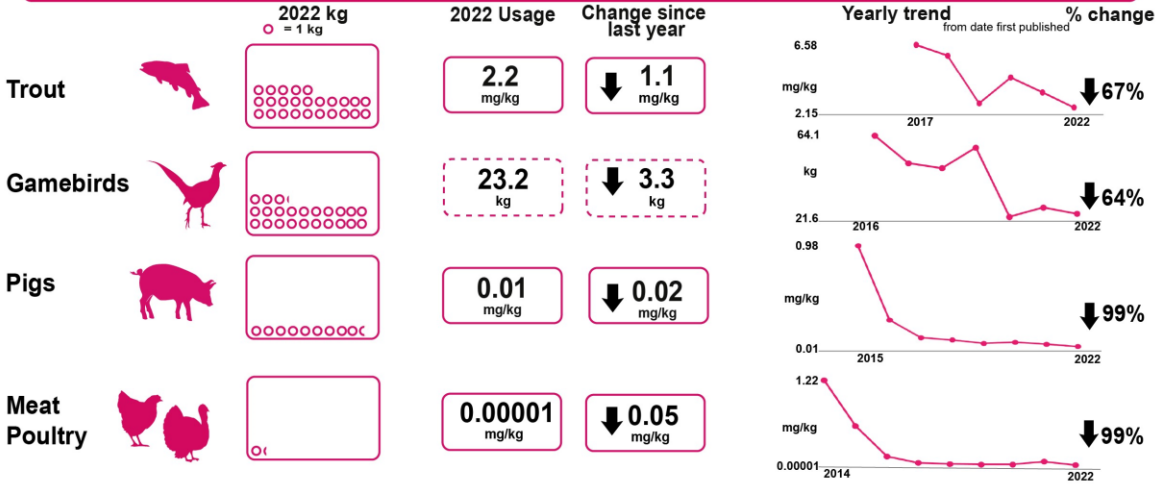
Antibiotic usage

Antibiotic usage refers to the amount of antibiotics prescribed and/or administered per sector. The data have been collected and provided to the VMD by the animal industry on a voluntary basis. Total coverage of all sectors is at least 90%.

Antibiotic usage by food-producing animal species



Highest Priority Critically Important Antibiotics by food-producing animal species



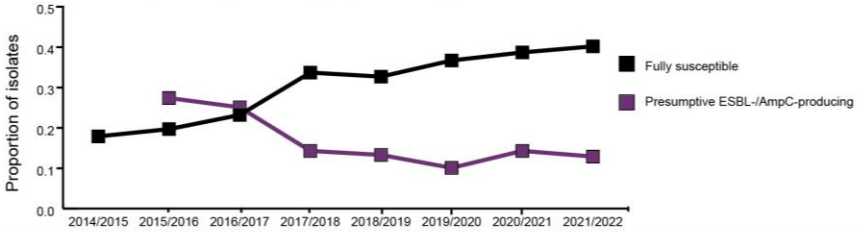
1 mg/kg relates to the amount of active ingredient standardised by kg biomass and calculated using ESVAC methodology, % bird days refers to 'actual daily bird-doses/100 bird-days at risk'

– – – indicates a different metric for usage

Antibiotic resistance in zoonotic and commensal bacteria from healthy animals at slaughter

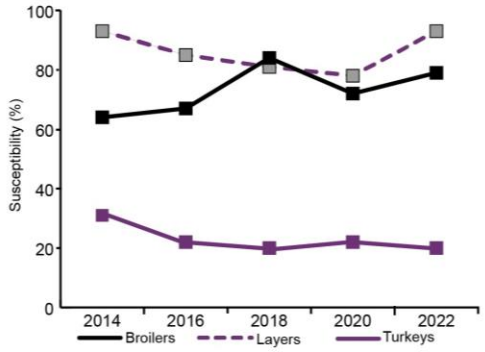
Key resistance outcome indicators: *E. coli*

The harmonised monitoring indicators combine results from healthy pigs and poultry at slaughter to give an idea of the major trends in UK AMR surveillance, and are internationally comparable. The overall picture for 2022 is positive. The proportion of isolates showing full sensitivity to the panel of antibiotics tested has continued to increase, and the proportion of presumptive ESBL-/AmpC-producing *E. coli* has remained stable.



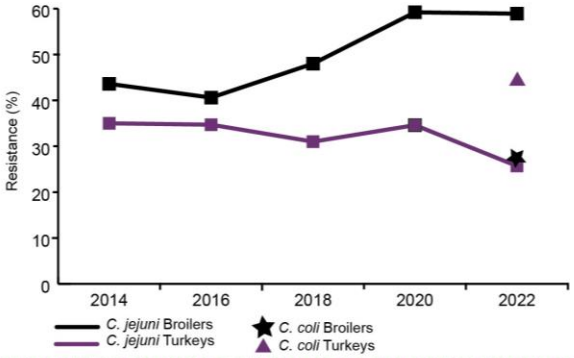
Resistance in *Salmonella* spp.

In 2022, full susceptibility in *Salmonella* increased in broilers and layers and remained stable in turkeys.



Resistance in *Campylobacter* spp.

In 2022, there were very high levels[2] of resistance to ciprofloxacin in *Campylobacter* from broilers and turkeys. This was the first year resistance in *C. coli* was tested.

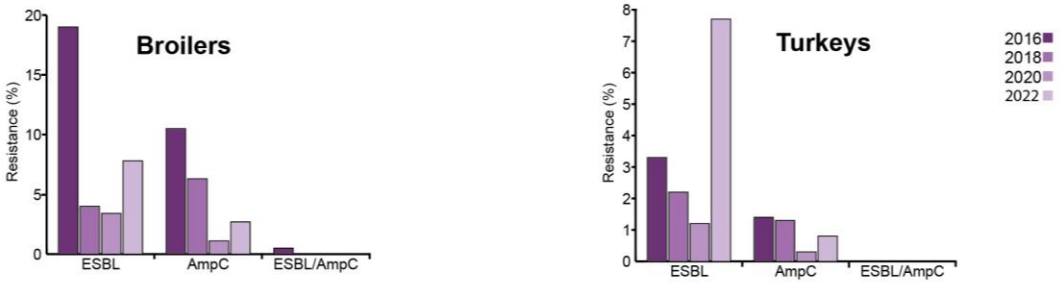


New surveillance for 2022

This year's harmonised monitoring includes three new species of bacteria: *Campylobacter coli*, *Enterococcus faecalis*, *Enterococcus faecium*. The addition of *Enterococcus* allows for detection of vancomycin resistance enterococci (VRE), which is of clinical importance. No VRE were detected.

Amplified detection of ESBL-/AmpC-producing *E. coli*

We also perform a more sensitive type of testing using selective media. This test inhibits the growth of susceptible bacteria but allows ESBL-/AmpC-producing *E. coli* to multiply, making them easier to detect. This tells us the proportion of individual birds carrying resistance to 3rd and 4th generation cephalosporins even at very low levels.



There was an increase in the prevalence of broilers and turkeys carrying ESBL- and AmpC-producing *E. coli* compared to 2020. Of these organisms from broilers, 77% were co-resistant to ciprofloxacin, an increase from 37% in 2020.

[2] Description of % resistance referenced: very high levels (50% to 70%)
ESBL= Extended Spectrum Beta Lactamase

Antibiotic resistance in clinical surveillance

Clinical surveillance aims to provide veterinarians with relevant treatment information using results from bacteria isolated from diagnostic samples. As scanning surveillance is subject to biases and differences in the number of samples, the results are not representative of the UK's wider animal populations.

Key findings

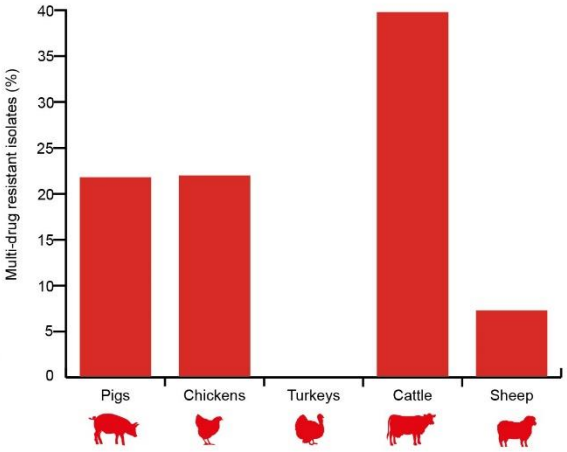
- 7,284 isolates were tested for AMR in England and Wales.
- *E. coli* and *Salmonella* were the most frequently tested bacteria.
- Resistance was usually highest to the most commonly used antibiotics: aminopenicillins and tetracyclines.
- Resistance tended to be higher in *E. coli* isolated from young animals, likely reflecting more frequent treatment.

Resistance in *Escherichia coli*

- Of the 984 *E. coli* isolates tested from all species, 24% were multi-drug resistant (resistant to three or more separate antibiotic classes). This was highest in cattle (40%).
- The highest levels of resistance were detected to the most commonly used antibiotics: the aminoglycoside streptomycin (54%), the aminopenicillin ampicillin (49%) and tetracycline (46%).
- In isolates from neonatal sheep, resistance to spectinomycin declined from 45% in 2021 to 23% in 2022. This is possibly due to withdrawal of this antibiotic from the market.

Highest priority critically important antibiotics (HP-CIAs): Resistance was low across all species: cefotaxime (3.7%), cefpodoxime (0.9%), ceftazidime (0.7%) and enrofloxacin (2.5%).

Percentage of isolates with multi-drug resistance

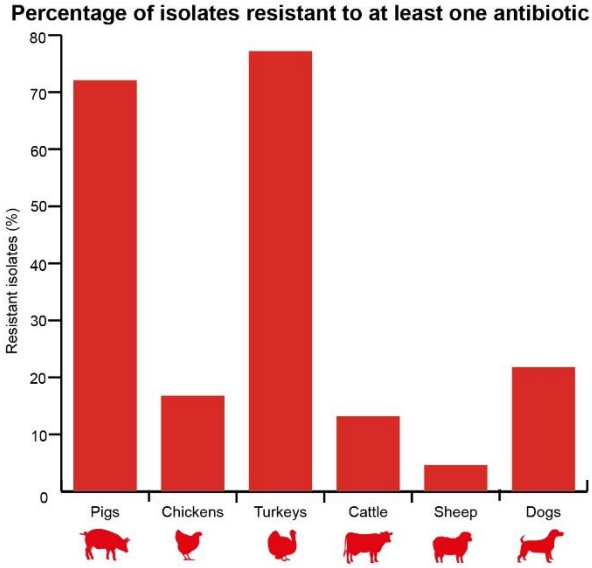


Resistance in *Salmonella* spp. from animals and their environment

- Of the 5,562 *Salmonella* isolates tested, 24% of isolates from all species showed resistance to at least one antibiotic. This was highest in turkeys (77%) and pigs (72%).
- A change to legislation in 2021 meant that *Salmonella* isolates from dogs became reportable under the Zoonoses Order in Great Britain. The number of isolates retrieved from dogs has increased from 105 in 2020 to 924 in 2022.

HP-CIA resistance was generally low (<2%), except to the quinolone nalidixic acid in turkeys (22%). This is difficult to interpret given the disruption to the poultry industry as a result of avian influenza during 2022 which impacted the number of samples submitted.

Percentage of isolates resistant to at least one antibiotic



Private Laboratory Initiative (PLI)

The PLI is a collaborative project between the VMD and APHA, which aims to routinely collect and analyse data from private veterinary laboratories, to provide an additional source of data for AMR surveillance. The PLI is feeding into the new National Biosurveillance Network (NBN) and will run pilot projects from April 2024 to April 2025.

Introduction

The Veterinary Antibiotic Resistance and Sales Surveillance report of the United Kingdom (UK-VARSS) presents combined data on veterinary antibiotic sales and antibiotic resistance in bacteria from food-producing animals in the UK.

The antibiotic sales data from 2014 to 2022 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. The first report on sales figures for antibiotic veterinary medicinal products, collated and published by the Veterinary Medicines Directorate (VMD), covered 1993 to 1998. The figures were provided voluntarily by the veterinary pharmaceutical companies marketing these products. Since 2005, sales data are collected as a statutory requirement (Veterinary Medicines Regulations), and in 2014 the first Veterinary Antibiotic Resistance and Sales Surveillance (UK-VARSS) report was published for the UK (presenting data from 2013).

However, many antibiotics are authorised for use in multiple animal species, and it is not possible to determine from sales data how much is used in each species. The UK-VARSS report has increasingly included data on usage in different animal production sectors and works in partnership with the livestock industry to develop, facilitate and coordinate antibiotic usage data collection systems. These data are reported voluntarily by the livestock sectors and are presented in **Chapter 2**.

While the term antimicrobial resistance (AMR) encompasses resistance of different types of organisms (bacteria, viruses, fungi, and parasites) to the drugs used to treat them, it is used throughout this report to refer to bacterial resistance to antibiotics specifically. The VMD collates data from government laboratories on antibiotic resistance in bacteria obtained from food-producing animals. This includes zoonotic bacteria, which are an integral part of our AMR surveillance, due to the potential for resistant bacteria and/or resistance genes to transfer between animals and people. This antimicrobial resistance data is collected under the framework of two surveillance schemes – harmonised monitoring and clinical surveillance. The harmonised monitoring scheme is a UK wide programme in which we test bacteria from the gut of healthy pigs and poultry at slaughter, giving us a representative picture of resistance in key livestock species entering the food chain, and results from this are presented in **Chapter 3**. Clinical surveillance involves testing of bacteria that have been isolated from diagnostic samples submitted by farmers and private veterinarians to government laboratories in England and Wales, and results from this are presented in **Chapter 4**.

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

For additional context whilst reading the report, please see below 1) a table containing a list of all antibiotics referred to throughout the report split by those authorised and not authorised

for use in animals and 2) a table of descriptions used throughout the resistance chapters used when referring to resistance levels.

Table 1: Antibiotics referred to throughout the report, grouped by antibiotic class.

Antibiotic class	Authorised for use in animals	Not authorised for use in animals
Aminoglycosides	Apramycin, framycetin, gentamicin, kanamycin, neomycin, paromomycin, spectinomycin, streptomycin	Amikacin
Amphenicols	Florfenicol	Chloramphenicol
Beta-lactams: 1st generation cephalosporins	Cefalexin, cefalonium, cefapirin	
Beta-lactams: 3rd generation cephalosporins	Cefoperazone, cefovecin, cefquinome, ceftiofur	Cefotaxime, cefpodoxime, ceftazidime
Beta-lactams: Carbapenems		Ertapenem, imipenem, meropenem
Beta-lactams: Penicillins	Amoxicillin, amoxicillin/clavulanate, ampicillin, benzylpenicillin, cloxacillin, phenoxymethylpenicillin	Temocillin
Glycylcyclines		Tigecycline
Lincosamide	Clindamycin, lincomycin, pirlimycin	
Macrolides	Erythromycin, gamithromycin, spiramycin, tildipirosin, tilmicosin, tulathromycin, tylosin, tylvalosin	Azithromycin
Polymyxins	Colistin	
Quinolones	Danofloxacin, enrofloxacin, marbofloxacin, orbifloxacin, oxolinic acid (under special import scheme), pradofloxacin	Nalidixic acid, ciprofloxacin
Tetracyclines	Chlortetracycline, doxycycline, oxytetracycline, tetracycline	
Trimethoprim/ sulphonamides	Sulfadiazine, sulfadimethoxine, sulfadimidine, sulfadoxine, sulfamethoxazole, trimethoprim	
Other	Novobiocin, metronidazole, tiamulin	Furazolidone

Table 2: Descriptions of percentage resistance levels referenced in this report (Chapter 3), using the EFSA definitions.

Description of resistance level	Equivalent percentage resistance range
Rare	<0.1%
Very low	0.1% to 1%
Low	>1% to 10%
Moderate	>10% to 20%
High	>20% to 50%
Very high	>50% to 70%
Extremely high	>70%

CHAPTER 1

Sales of veterinary antibiotics

1.1 Summary

UK sales of veterinary antibiotics for food-producing animals in 2022, adjusted for the animal population, were the lowest recorded to date at 25.7 mg/kg. This represents a 9% (2.6 mg/kg) decrease since 2021 and a 59% (36.6 mg/kg) decrease since 2014.

Sales of Highest Priority-Critically Important Antibiotics (HP-CIAs) for food-producing animals remain very low at 0.12 mg/kg. This represents a reduction of 82% (0.5 mg/kg) since 2014. Overall, in 2022, HP-CIAs accounted for less than 0.5% of the total antibiotic sales for food-producing animals.

The total quantity of antibiotic sold for all animals (which includes both companion animals and food-producing animals) was 193 tonnes in 2022, the lowest recorded amount to date. This represents a 9% (19.4 tonne) decrease since 2021, and a 57% (253.6 tonne) decrease since 2014. Sales of HP-CIAs for all animals was 0.91 tonnes representing a small increase of 0.01 tonnes (10 kg) since 2021 but a reduction of 81% (3.9 tonnes) since 2014. For the second year in a row, no colistin was sold for use in animals.

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 Supplementary Material 1 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 B.

Data have been analysed using methodology harmonised across Europe (ESVAC).

Note that, for ease of reading, the data has in most cases been rounded to one decimal place. However, the percentage changes have been calculated using the exact number. Antibiotics were considered HP-CIAs if they are within “Category B” in the Antimicrobial Expert Group report (AMEG), i.e. third- and fourth-generation cephalosporins, polymyxins (e.g. colistin) and quinolones/fluoroquinolones. Note that there are no quinolones licensed to be used in animals, so we refer to fluoroquinolones throughout this chapter. Data has been presented graphically throughout, but the raw data can be found in Supplementary Material 1.

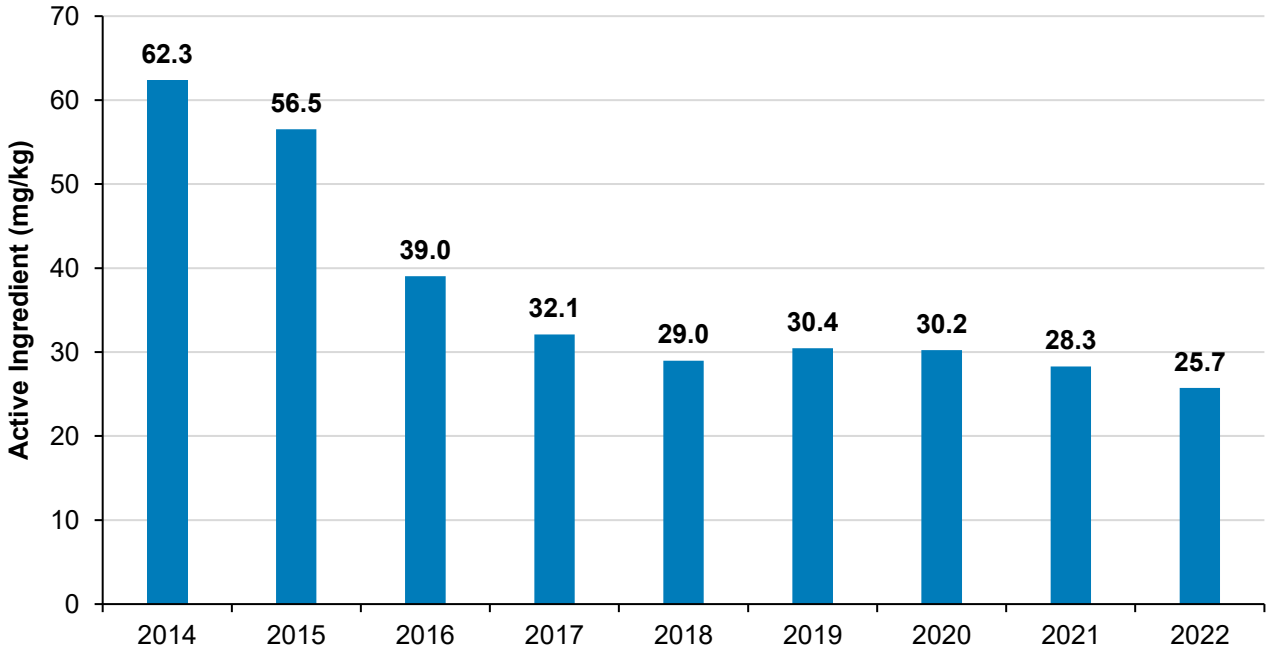
1.3 Results

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

1.3.1.1 Sales for food-producing animals (mg/kg)

The sales of antibiotics for food-producing animal species in 2022 were 25.7 mg/kg, the lowest recorded figure to date, representing a decrease of 9% (2.6 mg/kg) since 2021 and 59% (36.6 mg/kg) since 2014 (**Figure 1.1**).

Figure 1.1: Active ingredient adjusted for population (mg/kg) of antibiotics sold for use in food-producing animals, 2014 to 2022.



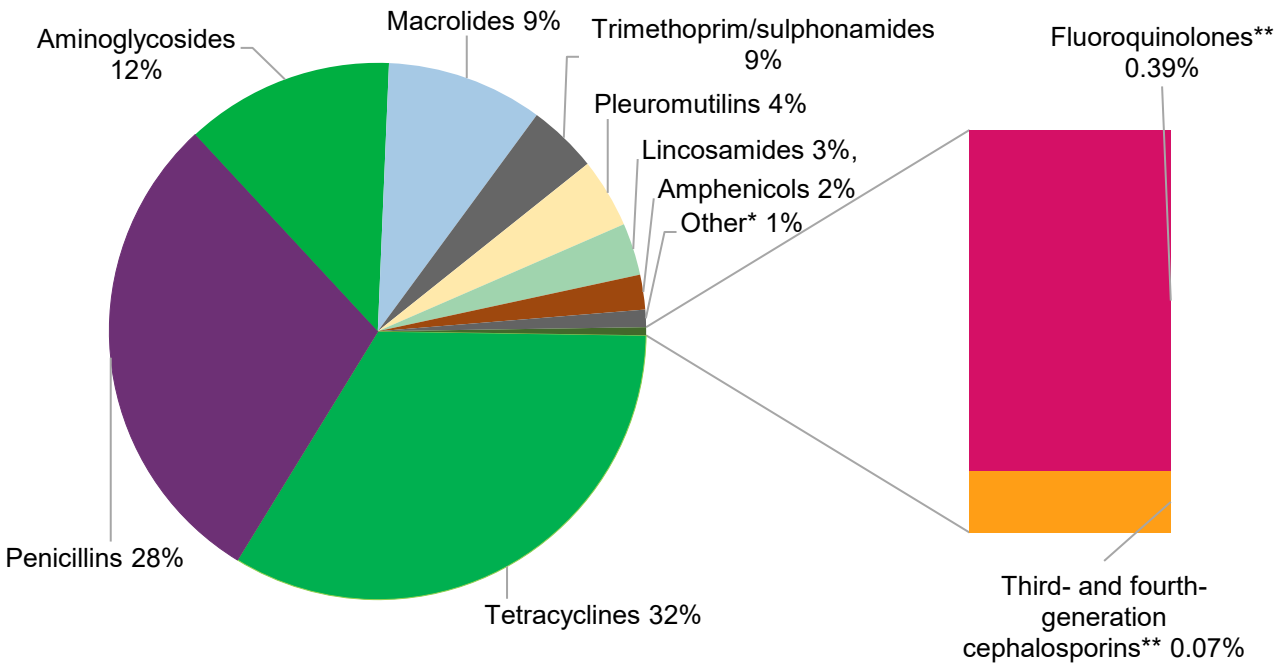
1.3.1.2 Sales by antibiotic class for food-producing animals (mg/kg)

Five antibiotic classes account for 90% of sales, tetracyclines (32%), penicillins (28%), aminoglycosides (12%), macrolides (9%) and trimethoprim/sulphonomides (9%) (**Figure 1.2**). Sales of all these antibiotic classes fell since 2021, except for aminoglycosides which rose slightly.

Sales of both tetracyclines and penicillins decreased between 2021 and 2022, by 14% (1.3 mg/kg) and 4% (0.3 mg/kg) respectively. Tetracycline sales have now decreased every year since 2014 (**Figure 1.3**).

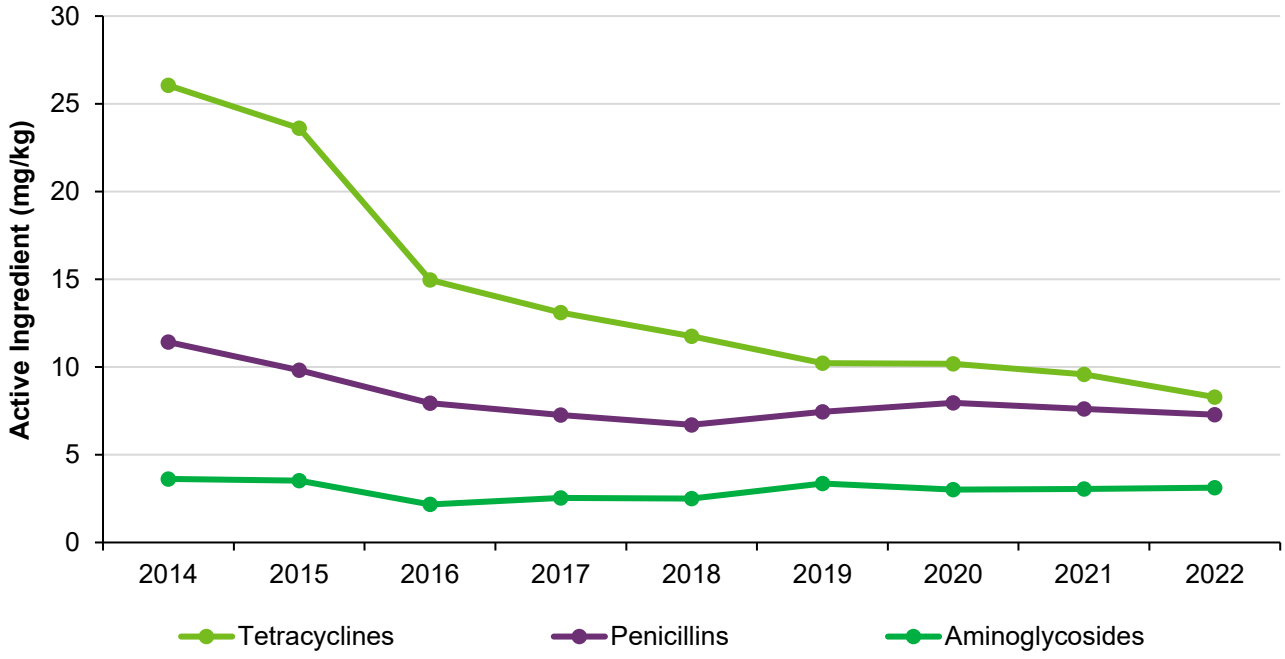
Sales of aminoglycosides increased between 2021 and 2022 by 3% (0.08 mg/kg) but have reduced by 14% (0.5 mg/kg) since 2014.

Figure 1.2: Active ingredient (% weight) of antibiotics by antibiotic class sold for use in food-producing animals, 2022.



* First and second generation cephalosporins and imidazole derivates
** Fluoroquinolones, third- and fourth-generation cephalosporins and colistin fall under the category of an HP-CIA

Figure 1.3: Top three active ingredients adjusted for population (mg/kg) of non-HP-CIA antibiotics by antibiotic class sold for use in food-producing animals, 2014 to 2022.

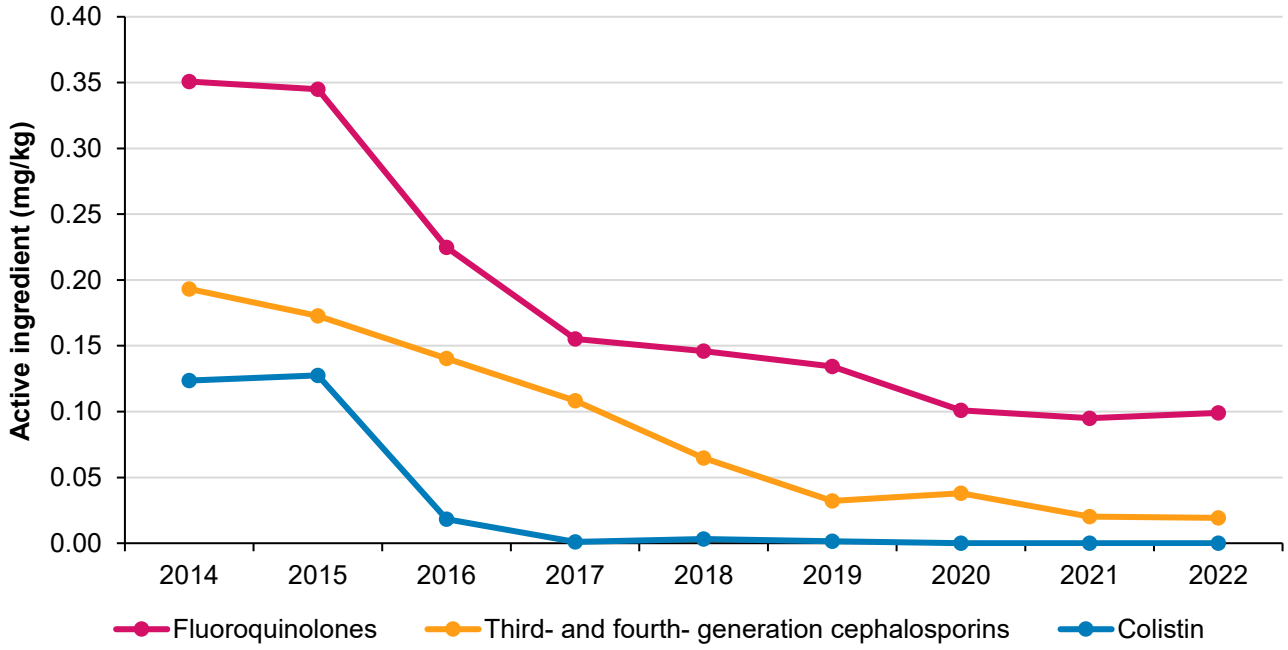


Sales over time of HP-CIAs for food-producing animals are shown in **Figure 1.4** and in 2022 were 0.12 mg/kg, which represents less than 0.5% of the overall antibiotic sales. Sales of HP-CIAs in food-producing animals reduced year on year between 2014 to 2021 but

increased very slightly by 0.003 mg/kg between 2021 and 2022. However, they still remain at very low levels and have reduced by 82% (0.5 mg/kg) since 2014.

Third- and fourth-generation cephalosporin sales were 0.02 mg/kg in 2022, a reduction of 0.0009 mg/kg since 2021 whereas fluoroquinolone sales were 0.10 mg/kg, an increase of 0.004 mg/kg since 2021. For the second year in a row, no colistin was sold in the UK for use in animals in 2022.

Figure 1.4: Active ingredient adjusted for population (mg/kg) of HP-CIAs sold for use in food-producing animals, 2014 to 2022.



1.3.1.3 Sales by route of administration for food-producing animals (mg/kg)

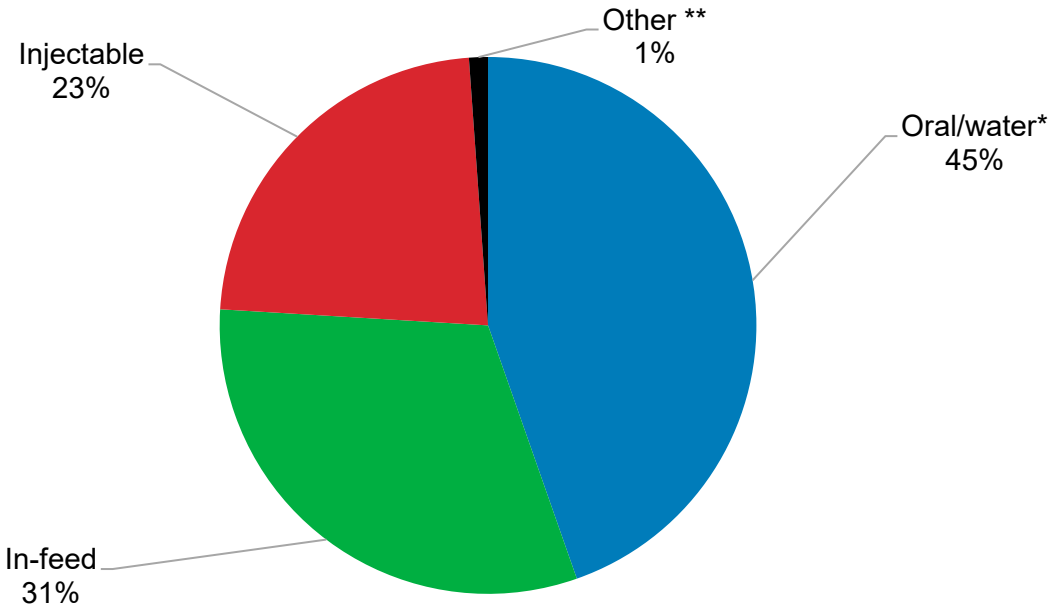
More targeted administration of antibiotics reduces the risk of development and spread of AMR. The agriculture industry and the vet profession has focused on encouraging more in-water use, which can allow for more targeted antibiotic administration than in-feed. In-feed use refers to premix products, whereas oral/water products refer to oral powders, pastes, solutions, and bolus preparations.

In 2022, 45% was indicated for oral/water use, 31% was for in-feed use, and 23% was injectables (**Figure 1.5**). Between 2021 and 2022, sales of in-feed products decreased by 16% (1.6 mg/kg) (**Figure 1.6**) whereas sales of oral/water decreased to a lesser degree, by 2% (0.2 mg/kg). Oral/water sales have increased as a percentage of total use from 28% in 2014 to 45% in 2022 and, for the second year running, is higher in-feed sales. This change demonstrates a change to more targeted antibiotic administration.

Sales of injectable antibiotics have remained fairly stable since 2014. Injectable treatments are considered to have a lesser risk of contributing to development of antimicrobial resistance compared to oral administration. This is because injectable treatments are less

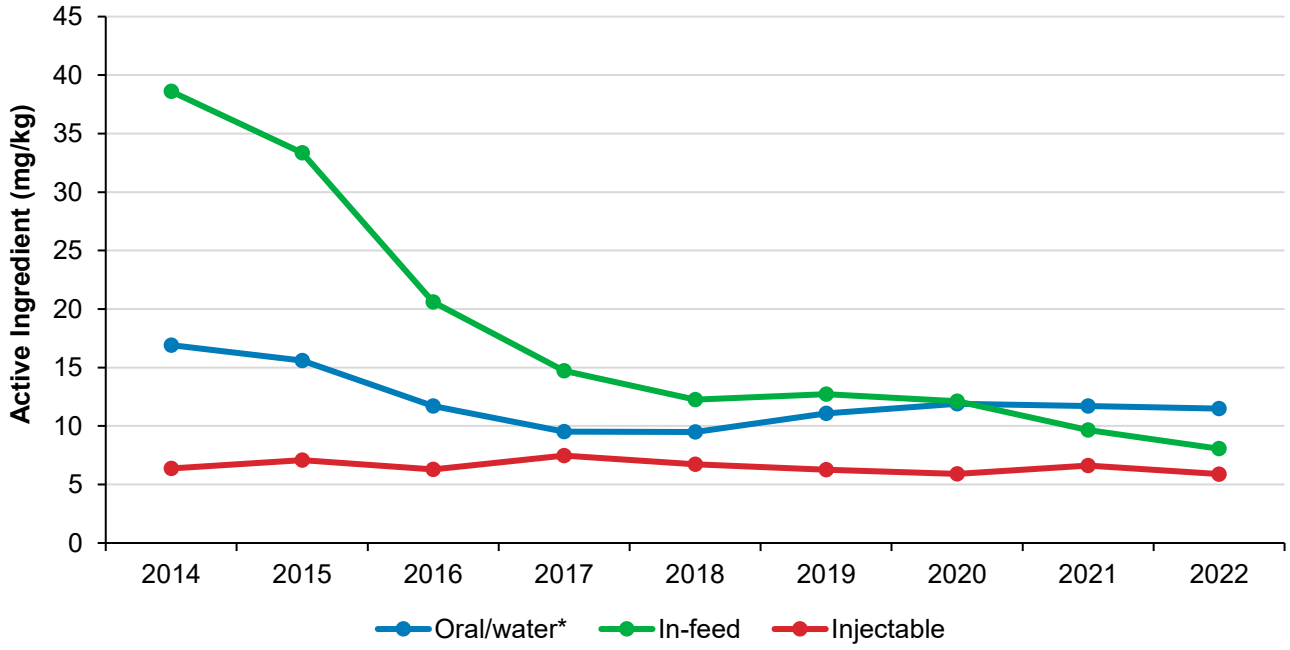
likely to result in the bacteria within the gut flora being exposed to antibiotics which lessens the risk of resistance developing (AMEG).

Figure 1.5: Pie chart depicting the active ingredient of antibiotics by route of administration sold for use food-producing animals in percentage weight for 2022.



* Oral powders, oral pastes, oral solutions, and bolus preparations.
** Includes intramammary dry and lactating cow, and intrauterine preparations

Figure 1.6: Active ingredient (mg/kg) of antibiotics by main routes of administration sold for use in food-producing animals, 2014 to 2022.



* Include oral powders, oral pastes, oral solutions, and bolus preparations

1.3.1.4 Sales of intramammary antibiotic products (course doses)

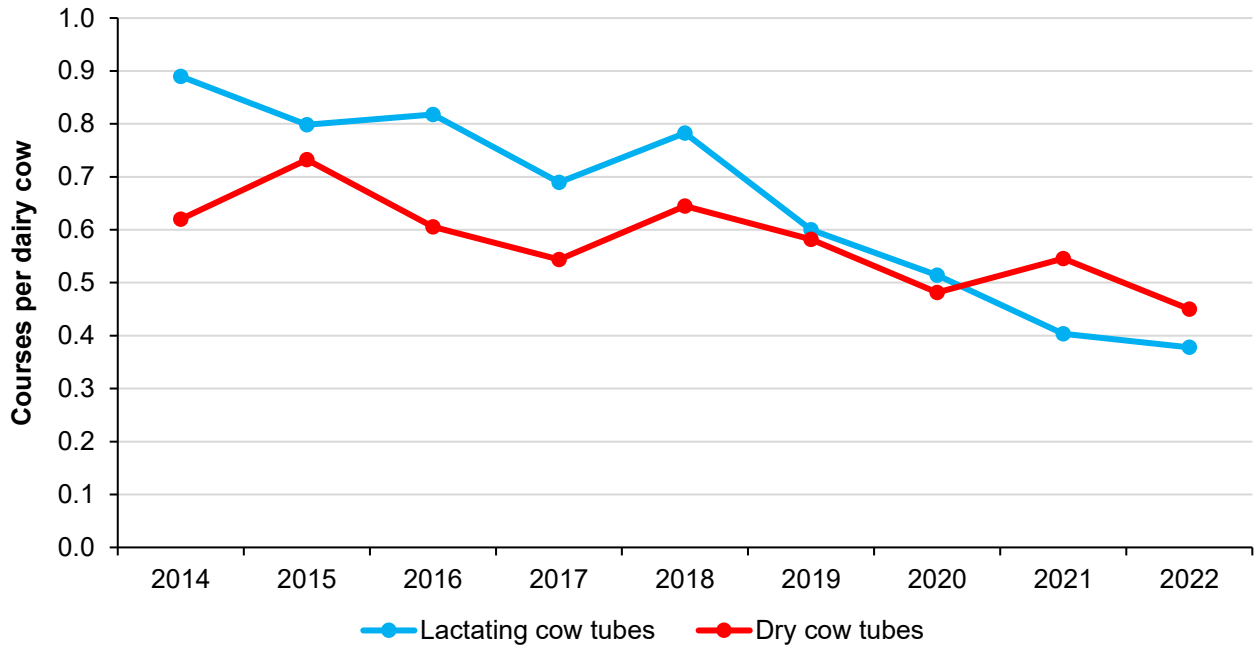
Sales of dry and lactating cow products analysed using the ESVAC defined course dose methodology (DCDvet) are shown in **Figure 1.7**. The DCDvet represents the average number of courses per dairy cow using a standard course dose of four tubes per dry cow and three tubes for lactating cow treatments.

Between 2021 and 2022, sales of lactating cow products reduced by 6% (0.03 course doses), a continuation of a year-on-year decrease seen since 2018. Sales of dry cow intramammary products decreased by 18% (0.10 course doses) between 2021 and 2022, reversing the increase in sales seen between 2020 and 2021 and representing the lowest sales recorded. Sales of HP-CIA intramammary products decreased by 13% (0.002 course doses) between 2021 and 2022 to 0.014 course doses, also the lowest figure to date. This represents a 96% (0.35 course dose) reduction since 2014.

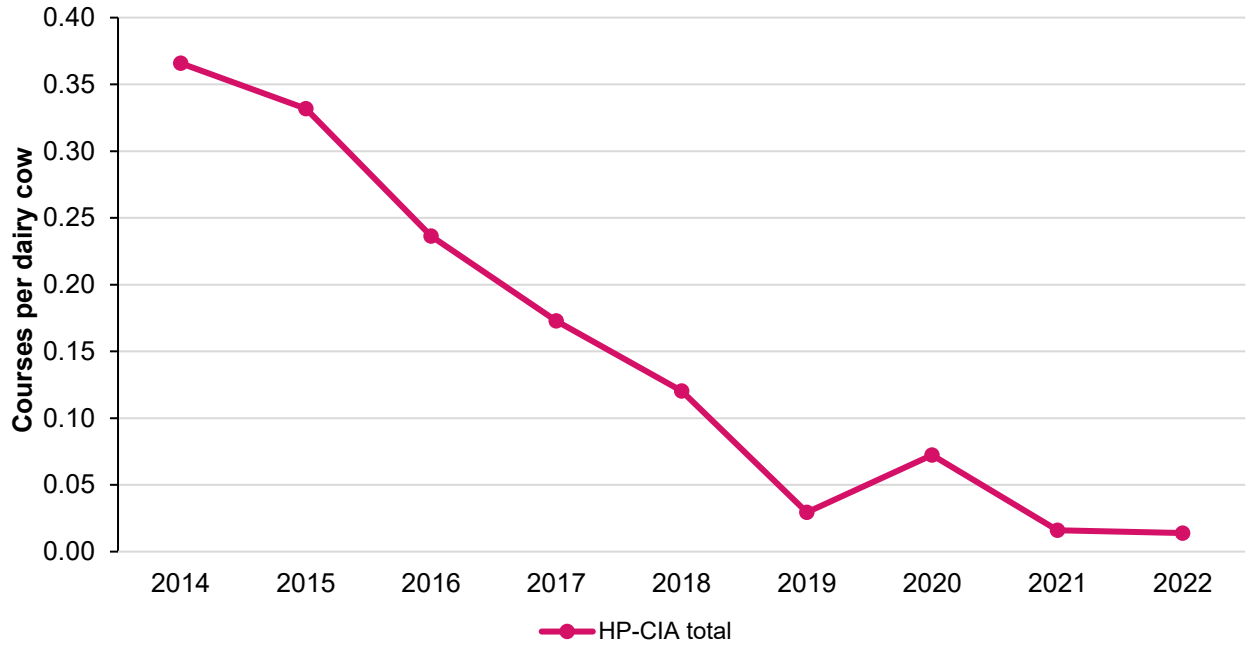
If the available products were considered clinically unsuitable by the veterinary surgeon, alternative products authorised outside the UK can be imported on a case-by-case basis under the Special Import Scheme. These lactating cow products are not captured in the antibiotic sales data.

Figure 1.7: Sales of (A) dry and lactating cow intramammary products (courses per dairy cow), 2014–2022, (B) Sales of HP-CIA intramammary products (courses per dairy cow, 2014 to 2022

(A)



(B)

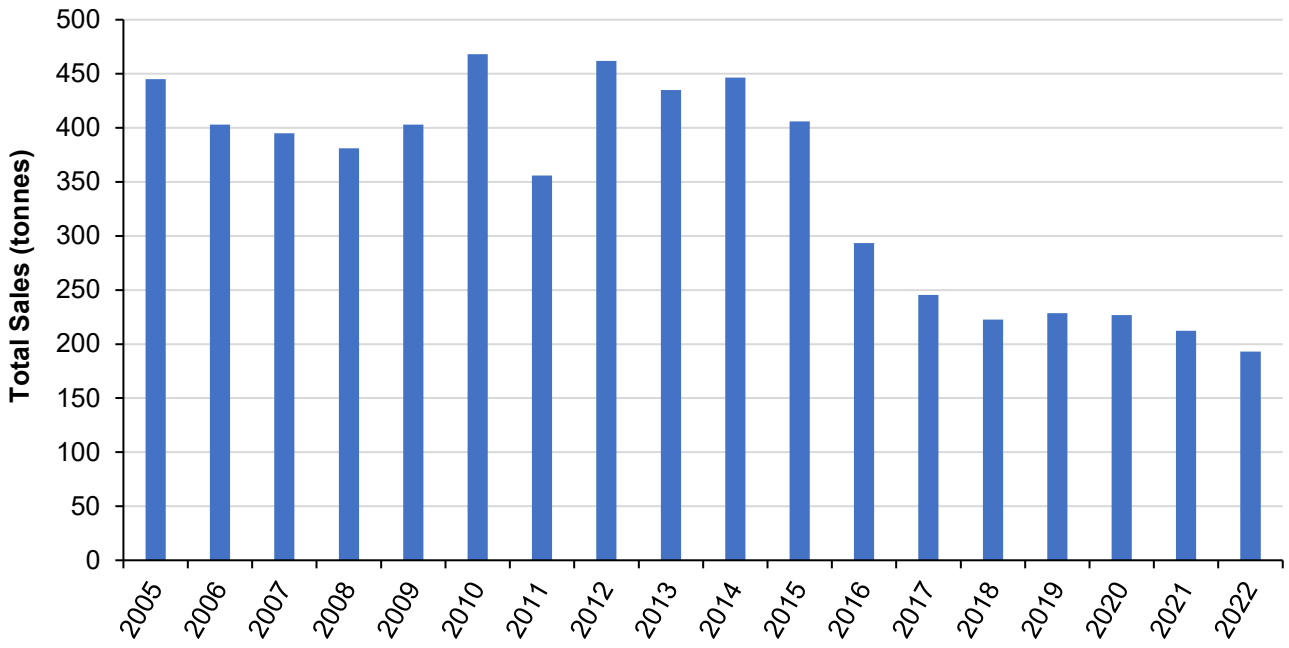


1.3.2 Total sales of antibiotics for all animals (tonnes)

Total sales of antibiotics for all animals (food-producing animals and companion animals) are measured in total weight (tonnes) as the mg/kg methodology only applies to food producing animals. Results are shown in **Figure 1.8**.

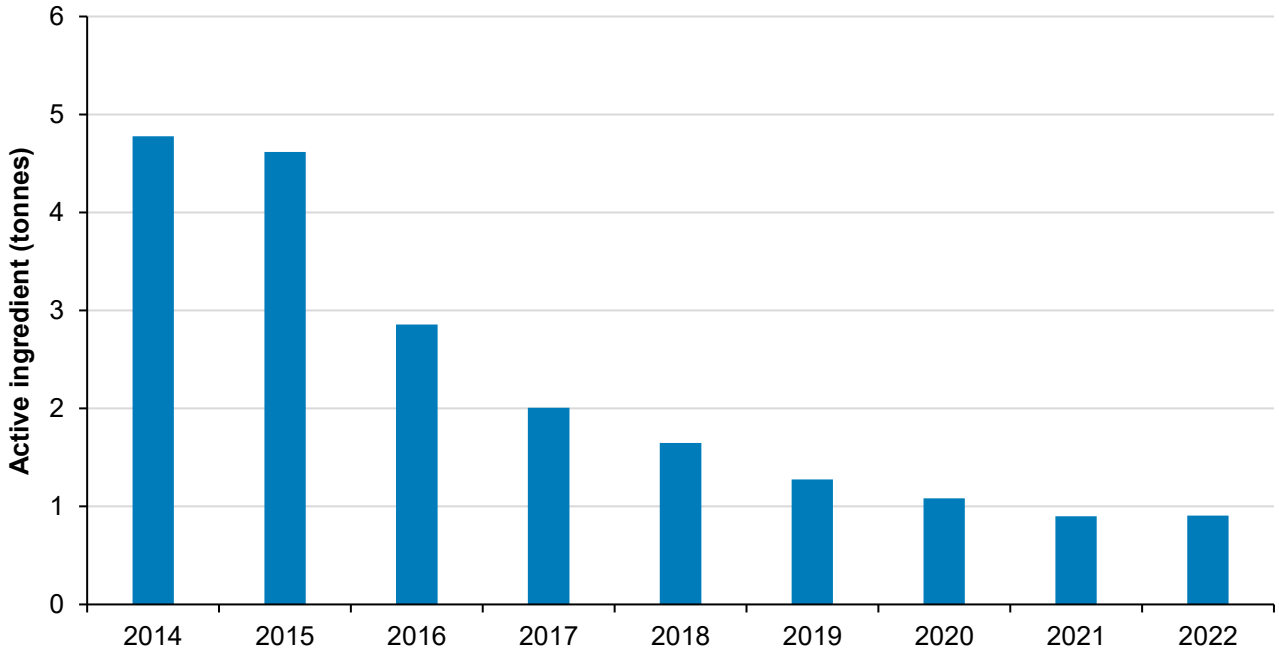
The total quantity of antibiotic active ingredient sold in 2022 was 193 tonnes, the lowest recorded figure to date. This is a 9% (19.4 tonnes) decrease since 2021, and a 57% (253.6 tonnes) decrease since 2014.

Figure 1.8: Active ingredient (tonnes) of antibiotics sold for use in all animals, 2005 to 2022.



Total sales of HP-CIAs for all animals are shown in **Figure 1.9**. Sales of HP-CIA in 2022 is 0.91 tonnes, representing a small increase of 0.01 tonnes (10 kg) since 2021 but a reduction of 81% (3.9 tonnes) since 2014. HP-CIA sales in tonnes accounted for less than 0.5% of total antibiotic sales in 2022. For the second year in a row, no colistin was sold for use in animals.

Figure 1.9: Active ingredient (tonnes) of HP-CIA sold for use in all animals, 2014 to 2022.



1.3.3 Total sales of antibiotics by species indication (tonnes)

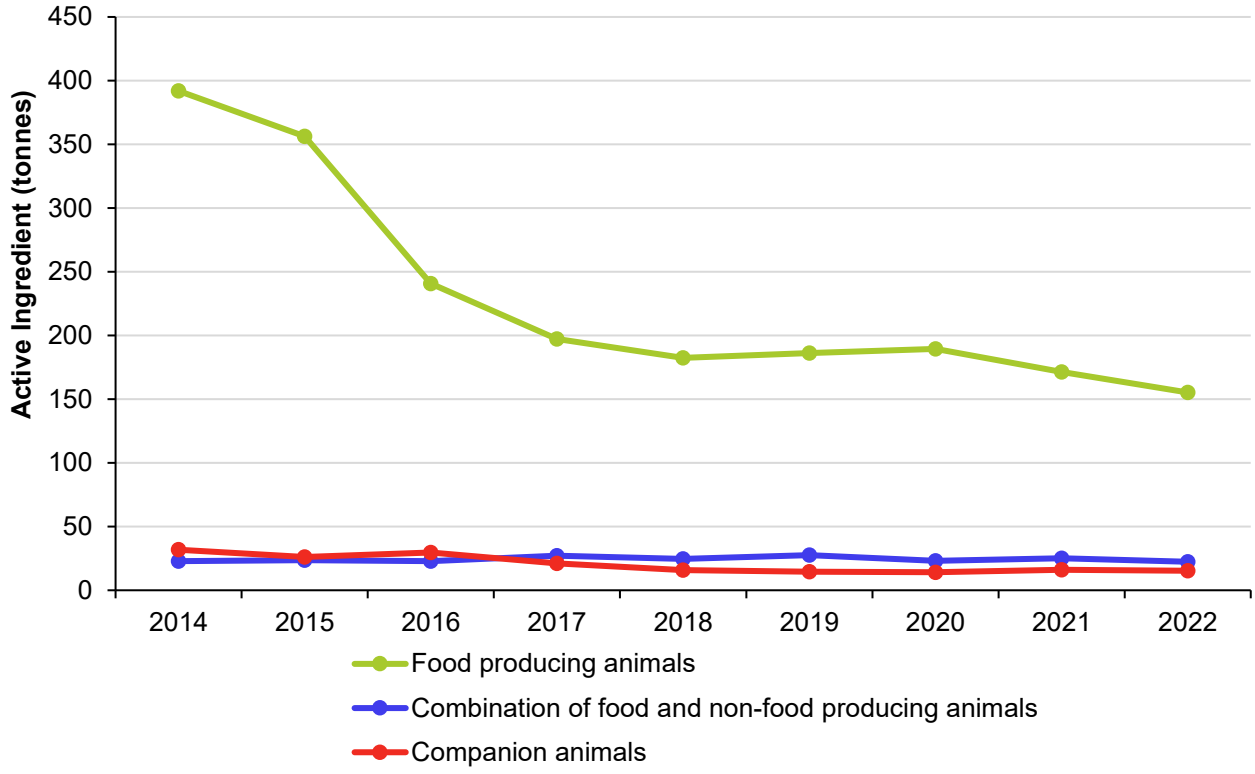
In 2022, 155.3 tonnes of antibiotic sales (80% of the total) were attributed to products licensed for food-producing animal species only (**Figure 1.10**). This is a decrease of 16 tonnes since 2021, largely due to a 15 tonne decrease in sales of products authorised for pigs and/or poultry.

Sales of products licensed for companion animals only accounted for 8% of total sales (15.3 tonnes) and this has decreased by 4.5% (0.72 tonnes) since 2021.

Sales of products indicated for both combination of food-producing and companion animals also decreased by 11% (2.71 tonnes) to 22.4 tonnes. This category is comprised of 99.8% injectable products.

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. For 2022, the sales and use data are showing a comparable trend.

Figure 1.10: Active ingredient (tonnes) of antibiotics sold by species indication, 2014 to 2022.

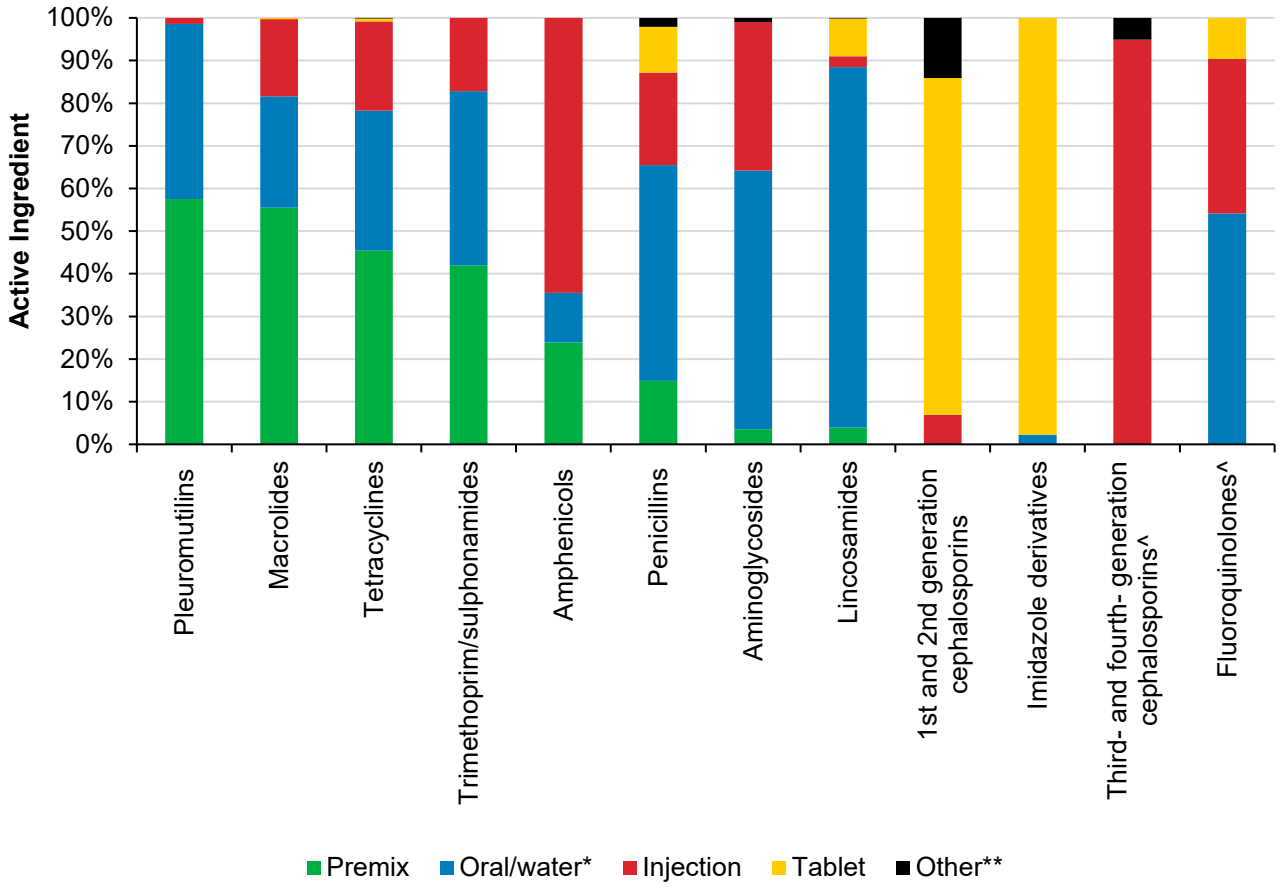


1.3.3.1 By antibiotic class and route of administration for all animal species (tonnes)

When looking at antibiotic sales of the most sold products for all animal species, 45% of tetracycline use was in-feed and 33% was for oral/water use whereas, for penicillins, 51% was indicated for oral/water use and 22% as an injection (**Figure 1.11**). Trimethoprim-sulphonamides and macrolides were mostly administered in-feed (accounting for 42% and 55% of their use respectively) whereas aminoglycosides were most administered by oral/water (61%) and injection (35%) (**Figure 1.11**).

Of the HP-CIAs, 95% of third- and fourth-generation cephalosporins sold were injectables, with the remainder being intra-mammary preparations for cattle. Thirty-six percent of fluoroquinolones were used as injectables, with the remainder used as oral/water (54%) and tablets (10%).

Figure 1.11: Active ingredient (% weight) of antibiotics by antibiotic class and route of administration sold for all animals, 2022.



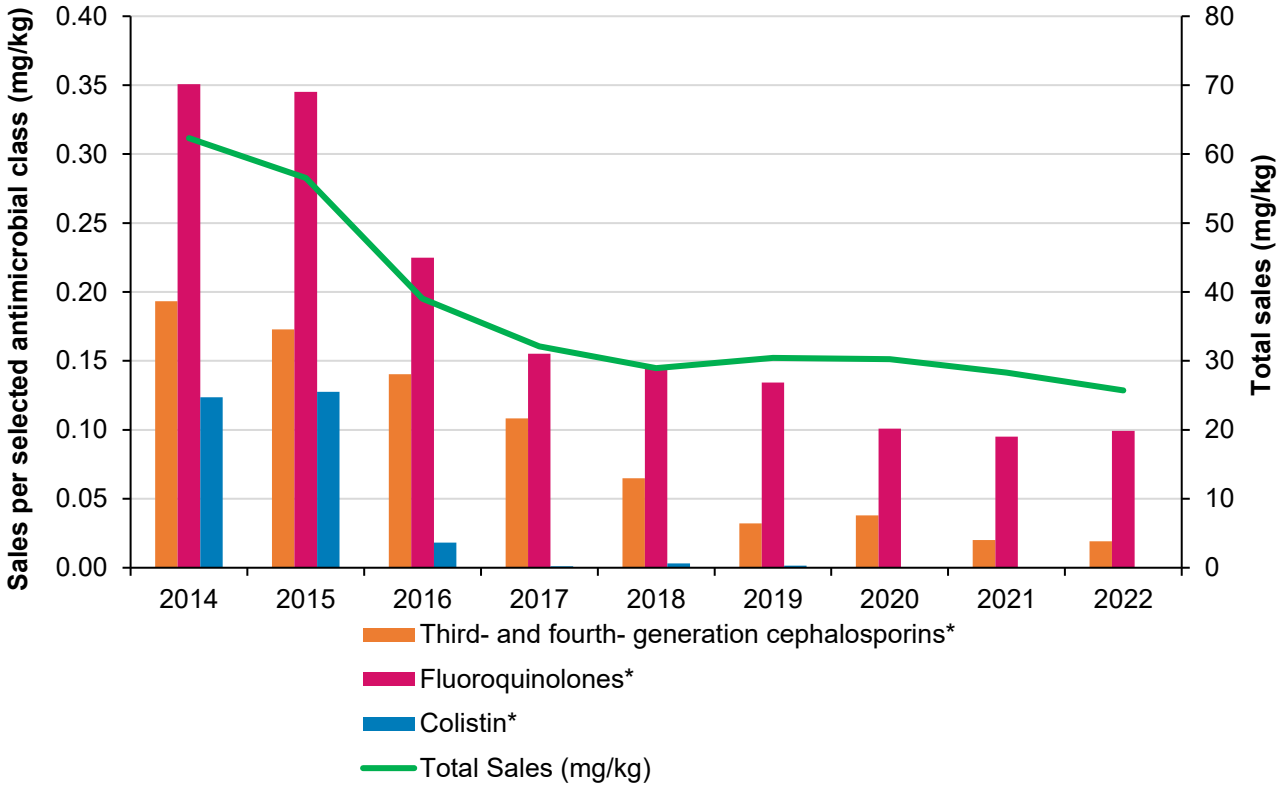
^ Fluoroquinolones and third- and fourth-generation cephalosporins fall under the category of an HP-CIA
* Oral powders, oral pastes, oral solutions and bolus preparations
** Intramammary and intrauterine preparations

1.3.4 Harmonised outcome indicators for antibiotic use

Harmonised indicators are important to monitor trends in a consistent way, and in a way that is comparable across different regions and countries. A number of different indicators for monitoring antibiotic sales in animals have been developed globally. To allow for consistency with previously published data and harmonisation with other countries in the European region, we are reporting the data using the EU harmonised indicators. These were published by the European Centre for Disease Prevention and Control (ECDC), European Food Safety Authority (EFSA) and EMA in 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 1.1**). Secondary indicators are the sales in mg/PCU of third- and fourth-generation cephalosporins, quinolones (and percentage of fluoroquinolones) and polymyxins, which measures HP-CIA use (**Figure 1.4**). In the UK, all quinolones sold for use in food-producing animals are fluoroquinolones (although the quinolone oxolinic acid is imported under the Special Import Scheme for use by the fish sector; see **Chapter 2.3.4**), and colistin is the only polymyxin that has been sold for use in food-producing animals. The data show that both primary and secondary indicators have decreased since 2016 (**Figure 1.12**).

Figure 1.12: Harmonised primary outcome indicators for antibiotic consumption in food-producing animal species in the UK; 2014 to 2022.



*Third- and fourth-generation cephalosporins, fluoroquinolones and colistin fall under the category of HP-CIA

A number of different indicators for monitoring antibiotic sales in animals have been developed globally, and overarching global indicators published by The Quadripartite [which consists of four main agencies: the Food and Agriculture Organization of the United Nations (FAO), United Nations Environment Programme (UNEP), World Health Organization (WHO) and World Organisation for Animal Health (WOAH)] and are described in more detail in the Supplementary Material 1.

1.4 Methods

Data collection and validation

Pharmaceutical companies supplied annual sales of all authorised veterinary antibiotics to the VMD in accordance with the Veterinary Medicines Regulations. Upon receipt, data were collated and validated, and product data entries were compared to those submitted in previous years. If there were large discrepancies between data provided in successive years, data validity was 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 C).

Tonnes of active ingredient

The weight of antibiotic active ingredient sold is calculated 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.

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 historic UK-VARSS methodology. Since UK-VARSS 2015 (published in 2016), sales data have been reported using ESVAC methodology in recognition of the utility of regional harmonisation of surveillance. Note that data presented in mg/kg for food-producing animals (which equals mg/PCU) do not include topical products or tablets as, in line with the ESVAC methodology, tablets 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 Supplementary Material 1. 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 (Supplementary Material 1).

Mg/kg Population Correction Unit (PCU) for food-producing animals

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 for food producing animals were analysed using the Population Correction Unit (PCU), which was formulated by the European Medicines Agency and represents the weight of the food producing animal population (in kg) at risk of antibiotic treatment by using standardised weights that represent the average weight at time of treatment. 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 kg 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 S1.2.1 of Supplementary Material 1 and full technical details on PCU methodology can be found in the 2011 ESVAC report. 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

The UK-VARSS methodology changed in 2021, with amendments to International Unit factors and corrections to a number of products active ingredients content and strength. As a result, minor changes can be seen in historical mg/kg figures.

CHAPTER 2

Usage of veterinary antibiotics by animal species

2.1 Summary

The key trends are as follows:

- **Pigs –** Antibiotic use decreased by 18% (15.5 mg/kg) between 2021 and 2022, from 87.3 to 71.8 mg/kg, which represents a 74% reduction since data was first published in 2015. Use of HP-CIAs also reduced from 0.03 mg/kg in 2021 to 0.01 mg/kg in 2022, which represents a 99% reduction since 2015. The sector continues to demonstrate an ongoing shift away from in-feed medication towards more targeted in-water delivery.
- **Turkeys –** Antibiotic use decreased by 17% (7.2 mg/kg) between 2021 and 2022, from 42.6 to 35.4 mg/kg, which represents an 84% reduction since data was first published in 2014. The only HP-CIAs used in turkeys are fluoroquinolones, and their use reduced from 0.006 mg/kg in 2021 to 0.0002 mg/kg in 2022.
- **Broilers –** Antibiotic use increased by 3% (0.4 mg/kg) between 2021 and 2022 from 13.7 mg/kg to 14.1 mg/kg, which represents a 71% reduction since data was first published in 2014. There were no HP-CIAs used in meat broilers in 2022.
- **Ducks –** Antibiotic use decreased by 83% (1.4 mg/kg) between 2021 and 2022 from 1.7 mg/kg to 0.3 mg/kg, which represents a 98% reduction since data was first published in 2014. There were no HP-CIAs used in 2022.
- **Laying Hens** – Antibiotic use decreased by 29% (0.1% bird days) between 2021 to 2022, from 0.33% bird days to 0.23% bird days, which represents a 65% reduction since data was first published in 2016. There were no HP-CIAs used in 2022.
- **Gamebirds –** Antibiotic use decreased by 25% (2.2 tonnes) between 2021 and 2022, from 8.9 tonnes to 6.7 tonnes, which represents a 66% reduction since data was first published in 2016. Use of HP-CIAs also reduced from 26.5 kg in 2021 to 23.2 kg in 2022, which represents a 64% reduction since data was first published in 2016. However, unlike other sectors, antibiotic use is not corrected for by the size of the underlying population, and therefore changes in usage are influenced by the gamebird population size. Between 2021 and 2022, the gamebird population decreased by an estimated 17% due to issues with sourcing eggs and chicks from France caused by avian influenza.
- **Salmon –** Antibiotic use decreased by 57% (24.5 mg/kg) between 2021 and 2022, from 43.1 mg/kg to 18.6 mg/kg, which represents a 15% increase since data was first published in 2017. There were no HP-CIAs used in 2022.

- **Trout –** Antibiotic use increased by 35.2 mg/kg between 2021 and 2022 from 9.0 mg/kg to 44.1 mg/kg. This is the highest use seen in the trout sector since data was first published in 2017 and was due to an outbreak of *Aeromonas salmonicida* on a small number of production sites. The only HP-CIA used in trout is the quinolone oxolinic acid, and its use reduced from 3.2 mg/kg in 2021 to 2.2 mg/kg in 2022, which represents a 67% reduction since 2017.

2.2 Introduction

All antibiotics used in UK animals must be prescribed by a veterinarian. Antibiotic use refers to the amount of antibiotics administered or to be administered, for example prescribed, dispensed, and/or delivered to the animal owner/vets for a defined animal sector and/or animal production sector.

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.

Capturing antibiotic use 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 explore any correlation between antibiotic use and antibiotic resistance. Data collection systems also allow for benchmarking, enabling vets and farmers to discuss antibiotic use, identify and share good practice and provide a stimulus for implementing effective stewardship interventions.

The VMD is working in partnership with all major food-producing animal sectors to develop, facilitate and coordinate antibiotic use data collection systems. This chapter describes the progress achieved so far. Data and commentary are provided by the food-producing animal sectors. Data has been presented graphically throughout, but full data sets can be found in Supplementary Material 1. Methodology is outlined in section 2.4.

2.3 Results

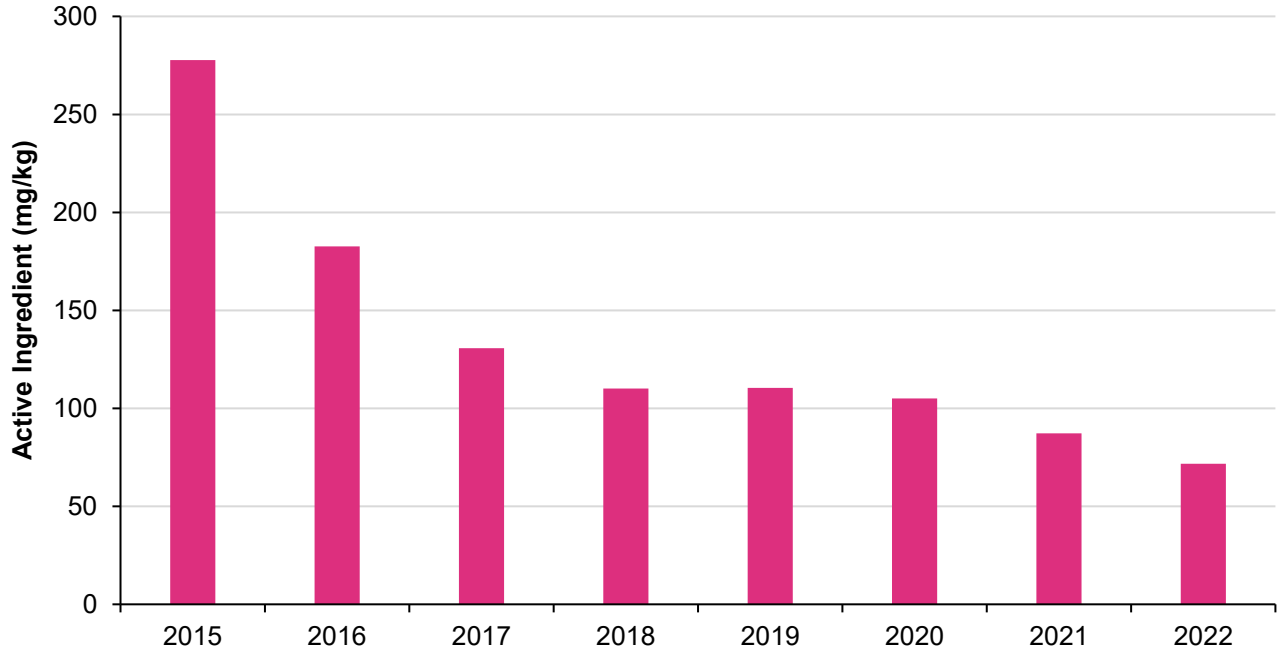
2.3.1 Pigs

2.3.1.1 Antibiotic use data

Data from the electronic Medicines Book for Pigs (eMB Pigs), representing greater than 95% of UK pig production, shows that total antibiotic use in pigs was 56.4 tonnes for 2022, which represents 71.8 mg/kg, when adjusted for population. This is a decrease of 18% (15.5 mg/kg) since 2021 and 74% (205.9 mg/kg) since data was first reported in 2015 (**Figure 2.1**). This means that the pig sector have already exceeded their sector target (which was to get to 73.5 mg/kg by 2024).

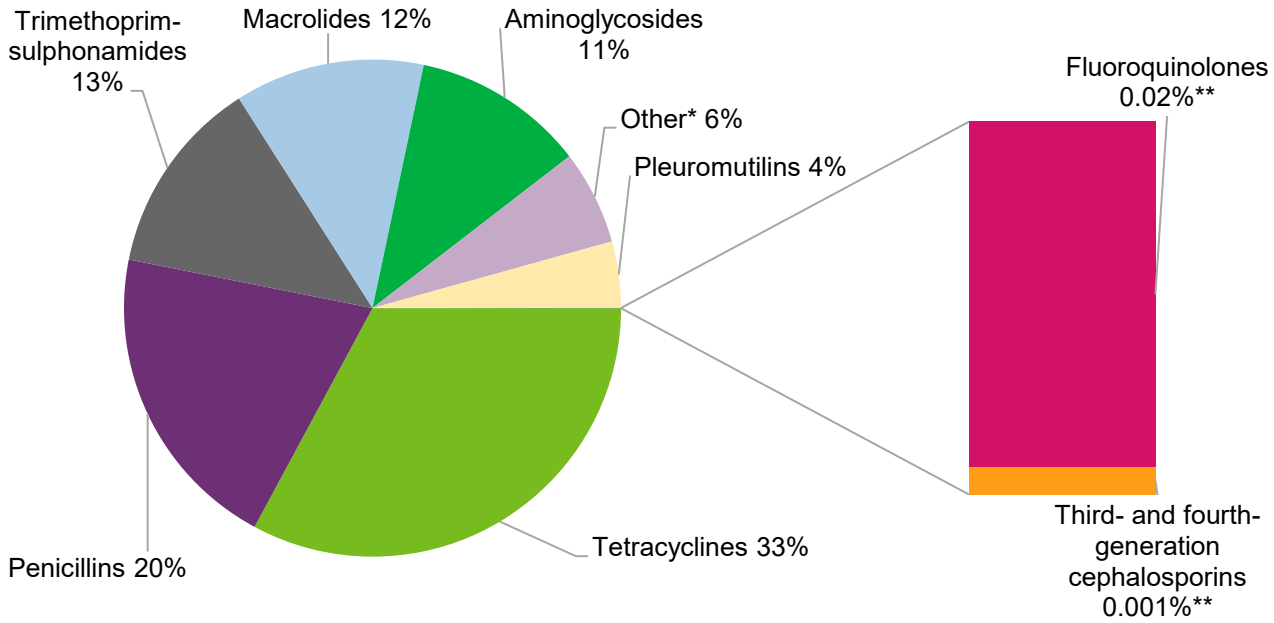
The use of antibiotics in pigs is broken down in **Figure 2.1**, **2.2** and **2.3**.

Figure 2.1: Active ingredient adjusted for population (mg/kg) of antibiotics reported in eMB pigs, 2015 to 2022.



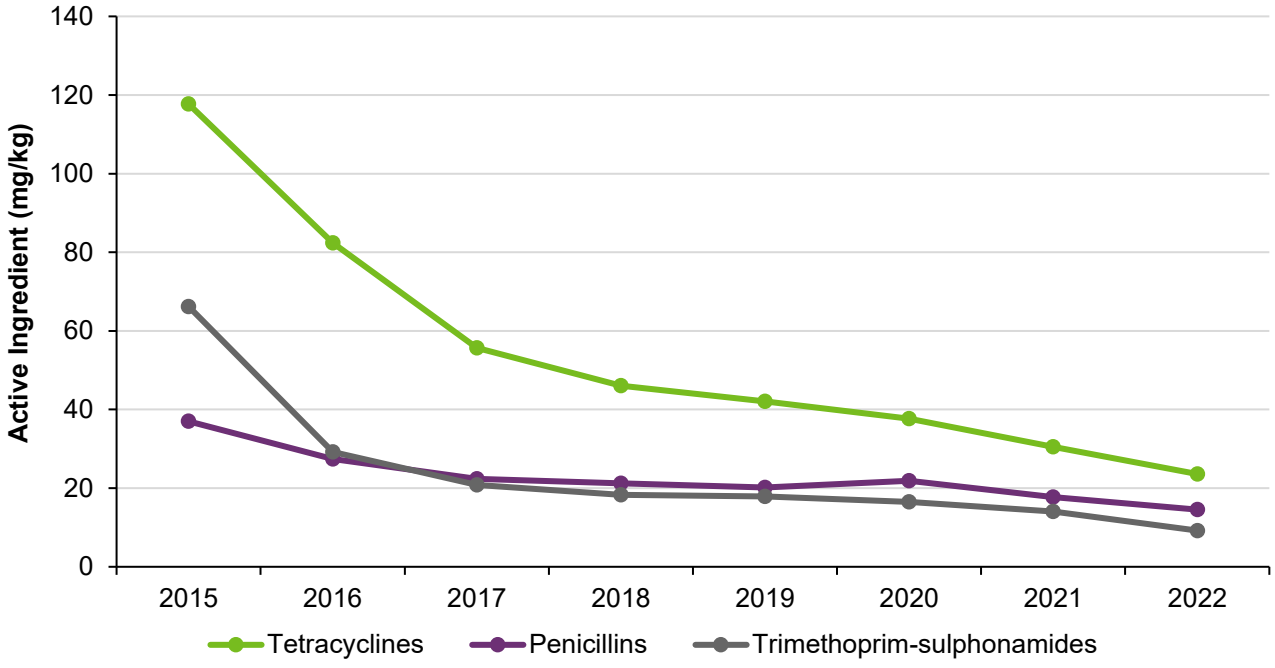
Tetracyclines remain the most used antibiotic class, representing 33% of antibiotic active ingredient used in 2022 (**Figure 2.2**), followed by penicillins (20%) and trimethoprim-sulphonamides (13%). Since data was first published in 2015, tetracyclines, penicillins and trimethoprim-sulphonamides have reduced by 80% (94.1 mg/kg), 61% (22.4 mg/kg) and 86% (57.0 mg/kg) respectively (**Figure 2.3**). All antibiotic classes decreased between 2021 and 2022 except for lincosamides, which increased by 1.5 mg/kg, but which still only accounts for 5% of overall use.

Figure 2.2: Active ingredient (% weight) of antibiotics by antibiotic class reported in eMB pigs, 2022.



* Lincosamides and amphenicols
** Fluoroquinolones and third-and fourth-generation cephalosporins fall under the category of an HP-CIA (no colistin was used)

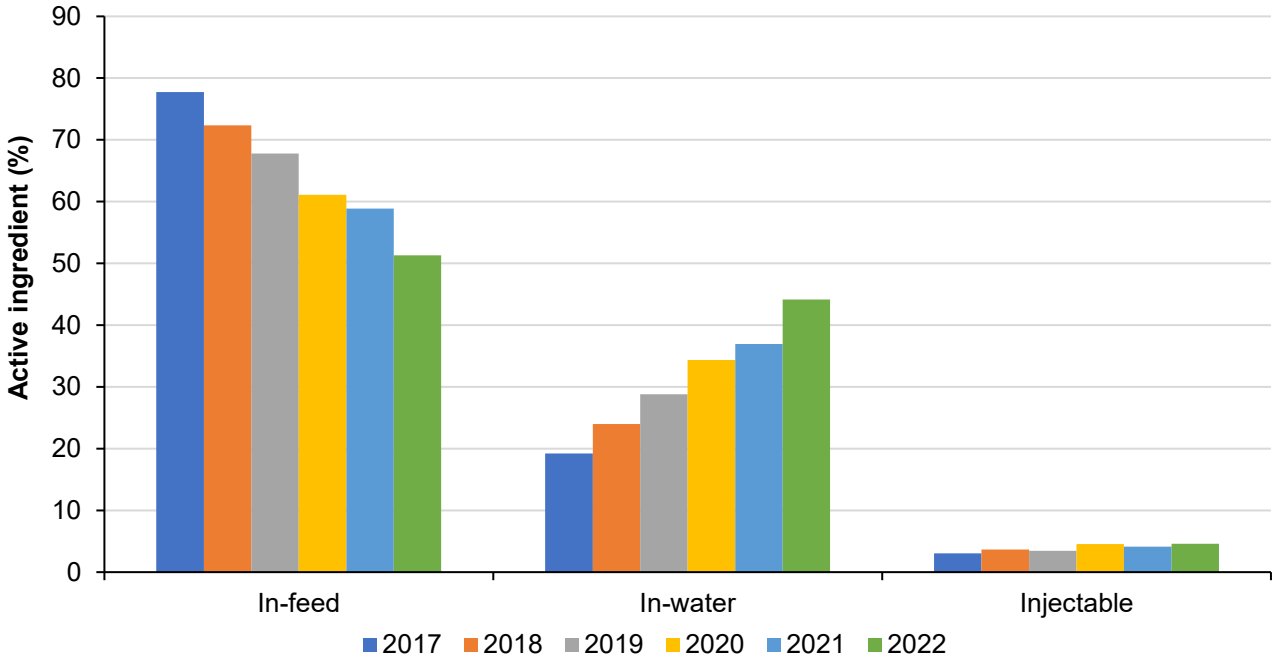
Figure 2.3: Active ingredient (mg/kg) of the top three antibiotics by antibiotic class reported in eMB Pigs, 2015 to 2022.



In-feed is the most common route of administration in pigs; however, relative use of in-feed antibiotics has fallen every year since 2017, representing 78% of total use in 2015 and 51% in 2022. Conversely, in-water administration now accounts for 44% active ingredient used

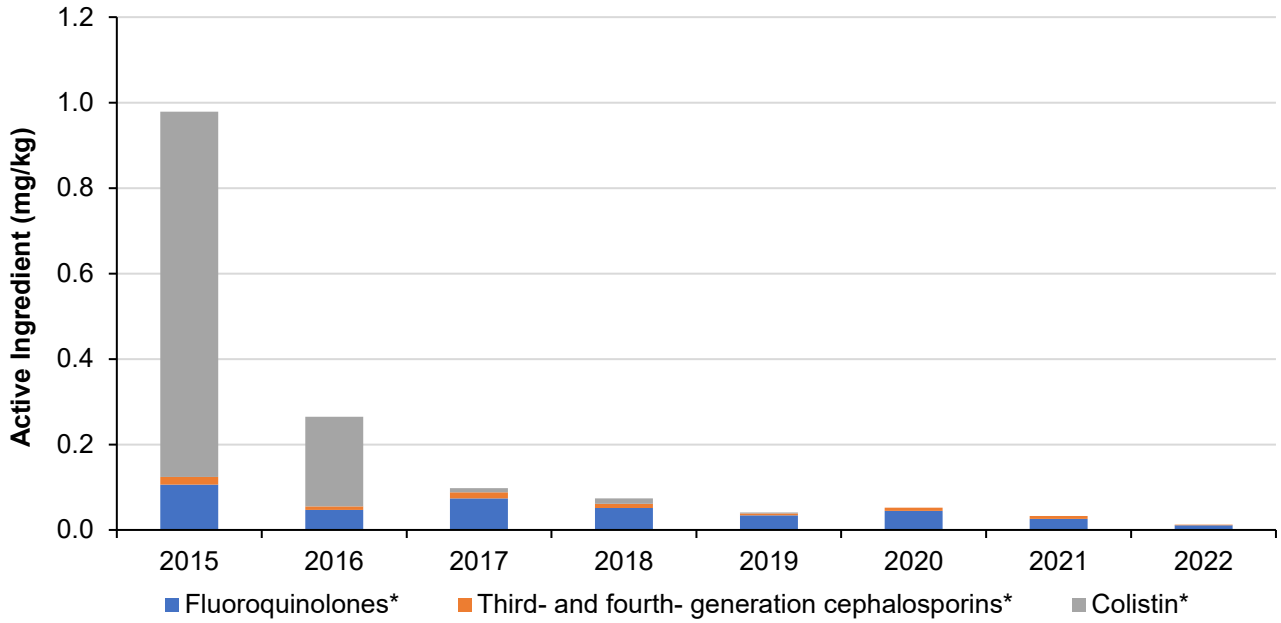
(compared with 19% in 2017) (see **Figure 2.4**). This shift is in line with the pig sector target to encourage producers to move from in-feed to in-water administration of antibiotics, which allows for more accurate targeting and thus more responsible use. The most common antibiotic classes for in-feed use in 2022 were tetracyclines (41% of total in-feed use), macrolides (18%) and penicillins (17%), whereas the most common antibiotic classes for in-water use in 2022 were tetracyclines (27% of total in-water use), aminoglycosides (21%) and penicillins (20%).

Figure 2.4: Active ingredient (% weight) of antibiotics by route of administration reported in eMB Pigs, 2017 to 2022.



The use of HP-CIAs in pigs is shown in **Figure 2.5**. In 2022, the use data represented 11.5 million pigs produced for the food-chain. Only 9.5 kg of HP-CIAs was used in these animals, which represents 0.01 mg/kg. Use of HP-CIAs in pigs reduced by 0.02 mg/kg between 2021 and 2022 to the lowest level recorded to date and accounting for 0.02% of overall use. HP-CIA use in the sector has now reduced by 99% (0.97 mg/kg) since 2015. All the third-generation cephalosporins and 99.9% of the fluoroquinolones were administered by injection, which means the use is targeted to individual animals. As in 2021, no products containing colistin were used in 2022.

Figure 2.5: Active ingredient (mg/kg) of HP-CIAs reported in eMB Pigs, 2015 to 2022.



* Colistin, third- and fourth-generation cephalosporins and fluoroquinolones fall under the category of an HP-CIA

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

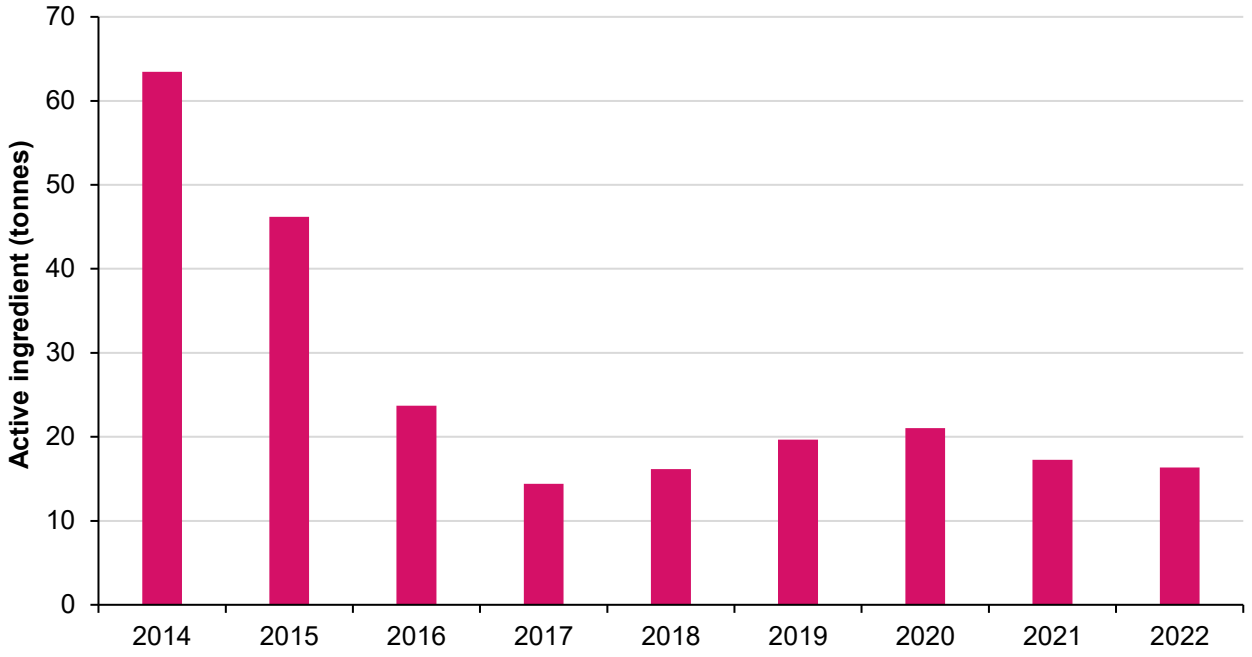
"In 2022, the UK pig industry's antibiotic use was the lowest level recorded so far at 71.8 mg/kg, continuing the downward trend in antibiotic use in UK pigs recorded over the last seven years, and totalling a 74% reduction in that time, with a continued recent 17.7% (15.5 mg/kg) reduction between 2021 and 2022. This means that in 2022 the pig sector achieved the RUMA sector target for antibiotic use (which was to get to 73.5 mg/kg by 2024). This has been facilitated by the delayed withdrawal of Zinc Oxide which had been anticipated in 2022 and is now expected to occur around the end of 2023. The loss of Zinc Oxide might still result in a rebound in use of antibiotic to treat Post Weaning Diarrhoea previously controlled by Zinc. The sector introduced a Persistently High Users scheme in 2021 where, through the farm assurance scheme Red Tractor, farms in the top 5% for antibiotic use per farm type are required to produce and action an antibiotic reduction plan with their vet. The use of all antibiotic classes reduced between 2021 and 2022, except for lincosamides, which increased by 1.5 mg/kg, and still only account for low levels of overall use (5%). The use of Highest-Priority Critically Important Antibiotics (HP-CIAs) in pigs remains at a very low level with a further decrease observed from 0.03 mg/kg in 2021 to 0.01 mg/kg in 2022. No colistin use was recorded in pigs for the third year running. Finally, as a result of the pig industry's continued move towards more targeted antibiotic delivery systems such as in-water delivery of medication, which present a reduced AMR risk compared to in-feed delivery, sales of antibiotics administered in-water increased for the second year in a row and sales of in-feed antibiotics decreased."

2.3.2 Meat poultry

2.3.2.1 Antibiotic usage data

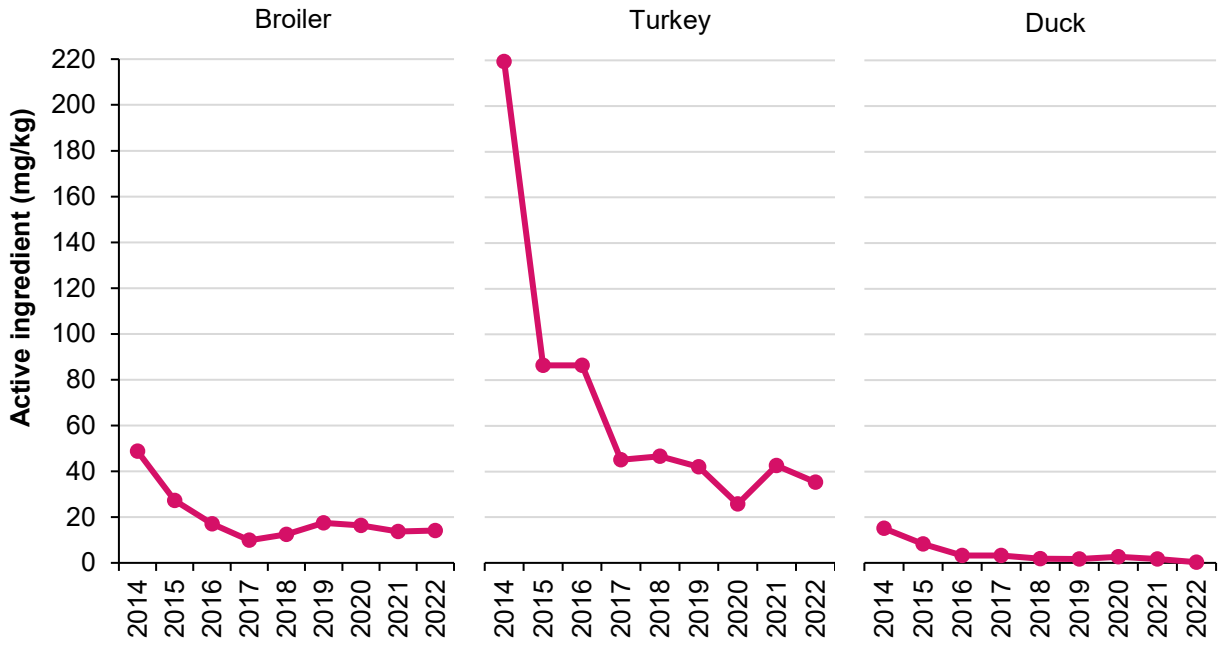
Data from the British Poultry Council (BPC) Antibiotic Stewardship, representing 90% of the meat poultry industry, reported the use of 16.4 tonnes of active ingredient combined for meat poultry and breeder birds in 2022. This is a 5% (0.9 tonne) decrease since 2021 and a 74% (47.1 tonnes) decrease since data was first published in 2014 (**Figure 2.6**).

Figure 2.6: Active ingredient (tonnes) of antibiotics used by members of BPC Antibiotic Stewardship, 2014 to 2022.



When adjusting for the size of the animal population, between 2021 and 2022 antibiotic usage in the boiler sector increased by 0.4 mg/kg to 14.1 mg/kg (**Figure 2.7**). However, this still represents a 71% (34.7 mg/kg) decrease since data was first published in 2014 and remains below the sector target of 25 mg/kg (**Figure 2.8**). Antibiotic use in the turkey sector decreased by 7.2 mg/kg to 35.4 mg/kg in 2022. It has now reduced by 84% (184.1 mg/kg) since 2014 and remains below the sector target of 50 mg/kg.(**Figure 2.8**). The duck sector demonstrated a decrease of 1.4 mg/kg to 0.3 mg/kg, and antibiotic use has now decreased by 98% (14.8 mg/kg) since 2014. Note that, unlike the tonnes figures, the mg/kg figures do not include use in breeder birds.

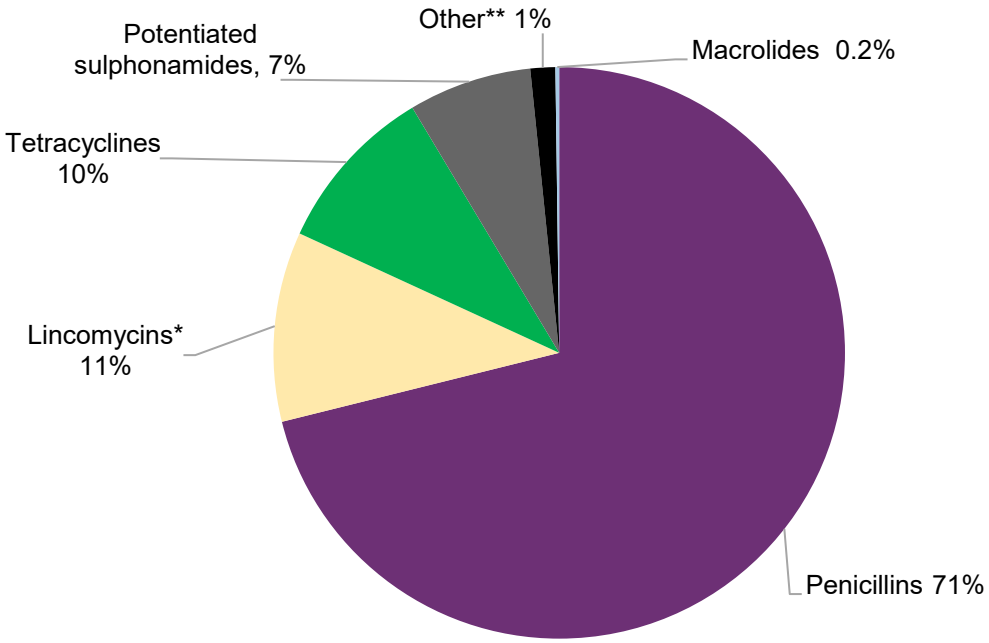
Figure 2.7: Active ingredient (mg/kg) of antibiotics by species used by members of BPC Antibiotic Stewardship, 2014 to 2022



In 2022, 71% of active ingredient classes comprised penicillins (over 99% of which is amoxicillin) (**Figure 2.9**), compared with 31% in 2014. Penicillin use decreased by 0.6 tonnes between 2021 and 2022. Tetracyclines and lincomycins are the second most commonly-used classes (accounting for 10% and 11% market share) and their use decreased by 0.02 tonnes and 0.8 tonnes respectively, between 2021 and 2022.

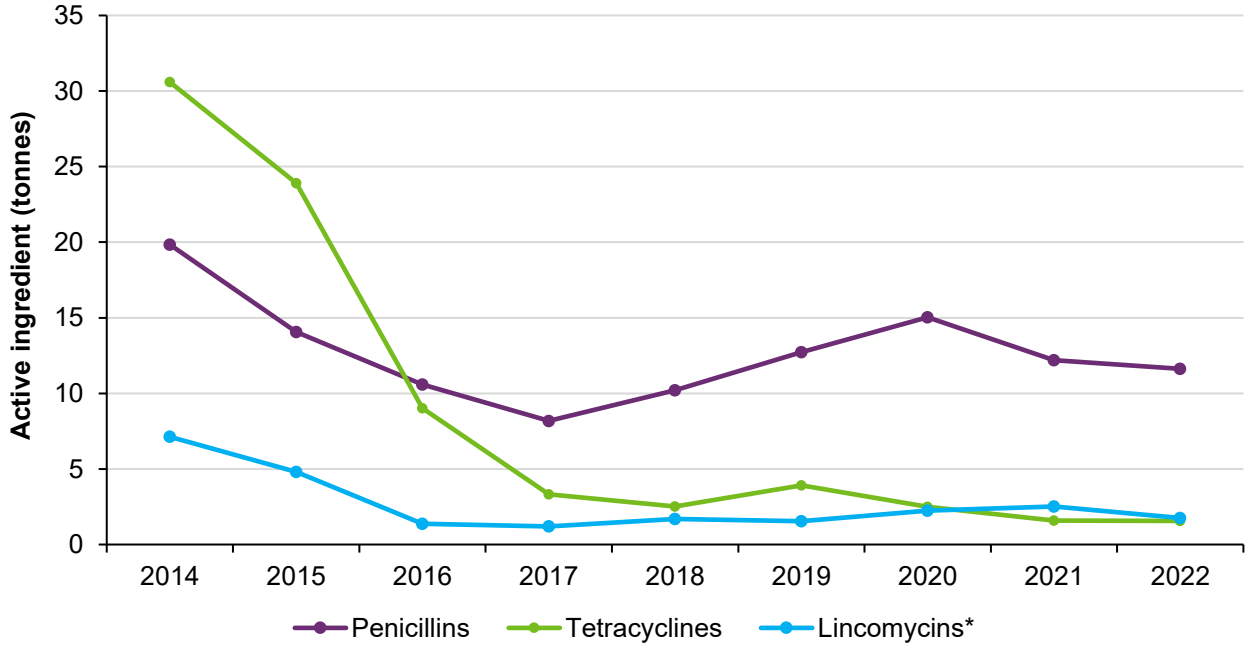
When considering HP-CIAs, colistin and third- and fourth-generation cephalosporins were once again not used by the meat poultry sectors and fluoroquinolones were not used by the duck sector in 2022. In 2022, BPC recorded use data representing 9.7 billion broilers and 8.1 million turkeys entering the food chain. However, only 1.3 kg of fluoroquinolones was used, which is a decrease of 55.3 kg since 2021. This represents 0.002% of overall use and a reduction of 99.9% (1.25 tonnes) since 2014. When looking only at slaughter animals, there was no fluoroquinolone use in slaughter broilers in 2022 and use in slaughter turkeys reduced from 0.006 mg/kg in 2021 to 0.0002 mg/kg.

Figure 2.8: Active ingredient (% weight) of antibiotics by antibiotic class used by members of BPC Antibiotic Stewardship, 2022.



* Includes products containing lincomycin in combination with spectinomycin
** Aminoglycosides and fluoroquinolones

Figure 2.9: Active ingredient (tonnes) of the top three antibiotics by antibiotic class used by members of BPC Antibiotic Stewardship, 2014 to 2022.



* Includes products containing lincomycin in combination with spectinomycin

Statement from British Poultry Council (BCP)

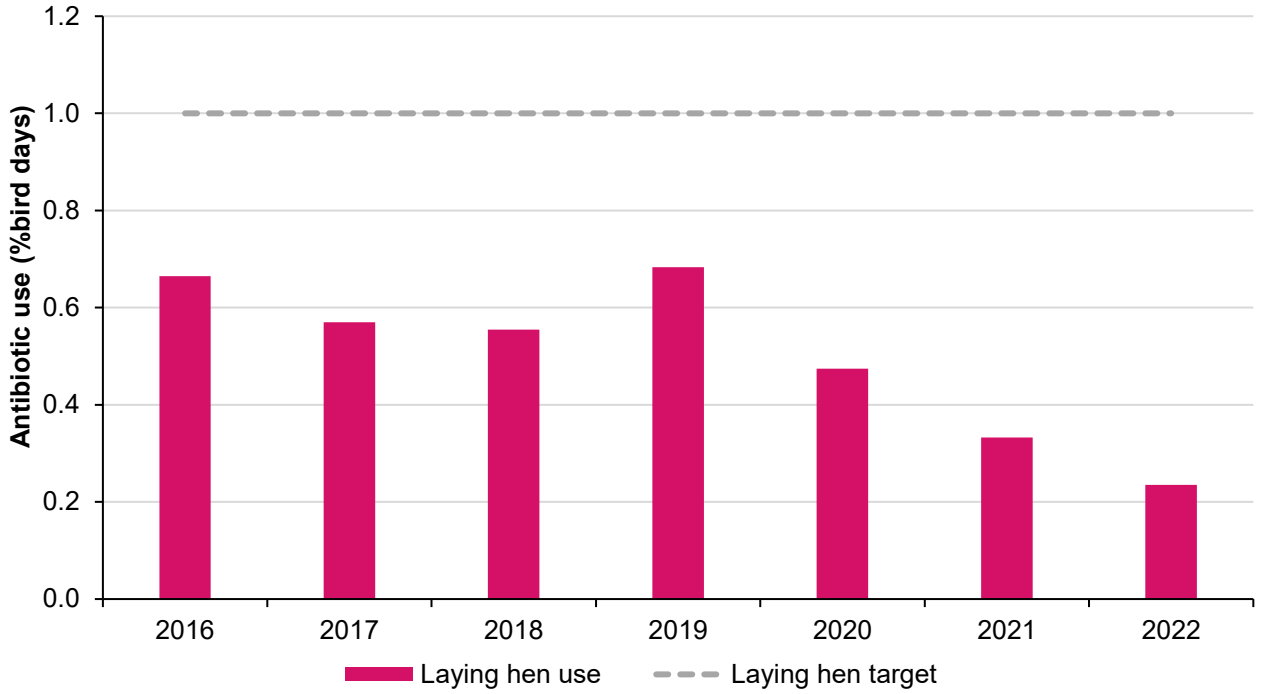
“The reductions seen in turkeys and ducks, and the stable pattern in broilers, highlights the continued focus on responsible antibiotic use despite the extreme challenges in 2022, which include the worse ever outbreak of highly pathogenic avian influenza in the UK alongside a cost of production and cost of living crisis. This is testament to the work of BPC Antibiotic Stewardship, which focuses on the sharing of best practice in a non-competitive manner, which is key to not only reducing overall antibiotic usage but preserving the effectiveness of the limited number of antibiotics licensed for use in poultry species. This is vital for the long-term sustainability of the industry. Only 1.3 kg of fluoroquinolone active ingredient was used in 2022 (in a single breeder flock and some meat turkeys, with no use in meat broilers). These high priority antibiotics were only used as a last resort following a detailed investigation into the causal problems, including antimicrobial sensitivity testing, and after alternative options for treatment had been explored. BPC members will continue to challenge antibiotic use levels and strive for further reductions, although it is important that birdkeepers do treat their birds under strict veterinary direction if required to ensure the health and the welfare of the livestock are not compromised.”

2.3.3 Laying hens

2.3.3.1 Antibiotic use data

In 2022 data collected by the British Egg Industry Council (BEIC), representing 90% of the laying hen industry, a total of 1.6 tonnes of antibiotic active ingredient was used, which represents 0.23% bird days (actual bird days treated/100 bird days at risk). This is a decrease of 30% (0.10% bird days) since 2021 and 65% (0.43% bird days) since data was first published in 2016 **(Figure 2.6**). The methodology for the metric is explained in section 2.4 of this report and represents the average number of days treatment administered per bird over a 100-day period.

Figure 2.10: Antibiotic use (% bird days) by members of the BEIC Lion Code, alongside the RUMA Targets Task Force sector target, 2016 to 2022.



Tetracyclines and pleuromutilins accounted for 78% of total use (**Figure 2.11**) and decreased by 25% (0.05% bird days) and 52% (0.05% bird days) respectively, between 2021 and 2022 (**Figure 2.10**). For the fifth year running, there were no HP-CIAs used by the laying hen sector in 2021.

Figure 2.11: Antibiotic use (% of total bird days) by antibiotic class by members of the BEIC Lion Code, 2022.

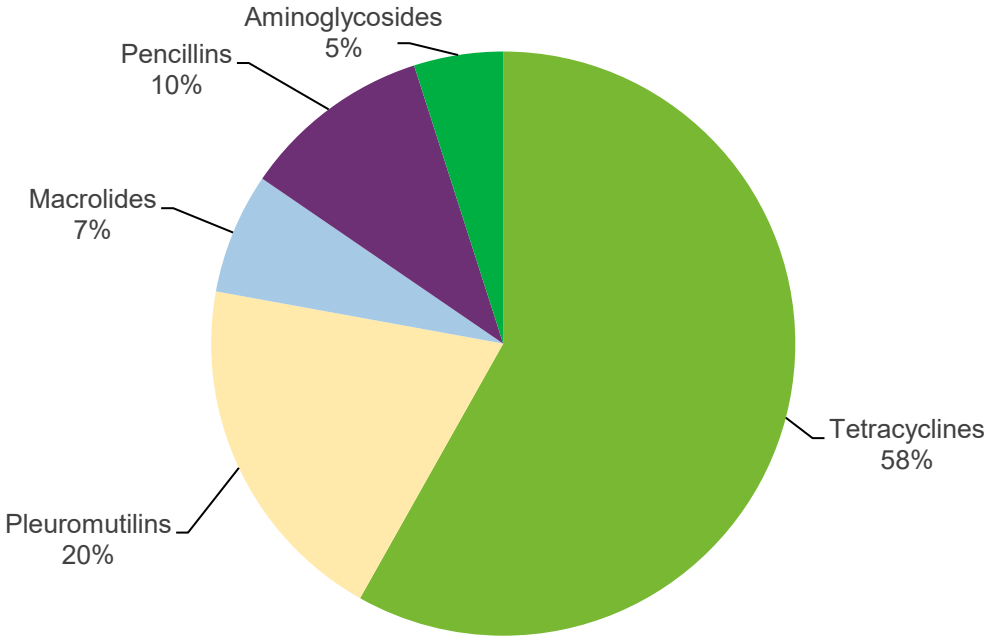
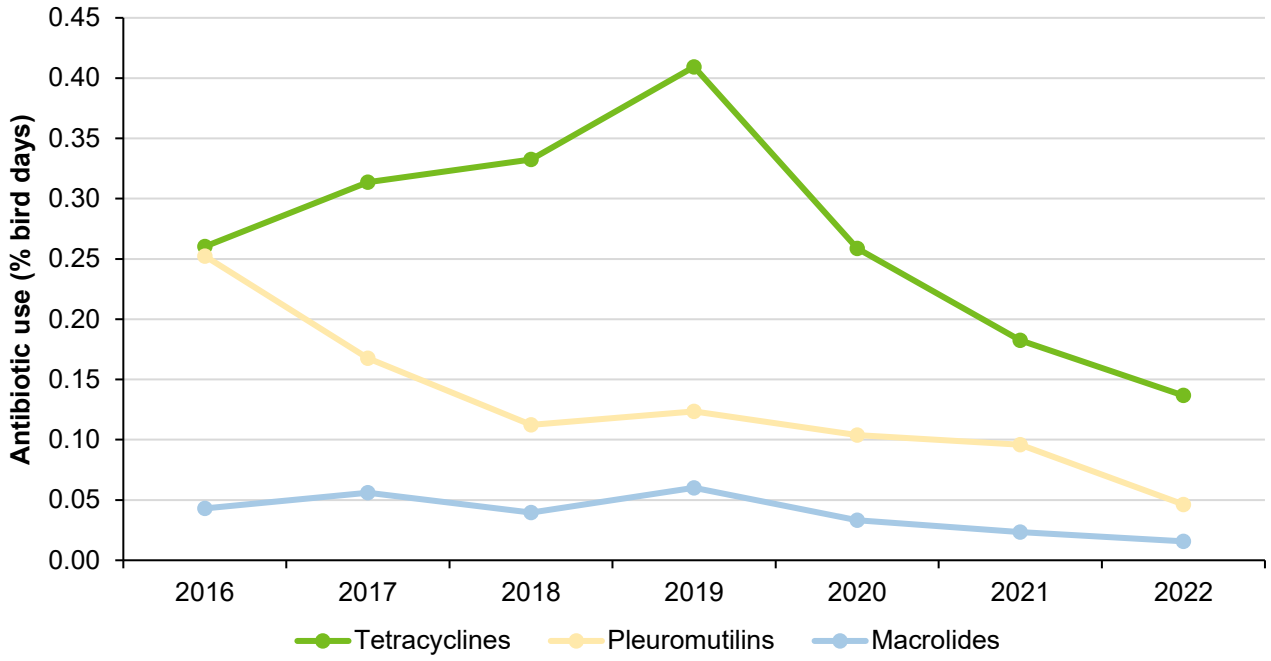


Figure 2.12: Antibiotic use (% bird days) of the top three antibiotics by antibiotic class by members of the British Egg Industry Council Lion code, 2016 to 2022.



2.3.3.2 Statement from the British Egg Industry Council (BEIC)

"The antibiotic use data from members of the British Egg Industry Council (BEIC) Lion Scheme for 2022 shows further reductions and continues to be below the target of 1% bird days, and for the sixth year running no HP-CIAs were used. This is a significant achievement, especially considering the major challenges in 2022, which included cost of production increases and bird flu outbreaks.

The Lion standard continues to focus on bird health through good biosecurity and hygiene, as well as feed and water quality. Version 8 of the Scheme has seen significant developments in biosecurity requirements. Compulsory training of the enhanced requirements of Version 8 of the Lion Scheme is also required, and the training modules also cover prudent use of antibiotics. All Lion accredited breeder, pullet rearing and laying farms also have to be registered with a vet and have an up-to-date veterinary health and welfare plan.

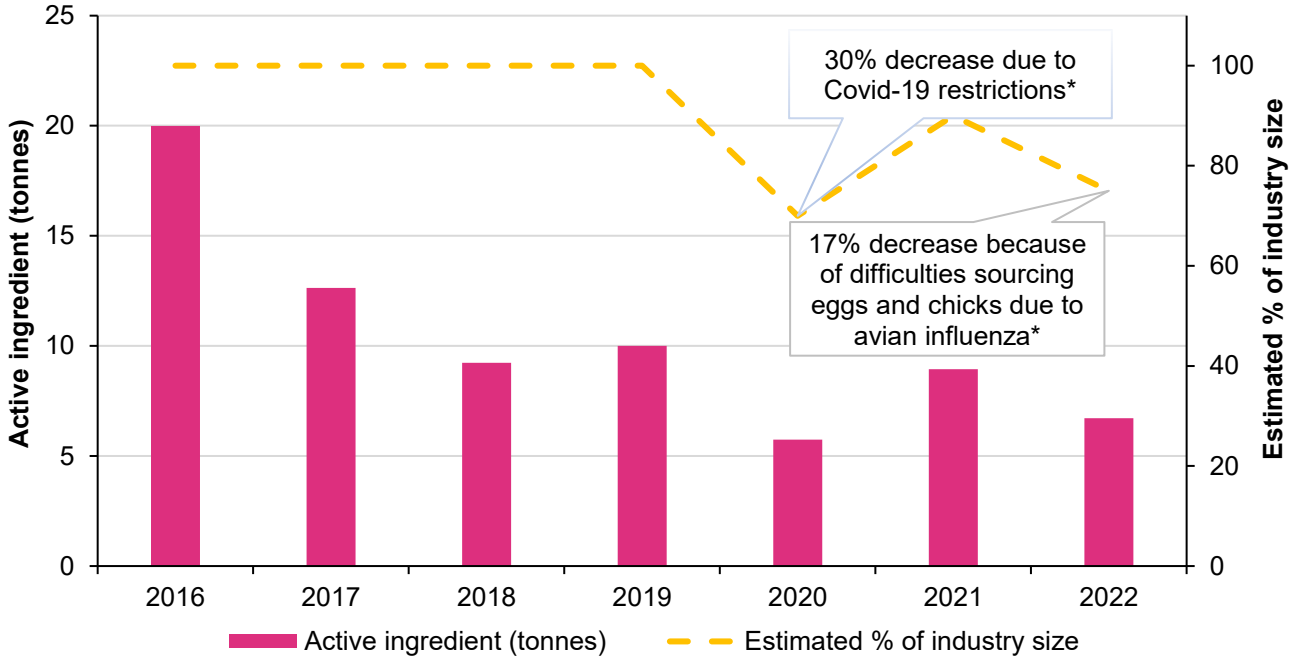
The industry is continuing the trend for retail supply away from enriched colony cage production and towards free-range and barn production. We are confident that we will continue to remain below our on-going antibiotic use target of 1% bird days, and 0.05% bird days for HP-CIAs."

2.3.4 Gamebirds

2.3.4.1 Antibiotic use data

In 2022, 6.7 tonnes of active ingredient were reported through the Game Farmers' Association (GFA) and British Veterinary Poultry Association (BVPA) gamebird subcommittee data collection programme, which represents 90% of the industry. The antibiotic use metric is not equivalent to that used in other sectors as the gamebird sector do not adjust antibiotic use for the underlying population. This means that changes in the yearly figure are influenced by changes in gamebird population. Overall, the 2022 tonnage represents a decrease of 25% (2.2 tonnes) since 2021 and, 66% (13.3 tonnes) since 2016 (**Figure 2.13**). However, due to issues with sourcing eggs and chicks from France due to avian influenza, the number of gamebirds reared is estimated to have fallen by 17%.

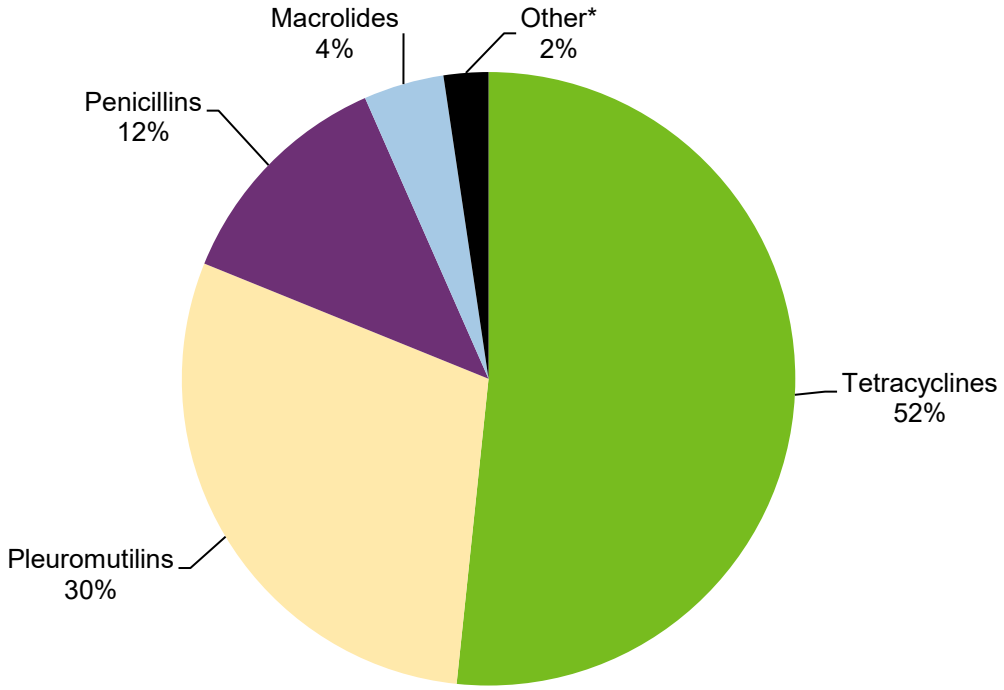
Figure 2.13: Active ingredient (tonnes) of antibiotics used in gamebirds, collected by the GFA and BVPA data collection programme, 2016 to 2022 and estimated population size (% of normal industry size).



* % change in industry size as estimated by the Game Farmers' Association

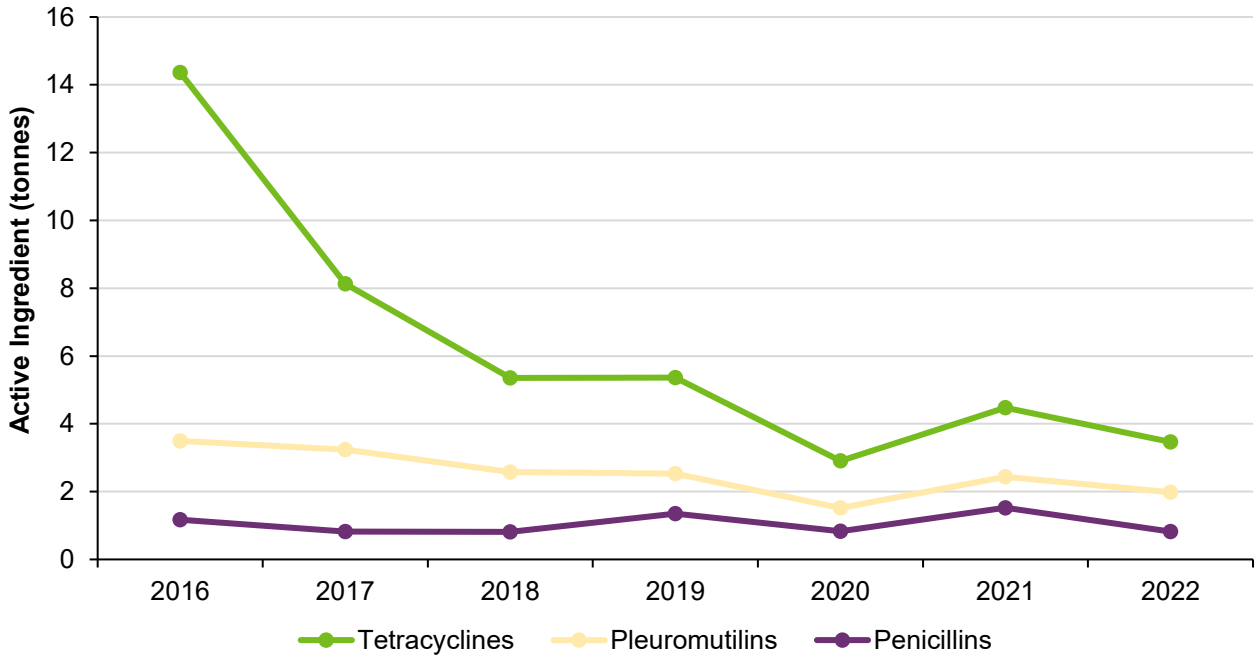
The use of antibiotics broken down by active ingredient is shown in **Figures 1.2** and **1.3**.

Figure 2.14: Active ingredient (% weight) of antibiotics by antibiotic class used in gamebirds, collected by the GFA and BVPA data collection programme, 2022.



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

Figure 2.15: Active ingredient (tonnes) of top three antibiotics by antibiotic class used in gamebirds, collected by the GFA and BVPA data collection programme, 2016 to 2022.



Tetracyclines remain the most commonly used active ingredient, representing 52% of antibiotics used in 2022, but this has dropped by 76% (10.9 tonnes) since 2016.

Analysis by route of administration shows that oral/water administration accounted for 61% of overall use and 39% of in-feed use. Since 2016, in-feed use has fallen by 82% (12.3 tonnes) whereas oral/water use has dropped to a lesser degree, by 19% (1 tonne). This shift is in line with the gamebird sector's focus of encouraging producers to move from in-feed to in-water administration of antibiotics, which allows for more accurate targeting and thus more responsible use.

The fluoroquinolone enrofloxacin is the only HP-CIA used by the gamebird sector and this has decreased by 12% (3.3 kg) since 2021 to 23.2 kg. This reduction is slightly less than the estimated 17% reduction in gamebirds reared during this period. However, HP-CIA use has decreased by 64% (41 kg) since data was first recorded 2016.

2.3.4.2 Statement from the Game Farmers' Association and the British Poultry Veterinary Association (BVPA) gamebird subcommittee

"2022 was a difficult year, with a 17% reduction in gamebirds reared due to avian influenza issues in France meaning that eggs and chicks couldn't be imported. However, the 25% reduction (in antimicrobial use) between 2021 and 2022 is greater than the reduction in gamebirds reared, showing that there has been a true reduction in antibiotic use – and overall antibiotic use has fallen by two thirds since 2015. During 2022, there was considerable uptake in the BVPA game sector training and the Agricultural Industries Confederation (AIC) game feed modules. Assurance and auditing in the game rearing sector also increased, with further development of the British Game Assurance (BGA) game farm and shoot assurance schemes and the Trusted Game Health and Welfare scheme which, alongside the training courses outlined and the pen scoring matrix developed by gamebird vets, all contribute to the aim of reducing antibiotic use by improving systems and health and welfare standards. Fluoroquinolone use reduced by 12% since 2021 but, given that the gamebird sector contracted by an estimated 17%, relative use did increase slightly. It is thought that a significant proportion of fluoroquinolone use is for the treatment of bacterial infections in chicks during the first week of life. The slight relative increase may have been related to the reduced availability of eggs/chicks from France resulting in more UK eggs being put in the incubator (including those with poorer grading) resulting in slightly poorer overall chick health. We will continue to work to reduce the use of fluoroquinolones and ensure that they are only used as a last resort and with good reason, e.g. where culture and sensitivity tests suggest it is the only suitable option. There is still more work to be done to meet the ambitious target of reducing antibiotic use by 40% (from a 2019 baseline) but by working together, and given the significant progress so far, we believe that this is achievable."

2.3.5 Aquaculture

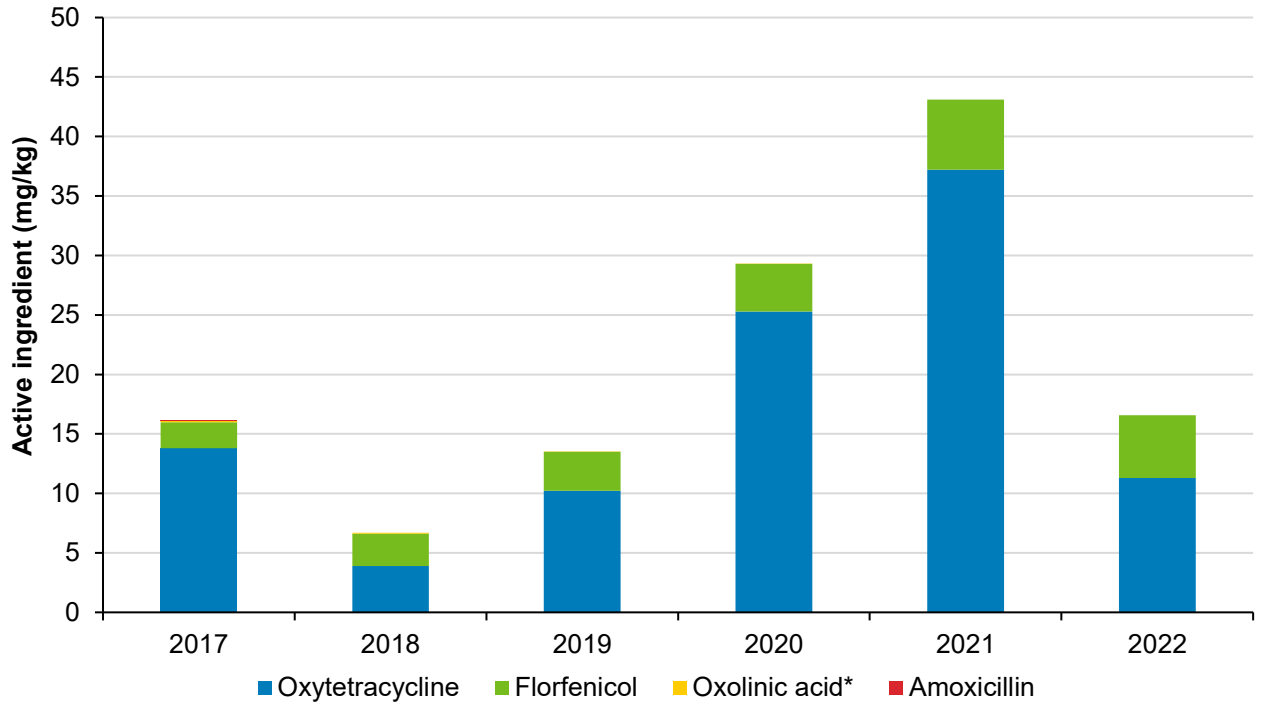
2.3.5.1 Salmon

Results

In data collected by Salmon Scotland representing 100% of the industry, 3.1 tonnes of antibiotic active ingredient were used in 2022, representing 18.6 mg/kg (**Figure 2.16**). This is a decrease of 57% (24.5 mg/kg) since 2021 but an increase of 15% (2.5 mg/kg) compared with 2017, when data was first published.

In 2022, oxytetracycline has remained the most-used antibiotic class, accounting for 68% of total use, with the rest being the amphenicol florfenicol. Oxytetracycline use has decreased by 65% (24.5 mg/kg) since 2021 whereas florfenicol remained at 5.9 mg/kg between 2021 and 2022. As with 2021, the HP-CIA oxolinic acid (a quinolone) was not used in salmon in 2022.

Figure 2.16: Antibiotic active ingredient (mg/kg) by antibiotic class used in salmon, 2017 to 2022.



* Oxolinic acid falls under the category of an HP-CIA

Statement from Salmon Scotland

“The data records a decrease in antibiotic use compared to 2021 and 2020. Decreases were recorded within both the freshwater and marine phases of production. It is important to state that antibiotic treatments are relatively infrequent in the salmon farming sector, with only 1.5% of freshwater farms and 8.7% of marine farms treated in 2022. Antibiotics are only

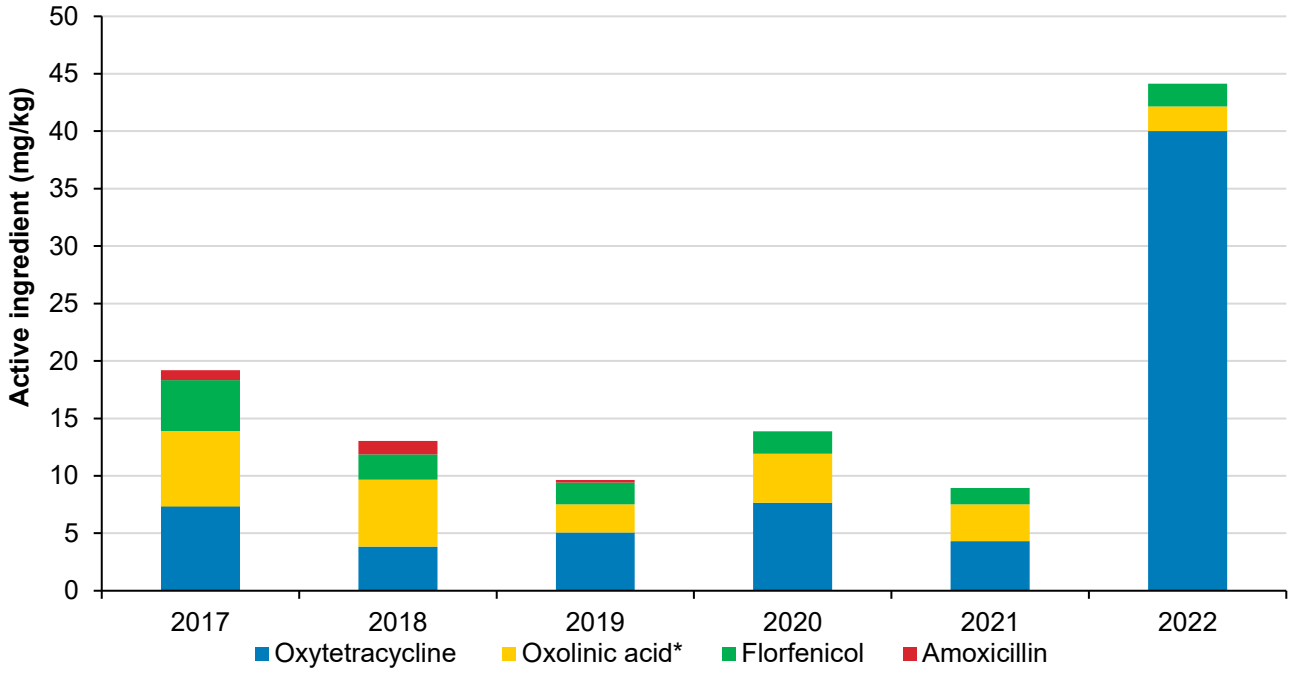
ever used in response to the clinical presentation of bacterial infection: there is no prophylactic use of antibiotics, and any use is supported by appropriate sensitivity testing. Similar to 2021, there was no use of the HP-CIA oxolinic acid in 2022. The Salmon sector continues to focus on a holistic and preventative approach to health management, including vaccination, antibiotic stewardship, biosecurity and health and welfare planning. The sector also continues to support the development of innovative approaches to fish health management, for example bacteriophages. Such approaches could support antibiotic stewardship in the future. Furthermore, antibiotic use and stewardship are routinely discussed within a dedicated Prescribing Vets forum. It should also be noted that the overall production cycle for Salmon is 3 years, so single year mg/kg figures can be difficult to interpret as the denominator relates to kg of fish slaughtered whereas the use may not have occurred in these animals. The sector remains committed to responsible use of antibiotics, balancing a drive to reduce use against the need to safeguard fish health and welfare."

2.3.5.2 Trout

Results

The data, obtained from veterinary practices that treat approximately 90% of UK trout production, demonstrates that a total of 0.51 tonnes of antibiotic active ingredient was used, representing 44.1 mg/kg; almost a 5 times increase since 2021. This is the highest usage seen in the trout sector since electronic recording began in 2017, representing a 24.9 mg/kg (130%) increase between 2017 and 2022 (see **Figure 2.17**). This increase is due to an outbreak of *Aeromonas salmonicida* on a small number of production sites.

Figure 2.17: Active ingredient (mg/kg) of antibiotics by antibiotic class used in trout, 2017 to 2022.



*Oxolinic acid falls under the category of an HP-CIA

When considering usage by class, the increase is primarily due to oxytetracycline which, in 2022, accounted for 91% of overall use.

In 2022, use of the HP-CIA oxolinic acid (a quinolone) dropped by 1.1 mg/kg to 2.2 mg/kg, which is a 67% (4.4 mg/kg) drop since 2017.

Statement from the British Trout Association

"The trout sector is committed to reducing antibiotic use through disease prevention, including vaccination, and promoting best practice through the Quality Trout UK standard. This year, as part of a project alongside VMD and Cefas, we also submitted over 150 bacterial samples for culture and sensitivity, which will help us to better understand the levels of resistance to the antibiotics which are used in the Trout sector. The significant rise in this year's antibiotic use figures are due to an outbreak of *Aeromonas salmonicida* on a small number of production sites with rainbow trout at a large size and therefore high biomass, meaning that antibiotics were needed for treating disease that would otherwise have had welfare consequences. This event is not anticipated to recur and it is expected that the Trout sector will fall back below the industry target of 20 mg/kg in 2023."

2.3.6 Cattle

2.3.6.1 Available antibiotic use data in cattle

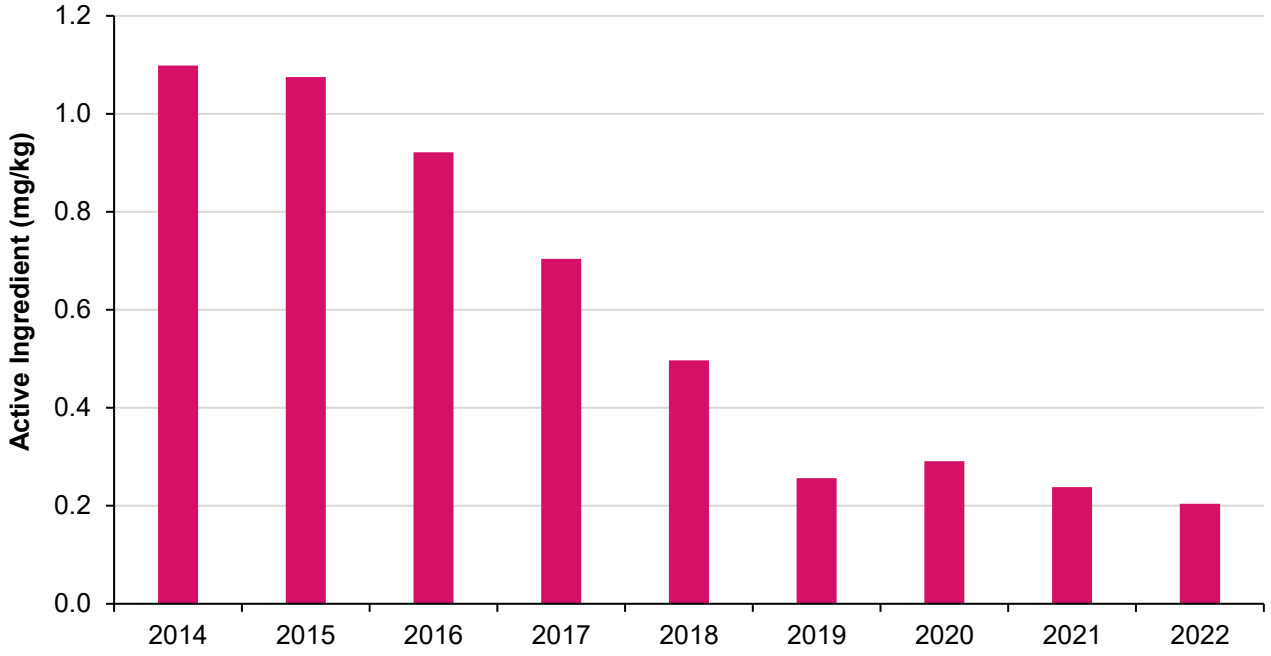
To assess trends in use of intramammary tubes, the dairy sector monitors total sales as a 3-year rolling average (for more information see here). The metric used is the Defined Course Dose (for) veterinary (DCDvet), see Annex A for further details on this metric.

Sales of antibiotic intramammary tubes for lactating cows showed a 15% reduction from 0.50 DCDvet (2019 to 2021 average) to 0.43 DCDvet (2020 to 2022 average).

Similarly, sales of antibiotic intramammary tubes for dry cows also showed an 8% reduction from 0.54 (2019 to 2021 average) to 0.49 (2020 and 2022 average).

Yearly sales of HP-CIA injectable products licenced for cattle decreased by 0.03 mg/kg from 2021, to 0.20 mg/kg in 2022. In total, sales of HP-CIA injectables licensed for cattle have decreased by 81% (0.89 mg/kg) since 2014.

Figure 2.18: Active ingredient adjusted for population (mg/kg) of sales of injectable HP-CIA products licenced for cattle, 2014 to 2022.



The Medicine Hub for ruminants

The Medicine Hub is a centralised national industry database for the collection and collation of antibiotic use data in sheep and cattle. It is a voluntary industry initiative launched by the Agriculture and Horticulture Development Board (AHDB) in 2021. Data provides a preliminary indication of antibiotic use in these sectors. The main limitations of the figures provided are outlined below:

- The figures presented below represent a low proportion of the dairy and sheep sectors (28% and 9% respectively) in comparison with other livestock sectors presenting use data within UK-VARSS (which have coverage of 90% or more). The data below can therefore not be interpreted as 'national' figures.
- Farms have voluntarily contributed data towards the figure, and, without greater coverage, the data may therefore not fully represent the diversity of farms within the UK.

For beef, dairy and sheep, there are different, and sometimes multiple, core metrics used to calculate population-adjusted antibiotic use. As different information is used in each calculation, the figures are not comparable to each other. More details on the different national and farm-level metrics used in the ruminant sectors can be found here. All mg/kg figures presented below are calculated using the national mg/PCU methodology for cattle and sheep (see Supplementary Material 1 for further details).

Dairy

The antibiotic use data from 2022 represents 28% of adult dairy cattle in 2022. Total antibiotic use in this sample is 16.6 mg/kg and use of HP-CIAs is 0.03 mg/kg.

Sheep

The antibiotic use data from for 2022 represents 9% of the sheep sector in 2022. Total antibiotic use in this sample is 7.7 mg/kg and use of HP-CIAs is 0.0004 mg/kg.

Beef

The antibiotic use data from for 2022 represents 6% of the beef sector (using the number of beef animals slaughtered) and is collated from 2132 UK beef enterprises.

Industry Statement regarding antibiotic use data for beef.

“The Cattle Antibiotic Guardian Group (CAGG) considers that whilst calculation of a mg/PCU figure for beef is possible using the data available from the AHDB Medicine Hub, it is not clear yet at this early stage in the data collection journey that the dataset held is sufficiently representative for the beef sector to give an accurate and meaningful national mg/PCU figure. Because the PCU methodology used in beef only looks at animals slaughtered, this increases the likelihood of the figure being inaccurate if the herd types in the sample (i.e. the balance of rearer and finisher farms) are not representative. An indicative antibiotic use figure based on data collected by Medicine Hub so far for beef, using a different metric, can be found in the RUMA TTF report along with an explanation of how this figure was derived”.

2.3.6.2 Statement from the Cattle Antibiotic Guardian Group

“The cattle sector has been working to collate antibiotic use data from cattle through a centralised and standardised antibiotic use data collection system for ruminants, the Medicine Hub. Antibiotic use data collected in 2022 represents 28% of adult dairy cattle in the dairy sector and 6% of slaughtered beef in 2022. Antibiotic use data was collated from across 2132 UK beef enterprises and 2430 dairy enterprises (there are approximately 7,500 dairy enterprises and approximately 60,000 beef enterprises in the UK).

The data collected in 2022 have been voluntarily provided and are not yet sufficient to be representative of the UK cattle population (and so cannot be used to provide a national figure). However, the figure calculated provides a useful snapshot of antibiotic use and demonstrates an important milestone in the industries’ journey towards collecting and collating national antibiotic use data. For example, use of antibiotics critically important to human health was low (0.03 mg/kg in the dairy sector sample). As more data are collated by Medicine Hub from a greater number and variety of farms, the antibiotic use figures are expected to change and are likely to better reflect use within the UK dairy and beef sectors.

The cattle sector continues to support uptake of national reporting mechanisms to monitor overall antibiotic use while at the same time focusing on improving responsible use of antibiotics on farms, for example by avoiding prophylactic use of antibiotics and increasing uptake of disease prevention measures on farms. For example, the British Cattle Veterinary Association (BCVA) offers training resources for cattle vets to support their efforts in promoting health and welfare and managing diseases, improving antibiotic selection and enhancing stewardship. Additionally, the Welsh project ARWAIN DGC aims to reduce the need to use antimicrobials such as antibiotics by improving productivity, animal health and welfare through new and innovative technology and further promotion of 'good practice'."

2.3.7 Sheep

2.3.7.1 Statement from the Sheep Antibiotic Guardian Group

"The sheep sector remains committed to using antibiotics as little as possible, and as much as necessary. The sector aims to balance responsible antibiotic use whilst ensuring sheep health and welfare is protected, with a focus on improvements on farm. Examples of this were showcased during the RCVS Knowledge Awards 2023 where veterinary surgeons championed changes on farm and in their practices, particularly focussing on reducing prophylactic use in lambs and during routine surgeries. The Antimicrobial Stewardship Award winners achieved improvements by implementing a range of actions including using training materials for vets, audits, risk assessments, awareness meetings and training and support materials for farmers as well as using SMART goals to help deliver on policy and practice changes, thus reducing the need for antibiotics and improving animal health and welfare.

The Medicine Hub, developed and resourced by AHDB, is a centralised national database for the collection and collation of antibiotic use data in sheep and cattle. It is a voluntary industry initiative which facilitates national reporting and builds evidence of the sector's responsible approach to antibiotic use. In 2022, the Hub captured antibiotic use data covering 9% of UK sheep production. This data provides a useful indication of antibiotic use in the sheep sector. Total antibiotic use was 7.7 mg/kg in these flocks in 2022 with HP-CIA use very low at 0.0004 mg/kg. This relatively small sample size represents the start of the data collation journey and provides a useful indication of antibiotic use in the sheep sector. The robustness of these figures will continue to improve as the sector submits high quality data and coverage of the dataset increases. These early figures evidence the positive results of the sheep sector's safeguarding of antibiotics which are most important to protect public health. In addition, Red Tractor, the UK's largest farm assurance scheme have included requirements for, for example, the use of HP-CIAs as a last resort alongside sensitivity and/or diagnostic testing (in October 2019), completing medicine training, having a health plan reviewed by a vet annually and antibiotic collation (in November 2021) and a recommendation to upload total antibiotics used onto Medicine Hub (or an equivalent system sharing data with the Hub), to be implemented in early 2024.

The sheep sector will continue to encourage uptake of antibiotic use recording systems to enable centralised data collation, ultimately to achieve a robust national figure.
The sector continues with a strong focus on consistent, coordinated, and collaborative communications on disease prevention and vaccination to support responsible antimicrobial stewardship and saw an increase of 13.9% in total number of vaccine doses sold between 2012 and 2022 despite some issues with vaccine supply."

2.3.8 Companion Animals

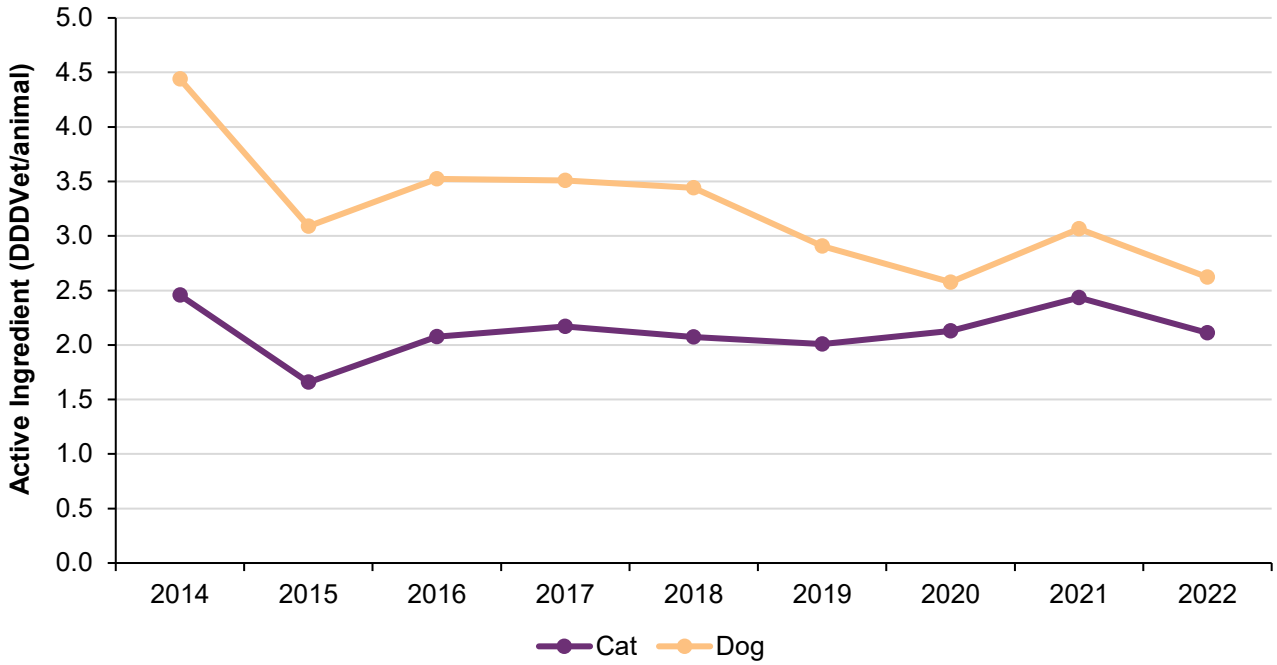
2.3.8.1 Antibiotic use in dogs and cats

In 2022, antibiotic use in dogs and cats has been estimated to be 57.3 mg/kg for dogs and 28.3 mg/kg for cats, and use of HP-CIAs is 0.41 mg/kg for dogs and 0.68 mg/kg for cats. This has been calculated by stratifying the sales data reported by veterinary pharmaceutical companies; the full methodology can be found in section 1.4 of this report and the Supplementary Material 1.

When monitoring trends, however, a different metric (DDDVet/animal) is also used, which relates to the average number of days that each dog or cat in the UK has received an antibiotic throughout the year. This is considered preferable as it accounts for the length of activity for long-acting products (which are commonly used in dogs and cats) as well as differences in dose rates used.

Sales of antibiotic products for dogs in 2022 decreased by 15% (0.4 DDDvet) since 2021 and 41% (1.8 DDDvet) since 2014 to 2.6 DDDvet (the same levels that were seen in 2020), (**Figure 2.19**). In comparison, sales of antibiotic products for cats decreased by 13% (0.32 DDDvet) since 2021 and 14% (0.35 DDDvet) since 2014 to 2.1 DDDvet (also to the same levels to those seen in 2020). It should be noted that the antibiotic use trends for dogs and cats seen in figure 2.19 follow a similar trend. One explanation for this could be that, in many cases, the same products are used in dogs and cats, and the sales are then split into dogs and cats based on estimated provided by the pharmaceutical companies. This may not reflect true usage trends, for example if data was based on veterinary practice records.

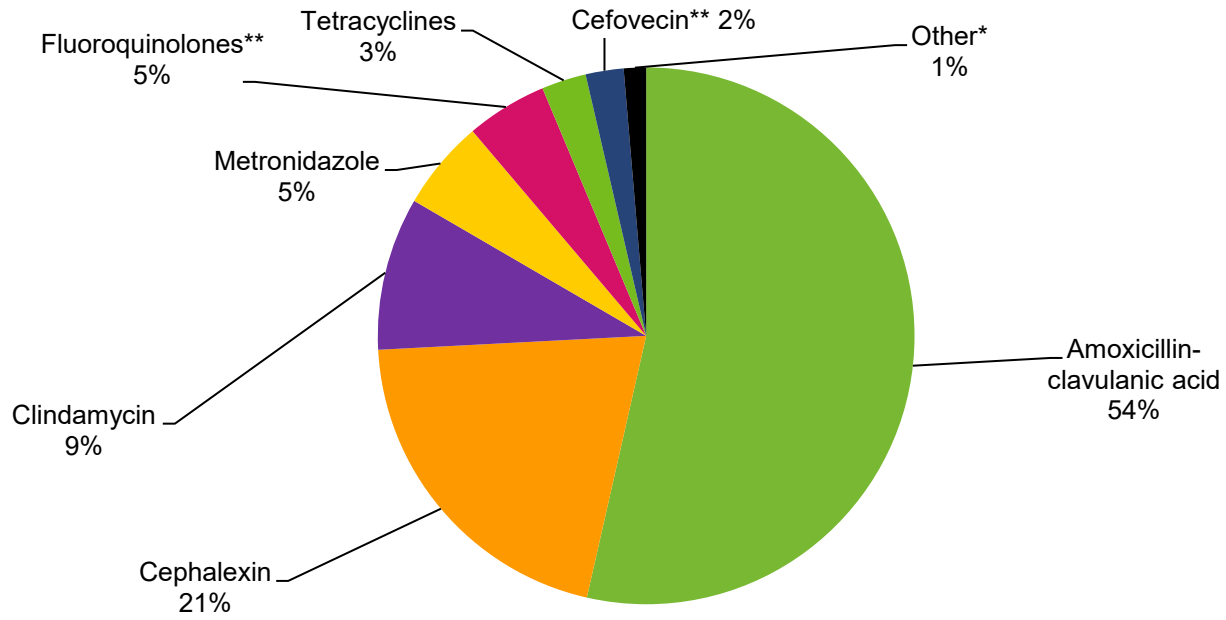
Figure 2.19: Active ingredient (DDDvet/animal) of antibiotics sold for use in dogs and cats, 2014 to 2022



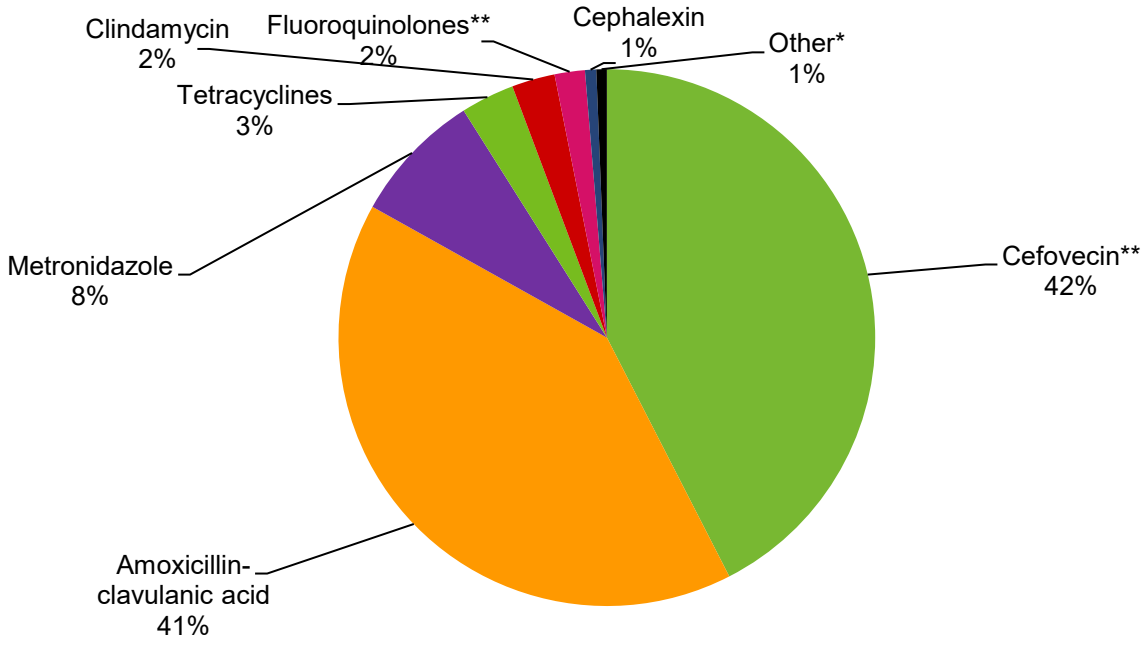
In dogs, products containing amoxicillin combined with the beta-lactamase inhibitor clavulanic acid were the most sold active ingredient in 2022 (**Figure 2.20**), representing 54% of total sales, followed by cephalexin (a first-generation cephalosporin), which represented 21% of total sales. In cats, cefovecin (a third-generation cephalosporin – an HP-CIA) was the most sold active ingredient in 2022 (**Figure 2.20**) representing 42% of total sales, closely followed by amoxicillin- clavulanic acid, representing 41% of total sales.

Figure 2.20: Active ingredient (DDDVet/animal) of antibiotics by active ingredient/antibiotic class sold for use in (a) dogs and (b) cats, 2022.

a)



b)

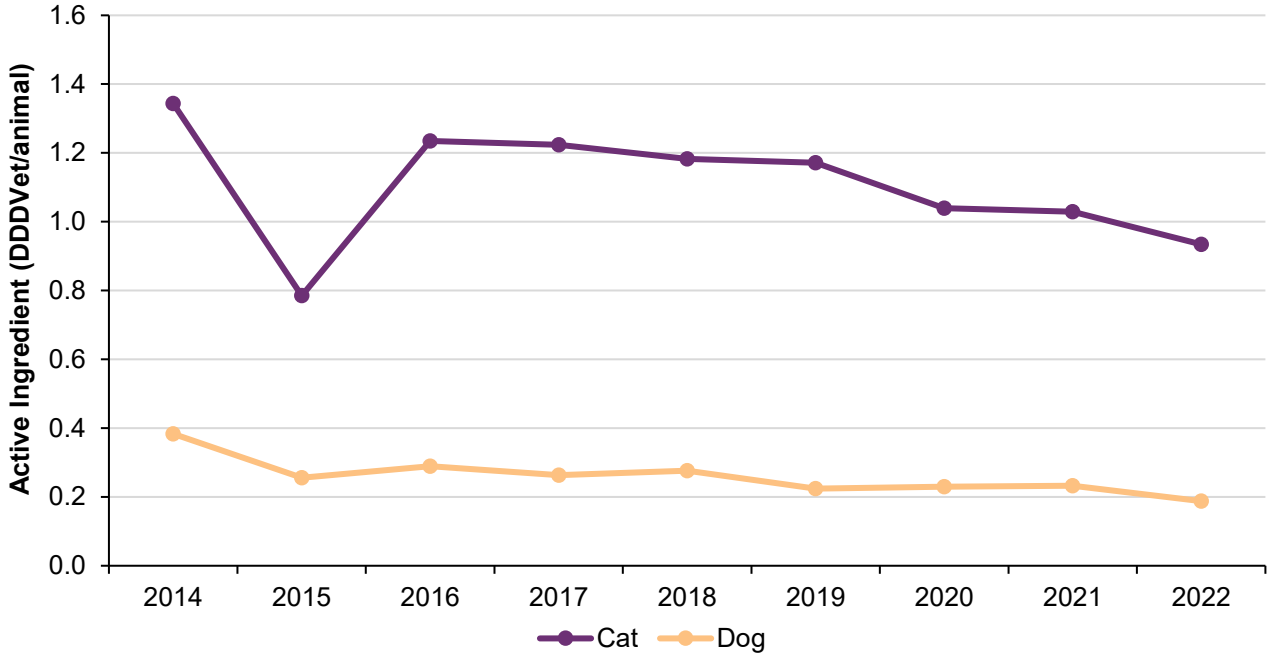


*Aminopenicillins (amoxicillin and ampicillin), trimethoprim-sulphonamides, metronidozole-spiramycin
** Fluoroquinolones and the third-generation cephalosporins cefovecin fall under the category of an HP-CIA

In dogs, sales of HP-CIAs (**Figure 2.21**) accounted for 7% of total sales (0.19 DDDVet/animal), which represents a reduction of 0.04 DDDVet since 2021 and 51% (0.20 DDDVet/animal) since 2014. In cats, however, HP-CIAs accounted for 44% of total sales

(0.9 DDDVet/animal), which represents a reduction of 0.09 DDDVet since 2021 and 30% (0.41 DDDVet/animal) since 2014. Fluoroquinolones represented 68% of HP-CIA use in dogs, whereas in cats, 96% of HP-CIA sales were for the third-generation cephalosporin, cefovecin. Note it is thought that the large reductions of HP-CIAs that were recorded in cats in 2015 are anomalous and relate to issues with supply.

Figure 2.21: Active ingredient (DDDVet/animal) of HP-CIAs, sold for use in dogs and cats, 2014 to 2022.



2.3.8.2 Horses

Antibiotic sales cannot be used to reliably determine antibiotic use in horses. This is because many products licensed in horses are also licensed for multiple other species, and because there is a higher use of off-label products (e.g. those licensed for other species or humans) or extemporaneous products under the prescribing cascade.

In the equine sector, a new study has been published exploring antibiotic use data. This was extracted using a custom report from the practice management software Eclipse® over a 10 year period (2012-2021), covering 14 practices, 6 of which were first opinion only and 8 had additional hospital referral facilities. A median 72,890 horses was seen annually (determined by counting the number of horses with any transactions recorded during the selected time-period) and, in total, this data covers up to 15% of the estimated UK equine population.

As with dogs and cats, mg/kg and DDDVet/animal metrics were calculated. The average weight of the horses within each practice was used for these calculations, which had a mean weight of 508 kg.

The study found total use was 46.32 mg/kg, accounting for 1.52 DDDVet/animal, a reduction in DDDvet/animal of 10% since 2012.

HP-CIA use[1] was 0.59 mg/kg in 2021, accounting for 0.11 DDDVet/animal/year, a reduction in DDDVet of 59% since 2012. Over 80% comprising tetracyclines and potentiated sulphonamides.

The study suggested that DDDVet/animal has advantages in the equine sector over mg/kg, especially due to the high use of potentiated sulphonamides in equine practice, which have high dose rates and therefore skew the mg/kg results.

The study also explains that the technique of extracting this data from the Practice Management systems Eclipse® was simple and other Practice Management systems could easily be adapted to produce similar information. Video instructions explaining how to generate the antibiotic usage report can be found here. The report then concludes that the results may serve as the foundation of future audits and represents the first step of what will hopefully become a reliable national audit.

2.3.8.3 Industry Updates

RUMA Companion Animal and Equine Group (RUMA CA&E)

"The RUMA Companion Animal and Equine group continue to meet regularly and focus on antibiotic stewardship within the companion animal and equine sectors, as identified in our 2022 annual progress report. In 2022, we held a stakeholder roundtable and identified clinical scenarios to prioritise for further exploration and activity, based on where the group, with their considerable expertise, considered there is the greatest scope to improve antibiotic stewardship. These included cat bite abscesses, kennel cough, acute diarrhoea and cat flu. At the same stakeholder roundtable and in conjunction with the work of our Targets and Measures Working Group (T&MWG), we focused on working together to agree a set of realistic metrics for monitoring and benchmarking antibiotic use at a national level for dogs and cats, with equine metrics to follow on in due course. These metrics were published in our first annual progress report in 2022.

2022 also saw the successful launch of the antibiotic amnesty, which was a campaign to encourage members of the public to return unused or unwanted antibiotics for safe disposal. This was a One Health initiative involving community pharmacies in the Midlands and Veterinary Practices across the United Kingdom and was so successful that it was repeated in 2023. The next steps for RUMA CA&E involve incorporating companion animal experts into the Independent Scientific Group (who provide independent, technical advice on the responsible use of medicines), further exploring antimicrobial usage data standardisation

[1] This was defined in the paper using the World Health Organisation definition which, unlike the ESVAC definition used in the rest of the UK-VARSS report, includes macrolides. However, the study showed macrolide use in horses was very low so this primarily represents fluoroquinolones and third generation cephalosporins

and gathering with stakeholders, including representatives from practice management systems, to improve data reporting (building on a workshop which we held this year), and encouraging the standardisation and collation of laboratory resistance data for the companion animal sectors."

Royal College of Veterinary Surgeons (RCVS) Knowledge

RCVS Knowledge is the charity partner of RCVS:

"As part of the VetTeam AMR initiative, this year saw the launch of a new online training initiative to vets and anyone within the practice team, which was funded by the VMD and provides over 20 hours of Continuous Professional Development (CPD) relating to improving how antibiotics are used in dogs, cats and horses – including practical modules looking at different diseases and conditions in relation to antibiotic use (e.g., cat-bite abscesses, diarrhoea in dogs, respiratory disease in horses etc) as well as modules on diagnostics, behaviour change and infection control. You can access the training here. This complements the other VetTeamAMR initiatives, which includes an auditing and benchmarking tool that is available free of charge for all companion animal and equine teams to collect data on antimicrobial prescribing. This pulls in antimicrobial usage data and allows vet practices to undertake antimicrobial usage audits to better understand what antibiotics are being used, why they are being used and to then monitor the effect of any implemented control measures. Finally, we are currently running an antimicrobial stewardship award scheme, to recognize individuals and teams who are driving continuous improvements in responsible antimicrobial use and are open to anyone who works within the veterinary industry. The closing date for applications is 12th January 2024."

2.4 Methods

Pigs

The antibiotic use 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 use calculated from individual unit data held in the eMB for pig farms across the UK.
- eMB uptake to date has been voluntary and this sample may not be representative for the whole of the UK.
- In terms of pig production, this eMB data covers English slaughter pigs only for 2015 and 2016, and UK slaughter pigs for 2017 to 2022. The eMB data as a percentage of the total clean pig slaughter figures for the relevant region are: 2015 - 61%, 2016 - 70%, 2017 - 87%, 2018 - 89% , 2019 - 95%, 2020 - >95% and 2021 - >95%, 2022 - > 95%

- 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 use and allow year on-year comparisons to be made.
- The data for 2021 were extracted from eMB on 12th August 2022 and these figures will now be fixed as the reference levels for 2021.
- The eMB database and the calculations within it are subject to a series of quality assurance checks to ensure national aggregated figures are as accurate as possible. As a result of this process, the eMB system is continuing to develop and work to further improve data accuracy is ongoing.
- The calculations used for the eMB data are in-line with the methods used by the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project, to allow comparisons to be made with European counterparts.

Meat poultry

The British Poultry Council (BPC) provided antibiotic use data for the poultry meat (broilers, 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 (broilers, duck) or annual (turkey and all breeders) antibiotic use data in the form of an aggregate spreadsheet. BPC then collate the data and report use 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 use figure. BPC calculates the population at risk of treatment by using annual slaughter numbers and standardised estimated weights at time of treatment (boilers: 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 use 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, a farm assurance 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 use 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 bird 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) and the British Veterinary Poultry Association (BVPA) gamebird subcommittee coordinated a comprehensive, voluntary data collection exercise to measure the use of antibiotics throughout the sector for 2022. 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.

Aquaculture

The trout data were collected from the main veterinary practices dealing with trout in England and Scotland and represent approximately 90% of UK trout production. The salmon use data were collected by Salmon Scotland 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.

Companion animals

Mg/kg for dogs and cats

In this metric, mg refers to the weight of antibiotic active ingredient sold for use in dogs and cats. As with the mg/PCU metric, topical products (e.g. those for treating eye, ear and skin infections) are excluded. The denominator is the estimated weight of the whole dog and cat population at risk. The total number of dogs and cats in the UK is estimated using statistics from the PDSA PAW report, which is a survey that is representative of the UK pet-owning population. This is then multiplied by the aggregated mean weight for all adult cats and all adult dogs registered at practices participating in the Small Animal Veterinary Surveillance Network (SAVSNET) between 2013 and 2021 (excluding animals aged under two years, over 22.5 years for dogs and 27.5 years for cats and/or with unrealistic weight measurements). We didn't have this data for 2022 so have used the 2021 dog and cat weights for the calculations.

The metric is calculated separately for dogs and cats, with the amount of antibiotic active ingredient separated by dog and cat. For products licensed for more than one species, the relative amount of total product sold which is consumed by dogs and cats have been estimated. Estimates are obtained by the VMD from stratification data provided by the Market Authorisation Holder (MAH) for each product. The stratification data indicates the percentage of each product which is estimated to have been used in dogs and in cats, respectively, in any given year. Only products which were licensed for dogs and/or cats +/- other species commonly seen in small animal practice (e.g. rabbits, rodents and exotics) were considered. Products indicated for dogs and/or cats alongside horses and/or food producing animals were not considered, as it is harder to accurately provide stratification estimates for these products, which are primarily injectables and are used increasingly in food producing animals.

The average number of Daily Defined Doses per animal per year (DDDVet/animal) for dogs and cats

The main issues with using mg/kg for trend monitoring in dogs and cats are that it underestimates the use of long acting injectables (which are very commonly used in cats) and there are also some big variations in dose rate. For example, marbofloxacin has a dose rate of 2 mg/kg/day, whereas metronidazole has a dose rate of 50 mg/kg/day. For this reason, dog and cat (companion animal) trend sales data for systemic antibiotics is presented and calculated using the average number of Daily Defined Doses (DDDVet) per animal per year(DDDVet/animal). This metric has been developed alongside, and with the support of, the RUMA Companion Animal and Equine group.

The DDDVet is defined as the assumed average dose per kg animal treated per species per day. These standard daily doses are extracted from the Summary of Product Characteristics (SPC) for each antibiotic product. If there is a dose range, then the lowest dose was chosen,

and where the dose rate varies between products with the same active ingredient/ route of administration, then the median dose rate was selected. For long-acting products, the DDDVet is calculated by dividing the daily dose rate with the length of activity for that product. A full list of the DDDVet figures used for each active ingredient/ route of administration can be found in Table S1.3.1 of Supplementary Material 1.

The DDDVet/animal is calculated (for each active ingredient/ route of administration and for both dogs and cats) using the method below:

$$\frac{\text{Total amount of active ingredient (mg)}}{\text{[DDDVet (mg/kg/day) * total animal population weight at risk (kg)]}}$$

The results are then added together to get the total figure. The mg of antibiotic active ingredient and total weight of animal population at risk is calculated in the same way as described above for the mg/kg calculation.

Ruminant data

The antibiotic use data for sheep and dairy were extracted from the Medicine Hub for Ruminants, which was developed by the ruminant industry with support from the VMD and launched by the Agriculture and Horticulture Development Board (AHDB) in 2021.

The scope and limitations of the data (as provided by Medicine Hub) are presented in the following bullet points:

- For sheep, these data are aggregated figures for antibiotic use calculated from individual enterprise data held in the Medicine Hub for participating sheep flocks across the UK.
- For dairy, these data are aggregated figures for antibiotic use calculated from individual enterprise data held in the Medicine Hub and from aggregate 'bulk data' supplied by third part data holders.
- Medicine Hub uptake to date has been voluntary and this sample may not be reflective of the antibiotic use situation across the whole of the UK
- The data are supplied by farmers, their vets, or bulk data holders and, although clear outliers have been identified and queried, AHDB is not able to validate every individual farmer's data. However, at an aggregated level, the data provide an initial indication of usage within the sample provided.
- The data for 2022 were extracted from Medicine Hub on 22nd September 2023
- The Medicine Hub database and the calculations within it are subject to a series of quality assurance checks to ensure aggregated antibiotic use figures are as accurate as possible. As a result of this process, the Medicine Hub system is continuing to develop and work to further improve data accuracy is ongoing.
- The calculations used for the Medicine Hub data are in-line with the methods used by the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project, to allow comparisons to be made with European counterparts.

The mg/PCU metric uses the number of living dairy cows for dairy AMU and the number of living sheep and lambs slaughtered multiplied by a standardised average weight for each

defined animal category at time of treatment with an antibiotic, for the dairy and sheep sectors respectively. For more details please see the Supplementary Material 1.

Total UK population data to calculate % coverage is obtained from Defra statistics on the total number of living dairy cows, the total number of beef animals slaughtered in 2022 and UK annual sheep and lambs slaughtered the UK in 2022.

CHAPTER 3

Harmonised monitoring of antibiotic resistance

This programme was originally developed to harmonise monitoring and reporting of antimicrobial resistance (AMR) in the food chain across Europe. It involves testing for resistance in zoonotic and commensal bacteria from healthy food-producing animals at slaughter, on-farm Salmonella isolates from the poultry National Control Programmes (NCP), and food products at retail. The UK is maintaining these surveillance activities to ensure the continuity of data outputs, trends, and indicators from this long-term programme. Maintaining international harmonisation in this area also facilitates comparability of AMR data with other countries across Europe.

In the UK, key livestock species are monitored in alternating years: poultry in even-numbered years, pigs in odd-numbered years. The 2022 data presented here originates from healthy poultry. The points in the food chain at which different poultry species are sampled are summarised in **Figure 3.1** and detailed in Table S1.1.1 in Supplementary Material 2. Sampling is designed to be representative of the UK poultry population.

In 2022, samples were collected from slaughterhouses processing 73% of domestically produced broilers, and 90% of fattening turkeys, which gives us an indication of the prevalence of resistance in these bacteria in meat poultry across the UK. Caecal samples collected from broilers and turkeys were used to isolate *Escherichia coli*, *Campylobacter coli*, *Campylobacter jejuni*, *Enterococcus faecium*, and *Enterococcus faecalis* bacteria, which were tested for AMR. *C. coli*, *E. faecium* and *E. faecalis* were included in the monitoring for the first time this year. *Salmonella* isolates collected from on-farm samples, taken as part of the National Control Programme (NCP) were also tested for AMR. Results of these tests are presented in this chapter as the percentage of individual isolates with resistance to individual antibiotics.

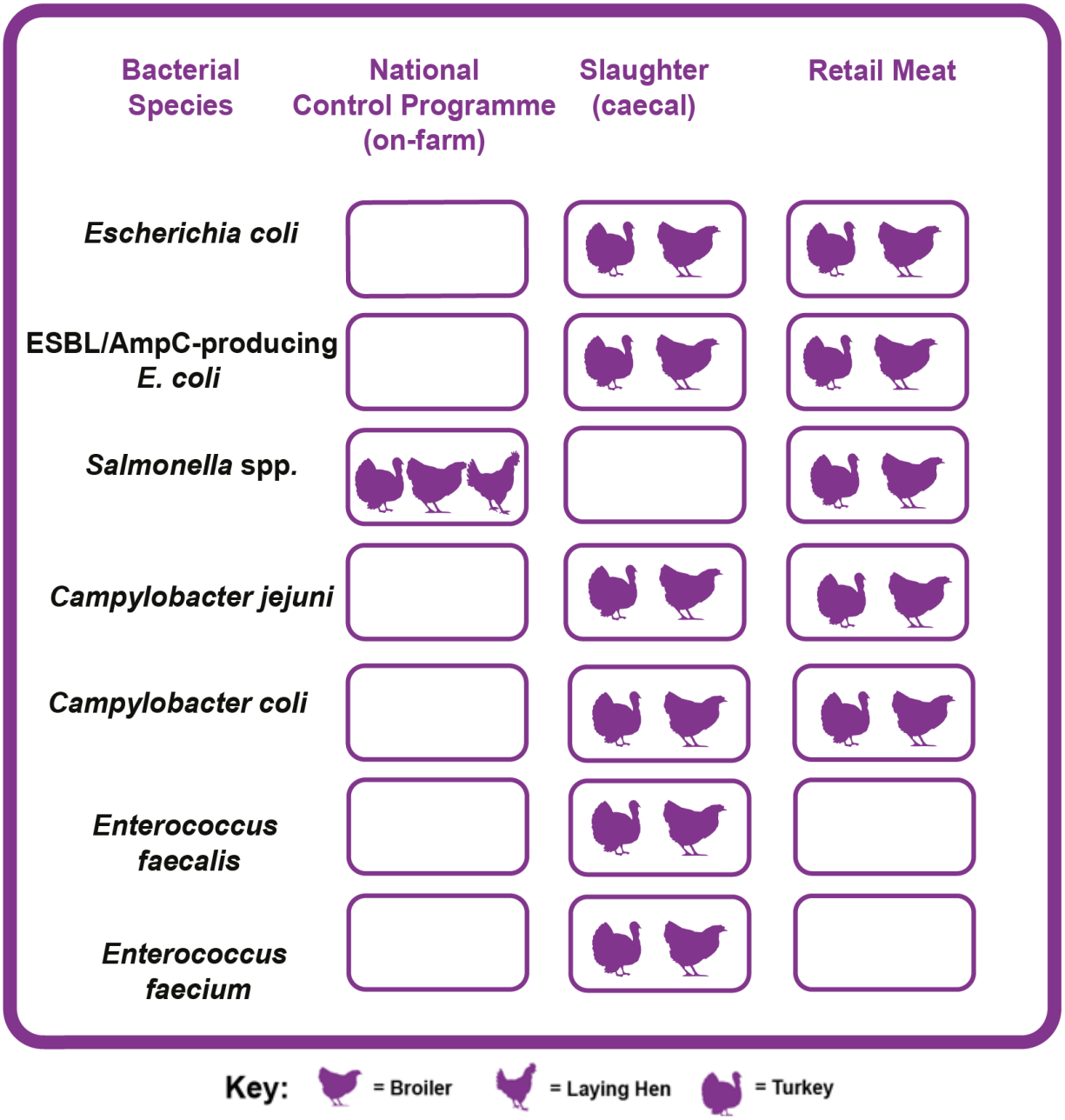
We also used selective media to detect the proportion of individual birds carrying extended spectrum beta lactamase (ESBL)- and AmpC-producing *E. coli*, also carbapenamase producing *E.coli*, which are resistant to specific highest priority critically important antibiotics (HP-CIAs). This measures the proportion of poultry carrying any *E. coli* resistant to third- and fourth-generation cephalosporins or carbapenems, even at very low levels.

Some of these results are combined to produce key outcome indicators for AMR in food-producing animals. These indicators are averaged over two years and are weighted by the size of pig and poultry populations, thereby providing an overall measure of AMR in these species in the UK.

Epidemiological cut-off values (ECOFFs) were used to assess resistance to the antibiotics tested. 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. ECOFFs are more sensitive than clinical breakpoints (CBPs) for detecting emerging resistance issues. A ‘decreased susceptibility’ or ‘resistant’ result based on ECOFFs does not necessarily imply a level of resistance that would correspond to clinical treatment failure.

The Food Standards Agency (FSA) lead on the testing and reporting of AMR in retail meat, which is published here.

Figure 3.1: Sampling for AMR harmonised monitoring in 2022.



3.1 Summary

- *E. coli* results are used to generate key harmonised outcome indicators, which give an overall measure of AMR in UK pig and poultry populations. These indicators show an overall positive picture for 2022.
- *Enterococcus faecalis* and *E. faecium* were added to the programme this year as indicator species for the detection of AMR in Gram-positive bacteria. This addition also allows for the detection of vancomycin-resistant enterococci (VRE) which are of clinical importance. No VRE were detected.
- For *Salmonella* spp., full susceptibility to the panel of antibiotics tested has increased in broilers (79%) and layers (93%) and remains stable in turkeys (20%).
- For *Campylobacter jejuni*, we continued to detect very high levels of resistance to the HP-CIA ciprofloxacin in broilers (59%). In turkeys, it reduced from 35% in 2020 to 26% in 2022.
- *Campylobacter coli* was added to the surveillance programme this year, as it is often more resistant than *C. jejuni* to several important antimicrobials and may transfer resistance genes to *C. jejuni*. In 2022, ciprofloxacin resistance was lower in *C. coli* isolated from broilers (27%) than in *C. jejuni*, whereas in turkeys, ciprofloxacin resistance was higher in *C. coli* (45%).
- We implemented testing for carbapenem resistance in *Campylobacter.* Ertapenem was included in the antibiotic panel to maintain international harmonisation and determine levels of resistance to this HP-CIA. However, methodological uncertainties make the results difficult to interpret (see **Box 3.1**).
- Selective media was used to detect the presence of ESBL/AmpC- and carbapenamase-producing *E. coli* in individual animals, even at very low levels. Carriage of ESBL-producing *E. coli* increased in both broilers (7.8%, up from 3.4% in 2020) and turkeys (7.7%, up from 1.2% in 2020). Results from the selective media also showed an increase in the carriage of AmpC-producing *E. coli* in broilers (2.7%, up from 1.1% in 2020). There was a marked increase in the co-resistance to ciprofloxacin in the ESBL/AmpC-producing *E. coli* from the selective media from broilers: 77% compared to 38% in 2020.

3.2 Methods

3.2.1 Sample collection and culture

Caecal samples were taken from healthy broilers and fattening turkeys at slaughter for the isolation of *E. coli*, *C. jejuni*, *C. coli*, *E. faecalis*, and *E. faecium*, as described in Decision (EU) 2020/1729. Enhancements to this year's programme included the addition of the bacterial species, *E. faecalis*, *E. faecium* and *C. coli*.

Boot/dust swabs were collected for the isolation of *Salmonella* in accordance with the National Control Programmes (NCP) for broilers, layers, and turkeys. This is the first year for

which the isolation of *Salmonella* from neck fold swabs, collected by Food Business Operators (FBO), was not included.

Caecal samples were also cultured on selective media for ESBL-, AmpC- and/or carbapenemase-producing *E. coli* following standardised methods. The use of selective media allows for the amplification and selection of *E. coli* resistant to the 3rd and 4th generation cephalosporins and to the carbapenems, in individual animals, at very low levels.

All countries within the UK were included in the sampling frame and contributed isolates from each of *E. coli*, *Salmonella*, *C. jejuni*, and *C. coli*. Isolates of *E. faecium* and *E. faecalis* were not taken from Northern Ireland in 2022. The sampling plan was randomised, stratified, and weighted by slaughter throughput.

3.2.2 Antibiotic susceptibility testing (AST)

AST was carried out by the national reference laboratories (NRLs) using European Committee on Antimicrobial Susceptibility Testing (EUCAST) methodology. Single typical colonies were selected for speciation and susceptibility testing. Standardised broth microdilution was used to determine the minimum inhibitory concentration (MIC) against a panel of antibiotics. The antibiotics used are listed in Table S1.4.1 of Supplementary Material 2**.** Antibiotics tested include those authorised for use in food producing animals, those critically important to human health and others which are representative of an antibiotic class or resistance mechanism.

Antibiotic panels have been updated since 2020. Updates include the addition of amikacin for *E. coli* and *Salmonella*, and the replacement by chloramphenicol and ertapenem of streptomycin and nalidixic acid for *Camplylobacter*.

3.2.3 Interpretation of results

The European Committee on Antimicrobial Susceptibility Testing (EUCAST) methodology for epidemiological cut-off values (ECOFF) was used in this report. Where possible EUCAST ECOFFs were used to interpret the MIC results. Where there were no EUCAST values available or where values have changed since 2020 the EFSA-recommended cut-off values were used.

Historical data presented in this report (other than fully-susceptible *Salmonella*) has been updated to reflect cut-off values used in 2022. Results are provided in full for ECOFFS and clinical breakpoints (CBPs)(S2.1 – S2.4) in Supplementary Material 2.

3.2.4 Whole genome sequencing

Whole genome sequencing (WGS) and *in silico* bioinformatic tools were used to detect the antibiotic resistance determinants present in the isolates with ESBL or AmpC phenotypes.

3.2.5 Harmonised AMR outcome indicators

The quadripartite (World Health Organisation WHO, Food and Agriculture Organisation of the United Nations FAO, World Organisation for Animal Health WOAH, and the United Nations Environment Programme UNEP) have recommended core outcome indicators. This report includes these indicators as well as one primary and three secondary indicators, weighted by population size.

E. coli is the indicator organism due to its ubiquitous nature in animals, food, and humans, and its ability to readily develop or transfer resistance. The indicators are averaged over two years due to the alternating schedule for AMR pig and poultry sampling and are weighted by population size, expressed in Population Correction Unit (PCU) (see section 2.4).

3.3 Results

Table 3.1: Classification of resistance as low, moderate, high etc. throughout the report is consistent with EFSA definitions for these terms.

Description of resistance level	Equivalent percentage resistance range
Rare	<0.1%
Very low	0.1% to 1%
Low	>1% to 10%
Moderate	>10% to 20%
High	>20% to 50%
Very high	>50% to 70%
Extremely high	>70%

Where a figure in this chapter shows no data for certain antibiotics or years, this is either because no resistance was detected or that the antibiotic was not included in the panel for that particular year.

3.3.1 Harmonised AMR outcome indicators

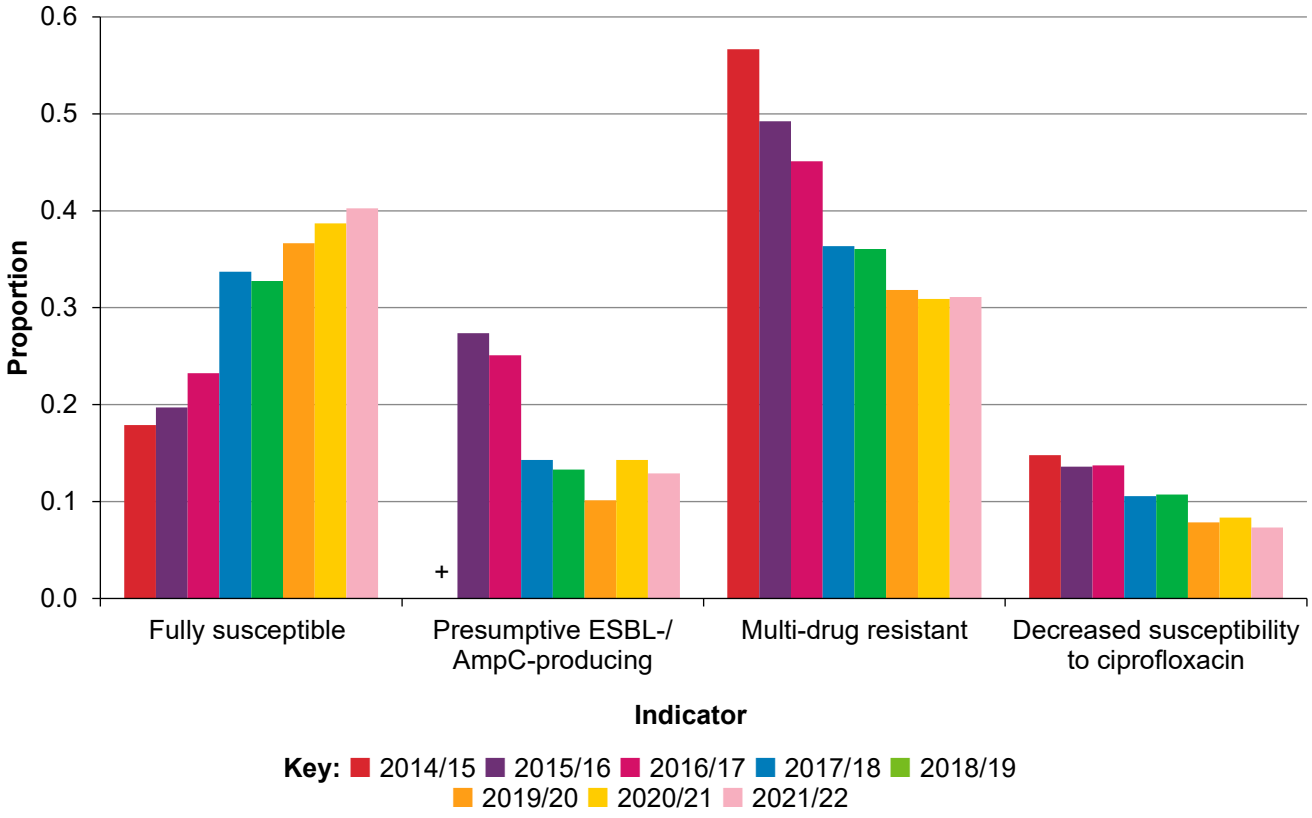
Indicators are an important tool for interpreting and comparing the results of AMR monitoring programmes. Indicators that are standardised and harmonised between different countries and livestock sectors allow for data to be reported in a consistent way over time, facilitating the assessment of trends, and enabling international comparison in a transparent way. These results therefore give us an indication of the UK's progress in combatting AMR in pigs and poultry. They are averaged over two years, encompassing AMR results from broilers, turkeys, and pigs, and weighted by livestock population size.

The primary indicator is the proportion of isolates fully susceptible to the entire panel of antibiotics. The secondary indicators are: the proportion of caecal samples on selective media with presumptive ESBL-/AmpC-producing *E. coli;* the proportion of MDR isolates; and the proportion of isolates with decreased susceptibility to the fluoroquinolone ciprofloxacin.

Thus, we would like to see a positive trend in the primary indicator and a negative trend in the secondary indicators.

For the 2021 to 2022 monitoring period, all indicators show considerable improvement since the start of the monitoring period (2015/2016 for presumptive ESBL-/AmpC-producing *E. coli*, and 2014/2015 for all other indicators, **Figure 3.2**). The primary indicator is at a new record high of 0.40. The secondary indicators remain substantially lower than those reported at the beginning of the monitoring period; however, they appear to have stabilised in recent years.

Figure 3.2: Proportion of harmonised monitoring *Escherichia coli* from broilers, fattening turkeys and fattening pigs weighted by PCU, averaged over two years. ESBL/AmpC results refer to caecal samples, all other indicators refer to isolates.



+ Data not available

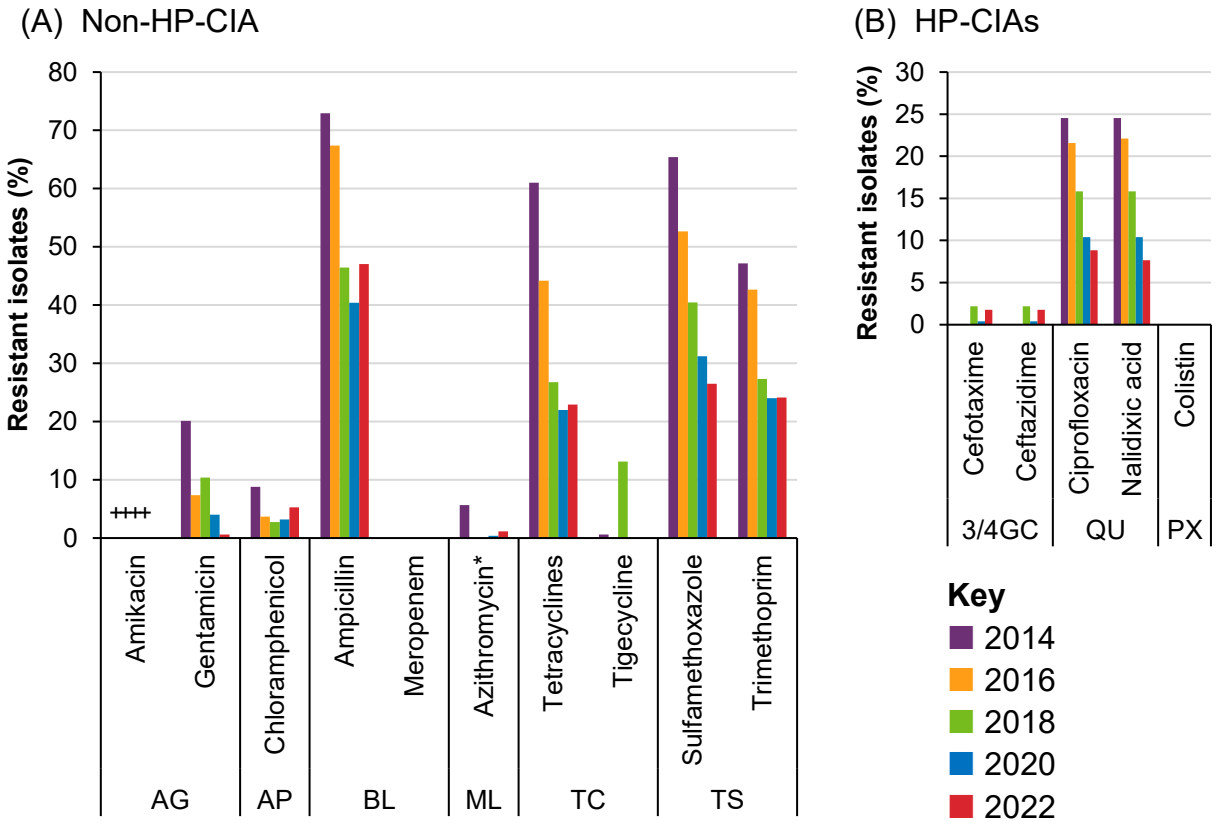
3.3.2 *Escherichia coli*

3.3.2.1 Broilers

Resistance of indicator *E. coli* isolates from broiler caecal samples is shown in **Figure 3.3**. A total of 170 *E. coli* isolates were tested. Full susceptibility to the panel of antibiotics tested increased from 42% in 2020 to 45% in 2022 and is substantially above 2014 levels (15%). The numbers of MDR isolates remained stable at 27%, which is considerably lower than 2014 levels (64%). Resistance to the non-HP-CIAs, shown in **Figure 3.3 (A)**, remained similar to levels detected in 2020, and substantially lower than in 2014.

For the HP-CIAs, shown in **Figure 3.3 (B)**, resistance to the third-generation cephalosporins, cefotaxime and ceftazidime, remained low at 1.8%. The three resistant isolates identified expressed the ESBL phenotype, and one was co-resistant to ciprofloxacin. Resistance to the quinolones continued a sharp downward trend, with 8.8% and 7.6% of isolates resistant to ciprofloxacin and nalidixic acid, respectively. One of these isolates expressed high-level resistance (MIC ≥4.0 mg/L to ciprofloxacin. Resistance to colistin was not detected.

Figure 3.3: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Escherichia coli* isolated from healthy broilers at slaughter. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



+ Not tested
* Interpreted using an EFSA-recommended ECOFF
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, PX: polymyxins, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

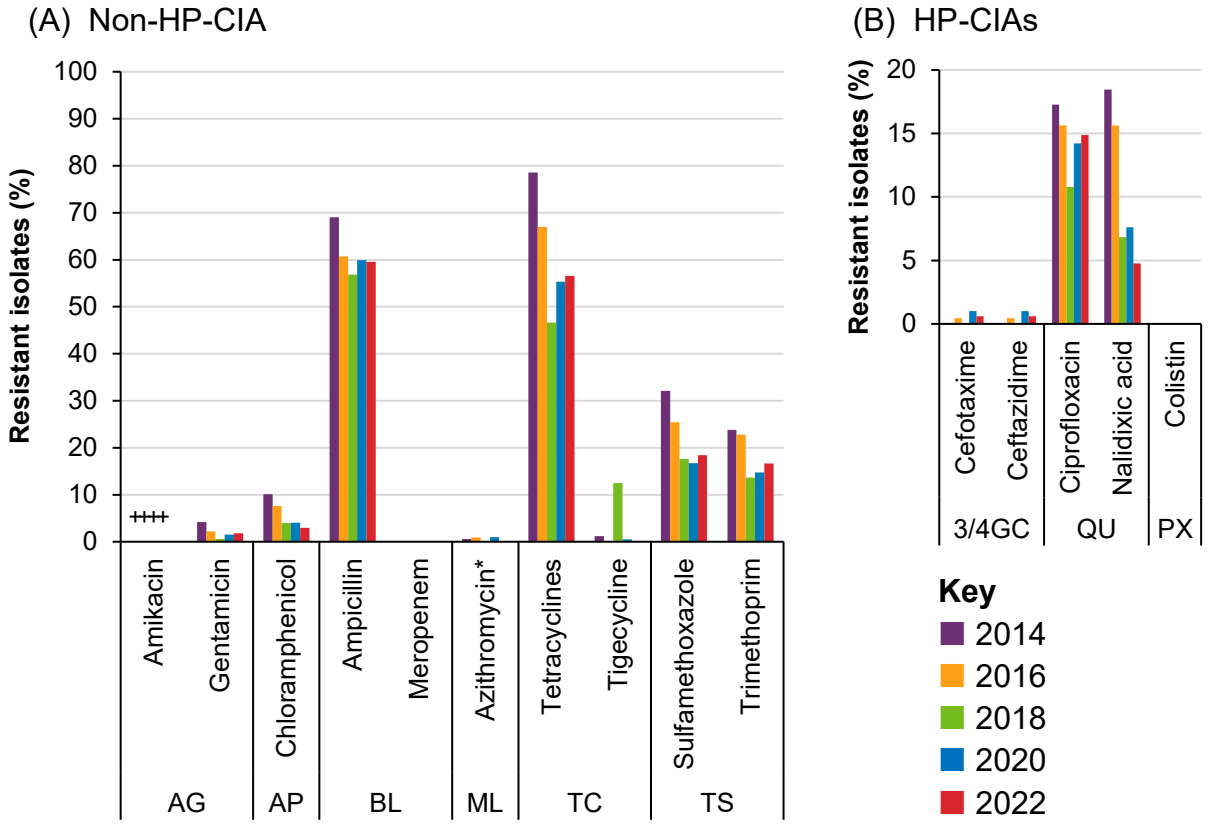
3.3.2.2 Turkeys

Resistance of *E. coli* isolated from turkey caecal samples is shown in **Figure 3.4**. A total of 168 *E. coli* isolates were tested. Full susceptibility of isolates to the panel of antibiotics tested decreased from 29% in 2020 to 22% in 2022 but remains above 2014 levels (11%). The numbers of MDR isolates have increased slightly since 2016, to 26% in 2022, but remain lower than 2014 levels (39%). Resistance to non HP-CIAs, shown in **Figure 3.4 (A)**, has remained relatively stable since 2018 and below the levels first recorded in 2014.

Of the HP-CIAs, shown in **Figure 3.4 (B)**, resistance to the third-generation cephalosporins, cefotaxime and ceftazidime, remained very low at 0.6%. This relates to a single isolate,

which expressed the ESBL phenotype and had high-level co-resistance to ciprofloxacin (MIC greater than 4 mg/L). Resistance to the fluoroquinolone ciprofloxacin was seen in 15% of isolates, which appears to be on an upward trend since 2018. High-level resistance to ciprofloxacin (MIC greater than 4mg/L) was observed in 8.0% of ciprofloxacin-resistant isolates. Colistin resistance remains undetected in *E. coli* isolated from turkeys.

Figure 3.4: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Escherichia coli* isolated from healthy turkeys at slaughter. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



\+ Not tested

* Interpreted using an EFSA-recommended ECOFF

AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, PX: polymyxins, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

3.3.3 *Enterococcus* spp.

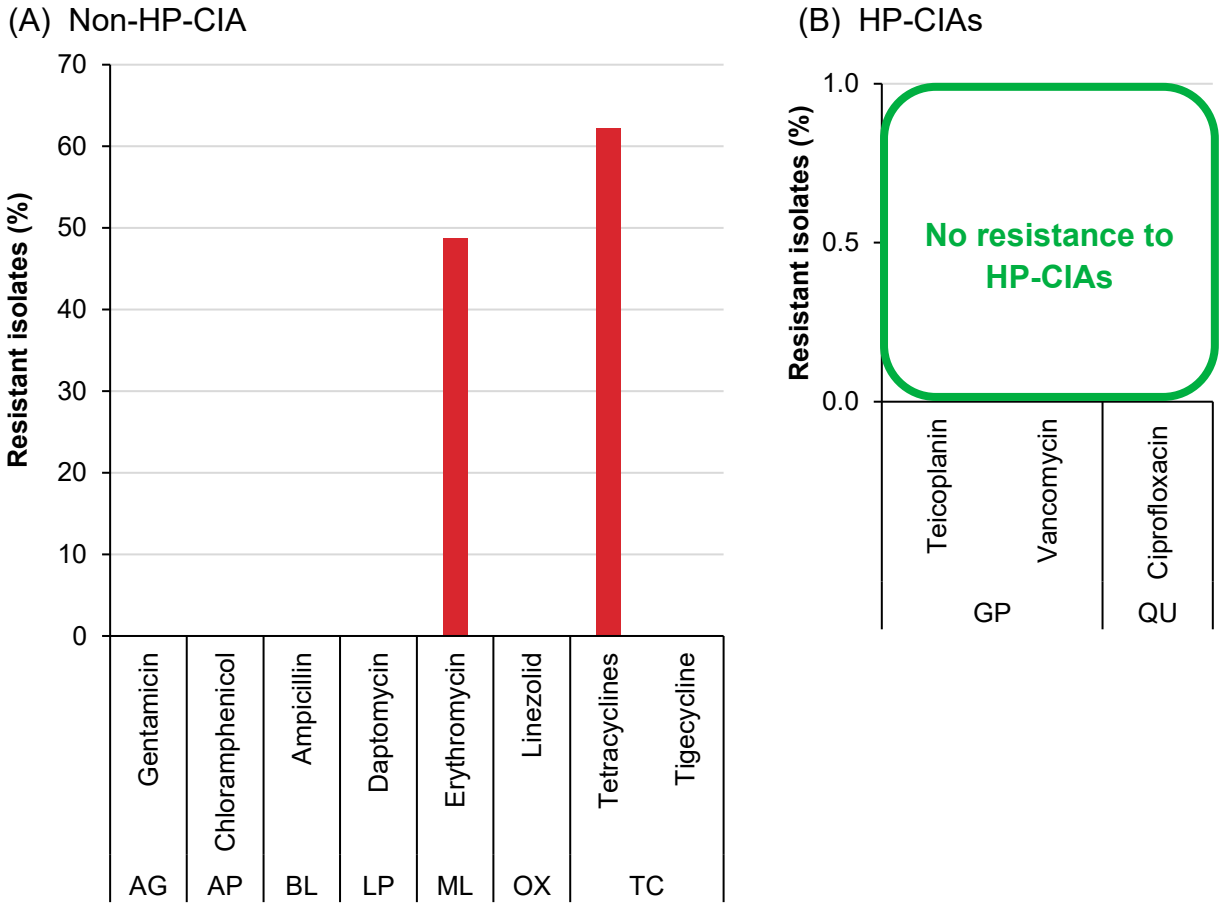
E. faecalis and *E. faecium* are new additions to our AMR surveillance programme. Enterococci were included as indicator species for resistance in Gram-positive bacteria. Also, vancomycin-resistant enterococci (VRE) are of particular concern, as they are associated with higher human mortality rates than vancomycin-sensitive enterococci.

3.3.3.1 *Enterococcus faecalis*

Broilers

A total of 74 *E. faecalis* isolates were tested from broilers. Of the 74 isolates, 23% were sensitive to all of the antibiotics in the panel and no isolates were MDR. VRE were not detected. High levels of resistance were seen to erythromycin (49%) and very high levels to tetracycline (62%). Resistance of *Enterococcus faecalis* isolates from broiler caecal samples is shown in **Figure 3.5**.

Figure 3.5: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Enterococcus faecalis* isolated from broilers at slaughter in 2022. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.

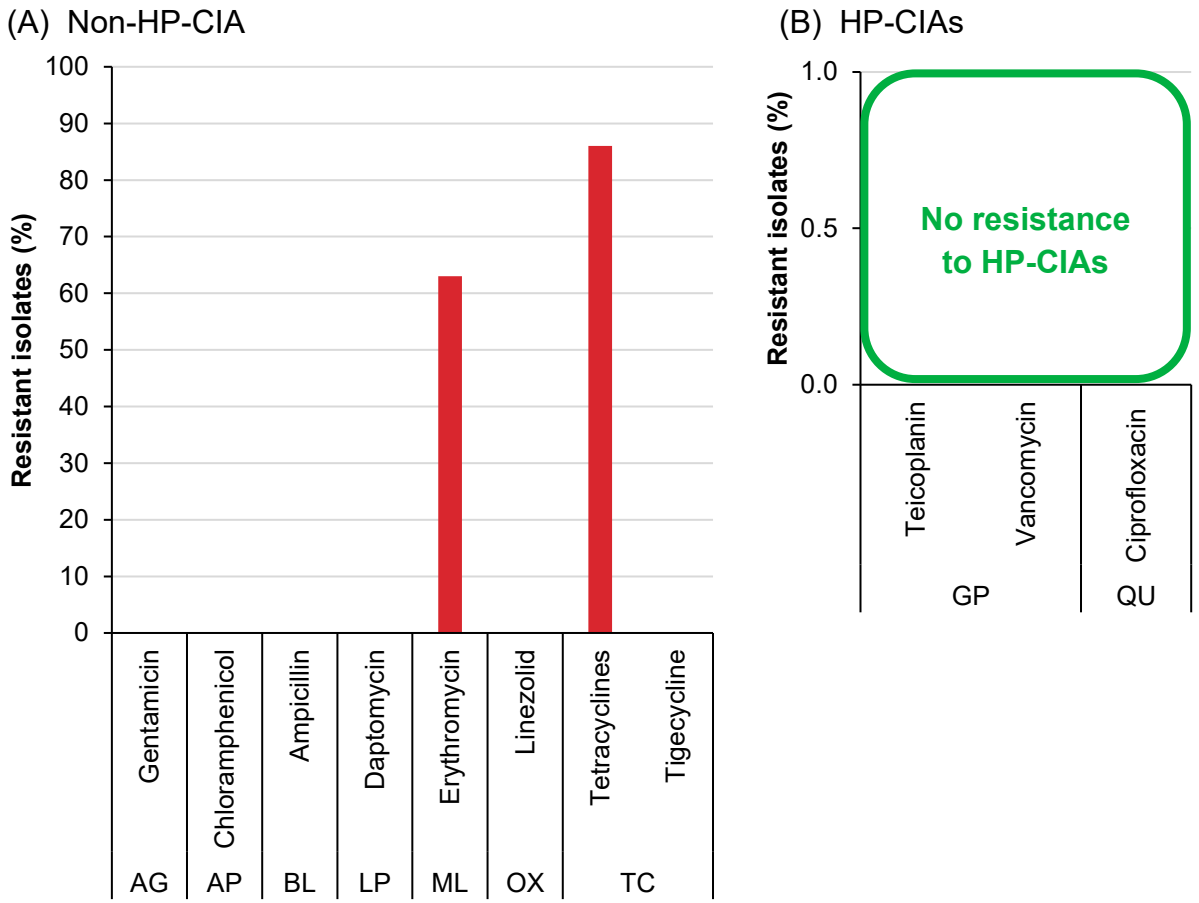


AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, GP: glycopeptide, LP: lipopeptide, ML: macrolides, OX: oxazolidinone, QU: quinolones, TC: tetracyclines

Turkeys

A total of 100 *E. faecalis* isolates were tested from turkeys. Of the 100 isolates, 12% were sensitive to all of the antibiotics in the panel and no isolates were MDR. VRE were not detected. Very high levels of resistance were seen to erythromycin (63%) and extremely high levels to tetracycline (86%). Resistance of *E. faecalis* isolates from turkey caecal samples is shown in **Figure 3.6**.

Figure 3.6: Resistance to non-HP-CIAs (A) and HP-CIAs in *Enterococcus faecalis* isolated from turkeys at slaughter in 2022. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, GP: glycopeptide, LP: lipopeptide, ML: macrolides, OX: oxazolidinone, QU: quinolones, TC: tetracyclines

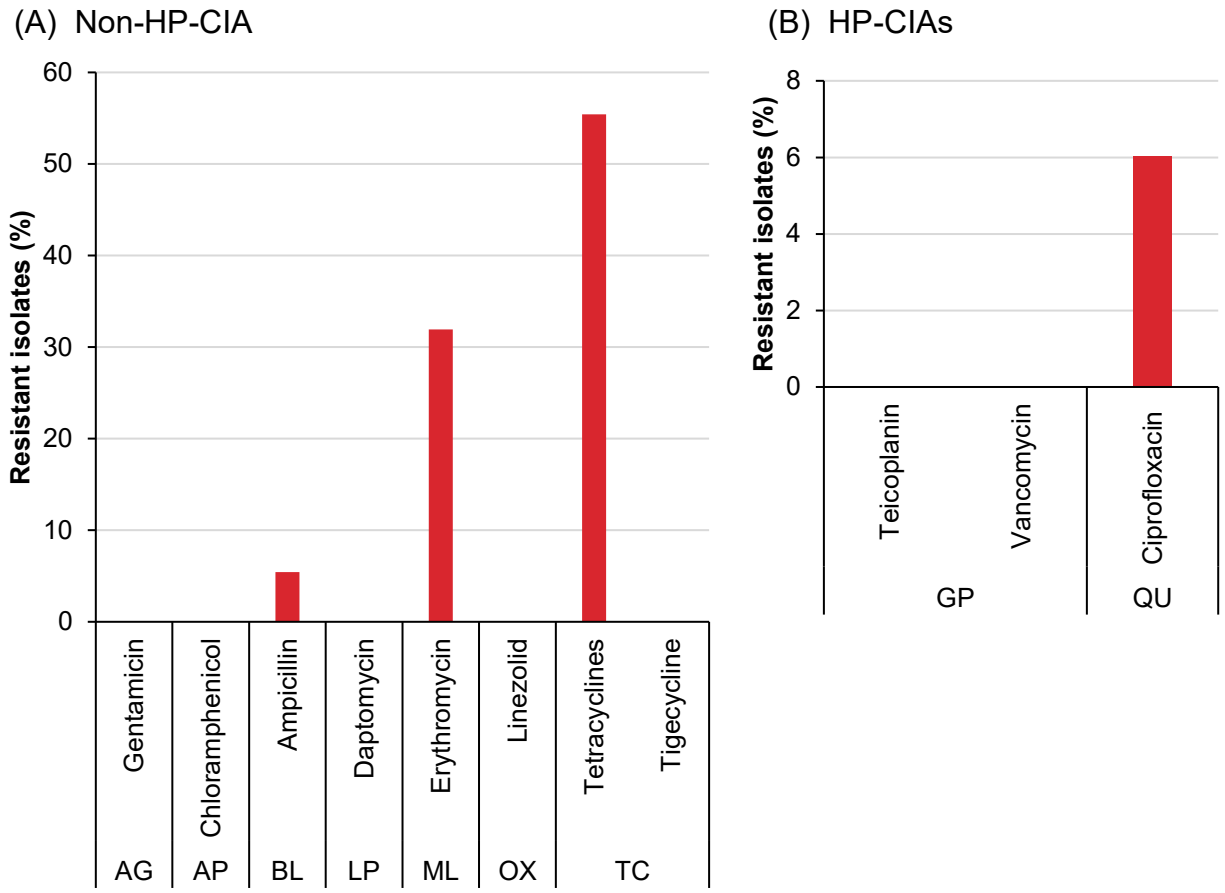
3.3.3.2 *Enterococcus faecium*

Broilers

A total of 166 *E. faecium* isolates were tested from broilers. Of the 166 isolates, 32% were sensitive to all of the antibiotics in the panel and 5% of isolates showed MDR. VRE were not detected. Very high levels of resistance were seen to tetracycline (55%) and high levels to erythromycin (32%) whilst low levels of resistance were seen to both ampicillin (5.4%) and

the HP-CIA, ciprofloxacin (6.0%). Resistance of *E. faecium* isolates from broiler caecal samples is shown in **Figure 3.7**.

Figure 3.7: Resistance to non-HP-CIAs (A), and HP-CIAs (B) in *Enterococcus faecium* isolated from broilers at slaughter in 2022. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.

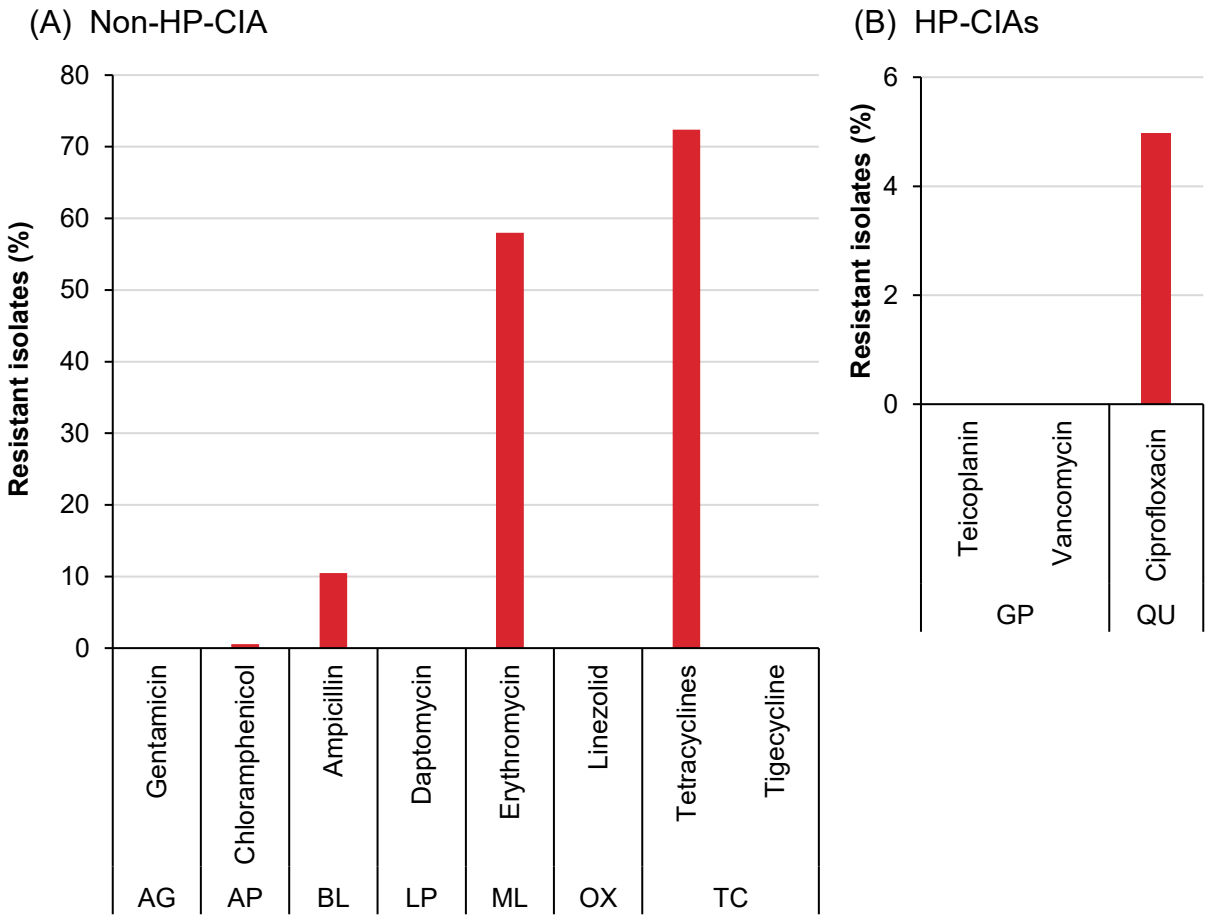


AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, GP: glycopeptide, LP: lipopeptide, ML: macrolides, OX: oxazolidinone, QU: quinolones, TC: tetracyclines

Turkeys

A total of 181 *E. faecium* isolates were tested from turkeys. Of the 181 isolates, 24% were sensitive to all of the antibiotics in the panel and 7% of isolates showed MDR. VRE were not detected. Extremely high levels of resistance were seen to tetracycline (72%) and very high levels to erythromycin (58%). Resistance of *E. faecium* isolates from turkey caecal samples is shown in **Figure 3.8**.

Figure 3.8: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Enterococcus faecium* isolated from turkeys at slaughter. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



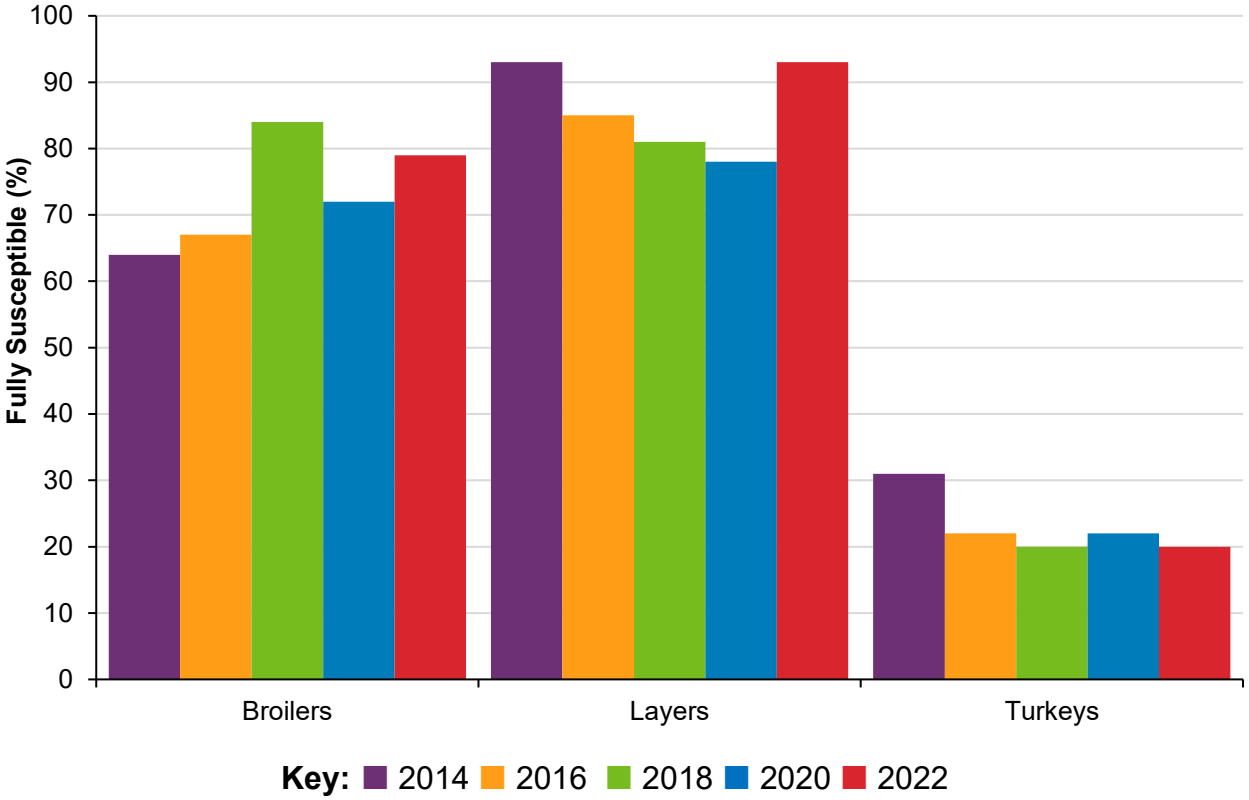
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, GP: glycopeptide, LP: lipopeptide, ML: macrolides, OX: oxazolidinone, QU: quinolones, TC: tetracyclines

3.3.4 *Salmonella* spp.

Salmonella is an important cause of foodborne disease in people and can cause disease in animals. The *Salmonella* National Control Programme (NCP) ensures effective surveillance of the UK's poultry industry for *Salmonella* that are considered to be a public health risk. The Harmonised Monitoring programme for AMR utilises representative samples taken under the NCP.

An important indicator of resistance is the number of isolates fully sensitive to the panel of antibiotics tested. This can be seen in **Figure 3.9** for resistance to *Salmonella* in broilers, layers, and turkeys. There was an increase in the numbers of fully susceptible isolates from broilers (79%) and layers (93%), and a slight decrease in the numbers from turkeys (20%).

Figure 3.9: *Salmonella* spp. isolates susceptible to all tested antibiotics, from broilers, layers and turkeys.



3.3.4.1 Broilers

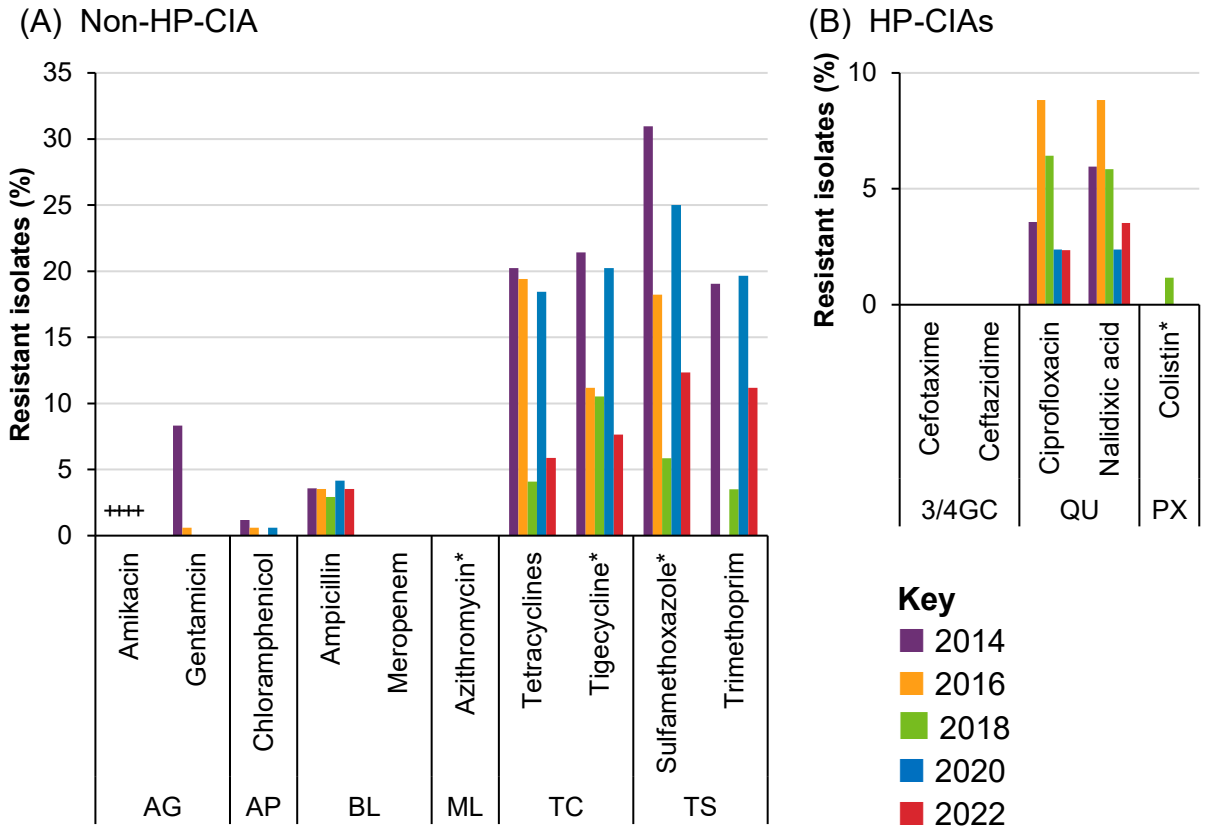
A total of 170 *Salmonella* isolates were tested from broiler flocks, collected through the NCP. Full details of NCP serovars are available here. The most tested serovars included *S.* Mbabdaka (54 isolates), the incomplete serovar 13,23:i:- (29 isolates), *S.* Montevideo (23 isolates), and *S.* Kedougou (20 isolates). Two isolates of monophasic *S.* Typhimurium 4,5,12:i:- were tested. No isolates of *S.* Enteritidis or *S.* Typhimurium were included in the randomised samples.

Resistance to *Salmonella* in broilers is shown in **Figure 3.10**. For the non HP-CIAs, shown in **Figure 3.10 (A)**, no resistance was detected to amikacin, azithromycin, gentamicin, meropenem or chloramphenicol. Resistance to the remaining antibiotics remained stable or has reduced since 2020. Resistance to the sulfonamides and tetracyclines is largely associated with the *S.* Kedougou serovar. Both of the monophasic *S.* Typhimurium isolates showed low-level resistance to ampicillin, sulphamethoxazole and tetracyclines, which is a resistance pattern typical of this serovar. An *S.* Infantis isolate was resistant to ciprofloxacin, nalidixic acid, sulphamethoxazole, tetracycline, tigecycline (marginal) and trimethoprim. This resistance pattern is typical of a clone of *S.* Infantis prevalent in parts of Europe in broilers, but which is rarely detected in the UK.

Of the HP-CIAs, shown in **Figure 3.10 (B)**, full susceptibility to the third-generation cephalosporins, cefotaxime and ceftazidime, was maintained between 2014 and 2022.

Levels of resistance to the fluoroquinolone ciprofloxacin remained low at 2.4% of isolates. These isolates were also resistant to nalidixic acid. No resistance to colistin was detected.

Figure 3.10: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Salmonella* isolated from broiler flock NCP samples. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



+ Not tested
* Interpreted using an EFSA-recommended ECOFF
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, PX: polymyxins, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

3.3.4.2 Layers

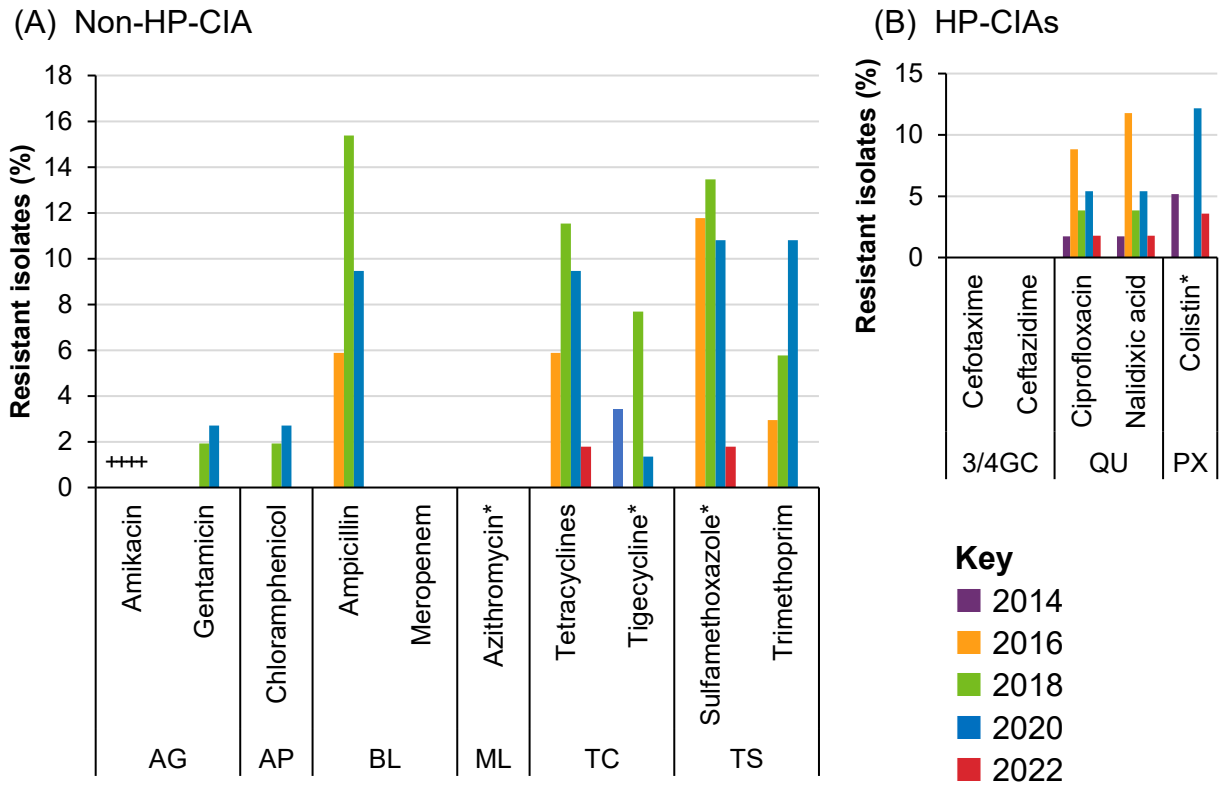
A total of 56 *Salmonella* isolates were tested from laying hen flocks collected through the NCP. These included *S*. Enteritidis (8 isolates), *S*. Typhimurium (eight isolates) and a single monophasic *S*. Typhimurium.

Resistance to *Salmonella* in laying hens is shown in **Figure 3.11**. For the non-HP-CIAs, shown in **Figure 3.11 (A)**, resistance was either low or not detected. The monophasic *S*. Typhimurium isolate was resistant to both sulfamethoxazole and to tetracycline.

Of the HP-CIAs, shown in **Figure 3.11 (B)**, full susceptibility to the third-generation cephalosporins, cefotaxime and ceftazidime, was maintained between 2014 and 2022. One isolate was resistant to both ciprofloxacin (1.8%), and nalidixic acid (1.8%). Two isolates

showed resistance to colistin (3.6%), both of which were *S*. Dublin, a Group D *Salmonella*, which have a degree of intrinsic resistance to colistin.

Figure 3.11: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Salmonella* isolated from layer flock NCP samples. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



+ Not tested
* Interpreted using an EFSA-recommended ECOFF
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, PX: polymyxins, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

3.3.4.3 Turkeys

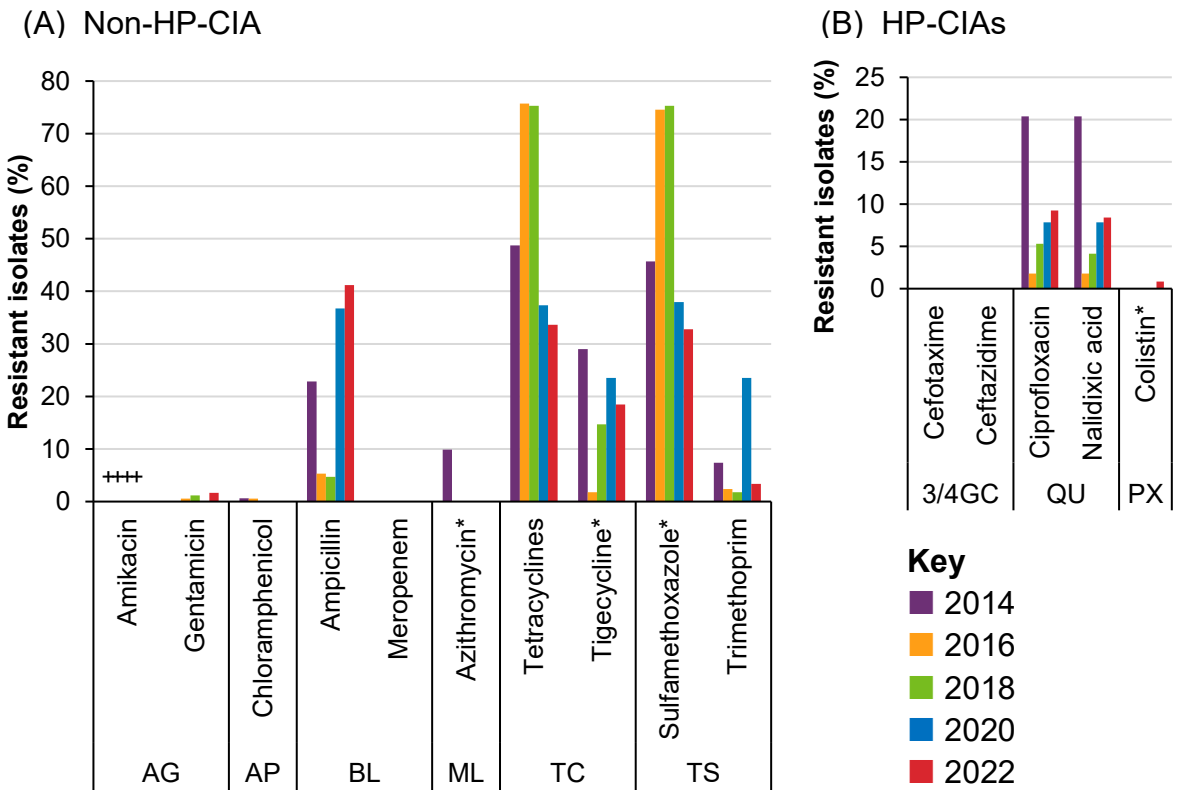
A total of 119 *Salmonella* isolates were tested for AMR from turkey flocks, collected through the NCP. These included *S*. Kedougou (28 isolates), *S*. Anatum (38 isolates), *S*. Derby (11 isolates), *S*. Senftenberg (eight isolates), and monophasic *S*. Typhimurium (4,5,12:i:-, 1 isolate and 4,12:i:-, 2 isolates). No *S*. Typhimurium or *S*. Enteritidis isolates were tested.

Resistance to *Salmonella* in turkeys is shown in **Figure 3.12**. For the non-HP-CIAs, shown in **Figure 3.12 (A)**, there was no resistance reported for amikacin, azithromycin, chloramphenicol, or meropenem. Levels of resistance to ampicillin were the highest recorded to date (41%). This figure included all of the *S*. Anatum isolates. The serovar *S*. Anatum accounted for 78% of the ampicillin-resistant isolates. This is similar to 2020, when *S*. Anatum accounted for 72% of the high levels seen then. It is possible that the high levels of resistance to ampicillin seen in both 2020 and 2022 were attributable to the high levels of *S*. Anatum that were tested compared to previous years. Levels of resistance to the other

antibiotics in the panel have declined since the highs recorded in 2014 and 2016. The three monophasic *S*. Typhimurium isolates showed the typical pattern of resistance seen in this serovar to sulfonamides, tetracyclines and ampicillin.

Of the HP-CIAs, shown in **Figure 3.12 (B)**, full susceptibility to the third-generation cephalosporins cefotaxime and ceftazidime was maintained between 2014 and 2022. Low-level resistance to the fluoroquinolone ciprofloxacin was detected in 9.2% of isolates, including all of the *S*. Senftenberg isolates. Of the ciprofloxacin-resistant isolates, 91% also showed resistance to nalidixic acid. Since the dramatic decreases in resistance to both ciprofloxacin and nalidixic acid observed between 2014 and 2016, the rates have been rising slowly but steadily, but remain low overall. A single isolate showed resistance to colistin (0.8%) in 2022. This is the first time colistin resistance has been recorded for *Salmonella* in turkeys in this programme.

Figure 3.12: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Salmonella* isolated from turkey flock NCP samples. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



+ Not tested
* Interpreted using an EFSA-recommended ECOFF
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, PX: polymyxins, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

3.3.5 *Campylobacter* spp.

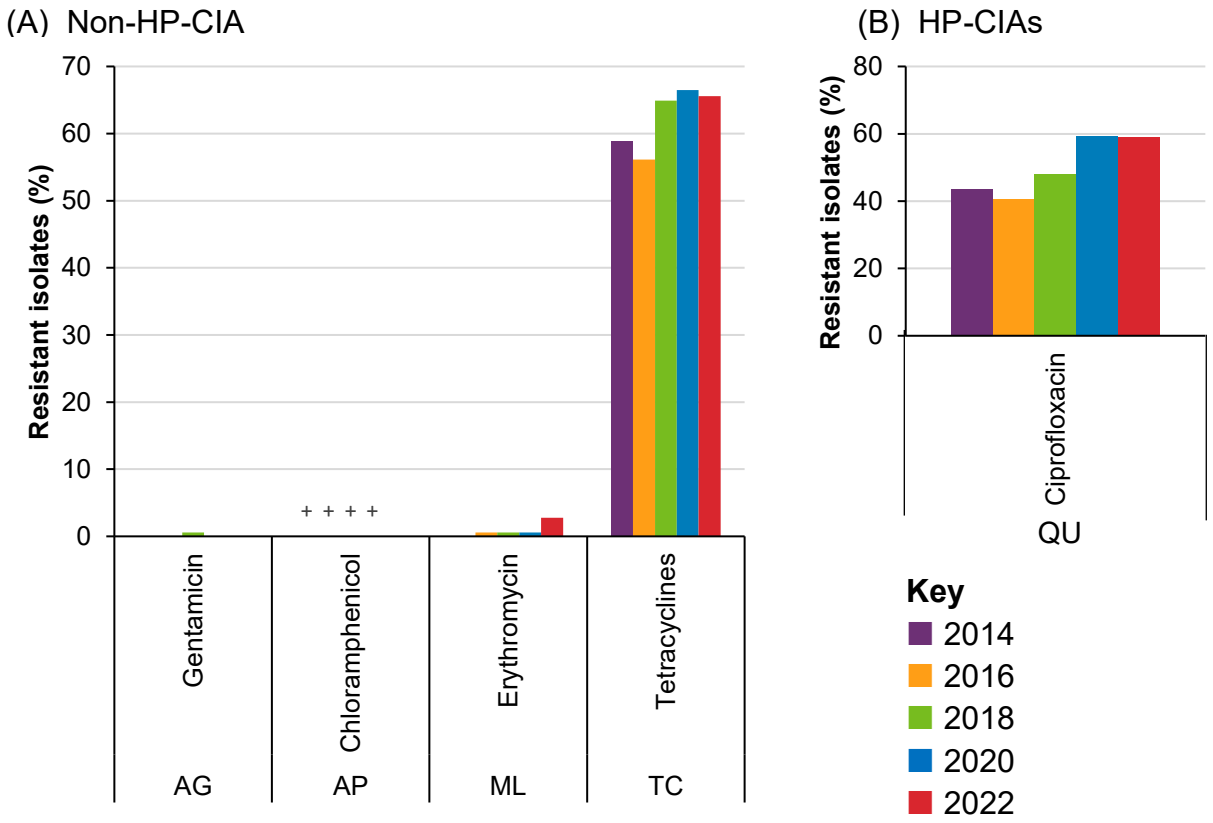
Campylobacter is the most common cause of food poisoning in humans in the UK. The majority of human *Campylobacter* infections are acquired from food, direct contact with animals or environmental cross contamination. We test for AMR in *C. jejuni* from poultry as it is the most prevalent species in poultry. For the first time this year we have isolated and tested for AMR in *C. coli* from poultry. This was added as *C. coli* is often more resistant than *C. jejuni* to several important antimicrobials and may transfer resistance genes to *C. jejuni*.

3.3.5.1 *Campylobacter jejuni*

Broilers

A total of 180 *C. jejuni* isolates were tested from broilers, of which 29% were fully susceptible to the panel of antibiotics tested and none were MDR. Levels of resistance to both tetracycline (66%) and to the fluoroquinolone ciprofloxacin (59%) remained very high (**Figure 3.13**). Levels of resistance to erythromycin were low (2.8%), and all of these isolates were susceptible to ciprofloxacin.

Figure 3.13: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Campylobacter jejuni* isolated from broilers at slaughter. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.

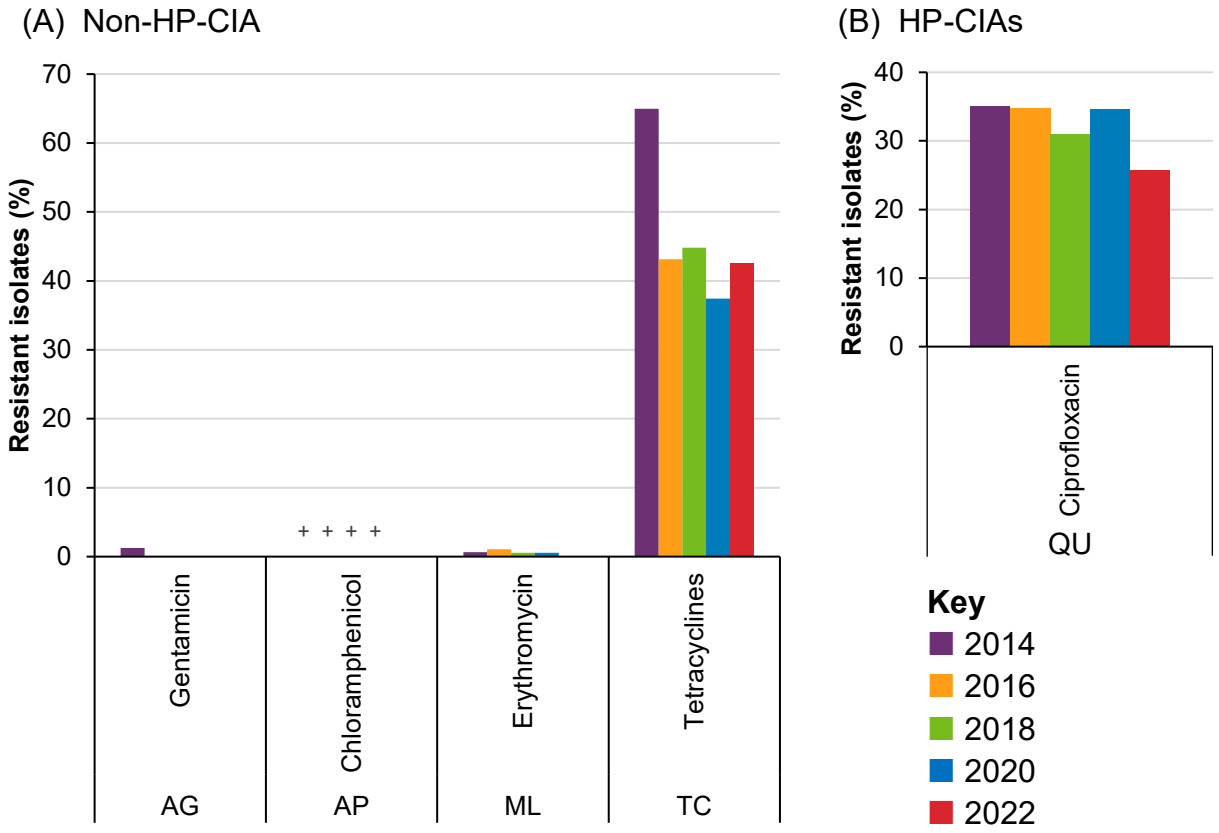


+ Not tested
AG: aminoglycosides, AP: amphenicols, ML: macrolides, QU: quinolones, TC: tetracyclines

Turkeys

A total of 136 *C. jejuni* isolates were tested from turkeys, of which 49% were fully susceptible to the panel of antibiotics tested and none were MDR. Resistance to tetracycline (43%) and to ciprofloxacin (26%) remained high (**Figure 3.14**), although ciprofloxacin resistance is at its lowest level since 2014 (35%).

Figure 3.14: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Campylobacter jejuni* isolated from turkeys at slaughter. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



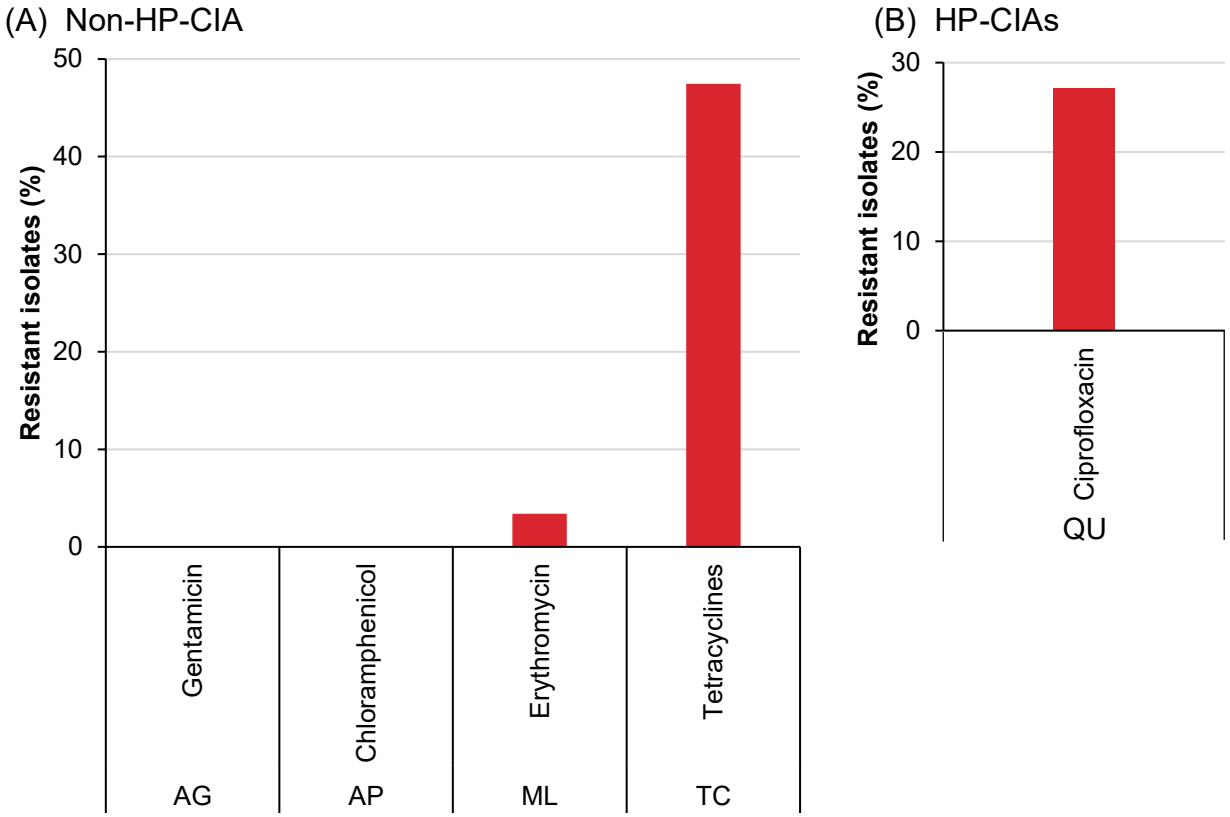
+ Not tested
AG: aminoglycosides, AP: amphenicols, ML: macrolides, QU: quinolones, TC: tetracyclines

3.3.5.2 *Campylobacter coli*

Broilers

This is the first year that *C. coli* isolates were tested from broilers. A total of 59 isolates were tested for resistance to antibiotics (**Figure 3.15**). Of these, 27% were fully sensitive to the panel of antibiotics tested and none were MDR. Resistance to both tetracycline (48%) and ciprofloxacin (27%) was high. A total of 3.4% of isolates were resistant to erythromycin, both of which were sensitive to the remainder of the antibiotics in the panel.

Figure 3.15: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Campylobacter coli* isolated from broilers at slaughter in 2022. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.

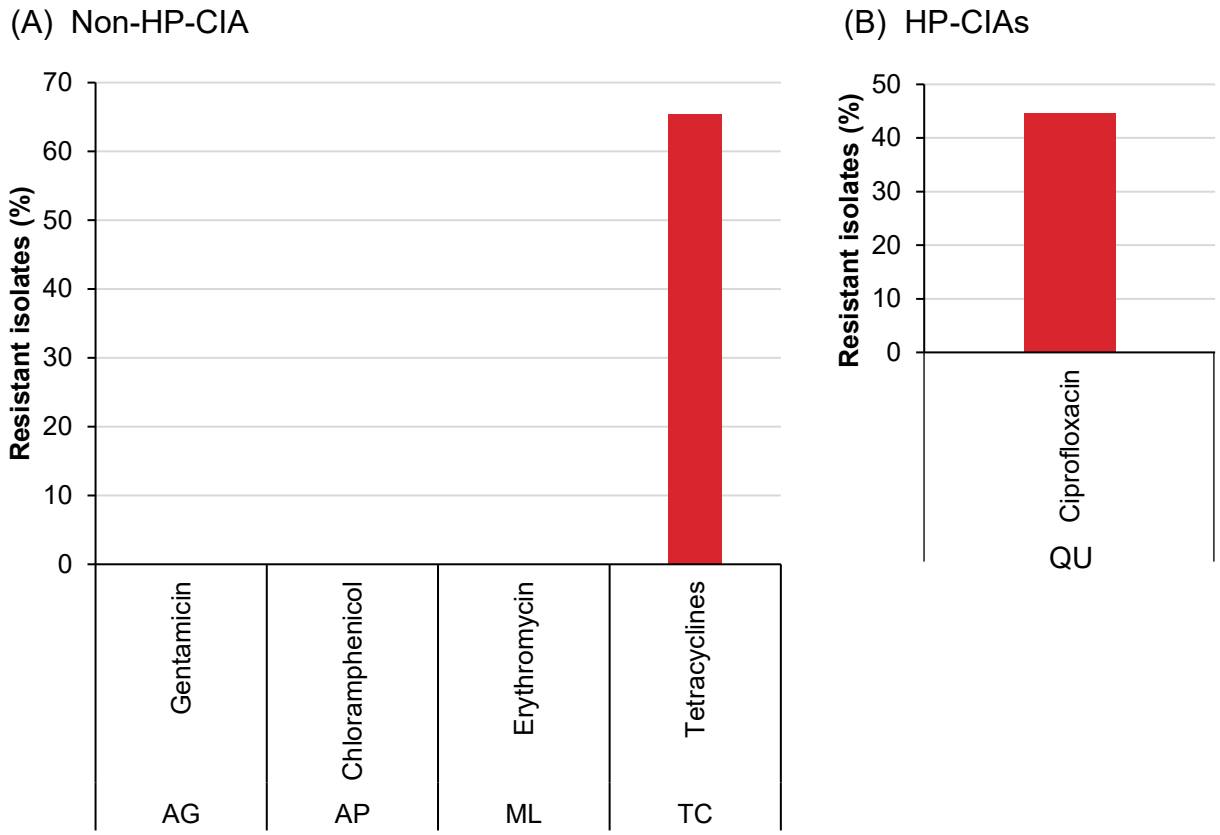


AG: aminoglycosides, AP: amphenicols, ML: macrolides, QU: quinolones, TC: tetracyclines

Turkeys

This is the first year that *C. coli* isolates were tested from turkeys. A total of 110 *C. coli* isolates were tested for antibiotic resistance (**Figure 3.16**). Of these, 13% were fully sensitive to the panel of antibiotics tested and none were MDR. Resistance to tetracycline was very high (66%) and to ciprofloxacin was high (45%).

Figure 3.16: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Campylobacter coli* isolated from turkeys at slaughter in 2022. Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



AG: aminoglycosides, AP: amphenicols, ML: macrolides, QU: quinolones, TC: tetracycline

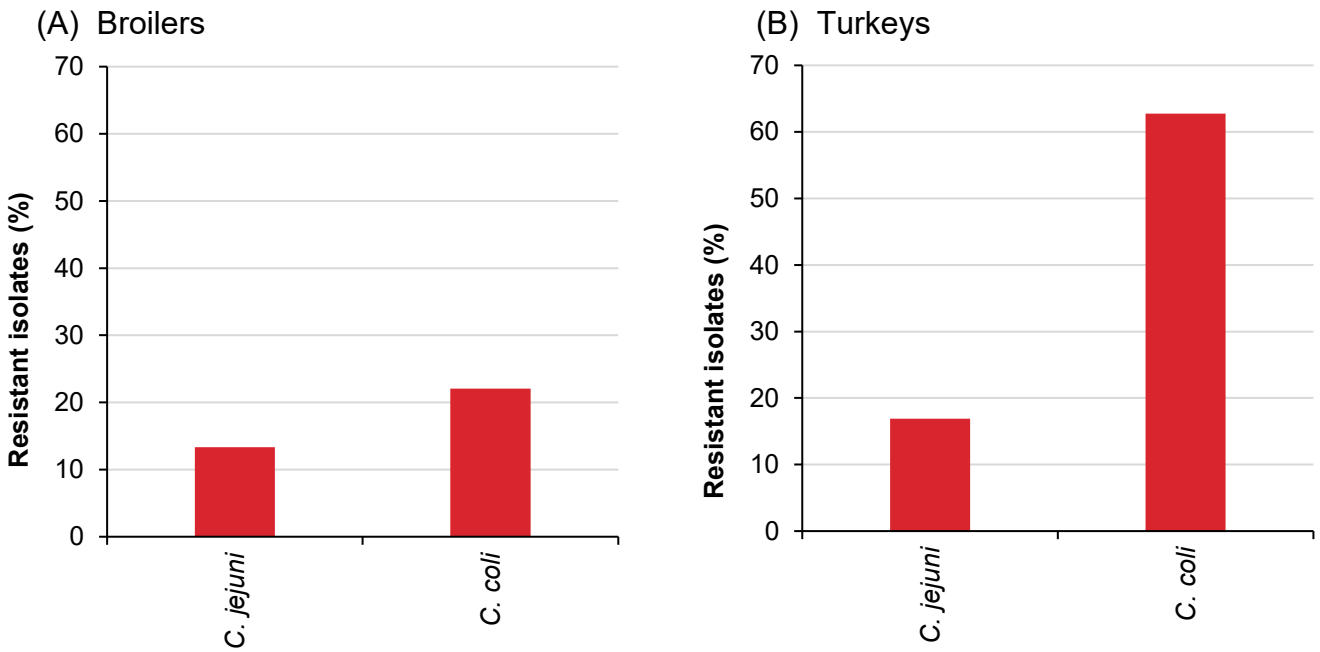
Box 3.1: Ertapenem resistance in *Campylobacter*

In 2022 ertapenem was included for the first time in the antibiotic panel used to test for resistance in *Campylobacter* species. There was a recognised need to include a member of the carbapenems as an HP-CIA and antibiotic of last resort in human health. Ertapenem is used in some countries to treat serious invasive *Campylobacter* infections in humans but is not approved for use in food-producing animals; it was added to our panel to maintain international harmonisation for this antibiotic class.

Figure 3.17 shows the tentative results achieved for resistance to ertapenem in both *C. jejuni* and *C. coli* in UK broilers and turkeys. In broilers levels of resistance were moderate in *C. jejuni* (13%) and high in *C. coli* (22%). In turkeys, levels of resistance were moderate in *C. jejuni* (17%) but very high in turkeys (63%). The MIC data were interpreted using the suggested EFSA-recommended ECOFF of 0.5 mg/L.

These results were surprising, particularly as third- and fourth-generation cephalosporins have not been used in UK poultry since usage data was collected. It must be noted, however, that the characteristics of *Campylobacter* with respect to ertapenem resistance are still not very well understood and there is currently a concerted program of work being undertaken to better understand these interactions. Also of note is the current absence of a EUCAST-validated ECOFF. As such the MIC values generated are difficult to interpret. We are further evaluating these isolates and consulting with public health colleagues as to the most appropriate One Health measure of carbapenem resistance within the UK context.

Figure 3.17: Resistance to ertapenem in *Campylobacter jejuni* and *Campylobacter coli* isolated from A) broilers and B) turkeys at slaughter in 2022. Interpreted using EFSA - recommended ECOFF.



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

The results in section 3.3.1 and **Figure 3.3** and **Figure 3.4** above show that the frequency of resistance to 3rd generation cephalosporins in *E. coli* isolated from the UK broiler/turkey population is less than 2%.

We also conducted additional, more sensitive, testing on selective media. This inhibits the growth of susceptible *E. coli* but allows the resistant bacteria to multiply, making them easier to detect. The results in the following sections (3.3.3.1 and 3.3.3.2) therefore represent the percentage of individual broilers and turkeys carrying any *E. coli* resistant to these antibiotics, even at very low levels.

Once these resistant bacteria have been amplified, they undergo WGS to confirm the genetic mechanisms underlying these resistances and are tested for susceptibility against other antibiotics.

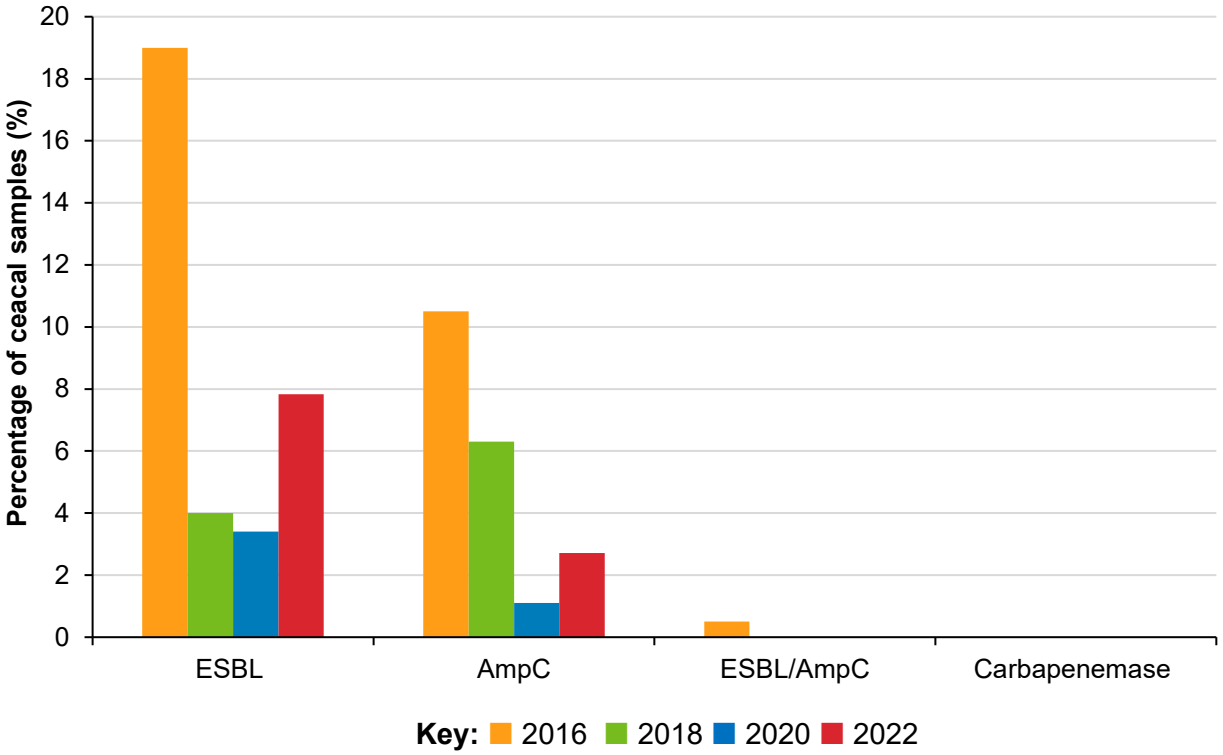
3.3.6.1 Broilers

From 2016 to 2020, there was a decline in the percentage of broilers carrying *E. coli* with ESBL and/or AmpC phenotypes, from 30% to 4.5%. However, we have seen an increase since 2020, and in 2022, 11% of broilers were carrying these bacteria. (**Figure 3.18**). In 2022, 7.8% of broilers were carrying ESBL-producing *E. coli* and 2.7% were carrying *E. coli* with the AmpC phenotype. None were carrying both phenotypes. No resistance to carbapenems was detected when using selective media.

Of the 36 isolates which grew on ESBL/AmpC selective media, no resistance was detected to amikacin, colistin, ertapenem, meropenem, imipenem, temocillin or tigecycline. Of the nine isolates with the AmpC phenotype, two were resistant to azithromycin (22%), which is the first time this has been recorded. All nine were resistant to tetracyclines, sulfonamides and trimethoprim, a difference from 2020, when resistance to these antibiotics was not observed.

Resistance to the fluoroquinolone ciprofloxacin was observed in 77% of isolates with either the AmpC (9/9) or the ESBL (18/26) phenotype. This has increased from 38% in 2020. In 2022, high-level ciprofloxacin resistance (MIC greater than 4mg/l) was detected in 31% of ESBL/AmpC-producing *E. coli*. This result demonstrates co-resistance to two classes of HP-CIAs. The last time this was observed was in a single AmpC-producing *E. coli* from broilers in 2018. This indicates a marked increase in the occurrence of high-level fluoroquinolone resistance in *E. coli* expressing either the AmpC or ESBL phenotypes.

Figure 3.18: ESBL/AmpC- and carbapenemase-producing *Escherichia coli* cultured on selective media, from caecal samples from healthy broilers at slaughter in the UK.



Whole genome sequencing (WGS) was carried out on 36 *E. coli* isolates from broilers, 27 with a putative ESBL phenotype and 9 with an AmpC phenotype. Of those with an ESBL phenotype, the most common antibiotic resistance genes (ARG) were *bla*$_{\text{CTX-M-15}}$ (33%) and *bla*$_{\text{SHV-12}}$ (33%). These were ascribed to four unique sequence types (ST). The other genes detected included *bla*$_{\text{CTX-M-15}}$ (15%), *bla*$_{\text{CTX-M-3}}$ (4%), *bla*$_{\text{TEM-52c}}$ (4%) and *bla*$_{\text{CTX-M-65}}$ with *bla*$_{\text{OXA-10}}$ (4%). For two isolates no known antibiotic resistance genes (ARG) for resistance to the third- and fourth-generation cephalosporins were detected.

Of the *E. coli* isolates which expressed the AmpC phenotype, 78% (7/9) were ST155, and all carried the *bla*$_{\text{CMY-2}}$ gene. Five of these were closely related but not sufficiently to suggest that they had the same ancestor. The remaining isolates (22%) carried the *bla*$_{\text{DHA-1}}$ gene.

3.3.6.2 Turkeys

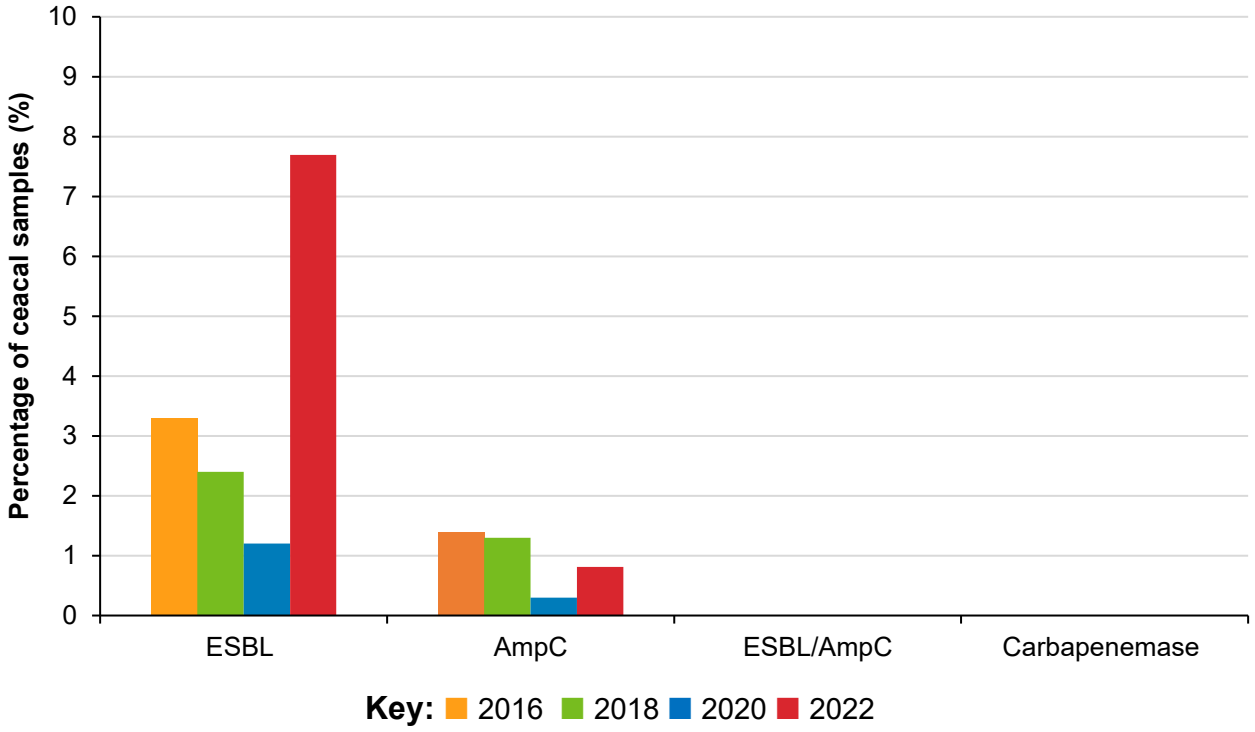
There was a decline in the percentage of turkey caecal samples containing *E. coli* which expressed either the ESBL and/or AmpC phenotypes: from 4.7% in 2016 to 1.5% in 2022. In 2022, we have seen an increase with 8.5% of turkeys carrying these bacteria (**Figure 3.19**). This rise is due to the marked increase in *E. coli* isolates expressing the ESBL phenotype, which rose from the 1.2% in 2020 to 7.7% in 2022. There was also a smaller increase in *E. coli* isolates expressing the AmpC phenotype, which rose from 0.3% in 2020 to 0.8% in 2022. No isolates exhibited both phenotypes. None of the 247 caecal samples grew on either of the selective media which were used to detect resistance to the carbapenems.

Of the 21 isolates which grew on the ESBL/AmpC selective media, no resistance was detected to amikacin, colistin, ertapenem, meropenem, imipenem, temocillin or tigecycline. All 21 were resistant to ampicillin as expected.

The *E. coli* isolates with an AmpC phenotype (n=2) showed the expected pattern of resistance to the beta-lactams but were otherwise relatively susceptible, showing only low-level resistance to tetracycline. In contrast, those expressing the ESBL phenotype (n=19) were frequently resistant to the sulfonamides (73.7%), or tetracyclines (68.4%). Resistance to gentamicin (10.5%) or trimethoprim (15.8%) was less common.

Lowe-level resistance to the fluoroquinolone ciprofloxacin was observed in 53% of isolates with an ESBL phenotype. No high-level ciprofloxacin resistance was detected. Nalidixic acid resistance was observed in 20% of the isolates with low-level resistance to ciprofloxacin. However, as all 10 isolates had a nalidixic acid MIC of less than 16mg/L, this would suggest a transferable mechanism of fluroquinolone resistance.

Figure 3.19: ESBL-/AmpC- and carbapenemase-producing *Escherichia coli* cultured on selective media, from caecal samples from healthy turkeys at slaughter in the UK.



Whole genome sequencing (WGS) was carried out on 19 *E. coli* isolates from turkeys, 17 with an ESBL phenotype and two with an AmpC phenotype. Of those with an ESBL phenotype, the most common ARG were *bla*$_{\text{OXA-10}}$ with *bla*$_{\text{SHV-12}}$ (35%), *bla*$_{\text{CTX-M-55}}$ (29%), *bla*$_{\text{SHV-12}}$ (18%), *bla*$_{\text{CTX-M-15}}$ (12%) and *bla*$_{\text{CTX-M-1}}$ (5.9%). The six isolates with the *bla*$_{\text{OXA-10}}$ with *bla*$_{\text{SHV-12}}$ phenotype were all ST515. The isolates in this group of ST515s showed some relatedness but were not from the same ancestor. The remaining isolates were from diverse STs.

Both isolates with an AmpC-producing phenotype harboured mutations in the promoter region of the *ampC* gene. No other AmpC-producing mechanism was detected.

CHAPTER 4

Clinical surveillance of antibiotic resistance

Our clinical surveillance is a programme of passive surveillance which evaluates antimicrobial resistance (AMR) in bacteria of relevance to animal health. Bacteria are isolated from post-mortem carcases or other diagnostic samples submitted by private veterinary surgeons to the Animal and Plant Health Agency (APHA) and partner veterinary laboratories in England and Wales. When a bacterial pathogen is identified, susceptibility testing is performed to provide the practitioner with relevant information for treatment. Similar programmes are conducted by Scottish (Scotland's Rural College Veterinary Services, SRUC) and Northern Irish (Agri-Food Biosciences Institute, AFBI-NI) laboratories. This chapter primarily reports the APHA methods and results; results from SRUC and AFBI-NI are included in the supplementary material.

As this is a passive programme, the results in this chapter should not be considered representative of AMR in animal populations, and should be interpreted with caution (see section 4.3 below). The primary aim of the programme is to provide scanning surveillance of animal disease. It also helps to identify new and emerging patterns of resistance, particularly since treatment failure is a frequent reason for submission of samples. In addition, the programme incorporates results from the susceptibility testing of *Salmonella* isolates recovered from animals, their feed and environment, in Great Britain, as part of the Zoonoses Order 1989. Any findings considered to pose a particular risk to human or animal health are reported to the Defra Antibiotic Resistance Coordination (DARC) group, and to the Veterinary Medicines Directorate (VMD) for management in accordance with protocols outlined in the VMD AMR Contingency Plan.

Clinical surveillance has historically been assessed by disc diffusion methods; however, broth microdilution testing interpreted by minimum inhibitory concentration (MICs) has continued to be developed for veterinary pathogens at APHA over the last two years. This enhancement has been developed in response to published recommendations for monitoring AMR in food-producing animals, in order to generate robust and comparable susceptibility testing outputs to detect emerging resistance issues in the UK. This gold standard technique is applied to an increasing number of organisms each year. This report features MIC results for the complete set of *Streptococcus suis* and *Brachyspira hyodysenteriae* isolated from pigs in 2022. MIC testing was performed on a subset of a further eight organisms in 2022; these results are presented in section S4.7 of Supplementary Material 2.

4.1 Summary

Clinical surveillance aims to provide veterinarians with relevant treatment information using results from bacteria isolated from diagnostic samples. This is a passive programme, subject to biases and differences in the numbers of samples, meaning results in this chapter cannot be extrapolated to the wider animal populations.

- 7,284 isolates were tested for AMR in England and Wales.
- The results are presented by animal species: pigs (13% of isolates), poultry (32%), cattle (34%), sheep (7.1%) and dogs (13%).
- Overall, resistance to the highest priority critically important antibiotics (HP-CIAs) was low or not detected, apart from to nalidixic acid in *Salmonella* isolated from turkeys (22%). This is difficult to interpret given the disruption due to avian influenza during 2022, which impacted the number of samples submitted.
- 24% of all clinical *Escherichia coli* isolates were multi-drug resistant (MDR), with the highest levels detected in isolates from cattle (40%).
- 76% of *Salmonella* isolates were fully susceptible to the panel of antibiotics tested. Full susceptibility was lowest in *Salmonella* isolated from pigs (28%) and turkeys (23%), and highest in those isolated from sheep (95%) and cattle (87%).
- **Pigs:** the most frequently isolated bacteria were: *E. coli* (49%), *Salmonella* (33%), *Streptococcus suis* (9%) and *Pasteurella multocida* (5%). In gastrointestinal pathogens, the highest levels of resistance were detected to the most commonly-used antibiotics: aminopenicillins, tetracyclines and trimethoprim/sulfonamides. Resistance levels in *E. coli* were higher in weaners than in neonates and adult pigs, likely reflecting more frequent antibiotic use in this age group.
- **Poultry:** the most frequently isolated bacteria were *Salmonella* (95%) and *E. coli* (4%). In these isolates, the highest levels of resistance were found to commonly-used antibiotics: aminopenicillins and tetracyclines.
- **Cattle:** the most frequently isolated bacteria were: *Salmonella* (44%), *E. coli* (30%, predominantly gastrointestinal), *P. multocida* (9.2%) and *M. haemolytica* (7.0%). AMR in mastitis samples varied by organism. MDR was more frequent in *E. coli* (13%) than streptococci (<3%). Higher levels of resistance were observed in *E. coli* from calves than in adult cattle, likely reflecting more frequent antibiotic usage in this age group.
- **Sheep:** the most frequently isolated bacteria were: *E. coli* (31%), *M. haemolytica* (30%), *Salmonella* (16%) and *Bibersteinia trehalosi* (6.9%). Resistance tended to be highest in neonates, again likely reflecting more frequent antibiotic use in this age group. A decline in *E. coli* resistance to spectinomycin from 45% in 2021 to 23% in 2022 was observed in neonates, possibly due to withdrawal of this antibiotic from the market.
- **Dogs:** the number of *Salmonella* isolates tested for AMR increased from 105 in 2021 to 924 in 2022, due to becoming reportable after a change in legislation. 78% of isolates were fully susceptible to the panel of antibiotics tested.
- Data from the Private Laboratories Initiative (PLI), which aims to collect and analyse AMR data from private veterinary laboratories, is presented for the third time this year.

4.2 Methods

4.2.1 Sample sources

Bacteria were isolated from clinical or post-mortem samples submitted to APHA and partner laboratories by practising veterinary surgeons in England and Wales. Submission of diagnostic material may be more likely in serious cases of disease or those resistant to treatment, and may therefore be subject to bias. Any laboratory isolating *Salmonella* spp., from animals and their environment, under the Zoonoses Order 1989 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

Detailed methodology for the susceptibility testing by disc diffusion and broth microdilution testing is presented in section S3.1 of Supplementary Material 2. Data presented in Box 4.3 (Private Laboratory Initiative) used different methods, which are described separately in Table S3.1.3 in Supplementary Material 2.

For the majority of the results presented in this chapter, the disc diffusion method used was formerly recommended by the British Society for Antimicrobial Chemotherapy (BSAC).

Broth microdilution testing under the clinical surveillance programme has historically been limited to specific organisms, such as *Brachyspira hyodysenteriae*, which causes swine dysentery. Bacterial susceptibility determined by MIC was introduced in UK-VARSS 2020 for key respiratory pathogens (section 4.3.1). A subset of isolates from multiple veterinary pathogens has been tested to continue methodological development of broth microdilution testing; these results are presented in the S4.7 of Supplementary Material 2. The aim for future years is to continue expanding this methodology to the full set of isolates.

4.2.3 Interpretation

Interpretative criteria are available in full in section S3.1 of Supplementary Material 2.

Disc diffusion resistance has been interpreted using BSAC clinical breakpoints. When not available, the historical APHA veterinary clinical breakpoint has been applied. MIC results have been interpreted using veterinary clinical breakpoints from Clinical and Laboratory Standards Institute (CLSI) in the first instance, or Committé Antibiogramme - Société Française de Microbiologie (CA-SFM) when these are not available; if veterinary clinical breakpoints were not available, human clinical breakpoints (CBPs) were used.

Multiple antibacterial resistance, or multi-drug resistance (MDR), is defined in this report as resistance to any of three or more separate antibiotic classes which were tested for a particular isolate.

4.3 Results

This section includes results of AMR testing for all the pathogens isolated. This year, results are presented by animal species and then body system. Summary results for the important zoonotic and multi-host organisms, *E. coli*, Salmonella *spp.*, livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) and *S. suis,* are presented in section 4.3.1.

Classification of resistance as low, moderate, high etc. throughout the report is consistent with the European Food Safety Authority (EFSA) definitions for these terms (**Table 4.1**).

Table 4.1: Classification of resistance as low, moderate, high etc. throughout the report is consistent with EFSA definitions for these terms.

Description of resistance level	Equivalent percentage resistance range
Rare	<0.1%
Very low	0.1% to 1%
Low	>1% to 10%
Moderate	>10% to 20%
High	>20% to 50%
Very high	>50% to 70%
Extremely high	>70%

Certain active compounds included in the antibiotic testing panels are not authorised for use in food-producing animals. These are included in the panels to allow us to monitor possible emergence of resistance to these antibiotics, or because they are representative of an antibiotic class. Panels of antibiotics can vary between years and individual isolates. Where a figure shows no data against specific antibiotics or years as a result of this panel variation, this has been identified in a footnote.

For some bacterial pathogens, very few numbers of isolates are recovered in any one year and therefore the prevalence of resistance and any trends need to be interpreted with caution. The complete dataset is available from Table S4.1 onwards in Supplementary Material 2, and only pathogens with test results for more than 20 isolates in 2022 are presented graphically in the main body of the report.

For *E. coli* isolated from ruminants and pigs, results are disaggregated by age, as summarised in **Table 4.2**, due to differences in disease presentation and antibiotic treatment across ages groups.

Table 4.2: Age categories of food-producing animals.

Animal	Neonatal	Pre-weaned	Post-weaned	Adult
Cattle	< 1 week	Unweaned and not known to be less than 1 week	From weaning to adult	≥ 24 months
Sheep	< 1 week	Unweaned and not known to be less than 1 week	From weaning to adult	≥ 12 months
Pigs	< 1 week	Unweaned and not known to be less than 1 week	From weaning to adult	≥ 5 months

4.3.1 Zoonotic organisms

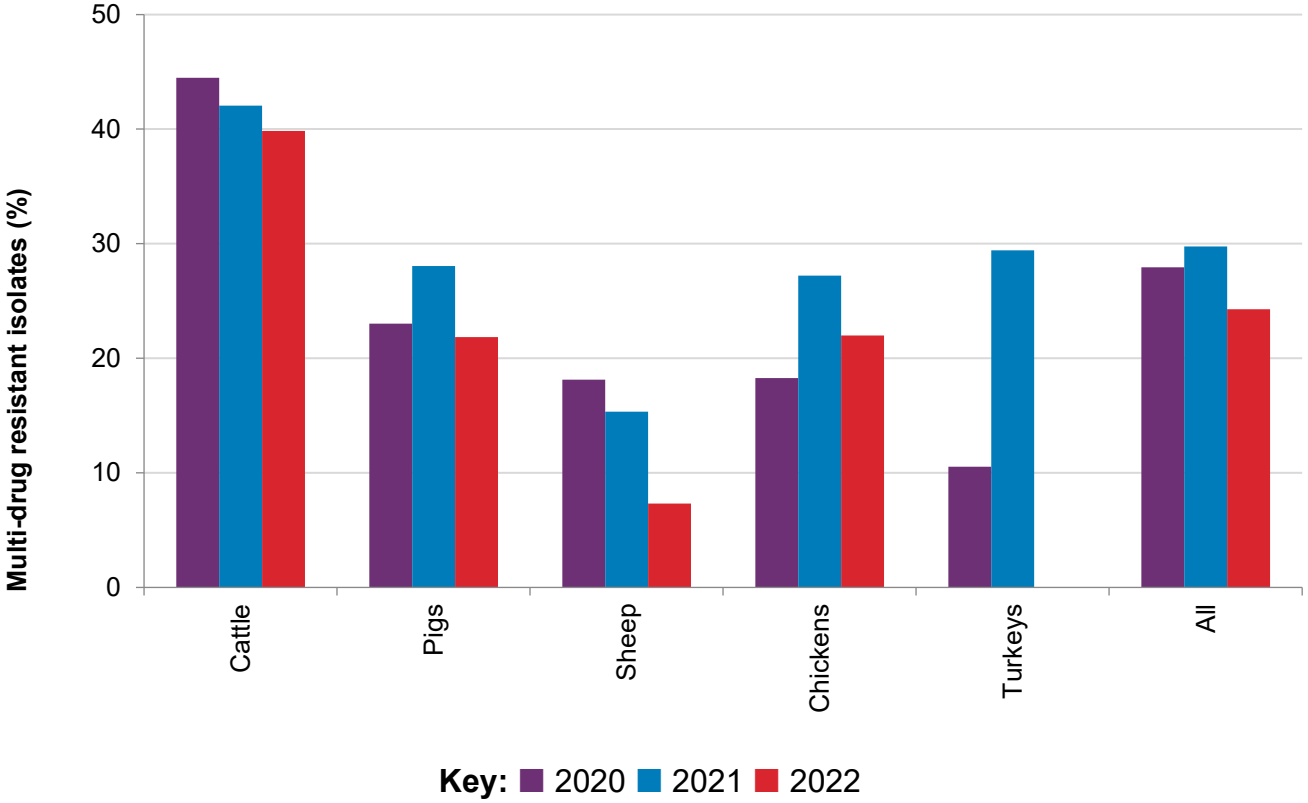
4.3.1.1 *Escherichia coli*

E. coli is an important zoonotic organism and a commensal of the gastrointestinal tract of animals and humans. The *E. coli* strains affecting animals are usually different to those affecting humans, but there is some overlap. *E. coli* can cause a range of clinical problems in food-producing animals, including diarrhoea and septicaemia. Some diseases caused by *E. coli* are related to pathogenicity, with particular strains possessing recognised virulence factors, whilst opportunistic *E. coli* infections can also occur. *E. coli* can also act as a reservoir of transferable resistance genes which can pass on to other bacterial species.

This section includes a summary of *E. coli* isolated from all species through clinical surveillance in England and Wales. Due to differences in methodology, data for Scotland and Northern Ireland are presented in Table S4.1.1 in Supplementary Material 2. Resistance in *E. coli* is further analysed by livestock species and age categories in the individual species sections.

Overall, 24% of all *E. coli* isolated from clinical submissions were MDR (**Figure 4.1**). Of the species tested, MDR was highest in cattle isolates (41%), followed by chickens (22%), pigs (22%), sheep (7.3%) and then finally turkeys (0%). The fluctuation of MDR in *E. coli* isolated from turkeys is difficult to interpret; given variation in the number of isolates tested (n=19 in 2020, n=17 in 2021 and n=6 in 2022). Across all species, there was a general trend towards higher resistance in isolates from neonates and weaners than adults. This likely reflects the more frequent treatment of young animals with antibiotics.

Figure 4.1: Multi-drug resistance in *E. coli* isolates, from different animal species (n=976 in 2022)



4.3.1.2 *Salmonella* spp.

Salmonella is an important cause of foodborne disease in people. It can be part of the normal gut flora in animals, but can also cause disease. *Salmonella* isolates are reported on a statutory basis and a culture of the organism must be provided to government laboratories when detected by private veterinary laboratories in Great Britain. All of these isolates undergo susceptibility testing. Data on *Salmonella* is published annually in the 'Salmonella in animals and feed in Great Britain' report.

Of the 5,562 *Salmonella* isolates recovered in Great Britain in 2022, 55% were from food-producing animals, 22% from non-food-producing animals, 22% from feed , and 1% from the environment.

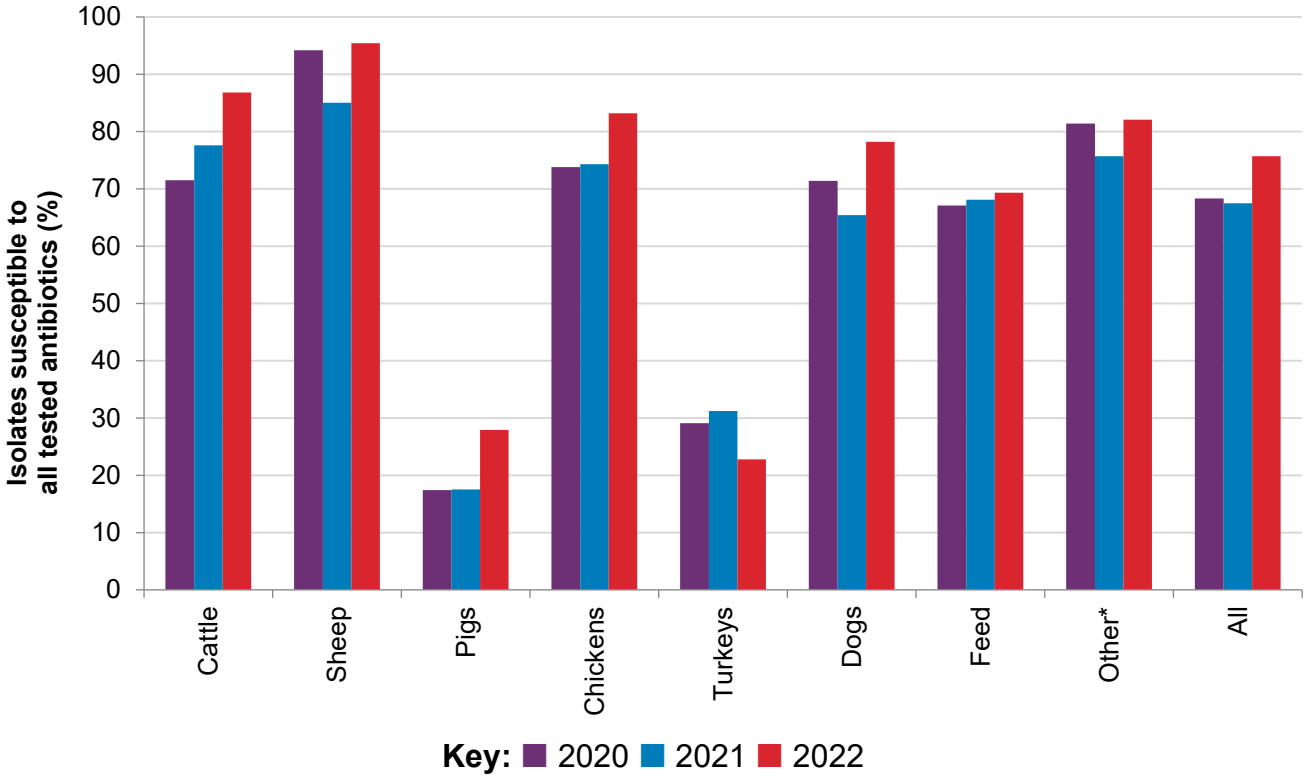
76% of *Salmonella* isolates from all species were fully susceptible (**Figure 4.2**). Of the species tested, full susceptibility was highest in sheep (95%), cattle (87%) and chickens (83%). The number of isolates was highly variable between species (sheep n=87, cattle n=431 and chickens n=2040 in 2022) and can fluctuate between years. Full susceptibility has increased in both cattle (72% in 2020 to 87% in 2022) and pigs (17% in 2020 to 28% in 2022).

In 2022, 96% of *S.* Dublin isolates from cattle and 48% of *S.* Typhimurium from all species were sensitive to all antibiotics tested. Monophasic *S.* Typhimurium was mostly isolated

from dogs and pigs and was often resistant to multiple antibiotics. Amikacin resistance, which is rarely found in samples originating from livestock, was detected in two *Salmonella* 4,12:i:- DT193 isolates from pigs.

Other resistances of note to HP-CIAs, include cefotaxime and ceftazidime resistance detected in nine *Salmonella* isolates; eight of which were MDR. One *S.* Kentucky isolate from a dog and one *S.* Infantis isolate from raw pet food were also resistant to ciprofloxacin. Additionally, four *S.* Infantis isolates were MDR and resistant to third-generation cephalosporins. Three of these isolates originated from chickens and one from raw pet food. Two of the chicken isolates were similar to a *S.* Infantis clone well-established in broiler flocks in continental Europe.

Figure 4.2: *Salmonella* spp. isolates susceptible to all tested antibiotics, from different source and animal species (n=5,562 in 2022).



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

4.3.1.3 Livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA)

LA-MRSA are, as the name suggests, commonly associated with livestock. They differ from other types of MRSA, such as hospital- or community-associated strains, which are more frequently found in humans. Anyone who has contact with farmed livestock can become colonised with LA-MRSA, although the risk is higher for those in frequent contact with livestock. LA-MRSA usually lives in the nose or on skin and is an opportunist

pathogen. When it causes disease, LA-MRSA most commonly causes a localised skin infection, but occasionally it can cause diseases such as pneumonia or bacteraemia.

LA-MRSA is prevalent in livestock around the world. It was detected in food-producing animals in the UK for the first time in 2014, and sporadic clinical cases are detected annually. Clonal complex (CC) 398 is a common LA-MRSA CC group isolated from food-producing animals. When detected, isolates undergo whole genome sequencing and are shared with the UK Health Security Agency (UKHSA) to investigate any possible associations with infections in humans.

In 2022, LA-MRSA CC398 *spa*-type t034 was recovered from infectious arthritis in an elbow joint of a young piglet. In a separate incident on a different farm, LA-MRSA *spa*-type t034, untypable by multi-locus sequence typing (MLST), was recovered from infectious arthritis in an elbow joint of a young piglet. LA-MRSA CC398 *spa*-type t011 was recovered from a case of bovine mastitis.

A summary of all LA-MRSA findings in 2022, identified by UK government veterinary laboratories, is provided in Table S4.1.3 in Supplementary Material 2.

4.3.1.4 *Streptococcus suis*

Streptococcus suis causes meningitis, arthritis and pneumonia in pigs. It is also zoonotic, although human infections are rare. Resistance, tested by disc diffusion (section 4.3.2.4) and broth microdilution (**Box 4.2**), in *S. suis* isolates are presented in the pig species section below.

4.3.2 Pigs

The complete pig dataset can be found in section S4.2 of Supplementary Material 2, and the subset of isolates tested by MIC in section S4.7 of Supplementary Material 2.

4.3.2.1 Gastrointestinal system

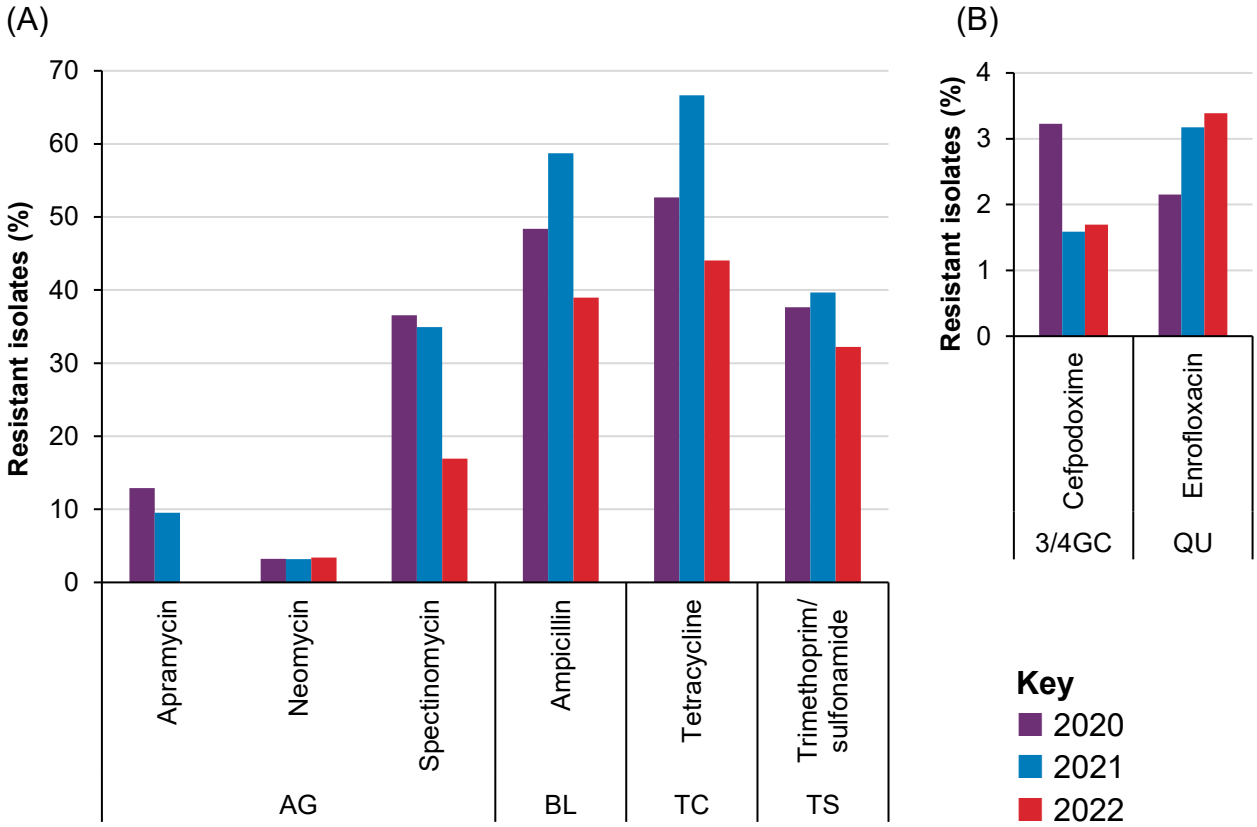
Escherichia coli

E. coli is an important zoonotic organism and a commensal of animals and humans. Isolates of porcine *E. coli* were predominantly collected from the post-weaning age category. High levels of resistance were detected to ampicillin, tetracycline and trimethoprim/sulfonamides across all age categories, despite varying numbers of isolates recovered (neonates n=59, post-weaning n=294 and adults n=32). The occurrence of resistance to the non-HP-CIA antibiotics tested was higher in post-weaning piglets than in neonates and adults. The increased occurrence of aminoglycoside resistance in post-weaned piglets, compared with neonatal piglets and adults, probably reflects the use of aminoglycosides for treating post-weaning diarrhoea.

The AMR in *E. coli* results from pigs are presented separately for neonates (**Figure 4.3**), pre-weaning piglets (**Figure 4.4**), and adults (**Figure 4.5**). The number of isolates tested are in Table S4.2.2 in Supplementary Material 2.

In neonatal piglets, 4.0% of isolates were MDR. High levels of resistance were detected to ampicillin (23%), tetracycline (44%) and trimethoprim/sulfonamides (32%), although these have reduced since 2020 (**Figure 4.3**). Resistance to the other antibiotics tested was generally low or not detected; and resistance to the HP-CIAs was low.

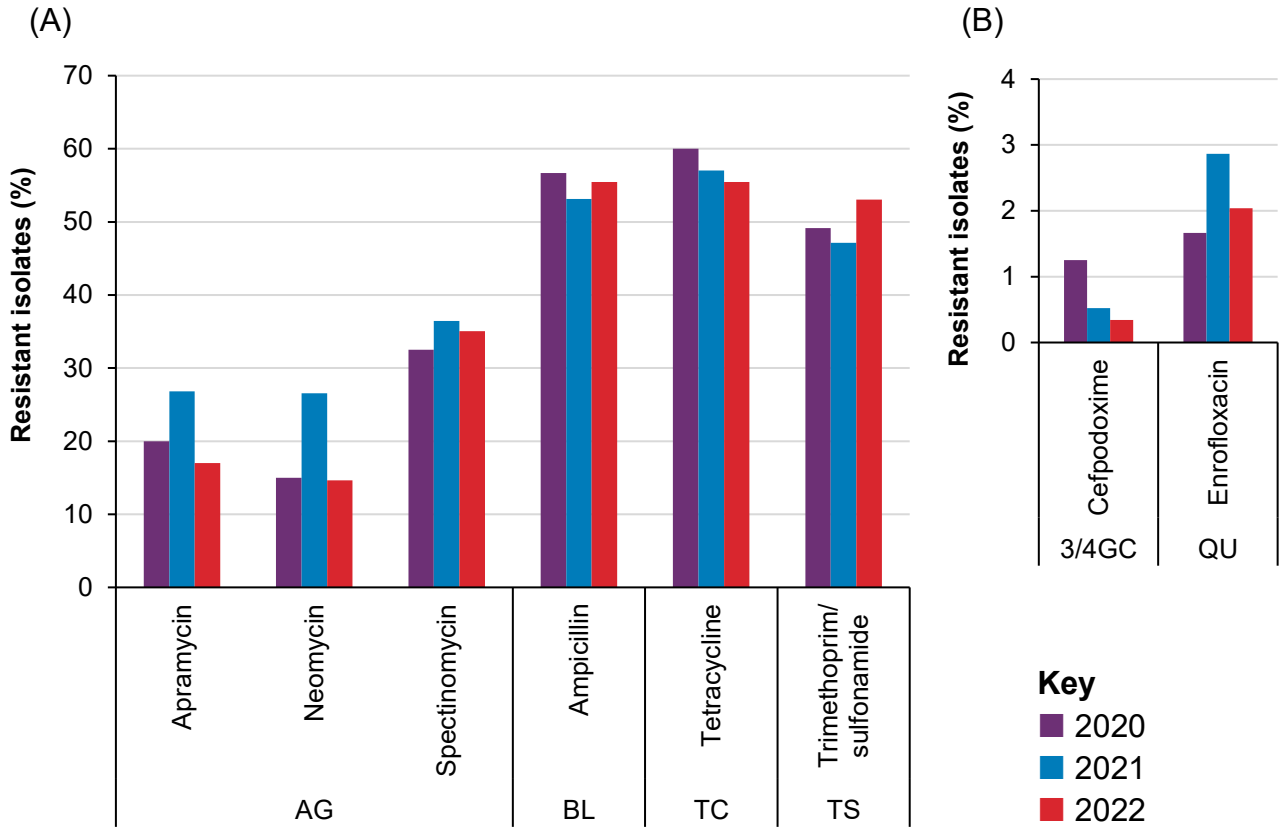
Figure 4.3: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolated from neonatal piglets (n=59 in 2022). Note scale differs between graphs.



AG: aminoglycoside, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

In post-weaned piglets, 28% of isolates were MDR. Very high levels of resistance were detected to ampicillin (55%), tetracycline (55%) and trimethoprim/sulfonamides (53%); high resistance to spectinomycin (35%), and appear little-changed since 2020 (**Figure 4.4**). Resistance to the other antibiotics tested was moderate and, resistance to HP-CIAs was very low.

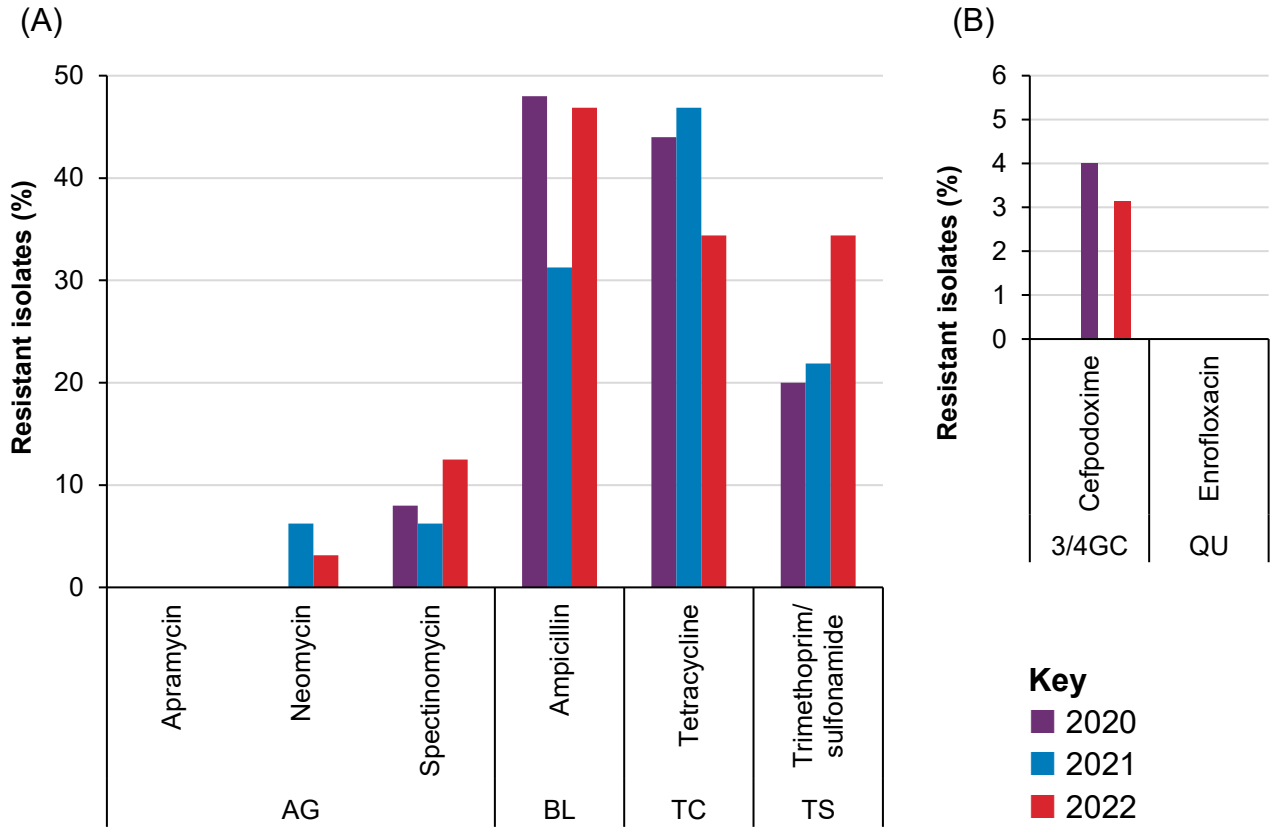
Figure 4.4: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from post-weaning piglets (n=294 in 2022). Note scale differs between graphs.



AG: aminoglycoside, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

In adult pigs, 9.4% of isolates were MDR. High levels of resistance were detected to ampicillin (47%), tetracycline (34%) and trimethoprim/sulfonamides (34%) (**Figure 4.5**). Resistance to the other antibiotics tested was generally low or not detected. No resistance was observed to the HP-CIA enrofloxacin, however, a single isolate (3.1%) was resistant to the HP-CIA cefpodoxime.

Figure 4.5: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from adult pigs (n=32 in 2022). Note scale differs between graphs.



AG: aminoglycoside, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

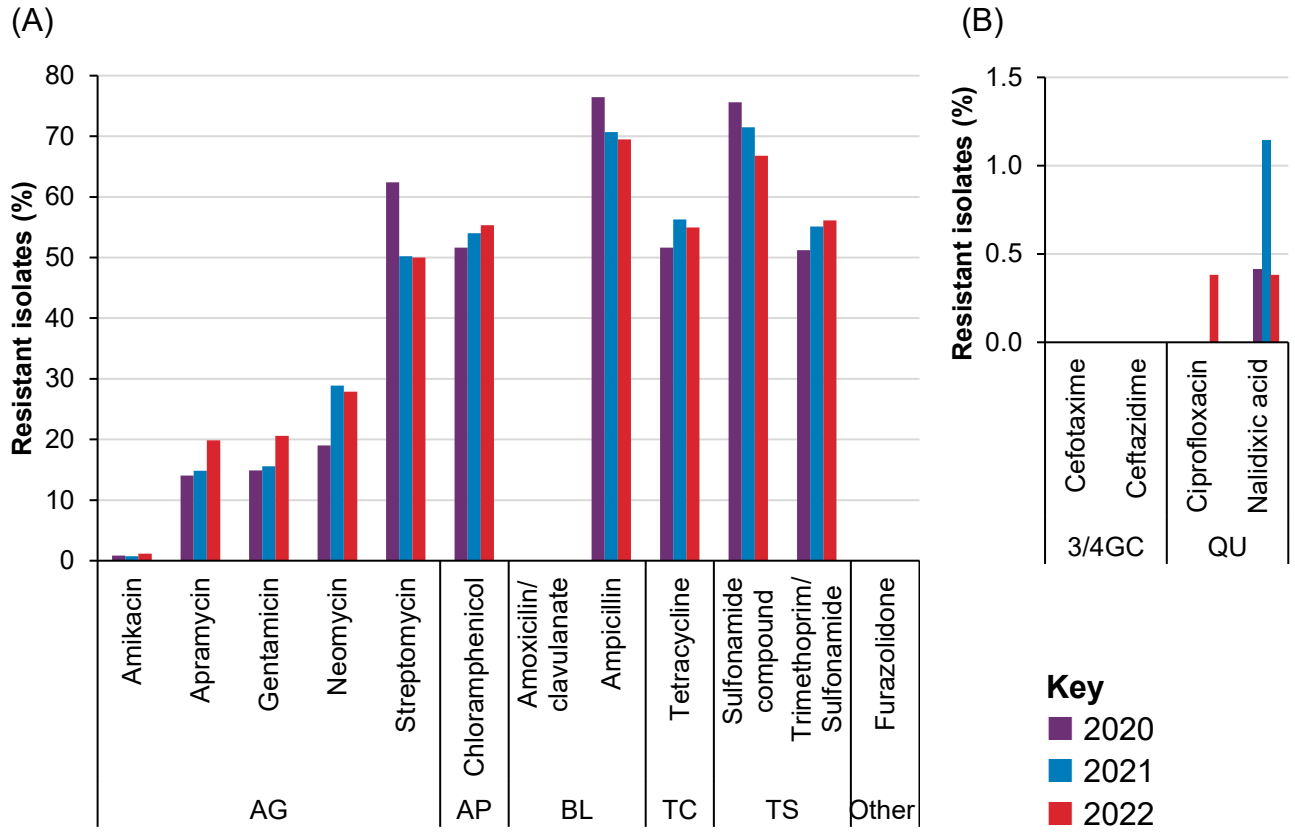
Salmonella spp.

Salmonella is an important cause of foodborne disease in people. It can be part of the normal gut flora in animals, but can also cause disease. *Salmonella* data for pigs is presented below for all age groups (**Figure 4.6**).

Of the 262 *Salmonella* isolates tested from pigs in 2022, 28% were susceptible to the full panel of antibiotics. Very high levels of resistance were detected to ampicillin (70%), sulfonamide compounds (67%), tetracycline (55%) and trimethoprim/sulfonamides (56%); and high resistance to gentamicin (21%) and neomycin (28%). No resistance to amoxicillin/clavulanate or furazolidone was detected between 2020 and 2022.

No resistance was observed to the HP-CIAs cefotaxime and ceftazidime, however, a single isolate (0.4%) was resistant to the HP-CIAs ciprofloxacin and nalidixic acid.

Figure 4.6: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Salmonella* isolates from pigs (n=262 in 2022). Note scale differs between graphs.



AG: aminoglycoside, AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

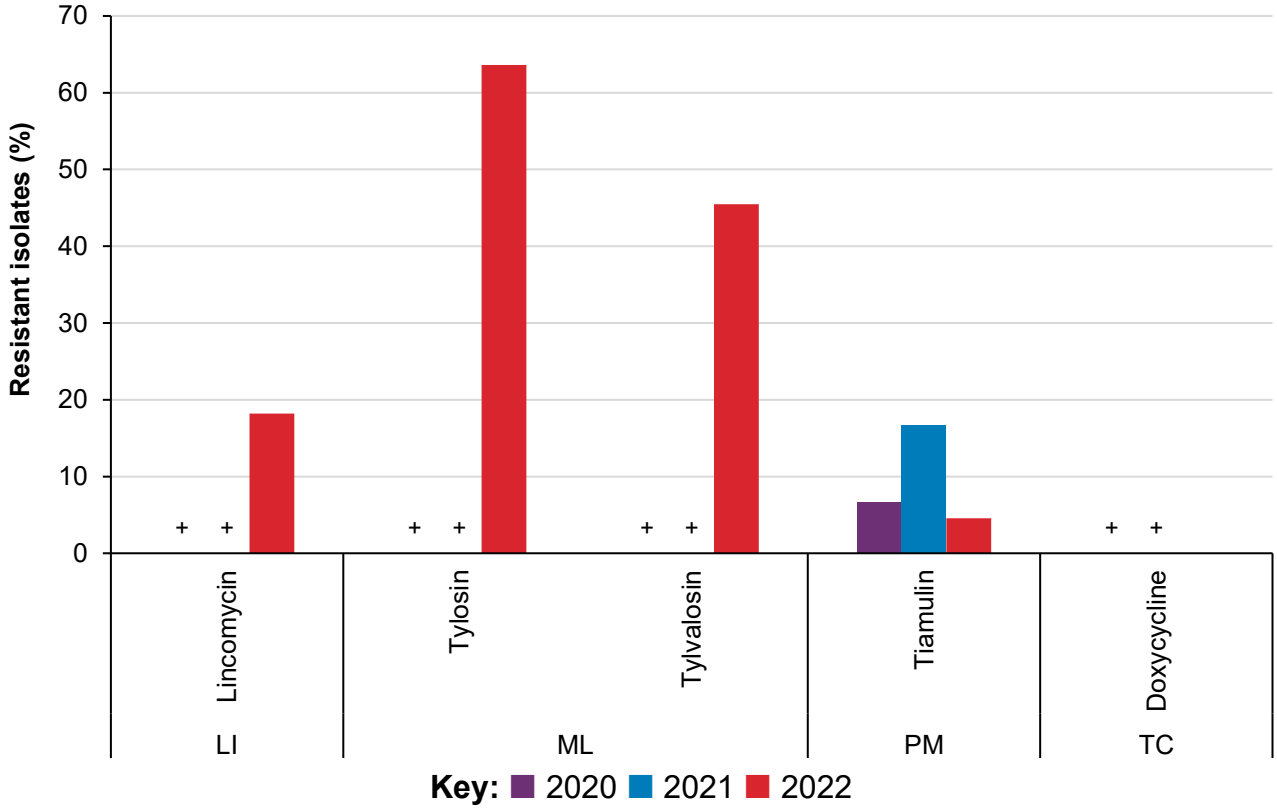
Box 4.1: *Brachyspira hyodysenteriae* MIC

Brachyspira hyodysenteriae is the causative organism of swine dysentery, an enteric disease of pigs which results in serious ill-thrift in its chronic form. A limited range of antibiotics are available for the treatment of swine dysentery and, as resistance to these treatments can develop, it is important that other aspects of disease control are addressed alongside treatment, such as hygiene and herd husbandry.

Tiamulin is an important veterinary antibiotic used in the treatment of swine dysentery and, because of the importance of this antibiotic in the clinical veterinary setting, all available isolates of *B. hyodysenteriae* are tested for tiamulin susceptibility each year, using broth microdilution and MICs. MIC testing has expanded this year to include a wider panel of antibiotics (**Figure 4.7**). The full breakpoints applied are available in Table S3.1.2.1 in Supplementary Material 2.

In 2022, 22 isolates were tested and one (4.5%) had a high tiamulin MIC of 8 mg/L, meaning that it was clinically resistant. Of the wider panel of antibiotics, we detected: no doxycycline resistance; moderate lincomycin resistance (18%); high tylvalosin resistance (46%); and very high tylosin resistance (64%).

Figure 4.7: Resistance in *Brachyspira hyodysenteriae* isolates from pigs (n=22 in 2022).



\+ Not tested
LI: lincosamides, ML: macrolides, PM: pleuromutilin, TC: tetracyclines

4.3.2.2 Respiratory system

Actinobacillus pleuropneumoniae

Actinobacillus pleuropneumoniae causes pneumonia in pigs. A total of seven isolates were tested in 2022 and results are available in full in Table S4.2.4 in Supplementary Material 2. No resistance was detected to ampicillin, tetracycline, or trimethoprim/sulfonamides. All isolates were resistant to neomycin and spectinomycin and 57% to apramycin.

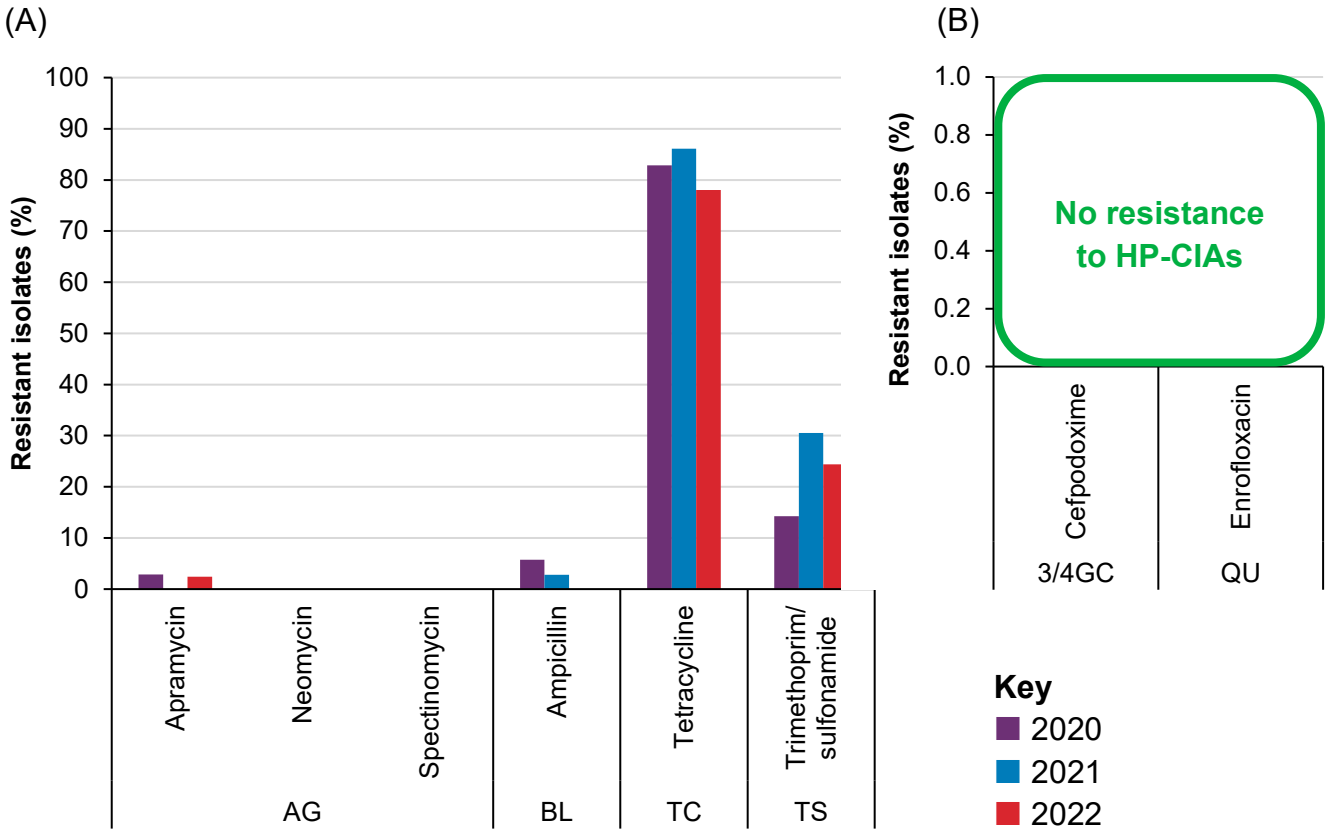
Glaesserella (*Haemophilus*) *parasuis*

Glaesserella (*Haemophilus*) *parasuis* causes Glasser's disease. Harmonised susceptibility testing methods and breakpoints for this organism are still being established. The results are available in full in Table S4.2.4 in Supplementary Material 2. Of the five *G. parasuis* isolates recovered in 2022, none were MDR and no resistance was detected to the antibiotics tested except three isolates resistant to neomycin and one isolate resistant to trimethoprim/sulfonamides.

Pasteurella multocida

P. multocida toxigenic strains are responsible for the development of atrophic rhinitis in pigs. A total of 41 isolates were recovered from diagnostic samples in 2022 (**Figure 4.8**). Of these, none were MDR. No resistance was detected to ampicillin, neomycin or spectinomycin. HP-CIA resistance was not observed between 2020 and 2022. Extremely high tetracycline (78%) resistance was detected, although this is probably an over-estimate, due to a legacy BSAC clinical breakpoint being applied. By contrast, MIC testing for this organism (performed on a subset of 28 isolates), indicated moderate resistance to tetracycline (18%).

Figure 4.8: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Pasteurella multocida* isolates from pigs (n=41 in 2022). Note scale differs between graphs.



AG: aminoglycosides, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

Trueperella (Arcanobacterium) pyogenes

There was no *Trueperella* (*Arcanobacterium) pyogenes,* from respiratory or systemic disease, isolated from pigs in 2022.

4.3.2.3 Integumentary system

Staphylococcus hyicus

Staphylococcus hyicus causes exudative epidermitis, otherwise known as 'greasy pig disease', in young pigs. A total of eight isolates were tested and the full results are presented in Table S4.2.6 in Supplementary Material 2. One isolate was MDR. No resistance was detected to trimethoprim/sulfonamides. Three isolates were resistant to tetracycline and two isolates were resistant to ampicillin, lincomycin and penicillin.

Staphylococcus xylosus

Staphylococcus xylosus causes dermatitis and one isolate was recovered in 2022. The results are available in full in Table S4.2.6 in Supplementary Material 2. No resistance was detected to the antibiotics tested, except ampicillin and penicillin.

4.3.2.4 Multi-system pathogens

Erysipelothrix rhusiopathiae

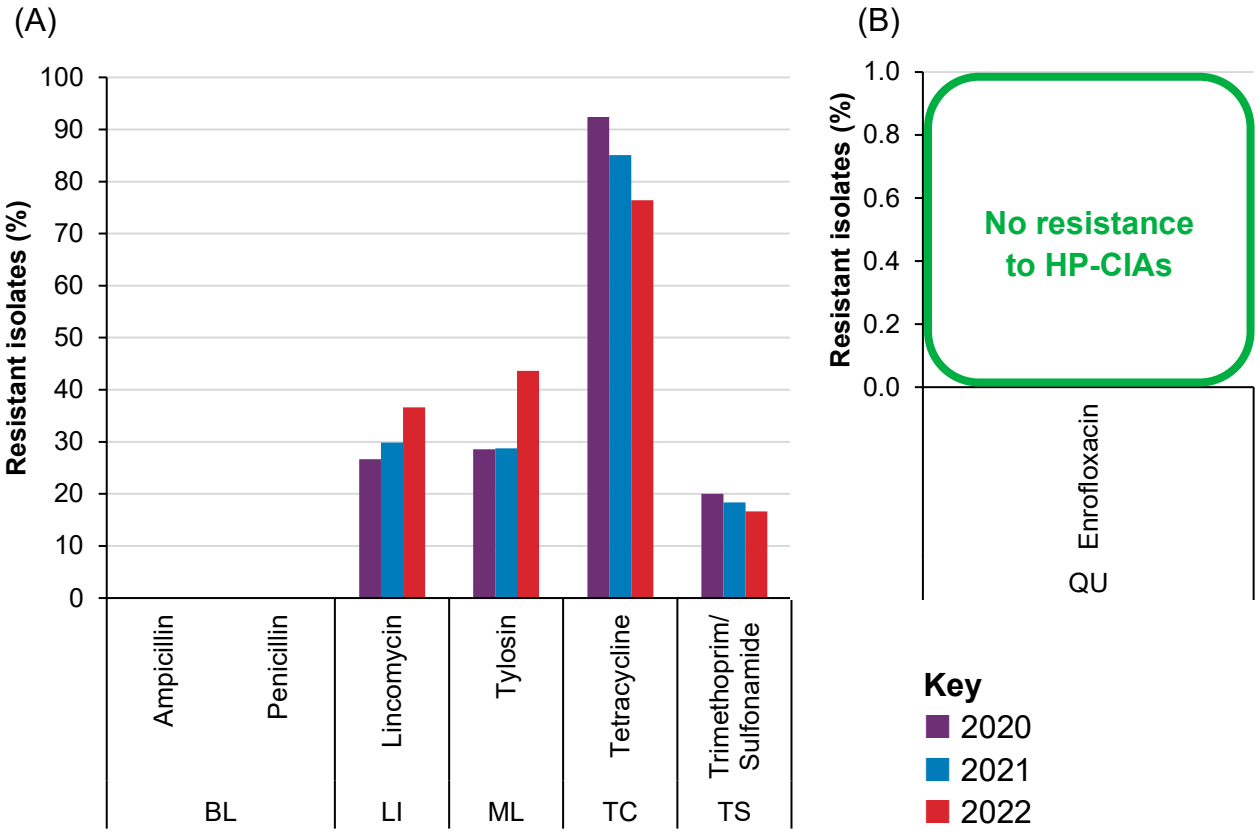
Erysipelothrix rhusiopathiae is widely distributed in nature and occurs as a commensal or pathogen of a very wide range of vertebrate and invertebrate species. In pigs, infection usually presents as septicaemia, arthritis and endocarditis. Three isolates were tested in 2022 and the full results presented in Table S4.2.6 in Supplementary Material 2. Isolates were susceptible to the antibiotics tested, including the usual treatment options penicillin and ampicillin, except for two isolates which were resistant to trimethoprim/sulfonamides.

Streptococcus suis

Streptococcus suis causes meningitis, arthritis and pneumonia in pigs. It is also zoonotic, although human infections are rare and usually occur following contact with affected pigs. A total of 72 isolates were tested by disc diffusion from diagnostic samples in 2022 (**Figure 4.9**). *S. suis* isolates have been utilised for further methodological development of broth microdilution (**Box 4.2**).

MDR was seen in 9.7% of isolates. No resistance was detected to ampicillin or penicillin, the usual treatment options. Very high levels of resistance were detected to tetracycline (76%); high resistance to both lincomycin (37%) and tylosin (44%); and moderate resistance to trimethoprim/sulfonamides (17%). HP-CIA resistance was not observed between 2020 and 2022.

Figure 4.9: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Streptococcus suis* isolates from pigs (n=72 in 2022). Note scale differs between graphs.



BL: beta-lactams, LI: lincosamides, ML: macrolides, TC: tetracyclines, TS: trimethoprim/sulfonamides, QU: quinolones

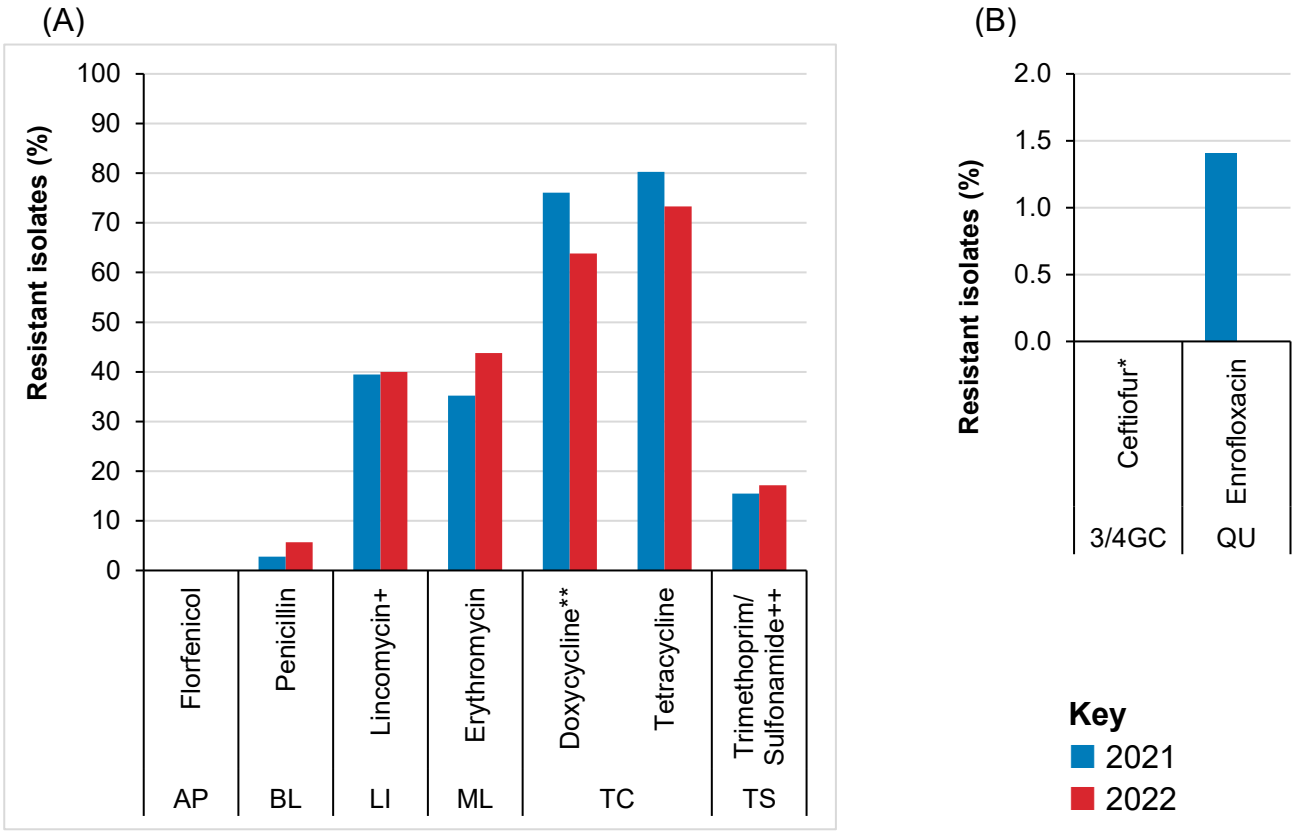
Box 4.2: *S. suis* MIC

Methodological development of broth microdilution, to generate robust and comparable susceptibility testing outputs, has continued with *S. suis.* 105 *S. suis* isolates from pigs underwent broth microdilution, these included several additional isolates from individual outbreaks not tested by disc diffusion (**Figure 4.10**). The full breakpoints applied are available in Table S3.1.2.1 in Supplementary Material 2.

Of the isolates, 37% were MDR and 24% susceptible to the full panel of antibiotics tested. No HP-CIA resistance was seen in 2022. Penicillin resistance was detected in 5.7% of isolates, indicating that beta-lactam compounds remain a viable first-line choice in the treatment of the majority of *S. suis* infections in pigs. No resistance was detected to florfenicol, an alternative treatment option, or to ceftiofur.

Resistance to erythromycin, lincomycin and tetracyclines was the most common MDR pattern observed (29%). Extremely high resistance was detected to tetracycline (73%) and very high resistance to doxycycline (64%).

Figure 4.10: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Streptococcus suis* isolates from pigs (n=105 in 2022) interpreted using CLSI veterinary breakpoints unless indicated otherwise.



* *S. uberis* in breakpoint for bovine isolates applied
** Interpreted using EUCAST human CBP for *S. pneumoniae*
+ Interpreted using CA-SFM veterinary CBP
++ Interpreted using EUCAST human CBP for *Streptococci*
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, LI: lincosamides, ML: macrolides, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

4.3.3 Poultry

The complete poultry dataset can be found in section S4.3 of Supplementary Material 2, and the subset of isolates tested by MIC in section S4.7 of Supplementary Material 2.

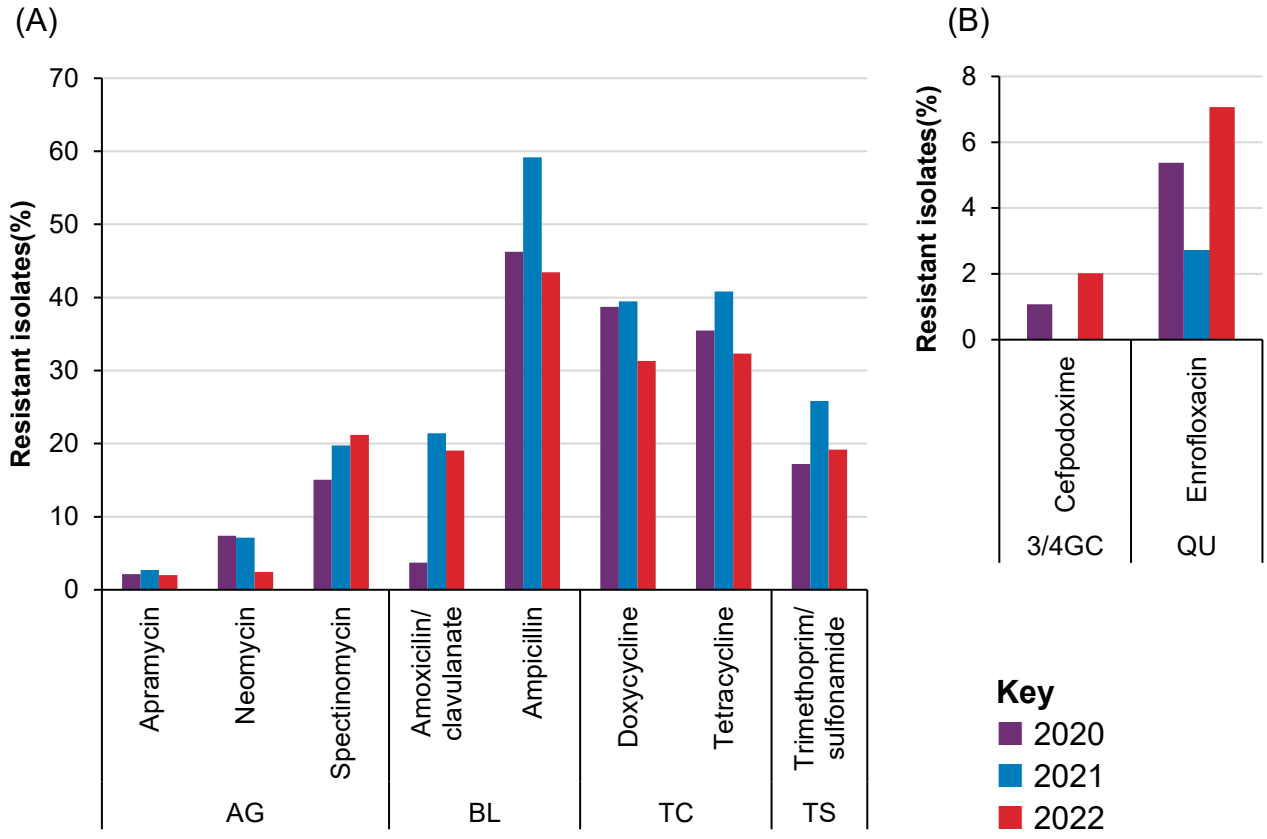
4.3.3.1 Gastrointestinal system

Escherichia coli

E. coli is an important zoonotic organism and a commensal of animals and humans. The clinical samples submitted for testing from chickens and turkeys includes flocks of various types and sizes, including commercial production, pet birds and small-scale poultry keepers. Much larger numbers of chicken isolates (n=99) were obtained compared to turkey isolates (n=6) between 2020 and 2022. Resistance in *E. coli* isolates from chickens is shown below in **Figure 4.11.** Full results from turkeys are shown in Table S4.3.2 in Supplementary Material 2; all isolates were fully susceptible

In chickens, MDR was detected in 22% of 99 isolates. Resistance to amoxicillin/clavulanic acid was 3.7% in 2020, 21% in 2021 and 19% in 2022; this potential increase is difficult to interpret given variation in the number of isolates tested. High resistance was detected to ampicillin (43%), doxycycline (31%), spectinomycin (21%) and tetracycline (32%). Resistance to the other antibiotics tested was moderate to low. Resistance to the HP-CIAs cefpodoxime (2%) and enrofloxacin (7.1%) was low.

Figure 4.11: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from chickens (n=99 in 2022). Note scale differs between graphs.



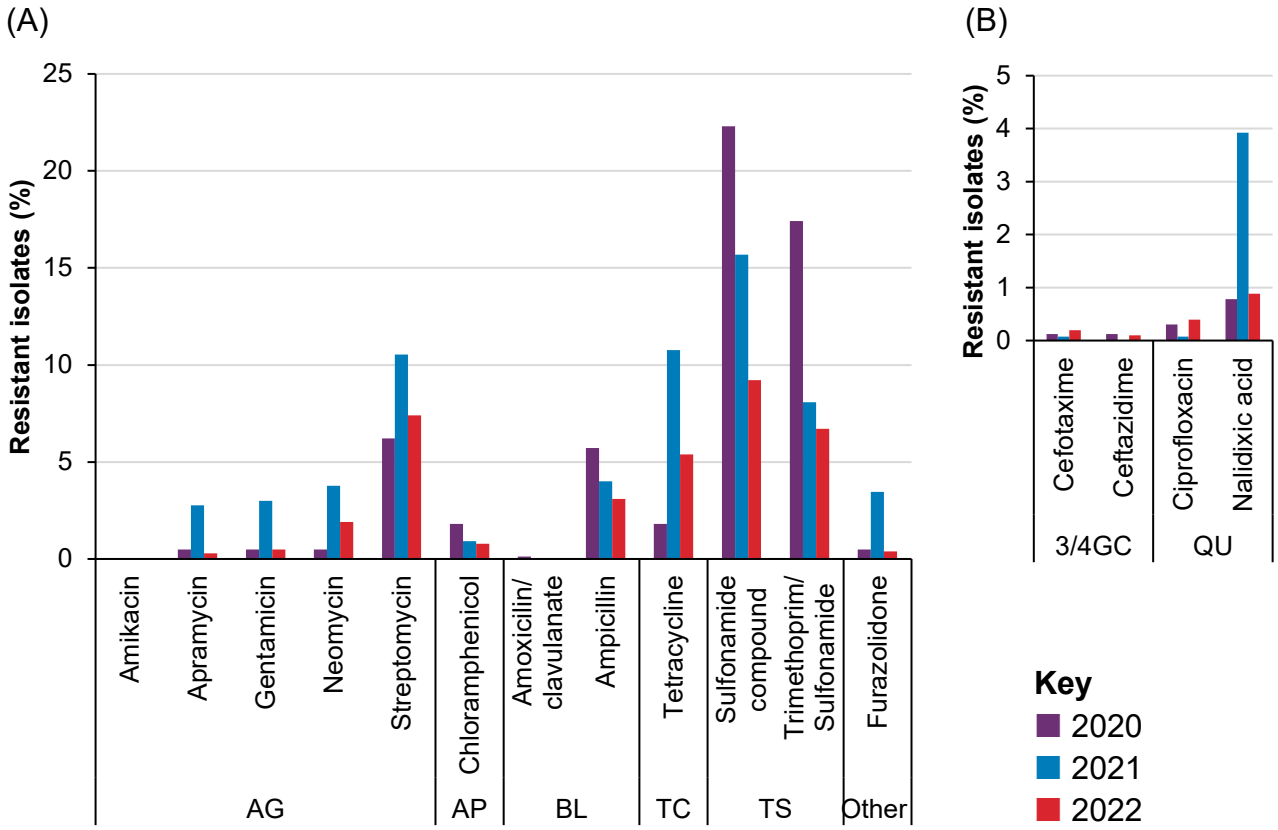
AG: aminoglycosides, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

Salmonella spp.

Salmonella is an important cause of foodborne disease in people. It can be part of the normal gut flora in animals, but can also cause disease.

In 2022, 2,040 isolates were recovered from chickens (**Figure 4.12**). No resistance was detected to amikacin and amoxicillin/clavulanate. Very low resistance was detected to apramycin (0.3%), furazolidone (0.4%), gentamicin (0.5%) and chloramphenicol (0.8%). The highest levels of resistance were seen to sulfonamides (9.2%) and streptomycin (7.4%). Resistance to the HP-CIAs was very low (<1%).

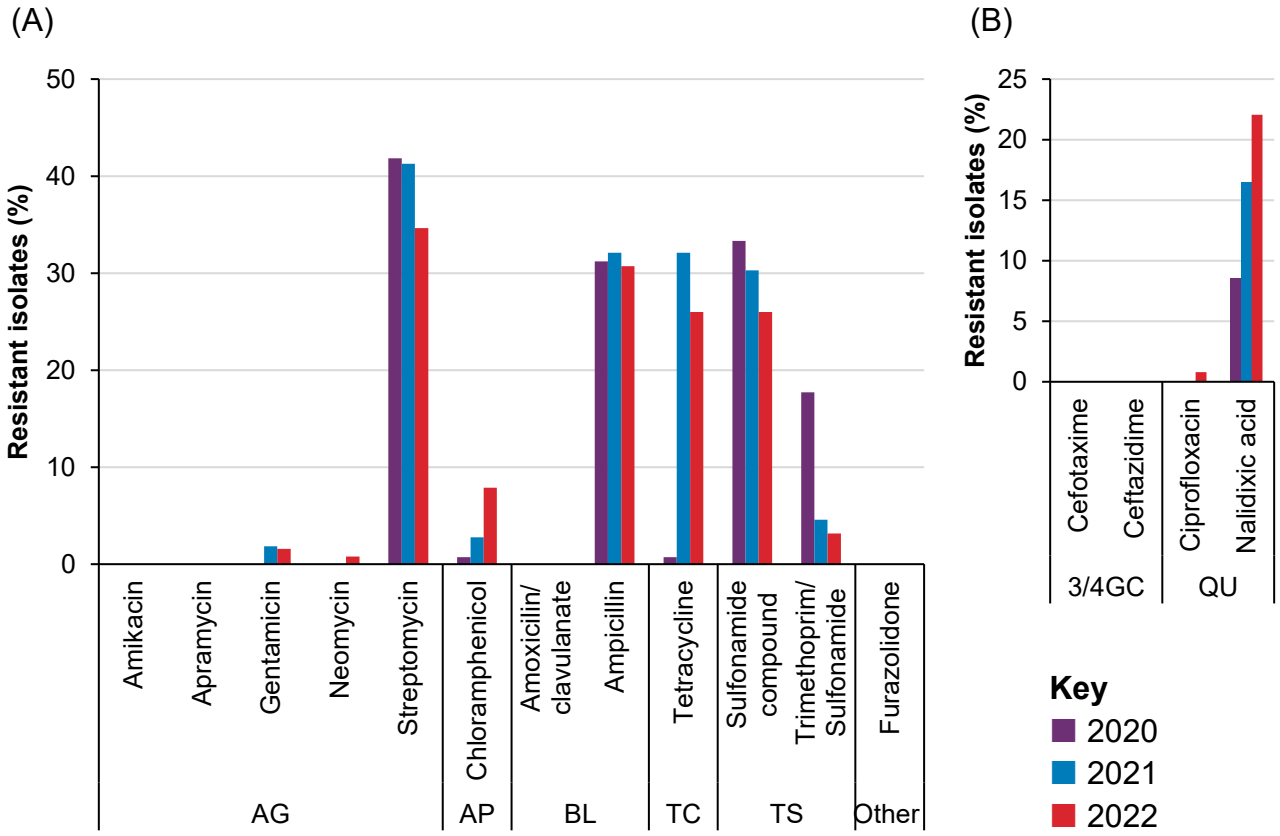
Figure 4.12: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Salmonella* isolates from chickens (n=2040 in 2022). Note scale differs between graphs.



AG: aminoglycosides, AP: amphenicols BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

In 2022, 127 isolates were recovered from turkeys (**Figure 4.13**). No resistance was detected to amikacin, apramycin, amoxicillin/clavulanate and furazolidone. Of the non HP-CIAs, high resistance was seen to streptomycin (35%), ampicillin (31%), sulfonamides (26%) and tetracycline (26%). Resistance to the other antibiotics tested was generally low (<8%) or not detected. Resistance to the HP-CIA quinolone nalidixic acid increased from 8.5% in 2020 to 22% in 2022; this potential increase is difficult to interpret given the decreased clinical submissions following significant disruption to the poultry industry as a result of avian influenza during 2022 and the COVID-19 pandemic prior. Resistance to the other HP-CIAS was very low (<0.8%) or not detected.

Figure 4.13: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Salmonella* isolates from turkeys (n=127 in 2022). Note scale differs between graphs.



AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

4.3.3.2 Respiratory system

Klebsiella pneumoniae

A single *Klebsiella pneumoniae* isolate was recovered from avian species. It was resistant to ampicillin, which is to be expected for a Gram-negative organism, and sensitive to the rest of the panel of antibiotics.

4.3.3.3 Multi-system pathogens

Erysipelothrix rhusiopathiae

Erysipelothrix rhusiopathiae is widely distributed in nature and occurs as a commensal or pathogen and can infect multiple species. In 2022, one isolate was recovered from a turkey. It was resistant to trimethoprim/sulfonamides and sensitive to the rest of the panel of antibiotics.

Staphylococcus aureus

Staphylococcus aureus causes a number of infections in poultry and game birds, including septicaemia, yolk sac infection, arthritis and osteomyelitis. In 2022, one isolate was recovered from a chicken. This was fully susceptible to the panel of antimicrobials tested. One MDR isolate was recovered from a pheasant. This was resistant to ampicillin, penicillin, tetracycline, doxycycline, erythromycin, tylosin and lincomycin.

4.3.4 Cattle

The complete cattle dataset can be found in section S4.4 of Supplementary Material 2, and the subset of isolates tested by MIC in section S4.7 of Supplementary Material 2.

4.3.4.1 Reproductive system

Bovine 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 highlight that acquired resistance does occur in England and Wales. Resistance should be considered when veterinarians and farmers develop mastitis control programs for individual farms.

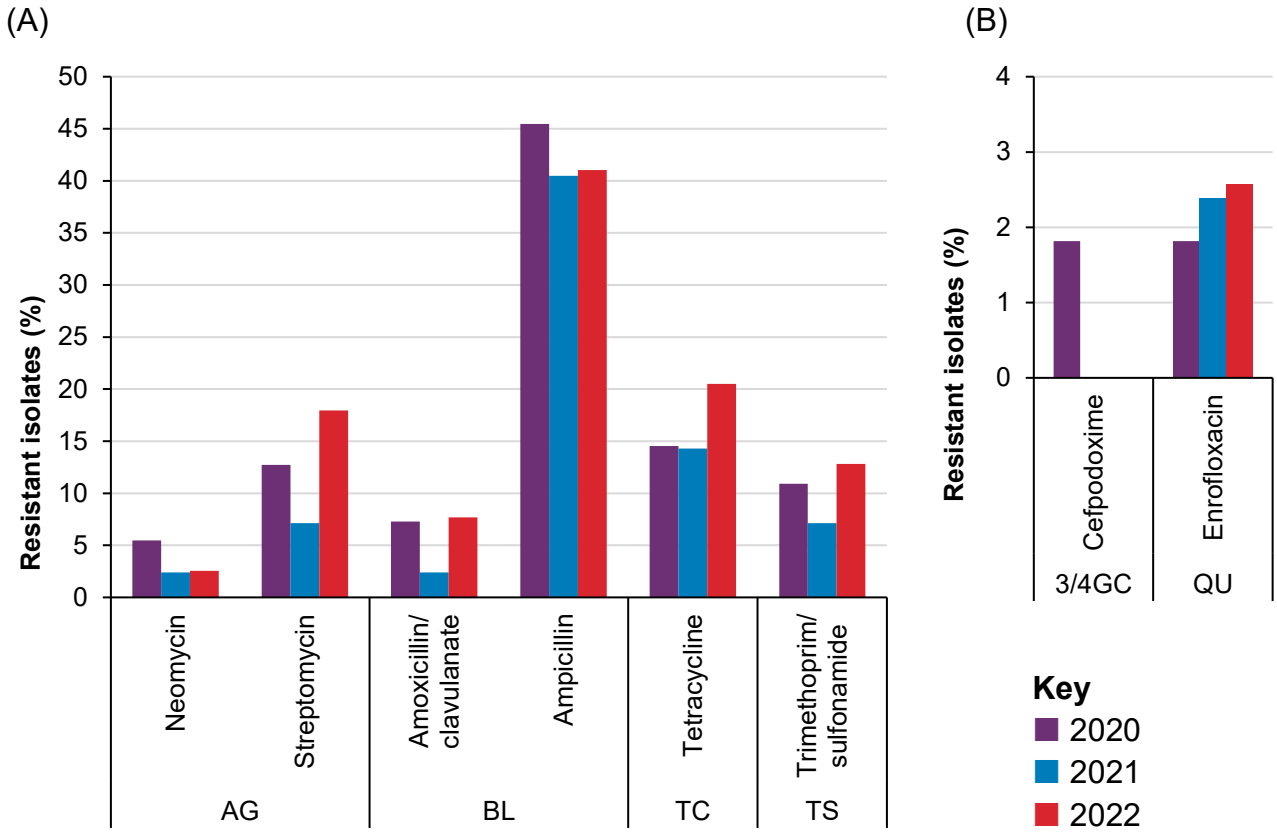
Note that Gram negative (*E. coli*) and Gram positive (*S. aureus* and streptococci) isolates are tested against different panels of antibiotics and that the number of isolates tested is highly variable, which is likely to impact the interpretation of resistance. Details on the number of tests performed on bovine mastitis pathogens are in S4.4 of Supplementary Material 2.

Escherichia coli

E. coli and other coliforms are major causes of bovine mastitis. Most *E. coli* strains originate from the immediate environment of the cow, and no particular virulence factors are required to infect the mammary gland. These *E. coli* isolates, therefore, mostly represent strains that are present in the environment of adult dairy cattle, particularly cattle sheds and cubicle houses, and are probably mainly of faecal origin. There were 39 isolates recovered from mastitis diagnostic samples in 2022 (**Figure 4.14**).

13% of isolates were MDR. There were high levels of resistance to ampicillin (41%) and tetracycline (21%), and moderate levels of resistance to streptomycin (18%) and trimethoprim/sulfonamides (13%). Resistance to the other antibiotics tested, including HP-CIAs, was low or not detected.

Figure 4.14: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Escherichia coli* isolated from mastitis samples from cattle (n=39 in 2022) in England and Wales. Note scale differs between graphs.



AG: aminoglycosides, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

Staphylococcus aureus

S. aureus is normally resident on the skin and mucous membranes of cattle and is a common cause of mastitis. There were 24 isolates recovered from diagnostic mastitis samples in 2022 (**Figure 4.15**).

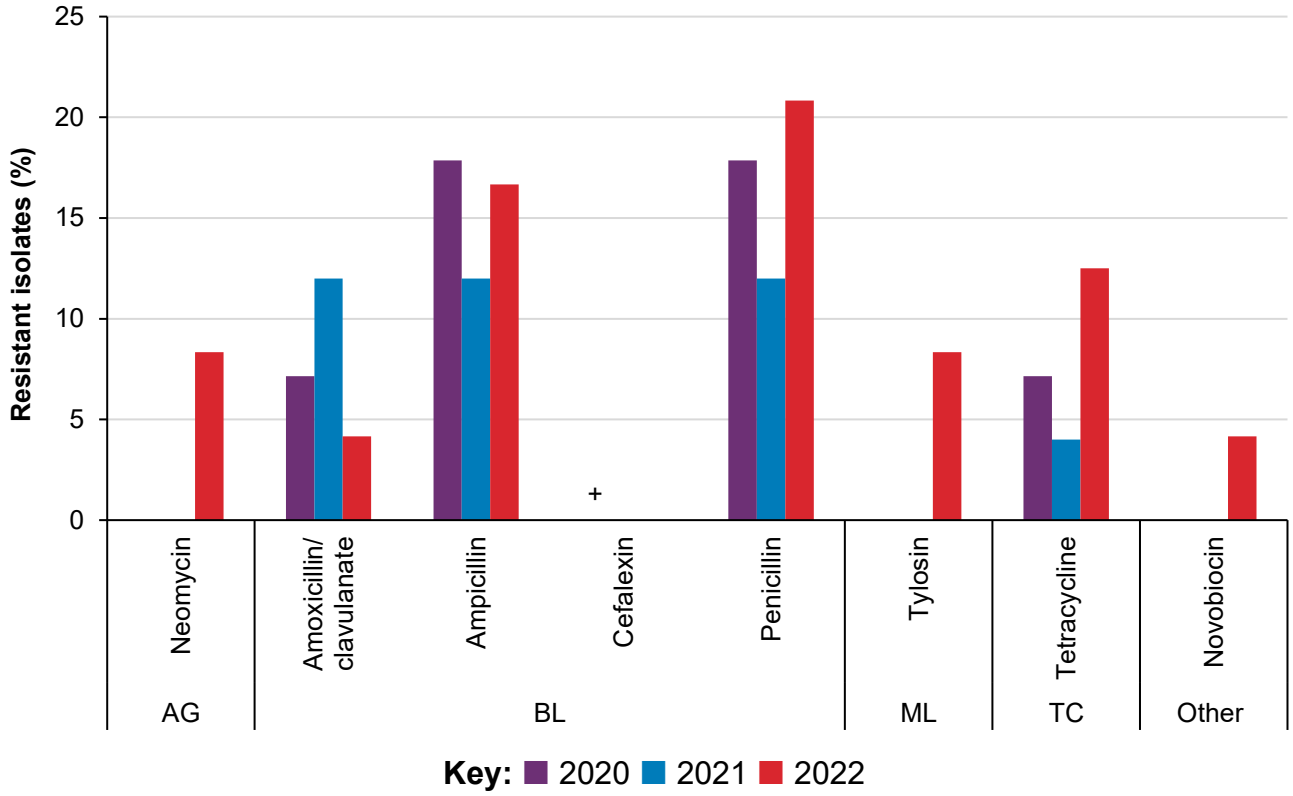
12% of isolates were MDR. There were high levels of resistance to penicillin (21%), and moderate levels of resistance to ampicillin (17%) and tetracycline (13%). Resistance to novobiocin (4.2%) and tylosin (8.3%) was detected in 2022. Resistance to HP-CIAs was not tested.

Resistance to penicillin was above 20% in 2022. Penicillin resistance in bovine *S. aureus* from England and Wales occurs most frequently via the production of beta-lactamases. The genes encoding beta-lactamases can be located on plasmids and often on transposons and may be readily transferable.

Resistance to amoxicillin/clavulanate, the combined beta-lactam and beta-lactamase inhibitor, was 4.2% in 2022. Isolates with this resistance are screened to check for the

presence of *mecA* and *mecC* genes, which confer methicillin resistance. One methicillin-resistant *S. aureus* (MRSA) isolate, carrying the *mecA* gene was detected in 2022, and confirmed as LA-MRSA CC398 spa-type. The isolate was resistant to ampicillin, penicillin, cefoxitin and tetracycline and was *mecA* positive by PCR.

Figure 4.15: Resistance in *Staphylococcus aureus* isolated from mastitis samples from cattle (n=24 in 2022) in England and Wales.



+ Not tested
AG: aminoglycosides, BL: beta-lactams, ML: macrolides TC: tetracyclines

Streptococcus dysgalactiae

Streptococcus dysgalactiae is a commensal of the mucous membranes of cattle and causes mastitis and occasionally other diseases. It is not considered zoonotic, and is a separate population to Group C streptococci that can cause disease in humans. 16 isolates were tested to the panel of antibiotics in 2022 and the full results are presented in Table S4.4.5 in Supplementary Material 2.

In 2022, all isolates were resistant to tetracycline (100%). This resistance is common. High resistance was detected to neomycin (29%) and novobiocin (21%), and moderate resistance to tylosin (13%). No resistance was detected to the other antibiotics tested.

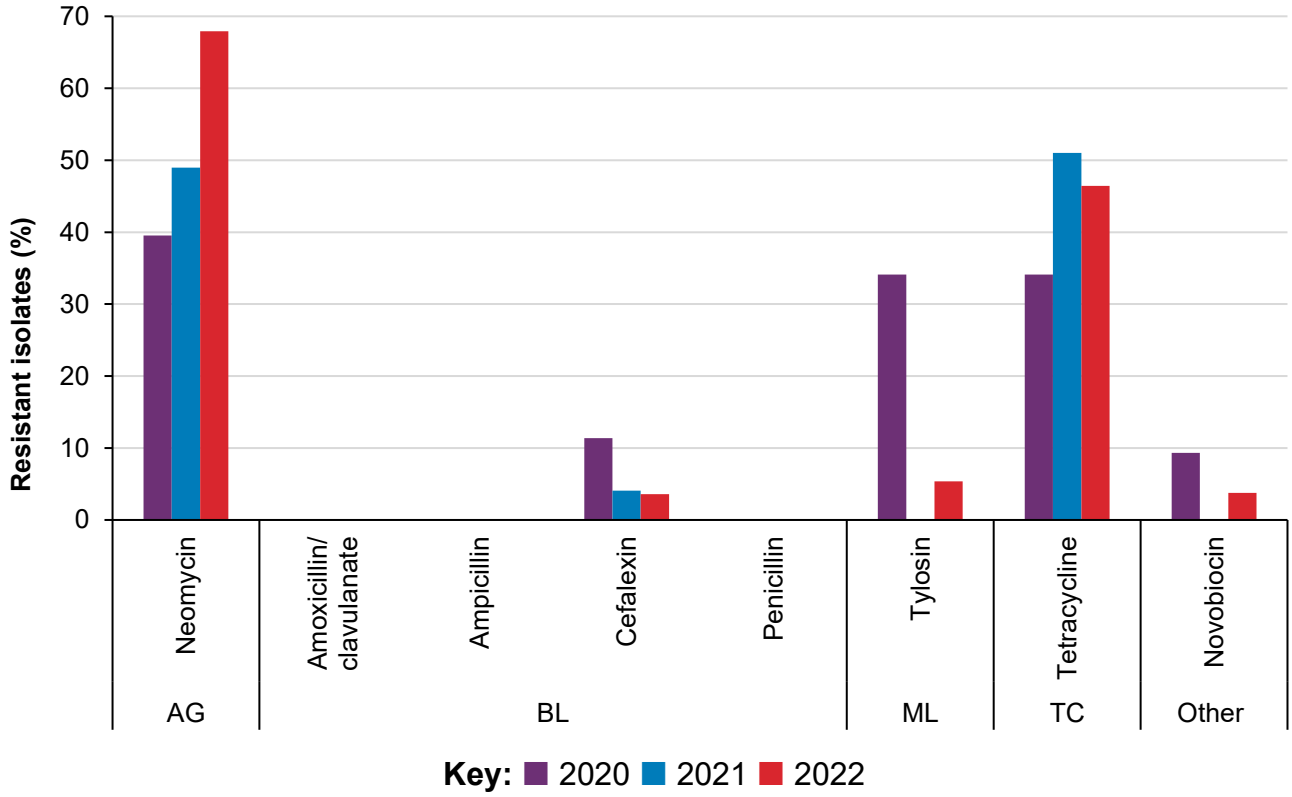
Streptococcus uberis

Streptococcus uberis is a well-recognised cause of bovine mastitis and is widely distributed in the environment of dairy cows, as well as being a commensal of the bovine

vagina, tonsil, and skin. It is not regarded as zoonotic. 56 isolates were tested to the panel of antibiotics in 2022 (**Figure 4.16**).

Resistance to neomycin was very high (68%), which may reflect a degree of intrinsic resistance to the aminoglycosides. Resistance to tetracycline (46%) was high. All isolates were sensitive to ampicillin, amoxicillin/clavulanate and penicillin. Resistance to HP-CIAs was not tested.

Figure 4.16: Resistance in *Streptococcus uberis* isolated from mastitis samples from cattle (n=56 in 2022) in England and Wales.



AG: aminoglycosides, BL: beta-lactams, ML: macrolides, TC: tetracyclines

Other mastitis pathogens

Very low numbers of additional mastitis pathogens were tested. Full results are available in Table S4.4.6 in Supplementary Material 2.

All eight of the *Klebsiella pneumoniae* isolated from bovine mastitis cases were resistant to ampicillin. This reflects the intrinsic resistance to ampicillin of this organism. One isolate was MDR and the remaining isolates were susceptible to the other antibiotics tested.

Six isolates of *Pseudomonas aeruginosa* were recovered in 2022 and were resistant to a range of antimicrobials. Efflux and impermeability are frequently responsible for resistance to beta-lactams in *P. aeruginosa* and likely accounted for the observed beta-lactam resistance in all isolates. All six isolates were susceptible to the anti-pseudomonal

cephalosporin antibiotic ceftazidime, which is not authorised for use in food-producing animals. Efflux pumps can also confer resistance to quinolones in *P. aeruginosa*; however, all isolates between 2020 and 2022 were susceptible to enrofloxacin.

One *Trueperella (Arcanobacterium) pyogenes* isolate was recovered in 2022, which was susceptible to the panel of antibiotics tested.

No *Streptococcus agalactiae* or *Staphylococcus xylosus* isolates were recovered in 2022.

Box 4.3: Private Laboratory Initiative

The Private Laboratory Initiative (PLI) is a collaborative project between the VMD and APHA. Many veterinarians send diagnostic samples to private veterinary laboratories for culture and sensitivity, the results of which do not ordinarily feed into AMR surveillance efforts. The purpose of the PLI project is to collect and analyse data from the private veterinary laboratories to supplement the AMR surveillance co-ordinated by the VMD. This initiative directly supports the UK's ambition to contain and control AMR by increasing the sensitivity of surveillance and providing a stronger evidence base for AMR in UK livestock.

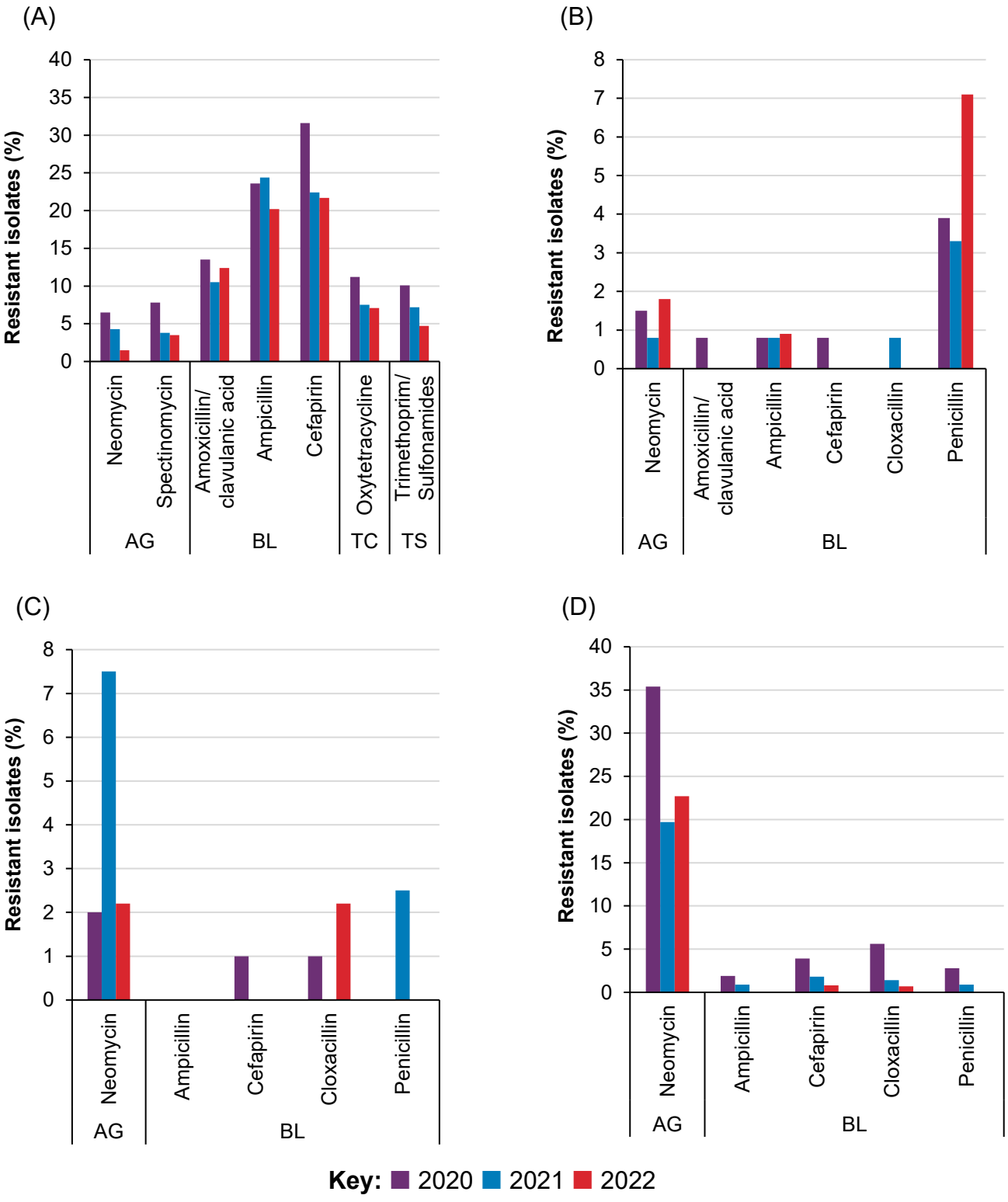
We are grateful to the Vale Veterinary Laboratory for providing data for this project. Presented in **Figure 4.17** are the results from antibiotic susceptibility testing of key mastitis pathogens isolated from cattle by the Vale Laboratory in 2020 to 2022. This data should be interpreted with caution, as there are differences in the laboratory methods, antibiotic panels and interpretation criteria used by government and private laboratories. A summary of the methodology and breakpoints applied can be found in Table S3.1.3 in Supplementary Material 2.

A total of 700 isolates were tested in 2022. Resistance to the aminoglycosides and oxytetracycline was low in 2022. Moderate to high resistance to beta-lactams was detected:12% of isolates were resistant to amoxicillin/ clavulanate , 20% to ampicillin, and 22% to cefapirin. In *S. uberis*, resistance was low or very low in 2022 to all beta-lactams tested. For *S. aureus,* resistance was detected to penicillin (7.1%), neomycin (1.8%) and ampicillin (0.9%). For *S. dysgalactiae* in 2022, resistance was only detected to neomycin and cloxacillin (both 2.2%).

These results broadly align with the cattle mastitis AMR results from the clinical surveillance programme (section 4.3.4.1), with the exception of the slightly lower percentage resistance to ampicillin in *E. coli,* and lower resistance to both ampicillin and penicillin in *S. aureus,* isolated by Vale compared to APHA. Additionally, for *S. dysgalactiae* in 2022, lower resistance to neomycin was detected by Vale compared to APHA. These discrepancies could be attributed to population and sampling differences, or variation in laboratory methodology and breakpoints used.

Whilst still in the early stages of this project, these results demonstrate the potential for broadening AMR surveillance by collaborating with the private sector. However, further work and investment are required to achieve greater parity between private and government laboratories. This will be progressed further in 2024 under the National Biosurveillance Network (NBN). The bringing together and reporting of data from additional sources will both improve representativeness of surveillance through an increased number of samples for testing, and provide greater information on AMR at a regional level. This will provide direct benefits to both farmers and vets by creating a more detailed picture of AMR in key veterinary pathogens, and better help inform disease management and treatment.

Figure 4.17: Resistance in (A) *Escherichia coli* (n=259 in 2022), (B) *Staphylococcus aureus* (n=113 in 2022), (C) *Streptococcus dysgalactiae* (n=46 in 2022) and (D) *Streptococcus uberis* (n=282 in 2022), isolated from bovine mastitis samples submitted to Vale Veterinary Laboratories.



AG: aminoglycosides, BL: beta-lactams, TC: tetracyclines, TS: trimethoprim/sulfonamides

4.3.4.2 Gastrointestinal system

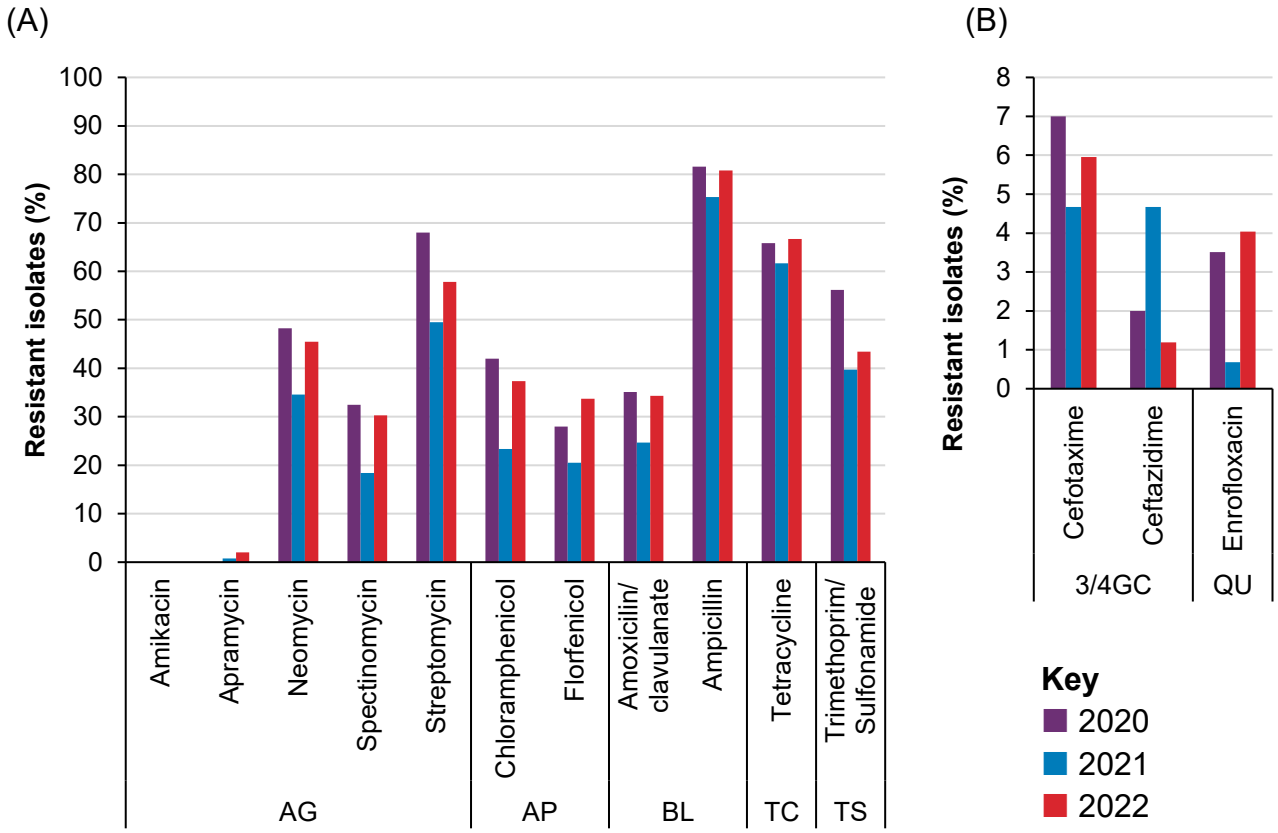
Escherichia coli

E. coli is an important zoonotic organism and a commensal of animals and humans. *E. coli* were predominantly collected from the neonatal category. The occurrence of resistance in neonatal calves was generally similar to that seen in pre-weaning calves, but mostly lower than what was observed in adults. The similar levels of resistance observed in neonatal and pre-weaning calves probably reflects the proximity in which these age groups are often kept in calf rearing accommodation on farms. Resistance to trimethoprim/sulfonamides was highest in neonates and declined with age. This could reflect relatively higher use of trimethoprim/sulfonamides in neonates for conditions such as calf scour.

The AMR in *E. coli* results from cattle are presented separately for neonates (**Figure 4.18**), pre-weaning calves (**Figure 4.19**), and adults (**Figure 4.20**). The number of isolates tested are in Table S4.4.2 in Supplementary Material 2.

In neonatal calves, 57% of isolates were MDR. Extremely high resistance was seen to ampicillin (81%) and high resistance was detected to all other antibiotics, apart from amikacin (0.0%) and apramycin (2.0%) (**Figure 4.18**). Low levels of resistance to the HP-CIAs cefotaxime, ceftazidime and enrofloxacin were detected.

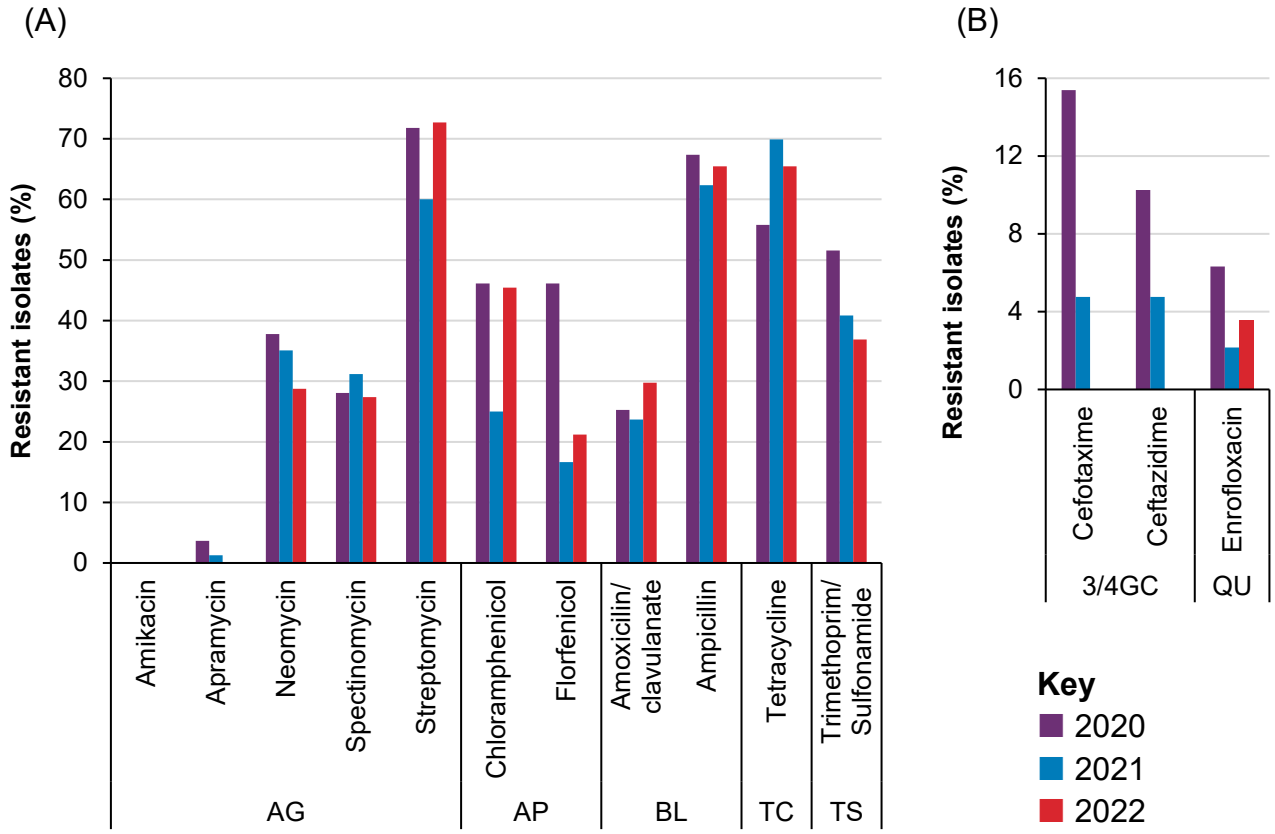
Figure 4.18: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from neonatal calves (n= 99 in 2022). Note scale differs between graphs.



AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

In pre-weaned calves, 44% of isolates were MDR. No resistance was detected to amikacin and apramycin (**Figure 4.19**). Resistance to most other antibiotics remains high to very high, with resistance to streptomycin (73%) extremely high. No resistance was detected to the third-generation cephalosporins, which could be related to recent reductions in use of these antibiotics in cows. Resistance to the HP-CIA quinolone enrofloxacin (3.6%) was low.

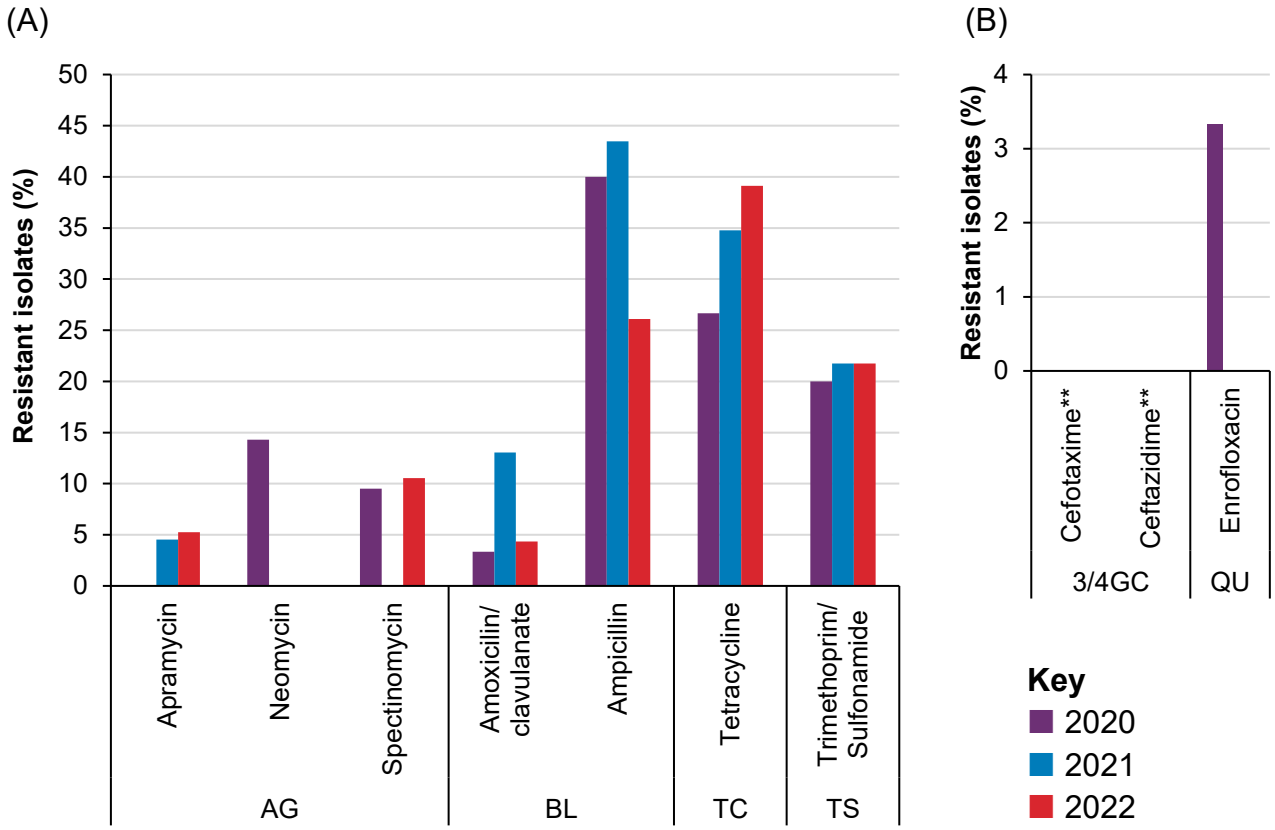
Figure 4.19: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from pre-weaned calves (n=84 in 2022). Note scale differs between graphs.



AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/ sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

In adult cattle, no resistance was detected to neomycin (**Figure 4.20**). Low levels of resistance were seen to apramycin (5.3%) and amoxicillin/clavulanate (4.3%). High levels of resistance were seen to ampicillin (26%), tetracycline (39%) and trimethoprim/sulfonamides (22%). No HP-CIA resistance was detected in 2022.

Figure 4.20: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from adult cows (n=23 in 2022). Note scale differs between graphs.



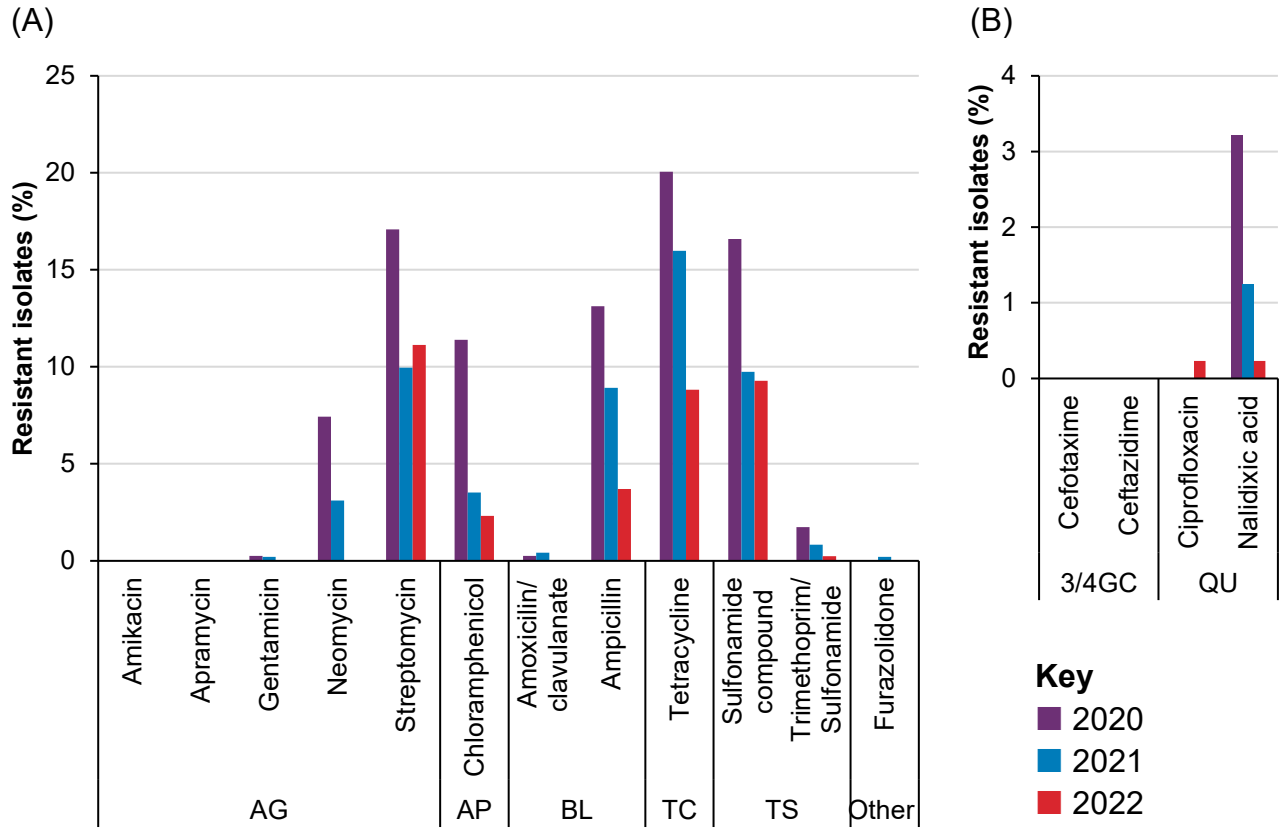
AG: aminoglycosides, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

Salmonella spp.

Salmonella is an important cause of foodborne disease in people. It can be part of the normal gut flora in animals, but can also cause disease. *Salmonella* data for cattle is presented below for all age groups (**Figure 4.21**).

In 2022, there were moderate levels of resistance to streptomycin (11%). Levels of resistance to the other antibiotics tested were either low or not detected. Resistance to the HP-CIAS was not detected in the third-generation cephalosporins, very low levels were seen in the quinolones: ciprofloxacin (0.2%) and nalidixic acid (0.2%).

Figure 4.21: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Salmonella* isolates from cattle (n=431 in 2022). Note scale differs between graphs.



AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

4.3.4.3 Respiratory system

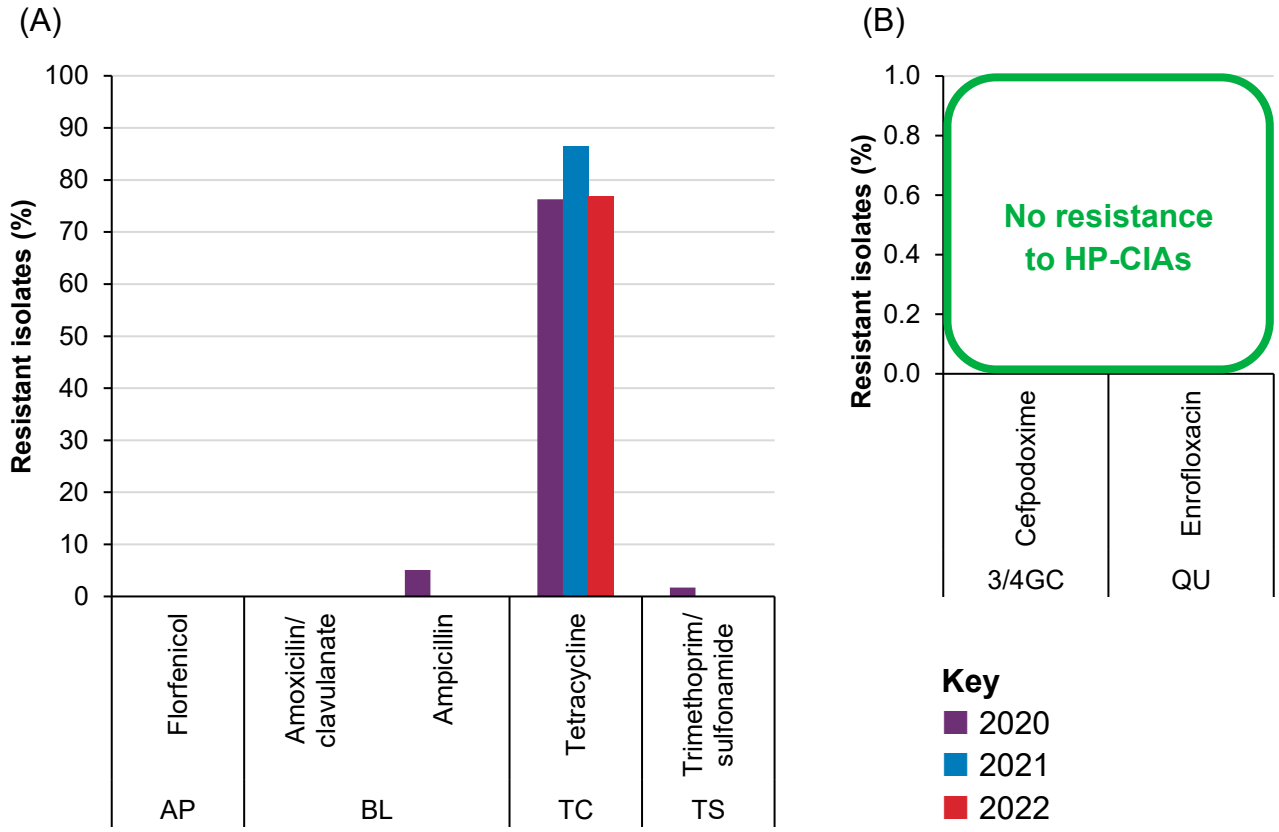
Histophilus somni

Histophilus somni (formerly known as *Haemophilus somnus*) causes pneumonia and thrombo-embolic meningo-encephalitis in calves. The three isolates tested between 2020 and 2022 were fully susceptible to the panel of antibiotics tested.

Mannheimia haemolytica

M. haemolytica causes respiratory disease in cattle in the UK, although the predominant serotypes differ from those in sheep. Healthy animals can carry the bacteria in the upper respiratory tract. A total of 69 isolates were recovered from diagnostic samples in 2022 (**Figure 4.22**). Of these, none were MDR and 23% fully susceptible to the panel of antimicrobials tested. HP-CIA resistance was not detected between 2020 and 2022. Very high tetracycline (77%) resistance was detected, although this is probably an over-estimate, due to use of an outdated BSAC clinical breakpoint. By contrast, MIC testing for this organism performed on a subset of 21 isolates indicated low resistance to tetracycline (9.5%). No resistance was detected to the other antibiotics on the panel.

Figure 4.22: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Mannheimia haemolytica* isolated from cattle (n=69 in 2022). Note scale differs between graphs.

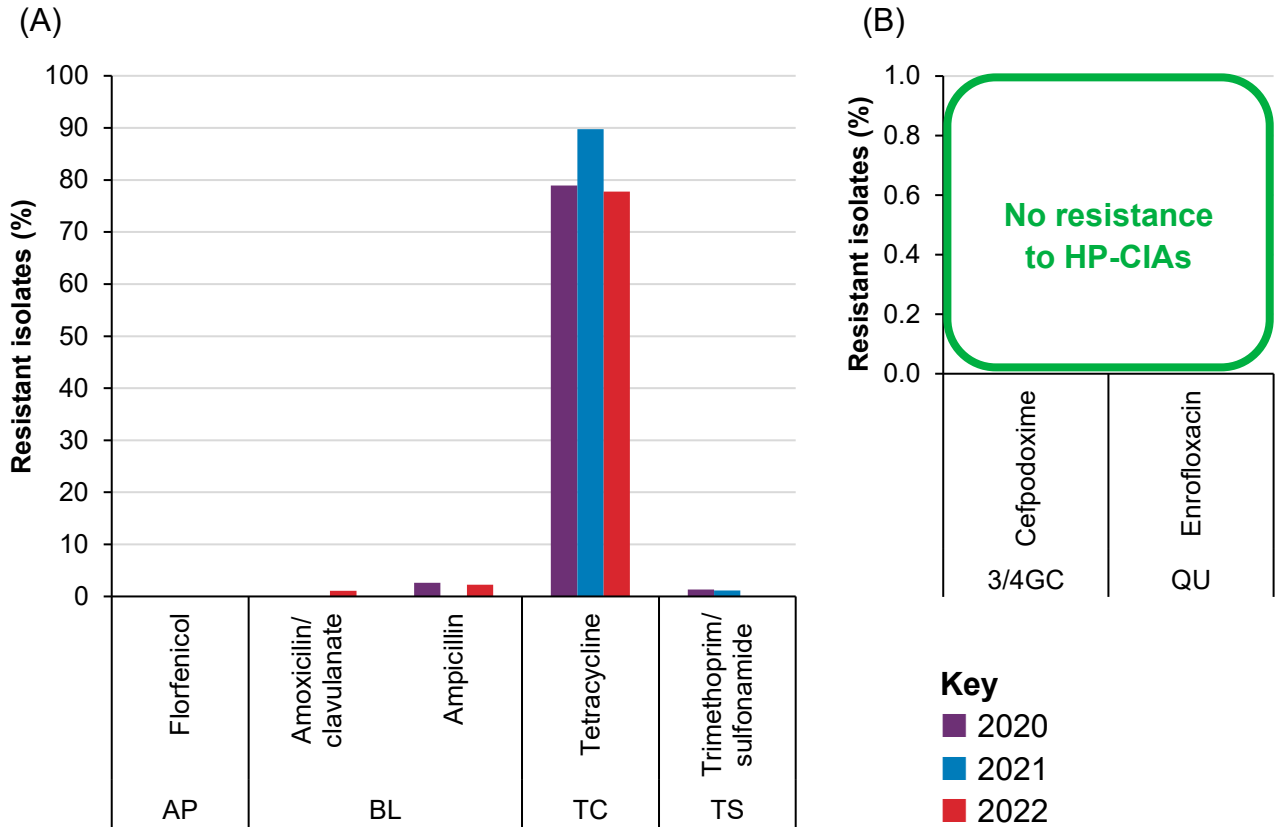


AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

Pasteurella multocida

P. multocida primarily causes respiratory disease in cattle in the UK. A total of 90 isolates were recovered from diagnostic samples in 2022 (**Figure 4.23**). Of these, 2.2% were MDR. No resistance was detected to florfenicol and trimethoprim/sulfonamides. Low levels resistance were seen to amoxicillin/clavulanate (1.1%) and ampicillin (2.3%), representing one and two isolates respectively. Very high tetracycline resistance (78%) was detected, although this is probably an over-estimate, due to the use of an outdated BSAC clinical breakpoint. By contrast, MIC testing for this organism performed on a subset of 33 isolates indicated high resistance to tetracycline (55%). HP-CIA resistance was not detected between 2020 and 2022.

Figure 4.23: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Pasteurella multocida* isolated from cattle (n=90 in 2022). Note scale differs between graphs.



AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/ sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

Trueperella (Arcanobacterium) pyogenes

No isolates of *Trueperella* (*Arcanobacterium*) *pyogenes* from respiratory or systemic disease in cattle were tested in 2022.

4.3.5 Sheep

The complete sheep dataset can be found in section S4.5 of Supplementary Material 2, and the subset of isolates tested by MIC in section S4.7 of Supplementary Material 2.

4.3.5.1 Gastrointestinal system

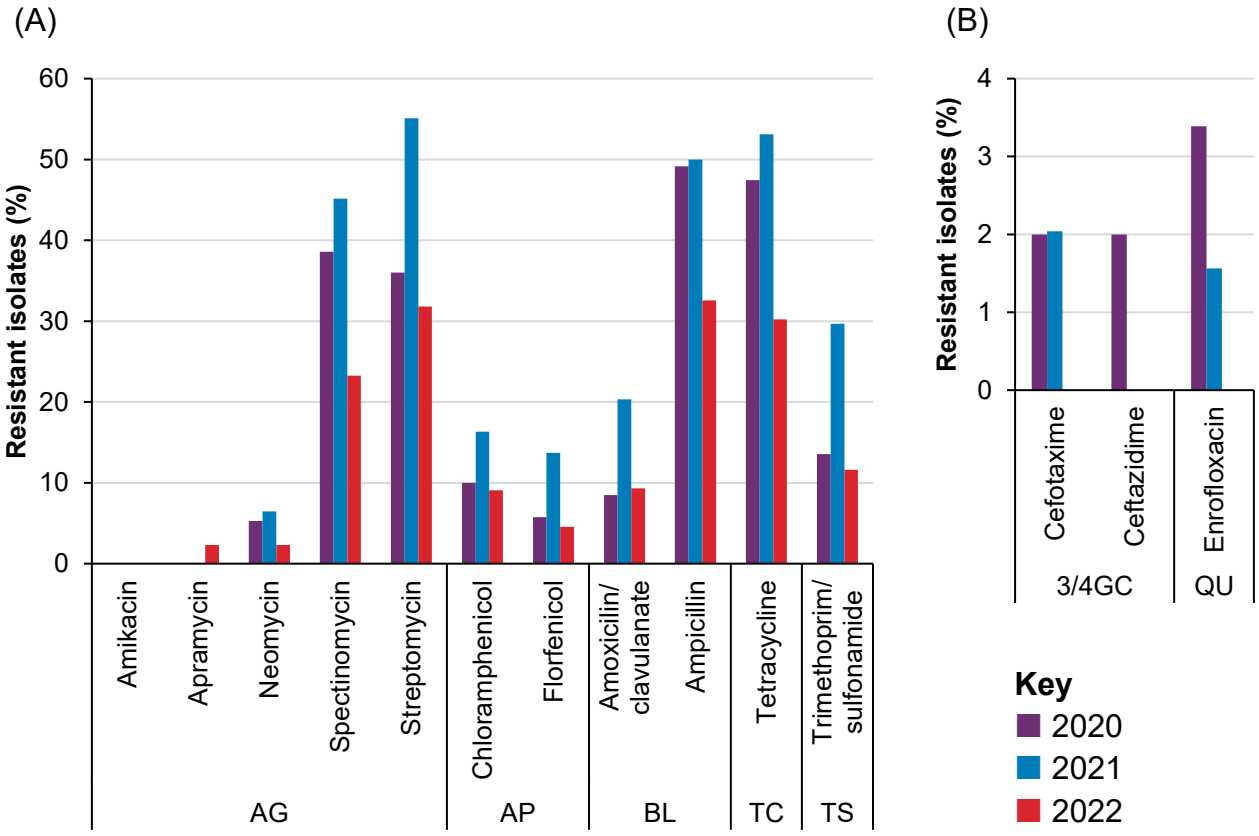
Escherichia coli

E. coli is an important zoonotic organism and a commensal of animals and humans. *E. coli* were predominantly collected from the neonatal and adult age categories. Non-HP-CIA resistance was generally highest in neonates and declined with age, except for tetracycline resistance which was higher in adult sheep. This could reflect relatively higher use of oxytetracycline in adult sheep for conditions such as lameness.

The AMR in *E. coli* results from sheep are presented separately for neonates (**Figure 4.24**), pre-weaning lambs (**Figure 4.25**), and adults (**Figure 4.26**). The number of isolates tested are in Table S4.5.2 in Supplementary Material 2.

In neonatal lambs, 19% of isolates were MDR. Resistance to spectinomycin decreased from 45.2% in 2021 to 23% in 2022 (**Figure 4.24**), which could reflect withdrawal of Spectam Scour Halt (the only oral antibiotic product authorised for the control of watery mouth in neonates) from the market. High levels of resistance were seen to ampicillin (33%), spectinomycin (23%), streptomycin (32%) and tetracycline (30%). Resistance to the other antibiotics tested was generally low or not detected, and resistance to HP-CIAs was not observed.

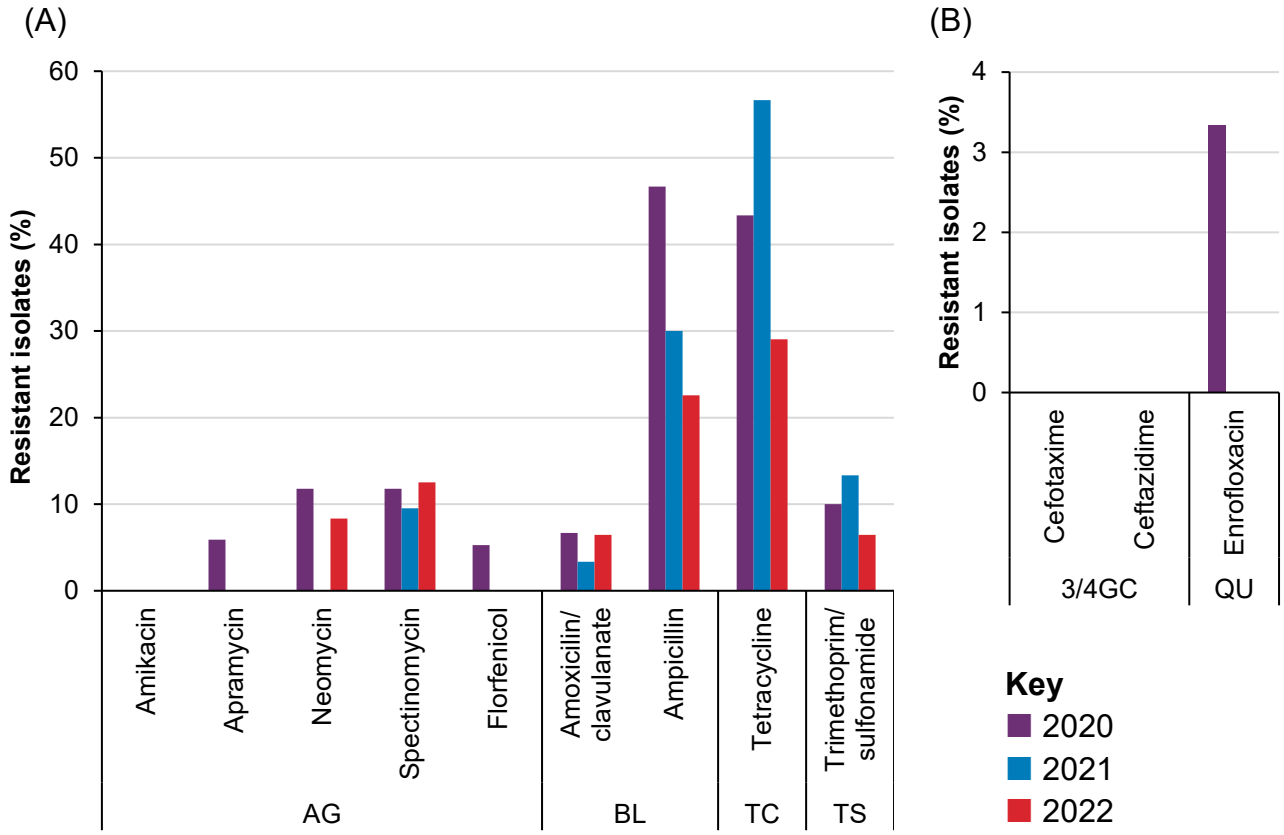
Figure 4.24: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from neonatal sheep (n=43 in 2022). Note scale differs between graphs.



AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

In pre-weaned lambs, 6.5% of isolates were MDR. High levels of resistance were detected to ampicillin (23%) and tetracycline (29%) (**Figure 4.25**). Resistance to other antibiotics was <13% and resistance to HP-CIAs was not detected.

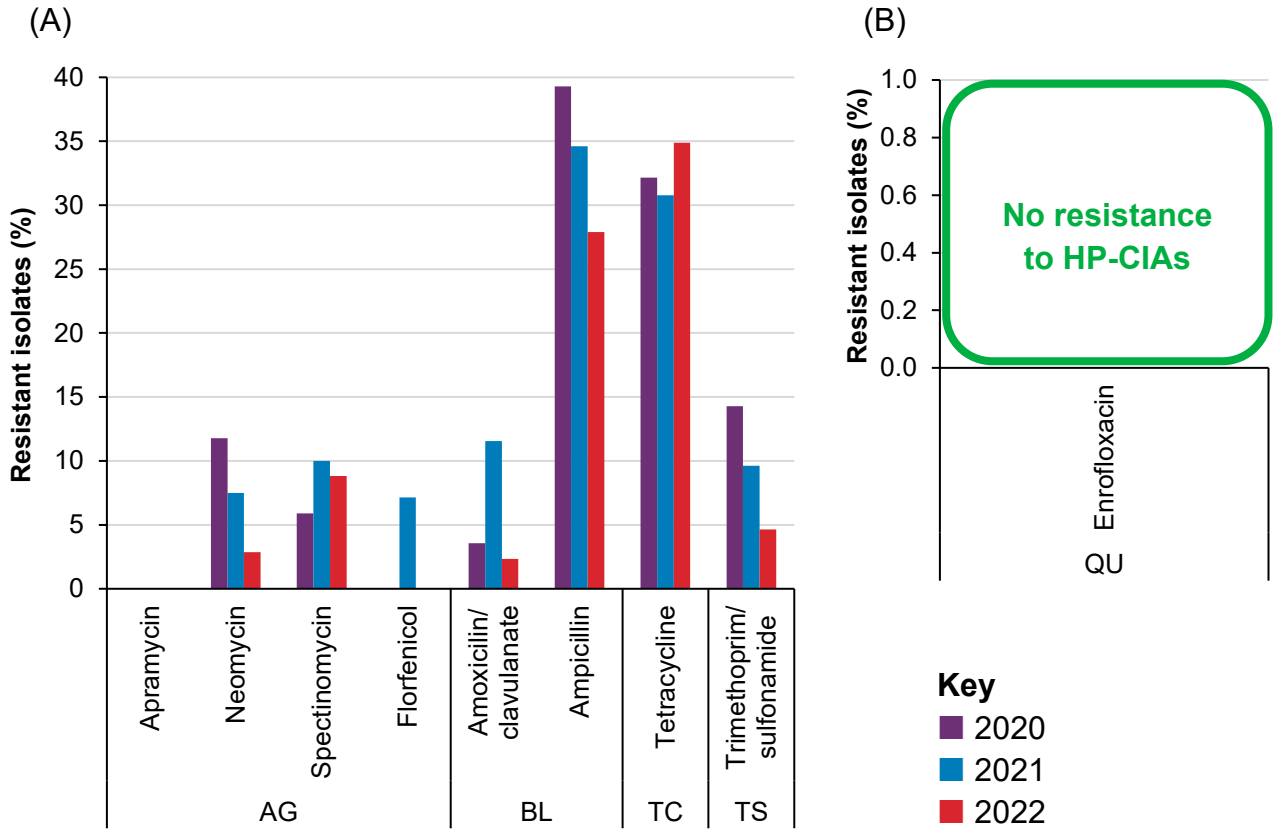
Figure 4.25: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from pre-weaning sheep (n=31 in 2022). Note scale differs between graphs.



AG: aminoglycosides, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

In adult sheep, one isolate (2.3%) was MDR. High levels of resistance were seen to ampicillin (28%) and tetracycline (35%) (**Figure 4.26**). Resistance to the other antibiotics was either low or not detected. HP-CIA resistance was not detected between 2020 and 2022.

Figure 4.26: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from adult sheep (n=43 in 2022). Note scale differs between graphs.



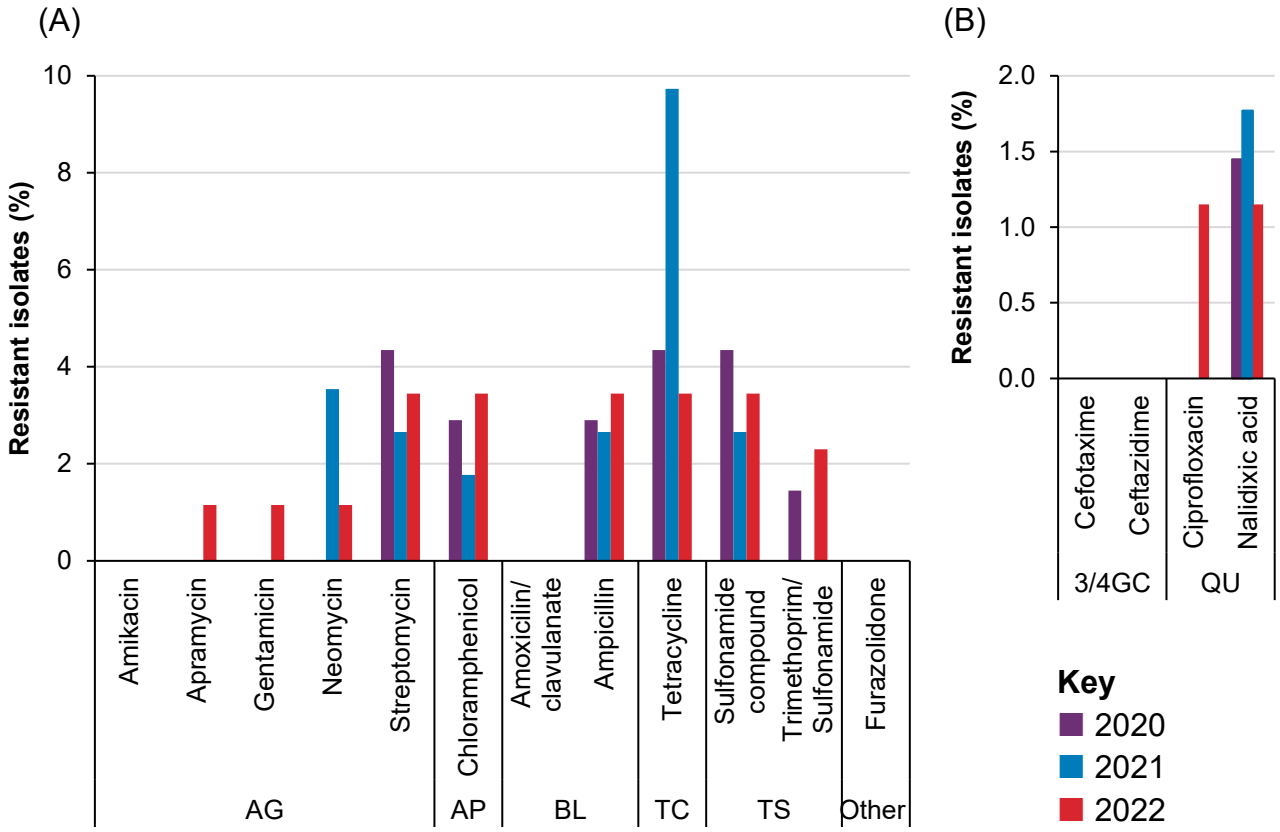
AG: aminoglycosides, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/ sulfonamides

Salmonella spp.

Salmonella is an important cause of foodborne disease in people. It can be part of the normal gut flora in animals, but can also cause disease. *Salmonella* data for sheep is presented below for all age groups (**Figure 4.27**).

Of the 87 isolates tested in sheep, 95% were susceptible to the full panel of antibiotics tested. Low levels of resistance were detected to known treatment options including ampicillin (3.4%) and sulfonamides (2.3%). Levels of resistance were either low or not detected to the other antibiotics. No resistance was observed to the HP-CIAs cefotaxime and ceftazidime, however, a single isolate (1.1%) was resistant to the HP-CIAs ciprofloxacin and nalidixic acid.

Figure 4.27: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Salmonella* isolates from sheep (n=87 in 2022). Note scale differs between graphs.



AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

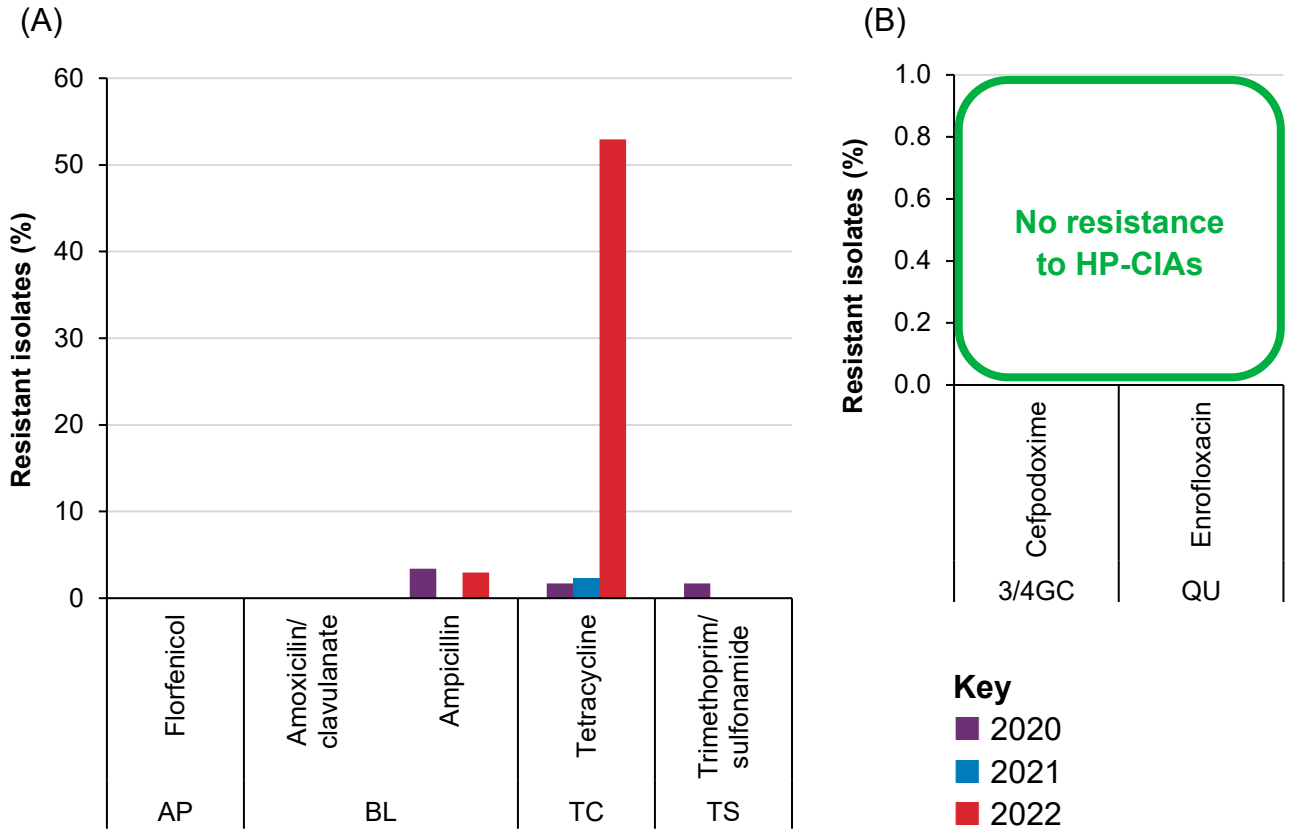
4.3.5.2 Respiratory system

Pasteurellosis complex is a respiratory disease that can cause severe morbidity and mortality in sheep. Many factors play a role in development of the disease. The most significant infectious agents are bacteria including *Mannheimia haemolytica*, *Pasteurella multocida*, and *Bibersteinia trehalosi*.

Bibersteinia trehalosi

B. trehalosi mainly causes septicaemia and systemic pasteurellosis in growing lambs. A total of 34 isolates were recovered in 2022 (**Figure 4.28**). Of these, 47% were susceptible to the full panel of antibiotics. High tetracycline resistance (53%) was detected, although this is probably an over-estimate, due to use of an outdated BSAC clinical breakpoint. The observed increase in 2022 is currently unexplained. By contrast, MIC testing for this organism performed on a subset of 8 isolates indicated no resistance to tetracycline. No resistance was detected to the other antibiotics tested in 2022, except one isolate (2.9%) was resistant to ampicillin. HP-CIA resistance was not detected between 2020 and 2022.

Figure 4.28: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Bibersteinia trehalosi* isolates from sheep (n=34 in 2022). Note scale differs between graphs.

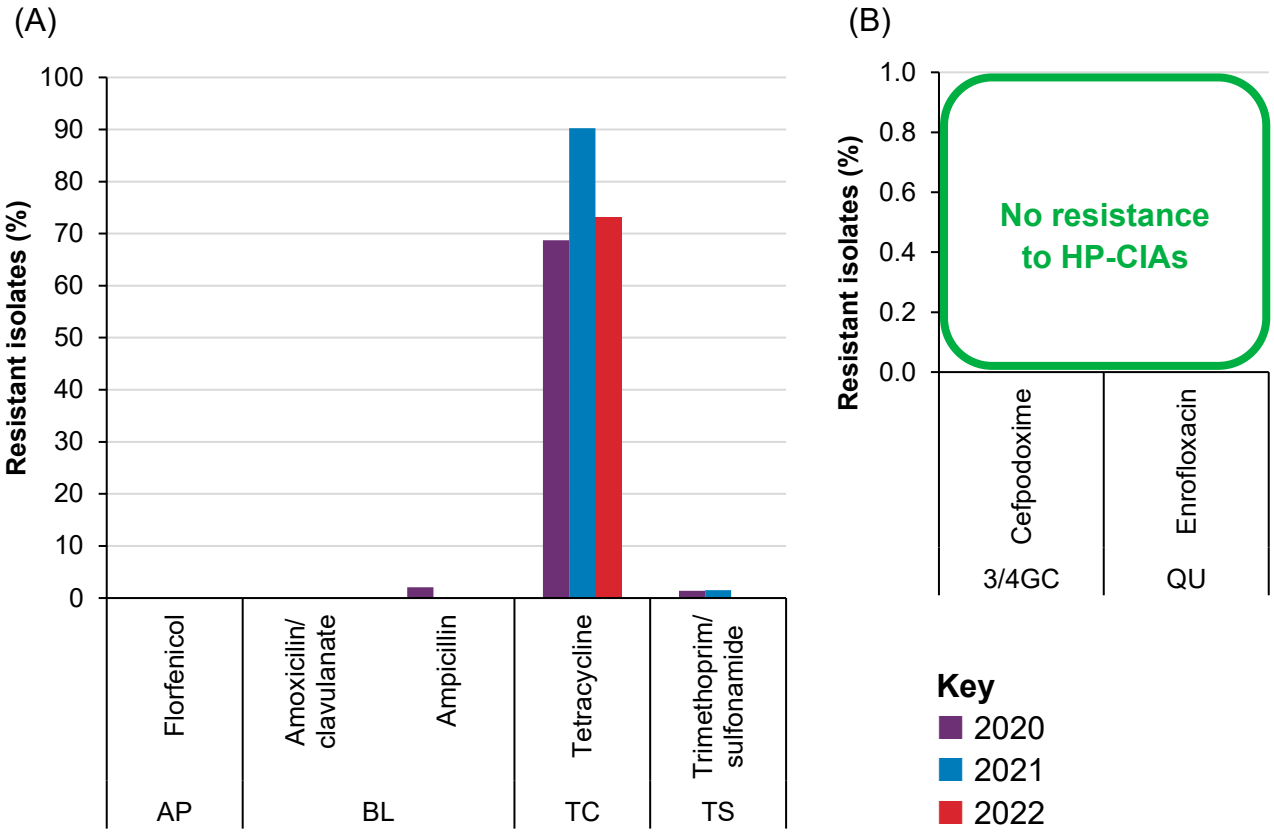


AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

Mannheimia haemolytica

M. haemolytica causes respiratory disease in sheep in the UK, although the predominant serotypes differ from those in cattle. Healthy animals can also carry the bacteria in the upper respiratory tract. A total of 145 isolates were recovered from diagnostic samples in 2022 (**Figure 4.29**). Of these, none were MDR and 27% fully susceptible to the panel of antimicrobials tested. Extremely high tetracycline (73%) resistance was detected, although this is probably an over-estimate, due to use of an outdated BSAC clinical breakpoint. By contrast, MIC testing for this organism performed on a subset of 40 isolates indicated no resistance to tetracycline. No resistance was detected to the other antibiotics tested on the panel in 2022. HP-CIA resistance was not detected between 2020 and 2022.

Figure 4.29: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Mannheimia haemolytica* isolates from sheep (n=145 in 2022). Note scale differs between graphs.

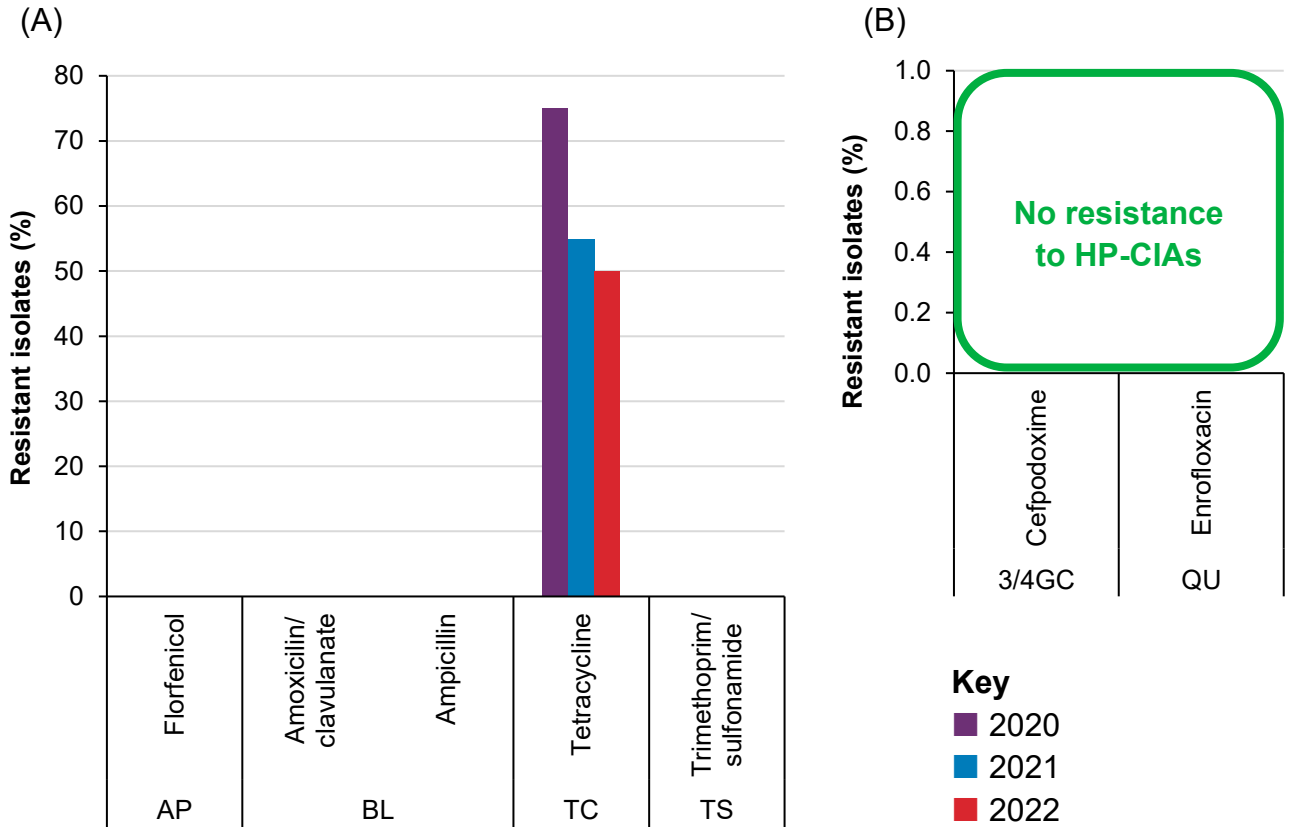


AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

Pasteurella multocida

P. multocida causes respiratory disease in sheep although rarely in the UK. A total of 20 isolates were recovered from diagnostic samples in 2022 (**Figure 4.30**). Of these, none were MDR and 10 (50%) were fully susceptible to the panel of antimicrobials tested. The remaining 10 (50%) were resistant to tetracycline only. The high tetracycline resistance detected is probably an over-estimate, due to use of an outdated BSAC clinical breakpoint. By contrast, MIC testing for this organism performed on a subset of 6 isolates indicated no resistance to tetracycline. HP-CIA resistance was not detected between 2020 and 2022.

Figure 4.30: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Pasteurella multocida* isolates from sheep (n=20 in 2022). Note scale differs between graphs.



AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

Trueperella (Arcanobacterium) pyogenes

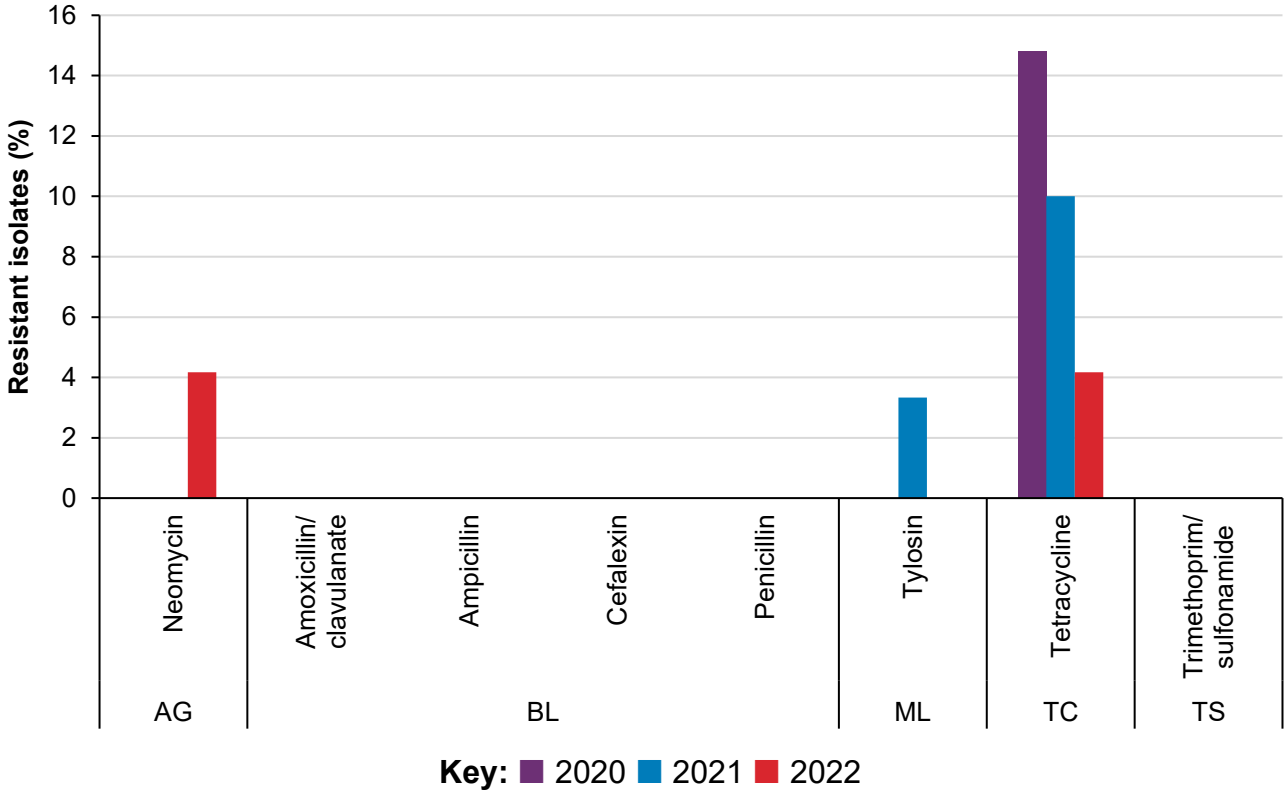
There was no *Trueperella* (*Arcanobacterium) pyogenes* isolated from sheep in 2022.

4.3.5.3 Integumentary system

Staphylococcus aureus

Staphylococcus aureus causes mastitis and tick pyaemia, as well as other infections, in sheep. 24 isolates were tested to the panel of antibiotics in 2022 (**Figure 4.31**) and none were MDR. One isolate was resistant to neomycin and tetracycline, and no resistance was detected to the other antibiotics tested on the panel. Resistance to HP-CIAs was not tested.

Figure 4.31: Resistance to non-HP-CIAs in *Staphylococcus aureus* isolates from sheep (n=24 in 2022). Note scale differs between graphs.



AG: aminoglycosides, BL: beta-lactams, ML: macrolides, TC: tetracyclines, TS: trimethoprim/ sulfonamides

Staphylococcus xylosus

There was no *Staphylococcus xylosus,* which causes dermatitis, isolated from sheep in 2022.

4.3.5.4 Musculoskeletal system

Streptococcus dysgalactiae

Streptococcus dysgalactiae causes infectious arthritis in young lambs and is thought to be carried on the mucous membranes of a small proportion of sheep. A total of 16 isolates were tested and the full results are presented in Table S4.5.5 in Supplementary Material 2. Extremely high tetracycline (94%) resistance was seen and no resistance was detected to the other antibiotics tested on the panel.

4.3.5.5 Multi-system

Erysipelothrix rhusiopathiae

Erysipelothrix rhusiopathiae is widely distributed in nature and occurs as a commensal or pathogen of a very wide range of vertebrate and invertebrate species. In sheep, infection usually presents as polyarthritis. One isolate was tested in 2022 and the full results are

presented in Table S4.5.5 in Supplementary Material 2. The isolate was resistant to trimethoprim/sulfonamides but no resistance was detected to the other antibiotics tested on the panel.

Listeria spp.

Listeria spp. are widely distributed in the environment and can be isolated from soil, decaying vegetation and poorly fermented silage. Asymptomatic faecal carriage occurs in humans and in many species of animal. The full results are presented in Table S4.5.5 in Supplementary Material 2.

Five *Listeria monocytogenes* isolates were tested in 2022. One isolate was resistant to cefalexin, reflecting intrinsic resistance of *Listeria* spp. to this compound, and no resistance was detected to the other antibiotics tested on the panel.

All ten *Listeria ivanovii* isolates tested in 2022 were susceptible to the full panel of antibiotics.

4.3.6 Dogs

The complete dog dataset can be found in section S4.6 of Supplementary Material 2.

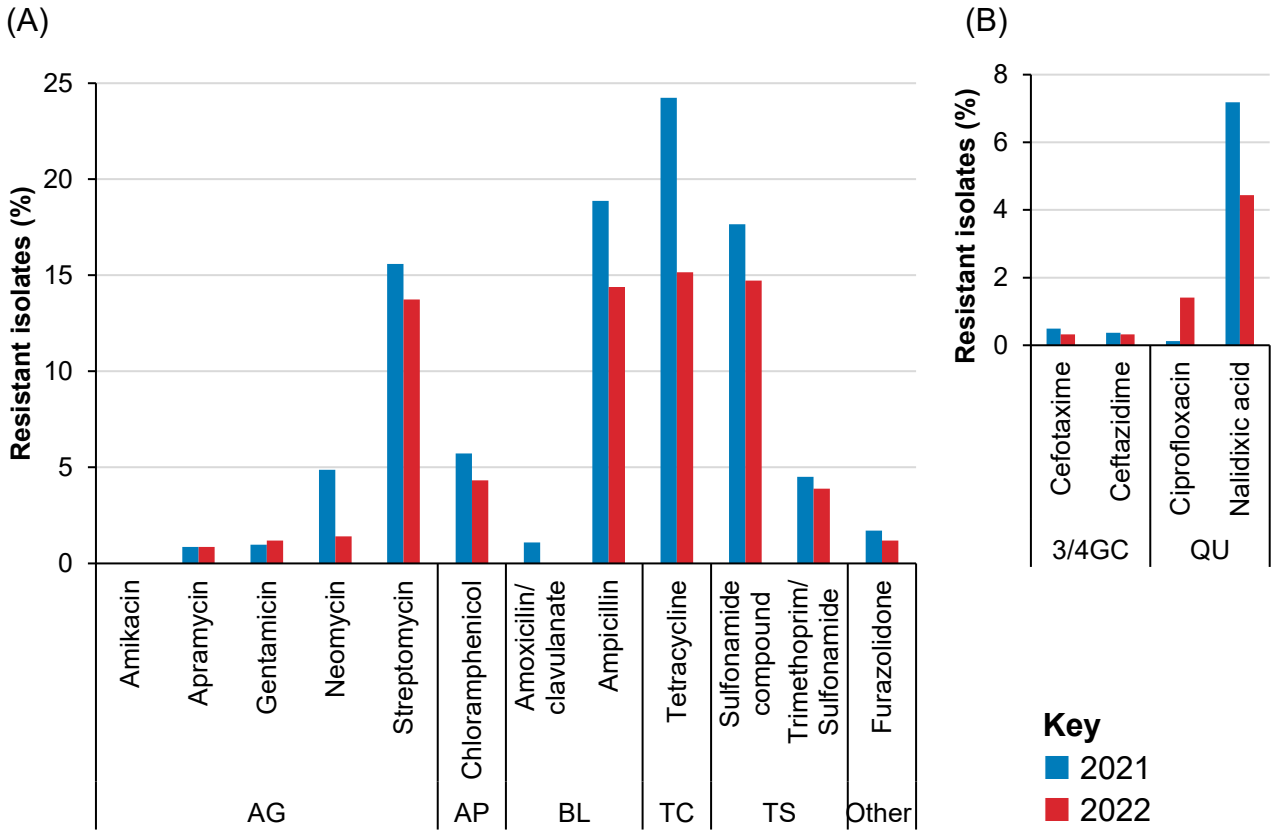
4.3.6.1 Gastrointestinal system

Salmonella spp.

Salmonella is an important cause of foodborne disease in people. It can be part of the normal gut flora in animals, but can also cause disease. In 2021, a change to legislation meant that *Salmonella* isolates from dogs became reportable under the Zoonoses Order in Great Britain, meaning we now have a more complete picture of AMR in *Salmonella* causing disease in dogs. *Salmonella* data for dogs is presented below (**Figure 4.32**).

Of the 924 isolates from dogs tested in 2022, 78% were susceptible to the full panel of antibiotics tested. One *S.* Infantis resistant to third-generation cephalosporins (HP-CIAs) was identified. Two *S.* Kentucky isolates from dogs were highly ciprofloxacin resistant. This highly ciprofloxacin resistant *S.* Kentucky clone is established in the poultry industry in many countries worldwide, but not yet in UK poultry.

Figure 4.32: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Salmonella* isolates from dogs (n=924 in 2022). Note scale differs between graphs.



AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

4.3.7 Trout

To further expand our clinical surveillance programme VMD is working with the Centre for Environment, Fisheries and Aquaculture Science (Cefas) to explore establishing regular clinical surveillance for AMR in the trout sector. In 2022, the focus was on establishing stakeholder engagement, sources of isolates, and robust procedures. The pilot programme will focus on the three pathogens: *Aeromonas salmonicida*, *Yersinia ruckeri* and *Flavobacterium psychrophilum*. 16 isolates were tested in 2022, with over 100 isolates submitted for testing in 2023. These will be reported together in VARSS 2023.

Annexes

Annex A: Glossary of terms

Active ingredient

The part of an antibiotic medicine that acts against the bacterial infection. Alternatively called 'active substance'.

AMEG

Antimicrobial Advice *ad hoc* Expert Group; AMEG is an *ad hoc* group established by the European Medicines Agency jointly under the Committee for Medicinal Products for Veterinary Use (CVMP) and the Committee for Medicinal Products for Human Use (CHMP). The AMEG was set up to provide guidance on the impact on public health and animal health of the use of antibiotics in animals, and on the measures to manage the possible risk to humans.

ATC vet

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.

BEIC

British Egg Industry Council

BPC

British Poultry Council

Broiler

A broiler is any chicken that is bred and raised specifically for meat production

BVPA

British Veterinary Poultry Association

CAGG

Cattle Antibiotic Guardian Group

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).

DCDVet

The Defined Course Doses represents the average number of courses per dairy cow using a standard course dose of four tubes per dry cow and three tubes for lactating cow treatments.

DDDVet

The Defined Daily Doses is the assumed average dose per kg animal per species per day. These standard daily doses are extracted from the Summary of Product Characteristics for each antibiotic product.

Defra

Department for Environment, Food and Rural Affairs

ECDC

European Centre for Disease Prevention and Control

HP-CIAs

Highest Priority Critically Important Antibiotics. In this report the classification according to the AMEG Category B has been used; therefore the following classes of antibiotics are included under HP-CIAs: quinolones (including fluoroquinolones); third and fourth generation cephalosporins and polymyxins (including 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.

EFSA

European Food Safety Authority

EMA

European Medicines Agency

eMB Pigs

Electronic Medicines Book for pigs

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.

GFA

Game Farmers' Association

Injectable product

A product which is administered to animals via injection.

Intramammary product

A product which is administered into the udder.

IU

International Units. A conversion factor used for the calculation of the mass of the active substance.

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.

OIE

Office International des Epizooties (now known as World Organisation for Animal Health)

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 (that is to say, 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.

RCVS

Royal College of Veterinary Surgeons

Red Tractor

Red Tractor Assured Food Standards is a UK company which licenses the Red Tractor quality mark, a product certification programme that comprises a number of farm assurance schemes for food products, animal feed and fertilizer.

RUMA

The Responsible Use of Medicines in Agriculture Alliance

SAGG

Sheep Antibiotic Guardian Group

SAVSNET

Small Animal Veterinary Surveillance Network

SPC

Summary of Product Characteristics

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).

WOAH

World Organisation for Animal Health

WHO

World Health Organization

Annex B: 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, for example 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 S1.5 of Supplementary Material 1.

Antibiotic use data

- In most cases, antibiotic use data represents the antibiotics that the vet and/or the feedmill has supplied for use on a farm, or for a particular species or sector (all under prescription from the veterinary surgeon). However, just because a product is supplied in a particular calendar year doesn't mean that it is necessarily used in that calendar year.

- Except in the Salmon sector, antibiotic use data doesn't have 100% coverage so the collected data may not be fully representative of the industry as a whole. For the majority of these sectors (pigs, meat poultry, laying hens, gamebirds and trout) coverage represents over 90%. However, for dairy, beef and sheep coverage is much smaller (28%,6% and 9% respectively) so the likelihood of this data not being representative of the whole sector is higher.

Resistance data, harmonised monitoring scheme

- The sampling size and strategy are designed to provide a sample which is representative of the wider population for each food-producing animal species (pigs, broiler, and turkeys) in the UK. However, pigs and poultry are monitored on alternating years, therefore not providing annual data.
- The organisms monitored are of direct relevance to human health.
- Antibiotics are considered HP-CIAs if they are within "Category B" in the Antimicrobial Expert Group (AMEG) report; these have been included in the panel of antibiotics against which these organisms are tested.
- The sampling methodology used is standardised and harmonised to produce robust susceptibility data that is comparable across species, years, and internationally.
- This year, European Committee on Antimicrobial Susceptibility Testing (EUCAST) epidemiological cut-off values (ECOFFs) were used to assess susceptibility of the bacterial isolates. 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. A 'decreased susceptibility' (or 'resistant') result based on ECOFFs does not necessarily imply a level of resistance that would correspond to clinical treatment failure. Minimum inhibitory concentrations (MICs) are also recorded and will enable any future changes in CBPs or ECOFFs to be taken into account.
- In 2022 ertapenem was included in the antibiotic panel for the *Campylobacter*. It was chosen to represent the carbapenem antibiotic class. Ertapenem is an HP-CIA and used in some countries to treat invasive Campylobacteriosis. However, the characteristics of *Campylobacter* with respect to ertapenem resistance are still not very well understood and there is currently a concerted program of work being undertaken to better understand these interactions. Also of note is the current absence of a EUCAST-validated ECOFF. As such the MIC values generated are difficult to interpret.
- 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 due to the population of ESBL-, AmpC- or carbapenemase-producing *E. coli* being a minority among the *E. coli* populations in the gut flora of these food-producing animals, so the probability of randomly picking a resistant 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.

Resistance data, clinical surveillance (including MIC testing of veterinary pathogens)

There are a number of limitations associated with the AMR data and they should be borne in mind when interpreting results from the veterinary clinical surveillance programme. Samples from this programme arise from diagnostic submissions in mostly diseased animals. This results in a biased sample of bacteria and cannot be considered to accurately reflect AMR within the general animal population in the UK. To note, the isolates that undergo MIC testing, excluding *Brachyspira hyodysenteriae,* are the same as those that undergo disc diffusion testing in the clinical surveillance program. Therefore, the same sampling limitations as those listed for the clinical surveillance program apply here.

Clinical surveillance limitations:

- Samples arise from diagnostic submissions, which involve mostly diseased animals, and don't reflect UK animal populations as a whole.
- 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 the severity of disease, impact on production or the value of the animals involved.
- The clinical 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 resistant bacterial clones, 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 veterinary clinical surveillance data details 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, although 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; that is to say, 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.

- 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 can include submissions from animals that have been unresponsive to initial antibiotic therapy, and thus the isolates recovered may have already been exposed to antibiotic pressure(s).
- APHA does not provide a veterinary diagnostic service for companion animals, with the exception of Salmonella isolated from dogs, which is now encompassed under the Zoonoses Order. Therefore, bacteria from these animal groups are under-represented in this report.
- 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. For example, AMR testing on *E. coli* isolates in Northern Ireland is mainly performed if samples are coming from less than 2-week-old calves and animals with bovine mastitis. 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.

Laboratory methodology:

- 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 undergoing disc diffusion, 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.
- For antibiotic susceptibility testing done by disc diffusion 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 Supplementary Material 3.

- 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.**
- The disc diffusion methodology used to date, for assessing susceptibility of veterinary pathogens from clinical surveillance, are limited in the availability of breakpoints for all relevant antibiotic and organism combinations. Assessing the susceptibility of veterinary pathogens by determination of the MIC using a standardised broth microdilution method provides a higher quality, internationally recognised output, which is comparable with other monitoring programmes.

Annex C: Sources for reporting of sales data

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

Marketing Authorisation Holders (MAHs)
It is mandatory for Marketing Authorisation Holders of manufactured antibiotics to provide the Veterinary Medicines Directorate with total annual sales data for each antibiotic product sold within the UK. Data were collected, verified and analysed to calculate the total weight, in tonnes, of each active ingredient sold for each antibiotic. Antibiotic sales data are collected as a proxy for antibiotic use.

Periodic Safety Update Reports (PSURs)
Sales figures submitted by MAHs in PSURs, for the purpose of Pharmacovigilance, were used to validate sales data published in this report. Where a PSUR had been returned to the VMD Pharmacovigilance team in the 2019 calendar year, reported sales were compared to those returned to the AMR team and any discrepancies were queried.

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

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

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

TRACES
Import and export figures obtained from TRACES were provided by the European

Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project and used in the calculation of the PCU.

Annex D: Contributors

Contributing Pharmaceutical Companies and Other Marketing Authorisation Holders (compiled by the VMD):

- Alfamed
- Alfasan Nederland B.V.
- Alivira Animal Health
- Alpha-Vet Allatgyogyaszati kft
- Andres Pintaluba S.A.
- Animalcare Limited
- aniMedica GmbH
- Audevard
- Avimedical B.V.
- Bela-Pharm GmbH & Co. KG
- Bimeda Animal Health Ltd
- Boehringer Ingelheim Animal Health Ltd
- Ceva Sante Animale
- Ceva Animal Health Ltd
- Chanelle Animal Health Ltd
- CP Pharma Handelsgesellschaft
- Cross Vetpharm Group Ltd
- Dechra Ltd
- Divasa Farmavic S.A.
- Dopharma Research B.V.
- ECO Animal Health
- Ecuphar Veterinaria S.L.U.
- Ecuphar N.V
- Elanco Europe Ltd
- Eli Lilly & Company Ltd
- Emdoka bvba
- Eurovet Animal Health B.V.
- Fatro S.P.A.
- Franklin Pharmaceuticals Ltd
- Global Vet Health S.L.
- Harkers Ltd
- Huvepharma SA
- Huvepharma N.V.
- I.C.F. Sri Industria Chimica Fine
- Industrial Veterinaria S.A.
- Intervet Ltd,
- Kela N.V.
- Kernfarm B.V.
- Krka Dd

- Labiana Life Sciences
- Laboratorios Calier S.A.
- Laboratorios e Industrias IVEN S.A.
- Laboratorios Maymo S.A.
- Laboratorios Hipra S.A.
- Laboratorios Karizoo S.A.
- Laboratorios SYVA S.A.U
- Lavet Pharmaceuticals Ltd
- Le Vet Beheer B.V.
- Livisto Int.'I.S.L
- Lohmann Pharma
- Nimrod Veterinary Products Ltd
- Norbrook Laboratories Ltd
- Orion Corporation
- Oropharma N.V.
- Pharmanovo Veterinararzneimittel GmbH
- Pharmaq Ltd
- Pharmsure International Ltd
- Phibro Animal Health S.A.
- Richter Pharma AG
- SP Veterinaria S.A.
- TVM UK
- Univet Ltd
- Vetcare Oy
- Vétoquinol SA
- Vétoquinol UK Ltd
- Vetpharma Animal Health S.L.
- Virbac S.A.
- VMD N.V.
- Zoetis UK Ltd