

UK Veterinary Antibiotic Resistance and Sales Surveillance Report

UK-VARSS 2023

Published November 2024





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

Authors

Veterinary Medicines Directorate (VMD):

- Dr Fraser Broadfoot MRCVS
- Dr Tamsin Dewé MRCVS
- Dr Aisling Glennie MRCVS
- Dr Kitty Healey MRCVS
- Dr Carolyn Hogan MRCVS
- Dr Catrina Prince MRCVS
- Elizabeth Anderson
- Charlotte Bailey
- Laura Biddle
- David Bradbury
- Anju Kirby
- Edel Light
- Sannah Malik
- Sophie Spalding

Animal and Plant Health Agency (APHA):

- Prof Muna Anjum
- Dr Manal AbuOun
- Dr Sam Connelly
- Dr Nick Duggett
- Dr Catherine Fearnley
- Dr Francesca Martelli
- Dr Chris Teale MRCVS
- Dr John Rodgers
- Dr James Carrier MRCVS
- Dr Silvia Stronati MRCVS
- Graham Hill
- Emma Stubberfield



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Foreword



This year's VARSS report presents antibiotic sales, use and resistance surveillance results in animals from the last year of the UK's previous National Action Plan on AMR (2019-2024). This allows us to reflect on progress made and provides an opportunity to look forward as we start delivering the new 5-year national action plan (NAP), which was published in May this year.

Over the last 5 years we have continued working collaboratively with the veterinary profession and farming industries to maintain and build upon the dramatic reductions in antibiotic use seen nearly 10 years ago. To help support this progress in reducing the unnecessary use of antibiotics, this year we strengthened our laws on antibiotic prescribing in the revised Veterinary Medicines Regulations, which came into effect in May 2024. We have stated our position for many years that antibiotics should not be used routinely or to compensate for poor animal husbandry or hygiene practices: now our law states this too. Provisions are also in place in the updated legislation to ensure that antibiotics are only prescribed for prophylactic use in animals under exceptional circumstances, where the risk of infection is very high and the consequences likely severe.

In this VARSS report we have introduced a new measure for total antibiotic sales in mg/kg across all species (not just food producing animals), alongside the headline metric we have been reporting for many years. The new metric is expected to be used across Europe from next year for the monitoring and reporting of sales data. We recognise the value in harmonised regional surveillance and publishing this new mg/kg metric will help ensure we can continue to compare our data and trends with neighbouring countries.

This year marks 10 years of collecting AMR data in the harmonised monitoring programme. We are now benefitting from this data by being able to look at long-term trends and carry out additional analysis, as well as observe the changes year-to-year. While we have been conducting active AMR surveillance across pigs and poultry for many years, we do not yet conduct this surveillance across other major livestock species in the UK. However, under the PATH-SAFE programme, we have been conducting AMR surveys to get some baseline data across sheep, beef, and bulk milk (as a measure of AMR in dairy cattle) and we are pleased to present these results in Chapter 3. This helps give us an indication of the levels of resistance in these sectors. We are also working to improve our clinical surveillance data by capturing AMR results from clinical samples sent to private labs in our surveillance outputs. We are grateful to our partners who have helped us develop our surveillance through both the PATH-SAFE and Private Labs Initiative.

This year's results from the antimicrobial resistance harmonised monitoring programme in pigs and poultry presents a positive picture for AMR trends in the UK for 2023, with our key indicators for resistance showing trends of decreasing resistance in the indicator commensal bacteria *E.coli*. In *E. coli* causing disease in animals, from the clinical AMR surveillance programme, we are also seeing reductions in resistance. These declining trends in resistance



are likely a reflection of the substantial reductions in antibiotic use and improved stewardship achieved by the sectors and veterinary profession over the past years.

Looking to antibiotic sales, this year we have seen very little change in UK-level sales of antibiotics for food producing animals since last year, maintaining the 59% reduction since 2014. However, this stable trend in total sales masks changes in antibiotic use in the individual sectors, highlighting by the importance and value of the usage data collected on a voluntary basis across many of the sectors. We are pleased to see that following a spike in use last year, the trout sector's antibiotic usage has reduced (by 84%) down to its lowest recorded use to date. While many other sectors have continued to see small reductions in use, this year the pig sector have not maintained the year-on-year reductions that they have achieved in the past (increasing by 18% this year). Likewise, we have seen increases in use in gamebirds, however the lack of accurate population numbers in this sector means it is not possible to produce a mg/kg figure, making it hard to determine how much the changes are explained by a changing pheasant population size.

If upticks in antimicrobial use become trends, we must anticipate this being reflected by increasing resistance trends in future years. This underlines the need to sustain and build on the progress to date. In many cases the most straightforward actions have already been taken, leaving the more complex challenges to be addressed.

In some areas we have made advances in AMR surveillance coverage but AMU data remains incomplete. In these cases our ability to draw conclusions from AMR data to make policy recommendations is compromised.

Our aspirations to improve surveillance will include looking ahead to the next round of revisions of the Veterinary Medicines Regulations. In the consultation period for the draft of the 2024 regulations we signposted the potential need to consider making reporting of veterinary antibiotic usage data a legal requirement; this will therefore be an area under review. Beyond our surveillance aspirations, we look forward to the Targets Task Force (TTF) ambitions and the new targets which the sectors will set in 2025.

This has been an important year for AMR and an opportunity to galvanise international action through the United Nation's High Level Meeting on AMR which took place on 26th September. We sought a political declaration which incorporates ambitious and action focused commitments on AMR globally. In particular, we advocated for the importance of committing to action and using data to measure progress. To that end we are pleased that member countries have adopted the political declaration which includes a robust mandate to allow the Quadripartite to establish an Independent Panel for Evidence on AMR , to provide guidance on science, data and evidence to inform global and national interventions and support progress on AMR.

The latest commitments are set: in the international political declaration, and more locally in our NAP, our legislation, and new targets that will be published shortly from the RUMA TTF. Now we turn our focus to implementation.

Dr Kitty Healey BVSc PhD MRCVS

Head of Surveillance Division, Head of Antimicrobial Resistance

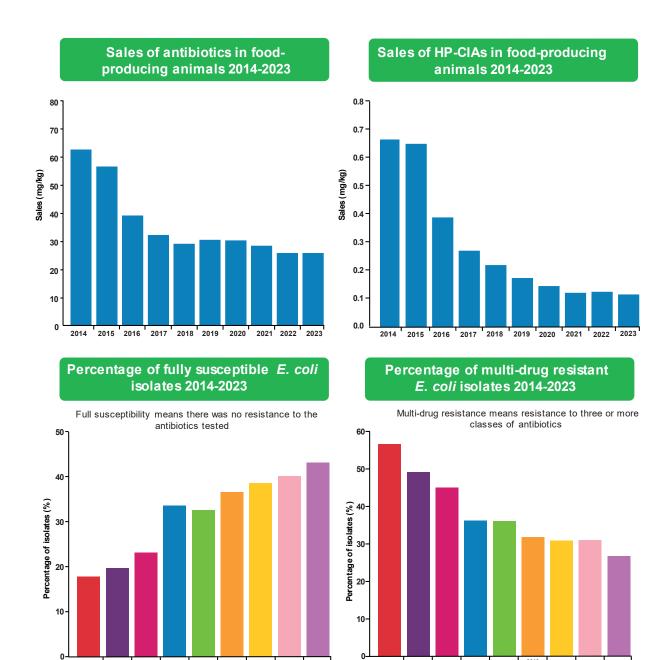


Highlights

Antibiotic use and resistance 2014-2023

A decade of bringing together antibiotic use and resistance data

This year's UK-VARSS report marks 10 years of bringing together data on antibiotic sales, usage and resistance. This allow s us to show long-term trends and demonstrates how reducing antibiotic use has been follow ed by a reduction in antimicrobial resistance (AMR) at a national level.



Indicators are an important tool for interpreting and comparing the results of AMU and AMR monitoring programmes. The indicators for sales are weighted by population size. *Escherichia coli* is the indicator organism for resistance. The outcome indicators for resistance are averaged over two years, due to the alternating schedule forAMR pig and poultry sampling, and are weighted by population size.

2015-2016

2014-2015 2016-2017 2017- 2018-2018 2019 2019-2020 2020-2021 2021-2022 2022-2023

2022-2023

2021 2022

2017-2018 2018-2019

2016-2017

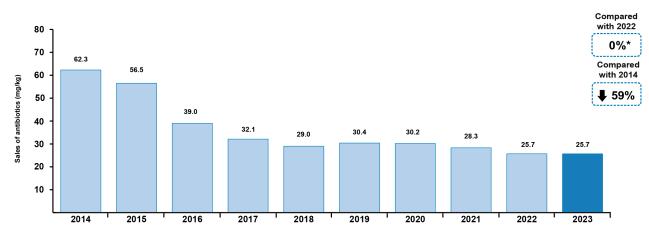
2014-2015 2015-2016 2019-2020 2020-2021



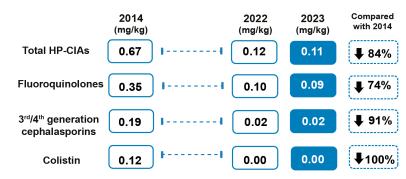
Antibiotic sales

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 2023; this represents no change since 2022 and an overall 59% (36.6 mg/kg) decrease since 2014.



Sales of highest priority critically important antibiotics (HP-CIAs) in food-producing animals remain at very low levels at 0.11mg/kg in 2023 and account for less than 0.5% of total sales.



New harmonised mg/kg metric for all animals

A new harmonised mg/kg metric for all animals has been developed for analysing sales data. This uses different animal categories and weights (meaning it is not comparable with the current food producing animal mg/kg metric). This metric is expected to be used when the EU publishes their 2023 sales in 2025. We have introduced this new metric as we recognise the value of harmonised regional surveillance. The 2023 UK sales using this metric is 16.5 mg/kg.

Sales of antibiotics for all animals (tonnes)

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	Compared with 2014
Tonnes	447	406	293	246	223	229	227	212	193	189	↓ 58%

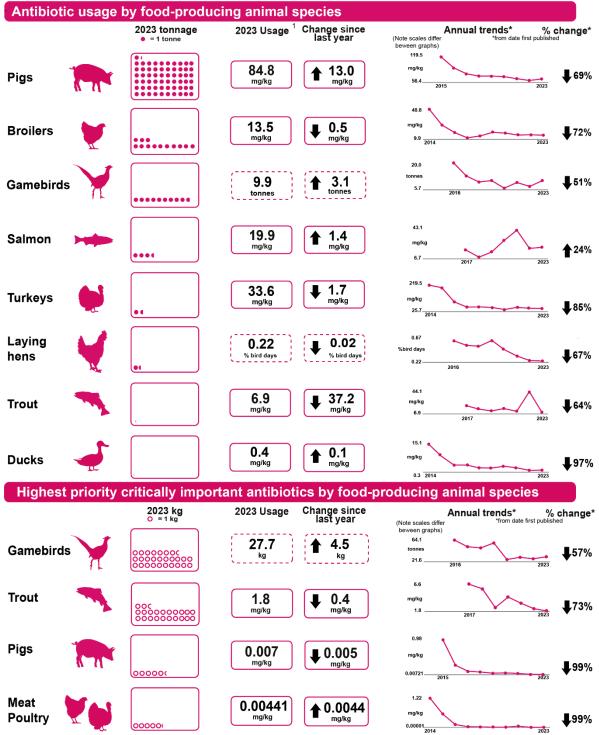
Over 60% of all antibiotics were sold were either tetracyclines (33%) or penicillins (28%).

Sales of HP-CIAs (not adjusted for animal population size) for 2023 was 0.82 tonnes representing a decrease of 9% (0.09 tonnes) since 2022 and an 83% decrease (3.96 tonnes) since 2014. Sales of HP-CIAs continue to respresent a small proportion (< 0.5%) of total veterinary antibiotic sales in tonnes.



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. Coverage is at least 85% for all sectors shown. Ruminant coverage of use data is low and may not be representative of the national sectors and is not included in this section of the report.

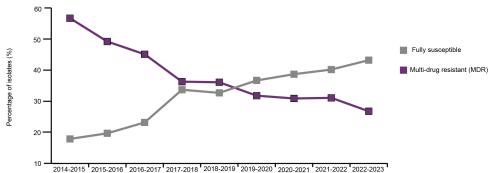


mg/kg relates to the amount of active ingredient standardised by kg biomass and calculated using ESVAC methodology, % bird days refers to 'actual daily bird-doses/100 bird-days at risk' indicates a different metric for usage

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

Key resistance outcome indicators: E. coli

The harmonised monitoring outcome indicators combine results from healthy pigs and poultry at slaughter to give an overall picture of antimicrobial resistance (AMR), and are internationally comparable. Results from 2023 are very positive, with considerable improvements since 2015. The percentage of *E. coli* isolates showing full susceptibility to the panel of antibiotics tested is at a new high of 43%, more than doubling since 2014/2015. The percentage of multi-drug resistant isolates (resistant to three or more antibiotic classes) is at a new low of 27%.



New AMR surveillance

This year's harmonised monitoring includes testing for three new species of bacteria in pigs: *Campylobacter coli*, *Enterococcus faecalis* and *Enterococcus faecium*. The addition of enterococci allows for detection of vancomycin-resistant enterococci (VRE), which are of clinical importance in people. No VRE were detected in pigs in 2023.

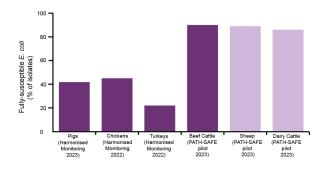
Pathogen Surveillance in Agriculture, Food and Environment (PATH-SAFE)

This year's report includes results from AMR surveillance pilots in milk from dairy cattle, beef cattle and sheep carried out under the PATH-SAFE programme. These surveys mirror the methodology used in our routine surveillance in pigs and poultry. However, the PATH-SAFE surveys were not conducted over an entire calendar year, and coverage of animal populations (27-28%) was less than that achieved in our routine harmonised monitoring (81% in 2023). Nonetheless these results provide an initial baseline for AMR in cattle and sheep. Results show that full susceptibility of *E. coli* from ruminants was extremely high (>86%), although there were some notable sector-specific findings, for example, carriage of ESBL/AmpC-producing *E. coli* in beef cattle (see below graph).

E. coli in different animal species

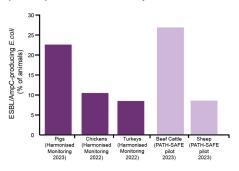
Full susceptibility in E.coli

- This graph shows the percentage of *E. coli* isolated from different animal species that are fully susceptible to the panel of antibiotics tested (i.e no resistance was found).
- These *E. coli* were isolated from our routine surveillance (harmonised monitoring, dark purple) and PATH-SAFE pilot surveys (light purple).



Using selective media to detect E.coli

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



Antibiotic resistance in clinical surveillance

Clinical surveillance aims to provide veterinarians with relevant treatment information using results from bacteria isolated from diagnostic samples. As this kind of 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.

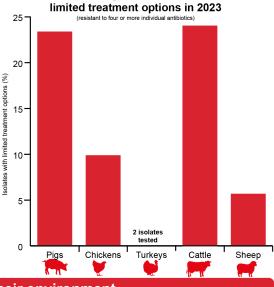
Key findings

- 7,415 isolates were tested for AMR in England and Wales, predominantly Salmonella and E. coli.
- Resistance in E. coli across all animal species mostly shows decreasing resistance since 2014.
- The percentage of isolates tested by animal species were: pigs (13%), poultry (30%), cattle (15%), sheep (7%), dogs (10%) and trout (<1%).

Resistance in Escherichia coli

- 1,168 E. coli isolates were tested from all species.
- 18% of isolates were resistant to four or more individual antibiotics, which could limit treatment options for veterinarians. This was most frequent in isolates from cattle (24%) and pigs (23%), as shown in adjacent graph.
- Across species, resistance tended to be higher in younger animals, which may reflect more frequent antibiotic use in this age group.

Highest priority critically important antibiotics (HP-CIAs): Resistance was low, very low or not detected in *E. coli*: cefotaxime (8.7%), cefpodoxime (0.7%), ceftazidime (4.9%) and enrofloxacin (1.7%).



Percentage of isolates with

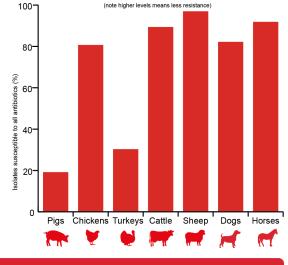
Resistance in Salmonella spp. from animals and their environment

- Of the 5,513 Salmonella isolates tested, 73% were fully susceptible. The lowest levels of susceptibility were in pigs (19%) and turkeys (30%), as shown in the adjacent graph.
- When looking at data since 2014, there are sector specific differences, with pigs, chickens and turkeys all showing trends of increasing full susceptibility. Full susceptibility in *Salmonella* from sheep and cattle remain high.
- 14% of Salmonella from all species indicated limited treatment options, that is, resistant to four or more individual antibiotics. This was most frequent in isolates from pigs (76%).

Highest priority critically important antibiotics (HP-CIAs) Resistance was low, very low or not detected in *Salmonella* spp.: cefotaxime and ceftazdime (>0.9%) and ciprofloxacin (<2.6%)

National Biosurveillance Network (NBN)

Percentage of isolates fully susceptible to all antibiotics tested in 2023



NBN is a major cross-government initiative to pilot and improve surveillance for biological threats across the One Health spectrum. It will assess how to better share and bring together surveillance outputs (including facilitating sharing of privately-held data) to generate better insights into threats. Most AMR data from animals in the UK is generated and held by private veterinary laboratories (PVLs) and does not ordinarily feed into AMR surveillance. Under the NBN pilot, the VMD is expanding on previous work with PVLs to facilitate data sharing with government across species sectors.

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Introduction

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

The antibiotic sales data from 2014 to 2023 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. These figures are provided by the veterinary pharmaceutical companies marketing these products, and this is a statutory requirement.

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 therefore also includes data on usage in different animal sectors and the VMD works in partnership with the livestock and companion animal sectors to develop, facilitate and coordinate antibiotic usage data collection systems. These data are reported voluntarily and 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 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 bacteria from the gut of healthy pigs and poultry at slaughter is tested, giving us a representative picture of resistance in key livestock species entering the food chain, and results from this are presented in **Chapter 3**. This year AMR surveillance pilots within the <u>PATH-SAFE</u> programme to address current surveillance gaps was also tested. Results from some of these AMR surveillance pilots are presented in **Chapter 3** and provide data on AMR in ruminants for 2023.

Clinical Surveillance involves testing of bacteria that have been isolated from clinical samples submitted by farmers and private veterinary surgeons to government laboratories in England and Wales. These results are published in **Chapter 4** which reflects AMR in bacteria causing disease in animals.

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 <u>veterinary antimicrobial resistance and sales surveillance</u>.

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. Please also see the glossary of terms within the annexes.

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

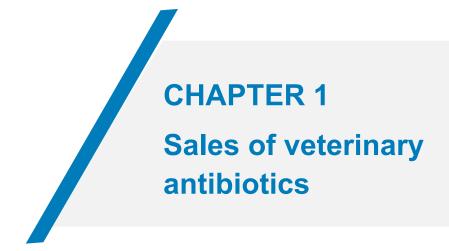
Antibiotic class	Authorised for use in animals	Not authorised for use in animals	
Aminoglycosides	Apramycin, framycetin, gentamicin, kanamycin, neomycin, paromomycin, spectinomycin, streptomycin	Amikacin	
Amphenicols	Florfenicol	Chloramphenicol	
Beta-lactams: 1 st generation cephalosporins	Cefalexin, cefalonium, cefapirin		
Beta-lactams: 2 nd generation cephalosporins		Cefoxitin	
Beta-lactams: 3 rd 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, methicillin	
Glycopeptides	Vancomycin	Teicoplanin	
Glycyclines		Tigecycline	
Lincosamide	Clindamycin, lincomycin, pirlimycin		
Lipopeptide		Daptomycin	
Macrolides	Erythromycin, gamithromycin, spiramycin, tildipirosin, tilmicosin, tulathromycin, tylosin, tylvalosin	Azithromycin	
Oxazolidinones		Linezolid	
Pleuromutilins	Tiamulin		
Polymyxins	Colistin		
Quinolones	Danofloxacin, enrofloxacin, marbofloxacin, oxolinic acid (Special Import Scheme only), pradofloxacin	Nalidixic acid, ciprofloxacin	
Streptogramins		Quinupristin/dalfopristin	
Tetracyclines	Chlortetracycline, doxycycline, oxytetracycline, tetracycline		
Trimethoprim/ sulfonamides	Sulfadiazine, sulfadimidine, sulfadoxine, sulfamethoxazole, trimethoprim		

Other	Metronidazole, novobiocin, fusidate	Furazolidone, mupirocin,
Other		rifampin

Table 2: Descriptions of percentage resistance levels referenced in this report, using the<u>EFSA definitions</u>.

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%







1.1 Summary

UK sales of veterinary antibiotics for food-producing animals in 2023, adjusted for the animal population, were 25.7 mg/kg. This represents essentially no change (0.007 mg/kg increase) since 2022 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 0.11 mg/kg. This represents essentially no change (0.01 mg/kg reduction) since 2022 and of 84% (0.6 mg/kg) since 2014. Overall, in 2023, HP-CIAs accounted for less than half a percent of the total antibiotic sales for food-producing animals.

The total quantity of antibiotics sold for all animals (which includes both companion animals and food-producing animals) was 188.6 tonnes in 2023, the lowest recorded amount to date. This represents a 2% (4.4 tonnes) decrease since 2022, and a 58% (257.9 tonnes) decrease since 2014. In 2023, sales of HP-CIAs for all animals were 0.82 tonnes, representing a decrease of 0.09 tonnes since 2022 and 83% (4.0 tonnes) since 2014. For the third year in a row, no colistin was sold for use in animals.

The main reason why tonnes of active ingredient sold for all animals reduced, whereas mg/kg for food producing animals remained essentially unchanged, relates to a 2% reduction in the weight of food producing animals at risk between 2022 and 2023, which includes a 10% reduction in pig production.

1.2 Introduction

Pharmaceutical companies have reported the quantity of authorised veterinary antibiotics sold throughout the UK to the VMD since 1993; this has been a statutory requirement since 2005 (see section S1.1 in Supplementary Material 1 for further details). The data reported in this chapter do not take into account imports of veterinary antibiotics, and some medicines sold may not be used in the same year (or at all if the products go out of date before being used). 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 E).

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 the equivalent category of the WHO List of <u>Medically Important Antimicrobials</u>, i.e. third- and fourth- generation cephalosporins, polymyxins (e.g. colistin) and quinolones/fluoroquinolones (which also aligns with "Category B" in the European Antimicrobial Expert Group report categorisation (<u>AMEG</u>)). Note that the only quinolones authorised to be used in animals are fluoroquinolones, so the latter are



referred to throughout this chapter. Data has been presented graphically throughout, but the raw data can be found in Supplementary Material 1.

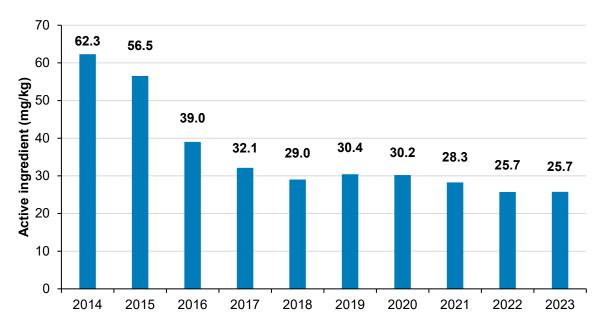
1.3 Results

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

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

Antibiotic sales for food-producing animal species in 2023 were 25.7 mg/kg, which is essentially unchanged (0.007 mg/kg increase) since 2022, and once again represents a reduction of 59% (36.6 mg/kg) since 2014 (**Figure 1.1**).

Figure 1.1: Antibiotic active ingredient sold for use in food-producing animals adjusted for population (mg/kg), 2014 to 2023.



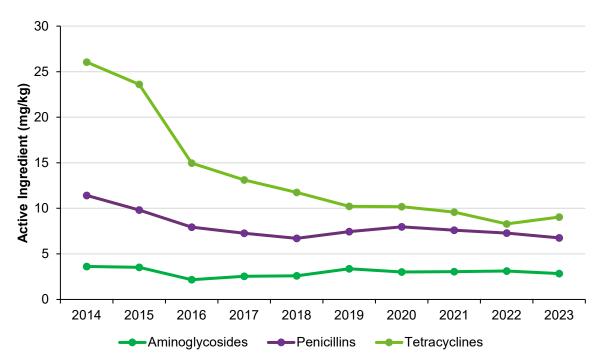
1.3.1.2 Sales by antibiotic class for food-producing animals (mg/kg)

In 2023, three antibiotic classes account for almost three quarters (72%) of total sales in food-producing animals: tetracyclines (35%), penicillins (26%) and aminoglycosides (11%).

Sales of penicillins and aminoglycosides decreased between 2022 and 2023 by 7% (0.5 mg/kg) and 9% (0.3 mg/kg), respectively. Tetracycline sales increased for the first time since 2014, by 9% (0.75mg/kg) (Figure 1.2).



Figure 1.2: Sales of the top three antibiotic classes (mg/kg) for food-producing animals, 2014 to 2023.

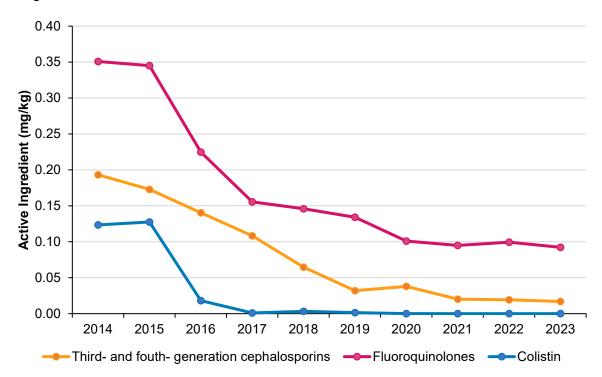


Sales of HP-CIAs for food-producing animals are shown in **Figure 1.3**. Sales remain very low at 0.11 mg/kg and are essentially unchanged (0.01 mg/kg reduction) since 2022 and 84% (0.6 mg/kg) lower than 2014. In 2023, HP-CIAs accounted for less than half a percent of the total antibiotic sales for food-producing animals.

In 2023, fluoroquinolones accounted for the majority (85%) of the total HP-CIAs sold for use in food-producing animals. For the third year in a row, no colistin was sold in the UK for use in animals.



Figure 1.3: Active ingredient adjusted for population (mg/kg) of HP-CIAs sold for use in food-producing animals, 2014 to 2023.



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

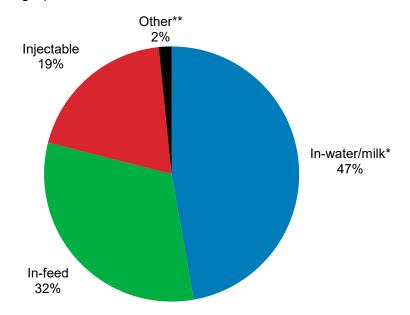
More targeted administration of antibiotics reduces the risk of development and <u>spread of</u> <u>AMR</u>. The pig, poultry and gamebird sectors have focused on encouraging more in-water administration, which can allow for more targeted antibiotic administration than in-feed. Infeed use refers to premix products, whereas in-water/milk products refer to oral powders and oral solutions.

In 2023, 47% of antibiotic sold for food-producing animals was indicated for in-water/milk use, 32% was for in-feed use, and 19% was injectable (**Figure 1.4**). In-water/milk sales rose to a greater degree than in-feed between 2022 and 2023 (7% versus 1% respectively) (**Figure 1.5**) and have exceeded in-feed sales for the third year running. By contrast, injectable product sales reduced by 15%.



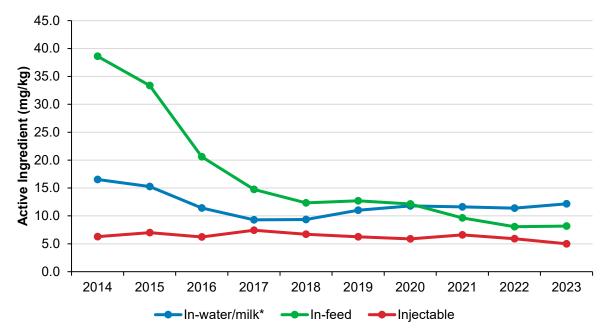


Figure 1.4: Antibiotic active ingredient sold for use in food-producing animals by route of administration (% weight), 2023.



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

Figure 1.5: Active ingredient (mg/kg) of antibiotics by main routes of administration sold for use in food-producing animals, 2014 to 2023.



* Includes oral powders and oral solutions

1.3.2 Sales of intramammary products authorised for cattle

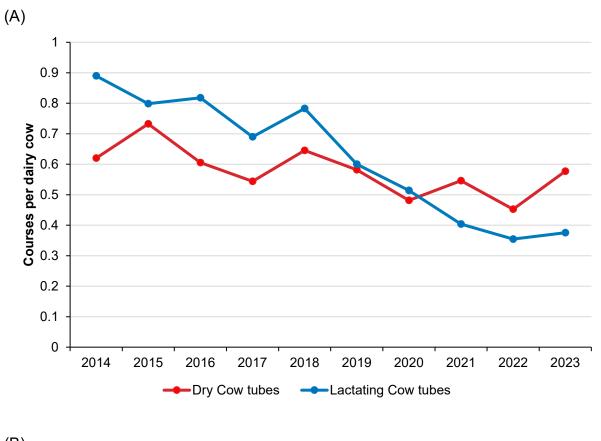
Sales of dry and lactating cow products analysed using the defined course dose methodology (DCDvet) are shown in **Figure 1.6**. The DCDvet represents the average number of courses per dairy cow using a standard course dose of four tubes for dry cow and three tubes for lactating cow treatments.

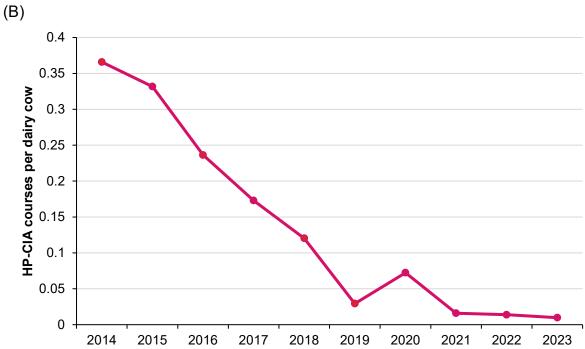
Between 2022 and 2023, sales of intramammary antibiotic dry cow products increased by 28% (0.13 course doses) but were still 7% (0.04 course doses) less than in 2014. Sales of lactating cow intramammary antibiotic products increased by 6% (0.02 course doses) between 2022 and 2023, but this still represents a 58% (0.51 course doses) decrease since 2014. Sales of HP-CIA intramammary products are very low (0.01 course doses), a reduction of 0.004 course doses since 2022 and 97% (0.36 course doses) 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 products are not captured in the antibiotic sales data.



Figure 1.6: Sales of (A) Dry and lactating cow intramammary products (courses per dairy cow) and (B) Sales of HP-CIA intramammary products.





1.3.3 Total sales of antibiotics for all animals (mg/kg)

This is a new section which shows mg/kg for all animals. This new metric has the following differences to the food- producing animal mg/kg metric presented earlier:

- Antibiotics for all animal species are now included (not just food producing animals)
- Slaughter weights used for food producing animals are higher (representing the liveweight at slaughter rather than average weight at treatment)
- New living animal categories have been added for cattle and dogs, cats, laying hens and ducks are now also included

This harmonised metric will be used <u>across Europe</u> for the monitoring and reporting of antibiotic sales data going forward. The value of harmonised regional surveillance is recognised and, in previous years, the UK has published its sales data for food producing animals alongside other countries in Europe in the <u>ESVAC report</u>. Publishing this new mg/kg metric for 2023 in VARSS will ensure that assessment of the data in this regional context can be continued when the first EU report using this new metric and <u>containing 2023 data is published in early 2025.</u>

As shown in **Figure 1.7**, this results in a mg/kg of 16.5, which is lower than the current mg/kg for food producing animals, but the trend remains comparable.



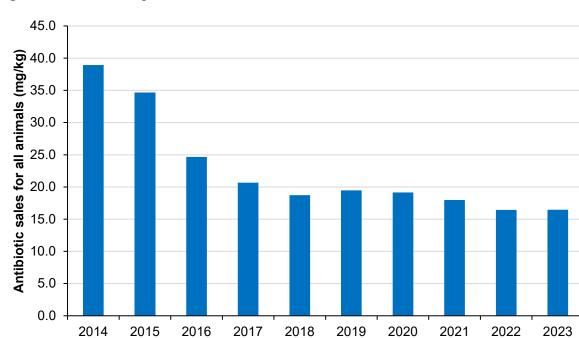


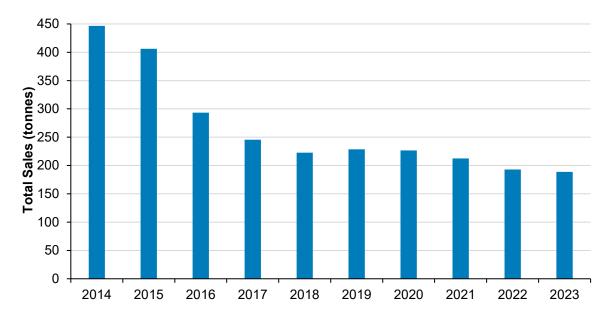
Figure 1.7: Active ingredient of antibiotics sold for use in animals, 2014 to 2023.

1.3.4 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). Results are shown in **Figure 1.8**. The total quantity of antibiotic active ingredient sold in 2023 was 188.6 tonnes, the lowest recorded figure to date. This is a 2% (4.4 tonnes) decrease since 2022, and a 58% (257.9 tonnes) decrease since 2014. The main reason why tonnes of active ingredient sold for all animals reduced, whereas mg/kg for food producing animals remained essentially unchanged, relates to a 2% reduction in the weight of food producing animals at risk between 2022 and 2023, which includes a 10% reduction in pig production.

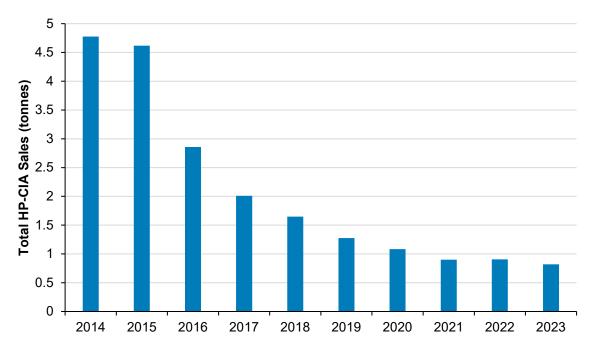


Figure 1.8: Active ingredient (tonnes) of antibiotics sold for use in all animals, 2014 to 2023.



Total sales of HP-CIAs in 2023 were 0.82 tonnes (**Figure 1.9**), representing a reduction of 83% (4.0 tonnes) since 2014. The total weight of HP-CIA sales accounted for less than half a percent of the total weight of antibiotics sold in 2023. For the third year in a row, no colistin was sold for use in animals.





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1.3.5 Total sales of antibiotics by species indication (tonnes)

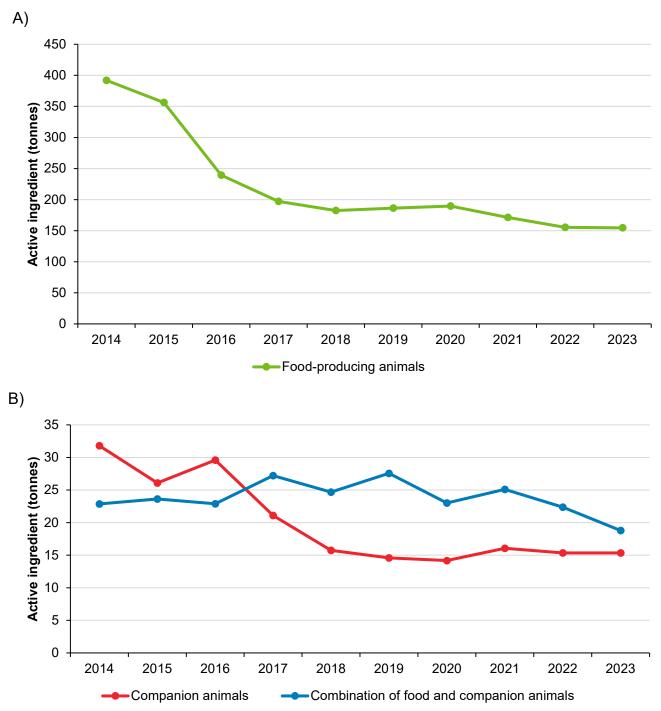
Veterinary antibiotics can be authorised for one or multiple species. Some products are authorised for food-producing animals only, some for companion animals (which for this analysis includes dogs, cats and horses) and others for a mixture of food producing and companion animals.

In 2023, 82% (154.5 tonnes) of total antibiotic sold were attributed to products authorised for food-producing animal species only (**Figure 1.10**), which is essentially unchanged compared to levels seen in 2022. Sales of products authorised for companion animals have also stayed constant since 2022 and account for a much smaller proportion of total sales (8%, 15.3 tonnes).

Sales of products indicated for both food-producing and companion animals decreased by 16% (3.6 tonnes) to 18.8 tonnes. This category is comprised of 99.8% injectable products.



Figure 1.10: Active ingredient (tonnes) of (A) antibiotics sold for food-producing animals, (B) companion animals and a combination of food and companion animals, 2014 to 2023.



1.3.6 Harmonised outcome indicators for antibiotic use

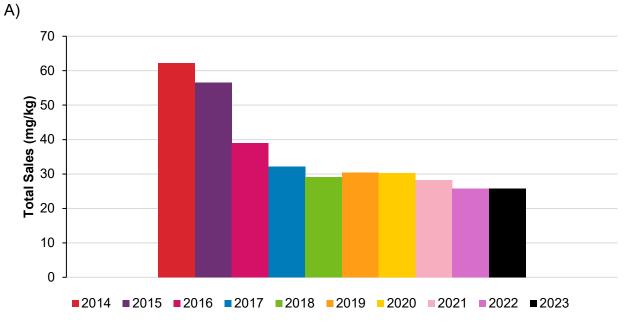
Harmonised indicators are important to monitor trends in a consistent way, and in a way that is comparable across different regions and countries. A number of different indicators for monitoring antibiotic sales in animals have been developed globally. For consistency with previously published data and harmonisation with other countries in the European region, the

data are reported using the EU harmonised indicators. These were <u>published</u> by the European Centre for Disease Prevention and Control (ECDC), European Food Safety Authority (EFSA) and EMA in 2017.

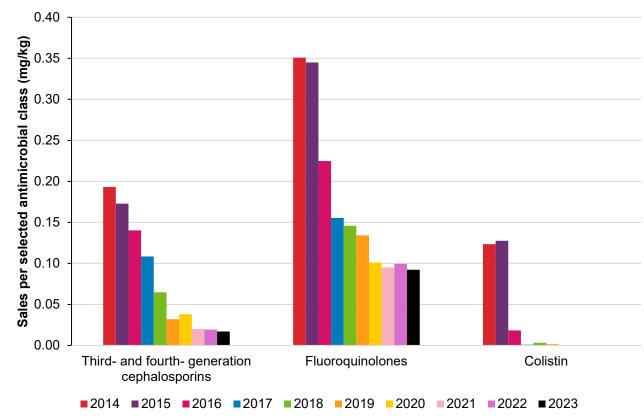
The primary indicator is "the overall sales of veterinary antibiotics in milligram of active substance per kilogram of estimated weight at treatment of livestock and of slaughtered animals in a country (mg/PCU)" (**Figure 1.1**). Secondary indicators are the sales in mg/PCU of third- and fourth- generation cephalosporins, quinolones (and percentage of fluoroquinolones) and polymyxins, which measures HP-CIA use (**Figure 1.3**). 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 2.3.5**), and colistin is the only polymyxin that has been on sale for use in food-producing animals. Both primary and secondary indicators have shown a decreasing trend since 2014 (**Figure 1.11**).



Figure 1.11: Harmonised outcome indicators for antibiotic consumption in food-producing animal species in the UK; Primary indicator (A) and Secondary indicators (B), 2014 to 2023.







A number of different indicators for monitoring antibiotic sales in animals have been developed globally, and overarching global indicators 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 <u>Veterinary Medicines Regulations</u>. 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 E).

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 <u>ATCvet Classification System</u> for veterinary medicinal products shown in Table S1.1.1 of 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 (Table S1.1.2 of 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



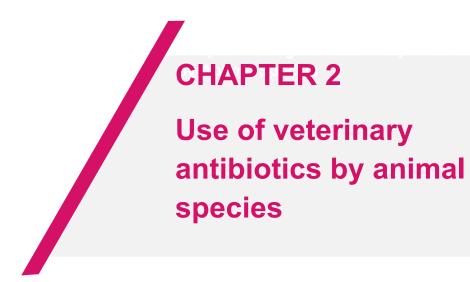
producing animals were analysed using the Population Correction Unit (PCU), which was formulated by the European Medicines Agency and represents the weight of the food producing animal population (in kg) at risk by using standardised weights that represent the average weight at time of treatment. Using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







2.1 Summary

The key trends are as follows:

- Pigs Antibiotic use increased by 18% (13.0 mg/kg) between 2022 and 2023, from 71.8 mg/kg to 84.8 mg/kg. This represents a total reduction since data was first published in 2015 of 69%. Use of HP-CIAs reduced from 0.012 mg/kg in 2022 to 0.007 mg/kg in 2023, which represents a greater than 99% reduction since 2015. Since 2015, the sector has also demonstrated a shift away from in-feed medication towards more targeted in-water delivery.
- Turkeys Antibiotic use decreased by 5% (1.7mg/kg) between 2022 and 2023, from 35.4 to 33.6 mg/kg. This represents an 85% reduction since data was first published in 2014. The only HP-CIAs used in turkeys are fluoroquinolones, and their use increased from 0.0002 mg/kg in 2022 to 0.0397 mg/kg in 2023.
- Broilers Antibiotic use decreased by 4% (0.5 mg/kg) between 2022 and 2023, from 14.1 mg/kg to 13.5 mg/kg. This represents a 72% reduction since data was first published in 2014. There were no HP-CIAs used in meat broilers in 2022, whereas fluoroquinolone use in 2023 was 0.0026 mg/kg.
- Ducks Antibiotic use increased by 0.1 mg/kg between 2022 and 2023 from 0.3 mg/kg to 0.4 mg/kg, but use remains very small. This represents a 97% reduction since data was first published in 2014. There were no HP-CIAs used in 2023.
- Laying Hens Antibiotic use decreased by 7% (0.02% bird days) between 2022 to 2023, from 0.23% bird days to 0.22% bird days. This represents a 67% reduction since data was first published in 2016. There were no HP-CIAs used in 2023.
- Gamebirds Antibiotic use increased by 47% (3.1 tonnes) between 2022 and 2023, from 6.7 tonnes to 9.9 tonnes. This represents a 51% reduction since data was first published in 2016. It should be noted that gamebird antibiotic use data is not corrected for by the size of the gamebird population, and fewer gamebirds were reared in 2022 due to issues with sourcing eggs and chicks caused by avian influenza. However, this increase in antibiotic use in 2023 is more than the 1/3 approximate increase in the number of gamebirds reared in 2023. Use of HP-CIAs increased by 19% (from 23.2 kg in 2022 to 27.7 kg in 2023), which is lower than the estimated increase in number of birds reared. Total HP-CIA use has reduced by 57% since data was first published in 2016.
- Salmon Antibiotic use increased by 7% (1.4 mg/kg) between 2022 and 2023, from 18.6 mg/kg to 19.9 mg/kg. This represents a 24% (3.9 mg/kg) increase since



data was first published in 2017, although levels are below those seen in 2020 and 2021. There were no HP-CIAs used in 2022.

Trout – Following the 35.2 mg/kg increase reported between 2021 and 2022, antibiotic use has reduced by 84% (37.2 mg/kg) from 44.1 mg/kg to 6.9 mg/kg. This is the lowest figure seen since data was first published in 2017. The only HP-CIA used in trout is the quinolone oxolinic acid, and its use decreased from 2.2 mg/kg in 2022 to 1.8 mg/kg in 2023. This is a 73% reduction since 2017.

2.2 Introduction

All antibiotics used in UK animals must be prescribed by a veterinary surgeon. Antibiotic use refers to the amount of antibiotics administered or intended to be administered (for example prescribed, dispensed, and/or delivered to the animal owner/ vets) for a defined animal species or production sector. This is different from sales data, which is collected from Marketing Authorisation holders and cannot be split by species or sector, as many antibiotics are authorised for use in multiple animal 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. Additionally, data collection systems 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 1.4 below.

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 2023, the sales and use data are showing a comparable trend.



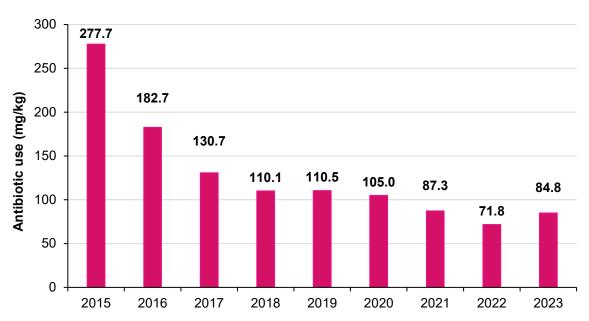
2.3 Results

2.3.1 Pigs

2.3.1.1 Antibiotic use data

Data from the electronic Medicines Book for Pigs (<u>eMB Pigs</u>), representing greater than 95% of UK pig production (9.5 million pigs produced for the food chain), show that in 2023 total antibiotic use in pigs was 61.2 tonnes, or 84.8 mg/kg when adjusted for population. This is an increase of 18% (13.0 mg/kg) since 2022, when use was the lowest recorded so far (71.8 mg/kg), and a total reduction of 69% (192.9 mg/kg) since data were first reported in 2015 (**Figure 2.1**). The <u>sector target</u> on antibiotic use is to achieve a national annual antibiotic usage figure of 73.5 mg/kg in 2024.

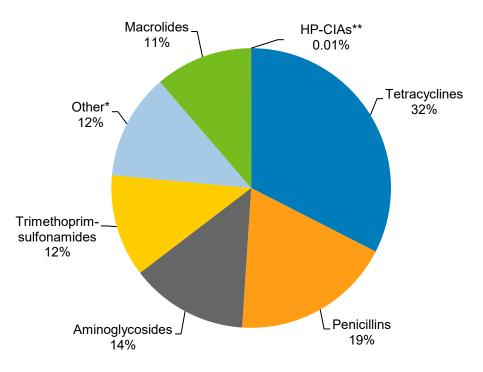
Figure 2.1: Active ingredient adjusted for population (mg/kg) of antibiotics reported in eMB pigs, 2015 to 2023.



Half (51%) of all antibiotics used in pigs were either tetracyclines or penicillins (**Figure 2.2**). In 2023, aminoglycosides (14%) replaced trimethoprim-sulfonamides (12%) as the third most used antibiotic class by active ingredient increasing from 3.5 mg/kg in 2015 to 11.5 mg/kg in 2023 (**Figure 2.3**).

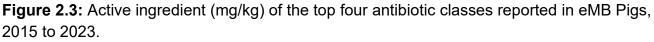
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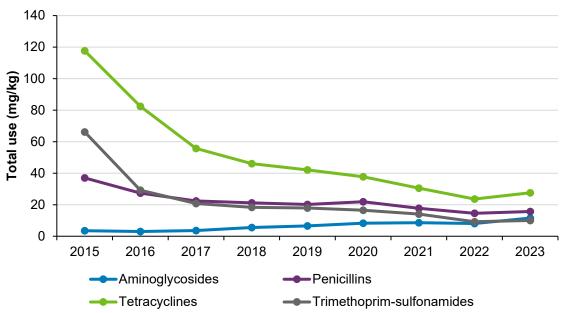
Figure 2.2: Active ingredient (% weight) of antibiotics by antibiotic class reported in eMB pigs, 2023.



*The category 'Other' contains the following antibiotics classes (% of total): Amphenicols (1%), Lincosamides (5%) and Pleuromutilins (6%).

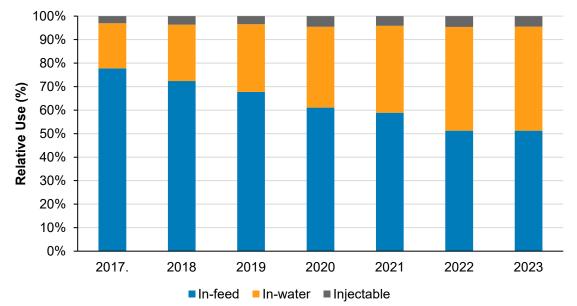
**HP-CIAs used were fluroquinolones or 3rd and 4th generation cephalosporins.





In-feed remains the most common route of antibiotic administration in pigs. However, relative use of in-feed antibiotic administration has fallen from 78% in 2017 to 51% in 2022 and this remains unchanged in 2023. Conversely, in-water administration has increased from 19% in 2017 to 44% in 2022 and this also remains unchanged in 2023 (see **Figure 2.4**). This shift reflects the pig sector's work to encourage in-water administration over in-feed to allow for more targeted administration of antibiotics.

Figure 2.4: Active ingredient (% weight) of antibiotics by route of administration reported in eMB Pigs, 2017 to 2023.



The use of HP-CIAs in pigs is shown in **Figure 2.5** and **Figure 2.6**. In 2023, only 5.2 kg of HP-CIAs were used, which represents 0.007 mg/kg. Use of HP-CIAs in pigs reduced by 0.005 mg/kg between 2022 and 2023, to the lowest level recorded to date. HP-CIAs account for one hundredth of a percent (0.01%) of overall antibiotic use in pigs. All the third-generation cephalosporins and 99.9% of the fluoroquinolones were administered by injection, which means that the use is targeted to individual animals. No products containing colistin have been used in the last four years.





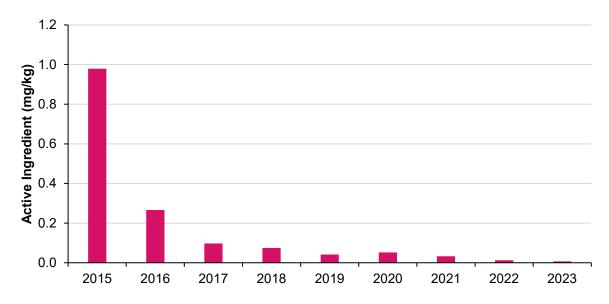
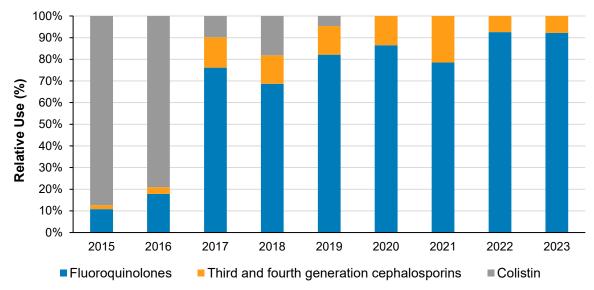


Figure 2.6: Active ingredient (% weight) of HP-CIAs reported in eMB Pigs, 2015 to 2023.



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

"The pig sector continues to promote the responsible use of antimicrobials and stands by the mantra 'as little as possible, but as much as necessary'. This includes ensuring that animals that are sick and need antimicrobials receive them. In 2023, the UK pig industry's antibiotic use was 84.8 mg/kg, an increase of 18% since 2022 and slightly lower than in 2021 (87.3 mg/kg). After a decision was made in 2017 by the European Commission to withdraw the marketing authorisation for veterinary medicines containing zinc oxide (ZnO) by 26 June 2022 (a product that is not an antimicrobial but was widely used to prevent diarrhoea), it was agreed that in the UK, products which were in the supply chain by that date could continue to be used until the end of shelf-life. If these products expired in 2023, some farmers are likely

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to have had to treat diarrhoeic pigs with antibiotics and so a slight increase in use was expected. It is likely a similar increase will occur in 2024 as the full impact of the withdrawal of ZnO veterinary medicinal products is seen. An increase in other diseases requiring antibiotic treatment was also seen, including enteric and respiratory diseases, such as PRRSv and Swine dysentery, in a range of age groups of pigs. Diseases in pigs are often caused by multiple, complex factors, but this increase may have been exacerbated by reduced vaccine availability during that year. These vaccine supply issues may also have impacted on the modest increase in antimicrobial use required in this year.

Overall, there has been a decrease in recorded antibiotic use in UK pigs over the last nine years, totalling a 69% reduction in that time. The RUMA sector target is for the annual national antibiotic use figure to be 73.5 mg/kg in 2024.

The use of Highest-Priority Critically Important Antibiotics (HP-CIAs) in pigs was at a very low level (0.007 mg/kg) and accounted for less than one hundredth of one percent (0.01%) of overall antibiotic use in pigs in 2023. This means that just 5.2 kg of HP-CIAs were used across 9.5 million pigs produced that year. Over 99.9% of HP-CIAs used were products administered by injection and therefore targeted to individual animals. No colistin use was recorded in pigs for the fourth 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 presents a reduced AMR risk compared to in-feed delivery, sales of antibiotics administered in-water have shown an increasing trend 2017-2022 and remained stable between 2022 and 2023."

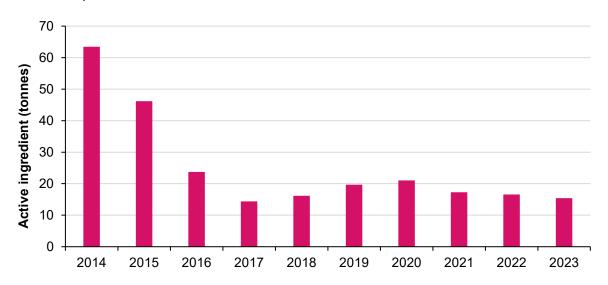
2.3.2 Meat poultry

2.3.2.1 Antibiotic usage data

Data from the British Poultry Council (BPC) Antibiotic Stewardship, representing 85% of the meat poultry industry (960 million chickens and 7.8 million turkeys entering the food chain and including breeding birds), reported the use of 15.4 tonnes of active ingredient in 2023. This is a 7% (1.1 tonne) decrease since 2022 and a 76% (48.0 tonnes) decrease since data was first published in 2014 (**Figure 2.7**).

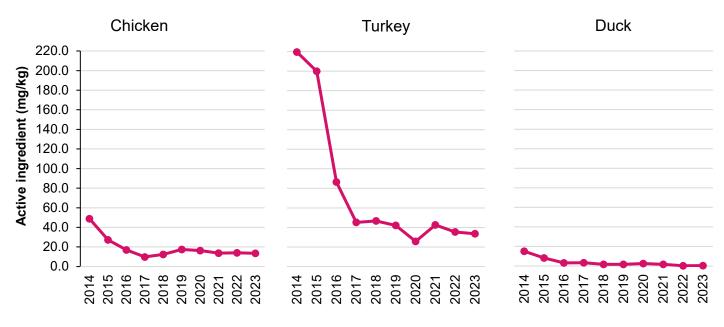


Figure 2.7: Active ingredient (tonnes) of antibiotics used by members of BPC Antibiotic Stewardship, 2014 to 2023.



When adjusting for the size of the animal population (and excluding breeding birds), between 2022 and 2023 antibiotic usage in the chicken sector decreased by 4% (0.5 mg/kg) to 13.5 mg/kg (**Figure 2.8**). This represents a 72% (35.2 mg/kg) decrease since data was first published in 2014 and remains below the <u>sector target</u> of 25 mg/kg (**Figure 2.9**). Antibiotic use in the turkey sector decreased by 5% (1.7 mg/kg) to 33.6 mg/kg in 2023. It has now reduced by 85% (185.9 mg/kg) since 2014 and remains below the sector target of 50 mg/kg (**Figure 2.9**). The duck sector demonstrated an increase of 0.1 mg/kg to 0.4 mg/kg, which remains a very low level, and antibiotic use has now decreased by 97% (14.7 mg/kg) since 2014.

Figure 2.8: Active ingredient (mg/kg) of antibiotics by species used by members of BPC Antibiotic Stewardship, 2014 to 2023.



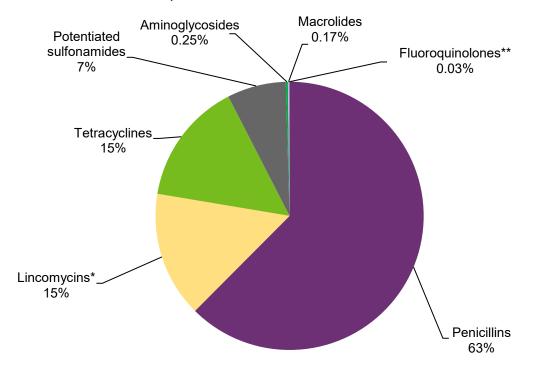


In 2023, 63% of active ingredients used were penicillins (all of which was amoxicillin) (**Figure 2.10**), compared with 73% in 2022. This is because the use of penicillins reduced by 2.5 tonnes between 2022 and 2023, whereas the use of lincomycins, potentiated sulfonamides and tetracyclines increased by 0.6, 0.5 and 0.3 tonnes respectively. Since 2014, the top three antibiotic classes (penicillins, tetracyclines and lincomycins) used in poultry have reduced by 51%, 93% and 67% respectively.

When considering HP-CIAs, colistin and third- and fourth- generation cephalosporins were once again not used by any of the meat poultry sectors in 2023, and fluoroquinolones were not used by the duck sector. In 2023, BPC recorded use data (which includes slaughter animals and breeding birds) of 5.1kg of fluoroquinolones, which is an increase of 3.8 kg since 2022 but still only represents 0.03% of overall use and has reduced by 99.6% (1.25 tonnes) since 2014. When looking only at slaughter animals, there was no fluoroquinolone use in slaughter broilers in 2022, whereas use was 0.0026 mg/kg in 2023, and use in slaughter turkeys increased from 0.0002 mg/kg in 2022 to 0.0397 mg/kg in 2023.



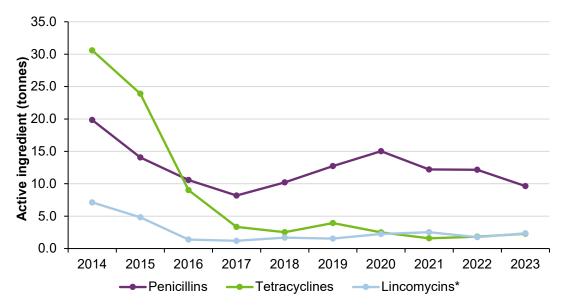
Figure 2.9: Active ingredient (% weight) of antibiotics by antibiotic class used by members of BPC Antibiotic Stewardship, 2023.



* Includes products containing lincomycin in combination with spectinomycin

** Fluoroquinolones fall under the category of an HP-CIA

Figure 2.10: Active ingredient (tonnes) of the top three antibiotics by antibiotic class used by members of BPC Antibiotic Stewardship, 2014 to 2023.



* Includes products containing lincomycin in combination with spectinomycin

Statement from British Poultry Council

"The reductions seen in broilers and turkeys, and the continued low use in ducks, highlights the continued focus on responsible antibiotic use and is testament to the work of BPC Antibiotic Stewardship, which focuses on ongoing collaboration, collective responsibility and the sharing of insights, experiences and best practice in a non-competitive manner to ensure continuous improvement. This is key to preserving the effectiveness of the limited number of antibiotics authorised for use in poultry species and is critical for the long-term resilience and sustainability of the industry. In 2023, the BPC also endorsed the International Poultry Council's <u>Antimicrobial Stewardship Principles</u>, recognizing the threat of AMR to local, national and global food security, as well as putting a strain on the effectiveness of treatment with subsequent risks to animal and human health.

There was a slight increase in fluoroquinolone use in broilers and turkeys. However, fluoroquinolones still only account for 0.03% of overall use in meat poultry. These highest priority antibiotics were only used as a last resort following a detailed clinical investigation by the prescribing vet, 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 antibiotics are used under strict veterinary direction if deemed necessary to ensure health and welfare are not compromised."

2.3.3 Laying hens

2.3.3.1 Antibiotic use data

In 2023, data collected by the <u>British Egg Industry Council (BEIC)</u>, representing 90% of the laying hen industry, reported that a total of 1.5 tonnes of antibiotic active ingredient was used, which represents 0.22% bird days (actual bird days treated/100 total bird days on the farm). This is a decrease of 7% (0.02% bird days) since 2022 and 67% (0.45% bird days) since data was first published in 2016 (**Figure 2.11**). The methodology for the metric is explained in section 2.4 of this report and represents the average number of days of treatment administered per chicken over a 100-day period.

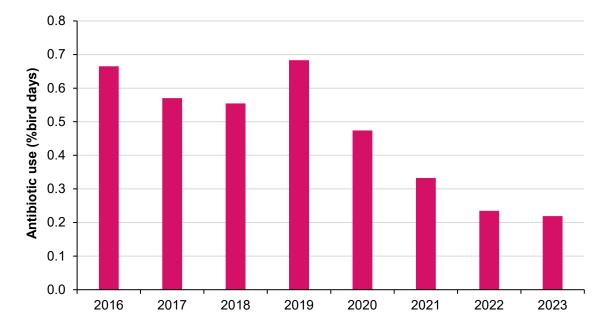


Figure 2.11: Antibiotic use (% bird days) by members of the BEIC Lion Code, 2016 to 2023

Tetracyclines, penicillins and pleuromutilins accounted for 92% of total use (Figure 2.12). Tetracyclines and pleuromutilins decreased by 6% (0.01% bird days) and 29% (0.01% bird days) respectively between 2022 and 2023, while penicillin use increased by 58% (0.01% bird days), overtaking pleuromutilins as the second most commonly used antibiotic class (Figure 2.13). For the seventh year running, there were no HP-CIAs used by the laying hen sector in 2023.



Figure 2.12: Antibiotic use (% of total bird days) by antibiotic class by members of the BEIC Lion Code, 2023.

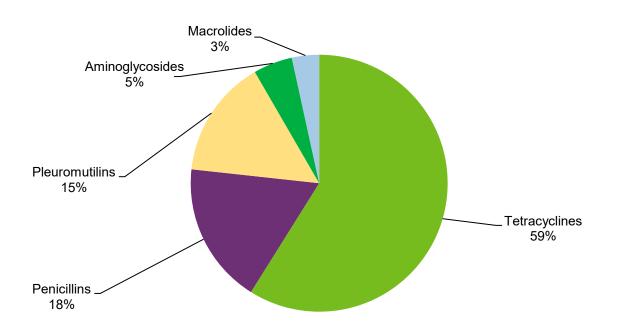
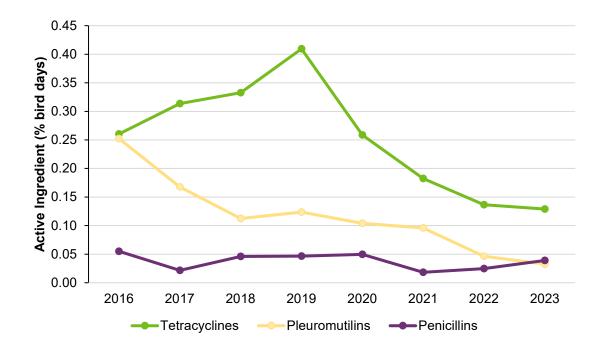


Figure 2.13: Antibiotic use (% bird days) of the top three antibiotics by antibiotic class by members of the British Egg Industry Council Lion code, 2016 to 2023.



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Statement from the British Egg Industry Council (BEIC)

"The antibiotic use data from members of the British Egg Industry Council (BEIC) Lion Scheme for 2023 shows further reductions and continues to be below the target of 1% bird days, and for the seventh year running no HP-CIAs were used. This is a significant achievement, especially considering the major challenges in 2023, which included cost of production increases and bird flu outbreaks. The laying hen sector continues to be a very low user of antibiotics.

The <u>Lion standard</u> continues to focus on bird health through good biosecurity and hygiene, as well as feed and water quality. Version 8 of the Scheme (which was launched in June 2023) has seen significant developments in biosecurity requirements and training modules on 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 current antibiotic use target of 1% bird days, and 0.05% bird days for HP-CIAs."

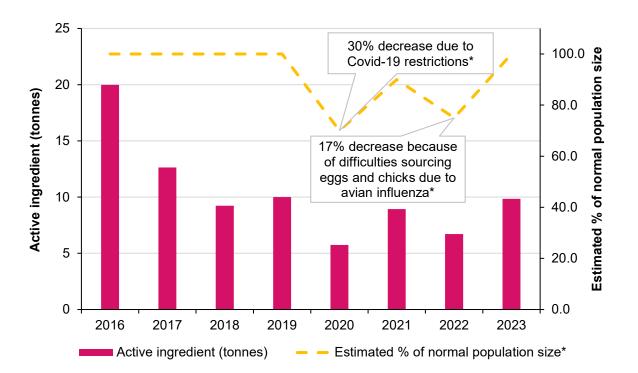
2.3.4 Gamebirds

2.3.4.1 Antibiotic use data

In 2023, 9.9 tonnes of active ingredient were reported through the <u>Game Farmers'</u> <u>Association (GFA)</u> and <u>British Veterinary Poultry Association (BVPA)</u> 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 the gamebird population. It is estimated by the industry that approximately 1/3 more gamebirds were reared in 2023, after challenges in 2022 with the sourcing of eggs and chicks caused by avian influenza in 2022. Overall, the 2023 tonnage represents an increase of 47% (3.1 tonnes) since 2022, which is more than the estimated increase in number of gamebirds reared, meaning that relative antibiotic use has increased. While this still represents a reduction of 51% (10.1 tonnes) since 2016, use remains at similar levels to those recorded in 2019 (the last year where there were an equivalent number of gamebirds reared) (**Figure 2.14**).



Figure 2.14: Active ingredient (tonnes) of antibiotics used in gamebirds, collected by the GFA and BVPA data collection programme, 2016 to 2023 and estimated population size (% of normal population size).



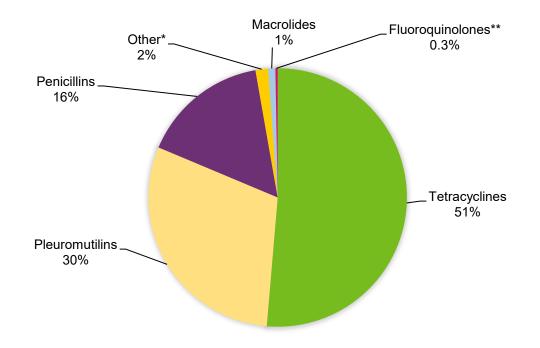
*% change in population size as estimated by the Game Farmers Association

The use of antibiotics broken down by active ingredient is shown in Figures 2.15 and 2.16.

Tetracyclines remain the most commonly used active ingredient, representing 51% of antibiotics used in 2023, but this has dropped by 65% (9.3 tonnes) since 2016. By contrast, penicillins (which account for 16% overall use in 2023) have increased by 34% (0.4 tonnes) over the same period.



Figure 2.15: Active ingredient (% weight) of antibiotics by antibiotic class used in gamebirds, collected by the GFA and BVPA data collection programme, 2023.

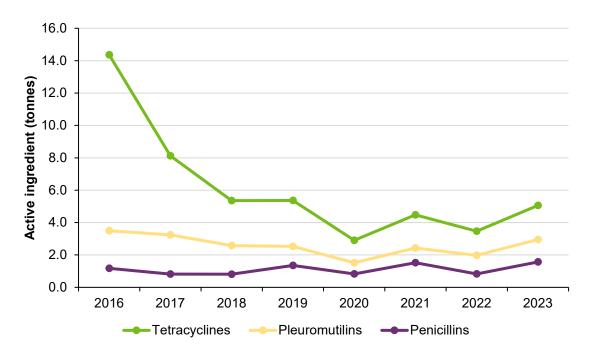


* Aminoglycosides, amphenicols, lincomycin, trimethoprim/sulfonamides

** Fluoroquinolones fall under the category of an HP-CIA



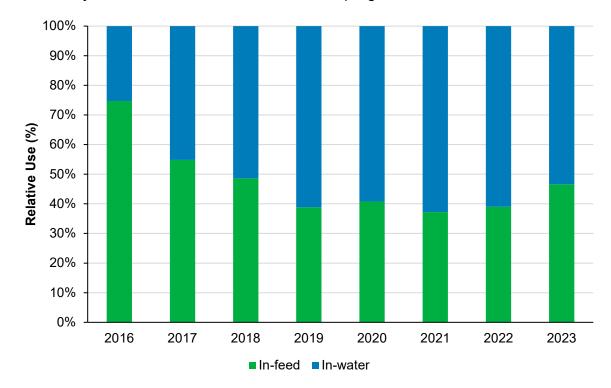
Figure 2.16: Active ingredient (tonnes) of top three antibiotics by antibiotic class used in gamebirds, collected by the GFA and BVPA data collection programme, 2016 to 2023.



Analysis by route of administration shows that relative use of in-feed has increased from 39% in 2022 to 47% in 2023 (**Figure 2.17**). This is contrary to the industry's focus on moving from in-feed to in-water medication where possible, which allows for more targeted treatment. However, it should be noted that relative in-feed use has dropped considerably since 2016 (when it accounted for 75% of antibiotic use).



Figure 2.17: Active ingredient (% relative use) by route of administration used in gamebirds, collected by the GFA and BVPA data collection programme, 2016 to 2023.



The fluoroquinolone enrofloxacin is the only HP-CIA used by the gamebird sector and this has increased by 19% (4.5kg) since 2022 to 27.7kg. However, this increase is less than the 1/3 approximate increase in gamebirds reared between 2022 and 2023, meaning that relative use has decreased. Since data was first recorded in 2016, HP-CIA use has decreased by 57% (36kg).

2.3.4.2 Statement from the Game Farmers' Association and the British Poultry Veterinary Association (BVPA) gamebird subcommittee (not finalised)

"Given the way the data are reported, the recorded increase in antibiotic use between 2022 and 2023 partially reflects the increase in number of birds reared. However, taking into consideration the changes in population size during the avian influenza outbreak, relative antibiotic use has effectively plateaued since 2019. The sector is therefore unlikely to meet their own industry-led target of reducing antibiotic use by 40% between 2019 and 2024. Apart from the changes in population size, the increase of antibiotic use between 2022 and 2023 is thought to relate to challenging weather conditions which increased the risk of enteric diseases such as coccidiosis and spironucleosis. An ongoing research project led by the sector is aiming to develop a better understanding of *Spironucleus* sp. during the release period and the sector is also actively promoting the GFA's Pen Scoring Matrix to raise the standards of the release environment. In line with current regulation, there is a commitment that prophylactic/metaphylactic treatment in one year should be followed by implementing and recording robust preventative measures to reduce the need for such treatment in future seasons. Other key initiatives going forward include a commitment to a voluntary transition away from in-feed antibiotics on rearing sites, development of a standard calculation of antibiotic use per reared bird for more meaningful data comparisons and promotion of the Veterinary Medicines Directorate's online and telephone-based reporting systems for suspected breaches of the Veterinary Medicines Regulations. The sector will also continue to develop and encourage engagement with veterinary-led training initiatives, developed by members of the BVPA game bird subcommittee in conjunction with gamekeeper and game farmers. Furthermore, assurance systems which audit the welfare of the birds such as Trusted Game and Aim To Sustain are being promoted. Part of this initiative is that by increasing the welfare of the birds, further meaningful and sustainable reductions in antibiotic use can be achieved.

It is encouraging that the use of the fluoroquinolone enrofloxacin has fallen relative to the estimated number of birds reared. We remain committed to collecting data relating to the use of fluoroquinolones and focusing on reducing their use, ensuring they are only used as a last resort and with good reason, e.g. where culture and sensitivity tests suggest they are the only suitable option."

2.3.5 Aquaculture

2.3.5.1 Salmon

2.3.5.1.1 Antibiotic use data

In data collected by <u>Salmon Scotland</u> representing 100% of the industry, 3.7 tonnes of antibiotic active ingredient were used in 2023, representing 19.9 mg/kg (**Figure 2.18**). This is an increase of 7% (1.4mg/kg) since 2022 and 24% (3.9 mg/kg) compared with 2017, when data was first published. It should be noted that 2023 usage figures are based on estimated production figures, as published in the Marine Production Survey 2022, as published figures were not available at the time of publication of the VARSS report.

In 2023, 50% of use was oxytetracycline and 50% florfenicol. Between 2022 and 2023, oxytetracycline use reduced by 21% (2.7 mg/kg) whereas florfenicol use increased by 69% (4.1 mg/kg). Since 2017, oxytetracycline use has reduced by 28% (3.8 mg/kg) whereas the use of florfenicol has increased by three and half times (**Figure 2.19**)

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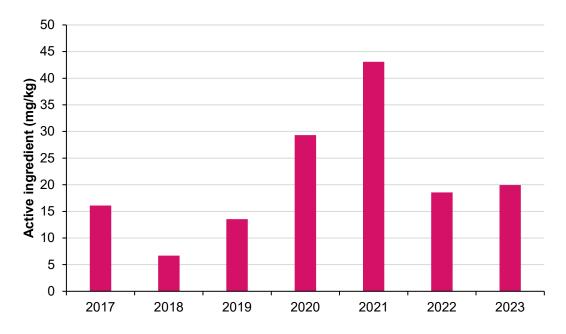
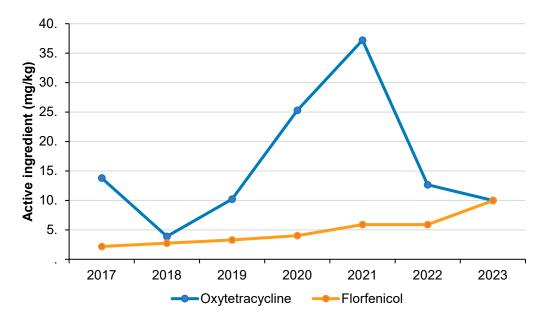


Figure 2.18: Antibiotic active ingredient (mg/kg) used in salmon, 2017 to 2023.

Figure 2.19: Antibiotic active ingredient (mg/kg) by antibiotic class used in salmon, 2017 to 2023.



2.3.5.1.2 Statement from Salmon Scotland

"The data records an increase in antibiotic use compared with 2022 but remains significantly below the levels recorded in 2020 and 2021. Increases 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 7.5% of freshwater farms and 9.8% of marine farms treated in 2023. 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 2022 and 2021, there was no

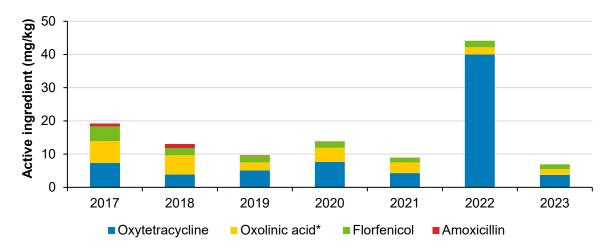
use of the HP-CIA oxolinic acid in 2023. The Salmon sector continues to focus on a holistic and preventative approach to health management, including vaccination, antibiotic stewardship, biosecurity and health and welfare planning. The sector also continues to support the development of innovative approaches 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. 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

2.3.5.2.1 Antibiotic use data

The data, obtained from veterinary practices that treat approximately 90% of UK trout production, demonstrates that a total of 0.09 tonnes of antibiotic active ingredient was used, representing 6.9 mg/kg, a reduction of 84% (37.2 mg/kg) between 2022 and 2023 and the lowest usage seen in the trout sector since electronic recording began in 2017. This follows the almost 5 times (35.2 mg/kg) increase between 2021 and 2022, which was linked to an outbreak of *Aeromonas salmonicida* on a small number of production sites (see **Figure 2.20**).

Figure 2.20: Active ingredient (mg/kg) of antibiotics by antibiotic class used in trout, 2017 to 2023.



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

When considering usage by class, oxytetracycline and florfenicol account for 75% of antibiotic use and, between 2022 and 2023, they decreased by 91% (36.3 mg/kg) and 27% (0.5 mg/kg) respectively.



In 2023, use of the HP-CIA oxolinic acid (a quinolone) accounted for 25% of overall use and, between 2022 and 2023, this decreased from 2.2 mg/kg to 1.8 mg/kg. It has now decreased by 73% (4.8 mg/kg) since 2017.

2.3.5.2.2 Statement from the British Trout Association

"After the increase in use in 2022, it is encouraging to see antibiotic use fall back down to more normal levels and well under the industry target of 20mg/kg, alongside reducing use of the HP-CIA oxolinic acid. This highlights the trout sector's ongoing commitment to reducing antibiotic use through disease prevention, including vaccination, and promoting best practice through the Quality Trout UK standard."

2.3.6 Cattle and sheep

2.3.6.1 Antibiotic use data

The Medicine Hub is a centralised national industry database for the collection and collation of antibiotic use data in UK dairy, beef and sheep. It is a voluntary industry initiative launched by the Agriculture and Horticulture Development Board (AHDB) in 2021 and published its first data, covering 2022, in 2023.

Medicine Hub coverage and antibiotic use data relating to the sheep and dairy sectors was provided to the VMD.

Currently, a low proportion of each ruminant sector is captured within the Medicine Hub compared to other livestock sectors (which have coverage of 85-100%). The data below can therefore not be interpreted as 'national' antibiotic use figures for these sectors.

Antibiotic use and coverage data from the beef sector was not provided for inclusion in this report.

The mg/kg figures presented below are calculated using the national mg/PCU methodology for dairy and sheep (see section 2.4 of this report for further details).



Dairy Cattle

The 2023 antibiotic use data is shown below:

% UK Dairy	Overall Use	HP-CIA Use	% HP-CIA Use
Cattle	(mg/kg)	(mg/kg)	
30	15.4	0.009	0.06

Sheep

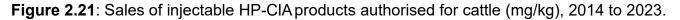
The 2023 antibiotic use data is shown below:

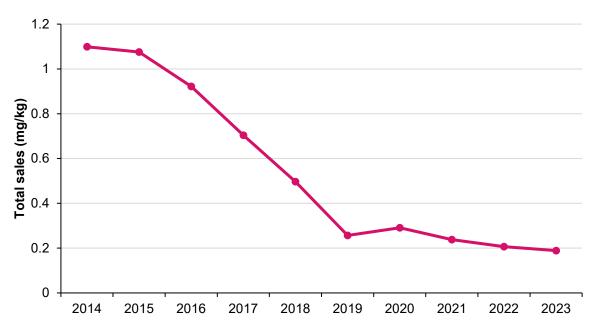
% UK Sheep	Overall Use	HP-CIA Use	% HP-CIA Use
Production	(mg/kg)	(mg/kg)	
11	5.6	0.0009	0.01

Sales (mg/kg) of injectable HP-CIA products authorised for use in cattle

Given the low coverage of antibiotic use data, antibiotic sales data can be used to estimate usage in some situations. Intramammary sales are included in the sales chapter. In addition, use of injectable HP-CIAs for cattle can be estimated using sales data. This is because over 80% of these products sold are either authorised for cattle alone or for cattle and pigs, and it is known from usage data that use of injectable HP-CIAs is very low in pigs.

Sales of injectable HP-CIA products authorised for cattle are shown in **Figure 2.21**. Sales were 0.19 mg/kg in 2023, representing a 9% (0.02 mg/kg) reduction between 2022 and 2023. Sales have now fallen by 83% (0.91 mg/kg) since 2014.





2.3.6.2 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. There is good collaboration between sheep veterinary, farming and industry groups with carefully coordinated work and messaging across all levels of the sector.

The Medicine Hub, developed and resourced by AHDB, is a centralised national database for the collection and collation of antibiotic use data in UK 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 2023, the Hub captured antibiotic use data from flocks representing 11% of UK finished lambs. This data provides a useful indication of antibiotic use in the sheep sector. Total antibiotic use was 5.6 mg/kg in these flocks in 2023 with HP-CIA use very low at 0.0009 mg/kg. It is important not to over-interpret this small proportion of national data but the reliability of these figures will continue to improve as the sector submits data from a wider number of flocks. 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). 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. Despite various external challenges (disease incursions, vaccine supply issues), the sector continues with a strong "Plan Prevent Protect" focus on consistent, coordinated, and collaborative communications to support responsible antimicrobial stewardship."

2.3.6.3 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, <u>the</u> <u>Medicine Hub</u>. Antibiotic use data collected in 2023 represents 30% of adult dairy cattle in the UK. Antibiotic use data was collated from across 2287 dairy enterprises (there are approximately 10,000 dairy enterprises in the UK). The data collected in 2023 have been voluntarily provided and are not yet sufficient to be representative of the UK dairy population (and so cannot be used to provide a national figure). For beef, the large variety of beef farm types within the UK (suckler, dairy beef, calf rearers and finishers) mean that the low coverage within this sector results in a higher chance of the mg/kg data not being representative of the national picture compared to other ruminant sectors and the figures are therefore not provided in this report (see the RUMA website for further details). However, the figure calculated for dairy provides a useful snapshot of antibiotic use in a subset of farms.

Once 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, in the future, the beef sector. The cattle sectors continue 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. The sample also demonstrates very low use of antibiotics critically important to human health (0.009 mg/kg in the dairy sector sample)."

2.3.7 Companion Animals

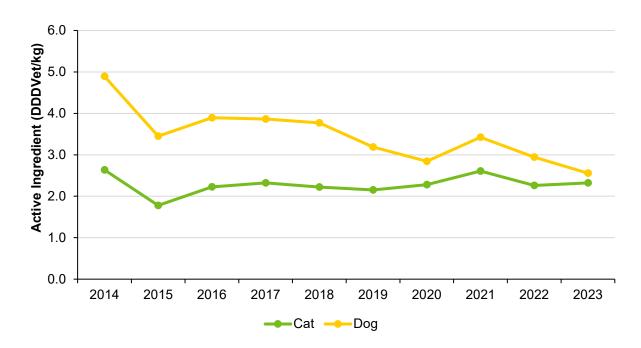
2.3.7.1 Antibiotic use in dogs and cats

Antibiotic use data is not available in the dog and cat sector. Therefore antibiotic use in dogs and cats is estimated by stratifying the sales data reported by veterinary pharmaceutical companies; the full methodology was developed in conjunction with the RUMA Companion Animal and Equine group and can be found in section 2.4 of this report and Supplementary Material 1. It should be noted that the figures presented differ slightly to previous VARSS reports, due to a change in methodology for determining average dog and cat weight (see methods section for further details).

In 2023, antibiotic use in dogs and cats has been estimated to be 54.6 mg/kg for dogs and 33.7 mg/kg for cats, and use of HP-CIAs is 0.40 mg/kg for dogs and 0.63 mg/kg for cats. However, mg/kg metrics underestimate the use of long acting injectable products (which are commonly used, particularly in cats) and so a different metric (DDDVet/animal) is preferable for monitoring trends. DDDVet/animal relates to the average number of days that each dog or cat in the UK has received an antibiotic throughout the year.

Sales of antibiotic products for dogs in 2023 have decreased by 13% (0.4 DDDvet) since 2022 and 48% (2.3 DDDvet) since 2014 to 2.6 DDDvet (Figure 2.22). In comparison, sales of antibiotic products for cats increased by 3% (0.06 DDDvet) since 2022 but have decreased by 12% (0.3 DDDvet) since 2014 to 2.3 DDDvet.

Figure 2.22: Active ingredient (DDDvet/animal) of antibiotics sold for use in dogs and cats, 2014 to 2023.



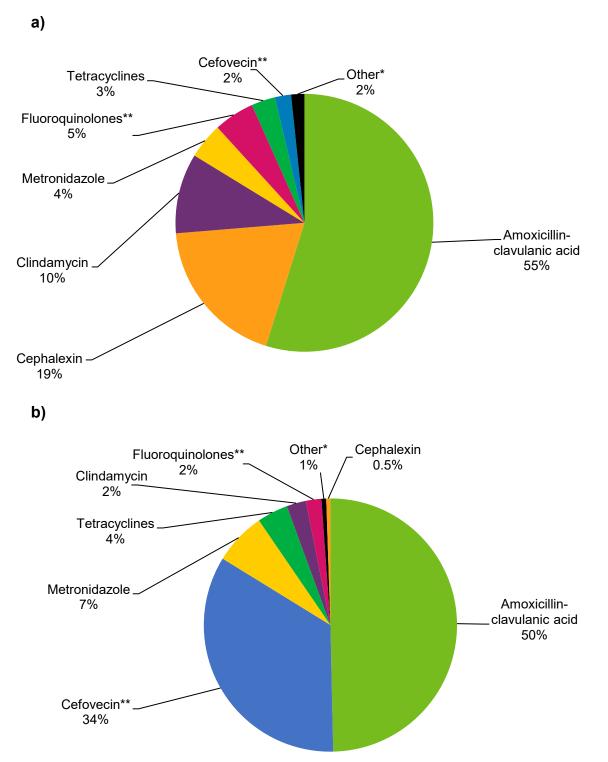
In dogs, products containing amoxicillin combined with the beta-lactamase inhibitor clavulanic acid were the most sold active ingredient in 2023 (**Figure 2.22**), representing 55% of total sales, followed by cephalexin (a first-generation cephalosporin), which represented 19% of total sales. In cats, amoxicillin-clavulanic acid has become the most sold active ingredient in 2023, representing 50% of total sales, overtaking the third generation cephalosporin cefovecin (an HP-CIA) which represented 34% of total sales (**Figure 2.23**).



Antibiotic usage

Chapter 2

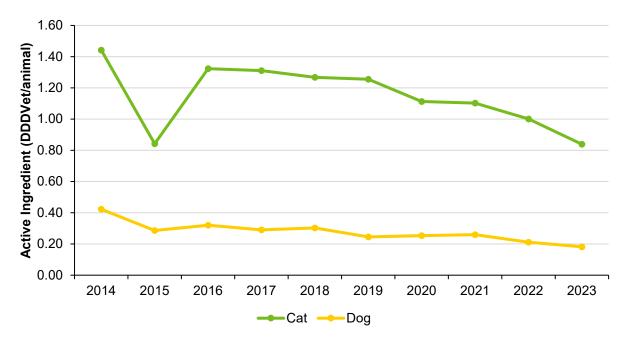
Figure 2.23: Active ingredient (DDDVet/animal) of antibiotics by active ingredient/antibiotic class sold for use in (a) dogs and (b) cats, 2023.



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

In dogs, sales of HP-CIAs (**Figure 2.24**) accounted for 7% of total sales (0.18 DDDVet/animal), which represents a reduction of 0.03 DDDVet since 2022 and 57% (0.24 DDDVet/animal) since 2014. In cats, however, HP-CIAs accounted for 36% of total sales (0.8 DDDVet/animal), which represents a reduction of 0.16 DDDVet since 2022 and 42% (0.60 DDDVet/animal) since 2014. Fluoroquinolones represented 72% of HP-CIA use in dogs, whereas in cats, 95% of HP-CIA sales were of 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 2.24: Active ingredient (DDDVet/animal) of HP-CIAs, sold for use in dogs and cats, 2014 to 2023.



2.3.7.2 Sector Update

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

"The reductions in antibiotic use in dogs and HP-CIA use in cats between 2022 and 2023 is testament to the extensive industry activities which are summarised in our <u>2023 annual</u> <u>progress report</u>. These are aimed at benchmarking antibiotic use in UK veterinary practices, evaluating practical and realistic novel interventions that can reduce antimicrobial prescribing in practice as well as supporting the profession in educating clients of the dangers of Antimicrobial Resistance (AMR). RUMA CA&E led and coordinated another successful <u>Antibiotic Amnesty</u> campaign in 2023 and joined RUMA Agriculture's Independent Scientific Group, which provides resources and discusses evidence relating to the responsible use of medicines in both human and animal medicine. In addition, in 2023, RUMA CA&E brought together stakeholders, including vets and practice management system companies to develop an approach to collecting antibiotic usage data across the CA&E sectors (as opposed to the manufacturer sales data currently available). RUMA CA&E also runs the



Targets and Measures Working Group (T&MWG) which is focused on evolving metrics for all sectors, engaging with stakeholders, and has progressed setting realistic targets for further improving the use of antibiotics in companion animals. RUMA CA&E also partnered with IVC Evidensia to produce a <u>social media toolkit</u> to support those who are interested in spreading the word about AMR. RUMA CA&E was pleased to see the <u>BSAVA/SAMSoc PROTECT</u> <u>ME poster</u> was also extensively updated in 2023, so it better aligns with current antibiotic stewardship advice, particularly reiterating that the use of fluoroquinolones (enrofloxacin, marbofloxacin, pradofloxacin, ciprofloxacin) and 3rd generation cephalosporins (cefovecin) should only be used in specific circumstances, to preserve their effectiveness, and samples should be submitted for antibiotic susceptibility testing before starting these agents where possible."

RCVS Knowledge

"RCVS Knowledge is a veterinary charity with a mission to advance the quality of veterinary care for the benefit of animals, the public, and society. RCVS Knowledge is the charity partner of the Royal College of Veterinary Surgeons (RCVS):

2023 saw the successful launch of RCVS Knowledge's <u>VetTeamAMR</u> learning platform, which was funded by the VMD and provides over 20 hours of free Continuous Professional Development (CPD) to veterinary practice teams. Designed to offer practical tips and bitesize modules, VetTeamAMR provides veterinary professionals with important advice on how to manage different diseases and conditions where antibiotics are most commonly used, as well as modules on diagnostics, behaviour change, and infection control. All of the content complements existing legal requirements and industry guidelines, including the new updated <u>BSAVA/SAMSoc PROTECT ME poster</u>. Users that complete enough of the course can become certified as a Bronze, Silver, Gold, or Platinum Antibiotic Guardian.

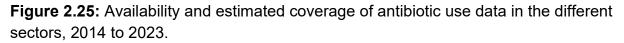
In 2023 the charity also added Antimicrobial Stewardship as a category in their annual RCVS Knowledge Awards for the first time. One of the winners was Paragon Veterinary Referrals, who provided an inspiring <u>case study</u> on reducing the use of antibiotics in cat bite abscesses. They formed an antimicrobial stewardship team and developed in-house guidelines, checklists and training. As a result, they were able to treat 86% of their patients successfully without antibiotics, and importantly without compromising welfare."

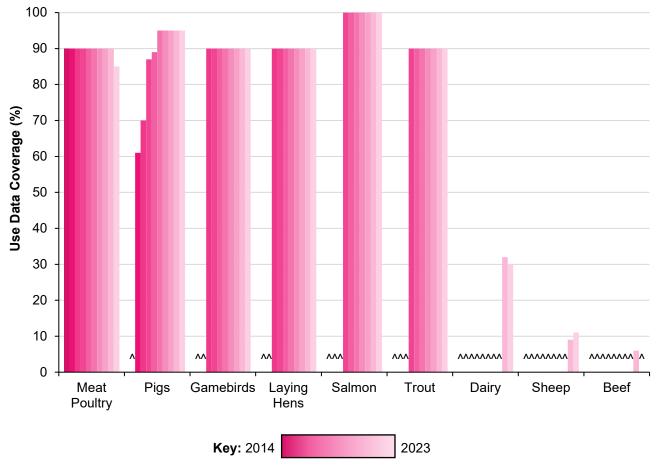
2.3.8 Antibiotic Use Coverage

The VMD's work with different livestock sectors means that antibiotic use data representing 85% or more of the pig, meat poultry, laying hen, trout, salmon and gamebird sectors can be published. The <u>Medicine Hub</u> for ruminants is also up and running with the aim of bringing together antibiotic use data for the dairy, beef and sheep sectors. However, all this data is still collected on a voluntary basis. There are currently no systems collecting antibiotic use data for dogs, cats and horses, but RUMA Companion Animal and Equine group are working with sector stakeholders to look into this.



In 2024, the GB Veterinary Medicines Regulations were revised and these included <u>new</u> <u>provisions relating to antibiotic use</u>. This includes a provision allowing the Secretary of State to require vets and keepers of food-producing animals to provide antibiotic use data on request. Given the progress highlighted, there are no plans to apply the above legal provisions to require antibiotic use data reporting at this time. However more progress is needed, particularly for the ruminant and companion animal sectors, and this may change if, upon review, it is considered that the voluntary model for antibiotic use collection does not deliver the desired outcomes. With this in mind, estimated coverage of antibiotic use data available in the different sectors is reported (see **Figure 2.25**).





^ Data not available

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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%, 2023 >95%
- The data are input 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 2023 were extracted from eMB on 29 May 2024 and these figures will now be fixed as the reference levels for 2023.
- 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)¹ provided antibiotic use data for the poultry meat (chicken, turkey and duck) sectors. BPC runs BPC Antibiotic Stewardship, which covers 85% of UK poultry meat production. This process of data collection started in 2012 and producers are responsible for submitting quarterly (chicken, duck) or annual (turkey and all breeders) antibiotic 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.

¹ https://britishpoultry.org.uk/

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 (chickens: 1.0 kg as derived by <u>ESVAC</u>; 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 <u>Lion</u> <u>Scheme</u>, 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 chicken over a 100-day period.

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

Gamebirds

The Game Farmers' Association (GFA) 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.

Dairy and Sheep

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 below:

- For dairy and 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.
- 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 2023 were extracted from Medicine Hub on 7 August 2024.
- 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.

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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 <u>PDSA PAW report</u>, which is a survey that is representative of the UK pet-owning population. This is then multiplied by the average weight of a dog and cat, which has been provided by the Royal Veterinary College using the VetCompass system (see summary below demonstrating how this is determined).

The metric is calculated separately for dogs and cats, with the amount of antibiotic active ingredient separated by dog and cat. For products authorised 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 authorised 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. Therefore the figures reported will slightly underestimate overall use.

VetCompass methods for calculation of standard bodyweight by species

Standard species bodyweights were calculated using clinical data on millions of animals under primary veterinary care in the UK derived from the <u>RVC VetCompass database</u>. A point mean population bodyweight describes the mean of the bodyweights of all individual animals in the population at a specific point in time. However, as animals tend to be weighed at *ad hoc* times when presented for routine veterinary care, veterinary records cannot provide the current updated bodyweights of all animals at any one single point in time. For example, juvenile animals weighed several weeks or months previously are likely to have a much higher bodyweight at a later point in time. The VetCompass method for calculation of standard point mean bodyweight by species solved this problem by modelling the bodyweight over time for all animals based on the available information on species and age along with recorded bodyweight values. Estimation of point mean population bodyweight that accounts for juvenile growth was achieved in four stages. Initially Loess models were used to define from observed data the age at which the juvenile growth period transitioned into stable adult weight for each species. Secondly, linear mixed effects models were developed to predict the magnitude and pattern of change in bodyweight expected during the identified

juvenile growth phase. Thirdly, the proportional increase in bodyweight was estimated for all individual juvenile animals from their last recorded weight in the clinical record prior to the target date for point mean calculation. For adult animals, the most recent recorded bodyweight prior to the point mean target date was included without adjustment. Finally, the point mean species bodyweight was calculated from the estimated point bodyweights of all individual animals at the target date of 31^{st} December for each year for annual reporting. Targeting of the last day of each year aimed to achieve the most representative annual mean bodyweight by maximising the number of bodyweight measurements in each annual data set. Outside this specific application the methods described are suitable for use on any selected target date. For the most recent full year of VetCompass data in 2023, calculations were derived from a sample of approximately 2 million dogs, 1 million cats, 100,000 rabbits, and 29,000 guinea pigs, of which 20 – 28% were juveniles depending on species.

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 <u>RUMA Companion Animal and Equine group</u>.

The <u>DDDVet</u> 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.

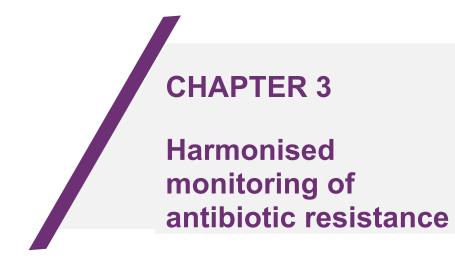
The DDDVet/animal is calculated (for each active ingredient/ route of administration and for both dogs and cats) using the method below:

Total amount of active ingredient (mg)

(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.







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 <u>National Control Programmes (NCP)</u>, and food products at retail. This surveillance is designed to be representative of food-producing animal populations, providing up-to-date data on AMR in poultry and pigs. Continuity of data from this long-term programme gives the ability to interrogate trends, identify emerging issues, and monitor the impact of the work to tackle AMR. Maintaining international harmonisation in this area also facilitates comparability of AMR data with other countries <u>across Europe</u>, which means the UK situation can be better contextualised and accurately understand risk.

In the harmonised monitoring programme, key livestock species are monitored for AMR in alternating years: poultry in even-numbered years, pigs in odd-numbered years. The 2023 data presented here originates from healthy pigs at slaughter in the UK and includes, for the first time, AMR in *Enterococcus* and *Campylobacter* species.

In this chapter, the results of baseline surveys are also presented of AMR in beef cattle and in bulk milk from dairy cattle in Great Britain (GB), and in sheep at slaughter in England and Wales, conducted under the <u>PATH-SAFE programme</u>. As such, they are not formally part of the harmonised monitoring programme, but they were designed to mirror the harmonised monitoring methodology. These surveys were conducted predominantly in 2023, but do not encompass an entire calendar year, and do not cover as much of the animal population, as the routine monitoring in pigs and poultry (section 3.2.1). Nonetheless, they give a more complete picture of AMR across the key food-producing species in GB. Further details are outlined in section 3.3.3.

The majority of the results in this chapter are reported as the percentage of individual bacterial isolates that are resistant to specific antibiotics. 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. Therefore, the results in this chapter do not necessarily indicate that a 'resistant' isolate would correspond to a clinical treatment failure (drug-resistant infection).

A second type of testing uses selective media to inhibit the growth of sensitive bacteria but allows the resistant bacteria to multiply, making them easier to detect. This allows detection of the proportion of individual animals (for pigs, beef cattle, and sheep at slaughter) or proportion of individual samples (for bulk milk from dairy cattle) carrying specific resistances, even at very low levels. This type of testing focuses on identifying the carriage of resistance to specific highest priority critically important antibiotics (HP-CIAs) or other antibiotics with human health relevance. Selective media was used in all species to detect the presence of extended spectrum beta lactamase (ESBL)-, AmpC-, and carbapenemase-producing *E. coli*

(**Fig. 3.3**), which are resistant to the third and fourth generation cephalosporins and carbapenems.

As part of the ongoing surveillance, some of the results from pigs are combined with those from poultry to produce <u>key outcome indicators</u> 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 for these species in the UK.

The Food Standards Agency (FSA) lead on the testing and reporting of AMR in retail meat, which is <u>published elsewhere</u>.

3.1 Summary

Routine UK-wide surveillance for AMR is conducted in pigs and poultry, in alternating years. This year, the results of baseline surveys are also presented of AMR arising from beef cattle, sheep, and dairy cattle in Great Britain, conducted under the PATH-SAFE programme. The PATH-SAFE surveys were conducted over shorter time periods than the routine surveillance, and covered less of the underlying animal populations. This means they could be less representative of national production, but nonetheless provide an important baseline for AMR in cattle and sheep.

In 2023, there were a small number of bacterial isolates detected that were resistant to antibiotics that are not used in food-producing animals in the UK: linezolid, colistin, and carbapenems.

Pigs

- *Escherichia coli* results from pigs are used to generate key harmonised outcome indicators, which are weighted by population size, and which give an overall measure of AMR in UK pig and poultry populations. These indicators show an overall positive picture for 2023.
 - The primary harmonised monitoring indicator has improved, showing an increasing trend in the percentage of *E. coli* isolates fully susceptible to the panel of antibiotics tested.
 - The secondary indicators have also improved over time, showing a decreasing trend in the percentage of multi-drug resistant (MDR) *E. coli* isolates. Levels of carriage of ESBL-/AmpC-producing *E. coli* and resistance to ciprofloxacin in *E. coli* remain low.
- *Campylobacter* was added to the pig surveillance programme this year. Moderate levels of ciprofloxacin resistance (20%) were detected in *C. coli.*
- *Enterococcus faecalis* and *E. faecium* were also added to the pig programme for the first time this year. Enterococci are indicator species for the detection of AMR in Grampositive bacteria. This addition also allows for the detection of vancomycin-resistant



enterococci (VRE), which are of clinical importance in people. No VRE were detected in pigs in 2023, but a low percentage of isolates were resistant to linezolid, which is not authorised for use in animals.

- In *Salmonella* species isolated from pigs, full susceptibility to the panel of antibiotics tested increased to 42% and MDR decreased to 38%, between 2021 and 2023.
- Selective media was used to detect carriage of specific resistances, even at very low levels within individual pigs. Carriage of ESBL-/AmpC-producing *E. coli* decreased from a high (30%) in 2021 to 23% in 2023. Amikacin-resistant *E. coli* were detected in 10% of pigs tested. For the first time in this programme, carriage of carbapenemase-producing and colistin-resistant *E. coli* were detected in individual pigs. These represent less than one third of a percent (0.3%) of the UK pig population entering the food chain.

PATH-SAFE

- Baseline surveys of AMR in beef cattle and sheep at slaughter, and in bulk milk from dairy cattle, were conducted under the <u>PATH-SAFE programme</u>. These surveys mirror the methodology used in the established surveillance in pigs and poultry, but cover a lower percentage of national populations, and were conducted over a shorter time period.
- An extremely high percentage (>86%) of *E. coli* arising from beef cattle, dairy cattle, and sheep were fully susceptible to the panel of antibiotics tested, and a low percentage (<9%) were MDR.
- No VRE were detected in beef cattle, sheep, or bulk milk.
- Selective media was used to detect the presence of specific resistances, even at very low levels within individual samples. This showed that 27% of beef cattle and 8.6% of sheep at slaughter were carrying ESBL-/AmpC-producing *E. coli* in their gut content. Using this technique, methicillin-resistant *Staphylococcus aureus* (MRSA) was detected in 1.3% of bulk milk samples prior to pasteurisation.
- In beef cattle, over 75% of *Campylobacter* tested were fully susceptible to the panel of antibiotics. Moderate resistance (16%) was detected in *C. jejuni* to the HP-CIA ciprofloxacin.
- In sheep, almost all *Salmonella* (99%) and over 70% of *Campylobacter* tested were fully susceptible to the panel of antibiotics.
- *Streptococcus uberis*, which causes mastitis, was detected in bulk milk. Using a tentative ECOFF, 42% of isolates were resistant to penicillin, which could be due to penicillins being the most commonly used antibiotic class in intramammary products sold.

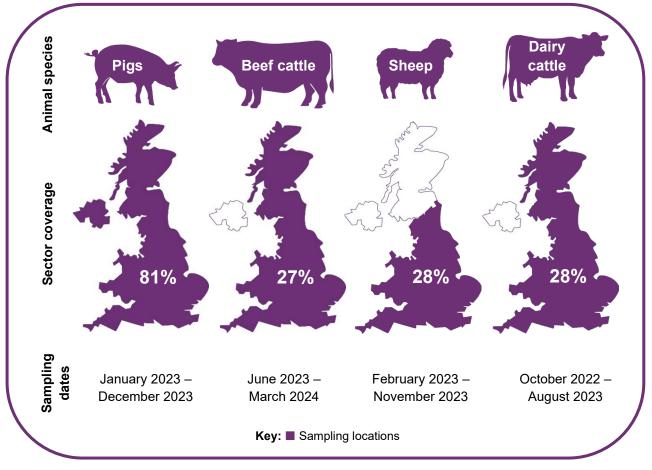


3.2 Methods

3.2.1 Sample collection and culture

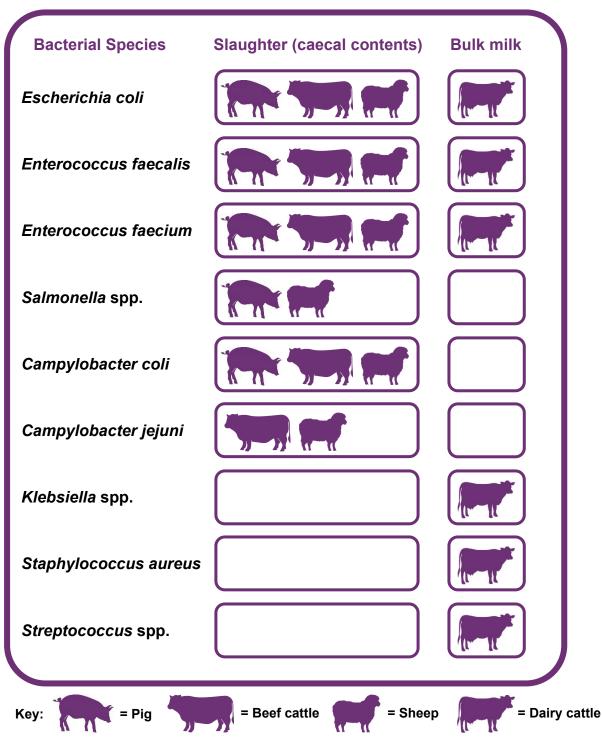
All countries within the UK were included in the sampling frame for pigs. Beef and dairy cattle surveys were conducted throughout Great Britain, and the sheep survey was conducted in England and Wales (**Fig 3.1**). The sampling plans were randomised, stratified, and weighted by slaughter throughput.

Figure 3.1: Summary of sampling locations, sector coverage and sampling dates for Harmonised Monitoring in pigs and PATH-SAFE surveys for beef cattle, sheep and dairy cattle in 2023.



Samples of faecal content were collected from the caeca of healthy pigs, beef cattle and sheep at slaughter as described in <u>Decision (EU) 2020/1729</u>. Bulk milk samples were collected from milk processors. These were cultured using <u>standardised methods</u>, or equivalent for bulk milk, and bacterial species were isolated, as summarised in **Fig. 3.2**. These bacteria underwent antimicrobial susceptibility testing (AST, see section 3.2.2), to give an indication of the prevalence of resistance in these bacteria across the UK population.

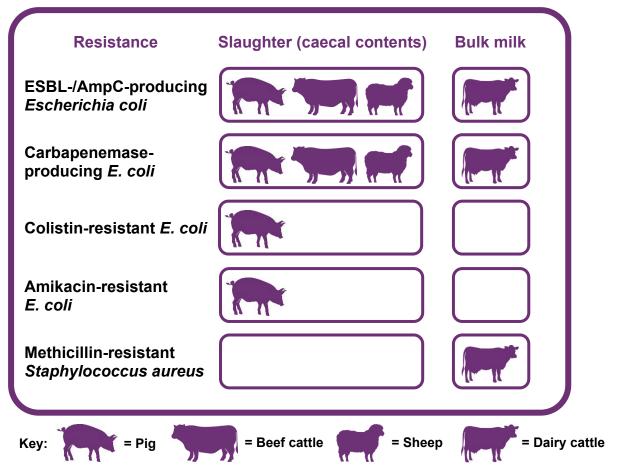
Figure 3.2: Summary of bacterial species isolated using non-selective media in 2023 according to sample origin.



Selective media was used to detect carriage of resistance to selected antibiotics, even at low levels, within individual animals and bulk milk samples, as summarised in **Fig. 3.3**. The selective media inhibits the growth of sensitive bacteria but allows the resistant bacteria to multiply, making them easier to detect. All samples were grown on media containing the third generation cephalosporin, cefotaxime, following <u>standardised methods</u>, to detect the growth

of *E. coli* which express the ESBL and/or AmpC phenotypes. Likewise, all samples were cultured onto media containing carbapenem antibiotics to detect *E. coli* resistant to this class of antibiotic. Pig caecal samples from GB were specifically cultured onto media containing colistin. This antibiotic, which is authorised for use but there have been no sales since 2020, is of increasing importance to human health. A subset of pig caecal samples from GB were also cultured onto media containing amikacin, to allow detection of *E. coli* which possess the *rmtb* gene. This gene encodes resistance to the aminoglycosides and is an emerging resistance mechanism in GB pigs. Bulk milk samples were additionally cultured for the presence of methicillin-resistant *Staphylococcus aureus* (MRSA). This bacterium can be zoonotic and usually has co-resistances to other antibiotics of human relevance.

Figure 3.3: Summary of resistances investigated using selective media in 2023 according to sample origin.



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 section S1.8 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.

In this chapter multidrug resistance (MDR) is defined as resistance to three or more antibiotic classes.

3.2.3 Interpretation of results

The European Committee on Antimicrobial Susceptibility Testing (<u>EUCAST</u>) methodology for epidemiological cut-off values (ECOFF) was used in this report. Where possible <u>EUCAST</u> <u>ECOFFs</u> were used to interpret the MIC results. EUCAST cut-off values are regularly under review and updated as new values and drug/bacteria species combinations are determined. Where no EUCAST values were available, European Food Safety Authority (<u>EFSA</u>) recommended cut-off values were used. Where neither defined EUCAST nor EFSA ECOFF values were available, tentative EUCAST ECOFF values were applied.

Historical data presented in this report has been updated to reflect cut-off values used in 2023. Results are provided in full for ECOFFS and clinical breakpoints CBPs (S2.1 – S2.7) 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, AmpC or carbapenem phenotypes detected from pigs and sheep, and bulk milk samples. Similar isolates from beef cattle are undergoing WGS in 2024.

3.2.5 Polymerase chain reaction

Polymerase chain reaction (PCR) was used to detect specific antibiotic resistance mechanisms in *E. coli* isolated from pigs using selective media: the *rmtB* gene present in amikacin-resistant isolates and selected *mcr* genes in colistin-resistant isolates.

3.2.6 Harmonised AMR outcome indicators

This report includes one primary and three secondary outcome indicators from the ongoing harmonised monitoring for AMR in pigs and poultry. The primary outcome indicator of complete susceptibility in *E. coli* is widely <u>recognised</u>. The secondary outcome indicators of percentage of MDR *E. coli*, percentage of *E. coli* resistant to the quinolone, ciprofloxacin, and the percentage of samples carrying ESBL- and/or AmpC-producing *E. coli* are also well <u>documented</u>. *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 outcome 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 1.4).

3.3 Results

Table 3.1: Classification of resistance as low, moderate, high etc. throughout the report is consistent with <u>EFSA definitions</u> 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 antibiotic was not tested (indicated with a ^).

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 an indication of the UK's progress in combatting AMR in pigs and poultry.

The primary indicator is the percentage of *E. coli* isolates fully susceptible to the entire panel of antibiotics. The secondary indicators are: the percentage of MDR *E. coli* isolates; the percentage of *E. coli* isolates with decreased susceptibility to the fluoroquinolone ciprofloxacin; and the percentage of caecal samples testing positive for presumptive ESBL-/AmpC-producing *E. coli*. Thus, seeing the primary indicator increase and the secondary indicators decrease is positive.

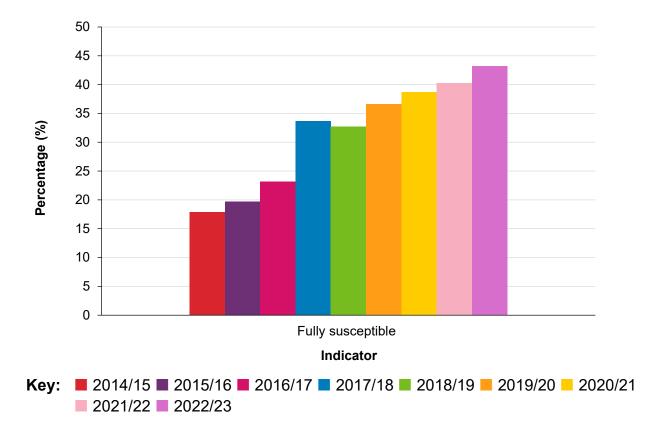
For the 2022 to 2023 monitoring period, all indicators show considerable improvement since the start of the programme (2015/2016 for presumptive ESBL-/AmpC-producing *E. coli*, and 2014/2015 for all other indicators). The primary indicator is at a new high of 43% and is 2.4 times what it was in 2014/2015 (**Fig. 3.4**).



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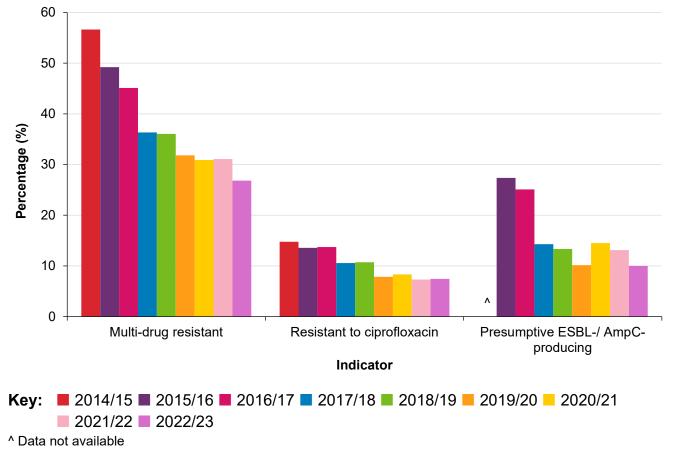
Figure 3.4: Primary outcome indicator: percentage of *Escherichia coli* isolates fully susceptible from broilers, turkeys and pigs weighted by PCU, averaged over two years.



The secondary outcome indicators remain substantially lower than those reported at the beginning of the monitoring period: the percentage of MDR isolates (27%) is at a new low and the percentage of presumptive ESBL-/AmpC-producing *E. coli* (10%) remains low (**Fig. 3.5**). Resistance to ciprofloxacin (7.5%) appears to have stabilised since 2019/20.



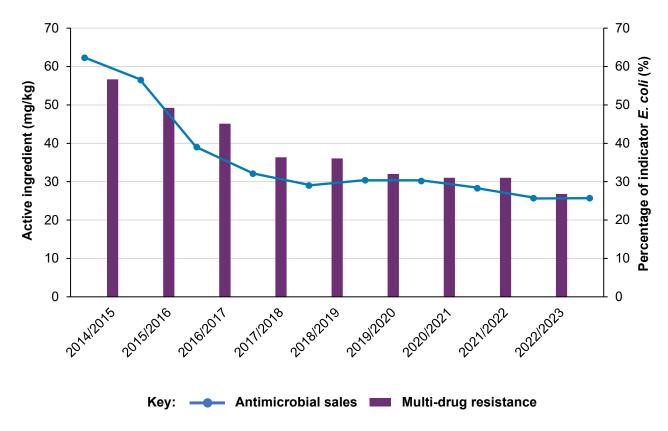
Figure 3.5: Secondary outcome indicators: percentage of *Escherichia coli* from broilers, turkeys and pigs weighted by PCU, averaged over two years. ESBL/AmpC results refer to caecal samples, all other indicators refer to isolates (see section 3.3.1).



Harmonised outcome indicators are also measured for antibiotic sales (see section 1.3.6). Overlaying indicators for sales with those for resistance illustrates how reductions in antibiotic sales since 2014 have been reflected in reductions in resistance over the same time period. In **Fig. 3.6**, the primary indicator for antibiotic consumption is shown along with the secondary indicator of multi-drug resistant *E. coli*.



Figure 3.6: Antibiotic active ingredient sold for use in food-producing animals adjusted for population (mg/kg) and percentage of multi-drug resistant *Escherichia coli* isolates from broilers, turkeys and pigs weighted by PCU, averaged over two years, 2014 to 2023.



3.3.2 Pigs

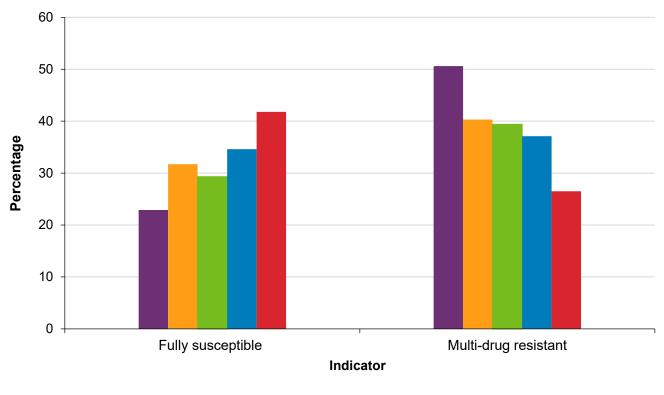
Samples were collected from January to December 2023 from slaughterhouses processing 81% of domestically-produced pigs.

3.3.2.1 Escherichia coli

A total of 170 *E. coli* isolates from pig caecal samples were tested. Full susceptibility to the entire antibiotic panel increased from 35% in 2021 to 42% in 2023, and has substantially improved from 2015 levels (23%) (**Fig. 3.7**). MDR decreased from 37% of isolates in 2021 to 27% of isolates in 2023, a consistent improvement from 2015 (51%).



Figure 3.7: Percentage of fully susceptible and multi-drug resistant *Escherichia coli* isolated from healthy pigs at slaughter (n=170 in 2023).



Key: 2015 2017 2019 2021 2023

Resistance to non-HP-CIAs is shown in **Fig. 3.8 (A)**. Between 2021 and 2023, there were reductions in resistance to chloramphenicol (11%), tetracycline (43%), sulfamethoxazole (30%), and trimethoprim (26%). Resistance to these antibiotics has reduced by 20 to 30 percentage points since 2015, which is most likely attributable to reductions in antibiotic use. Chapter 2 shows that usage of tetracyclines and trimethoprim-sulfonamides decreased by 80% and 86% respectively between 2015 to 2022, although these have increased between 2022 and 2023 (**Fig. 2.3**). No resistance was detected to amikacin, meropenem or tigecycline.

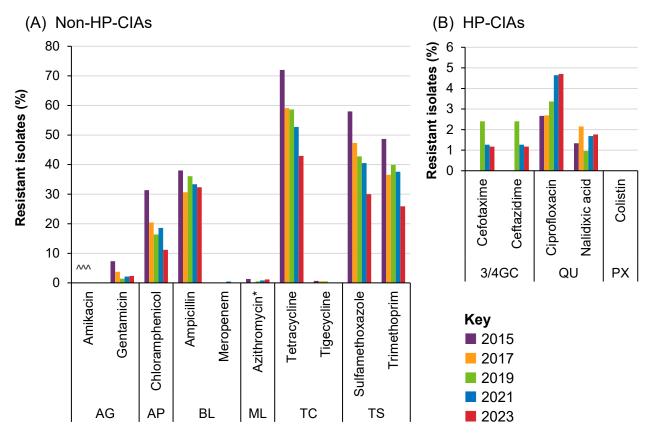
Resistance to HP-CIAs is shown in **Fig. 3.8 (B)** and has remained low. Two isolates (1.2%) were resistant to the third-generation cephalosporins cefotaxime and ceftazidime. One of these expressed the ESBL phenotype. The other expressed both ESBL and AmpC phenotypes. Both isolates were sensitive to ciprofloxacin. Resistance to ciprofloxacin increased from 2.7% to 4.6% between 2015 and 2021 but has remained stable in 2023 (4.7%). No resistance was detected to colistin.



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Figure 3.8: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Escherichia coli* isolated from healthy pigs at slaughter (n=170 in 2023). 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 Enterococcus spp.

E. faecalis and *E. faecium* are new additions to the AMR surveillance programme, first introduced for poultry in 2022 and pigs in 2023. Enterococci were included as indicator species for resistance in Gram-positive bacteria. This also allows us to test for resistance against a wider antibiotic panel including vancomycin and linezolid. Vancomycin-resistant enterococci (VRE) are of particular concern to public health, as they are associated with higher human mortality rates than vancomycin-sensitive enterococci. Linezolid is one of the few remaining treatment options for MRSA and for VRE. *E. faecium* is the more prevalent species in pigs, and is commonly involved in acquisition and transfer of AMR genes. *E. faecalis* is more relevant to human health.



Enterococcus faecalis

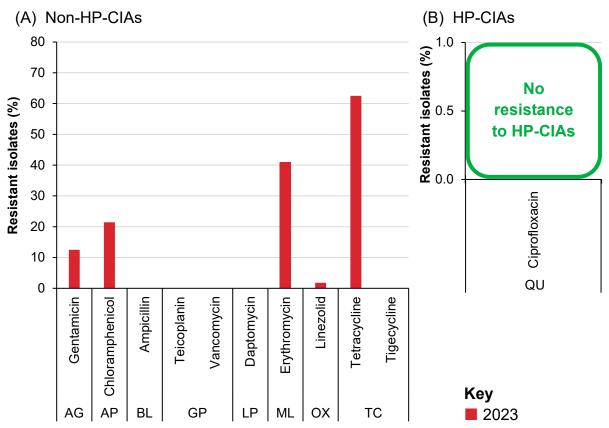
Resistance in *E. faecalis* isolated from pig caecal samples is shown in **Fig. 3.9**. A total of 56 isolates were tested. Full susceptibility to the antibiotic panel was 36%. MDR was detected in 30% of isolates and VRE were not detected.

Very high levels of resistance were seen to tetracyclines (63%) and high levels to erythromycin (41%) and chloramphenicol (21%). Similar levels of resistance to tetracycline and erythromycin were seen last year in broilers and even higher levels in turkeys. As shown in **Fig. 2.2**, tetracyclines are the most-used antibiotic class in pigs. HP-CIA resistance was not detected.

Detection of resistance to linezolid (1.8%) is notable, as this antimicrobial is not authorised for use in pigs in the UK but is used to treat MDR human infections such as VRE. Gentamicin (13% resistance in *E. faecalis*) and chloramphenicol (21%) are also not authorised in the UK, but products containing aminoglycosides other than gentamicin and amphenicols other than chloramphenicol are authorised. Gentamicin is also occasionally used in pigs in exceptional circumstances under the prescribing cascade (2.57 kg and 0.004 mg/kg in 2023).



Figure 3.9: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Enterococcus faecalis* isolated from healthy pigs at slaughter in 2023 (n=56). 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

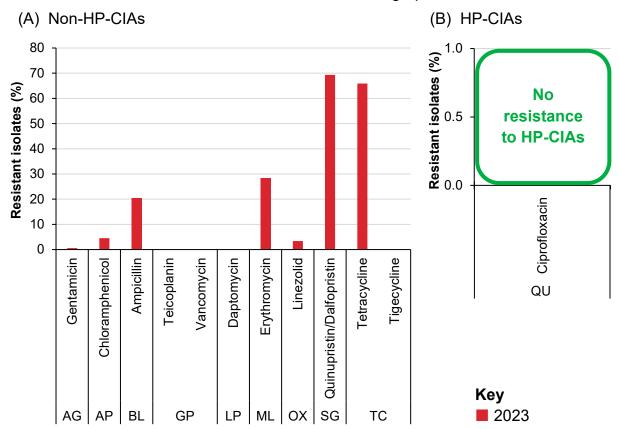
Enterococcus faecium

Resistance in *E. faecium* isolated from pig caecal samples is shown in **Fig. 3.10**. A total of 176 isolates were tested. Full susceptibility to the antibiotic panel was 18%. MDR was detected in 31% of isolates and VRE were not detected.

Very high levels of resistance were seen to tetracyclines (66%) and high levels to erythromycin (28%) and ampicillin (21%). This is consistent with use of these antibiotic classes in pigs. As shown in **Fig. 2.2**, tetracyclines, penicillins and macrolides account for 32%, 19% and 11% of antibiotic use in pigs respectively in 2023. Similar resistance levels to tetracycline and erythromycin were seen in 2022 in broilers and even higher levels in turkeys. Resistance levels to quinupristin-dalfopristin were very high (69%); however, contextualisation of this result is difficult, as other reports use a variety of cut-off values. HP-CIA resistance was not detected.

Detection of resistance to linezolid (3.4%) is notable as this antimicrobial is not authorised for use in pigs in the UK but is used to treat MDR infections in humans, including VRE.

Figure 3.10: Resistance to non-HP-CIAs (A), and HP-CIAs (B) in *Enterococcus faecium* isolated from healthy pigs at slaughter in 2023 (n=176). 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, SG: streptogramins, TC: tetracyclines

3.3.2.3 Salmonella spp.

Salmonella is an important cause of foodborne disease in people and can cause disease in animals. The UK has been monitoring AMR in *Salmonella* obtained from pig caecal samples since 2021. Prior to this (2015-2019), *Salmonella* were isolated from carcass swabs. The prevalence of *Salmonella* in gut contents is much higher than on <u>carcasses</u> and so the results presented here offer a better reflection of AMR in *Salmonella* in healthy pigs at slaughter.

A total of 97 *Salmonella* isolates were tested. There are many serovars of *Salmonella* and their differences impact on overall resistance trends. The most prevalent serovars identified included: monophasic *S.* Typhimurium (29%), *S.* Derby (29%), *S.* Panama (14%), *S.* Typhimurium (9%) and *S.* Kedougou (5%).

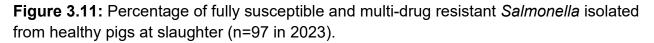
Full susceptibility to the panel of antibiotics tested increased to 42% in 2023 from 39% in 2021 (**Fig. 3.11**). Within individual serovars, 89% of the *S*. Derby isolates and 80% of the *S*.

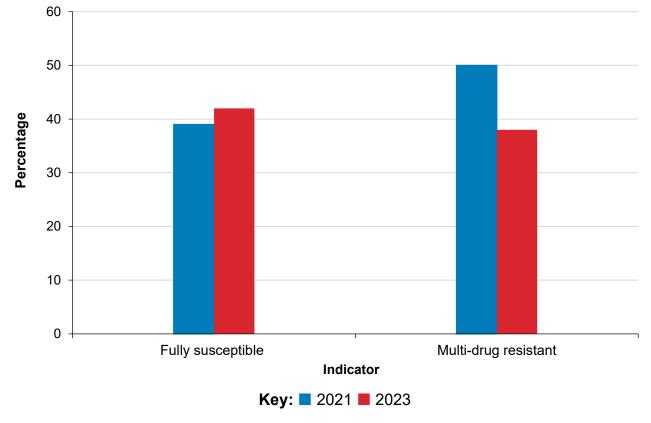


Harmonised monitoring

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Kedougou isolates were fully susceptible. The number of MDR isolates decreased to 38% in 2023 from 50% in 2021.



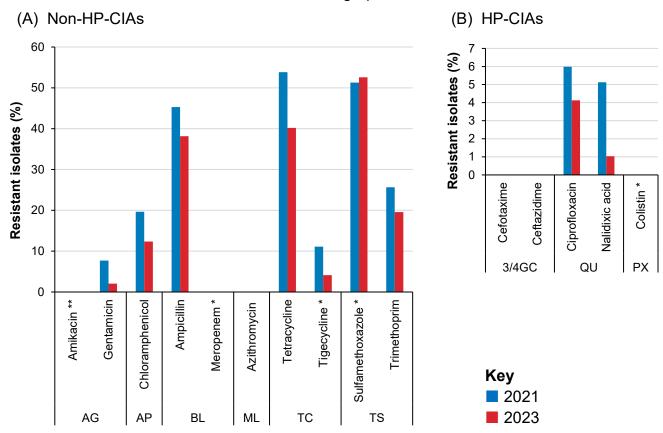


As in 2021, the highest levels of resistance were to antibiotics in the most-used antibiotic classes in pig medicine: sulfamethoxazole (53%, trimethoprim/sulfonamide class), tetracycline (40%, tetracyclines) and ampicillin (38%, beta-lactams) (**Fig. 3.12 (A)**). Resistance to several non-HP-CIAs reduced between 2021 and 2023, including to tetracyclines which reduced by 14 percentage points. Resistance was not detected to amikacin, meropenem or azithromycin.

No resistance to the HP-CIAs third-generation cephalosporins (cefotaxime and ceftazidime) or to colistin was detected in either 2021 or 2023 (**Fig. 3.12 (B)**). Resistance to the fluoroquinolones ciprofloxacin (4.1%) and nalidixic acid (1.0%) was lower in 2023 than in 2021. This corresponds with the 41% reduction in the use of fluroquinolones in the pig sector between 2021 and 2023 to just 0.007 mg/kg (4.8 kg active ingredient, **Fig 2.5**).



Figure 3.12: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Salmonella* isolated from healthy pigs at slaughter (n=97 in 2023). Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



* Interpreted using an EFSA-recommended ECOFF

** Interpreted using a tentative EUCAST 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

3.3.2.4 Campylobacter coli

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. *Campylobacter* was added to the pig surveillance programme for the first time this year, by testing AMR in *C. coli*. *C. coli* is the more prevalent *Campylobacter* species found in pigs and is usually more resistant to antibiotics than *C. jejuni*. *C. coli* can also transfer resistance genes to *C. jejuni* which is more commonly associated with human gastrointestinal disease.

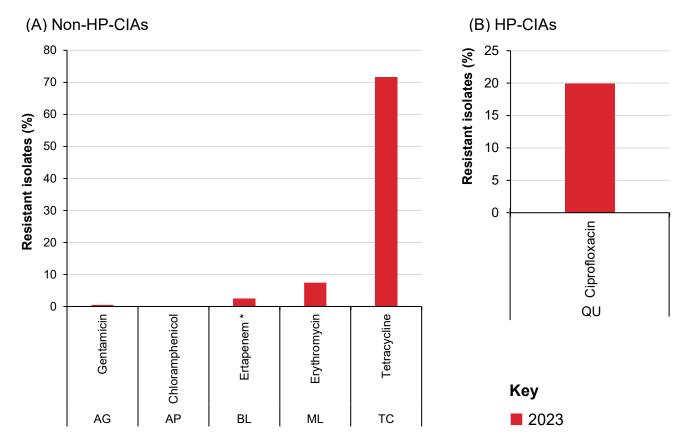
Resistance in *C. coli* isolated from pig caecal samples is shown in **Fig. 3.13**. A total of 201 isolates were tested, of which 21% were susceptible to all of the antibiotics tested, and 2% were MDR.

Levels of resistance to tetracycline (72%) were extremely high, and resistance to the fluroquinolone ciprofloxacin was moderate (20%) despite decreasing use of fluroquinolones

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by the pig sector (**Fig. 2.5**). Co-resistance to ciprofloxacin and erythromycin was rare, with only one isolate (0.5%) expressing resistance to both. Erythromycin is a first-line antibiotic for treating *Campylobacter* infection in people.

Figure 3.13: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Campylobacter coli* isolated from healthy pigs at slaughter in 2023 (n=201). Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



* Interpreted using an EFSA-recommended ECOFF

AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, QU: quinolones, TC: tetracyclines



Box 3.1: Ertapenem resistance in *Campylobacter* spp.

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 a HP-CIA and antibiotic of last resort in human health. Carbapenems are illegal to use in food-producing animals in the UK. Ertapenem is used in some countries to treat serious invasive *Campylobacter* infections in humans and was added to the panel to maintain international harmonisation of surveillance for this antibiotic class.

In 2022, the tentative results of resistance to ertapenem in UK broilers and turkeys were presented using the suggested EFSA-recommended ECOFF of 0.5 mg/L, as no EUCAST validated ECOFFs were available. This remains the same in 2023 and so ertapenem resistance in UK pigs was analysed using the EFSA-recommended ECOFF.

In 2023, levels of resistance to ertapenem in *C. coli* from UK pigs was low (2.5%). This result is difficult to interpret as work is still ongoing to explore whether this antibiotic is the best representative of this class. The isolates are being further evaluated along with consultation with public health colleagues as to the most appropriate One Health measure of carbapenem resistance within the UK context.

3.3.3 Pathogen Surveillance in Agriculture, Food and Environment (PATH-SAFE)

The Pathogen Surveillance in Agriculture, Food and Environment (<u>PATH-SAFE</u>) is a UKwide cross-government programme. PATH-SAFE was launched in 2021 and concludes in March 2025. It has provided departments across government the opportunity to investigate knowledge gaps in AMR and foodborne disease within agri-food chains.

AMR surveillance is well-established in pigs and poultry entering the food chain in the UK, as demonstrated in the UK-VARSS annual reports. However, there is no equivalent programme to measure the prevalence of AMR in cattle or sheep. Under PATH-SAFE, a number of AMR surveillance pilots were carried out to address these gaps. These pilots were made possible through extensive collaboration between government departments and industry partners.

The following sections report the results from AMR surveillance pilots in dairy cattle, beef cattle, and sheep. They were designed to mirror the methodology used in the routine surveillance in pigs and poultry. The PATH-SAFE surveys were conducted over shorter time periods than the routine surveillance and covered less of the underlying animal populations. This means they could be less representative of national production, but nonetheless provide an important baseline for AMR in cattle and sheep.

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3.3.4 Beef cattle (PATH-SAFE)

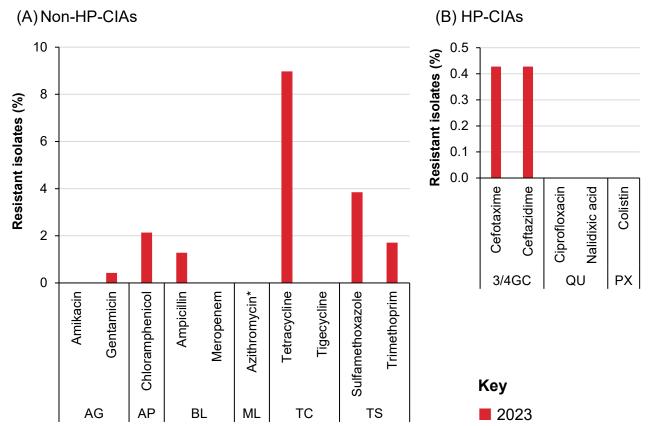
This pilot survey was conducted as part of the PATH-SAFE programme (section 3.3.3). Samples were collected from June 2023 to March 2024 from slaughterhouses processing 27% of domestically-produced prime cattle in Great Britain.

3.3.4.1 Escherichia coli

Resistance of *E. coli* isolated from cattle is shown in **Fig. 3.14**. A total of 234 *E. coli* isolates were tested. Full susceptibility to the antibiotic panel was extremely high (90%) and 2.6% of isolates were MDR.

Levels of resistance were generally low (<9%) or not detected. Of the HP-CIAs, one isolate (0.4%) was resistant to the third-generation cephalosporins cefotaxime and ceftazidime. No resistance was seen to the other HP-CIAs tested.

Figure 3.14: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Escherichia coli* isolated from healthy cattle at slaughter in 2023 (n=234). Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



* 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 Enterococcus spp.

Enterococci were included as indicator species for resistance in Gram-positive bacteria. This also allows us to test for resistance against a wider antibiotic panel including vancomycin and linezolid. Vancomycin-resistant enterococci (VRE) are of particular concern to public health, as they are associated with higher human mortality rates than vancomycin-sensitive enterococci. Linezolid is one of the few remaining treatment options for MRSA and for VRE. *E. faecium* is the more prevalent species in beef cattle and is commonly involved in acquisition and transfer of AMR genes. *E. faecalis* is more relevant to human health.

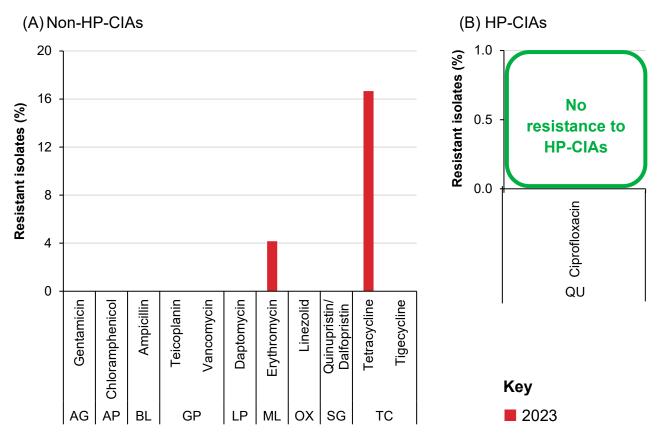
Enterococcus faecalis

Resistance in *E. faecalis* isolated from cattle is shown in **Fig. 3.15**. A total of 24 isolates were tested. Full susceptibility to the antibiotic panel was 83%. No isolates were MDR and VRE were not detected.

Four isolates (17%) were resistant to tetracycline and one isolate (4.2%) was also resistant to erythromycin. No resistance was detected to the other antibiotics tested on the panel. HP-CIA resistance was not observed.



Figure 3.15: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Enterococcus faecalis* isolated from healthy cattle at slaughter in 2023 (n=24). 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

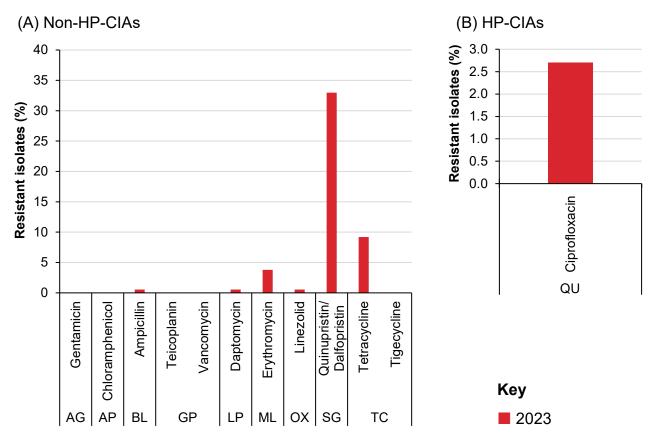
Enterococcus faecium

Resistance in *E. faecium* isolated from cattle is shown in **Fig. 3.16**. A total of 185 isolates were tested. Full susceptibility to the antibiotic panel was 54%. Two isolates (1.1%) were MDR. VRE were not detected.

Low levels of resistance were seen to tetracycline (9.2%) and erythromycin (3.8%). Resistance levels to quinupristin-dalfopristin were high (33%); however, contextualisation is difficult, as other reports use a variety of cut-off values. Resistance to the other non-HP-CIAs tested was generally very low or not detected. Resistance levels to the fluoroquinolone ciprofloxacin (a HP-CIA) were low (2.7%).



Figure 3.16: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Enterococcus faecium* isolated from healthy cattle at slaughter in 2023 (n=185). 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, SG: streptogramins, TC: tetracyclines

3.3.4.3 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. *C. coli* is the more prevalent *Campylobacter* species found in pigs and tends to be more resistant to antibiotics than *C. jejuni*. *C. coli* can also transfer resistance genes to *C. jejuni* which is more commonly associated with human gastrointestinal disease.

Campylobacter coli

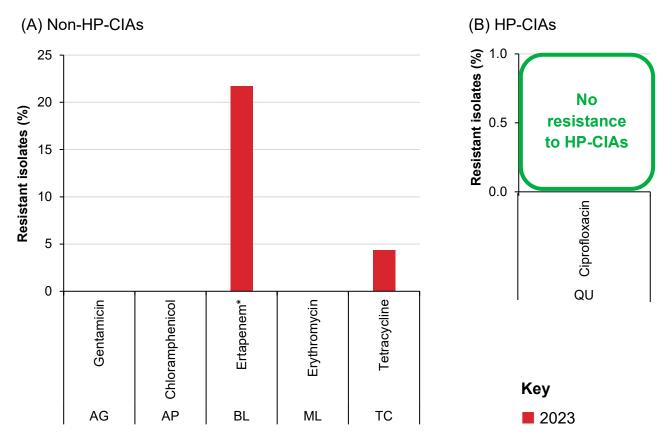
Resistance in *C. coli* isolated from cattle is shown in **Fig. 3.17**. A total of 23 isolates were tested. Full susceptibility to the entire panel was 78% and none were MDR.

One isolate (4.3%) was resistant to tetracycline. High resistance was detected to ertapenem (22%). This result is difficult to interpret as there is still scientific debate into the suitability of using ertapenem to represent the carbapenem antibiotic class (see **Box 3.1**). No resistance



was seen to the other antibiotics tested on the panel. Resistance to the fluoroquinolone ciprofloxacin (a HP-CIA) was not detected.

Figure 3.17: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Campylobacter coli* isolated from cattle in 2023 (n=23). Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



* Interpreted using an EFSA-recommended ECOFF

AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, QU: quinolones, TC: tetracyclines

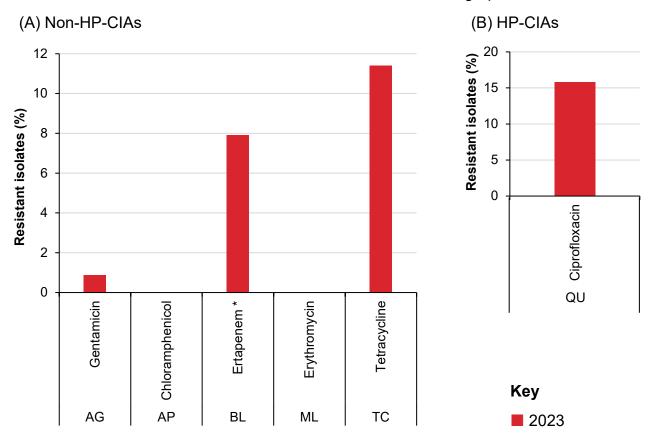
Campylobacter jejuni

Resistance in *C. jejuni* isolated from cattle is shown in **Fig. 3.18**. A total of 114 isolates were tested. Full susceptibility to the entire panel was 76% and one isolate (0.9%) was MDR.

Moderate levels of resistance were seen to tetracycline (11%) and very low levels to gentamicin (0.9%). Low resistance was detected to ertapenem (7.9%). This result is difficult to interpret as there is still scientific debate into the suitability of using ertapenem to represent the carbapenem antibiotic class (see **Box 3.1**). Resistance levels to the fluoroquinolone ciprofloxacin (a HP-CIA) was moderate (16%). Resistance was not detected to the other antibiotics tested on the panel.



Figure 3.18: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Campylobacter jejuni* isolated from healthy cattle at slaughter in 2023 (n=114). Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



* Interpreted using an EFSA-recommended ECOFF

AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, QU: quinolones, TC: tetracyclines

3.3.5 Sheep (PATH-SAFE)

This pilot survey was conducted as part of the PATH-SAFE programme (section 3.3.3). Samples were collected from February to November 2023 from slaughterhouses processing 28% of domestically-produced sheep in England and Wales.

Of the animals sampled, 95 were adult sheep (over 12 months old, adult animals which have a permanent incisor erupted through the gum), and 473 were lambs (under 12 months, young animals lacking permanent teeth). Results presented here are for all animals sampled, but additional analysis was performed, where appropriate, to test for differences between the age groups.

3.3.5.1 Escherichia coli

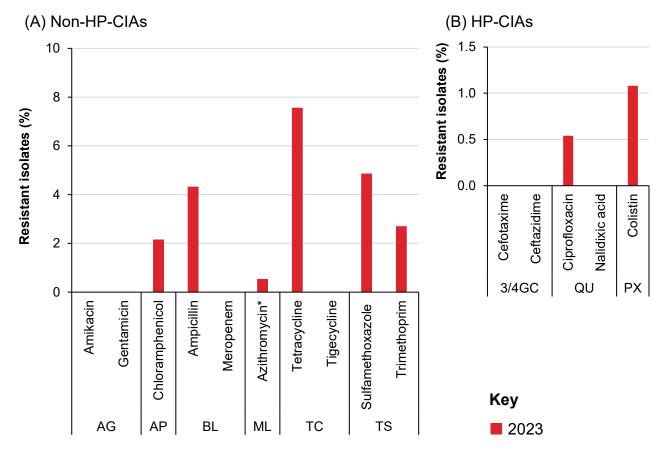
185 caecal samples were tested for *E. coli* and a total of 185 isolates were recovered. Resistance of these isolates is shown in **Fig. 3.19**. Full susceptibility to the entire panel was



extremely high at 89% and was similar between adult sheep (80%) and lambs (90%). 7 isolates (3.8%) were MDR.

Resistance to the non-HP-CIAs tested was generally low (<8%) or not detected. Of the HP-CIAs, two isolates (1.1%) were resistant to colistin. No plasmid-mediated *mcr* genes were detected, which is reassuring because plasmids can facilitate transmission of resistance genes between different bacterial strains and species. One isolate (0.5%) was resistant to the fluoroquinolone ciprofloxacin. No resistance was seen to the other HP-CIAs tested.

Figure 3.19: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Escherichia coli* isolated from healthy sheep at slaughter in 2023 (n=185). Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



* 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

3.3.5.2 Enterococcus spp.

Enterococci were included as indicator species for resistance in Gram-positive bacteria. This also allows us to test for resistance against a wider antibiotic panel including vancomycin and linezolid. Vancomycin-resistant enterococci (VRE) are of particular concern to public health, as they are associated with higher human mortality rates than vancomycin-sensitive enterococci. Linezolid is one of the few remaining treatment options for MRSA and for VRE.

E. faecium is the more prevalent species in sheep, and is commonly involved in acquisition and transfer of AMR genes. *E. faecalis* is more relevant to human health.

Enterococcus faecalis

E. faecalis was detected in 13% of 485 samples tested. Of these isolates, 52 were tested for AMR. Full susceptibility to the entire panel was 90%. None were MDR, and VRE were not detected.

Five isolates (9.6%) were resistant to tetracycline and no resistance was detected to the other antibiotics tested on the panel, including HP-CIAs (Table S2.6.4 in Supplementary Material 2).

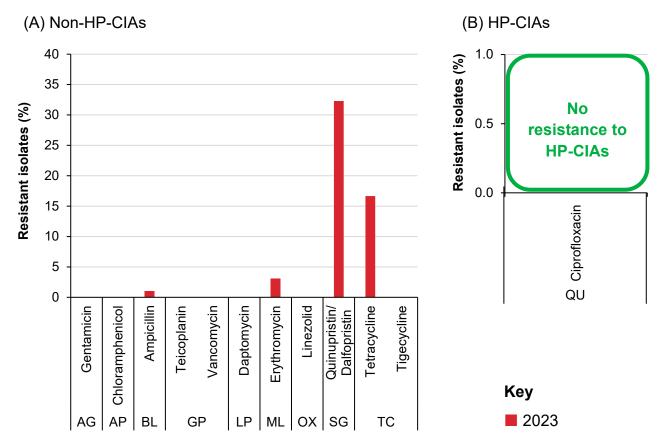
Enterococcus faecium

E. faecium was detected in 21% of 485 samples tested. Of these isolates, 96 were tested and their resistance is shown in **Fig. 3.20**. Full susceptibility to the entire panel was 57%. MDR was detected in 4.2% isolates and VRE were not detected.

Moderate levels of resistance were seen to tetracycline (17%), low levels to erythromycin (3.1%) and very low levels to ampicillin (1.0%). Resistance levels to quinupristin-dalfopristin were high (32%); however, contextualisation is difficult, as other reports use a variety of cutoff values. No resistance was detected to the other antibiotics tested on the panel, including HP-CIAs.



Figure 3.20: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Enterococcus faecium* isolates from healthy sheep at slaughter in 2023 (n=96). 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, SG: streptogramins, TC: tetracyclines

3.3.5.3 Salmonella

Salmonella was detected in 8.9% of caecal samples. The most prevalent serovars identified included *S. enterica* spp. *diarizonae* (77%), a low pathogenicity sheep-adapted strain, and *S.* Typhimurium (20%). Full susceptibility to the entire panel was extremely high (99%), and none were MDR (Table S2.6.6 in Supplementary Material 2).

Of the HP-CIAs, one isolate (0.9%) was resistant to colistin; however, no known *mcr* genes were detected though WGS. This is not an exceptional finding in Group D *Salmonella*. No resistance was detected to the other antibiotics tested on the panel.

3.3.5.4 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. *C. coli* is the more prevalent *Campylobacter* species found in pigs and tends to be more resistant to antibiotics than *C. jejuni. C. coli* can

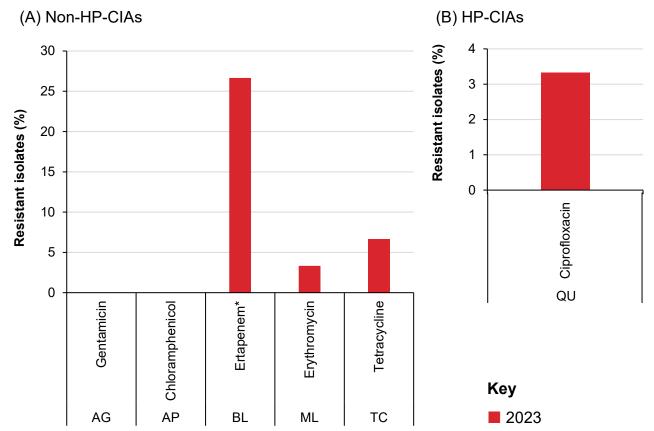
also transfer resistance genes to *C. jejuni* which is more commonly associated with human gastrointestinal disease.

Campylobacter coli

C. coli was detected in 8% of 411 samples tested. Of these isolates, 30 were tested and their resistance is shown in **Fig. 3.21**. Full susceptibility to the entire antibiotic panel was very high at 70%, and one isolate (3.3%) was MDR.

Low levels of resistance were detected to tetracycline (6.7%) and erythromycin (3.3%). Erythromycin is a first-line antibiotic for treating *Campylobacter* infection in people. No resistance was detected to chloramphenicol or gentamicin. High resistance was detected to ertapenem (27%). There is still scientific debate into the suitability of using ertapenem to represent the carbapenem antibiotic class (see **Box 3.1**). Resistance levels to the fluoroquinolone ciprofloxacin was low (3.3%).

Figure 3.21: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Campylobacter coli* isolates from healthy sheep at slaughter in 2023 (n=30). Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



^{*} Interpreted using an EFSA-recommended ECOFF AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, QU: quinolones, TC: tetracyclines

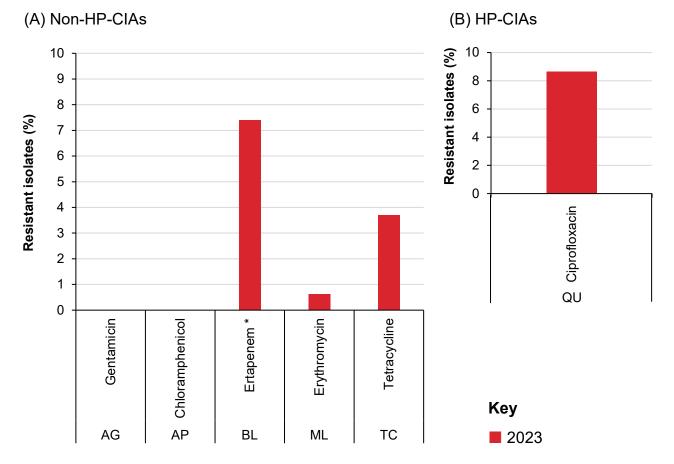


Campylobacter jejuni

C. jejuni was detected in 41% of 411 samples tested. Of these isolates, 162 were tested and their resistance is shown in **Fig. 3.22**. Full susceptibility to the entire antibiotic panel was extremely high at 87%, and one isolate (0.6%) was MDR.

Low levels of resistance was detected to tetracycline (3.7%) and very low levels to erythromycin (0.6%). Erythromycin is a first-line antibiotic for treating *Campylobacter* infection in people. Resistance levels to ertapenem was also low (7.4%). There is still scientific debate into the suitability of using ertapenem to represent the carbapenem antibiotic class (see **Box 3.1**). No resistance was detected to chloramphenicol or gentamicin. Resistance to the fluoroquinolone ciprofloxacin was low (8.6%).

Figure 3.22: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Campylobacter jejuni* isolates from healthy sheep at slaughter in 2023 (n=162). Interpreted using EUCAST ECOFFs unless otherwise indicated.



* Interpreted using an EFSA-recommended ECOFF

AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, QU: quinolones, TC: tetracyclines



3.3.6 Dairy cattle (PATH-SAFE)

This pilot survey was conducted as part of the PATH-SAFE programme (section 3.3.3) and covered 28% of dairy farms in Great Britain. 1,055 bulk milk samples collected by National Milk Records (NMR) were tested by APHA for resistance genes and resistant bacteria.

Bulk milk is raw, refrigerated milk collected from multiple cows on a farm. The presence of bacteria in bulk tank milk can be due to faecal contamination (e.g. *E. coli*, enterococci) or the transfer of bacteria from the mammary gland during the milking process (e.g. streptococci). This milk subsequently undergoes pasteurisation.

3.3.6.1 Escherichia coli

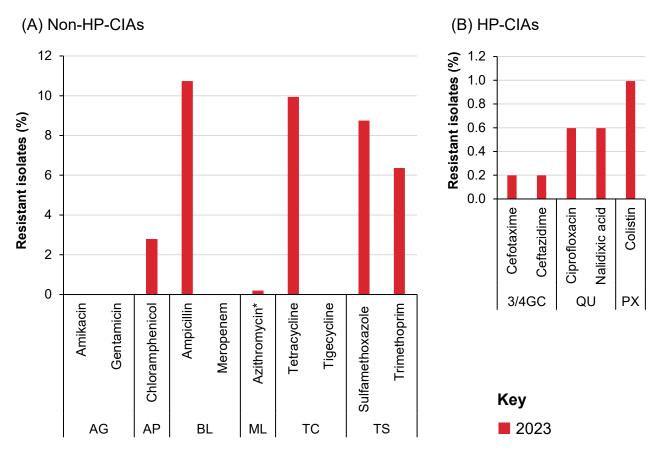
E. coli are part of the normal gut flora. A total of 503 *Escherichia coli* were isolated from bulk milk. 86% of these were fully susceptible to all antibiotics in the panel and 8.2% of isolates were MDR. Results of AST are shown in **Fig. 3.23**.

Moderate levels of resistance were seen to ampicillin (11%), and low levels of resistance to tetracycline (9.9%), sulfamethoxazole (8.7%), trimethoprim (6.4%) and chloramphenicol (2.8%). Antibiotic use data which has been voluntarily collated from a sub-section of the dairy industry has not been published by breakdown of antibiotic class (see section 2.3.6.1). Previous <u>dairy sample survey estimates</u> from 2019 suggest that tetracyclines and beta-lactams each accounted for around 20% of antibiotic active ingredient administered to dairy cows.

Very low levels of resistance were detected to HP-CIAs, including the third-generation cephalosporins cefotaxime and ceftazidime (both 0.2%), the fluoroquinolone ciprofloxacin (0.6%), and colistin (1.0%). Antibiotic use data from 2023 has been voluntarily submitted by a sub-section of the dairy industry (30%) and, whilst it is not representative of the national sector, it does indicate very low HP-CIA use (0.06% of total use) which is consistent with this finding.



Figure 3.23: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Escherichia coli* isolated from bulk milk samples in 2023 (n=503). Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



* 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

3.3.6.2 Enterococcus spp.

Enterococci were included as indicator species for resistance in Gram-positive bacteria. This also allows us to test for resistance against a wider antibiotic panel including vancomycin and linezolid. Vancomycin-resistant enterococci (VRE) are of particular concern to public health, as they are associated with higher human mortality rates than vancomycin-sensitive enterococci. Linezolid is one of the few remaining treatment options for MRSA and for VRE. *E. faecium* is commonly involved in acquisition and transfer of AMR genes. *E. faecalis* is more relevant to human health.

Enterococcus faecalis

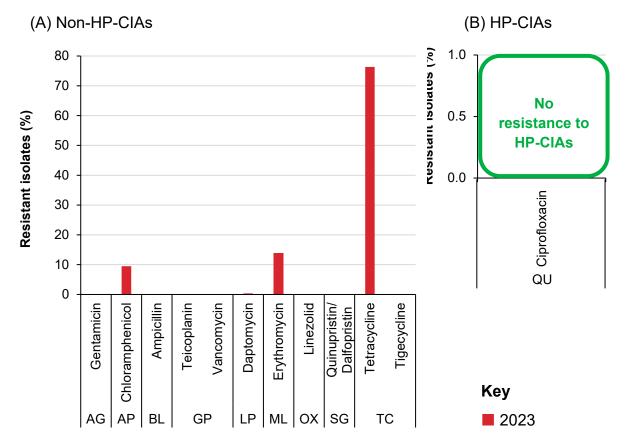
Resistance in *E. faecalis* isolated from bulk milk samples is shown in **Fig. 3.24**. All 296 isolates recovered were tested. Full susceptibility to the antibiotic panel was 23%. MDR was detected in 5.7% of isolates and VRE were not detected.



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Extremely high levels of resistance were seen to tetracycline (76%), which is also observed in other animals and bacterial species. This could reflect historically high use of this class of antibiotics in veterinary medicine. Dairy sample survey estimates from 2019 suggest that tetracyclines account for <u>around 20%</u> of antibiotic active ingredient administered to dairy cows. Moderate levels of resistance to erythromycin (14%) and low levels to chloramphenicol (9.5%) were detected. A very low level of resistance to daptomycin (0.3%) was observed which is not authorised for use in animals in the UK. HP-CIA resistance was not detected.

Figure 3.24: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Enterococcus faecalis* isolated from bulk milk samples in 2023 (n=296). 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

Enterococcus faecium

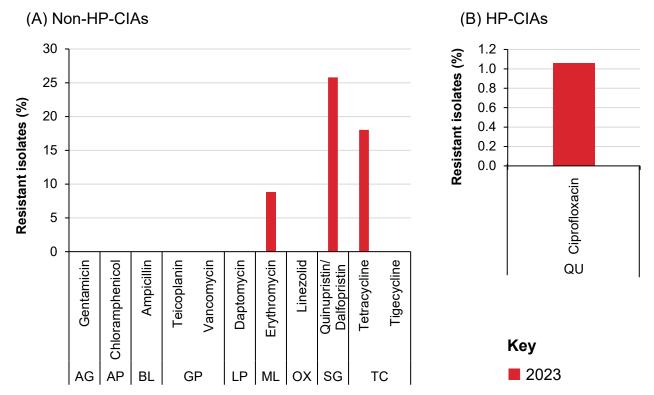
Resistance in *E. faecium* isolated from bulk milk samples is shown in **Fig. 3.25**. A total of 283 isolates were tested. Full susceptibility to the antibiotic panel was 75%. No MDR isolates were found and VRE were not detected.

Moderate levels of resistance were seen to tetracycline (18%) and low levels to erythromycin (8.8%). Resistance levels to quinupristin-dalfopristin were high (26%), however

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contextualisation is difficult as other reports use a variety of cut-off values. Of the HP-CIAs, three isolates (1.1%) were resistant to the fluoroquinolone ciprofloxacin. In the UK, there are no intramammary products authorised for dairy cattle which contain fluoroquinolones. Sales of fluoroquinolone containing injectable products authorised for cattle can be analysed to estimate use of these products in the sector (see section 2.4). In 2023, UK sales of injectable fluoroquinolone products authorised for cattle were extremely low (0.14 mg/kg). No resistance was detected to the other antibiotics tested on the panel.

Figure 3.25: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Enterococcus faecium* isolated from bulk milk samples in 2023 (n=283). 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, SG: streptogramins, TC: tetracyclines

3.3.6.3 Klebsiella spp.

Klebsiella spp. is a zoonotic organism and an important cause of <u>bovine mastitis</u>, with *K. pneumoniae* and *K. oxytoca* being the most prevalent species in dairy cattle. *Klebsiella* isolation was started from 3rd March 2023 compared to the other bacterial species which started 11th January 2023.

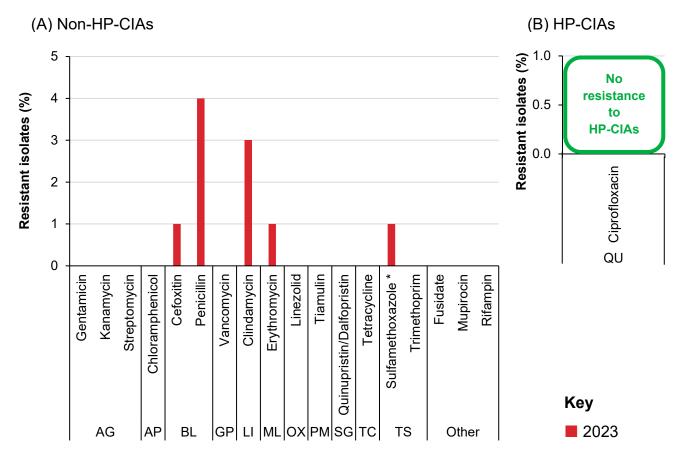
Nine *Klebsiella pneumoniae* isolates were obtained from bulk milk and none were MDR. Very high resistance was seen to tetracycline (56%, Table S2.7.6 in Supplementary Material 2). Of the HP-CIAs, two isolates (22%) were resistant to colistin, although these isolates did not carry any known *mcr* gene. There are two colistin products authorised for use in cattle, but there have been no sales of either product since 2020. No resistance was detected to the third-generation cephalosporins, the quinolones, or other antibiotics tested.

Four *Klebsiella oxytoca* isolates were recovered from bulk milk and none were MDR. One isolate (25%) was resistant to tetracycline (Table S2.7.6 in Supplementary Material 2). No resistance was detected to the third-generation cephalosporins or other antibiotics tested.

3.3.6.4 Staphylococcus aureus

S. aureus is normally resident on the skin and mucous membranes of cattle and is a common cause of mastitis. 100 *S. aureus* isolates were obtained from bulk milk and tested for AMR. Of these, 92% were susceptible to all antibiotics in the panel and none were MDR. Resistance to the non-HP-CIAs was low (<4%) or not detected (**Fig. 3.26**). No resistance was detected to the fluoroquinolone ciprofloxacin (a HP-CIA).

Figure 3.26: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Staphylococcus aureus* isolated from bulk milk samples in 2023 (n=100). Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



* Interpreted using an EFSA-recommended ECOFF

AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, GP: glycopeptide, LI: lincosamides, ML: macrolides, OX: oxazolidinone, PM: pleuromutilin, QU: quinolones, SG: streptogramins, TC: tetracyclines, TS: trimethoprim/sulfonamides



3.3.6.5 Streptococcus spp.

Streptococcus spp. are commensals of the mucous membranes of cattle. They can cause mastitis and occasionally other diseases. They are not regarded as zoonotic in cattle.

Streptococcus dysgalactiae

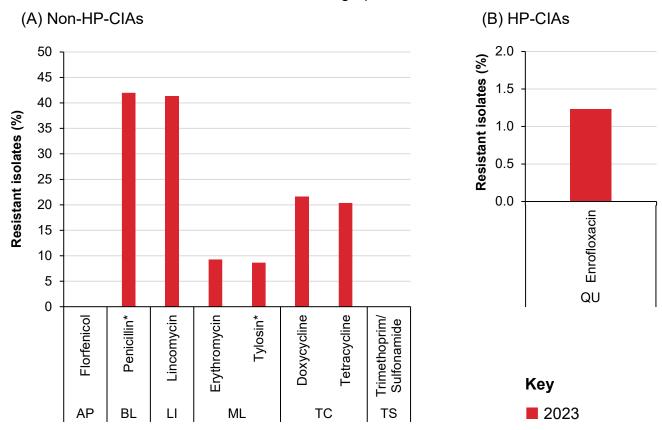
A total of six isolates were recovered from bulk milk and one of these (17%) was MDR. Three isolates (50%) were resistant to doxycycline (Table S2.7.9 in Supplementary Material 2). One of these isolates was MDR (17%), with co-resistance to erythromycin and tylosin. Of the HP-CIAs, none were resistant to the fluoroquinolone enrofloxacin.

Streptococcus uberis

A total of 162 isolates were recovered from bulk milk. 48% of isolates tested were susceptible to all antibiotics in the panel and 4.9% were MDR. High levels of resistance were detected to lincomycin (41%), doxycycline (22%) and tetracycline (20%, **Fig. 3.27**). There are no authorised intramammary tetracycline products, and lincosamides only accounted for 0.4% intramammary active ingredient sales in 2023. Using a tentative EUCAST ECOFF, high levels of resistance were also seen to penicillin (42%), which may be due to penicillins being the most commonly used antibiotic class in intramammary products sold. In 2023, penicillins are included in 46% intramammary lactating cow and 71% intramammary dry cow tubes sold. Of the HP-CIAs, low levels of resistance were seen to the fluoroquinolone enrofloxacin (1.2%).



Figure 3.27: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Streptococcus uberis* isolated from bulk milk samples in 2023 (n=162). Interpreted using EUCAST ECOFFs unless otherwise indicated. Note scale differs between graphs.



* Interpreted using a tentative EUCAST ECOFF

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

3.3.7 Using selective media to detect resistance

Additional, more sensitive, testing was conducted using selective media (see S1.4 in Supplementary Material 2). This inhibits the growth of susceptible *E. coli* in a sample but allows the resistant bacteria to multiply, making them easier to detect. The results below therefore represent the percentage of samples containing any *E. coli* resistant to these antibiotics, even at very low levels. This means that for pigs, cattle and sheep at slaughter, these results can be interpreted as the percentage of resistance to three different HP-CIAs is tested in this way: 3/4th generation cephalosporins (ESBL-/AmpC-producers); carbapenems; and colistin. Selective media has also been used to test for resistance to the non-HP-CIA amikacin in pigs.

These resistant bacteria then undergo molecular testing to confirm the genetic mechanisms underlying these resistances (see S1.6 and S1.7 in Supplementary Material 2) and are tested for susceptibility against other antibiotics.



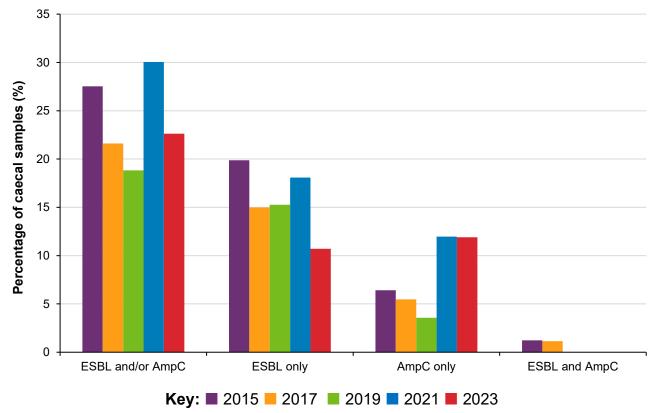
The PATH-SAFE surveys were conducted over shorter time periods than the routine surveillance and covered less of the underlying animal populations (see section 3.3.3). This means they could be less representative of national production, but nonetheless provide an important baseline for AMR in cattle and sheep.

3.3.7.1 Pigs

ESBL- and/or AmpC-producing E. coli

The results in section 3.3.2 and **Fig. 3.8** above show that the frequency of resistance to third generation cephalosporins in *E. coli* isolates from caecal samples of UK pigs is less than 2%. However, the use of selective media shows that the percentage of individual pigs carrying any *E. coli* expressing ESBL and/or AmpC phenotypes was 23% in 2023 (**Fig. 3.28**). This has reduced from a high of 30% in 2021. In 2023, carriage of *E. coli* with the ESBL phenotype was at lowest-ever levels in UK pigs (11%) but carriage of *E. coli* with the AmpC phenotype was unchanged (12%). No isolates were detected with both ESBL and AmpC phenotypes.

Figure 3.28: ESBL-/AmpC-producing *Escherichia coli* cultured on selective media, from caecal samples from healthy pigs at slaughter in the UK.



Of the 76 isolates which grew on ESBL/AmpC selective media, co-resistance to the HP-CIA fluoroquinolone ciprofloxacin was seen in 25% of isolates with ESBL and/or AmpC phenotypes. This means that 5.7% of UK pigs are carrying *E. coli* showing resistance to two HP-CIA classes (third/fourth-generation cephalosporins, and fluoroquinolones) within their

gut content, even at very low levels. It is important to note that these results are measured using ECOFFs, so these isolates are not necessarily clinically resistant. This percentage has increased since 2021 (4.7%). Of these co-resistant isolates 89% were ESBL producers and 11% were AmpC producers.

Whole genome sequencing (WGS) was carried out on all isolates. The isolates came from a large variety of sequence types (STs), indicating that the *E. coli* harbouring ESBL/AmpC genes were highly diverse.

Of the 36 isolates with an ESBL phenotype, the most common antibiotic resistance genes were *bla*_{CTX-M-1} (50%) and *bla*_{CTX-M-15} (28%). These genes are commonly found on plasmids and are associated with resistance to other antibiotics. The other genes detected included *bla*_{CTX-M-14} (8.3%), *bla*_{TEM-52b} (8.3%), *bla*_{CTXM-55} (2.8%) and *bla*_{SHV-12} (2.8%).

Of the 40 *E. coli* isolates which expressed the AmpC phenotype, 88% had a mutation in the *ampC* promoter region, 7.5% harboured the bla_{CMY-2} gene and 5.0% harboured the bla_{DHA-1} gene. Mutations in the *ampC* promoter region are located on the chromosome, are not associated as strongly with resistance to other antibiotics or as readily transmitted to other bacteria as those resistances which are found on plasmids.

Carbapenemase-producing E. coli

It is illegal to use carbapenems in food-producing animals in the UK. Carriage of carbapenem resistance has been routinely tested using selective media since the surveillance programme started in 2015. For the first time, in 2023 one carbapenemase-producing *E. coli* isolate was detected, representing 0.3% of pigs. The isolate was MDR and additionally resistant to beta-lactams, including 3rd and 4th generation cephalosporins; macrolides; quinolones; tetracyclines and trimethoprim/sulfonamides. WGS confirmed the isolate was ST38 and carried the *bla*_{OXA-48} gene.

Colistin-resistant E. coli

Screening for colistin-resistant *E. coli* has been routinely conducted in Great Britain since 2016. For the first time within the harmonised monitoring programme, one colistin-resistant *E. coli* was detected in a pig (0.3%). It was also resistant to ampicillin, but was sensitive to all other antibiotics tested, including the cephalosporins and quinolones. Following molecular testing, the isolate was identified as ST86. It possessed the *bla*_{TEM-1B} gene, which encodes resistance to penicillins and early cephalosporins, in addition to the *mcr-1* gene for colistin resistance, both present on a plasmid. Plasmids enable transmission of AMR genes to other bacterial strains and species.

Amikacin-resistant E. coli

The results in section 3.3.2 and **Fig. 3.8** above show that resistance to amikacin in individual *E. coli* isolates arising from representative caecal sampling of UK pigs was not detected.



The *rmtB* gene, conferring resistance to aminoglycosides, was first detected in UK pigs in 2020 from a herd with clinical signs of diarrhoea and sudden death. To better understand its presence in pig populations, selective media was used opportunistically to screen for amikacin resistance in harmonised monitoring samples taken in Great Britain between May to December 2023. The percentage of individual pigs carrying any *E. coli* resistant to amikacin, using selective media, was 10%, and PCR was used to confirm the presence of the *rmtB* gene in all these isolates. Amikacin is not used in pigs, but use of other aminoglycosides represents 14% of total use in pigs.

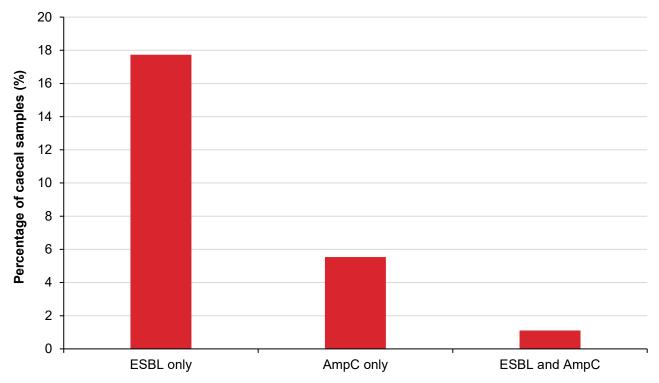
3.3.7.2 Beef cattle

ESBL- and/or AmpC-producing E. coli

The results in section 3.3.4.1 and **Fig. 3.14** above show that the frequency of resistance to third generation cephalosporins in *E. coli* isolated caecal samples of beef cattle in Great Britain was very low (0.4%). However, use of selective media showed that the percentage of individual animals carrying any *E. coli* expressing ESBL and/or AmpC phenotypes was 27%. The carriage of *E. coli* with the ESBL phenotype only was 18%, and carriage of the AmpC phenotype only was 5.5%. A small proportion of cattle (1.1%) were carrying *E. coli* with both ESBL and AmpC phenotypes (**Fig. 3.29**). Phenotypic classification for 2.5% of the isolates was inconclusive. These are being investigated further through WGS. This means that 27% of British cattle are carrying *E. coli* showing resistance to third/fourth-generation cephalosporins within their gut content, even at very low levels. It is important to note that these are not necessarily clinically resistant.



Figure 3.29: ESBL-/AmpC-producing *Escherichia coli* cultured on selective media, from caecal samples from healthy cattle at slaughter in the UK in 2023.



Of the 97 isolates which grew on ESBL/AmpC selective media, co-resistance to the HP-CIA fluroquinolone ciprofloxacin was seen in 67% of isolates.

Carbapenemase-producing E. coli

No carbapenemase producing *E. coli* were detected in 97 caecal samples from beef cattle tested using selective media.

3.3.7.3 Sheep

ESBL- and/or AmpC-producing E. coli

The results in section 3.3.5.1 and **Fig. 3.19** above show that resistance to third generation cephalosporins in *E. coli* isolates from a subset of caecal samples of sheep was not detected.

However, use of selective media showed that the percentage of individual animals carrying any *E. coli* expressing ESBL and/or AmpC phenotypes was 8.6%. The carriage of *E. coli* with the ESBL phenotype only was 3.1%, the carriage of the AmpC phenotype only was 5.2%. A small proportion of sheep (0.3%) were carrying *E. coli* with both ESBL and AmpC phenotypes (**Fig. 3.30**). The higher prevalence of carriage of AmpC compared to ESBL phenotypes could be explained by use of beta-lactamase inhibitors such as clavulanic acid which select for the AmpC phenotype. However, representative usage data is needed to test this hypothesis, which is not currently available.



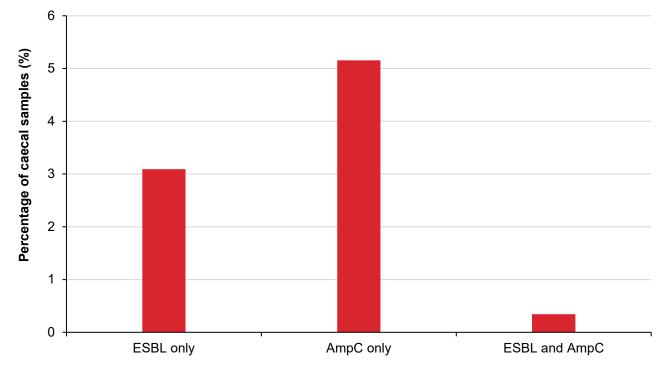
Of the 25 isolates which grew on ESBL/AmpC selective media co-resistance to the HP-CIA fluoroquinolone ciprofloxacin was seen in 36% of isolates with ESBL and/or AmpC phenotypes. This means that 3% of UK sheep are carrying *E. coli* showing resistance to two HP-CIA classes (third/fourth-generation cephalosporins, and fluoroquinolones) within their gut content, even at very low levels. It is important to note that these results are measured using ECOFFs, so these isolates are not necessarily clinically resistant. Of these co-resistant isolates, 78% were ESBL phenotype and 22% were AmpC phenotype.

WGS was carried out on all isolates. The isolates came from a large variety of sequence types (STs), indicating that the *E. coli* harbouring ESBL/AmpC genes were highly diverse. The most common sequence type was ST58 (32%). ST58 is widespread, commonly found in livestock, and occasionally associated with disease in people.

Of 9 isolates with an ESBL phenotype, the antibiotic resistance genes detected were *bla*_{CTX-M-15} (78%), *bla*_{CTX-M-14} (11%) and *bla*_{CTX-M-55} (11%). Of the 15 *E. coli* isolates which expressed the AmpC phenotype, 87% had a mutation in the *ampC* promoter region. These resistances are borne on the chromosome, not on plasmids (which can transfer to other bacterial strains and species). These isolates belonged to diverse sequence types, indicating resistance is occurring sporadically, perhaps in response to local selection pressure. The other genes detected included *bla*_{DHA-1} (6.7%) and *bla*_{DHA-1} with *bla*_{TEM-192} (6.7%). The *E. coli* isolate with both ESBL and AmpC phenotypes was ST297 and harboured a mutation in the *ampC* promoter region. No known ESBL genes were detected in this isolate through WGS.



Figure 3.30: ESBL-/AmpC- and carbapenemase-producing *Escherichia coli* cultured on selective media, from caecal samples from healthy sheep at slaughter in the UK in 2023.



Carbapenemase-producing E. coli

No carbapenemase producing *E. coli* were detected in 291 caecal samples from sheep tested using selective media.

3.3.7.4 Dairy cattle (bulk milk)

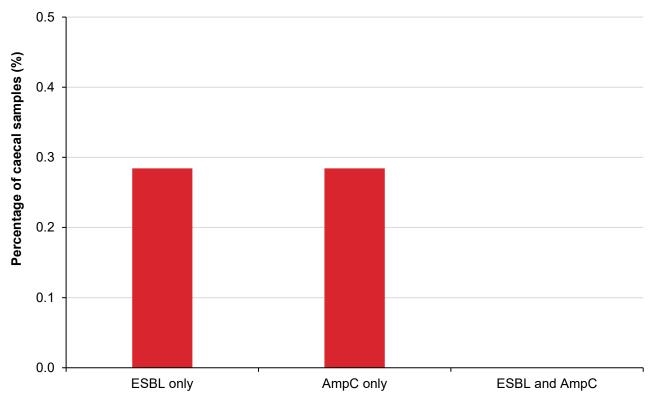
ESBL- and/or AmpC-producing E. coli

The results in section 3.3.6.1 and **Fig. 3.23** above show that the frequency of resistance to third generation cephalosporins in *E. coli* isolates from bulk milk samples was 0.2%.

Using selective media, the percentage of individual bulk milk samples carrying any *E. coli* expressing ESBL and/or AmpC phenotypes was 0.6% (**Fig. 3.31**).



Figure 3.31: ESBL-/AmpC- and carbapenemase-producing *Escherichia coli* cultured on selective media, from bulk milk samples in the UK in 2023.



WGS was carried out for 6 isolates, three *E. coli* isolates with an ESBL phenotype and three isolates with an AmpC phenotype. The isolates came from six sequence types (ST58, 88, 362, 442, 1126, 4624), indicating that the *E. coli* harbouring ESBL/AmpC genes were diverse.

Of the three isolates with an ESBL phenotype, all (100%) had ESBL genes identified. The genes detected were *bla*_{CTX-M-39} (33%), *bla*_{CTX-M-15} (33%) and *bla*_{CTX-M-32} (33%). Of the three isolates which expressed the AmpC phenotype, all (100%) had a mutation in the *ampC* promoter region. No other AmpC-producing mechanism was detected.

Carbapenemase-producing E. coli

No carbapenemase producing *E. coli* were detected in 1,055 bulk milk samples from dairy cattle tested using selective media.

Methicillin-resistant Staphylococcus aureus (MRSA)

The percentage of bulk milk samples carrying any MRSA, as identified from selective media, was 1.3%. A total of 14 isolates were isolated and three were MDR (21%). Two isolates (14%) were resistant to the fluoroquinolone ciprofloxacin in addition to methicillin.

Whole genome sequencing was carried out on 11 MRSA isolates. The isolates belonged to 7 sequence types (STs): the most common were ST398 (36%), which is the majority sequence

type in livestock-associated MRSA (LA-MRSA), and ST425 (18%). The remaining five STs were only identified once (14%). Two of the ST398 isolates were MDR.

As expected, the most common predicted resistance was to beta-lactams, which was encoded by either *mecA* or *mecC* in 82% of MRSA isolates sequenced. Two isolates only harboured the *blaz* beta-lactam gene (18%). The next most common predicted resistance was to tetracycline (64%).



CHAPTER 4

Clinical surveillance of antibiotic resistance



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The clinical surveillance is a programme of passive surveillance which evaluates antimicrobial resistance (AMR) in bacteria of relevance to animal health. The majority of AMR testing of sick animals in the UK is conducted by private veterinary laboratories at the request of private veterinary surgeons, and does not feed into government surveillance. However, some diagnostic samples, as well as carcasses for post-mortem, are submitted by veterinary surgeons to the Animal and Plant Health Agency (APHA) and partner veterinary laboratories in England and Wales. When a bacterial pathogen is isolated from these samples, susceptibility testing is performed to provide the practitioner with relevant information for treatment. Similar programmes are conducted by Scottish (<u>Scotland's Rural</u> <u>College Veterinary Services</u>, SRUC) and Northern Irish (<u>Agri-Food Biosciences Institute</u>, AFBI-NI) laboratories. This chapter primarily reports the APHA methods and results; results from SRUC and AFBI-NI are included in Supplementary Material 2.

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 within these limits (see section 4.3 below). The primary aim of the clinical surveillance programme is to provide scanning surveillance of animal disease. The clinical AMR results, as reported in this chapter, are used to identify new and emerging patterns of resistance, particularly since treatment failure is a frequent reason for submission of samples. In addition, this chapter incorporates results from the susceptibility testing of *Salmonella* isolates recovered by both governmental and private laboratories 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 Antimicrobial Resistance Coordination (DARC) group, and to the Veterinary Medicines Directorate (VMD) for management in accordance with protocols outlined in the VMD AMR <u>Contingency Plan</u>.

Clinical surveillance has historically been carried out using disc diffusion methods. However, broth microdilution testing providing minimum inhibitory concentration (MIC) values has continued to be developed for veterinary pathogens at APHA over the last four years, as laid out by APHA and VMD in the <u>Vet Record</u>. This enhancement should generate robust and comparable susceptibility testing outputs to detect emerging resistance issues in the UK. This chapter features MIC results for respiratory pathogens, in addition to *Streptococcus suis* and *Brachyspira hyodysenteriae*, isolated in 2023. The aim for future years is to continue expanding this methodology to further bacteria.

4.1 Summary

Clinical surveillance aims to provide veterinary surgeons 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 wider animal populations.

- 7,415 isolates were tested for AMR in England and Wales in 2023. The percentage of isolates tested by animal species were: pigs (13% of isolates), poultry (30%), cattle (15%), sheep (7%), dogs (10%) and trout (<1%).
- Resistance in *Escherichia coli* from all animal species shows a decreasing trend since 2014. 18% of all clinical *E. coli* isolates tested were resistant to four or more individual antibiotics, meaning that treating veterinary surgeons are likely to have reduced treatment options. This was most frequent in isolates from cattle (24%) and pigs (23%), and less frequent in chickens (10%) and sheep (6%).
- 73% of Salmonella isolates tested were fully susceptible to the panel of antibiotics tested. Full susceptibility was highest in those isolated from sheep (97%), horses (92%), and cattle (89%), and lowest in Salmonella isolated from pigs (19%) and turkeys (30%). Full susceptibility in pigs, chickens, turkeys, and dogs all show increasing trends since 2014, whereas it has remained fairly stable in cattle and sheep. Full susceptibility of Salmonella isolated from feed appears to be decreasing over time.
- The transition from disc diffusion to broth microdilution, interpreted using Minimum Inhibitory Concentrations (MIC), continues, as use of this gold-standard testing is further established.

Important findings from individual animal species are as follows:

- **Pigs:** the most frequently tested bacteria were *E. coli* (49%) and *Salmonella* (35%). Increases in resistance between 2022 and 2023 were observed in these pathogens to the majority of antibiotics tested. Full susceptibility in *Salmonella* isolated from pigs decreased from 28% in 2022 to 19% in 2023. Resistance to aminoglycosides in *E. coli* was higher in weaners than in neonates and adult pigs, likely reflecting more frequent use of these antibiotics in this age group for treating post-weaning diarrhoea.
- **Poultry:** the most frequently tested bacteria were *Salmonella* (94%) and *E. coli* (6%). Higher levels of resistance in *E. coli* isolates were found to the most commonly-used antibiotic classes: aminopenicillins and tetracyclines. Resistance in *E. coli* from broilers declined between 2022 and 2023 to each antibiotic tested. Resistance was more common in *Salmonella* isolated from turkeys compared to broilers.
- **Cattle:** the most frequently tested bacteria were *Salmonella* (41%) and *E. coli* (29%, predominantly gastrointestinal). Mastitis caused by *E. coli* was more likely to be resistant (9.1% of isolates indicating limited treatment options) than that caused by other organisms. Higher levels of resistance were observed in *E. coli* from calves than in adult cattle, which may reflect more frequent antibiotic usage in this age group.



- **Sheep:** the most frequently tested bacteria were *E. coli* (49%) and *Mannheimia haemolytica* (18%). Resistance tended to be highest in younger animals, which may reflect more frequent antibiotic use in this age group.
- **Dogs:** Only *Salmonella* bacteria were tested. 82% of *Salmonella* were susceptible to the full panel of antibiotics. 10% of *Salmonella* isolates were resistant to four or more antibiotics, limiting treatment options. Resistance to many antibiotics tested has reduced since 2022.

In addition, results are presented from:

- The AMR surveillance pilot in trout. 13 isolates were tested from 2023, and indicated possible emerging resistance to oxolinic acid in *Yersinia ruckeri*, which causes enteric redmouth disease. Resistance to highest priority critically important antibiotics (HP-CIAs) and to the carbapenem meropenem was also detected, and is undergoing further investigation.
- The Private Laboratories Initiative (PLI), which aims to collect and analyse AMR data from private veterinary laboratories. Data on AMR in bacteria causing mastitis is presented for the fourth consecutive 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, including private veterinary laboratories, isolating *Salmonella* spp., from animals and their environment, under the <u>Zoonoses Order 1989</u> in Great Britain and subsequent <u>Zoonoses (Amendment) Order 2021</u>, is required to notify and submit an isolate to a Defra-approved laboratory for characterisation, including antibiotic sensitivity testing.

Where total isolate numbers are stated, this refers to the total number of isolates tested against any antibiotic. Individual isolates are not always tested to all antibiotics shown.

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 section 4.3.4.1 (Private Laboratory Initiative) used different methods, which are described separately in Table S3.1.2 in Supplementary Material 2.



For the majority of the results presented in this chapter, the disc diffusion method was used, as formerly recommended by the British Society for Antimicrobial Chemotherapy (<u>BSAC</u>). Disc diffusion results are measured by the zone of inhibition.

Broth microdilution testing under the clinical surveillance programme has historically been limited to specific organisms, such as *Brachyspira hyodysenteriae*, which causes swine dysentery. Broth microdilution results are measured using minimum inhibitory concentrations (MIC), and was introduced in <u>UK-VARSS 2020</u> for key respiratory pathogens (section 4.3.1) following joint APHA/VMD recommendations. In 2023, the respiratory pathogens: *Actinobacillus pleuropneumoniae*, *Bibersteinia trehalosi, Mannheimia haemolytica, Pasteurella multocida* along with *Streptococcus suis* and *B. hyodysenteriae* results are presented by broth microdilution method.

4.2.3 Interpretation

Interpretative criteria are available in full in section S3.1 of Supplementary Material 2. In Chapter 4, results are interpreted using clinical breakpoints (CBPs). Where these are veterinary-specific the results can be used to imply likely treatment success (sensitive) or failure (resistant). Some results have been interpreted using human CBPs, where veterinary CBPs were unavailable. These results should be interpreted with caution. This contrasts with the results presented in Chapter 3, which are interpreted using ECOFFs. ECOFFs are a more sensitive way to detect emerging resistance, but don't necessarily correspond to treatment failure.

Disc diffusion data has been interpreted using BSAC clinical breakpoints. When not available, the historical APHA or Animal Health and Veterinary Laboratory Agency (AHVLA) veterinary clinical breakpoint has been applied.

MIC results have been interpreted using veterinary clinical breakpoints from <u>Clinical and</u> <u>Laboratory Standards Institute</u> (CLSI) in the first instance, or <u>Committé Antibiogramme</u> -<u>Société Française de Microbiologie</u> (CA-SFM) when these are not available; if veterinary clinical breakpoints were not available, <u>human clinical breakpoints</u> were used.

Multi-drug resistance (MDR) is defined in this chapter for isolates tested by broth microdilution as resistance to three or more antibiotic classes. Isolates tested by disc diffusion which were resistant to four or more antibiotics have been referred to as having limited treatment options.

4.3 Results

This section presents the AMR results for all the pathogens tested. Summary results are first presented for the important zoonotic and multi-host organisms, *E. coli*, Salmonella *spp*., livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) and *Streptococcus suis*, in section 4.3.1. AMR results for veterinary pathogenic bacteria are then presented, organised by animal species followed by body system.



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

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 (**Table 1**). These are included in the panels to allow monitoring of 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 changes seen between years need to be interpreted with caution. Only pathogens with test results for more than 20 isolates in 2023 are presented graphically in the main body of the report. The complete dataset is available from section S4.1 onwards in Supplementary Material 2.

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 age groups.

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

Table 4.2: Age categories of food-producing animals.



4.3.1 Zoonotic organisms

Summary results for important zoonotic and multi-host organisms are presented in this section. Most testing reported here was performed using disc diffusion methodology (see section S3.1.1 in Supplementary Material 2), with the exception of *S. suis*, for which broth microdilution was used, and measured by MIC (see section S3.1.3 in Supplementary Material). The complete dataset can be found in section S4.1 of Supplementary Material 2.

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.

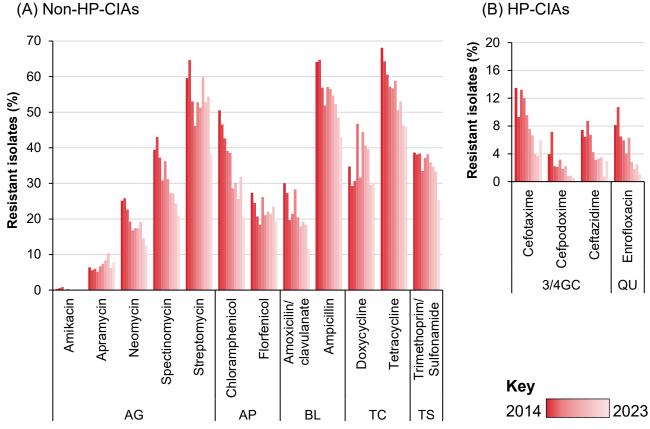
Resistance in all veterinary clinical *E. coli* isolates from England and Wales since 2014 is shown in **Fig. 4.1**. These results clearly demonstrate a decline in clinical resistance to most antibiotics between 2014 and 2023, including to the HP-CIAs tested.



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Figure 4.1: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from pigs, chickens, turkeys, cattle and sheep from 2014 to 2023 (n=1,141 in 2023). 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

Overall, 18% of all *E. coli* isolated from clinical submissions indicated limited treatment options (**Fig. 4.2**). This was most frequently detected in cattle isolates (24%), followed by pigs (23%), chickens (10%) and sheep (5.7%). Very small numbers of isolates from turkeys were submitted (see section 4.3.3.1).

Across all species, there was a general trend towards higher resistance in isolates from neonates and weaners than adults. This may reflect the more frequent treatment of young animals with antibiotics.



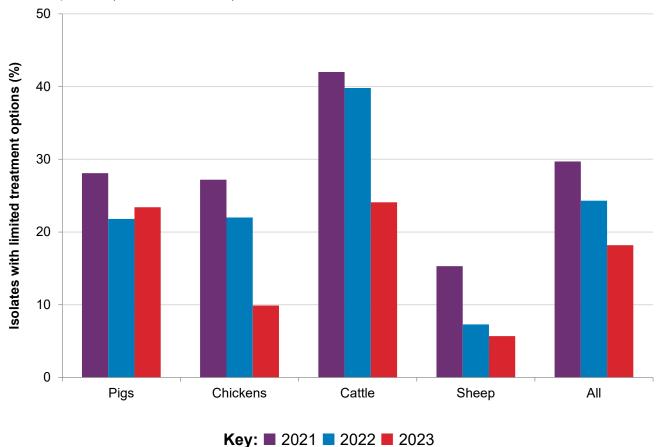


Figure 4.2: Percentage of *E. coli* isolates with limited treatment options, from different animal species (n=1,141 in 2023).

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 '<u>Salmonella in</u> animals and feed in Great Britain' report.

Of the 5,513 *Salmonella* isolates tested in Great Britain in 2023, 54% were from foodproducing animals, 14% from companion animals, 23% from feed, and 5.2% from the environment. The number of isolates was highly variable between species (for example, 62 isolates were submitted from horses, whereas 471 were submitted from cattle, and can fluctuate between years.

A total of 73% of *Salmonella* isolates from all species were fully susceptible. Of the species tested, full susceptibility was highest in sheep (97%), horses (92%) and cattle (89%), and lowest in pigs (19%) and turkeys (30%). Full susceptibility increased in cattle (78% in 2021 to 89% in 2023), sheep (85% in 2021 to 97% in 2023) and dogs (65% in 2021 to 82% in 2023).



Looking back over data from 2014, trends of increasing fully-susceptible *Salmonella* from pigs, chickens and turkeys are clear (**Fig. 4.3**). This could be explained by reductions in antibiotic usage achieved in these sectors over the same time period (see Section 1.3). Full susceptibility also appears to be increasing in dogs, however, *Salmonella* only became reportable for dogs in 2021, so data from earlier years is less complete. Full susceptibility in *Salmonella* in cattle and sheep appears largely stable between 2014 and 2023 (**Fig. 4.3**). Full susceptibility in isolates from animal feed appears to be decreasing.

Overall, 14% of *Salmonella* from all species tested in 2023 had limited treatment options. This was highest in pigs (76%) and feed (21%). Resistance to the HP-CIAs cefotaxime and ceftazidime was detected in eight (0.1%) *Salmonella* isolates: seven isolates from dogs and one from raw pet food, all of which had limited treatment options. Four of these isolates, one *S*. Saintpaul and three *S*. Kentucky, were co-resistant to the quinolone ciprofloxacin.

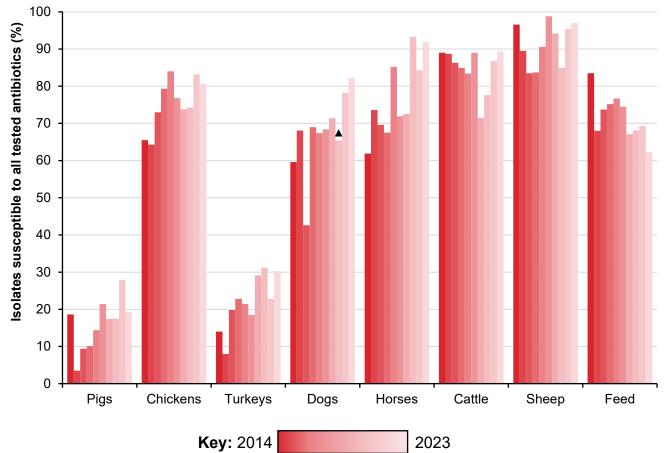


Figure 4.3: *Salmonella* spp. isolates susceptible to all tested antibiotics, from different sources and animal species, from 2014 to 2023 (n=5,513 in 2023).

▲ Salmonella in dogs became reportable in 2021

Overall patterns of resistance in *Salmonella* species can be affected by which serovars are circulating. Full details can be found <u>here</u>. In 2023, 96% of *S*. Dublin isolates from cattle and 55% of *S*. Typhimurium from all species were sensitive to all antibiotics tested. Monophasic *S*. Typhimurium was mostly isolated from dogs and pigs. Of these, 78% of dog isolates and 1.7% of pig isolates were fully susceptible, reflecting the occurrence of different phage types,

each with specific resistance patterns. An increase in resistance was seen to tetracyclines (13% in 2022 to 15% in 2023) and trimethoprim/sulfonamides (7.8% in 2022 to 12% in 2023), although remaining at low levels. This could possibly be linked to an increase in *S*. Kedougou isolates which typically have this resistance pattern.

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

LA-MRSA are, as the name indicates, 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 <u>contact with livestock</u>. LA-MRSA usually lives in the nose or on skin and is an opportunistic 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 <u>first time in 2014</u>, 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 2023 a single LA-MRSA CC398 *spa*-type t4838 isolate was recovered from a skin swab taken from a young piglet. The presence of the *cfr* gene was confirmed. This confers resistance to multiple antimicrobials, including linezolid. This antimicrobial is not authorised for use in pigs in the UK, but is used to treat MDR human infections including vancomycin-resistant enterococci (VRE).

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 broth microdilution (section 4.3.2.4), in *S. suis* isolates are presented in the pig species section below.

4.3.2 Pigs

Results for pathogenic bacteria isolated from pigs are presented in this section and are organised by body system. Most testing reported here was performed using disc diffusion methodology (see section S3.1.1 in Supplementary Material), with the exception of selected respiratory pathogens, for which broth microdilution was used, as measured by MIC (see section S3.1.3 in Supplementary Material). The complete pig dataset can be found in section S4.2 of Supplementary Material 2.



4.3.2.1 Gastrointestinal system

Escherichia coli

E. coli is one of the major causes of diseases in pigs presenting primarily as diarrhoea with rapid dehydration and can cause sudden death.

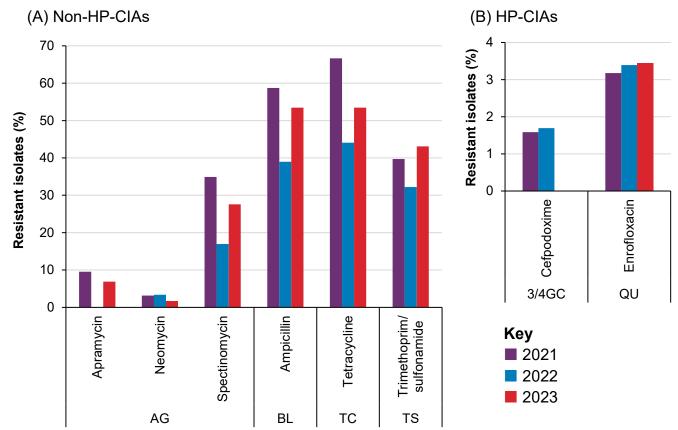
Isolates of porcine *E. coli* were predominantly collected from the post-weaning age category (63% of 453 isolates), with smaller numbers from neonates (13%) and adult pigs (8.2%). High levels of resistance were detected to ampicillin and tetracycline across all age categories. For context, in use data representing >95% of the pig sector, the most commonly used antibiotic classes in 2023 were tetracyclines (32%), penicillins (19%), aminoglycosides (14%) and trimethoprim-sulfonamides (12%) (see Section 1.3.1).

The AMR in *E. coli* results from pigs are presented separately for neonates (**Fig. 4.4**), preweaning piglets (**Fig. 4.5**), and adults (**Fig. 4.6**). Like in other species, resistance tends to be higher in younger age groups. Usage data split by farm type is not available, but there is some <u>published evidence</u> using English data from 2017 and 2018 that use in breederfinisher and nursery-finisher farms is significantly higher than finisher farms, which likely reflects higher use in neonates and weaner pigs compared with adult finishers.

In neonatal piglets, 17% of isolates had limited treatment options. Very high levels of resistance were detected to ampicillin (53%) and tetracycline (53%) and high resistance to trimethoprim/sulfonamides (43%) (**Fig. 4.4**). Resistance to the other antibiotics tested was moderate to low; and resistance to the HP-CIAs was low.



Figure 4.4: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolated from neonatal piglets (n=58 in 2023). Note scale differs between graphs.

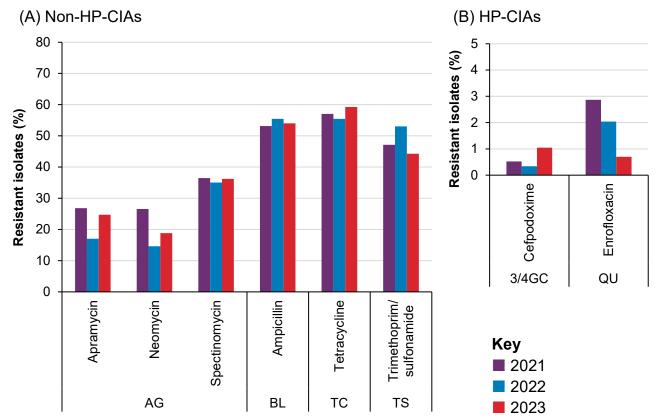


AG: aminoglycoside, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

In post-weaned piglets, 29% of isolates had limited treatment options, more than in other age groups. Very high levels of resistance were detected to ampicillin (54%) and tetracycline (59%), and high resistance to trimethoprim/sulfonamides (44%), spectinomycin (36%) and apramycin (25%) (**Fig. 4.5**). These appear little-changed since 2021. Resistance to the HP-CIAs was very low. There were higher levels of aminoglycoside resistance in *E. coli* from post-weaned piglets (up to 36%), compared with neonatal piglets (27% for spectinomycin, but much less for other aminoglycoside antibiotics) and adults (up to 14%), which probably reflects the use of aminoglycosides for treating post-weaning diarrhoea.



Figure 4.5: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from post-weaning piglets (n=287 in 2023). Note scale differs between graphs.

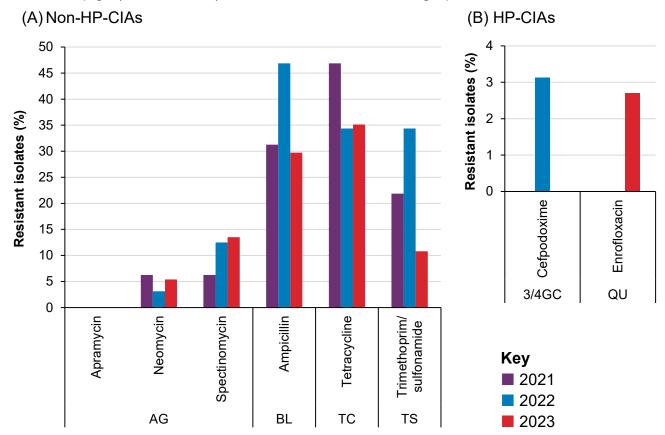


AG: aminoglycoside, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

In adult pigs, 2.7% of isolates had limited treatment options. High levels of resistance were detected to ampicillin (30%) and tetracycline (35%) (**Fig. 4.6**). Resistance to the other non-HP-CIA antibiotics tested was moderate to low. Of the HP-CIAs, no resistance was observed to the third-generation cephalosporin cefpodoxime, however, a single isolate (0.7%) was resistant to the quinolone enrofloxacin. In pigs, fluoroquinolone use is low and, in usage data from 2023, it accounts for 0.008% of total use.



Figure 4.6: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from adult pigs (n=37 in 2023). 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.

Salmonellosis primarily presents as diarrhoea in pigs, but can cause a range of clinical signs including fever, loss of appetite and laboured breathing. *Salmonella* data for pigs is presented below for all age groups (**Fig. 4.7**).

Of the 328 *Salmonella* isolates tested from pigs in 2023, 19% were susceptible to the full panel of antibiotics, which is a reduction from 28% in 2022. In 2023, 76% of isolates had limited treatment options. Levels of resistance in *Salmonella* isolated from pigs increased this year to all antibiotics apart from ciprofloxacin. These results correlate with usage data (Section 1.3.1), where use of all antibiotic classes (except for the HP-CIAs, which include fluoroquinolones and third and fourth generation cephalosporins) in pigs increased between 2022 and 2023.

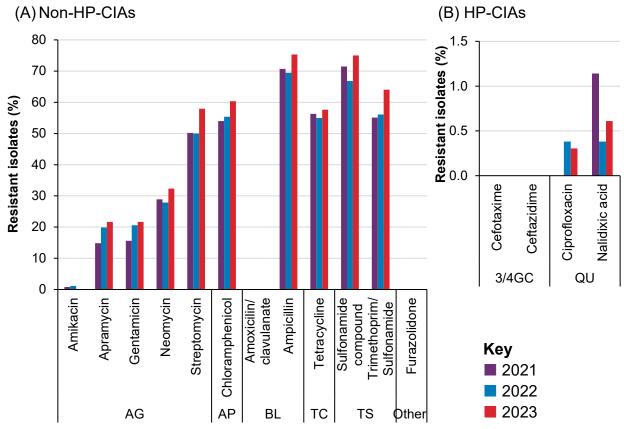
Extremely high levels of resistance were detected to ampicillin (75%) and sulfonamides (75%), very high levels of resistance were detected to tetracycline (58%) and trimethoprim/sulfonamides (64%); and high levels of resistance were detected to gentamicin (22%) and neomycin (32%). No resistance to amoxicillin/clavulanate or furazolidone was detected in 2023.



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Of the HP-CIAs, no resistance was observed to the third-generation cephalosporins cefotaxime and ceftazidime, however, a single isolate (0.3%) was resistant to the quinolone ciprofloxacin and two isolates (0.6%) were resistant to nalidixic acid. In pigs, the only quinolones used are fluoroquinolones, and usage data from 2023 show that these account for 0.008% of total use.

Figure 4.7: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Salmonella* isolates from pigs (n=328 in 2023). 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

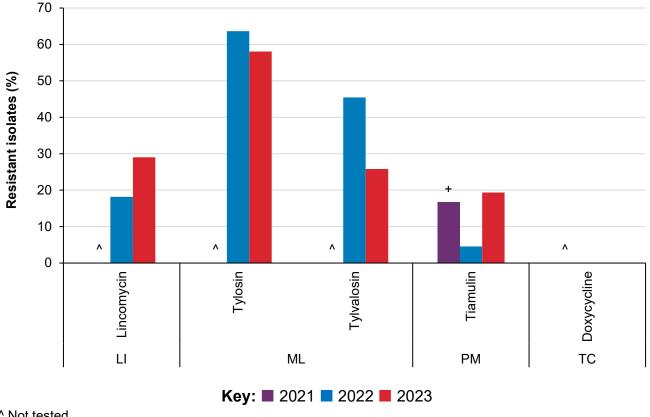
Brachyspira hyodysenteriae

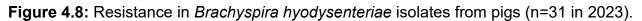
Brachyspira hyodysenteriae is the causative organism of swine dysentery, an enteric disease of pigs which results in serious ill-thrift in its chronic form. A limited range of antibiotics is available for the treatment of swine dysentery and other aspects of disease control, such as hygiene and herd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

Tiamulin is an important veterinary antibiotic used in the treatment of swine dysentery. All available isolates of *B. hyodysenteriae* are tested for tiamulin susceptibility each year, using broth microdilution and measured by MIC. Since 2022, MIC testing has been expanded to include a wider panel of antibiotics. The full breakpoints applied are available in Table S3.1.3.1 in Supplementary Material 2.



In 2023, 31 isolates were tested and 19% were clinically resistant. Of the wider panel of antibiotics, no resistance was detected to doxycycline whereas high levels of resistance were detected to both lincomycin (29%) and tylvalosin (26%), and very high levels to tylosin (58%) (Fig. 4.8).





^ Not tested

+ Less than 20 isolates tested

LI: lincosamides, ML: macrolides, PM: pleuromutilin, TC: tetracyclines

4.3.2.2 **Respiratory system**

Results presented for the majority of the key respiratory pathogens are generated using MICs, as outlined in S3.1.3 of Supplementary Material 2, unless indicated otherwise.

Actinobacillus pleuropneumoniae

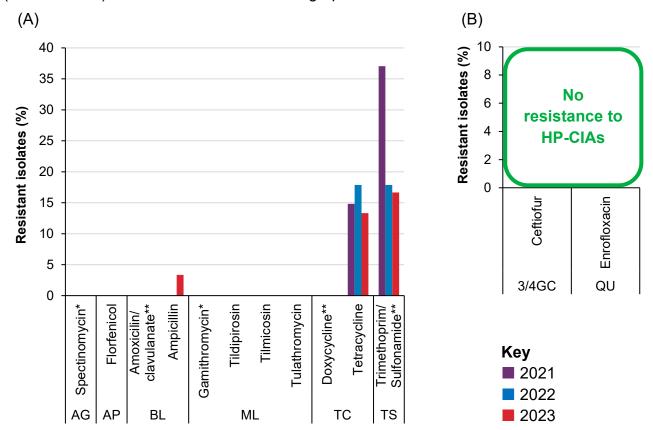
Actinobacillus pleuropneumoniae causes pneumonia in pigs. Of the six isolates recovered in 2023, 50% were susceptible to the full panel of antibiotics and 17% were multi-drug resistant (MDR, resistant to three or more antibiotic classes). Resistance was detected to ampicillin in 33% of isolates, and 17% were resistant to tetracycline and trimethoprim/sulfonamide (Table S4.2.5 in Supplementary Material 2). No resistance was detected to the other antibiotics tested on the panel.



Pasteurella multocida

P. multocida toxigenic strains are responsible for the development of atrophic rhinitis in pigs. A total of 30 isolates were recovered from diagnostic samples in 2023, 73% were susceptible to the full panel of antibiotics and none were MDR. Moderate levels of resistance were detected to tetracycline (13%) and trimethoprim/sulfonamide (17%), and low resistance to ampicillin (3.3%, **Fig. 4.9**). HP-CIA resistance was not observed in 2023.

Figure 4.9: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Pasteurella multocida* isolated from pigs interpreted using CLSI veterinary breakpoints unless indicated otherwise (n=30 in 2023). Note scale differs between graphs.



* Spectinomycin and gamithromycin breakpoint for bovine isolates applied

** Interpreted using CA-SFM veterinary CBP

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

Trueperella (Arcanobacterium) pyogenes

No *Trueperella* (*Arcanobacterium*) *pyogenes* was isolated from respiratory or systemic disease in pigs in 2023.



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 five isolates were tested and of these, two isolates (40%) had limited treatment options. No resistance was detected to trimethoprim/sulfonamides. Three isolates (60%) were resistant to ampicillin, lincomycin, penicillin and tetracycline (Table S4.2.6 in Supplementary Material 2).

Staphylococcus xylosus

Staphylococcus xylosus causes dermatitis and one isolate was recovered in 2023. No resistance was detected to the antibiotics tested.

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. Four isolates were tested in 2023. Three isolates (75%) were resistant to trimethoprim and no resistance was detected to the other antibiotics tested on the panel, including the usual treatment options penicillin and ampicillin (Table S4.2.6 in Supplementary Material 2).

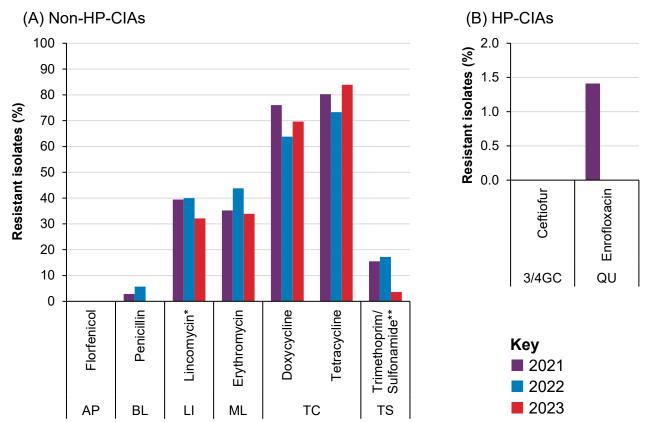
Streptococcus suis

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.

Methodological development of broth microdilution, to generate robust and comparable susceptibility testing outputs, has continued with *S. suis*. A range of breakpoints are used for this organism, because all drug/bacteria species combinations are not available from the same source. Of the 56 *S. suis* isolates tested by broth microdilution, 16% were susceptible to the full panel of antibiotics tested and 29% were MDR . Penicillin resistance was not detected in 2023, indicating that penicillins remain a viable first-line choice in the treatment of the majority of *S. suis* infections in pigs (**Fig. 4.10**). No resistance was detected to florfenicol, an alternative treatment option, or to ceftiofur. Extremely high resistance was detected to tetracycline (84%) and very high resistance to doxycycline (70%). No HP-CIA resistance was seen in 2023.



Figure 4.10: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Streptococcus suis* isolates from pigs (n=56 in 2023). Interpreted using CLSI veterinary breakpoints unless indicated otherwise.



* Interpreted using CA-SFM veterinary CBP

** Interpreted using EUCAST human CBP for streptococci

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

Results for pathogenic bacteria isolated from poultry are presented in this section and are organised by body system. Testing reported here was performed using disc diffusion methodology (see section S3.1.1 in Supplementary Material). The complete poultry dataset can be found in section S4.3 of Supplementary Material 2.

4.3.3.1 Gastrointestinal system

Escherichia coli

E. coli can cause a range of clinical problems in poultry, including respiratory illness, reduced appetite and poor growth.

The clinical samples submitted for testing from chickens and turkeys arise from flocks of various types and sizes, including commercial farms, pet birds and small-scale poultry



keepers. Much larger numbers of chicken isolates (n=121) were obtained compared to turkey isolates (n=2) in 2023.

Resistance in *E. coli* isolates from chickens is presented below (**Fig 4.11**). In chickens, 10% of isolates had limited treatment options. High levels of resistance were detected to ampicillin (38%), doxycycline (30%) and tetracycline (31%). Resistance to the other antibiotics tested was moderate to low and reduced since 2022. For context, in data representing 85% of the meat poultry sector (Section 1.3.2), the most commonly used antibiotic classes used in meat poultry in 2023 were penicillins (63%), lincomycins (which includes lincosamide/ aminoglycoside combination products) (15%), tetracyclines (15%) and trimethoprim-sulfonamides (7%).

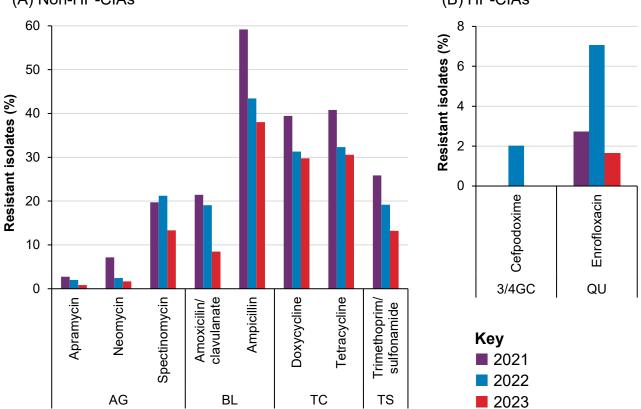
Of the HP-CIAs, resistance to the third-generation cephalosporin cefpodoxime was not detected, and resistance to the quinolone enrofloxacin (1.7%) was low. Third and fourth generation cephalosporins were not used in commercial broilers in 2023 and fluoroquinolone use accounted for 0.02% of total sales.

 Figure 4.11: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates

 from chickens (n=121 in 2023). Note scale differs between graphs.

 (A) Non-HP-CIAs

 (B) HP-CIAs



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

Both isolates recovered from turkeys were resistant to ampicillin (100%) and one isolate was resistant to doxycycline (50%) and tetracycline (50%) in addition.



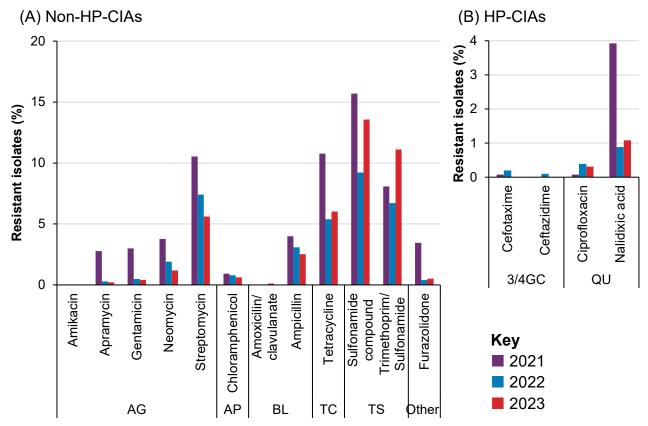
Salmonella spp.

Salmonellosis can cause a wide range of clinical signs in poultry including lethargy, loss of appetite and poor growth.

In 2023, 1,945 *Salmonella* isolates were recovered from samples from chickens. 81% of isolates were susceptible to the full panel of antibiotics, which is a slight reduction from 83% in 2022. 4.5% of isolates had limited treatment options. Levels of resistance were moderate to sulfonamides (14%) and trimethoprim/sulfonamide (11%), although both of these have increased substantially since 2022 (**Fig. 4.12 (A)**). Resistance to the other antibiotics tested was either low, very low or not detected.

Of the HP-CIAs, no resistance was observed to the third-generation cephalosporins cefotaxime and ceftazidime (**Fig. 4.12 (B)**). Resistance levels to the quinolones ciprofloxacin (0.3%) and nalidixic acid (1.1%) were very low and low, respectively.

Figure 4.12: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Salmonella* isolates from chickens (n=1,945 in 2023). 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 2023, 76 *Salmonella* isolates were recovered from turkeys. 30% of isolates were susceptible to all antibiotics tested and 22% had limited treatment options. The highest levels of resistance were seen to tetracycline (45%) and sulfonamide (40%) (**Fig 4.13**). High levels of resistance to ampicillin (21%) and streptomycin (22%); and moderate levels of resistance

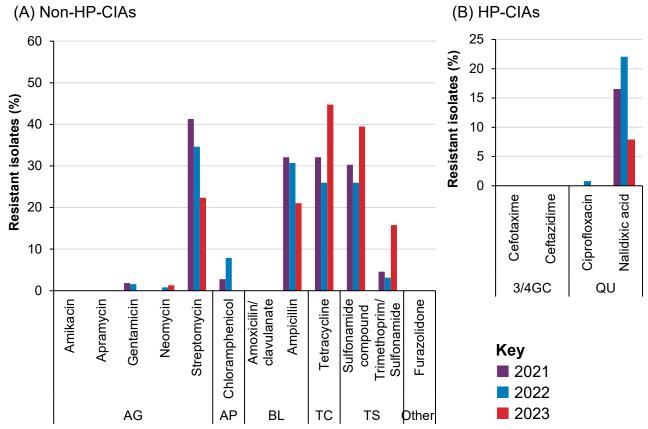


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to trimethoprim/sulfonamide (16%) were also detected. As in broilers, resistance to sulfonamide and trimethoprim/sulfonamide has increased substantially since 2022. Resistance to tetracycline in *Salmonella* isolated from turkeys has also increased. Resistance to the other antibiotics tested including HP-CIAs was either low, very low or not detected.

Figure 4.13: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Salmonella* isolates from turkeys (n=76 in 2023). 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 a chicken. It was resistant to ampicillin, reflecting the intrinsic resistance to this organism, but sensitive to the rest of the panel of antibiotics (Table S4.3.4 in Supplementary Material 2).

4.3.3.3 Multi-system pathogens

Erysipelothrix rhusiopathiae

Erysipelothrix rhusiopathiae is widely distributed in nature and occurs as a commensal. It is also a pathogen and can infect multiple species, causing a range of clinical disease, including lethargy, decreased egg production and sudden death. In 2023, one isolate was

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recovered from a turkey. It was resistant to trimethoprim/sulfonamides and susceptible to the rest of the panel of antibiotics tested (Table S4.3.5 in Supplementary Material 2).

Staphylococcus aureus

Staphylococcus aureus causes a number of infections in poultry and game birds, including septicaemia, yolk sac infection, arthritis and osteomyelitis. In 2023, three isolates were recovered from chickens and all were fully susceptible to the panel of antibiotics tested.

Staphylococcus xylosus

Staphylococcus xylosus causes dermatitis and two isolates were recovered from chickens in 2023. Both isolates were resistant to ampicillin and penicillin, and susceptible to the other antibiotics tested (Table S4.3.5 in Supplementary Material 2).

4.3.4 Cattle

Results for pathogenic bacteria isolated from cattle are presented in this section and are organised by body system. Most testing reported here was performed using disc diffusion methodology (see section S3.1.1 in Supplementary Material), with the exception of selected respiratory pathogens, for which broth microdilution was used, as measured by MIC (see section S3.1.3 in Supplementary Material). The complete cattle dataset can be found in section S4.4 of Supplementary Material 2.

4.3.4.1 Reproductive system

Bovine mastitis is complex, and involves a range of pathogens. The data presented are aggregated at a national level and therefore have limited ability to inform treatment protocols on individual farms. However, they highlight that acquired resistance does occur in England and Wales. Resistance should be considered when veterinary surgeons 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.

Escherichia coli

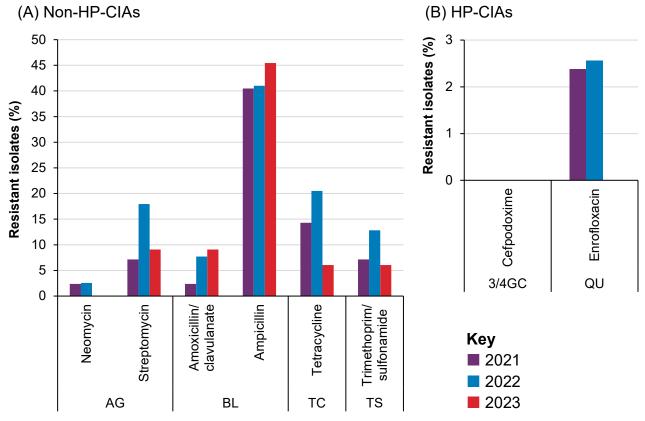
E. coli and other coliforms are major causes of bovine mastitis. Most *E. coli* strains originate from the cow's immediate environment, and no particular virulence factors are required to infect the mammary gland. These *E. coli* isolates, therefore, are probably mainly of faecal origin. There were 33 isolates recovered from mastitis diagnostic samples in 2023.

Of the 33 isolates tested, 9.1% had limited treatment options. There were high levels of resistance to ampicillin (46%) and low levels of resistance to streptomycin (9.1%), tetracycline (6.1%) and trimethoprim/sulfonamides (6.1%, **Fig. 4.14**). This may be linked to



penicillins being the most commonly used antibiotic class in intramammary products sold. 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 in England and Wales (n=33 in 2023). Note scale differs between graphs.



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

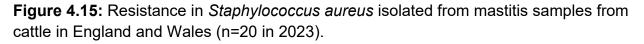
Staphylococcus aureus

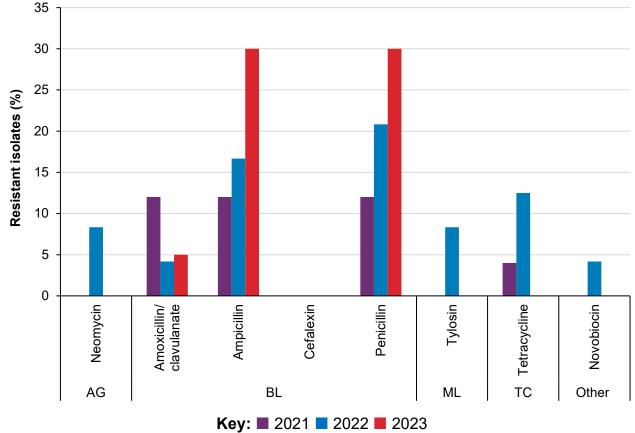
S. aureus is normally resident on the skin and mucous membranes of cattle and is a common cause of mastitis. There were 20 isolates recovered from diagnostic mastitis samples in 2023.

No isolates indicated limited treatment options. There were high levels of resistance to ampicillin (30%) and penicillin (30%), and both of these have increased substantially since 2022 (**Fig. 4.15**). This is consistent with a 9% increase in the sales of intramammary lactating cow products containing penicillins (Section 1.3.2); however, it is difficult to draw firm conclusions, as the AMR results represented here arise from a small number of isolates. Penicillin resistance in bovine *S. aureus* from England and Wales occurs most frequently via the production of beta-lactamases. Resistance to the other antibiotics tested was either low or not detected.

One isolate (5%) was resistant to amoxicillin/clavulanate, which combines a beta-lactam antibiotic and beta-lactamase inhibitor. Isolates with this resistance are screened to check for

the presence of *mecA* and *mecC* genes, which confer methicillin resistance. The isolate was not methicillin-resistant *S. aureus* (MRSA).





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 separate from the Group C streptococci that can cause disease in humans. A total of 13 isolates were tested to the panel of antibiotics in 2023.

In 2023, all isolates were resistant to tetracycline (100%, Table S4.4.2 in Supplementary Material 2). This resistance is <u>well-recognised</u>. Moderate resistance was detected to tylosin (15%) and low resistance to neomycin (8.3%). No resistance was detected to the other antibiotics tested.

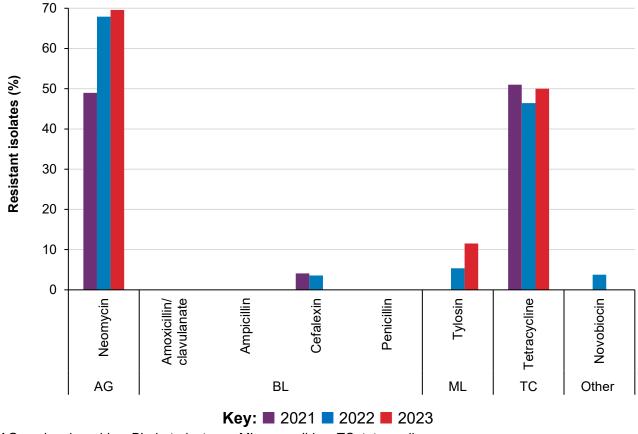


Streptococcus uberis

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. A total of 26 isolates were tested to the panel of antibiotics in 2023 and none had limited treatment options.

Resistance to neomycin was very high (70%), which may reflect a degree of intrinsic resistance to the aminoglycosides (**Fig. 4.16**). Resistance to tetracycline (50%) was high. All isolates were sensitive to ampicillin, amoxicillin/clavulanate and penicillin.

Figure 4.16: Resistance in *Streptococcus uberis* isolated from mastitis samples from cattle in England and Wales (n=26 in 2023).



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

Other mastitis pathogens

Very low numbers of additional mastitis pathogens were tested.

A total of 16 isolates of *Klebsiella pneumoniae* were isolated from bovine mastitis cases. Of these 94% were resistant to ampicillin, reflecting the intrinsic resistance of this organism to ampicillin (Table S4.4.3 in Supplementary Material 2). Resistance to the other antibiotics tested, including HP-CIAs, was not detected.



Five isolates of *Pseudomonas aeruginosa* were recovered in 2023 and all (100%) had limited treatment options. All (100%) isolates were resistant to amoxicillin/clavulanic acid, ampicillin, cefotaxime, tetracycline and trimethoprim/sulfonamide (Table S4.4.3 in Supplementary Material 2). One isolate (20%) was resistant to the anti-pseudomonal cephalosporin antibiotic ceftazidime, an HP-CIA, which is not authorised for use in food-producing animals. 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.

One *Trueperella (Arcanobacterium) pyogenes* isolate was recovered in 2023, which was susceptible to the full panel of antibiotics tested (Table S4.4.3 in Supplementary Material 2).

No Streptococcus agalactiae or Staphylococcus xylosus isolates were recovered in 2023.

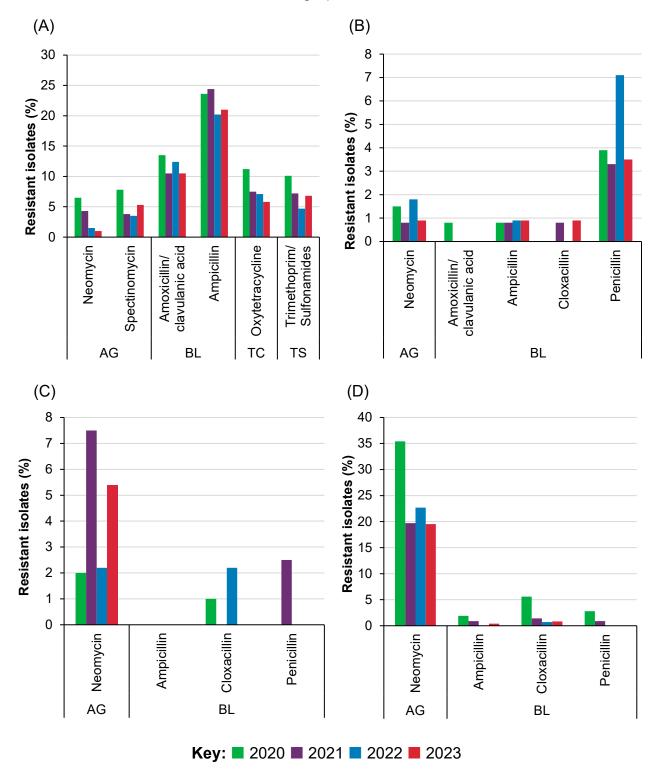
Private Laboratory Initiative (PLI)

The Private Veterinary Laboratory Initiative (PLI) is a collaborative project between the VMD and APHA, which aims to collect and analyse data from the private veterinary laboratories (PVLs) to supplement the AMR surveillance co-ordinated by the VMD. The inclusion of PVL data in this report has demonstrated the potential for broadening AMR surveillance by collaborating with the private sector. Further work in this area is ongoing under a pilot for the UK's National Biosurveillance Network (NBN), see **Box 4.1**.

With thanks to the Vale Veterinary Laboratory for providing data for the PLI. Presented in **Fig. 4.17** are the results from antibiotic susceptibility testing of key mastitis pathogens isolated from cattle by the Vale Laboratory during 2020-2023. Direct comparison with results elsewhere in the chapter should be made with caution, as there are differences in the laboratory methods, antibiotic panels and interpretation criteria used by government and private veterinary laboratories. These isolates were tested by disc diffusion following CLSIVet01 methodology. A summary of the methodology and breakpoints applied can be found in Table S3.1.2 in Supplementary Material 2.

A total of 607 isolates were tested by Vale in 2023. Resistance to aminoglycosides and oxytetracycline was low (<5.8%) for all bacteria tested, aside from *S. uberis*, which showed moderate resistance to aminoglycosides (20%). Moderate to high resistance to beta-lactams was detected in *E. coli*: 11% of isolates were resistant to amoxicillin/clavulanate, and 21% to ampicillin. In *S. uberis*, resistance was <0.8% in 2023 to all beta-lactams tested. Only 3.5% of *S. aureus* tested were resistant to penicillin. In *S. dysgalactiae*, low levels of resistance were seen to neomycin (5.4%) and no resistance was detected to the other antibiotics tested on the panel.

Figure 4.17: Resistance of (A) *Escherichia coli* (n=210 in 2023), (B) *Staphylococcus aureus* (n=113 in 2023), (C) *Streptococcus dysgalactiae* (n=37 in 2023) and (D) *Streptococcus uberis* (n=247 in 2023) isolated from bovine mastitis samples submitted to Vale Veterinary Laboratories. Note scale differs between graphs.



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



Box 4.1: National Biosurveillance Network (NBN)

The National Biosurveillance Network (NBN) is a major cross-government initiative to pilot and improve surveillance for biological threats. The NBN aims to improve the UK's ability to characterise and report biological risks across the One Health spectrum, reliably and rapidly, and is a key component of the UK's Biological Security Strategy (BSS). The NBN pilot is running until April 2025 and will assess how to better record, share and utilise surveillance outputs, and bring together data (including facilitating sharing of privately held data) to generate better insights into threats.

The majority of diagnostic samples originating from animals in the UK are sent to private veterinary laboratories (PVLs) for culture and sensitivity, meaning that the results do not ordinarily feed into AMR surveillance. Under the NBN pilot, the VMD is expanding on previous work (Private Laboratories Initiative, section 4.3.4.1) to involve a greater number of PVLs across multiple species sectors. VMD aims to understand what AMR data is being generated by veterinary laboratories across the private sector, and to facilitate sharing of this data with government. This work will explore possible concerns around data-sharing, as well as technical and other barriers, and try to propose solutions.

This expansion directly supports the UK's One Health AMR objectives, as outlined in the <u>UK</u> <u>National Action Plan</u>, to contain and control AMR by optimising surveillance. Collaboration is integral to the success of this project, and the project team is grateful to the participating PVLs, who have engaged so willingly, and whose input is integral to understanding how government can work with the private sector to enhance AMR surveillance. The VMD is committed to working together to create a more detailed picture of AMR in key veterinary pathogens, to better inform disease management and treatment nationally.

4.3.4.2 Gastrointestinal system

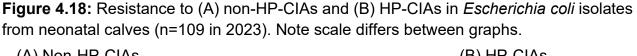
Escherichia coli

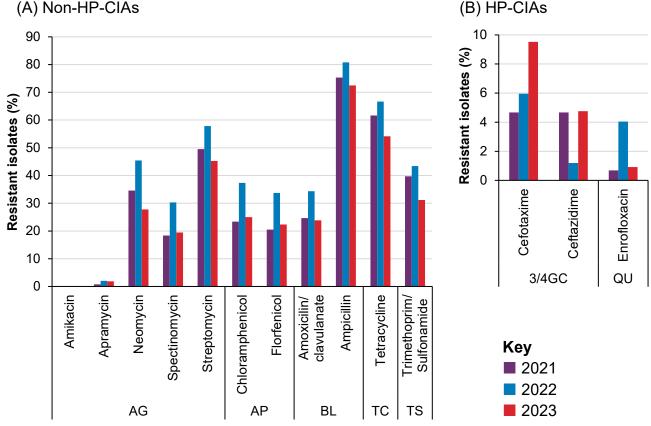
E. coli is a common cause of diarrhoea and dehydration in cattle, and can lead to rapid death. The AMR in *E. coli* results from cattle are presented separately for neonates (**Fig. 4.18**), pre-weaning calves (**Fig. 4.19**), and adults (**Fig. 4.20**).

E. coli in cattle 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 in adults. This is consistent with other animal species, where resistance tends to be higher in younger animals, probably linked to higher antibiotic use in this age group. The similar levels of resistance observed in neonatal and pre-weaning calves could reflect the proximity in which these age groups are often kept on farm. Resistance to trimethoprim/sulfonamides was highest in pre-weaned calves and declined with age. This could reflect relatively higher use of trimethoprim/sulfonamides in this age group for

conditions such as calf scour. A decline in the occurrence of *E. coli* with limited treatment options was noted in neonatal calves, pre-weaning calves and in adult animals. This may be linked to decreased use, although there is not sufficient coverage of usage data in the dairy sector to confirm this (see Section 1.3.9).

In neonatal calves, 37% of isolates had limited treatment options. Extremely high resistance was seen to ampicillin (73%) (**Fig. 4.18**). Resistance to most other antibiotics was high (>20%), apart from amikacin (none detected) and apramycin (1.9%). Of the HP-CIAs, resistance to third-generation cephalosporins cefotaxime (9.5%) and ceftazidime (4.8%) were low and resistance to the quinolone enrofloxacin (0.9%) was very low. With the exception of third-generation cephalosporins, to which resistance increased since 2022, resistance to individual antibiotics in *E. coli* arising from this age group decreased between 2022 and 2023.





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, 27% of isolates had limited treatment options. Resistance was very high to tetracycline (63%), and very high to ampicillin (53%) (**Fig. 4.19**). Resistance to most other antibiotics tested was high. Of the HP-CIAs, resistance levels to the quinolone enrofloxacin (3.6%) was low.



Oral products specifically authorised for calves (either for scours or respiratory disease) accounted for 3.8 tonnes of active ingredient sold in 2023 and these contain tetracyclines, aminoglycosides or sulfonamides, which may account for the resistance level seen in neonatal and pre-weaned calves.

A subset of isolates was tested to additional antibiotics perhaps due to treatment failure. Of the 18 isolates tested against streptomycin, ten (56%) were resistant. Of the HP-CIAs, one isolate (5.3%) of 19 tested was resistant to the third-generation cephalosporins cefotaxime and ceftazidime.

(B) HP-CIAs (A) Non-HP-CIAs 80 8 Resistant isolates (%) 70 6 60 Resistant isolates (%) 4 50 2 40 0 30 Cefotaxime Ceftazidime Enrofloxacin 20 10 0 3/4GC QU Neomycin Spectinomycin Streptomycin clavulanate Amikacin Ampicillin Tetracycline Apramycin Chloramphenicol Florfenicol **Frimethoprim**/ Amoxicilin/ Sulfonamide Key 2021 2022 AG AP ΒL 2023 ΤС ΤS

Figure 4.19: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from pre-weaned calves (n=87 in 2023). Note scale differs between graphs.

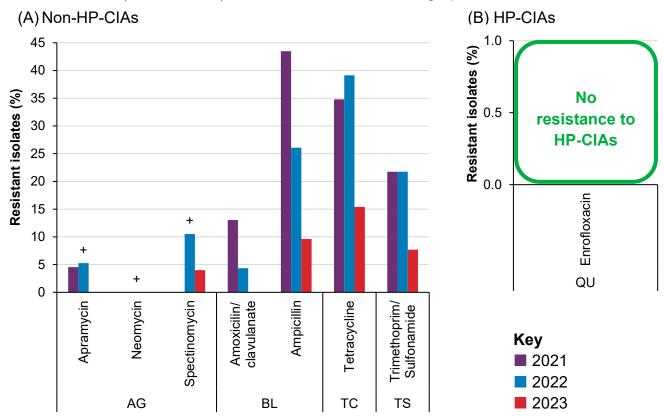
+ Less than 20 isolates tested

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

In adult cattle, one isolate (1.7%) had limited treatment options. Moderate levels of resistance were seen to tetracycline (15%) (**Fig. 4.20**). Levels of resistance to the other antibiotics tested were either low or not detected. No HP-CIA resistance was detected in 2023.

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Figure 4.20: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from adult cattle (n=52 in 2023). Note scale differs between graphs.



+ Less than 20 isolates tested

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

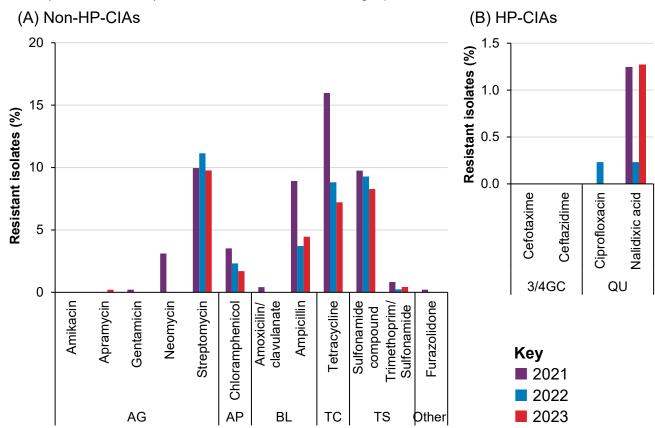
Salmonella spp.

Salmonellosis can cause a wide range of clinical signs in cattle including diarrhoea, joint infections, chronic pneumoniae, abortion and sudden death from septicaemia. *Salmonella* data for cattle is presented below for all age groups (**Fig. 4.21**).

Of the 471 *Salmonella* isolates tested from cattle in 2023, 89% were susceptible to the full panel of antibiotics. This is a reduction from 87% in 2022. 8.1% of *Salmonella* isolated from cattle in 2023 had limited treatment options. Low levels of resistance were detected to ampicillin (4.5%), chloramphenicol (1.7%), streptomycin (9.8%), sulfonamides (8.3%) and tetracycline (7.2%). Levels of resistance to the other antibiotics tested were either very low (<1%) or not detected. Of the HP-CIAs, resistance to the third-generation cephalosporins or to the quinolone ciprofloxacin was not detected; low levels of resistance were detected to the quinolone nalidixic acid (1.3%).



Figure 4.21: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Salmonella* isolates from cattle (n=471 in 2023). 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

Results presented for the majority of the key respiratory pathogens are generated using MICs, as outlined in S3.1.3 of Supplementary Material 2, unless indicated otherwise.

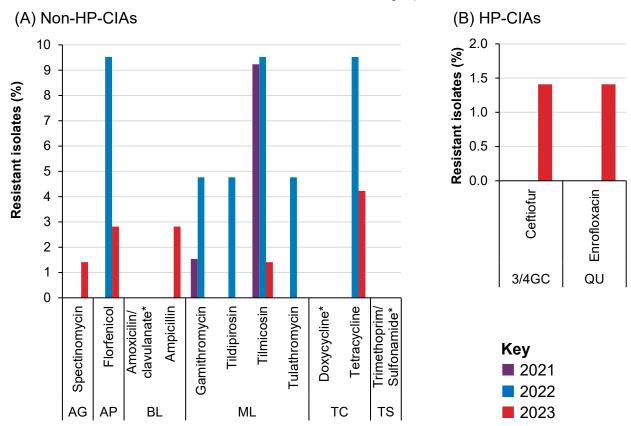
Mannheimia haemolytica

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 71 isolates were recovered from diagnostic samples in 2023. Of these, 93% were susceptible to the full panel of antibiotics tested and 2.8% were MDR. Resistance to the antibiotics tested was low (<4.2%) or not detected (**Fig. 4.22**). Of the HP-CIAs, one isolate (1.4%) was resistant to the third-generation cephalosporin ceftiofur and one isolate (1.4%) was resistant to the quinolone enrofloxacin.



Figure 4.22: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Mannheimia haemolytica* isolated from cattle (n=71 in 2023). Interpreted using cattle CLSI veterinary breakpoints unless indicated otherwise. Note scale differs between graphs.



* Interpreted using CA-SFM veterinary CBP

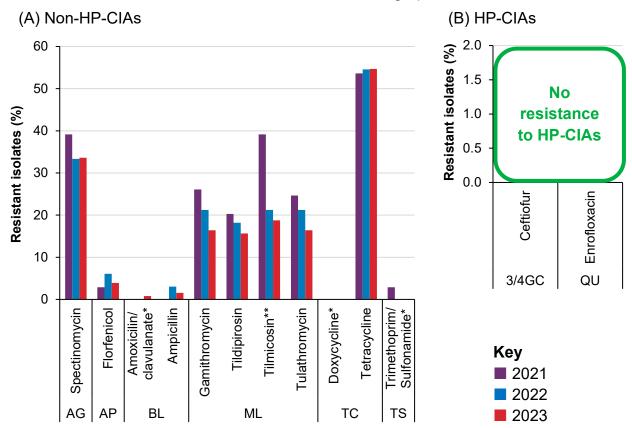
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third and fourth generation cephalosporins

Pasteurella multocida

P. multocida primarily causes respiratory disease in cattle in the UK. Of the 128 isolates recovered from diagnostic samples in 2023, 41% were susceptible to the full panel of antibiotics tested and 7.8% were MDR. Very high levels of resistance were detected to tetracycline (55%) and high levels to spectinomycin (34%) (**Fig. 4.23**). Levels of resistance to the other antibiotics tested were much lower (<19%) or not detected. All tetracycline-resistant isolates were susceptible to doxycycline, indicating that this may be a viable treatment choice, even when tetracycline resistance is detected. No HP-CIA resistance was detected in 2023.



Figure 4.23: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Pasteurella multocida* isolated from cattle (n=128 in 2023). Interpreted using cattle CLSI veterinary breakpoints unless indicated otherwise. Note scale differs between graphs.



* Interpreted using CA-SFM veterinary CBP

** Tilmicosin breakpoint for porcine isolates applied

AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, 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 2023.

Histophilus somni

Histophilus somni (formerly known as *Haemophilus somnus*) causes pneumonia and thrombo-embolic meningoencephalitis in calves. These bacteria are tested using the disc diffusion method. 27 isolates were recovered in 2023 and all isolates were fully susceptible to the panel of antibiotics tested (Table S4.4.8 in Supplementary Material 2).



4.3.4.4 Multi-system pathogens

Listeria monocytogenes

Listeria spp. are widely distributed in the environment and can be isolated from soil, decaying vegetation and poorly fermented silage. Listeriosis can cause a wide range of clinical signs in cattle including neurological symptoms, abortion and sepsis.

All four *Listeria monocytogenes* isolates tested in 2023 were susceptible to the full panel of antibiotics (Table S4.4.9 in Supplementary Material 2).

Staphylococcus xylosus

Staphylococcus xylosus causes dermatitis and two isolates were recovered in 2023. One isolate (50%) was resistant to ampicillin and penicillin (Table S4.4.9 in Supplementary Material 2). No resistance was detected to the other antibiotics tested on the panel.

4.3.5 Sheep

Results for pathogenic bacteria isolated from sheep are presented in this section and are organised by body system. Most testing reported here was performed using disc diffusion methodology (see section S3.1.1 in Supplementary Material), with the exception of selected respiratory pathogens, for which broth microdilution was used, as measured by MIC (see section S3.1.3 in Supplementary Material). The complete sheep dataset can be found in section S4.5 of Supplementary Material 2.

4.3.5.1 Gastrointestinal system

Escherichia coli

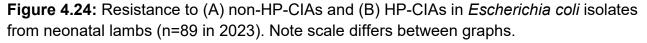
E. coli causes diarrhoea in sheep and watery mouth disease in newborn lambs.

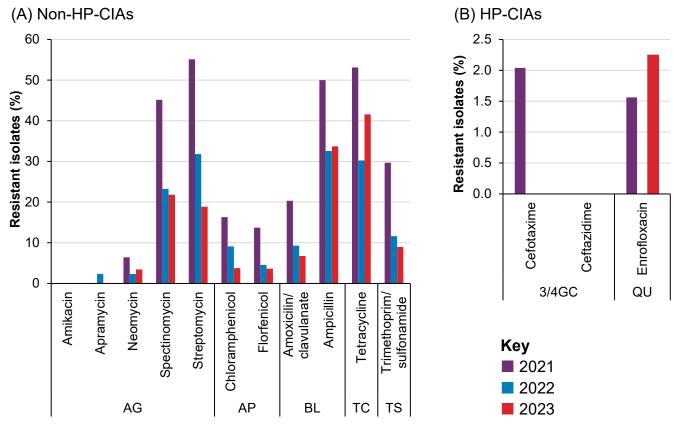
The AMR in *E. coli* results from sheep are presented separately for neonates (**Fig. 4.24**), pre-weaning lambs (**Fig. 4.25**), and adults (**Fig. 4.26**). Isolates of ovine *E. coli* were predominantly collected from neonates (36% of 264 isolates), with smaller numbers from pre-weaned (17%) and adult sheep (24%). Across all age categories, a total of 5.7% of isolates had limited treatment options. This occurred most frequently in pre-weaned lambs (13%), and was similar in neonates (9.6%), but was not detected in adults. Non-HP-CIA resistance was generally highest in pre-weaned lambs and declined with age.

In neonatal lambs, 9.6% of isolates had limited treatment options. High levels of resistance were seen to ampicillin (34%), spectinomycin (22%) and tetracycline (42%) (**Fig. 4.24**). Streptomycin resistance was observed in 19% of isolates. In 2023, due to a product being discontinued, there were no longer any sales of oral spectinomycin for treating watery mouth in lambs. Resistance to spectinomycin and streptomycin reduced between 2022 and 2023; it will be interesting to see if further reductions are detected in 2024. Resistance to the other



antibiotics tested was low (<9%) or not detected, and resistance to HP-CIAs was not observed.





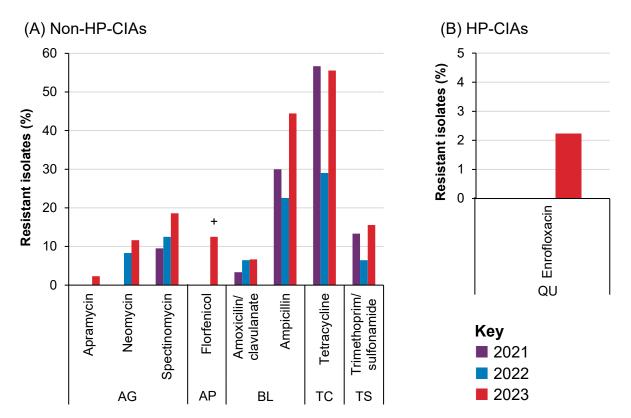
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulfonamides, 3/4GC: third- and fourth-generation cephalosporins

In pre-weaned lambs, 13% of isolates had limited treatment options. Very high levels of resistance were detected to tetracycline (56%) and high levels of resistance to ampicillin (44%, **Fig. 4.25**). This may be linked to antibiotic use, as tetracyclines and penicillins have been reported to be the <u>most commonly used</u> antibiotic classes in this sector. Of the HP-CIAs, one isolate (2.2%) was resistant to the quinolone enrofloxacin.

A subset of six isolates were tested to additional antibiotics perhaps due to treatment failure. All six isolates (100%) were resistant to streptomycin and one isolate (16.7%) was resistant to the third-generation cephalosporin cefotaxime. Resistance to the third-generation cephalosporin ceftazidime was not detected.



Figure 4.25: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from pre-weaning lambs (n=45 in 2023). Note scale differs between graphs.



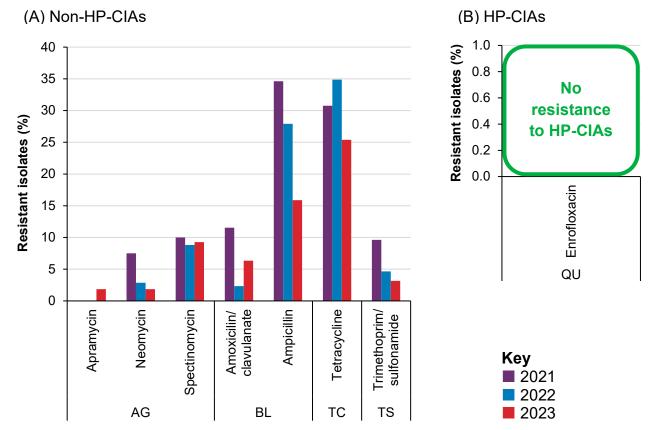
+ Less than 20 isolates tested

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

In adult sheep, no isolates showed limited treatment options. Levels of resistance to tetracycline (25%) was high but were lower than in the preceding two years (**Fig. 4.26**). Resistance to the other antibiotics was lower (<16%). HP-CIA resistance was not detected between 2021 and 2023.



Figure 4.26: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Escherichia coli* isolates from adult sheep (n=63 in 2023). Note scale differs between graphs.



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

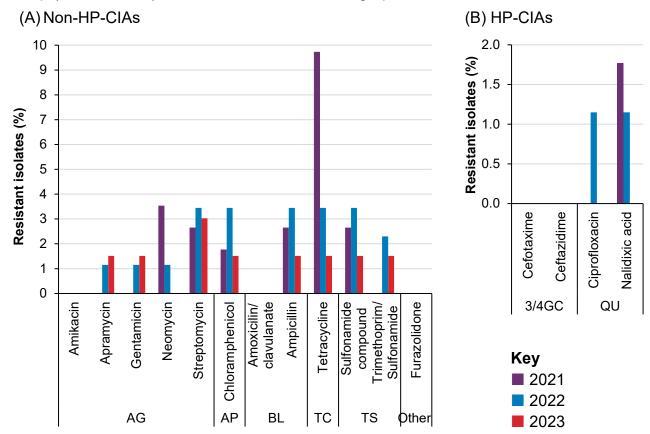
Salmonella spp.

Salmonellosis can cause a wide range of clinical signs in sheep including diarrhoea, fever, abortion and sudden death from septicaemia. *Salmonella* data for sheep is presented below for all age groups (**Fig. 4.27**).

Of the 66 isolates tested in sheep, 97% were susceptible to the full panel of antibiotics tested. This is an increase from 95% in 2022. A single isolate (1.5%) had limited treatment options. Low levels of resistance were detected to known treatment options including ampicillin (1.5%) and sulfonamides (1.5%). Levels of resistance to the other antibiotics tested were either low or not detected. No resistance was observed to the HP-CIAs in 2023.



Figure 4.27: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Salmonella* isolates from sheep (n=66 in 2023). 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 *Bibersteinia trehalosi, Mannheimia haemolytica* and *Pasteurella multocida*.

Results presented for the majority of the key respiratory pathogens are generated using MICs, as outlined in S3.1.3 of Supplementary Material 2, unless indicated otherwise.

Bibersteinia trehalosi

B. trehalosi mainly causes septicaemia and systemic pasteurellosis in growing lambs. A total of 47 isolates were recovered from diagnostic samples in 2023. Of these, 96% were susceptible to the full panel of antibiotics tested and none were MDR. Resistance was detected to ampicillin in 4.3% of isolates, and to amoxicillin/clavulanate and tilmicosin in 2.1% of isolates (Table S4.5.4 in Supplementary Material 2). HP-CIA resistance was not observed and no resistance was detected to the other antibiotics tested on the panel.



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. All 96 isolates recovered from diagnostic samples in 2023 were susceptible to the full panel of antibiotics (Table S4.5.4 in Supplementary Material 2).

Pasteurella multocida

P. multocida causes respiratory disease in sheep although rarely in the UK. A total of 23 isolates were recovered from diagnostic samples in 2023. Of these, 96% were susceptible to the full panel of antibiotics tested and none were MDR. Low levels of resistance were detected to gamithromycin, spectinomycin, tildipirosin, tilmicosin and tulathromycin (all 4.3%, Table S4.5.4 in Supplementary Material 2). HP-CIA resistance was not observed and no resistance was detected to the other antibiotics tested on the panel.

Trueperella (Arcanobacterium) pyogenes

A single *Trueperella (Arcanobacterium) pyogenes* isolate was recovered in 2023, which was tested by disc diffusion method and was susceptible to the panel of antibiotics tested (Table S4.5.5 in Supplementary Material 2).

4.3.5.3 Integumentary system

Staphylococcus aureus

Staphylococcus aureus causes mastitis and tick pyaemia, as well as other infections, in sheep. 18 isolates were tested to the panel of antibiotics in 2023 and none had limited treatment options. Resistance to tetracycline was detected in 22% of isolates (Table S4.5.6 in Supplementary Material 2). Resistance to HP-CIAs was not tested and no resistance was detected to the other antibiotics tested on the panel.

Staphylococcus xylosus

Staphylococcus xylosus causes dermatitis. No isolates were recovered from sheep in 2023.

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 20 isolates were tested and none had limited treatment options. All isolates (100%) were resistant to tetracycline and one isolate (5%) was resistant to tylosin (Table S4.5.6 in Supplementary Material 2). Resistance to HP-CIAs was not tested and no resistance was detected to the other antibiotics tested on the panel.



4.3.5.5 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 sheep, infection usually presents as polyarthritis. A single isolate was tested in 2023 and was resistant to trimethoprim/sulfonamides (Table S4.5.7 in Supplementary Material 2). Resistance was not 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. Listeriosis can cause a wide range of clinical signs in sheep including neurological symptoms, abortion and sepsis.

All three *Listeria monocytogenes* and four *Listeria ivanovii* isolates tested in 2023 were susceptible to the full panel of antibiotics (Table S4.5.7 in Supplementary Material 2).

4.3.6 Dogs

Results for *Salmonella* isolated from dogs are presented in this section and are organised by body system. Testing reported here was performed using disc diffusion methodology (see section S3.1.1 in Supplementary Material). The complete dog dataset can be found in section S4.6 of Supplementary Material 2.

A change in legislation in 2021 meant that *Salmonella* isolates from dogs became reportable under the <u>Zoonoses Order</u> in Great Britain.

4.3.6.1 Gastrointestinal system

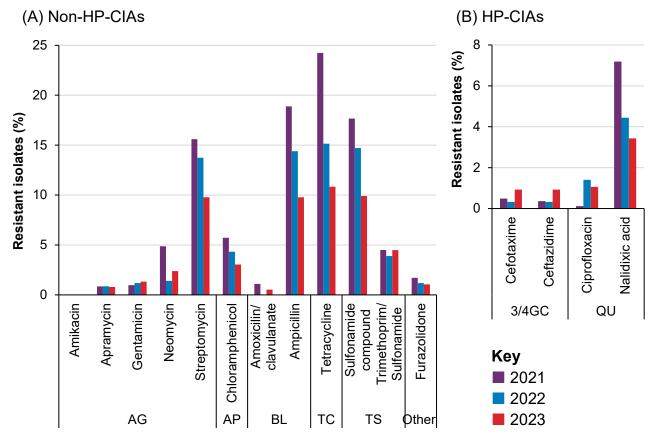
Salmonella spp.

Salmonellosis can cause a wide range of clinical signs in dogs including diarrhoea, fever, decreased appetite and lethargy.

Of the 757 *Salmonella* isolates tested from dogs in 2023, 82% were susceptible to the full panel of antibiotics tested and 10% had limited treatment options. Levels of resistance were highest to streptomycin (9.8%), ampicillin (9.8%), tetracycline (10.8%) and sulfonamide compounds (9.9%) (**Fig. 4.28**). All of these were noticeably lower than those reported in both 2021 and 2022, and is consistent with the reduction in antibiotic sales for dogs between 2022 and 2023 reported in chapter 2 (Section 1.3.5). Seven isolates (0.9%) were resistant to the HP-CIA third-generation cephalosporins, all of which had limited treatment options. Resistance to the quinolones ciprofloxacin (1.1%) and nalidixic acid (3.4%) were low. Sales data estimates suggest that third generation cephalosporins and fluoroquinolones account for 2 and 5% of overall antibiotic use in dogs respectively (Section 1.3.8).



Figure 4.28: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Salmonella* isolates from dogs (n=757 in 2023). 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 the clinical surveillance programme, the VMD is working with the Centre for environment, fisheries and aquaculture science (Cefas) to explore clinical surveillance for AMR in the trout sector. In 2022, the focus was on establishing stakeholder engagement, sources of isolates, and robust procedures. In 2023, the pilot programme focused on three fish pathogens: *Aeromonas salmonicida*, which causes furunculosis; *Yersinia ruckeri*, which causes enteric red mouth disease (ERM); and *Flavobacterium psychrophilum*, which causes rainbow trout fry syndrome. These are three of the most important bacterial pathogens affecting farmed trout and salmon in Great Britain. These diseases are controlled by vaccination, but in instances of vaccine failure or supply shortages, outbreaks can occur.

In 2023, Cefas' Weymouth laboratory analysed 188 isolates, recovered from post-mortem carcasses or other diagnostic samples from trout by private veterinary surgeons, fish health specialists, and partner veterinary laboratories in England and Wales. All but 15 isolates precede 2023 and are being tested for AMR to provide historic baseline data. Results from the 15 isolates submitted from diseased trout in 2023 are presented here. Two of the isolates were *A. salmonicida*, 11 were *Y. ruckeri*, and two were discarded as unintended species.



AST was performed using broth microdilution following Clinical and Laboratory Standards Institute (CLSI 2020) protocols, against a panel of antibiotics relevant to fish and/or human health. Results were interpreted using CLSI epidemiological cut-off values where available. However, as AMR surveillance in fish is not well-established globally, published cut-off values are not available for some of the bacterial species/antibiotic combinations tested. In these occasions, the normalized resistance interpretation (NRI) method was chosen to determine the wild type cut-off value (COwt). Resistances reported using these cut-off values do not necessarily imply clinical resistance.

Of the two *A. salmonicida* isolates tested by broth microdilution, neither were fully sensitive, nor MDR. Levels of resistance to the carbapenem meropenem, sulfamethoxazole, and the HP-CIA oxolinic acid were 50% (Table S4.7.1 in Supplementary Material 2).

Of the 11 *Y. ruckeri* isolates, no isolates were fully sensitive, and a single isolate (9.1%) was MDR. Levels of resistance to sulfamethoxazole were extremely high (91%), although this result needs to be interpreted with caution, as the numbers of isolates used to generate the local cut-off were very small (**Fig. 4.29**). Levels of resistance to ampicillin (9.1%) and to the carbapenem meropenem (9.1%) were low. WGS is being conducted to better understand these findings. Resistance was also found to the HP-CIAs oxolinic acid (55%), enrofloxacin (55%) and ceftazidime (9.1%). This indicates emerging resistance to these antibiotics, most critically oxolinic acid, which is the treatment of choice for ERM. Antibiotic use data representing around 90% of the UK trout sector shows that oxolinic acid accounts for 25% overall use, although this has reduced by 73% since 2017 (see section 1.3.5.2). It should be noted that these results do not necessarily imply treatment failure, and that the number of isolates tested in 2023 was small.

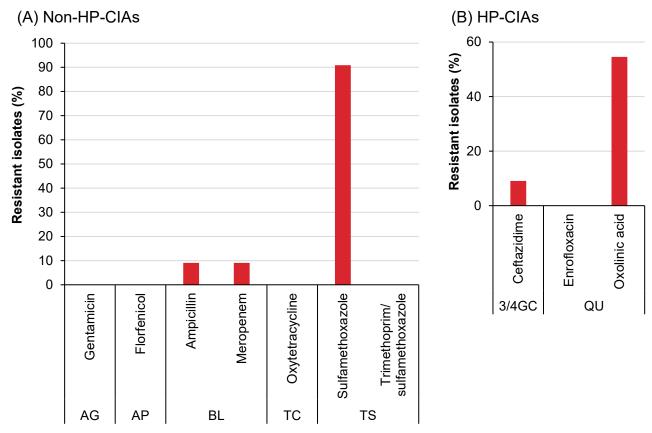
Understanding the relevance of these results to trout health would be improved by testing larger numbers of isolates for AMR. Cefas are continuing to work with the British Trout Association (BTA) to explore barriers to sample submission.



Clinical surveillance

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Figure 4.29: Resistance to (A) non-HP-CIAs and (B) HP-CIAs in *Yersinia ruckeri* isolates from trout in 2023 (n=11 in 2023). Interpreted using Cefas internally generated breakpoints unless indicated otherwise. 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





Annex A: Glossary of terms

Active ingredient

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

AFBI

Agri-Food Biosciences Institute

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.

APHA

Animal and Plant Health Agency, an Executive Agency of the Department for Environment, Food and Rural Affairs (Defra)



AST

Antibiotic susceptibility testing: testing used to determine which antibiotics will inhibit the growth of, or kill, a bacterium/micro-organism.

BEIC

British Egg Industry Council

BPC

British Poultry Council

Broiler

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

BSAC

British Society for Antimicrobial Chemotherapy

BTA

British Trout Association

Bulk Milk

Refrigerated milk from multiple cows within a herd stored for transportation from the farm to processing facilities i.e. to go on to be pasteurised.

BVPA

British Veterinary Poultry Association

CAGG

Cattle Antibiotic Guardian Group

CA-SFM

Committé Antibiogramme - Société Française de Microbiologie

СВР

Clinical Break Point: relates the laboratory results to the likelihood of clinical treatment success or failure.

Cefas

Centre for environment, fisheries and aquaculture science

CHAWG

Cattle Health and Welfare Group

CLSI

Clinical and Laboratory Standards Institute



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).

DARC

Defra Antimicrobial Resistance Coordination group

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 has been used; therefore the following classes of antibiotics are included under HP-CIAs fluoroquinolones; third and fourth generation cephalosporins and polymyxins (including colistin).

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

ESBL-producing

Extended spectrum beta lactamase producing: the bacteria is able to produce betalactamase enzymes that may make them resistant to some antibiotics.

ESVAC

European Surveillance of Veterinary Antimicrobial Consumption

EUCAST

European Committee on Antimicrobial Susceptibility Testing

Food-producing animal (species)

Animals used for food production including (but not limited to): cattle, sheep, pigs, poultry, salmon, trout and bees.

FSA

Food Standards Agency

FSS

Food Standards Scotland

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.

Limited treatment options

Isolates resistant to four or more individual antibiotics

Medicated feeding stuff

Feeding stuffs that contain a veterinary medicine and that are intended for feeding to animals without further processing.

MDR

Multi-drug resistance, isolates resistant to three or more antibiotic classes.



MIC

Minimum inhibitory concentration, the lowest concentration of an antibiotic that inhibits visible growth of a bacterium after overnight incubation.

MH

Medicine Hub for ruminants

NMR

National Milk Records

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.

NRL

National reference laboratories

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.

PATH-SAFE

Pathogen Surveillance in Agriculture, Food and Environment

PCR

Polymerase chain reaction: a laboratory technique used to amplify DNA sequences for further analysis.

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

SRUC

Scotland's Rural College Veterinary Services

ST

Sequence type, the characterised unique sequences combined into an allelic profile present within a bacterium.

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)



VRE

Vancomycin-resistant enterococci

WGS

Whole genome sequencing, a laboratory method to DNA sequence the genome.

WHO

World Health Organization

WOAH

World Organisation for Animal Health



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 has been used across EU Member States and is currently the best approximation of consumption. This form of analysis is used 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 85%. However, for dairy and sheep coverage is much smaller (30% and 11% 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 chickens, 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 (<u>AMEG</u>) 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.
- Defined EUCAST ECOFFs are not available for all drug/bug combinations. Where these were not available European Food Safety Authority (EFSA) cut-off values were applied. In the absence of both then tentative EUCAST ECOFF were considered.
- Since 2022 ertapenem has been 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.
- It should be noted that when using selective culture methods, the occurrence of ESBL-, AmpC- or carbapenemase-producing *E. coli*, colistin- and amikacin-resistant *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 these organisms being a minority among the populations in the gut flora of these food-

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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, PATH-SAFE surveys

- For the PATH-SAFE AMR pilot surveys, the same approach as the harmonised monitoring scheme above was used. However, for each of these surveys the >60% coverage that was aimed for was not achieved.
- The equivalent sampling methodology was used in the case of bulk milk samples from dairy cattle.
- In addition to the selective culture methods above, the occurrence of methicillinresistant *Staphylococcus aureus* was also assessed.

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.

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 the extent to which the samples processed by APHA, SRUC Veterinary Services and AFBI are representative of total diagnostic submissions is not known.
- 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

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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 <u>Zoonoses Order</u>. 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 wellestablished; 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 veterinary surgeons 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 2.
- Different antibiotic susceptibility testing methodologies are used in England and Wales (APHA), Scotland (SRUC Veterinary Services), and Northern Ireland (AFBI). APHA use BSAC methodology to determine resistance/susceptibility based on human clinical breakpoints, whilst AFBI use CLSI. SRUC Veterinary Services are in the process of changing from BSAC methodology to EUCAST. Isolates from pigs and poultry in 2023 have been tested by SRUC Veterinary Services using EUCAST methodology and breakpoints, cattle and sheep isolates were tested using BSAC methodology. 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.
- The breakpoints used for determining resistance for isolates undergoing broth microdilution to generate MIC values, recovered under the veterinary clinical



surveillance programme in GB, are those recommended by CLSI. These veterinary-specific breakpoints have been established to decrease reliance on human breakpoints and continue to be developed and reviewed. In the case of some veterinary drug-bug combinations a CLSI veterinary CBP value may not exist. In this case in the first instance CA-SFM veterinary CBPs have been used, and if veterinary CBPs were not available, EUCAST human CBPs were used.

Private Laboratory Initiative (PLI):

• The Private Laboratory Initiative (PLI) is a collaborative project between the VMD and APHA. The purpose is to collect and analyse data from the private veterinary laboratories to supplement the AMR surveillance co-ordinated by the VMD. There are differences in the laboratory methods, antibiotic panels and interpretation criteria used by government and private laboratories so the data should be interpreted with caution. The methods used to determine antimicrobial susceptibility in this data are based on those in CLSI Vet01 July 2013.



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
- Animalcare Limited
- aniMedica GmbH
- Bela-Pharm GmbH & Co. KG
- Bimeda Animal Health Ltd
- Boehringer Ingelheim Animal Health Ltd
- Ceva Animal Health Ltd
- Chanelle Animal Health Ltd
- Dechra Ltd
- Divasa Farmavic S.A.
- Dopharma Research B.V.
- ECO Animal Health
- Ecuphar N.V
- Elanco Europe Ltd
- Emdoka bvba
- Eurovet Animal Health B.V.
- Fatro S.P.A.
- Franklin Pharmaceuticals Ltd
- Global Vet Health S.L.
- Huvepharma N.V.
- Industrial Veterinaria S.A.
- Intervet International B.V.
- Kela N.V.
- Kernfarm B.V.
- Krka Dd
- Laboratorios Hipra S.A.
- Laboratorios Karizoo S.A.
- Laboratorios SYVA S.A.U
- Lavet Pharmaceuticals Ltd
- Le Vet B.V.
- Livisto Int.'I.S.L
- MSD Animal Health UK Limited
- Nextmune Italy S.R.L.
- Nimrod Veterinary Products Ltd
- Norbrook Laboratories Ltd
- Orion Corporation
- SP Veterinaria S.A.
- TVM UK
- Univet Ltd
- Vetcare Oy



- Vétoquinol UK Ltd
- Vetpharma Animal Health S.L.
- VetViva Richter GmbH
- Virbac S.A.
- VMD N.V.
- Zoetis UK Ltd

