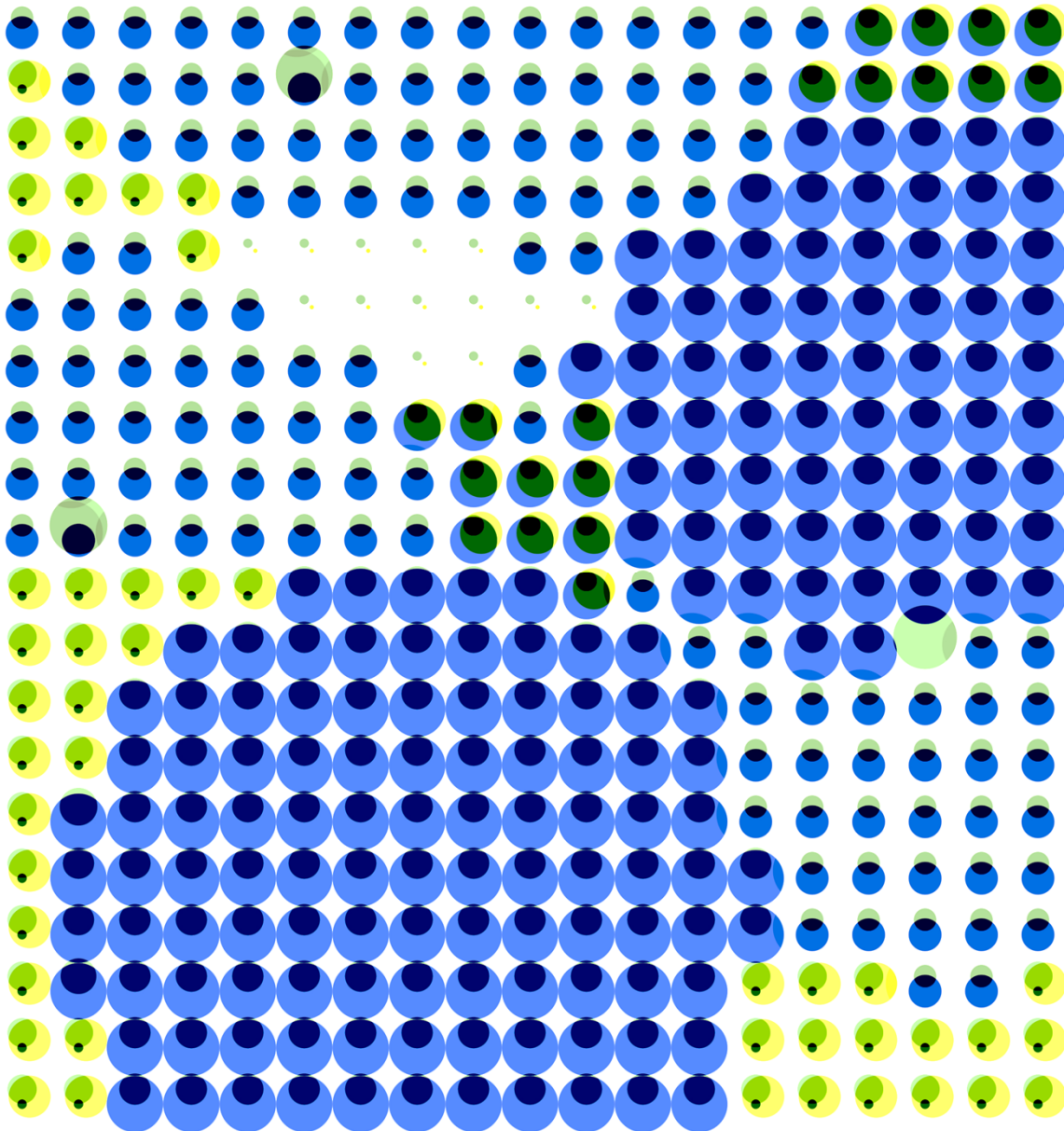


JVARM REPORT

2023



Veterinary AMR Center
National Veterinary Assay Laboratory,
Ministry of Agriculture, Forestry and Fisheries



Sep 2026

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I. Introduction

Antimicrobial agents are essential for protecting animal health, ensuring a stable supply of livestock and aquatic products, and treating infectious diseases in animals, but there is always a risk that antimicrobial resistant bacteria selected by antimicrobial use may affect the medical care of humans, livestock, companion animals, and aquatic animals. For this reason, the Ministry of Agriculture, Forestry and Fisheries (MAFF) conducts monitoring of antimicrobial resistant bacteria and, based on the results of the survey, formulates and implements risk management measures according to the assessed level of risk.

The problem caused by antimicrobial resistant bacteria is not only a problem in Japan, but has become one of the most important international issues. In 2015, the World Health Organization (WHO) formulated the “Global Action Plan on Antimicrobial Resistance” and requested member countries to promote measures to combat antimicrobial resistance. In response, Japan formulated the “National Action Plan on Antimicrobial Resistance (AMR) (2016-2020)” in 2016, and a “new National Action Plan on Antimicrobial Resistance (2023-2027)” is currently underway from 2023.

The nationwide monitoring of antimicrobial resistant bacteria is considered one of the key pillars of control measures outlined in the National Action Plan on AMR. The MAFF has been carrying out the Japanese Veterinary Antimicrobial Resistance Monitoring (JVARM) since 1999 in conjunction with prefectures and the Food and Agricultural Materials Inspection Center (FAMIC) as well as other related public and private institutions.

This report provides an overview of the monitoring of antimicrobial-resistant bacteria isolated from healthy and diseased animals in 2023, as well as monitoring of antimicrobial sales in 2023. The number of samples and resistance rates for each bacterial species, as well as trends in antimicrobial sales volume, are published on the website of the National Veterinary Assay Laboratory (https://www.maff.go.jp/nval/yakuzai/yakuzai_p3.html).

2. Summary of Monitoring Results 2023

Resistance rates are not presented when fewer than 20 isolates were collected. For trends in resistance rates, please refer to the National Veterinary Assay Laboratory website (https://www.maff.go.jp/nval/yakuzai/yakuzai_AMR_2.html).

2.1. Outcome Indices of the National Action Plan

2.1.1. Resistance Rates

Based on the status of achievement of the outcome indices set in the National Action Plan on Antimicrobial Resistance (AMR) 2016–2020, the National Action Plan on Antimicrobial Resistance (AMR) 2023–2027 (hereinafter referred to as the “new Action Plan”) retained, from the perspective of continuity, the resistance rates of *Escherichia coli* to tetracyclines, third-generation cephalosporins, and fluoroquinolones as outcome indices for the animal sector. In addition, because antimicrobial resistance status and hygiene management differ by livestock species, target values to be achieved by 2027 were established for each livestock species in order to serve as indicators of the outcomes of measures addressing species-specific issues (Table 2-1-1).

In 2023, the resistance rates of *E. coli* isolated from healthy livestock to tetracyclines, one of the outcome indices in the new Action Plan, were 20.0% in cattle, 56.3% in pigs, and 53.5% in chickens. The corresponding resistance rates to third-generation cephalosporins were 1.0%, 0.0%, and 3.9%, respectively, while those to fluoroquinolones were 0.5%, 0.7%, and 16.1%, respectively. No substantial increases or decreases were observed for any of these antimicrobial classes in any livestock species (Figures 2-1-1-1 to 2-1-1-3).

Table 2-1-1 Outcome indices in the new Action Plan

Indicator (Resistance rates of <i>Escherichia coli</i>)	2027 target value		
	Cattle	Pigs	Chickens
Tetracyclines	≤20%	≤50%	≤45%
Third-generation cephalosporins	≤1%	≤1%	≤5%
Fluoroquinolones	≤1%	≤2%	≤15%

Fig. 2-1-1-2

Third-generation cephalosporin resistance rates

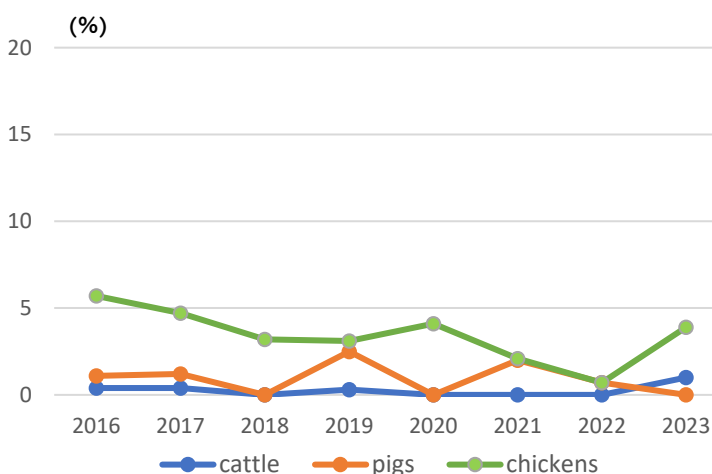


Fig. 2-1-1-1 Tetracycline resistance rates

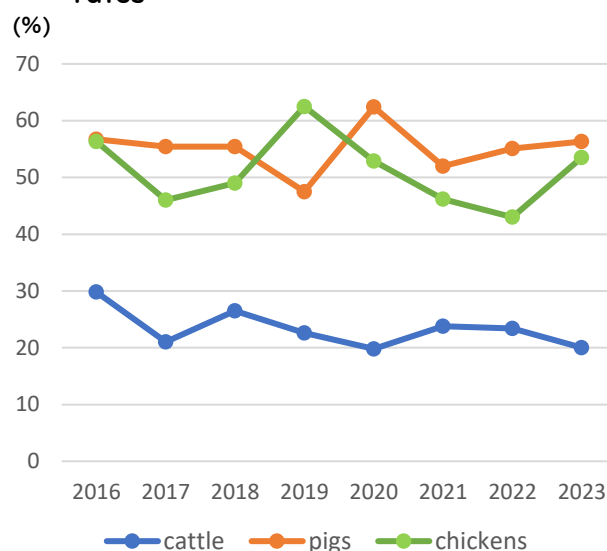
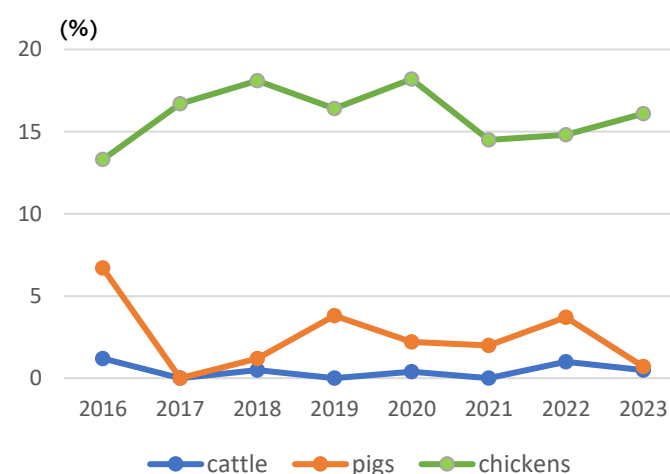


Fig. 2-1-1-3 Fluoroquinolone resistance rates



2.1.2. Antimicrobial Sales Volume

In addition to resistance rates, the new Action Plan established targets for antimicrobial use as outcome indices for the animal health sector. One target is to reduce the total use of veterinary antimicrobials in the livestock sector by 15% from the 2020 level of 626.8 tons by 2027. The other is to limit the total use of second-line antimicrobials in the livestock sector, including third-generation cephalosporins, 15-membered ring macrolides (tulathromycin and gamithromycin), fluoroquinolones, and colistin, to no more than 27 tons in 2027.

In 2023, the total use of veterinary antimicrobials in the livestock sector was 559.4 tons, representing a 10.8% reduction from the 2020 level (Figure 2-1-2-1). The total use of second-line antimicrobials in the livestock sector was 23.481 tons in 2023, which was below the target of 27 tons (Figure 2-1-2-2).

Fig. 2-I-2-I Trends in antimicrobial sales volume in the livestock sector

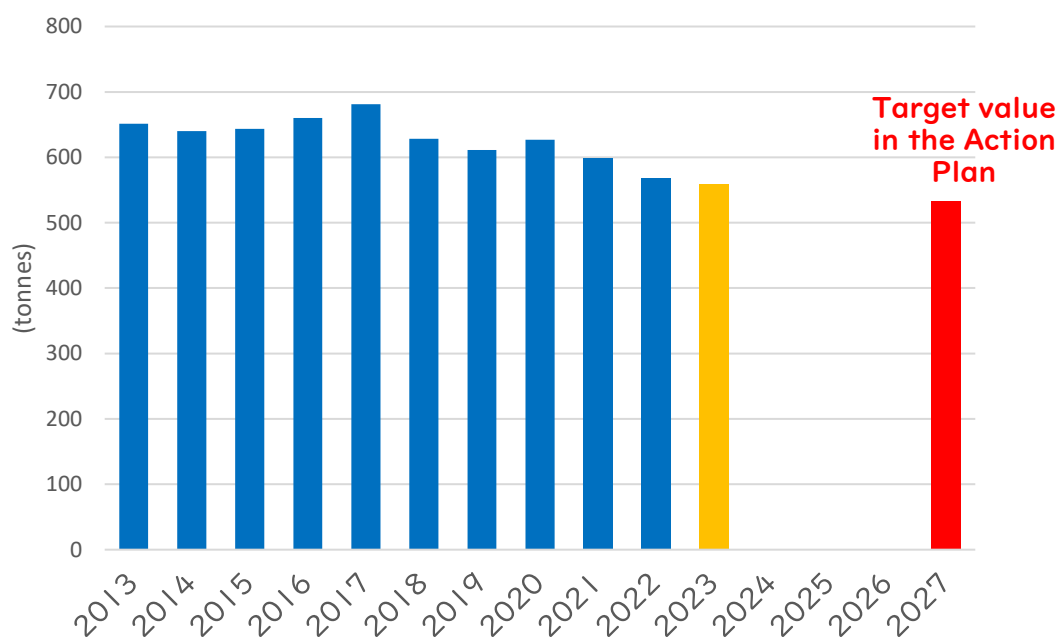
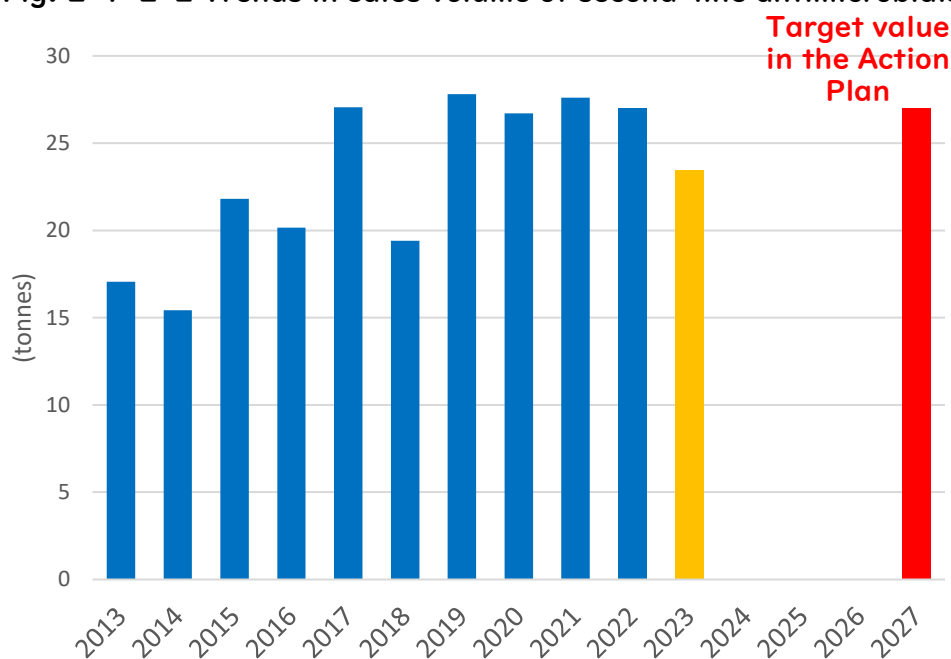


Fig. 2-I-2-2 Trends in sales volume of second-line antimicrobials in the livestock sector



2.2. Overview

Healthy livestock

In addition to the low resistance rates of *Escherichia coli* isolated from healthy livestock to third-generation cephalosporins and fluoroquinolones, which are medically important antimicrobials included as outcome indices in the National Action Plan on Antimicrobial Resistance (AMR) (2023–2027), the resistance rate to colistin, which is also critically important in human medicine, remained low. This was considered to reflect efforts by livestock farmers, veterinarians, and other stakeholders to ensure the prudent use of these

antimicrobials as second-line antimicrobials. Furthermore, resistance rates to MEPM and VCM, which are not approved for veterinary use but are regarded as last-resort treatments for multidrug-resistant bacterial infections in human medicine, were 0.0%.

In contrast, although sales volume of tetracyclines, which are widely used in animals, has decreased in pigs, no change was observed in the resistance rate. An analysis of antimicrobial resistance patterns among *E. coli* isolates from pigs in 2023 showed that 9.0% of the isolates were resistant to TC alone, whereas 47.2% were resistant to TC as well as to other antimicrobials. These findings suggested that reducing selective pressure from TC alone would be unlikely to reduce the TC resistance rate and that selective pressure from multiple antimicrobials needs to be reduced simultaneously. It is therefore important to reduce opportunities for the overall use of antimicrobials, rather than TC alone, by promoting the prevention of infectious diseases through appropriate livestock hygiene management, vaccination, and other measures set out in the National Action Plan on Antimicrobial Resistance.

Diseased livestock

Among *Escherichia coli* isolates from cattle and pigs, resistance rates to TC remained high at over 50% from 2015 to 2023. A similar trend was observed in chickens, although the resistance rate decreased to 38.5% in 2023. Resistance rates to ABPC were also high, at 40% or higher in all livestock species in 2023. In contrast, resistance rates to CPFY and CTX remained at or below 35% overall. In chickens in particular, the resistance rate to CPFY decreased to below 20% in 2022 and remained below this level thereafter. Resistance to CL in pigs declined after CL was designated as a second-line antimicrobial, reaching 7.7% in 2023.

Among *Salmonella* spp. isolates from cattle and pigs, resistance rates to TC remained above 30% throughout the period from 2014 to 2023. In cattle in particular, the resistance rate increased sharply from 2020 onward, reaching 73.7% in 2023. The resistance rate to ABPC increased in cattle to 69.7% in 2023, whereas it decreased to 21.7% in pigs. The resistance rate to CTX remained at or below 5% in pigs but increased in cattle in 2023, with the Dublin serotype accounting for most of the resistant isolates. The resistance rate to CL decreased to 0% in pigs but increased in cattle, indicating the need to monitor differences among serotypes.

Among *Streptococcus* spp. isolates associated with bovine mastitis, the highest resistance rate was 29.4% for TC, while susceptibility to the other antimicrobials was generally maintained.

Among *Staphylococcus aureus* isolates from cattle in 2023, resistance rates to all tested antimicrobials (PCG, MPIPC, EM, TC, and CPFY) were below 10%. In contrast, isolates from pigs showed high resistance rates to PCG (70.8%) and TC (41.7%). MPIPC-resistant, *mecA*-positive isolates continued to be detected in pigs, as in the previous year. The *mecA* gene was also detected in isolates from chickens.

Resistance to approved veterinary drugs was identified in all bacterial species isolated from diseased livestock. Although resistance rates to second-line antimicrobials were generally

maintained at low levels, increasing trends were observed in some cases. Therefore, when treating animals with antimicrobials, it is important to perform antimicrobial susceptibility testing and use an appropriate effective antimicrobial only when truly necessary.

Healthy companion animals

Among *E. coli* and *Enterococcus* spp. isolated from healthy dogs and cats, resistance rates to many of the tested antimicrobials, including second-line antimicrobials, were 20% or lower. In addition, the resistance rate was 0.0% for both *E. coli* resistant to carbapenems, which are not approved for veterinary use but are important as last-resort treatments for multidrug-resistant bacterial infections, and VCM-resistant *Enterococcus* spp., which pose a major concern in human medicine, particularly in relation to nosocomial infections. For many of the tested antimicrobials, resistance rates were lower than those among bacteria isolated from diseased dogs and cats, confirming that antimicrobial susceptibility was well maintained among commensal bacteria carried by healthy dogs and cats.

Diseased companion animals

For *E. coli*, *Klebsiella* spp., coagulase-positive *Staphylococcus* spp., and *Enterococcus* spp., which have been continuously collected since the surveys began, the overall trends were generally similar to those observed previously. Among *Enterobacter* spp. collected in 2023, resistance rates to third-generation cephalosporins and fluoroquinolones tended to be high in isolates from both dogs and cats. In contrast, all resistance rates among *Acinetobacter* spp. were below 20%.

For second-line antimicrobials, resistance rates to CTX were high in *Enterobacter* spp., *Klebsiella* spp., and *S. aureus* isolated from cats, but were 30% or lower in the other bacterial species. Resistance rates to CPM varied widely, ranging from 11.1% to 100.0%. Resistance rates to AZM, a 15-membered ring macrolide, were 50% or higher among coagulase-positive *Staphylococcus* spp. No *mcr* genes were detected among the CL-resistant isolates. Carbapenem-resistant isolates were also detected, including one *Klebsiella* spp. isolate from a dog, one *Acinetobacter* spp. isolate from a dog, and two *Acinetobacter* spp. isolates from cats. In contrast, the resistance rate to VCM among *Enterococcus* spp. was 0.0%.

Some bacterial species exhibited high resistance rates to multiple antimicrobials. To preserve the effectiveness of antimicrobials for the future treatment of bacterial infections, the prudent use of antimicrobials is essential. This includes selecting effective antimicrobials based on antimicrobial susceptibility testing conducted before treatment and considering alternatives to antimicrobial administration, such as cleansing and disinfection, for conditions such as dermatitis.

In both livestock and companion animals, bacteria isolated from diseased animals showed higher resistance rates than those isolated from healthy animals. This was presumed to reflect the effects of antimicrobial treatment and raises concerns regarding a potential decline in the effectiveness of antimicrobials for treating infectious diseases in animals. In

contrast, resistance rates among bacteria isolated from healthy animals were generally low, and it is important to maintain this favorable status. To achieve this, the prudent use of antimicrobials must continue to be thoroughly implemented.

Sales volume of antimicrobials

The sales volume of veterinary antimicrobials in 2023 was 717.5 tons, representing a decrease of approximately 30% from 2001. In recent years, the annual sales volume has remained below 800 tons. By antimicrobial class, tetracyclines accounted for the largest sales volume. However, sales of tetracyclines have declined, and their share of the total sales volume has remained below 40% since 2018. By estimated target animal species, pigs accounted for the largest sales volume. Sales for pigs have declined in recent years, mainly because of a decrease in tetracycline sales. In 2023, the sales volume of tetracyclines for pigs was half that recorded in 2001. Seawater fish accounted for the second-largest sales volume after pigs. Sales increased between 2015 and 2019, mainly because of increased sales of macrolides, particularly EM. This increase was considered to be associated with the treatment of type II α -hemolytic lactococcosis, which has been reported since around 2013. In 2020, the upward trend reversed, and sales began to decline, possibly because of improvements in vaccines and other measures.

Among second-line antimicrobials, CL had the largest sales volume, followed by fluoroquinolones. By animal species, sales were highest for pigs, and CL accounted for approximately 80% of second-line antimicrobial sales for pigs. Sales of CL increased after the revocation of its designation as a feed additive in 2018. However, following the development of a vaccine against edema disease, for which CL is indicated, sales are expected to decrease in the future. Broilers accounted for the second-largest sales volume of second-line antimicrobials, of which fluoroquinolones accounted for 66%.

The distribution volume of antimicrobial feed additives remained generally stable, although it increased from 203.3 tons in 2022 to 219.2 tons in 2023. By antimicrobial class, polyethers, which consist mainly of ionophores and are not used in humans, accounted for most of the distribution volume and showed an increasing trend. Their share of the total distribution volume increased from 57.8% in 2013 to 79.1% in 2023.

The sales volume of antimicrobials for human use sold to companion animal clinics decreased from 4.4 tons in 2022 to 4.2 tons in 2023, the lowest level since the survey began in 2016. There were no substantial changes in the shares of individual antimicrobial classes or products in the total sales volume of antimicrobials for human use. First-generation cephalosporins and penicillins accounted for the largest shares. Antimicrobials that are neither approved nor marketed for dogs and cats and are classified as “Reserve” under the WHO AWaRe classification accounted for 2% of sales as in 2022. The AWaRe classification is a tool designed to promote the appropriate use of antimicrobials in consideration of antimicrobial resistance, and antimicrobials in the Reserve group should be preserved as last-resort treatments for conditions such as multidrug-resistant bacterial

infections. It is therefore necessary to recognize that, in principle, these antimicrobials should not be used.

List of bacteria collected in 2023

	Healthy/Diseased	Animal species	Species						
Livestock	Healthy (3-1)	Cattle	<i>Escherichia coli</i>	<i>Enterococcus</i> spp.	<i>Campylobacter</i> spp.				
		Pigs							
		Chicken				<i>Salmonella</i> spp.			
	Diseased (clinical isolates) (3-2)	Cattle		<i>Salmonella</i> spp.	<i>Staphylococcus aureus</i>	<i>Streptococcus</i> spp. associated with mastitis			
		Pigs				<i>Glaesserella parasuis</i>			
		Chicken							
Companion animals	Healthy (3-3)	Dogs Cats	<i>Escherichia coli</i>	<i>Enterococcus</i> spp.					
	Diseased (3-4)	Dogs Cats							<i>Klebsiella</i> spp.

Appendix: Class and abbreviations of the tested antimicrobials

Antimicrobial class		Antimicrobials	Abbreviations
β -lactam	Penicillins	Ampicillin	ABPC
		Benzylpenicillin	PCG
		Oxacillin	MPIPC
	Cephalosporins	Cefazolin	CEZ
		Cephalexin	CEX
		Cefoxitin	CFX
		Cefotaxime	CTX
		Cefquinome	CQN
		Ceftiofur	CTF
		Cefuroxime	CXM
	Carbapenems	Meropenem	MEPM
Aminoglycosides		Streptomycin	SM
		Dihydrostreptomycin	DSM
		Gentamicin	GM
		Kanamycin	KM
Macrolides		Erythromycin	EM
		Azithromycin	AZM
		Tylosin	TS
		Tilmicosin	TMS
Lincosamides		Lincomycin	LCM
		Clindamycin	CLDM
Tetracyclines		Tetracycline	TC
		Oxytetracycline	OTC
Amphenicols		Chloramphenicol	CP
		Florfenicol	FFC
		Thiamphenicol	TP
Polypeptides		Colistin	CL
		Bacitracin	BC
Glycopeptides		Vancomycin	VCM
Quinolones		Nalidixic acid	NA
Fluoroquinolones		Ciprofloxacin	CPFX
		Enrofloxacin	ERFX
		Levofloxacin	LVFX
Polyethers		Salinomycin	SNM
Sulfonamides		Trimethoprim	TMP
Other		ST (sulfamethoxazole/trimethoprim)	ST (SMX/TMP)
		Fosfomycin	FOM

3. Monitoring Results of Resistance Rates

3.1. Healthy Livestock

This section provides a summary of the results of antimicrobial-resistant bacteria monitoring conducted in fiscal year 2023. The monitoring covered *Escherichia coli* and *Enterococcus* spp., which are indicator bacteria, as well as *Campylobacter* spp. and *Salmonella* spp., which are foodborne pathogens of public health concern. These bacteria were isolated from healthy livestock (cattle, pigs, and broilers) at slaughterhouses and poultry slaughterhouses. The results for *Enterococcus* spp. were compiled based on data provided by the Food and Agricultural Materials Inspection Center (FAMIC).

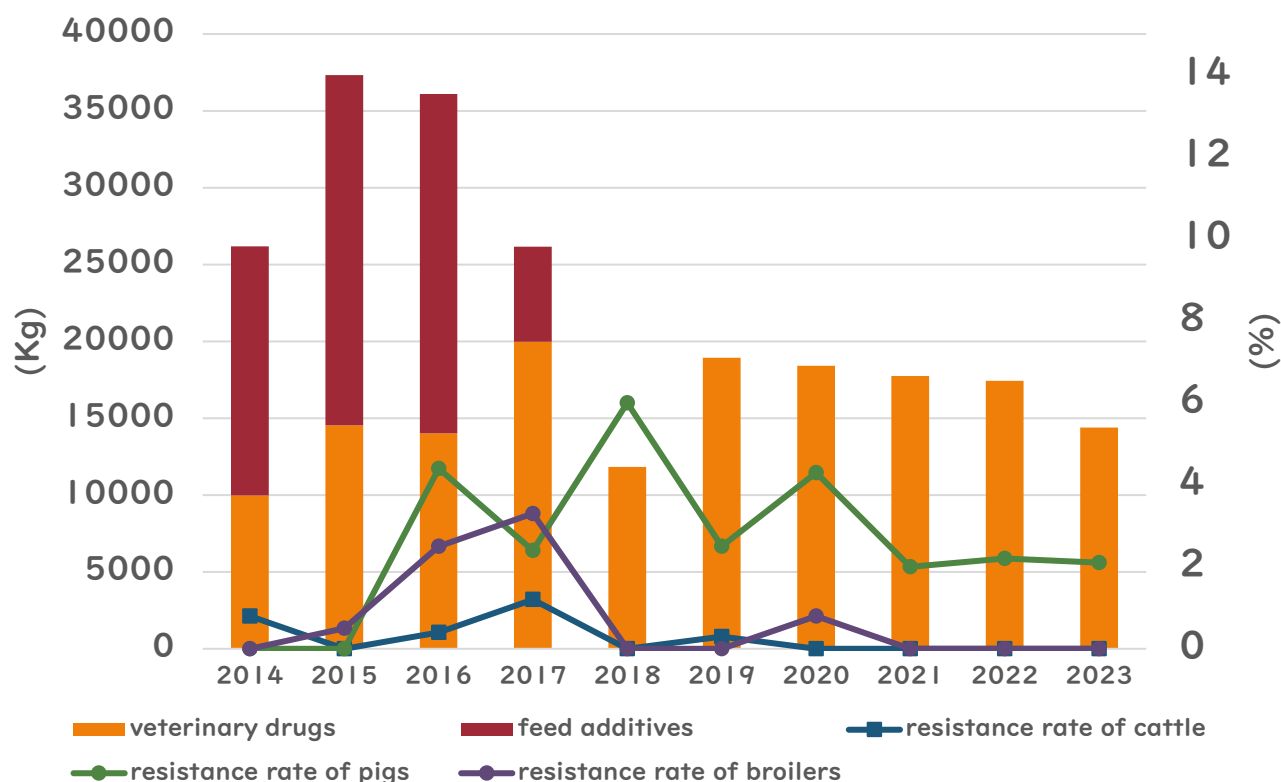
3.1.1. Resistance Rates by Species

The major changes in antimicrobial resistance in each bacterial species are described below. For specific resistance rates and graphs showing trends over time, please refer to the National Veterinary Assay Laboratory website (https://www.maff.go.jp/nval/yakuzai/yakuzai_AMR_2.html).

3.1.1.1. *Escherichia coli* (Cattle, Pigs, Broilers)

Based on the risk assessment conducted by the Food Safety Commission of Japan, CL was designated for use as a second-line antimicrobial in veterinary medicine in 2019, and its designation as a feed additive was revoked. Resistance rates to CL among *E. coli* isolated from healthy livestock have remained low, at 6% or lower, since before 2019. In 2022, the resistance rate to CL was 0.0% in broilers, for which CL is not approved as a veterinary drug, and in cattle, for which CL is approved but rarely sold. The resistance rate in pigs was also low, at 2.1% (Figure 3-1-1).

Fig. 3-1-1 Trends in CL Sales Volume and Resistance Rates of *Escherichia coli* Derived from Healthy Livestock



The resistance rate to MEPM, a carbapenem that is considered one of the most critically important antimicrobials in human medicine*, was 0.0% in all animal species.

* Not approved for veterinary use.

With regard to the resistance rate to TC, which is an outcome index in the National Action Plan on Antimicrobial Resistance, sales volume of TC for pigs has decreased, whereas the resistance rate has not declined (Figure 3-1-2). An analysis of antimicrobial resistance patterns among *Escherichia coli* isolates from pigs in 2023 showed that 9.0% of the isolates were resistant to TC alone, whereas 47.2% were resistant to TC and other antimicrobials (Figure 3-1-3). Among the multidrug-resistant isolates resistant to TC, 17.6% were also resistant to ABPC, CP, SM, and ST. In addition, 8.8% were resistant to ABPC, while 7.4% were resistant to each of the following patterns: ABPC and CP; CP, SM, and ST; or SM alone (Figure 3-1-4). Thus, the TC-resistant isolates were also resistant to one or more other antimicrobials. Although the effects of selective pressure from other antimicrobials may vary depending on whether the resistance genes for TC and those for other antimicrobials are located on the same mobile genetic elements or other transmission-related factors, these findings suggest that reducing selective pressure from TC alone would be insufficient to reduce the TC resistance rate. Therefore, selective pressure from multiple antimicrobials needs to be reduced. It is important to reduce opportunities for the overall use of antimicrobials, rather than TC alone, by promoting the prevention of infectious diseases through appropriate livestock hygiene management, vaccination, and other measures included in the National Action Plan on Antimicrobial Resistance.

Fig. 3-I-2 Trends in TC sales volume and TC resistance rates among *Escherichia coli* isolates from healthy pigs

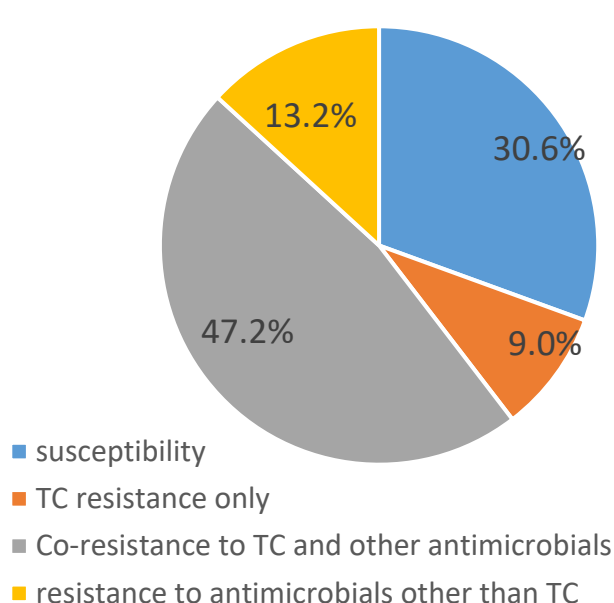
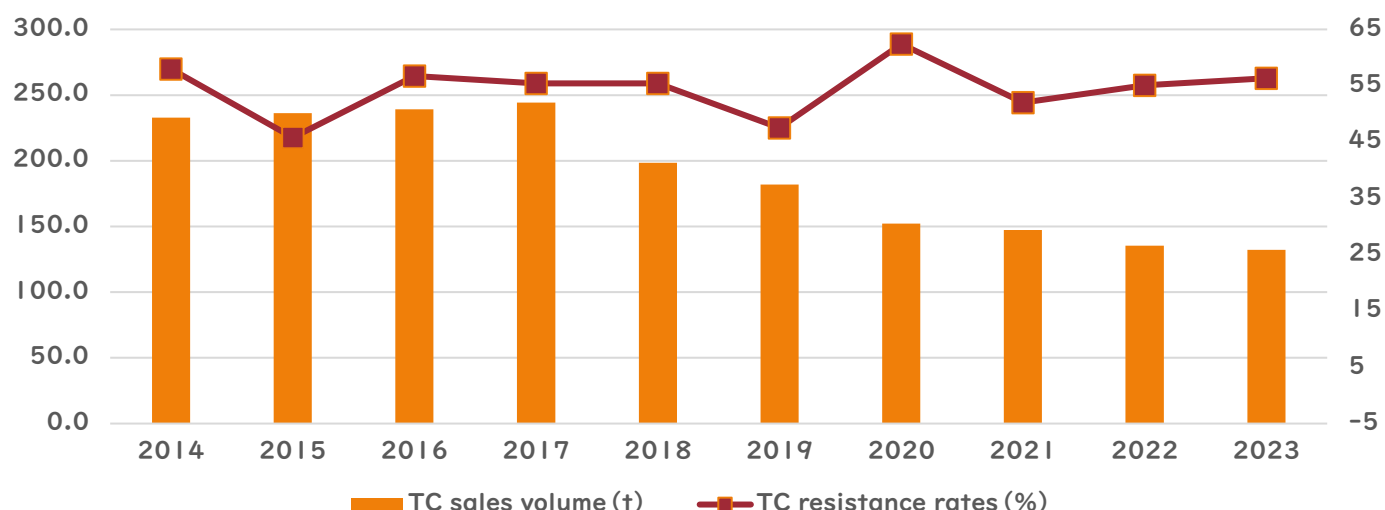


Fig. 3-I-3 Resistance patterns to TC and other antimicrobials among *Escherichia coli* isolates from healthy pigs

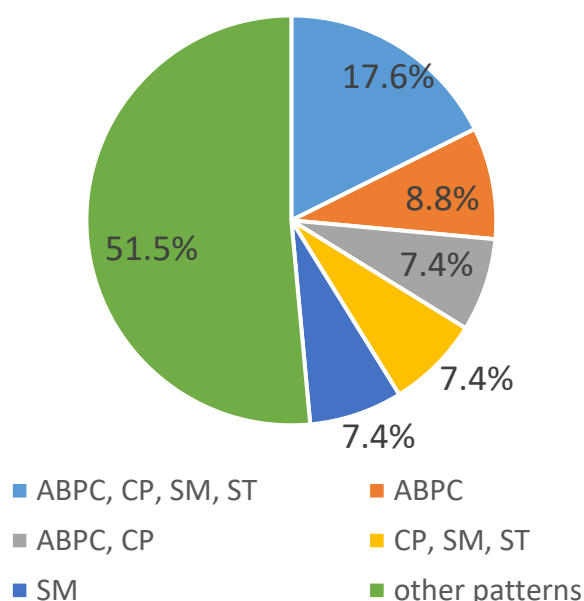


Fig. 3-I-4 Patterns of resistance to other antimicrobials among TC-resistant *Escherichia coli* isolates from healthy pigs

3.1.1.2. *Enterococcus* spp. (Cattle, Pigs, Broilers)

The resistance rate to VCM*, which is considered one of the most critically important antimicrobials in human medicine, was 0.0% in *Enterococcus* spp. from all animal species. Resistance rates to TS, a macrolide for which antimicrobial susceptibility cannot be assessed in *Escherichia coli*, remained higher in broilers and pigs than in cattle (Figure 3-I-5). The designation of tylosin phosphate as a feed additive for use in pigs was revoked in 2019 based on the results of a risk assessment conducted by the Food Safety Commission of Japan. Sales volume of macrolides as veterinary drugs for pigs increased from 2014 to 2016 and subsequently remained stable. After a decrease was observed in 2022, sales increased in 2023 to approximately the 2021 level (Figure 3-I-6). In contrast, the

resistance rate to TS in pigs remained stable through 2020, decreased slightly only in 2021, and returned to its previous level in 2022 and remained at approximately that level thereafter. In broilers, the resistance rate to TS had declined since 2017 but increased in 2023. Although the interpretive criterion for TS resistance was changed in 2023, a similar resistance rate was obtained when the previous criterion was applied. Therefore, the increase was not considered attributable to the change in the criterion. Possible contributing factors included the increase in sales volume of macrolides for broilers and the increase in the proportion of *E. faecalis* among chicken-derived enterococci, from approximately 30%–40% through 2022 to approximately 70% in 2023 (Figure 3-1-7). *E. faecalis* has higher resistance rates to macrolides, including TS, than the other bacterial species.

* Not approved for veterinary use.

Fig. 3-1-5 Resistance rates to TS among *Enterococcus* spp. isolated from healthy livestock

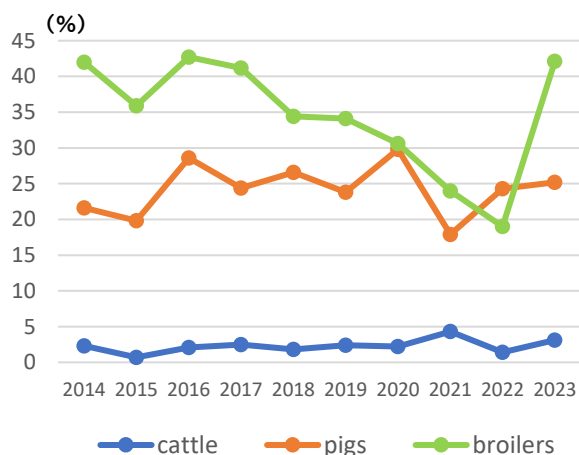
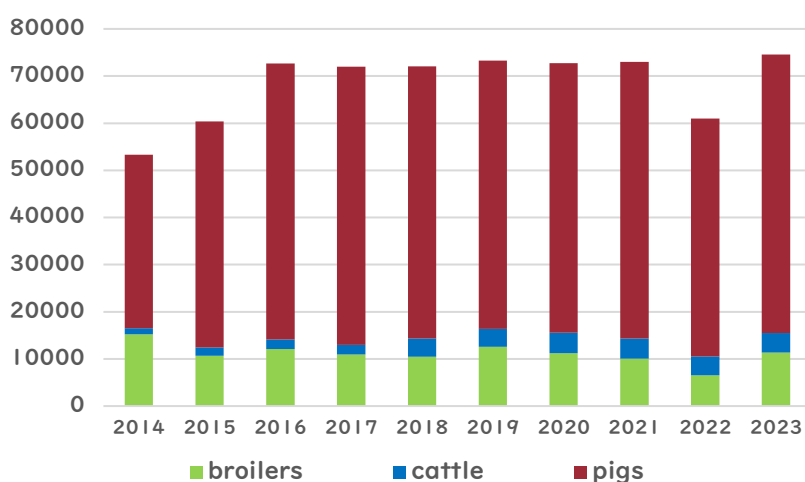


Fig. 3-1-6 Sales volume of macrolides



Interpretive criterion:

Through 2022: 64 µg/mL from 2023: 16 µg/mL

Note: If the previous interpretive criterion of 64 µg/mL were applied to the 2023 results, the resistance rates would be 2.7% in cattle, 25.2% in pigs, and 41.4% in broilers.

Enterococcus spp. comprises many bacterial species, and trends in resistance rates may differ among species. It is therefore important to monitor changes in the proportions of the species isolated. Although *E. faecalis* and *E. faecium* are of concern in human medicine, *E. hirae* was the most frequently isolated species among *Enterococcus* spp. from cattle and pigs in 2023, accounting for 88.3% of cattle-derived isolates (197 of 223 isolates) and 59.3% of pig-derived isolates (80 of 135 isolates), respectively. In contrast, *E. faecalis* was the most frequently isolated species from broilers, accounting for 71.7% of the isolates (109 of 152 isolates). The proportions of *E. faecalis* isolates from cattle and pigs were 3.1% (7 of 223 isolates) and 20.7% (28 of 135 isolates), respectively. The proportions of *E. faecium*

isolates were 1.8% in cattle (4 of 223 isolates), 6.7% in pigs (9 of 135 isolates), and 6.6% in broilers (10 of 152 isolates) (Figure 3-I-8).

Among *E. faecalis* isolates from broilers, for which at least 20 isolates were collected, resistance rates to KM, TC, EM, LCM, and TS exceeded 40%. In contrast, the resistance rate to CPFX, a fluoroquinolone that is important in human medicine, was 6.4%, while the resistance rate to VCM was 0.0%.

Fig. 3-I-7 Annual changes in the species distribution of *Enterococcus* spp. isolated from broilers

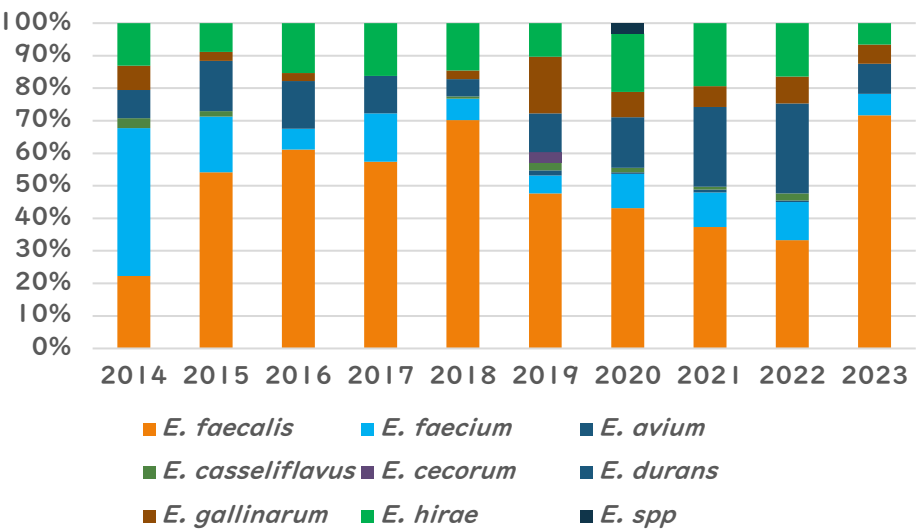
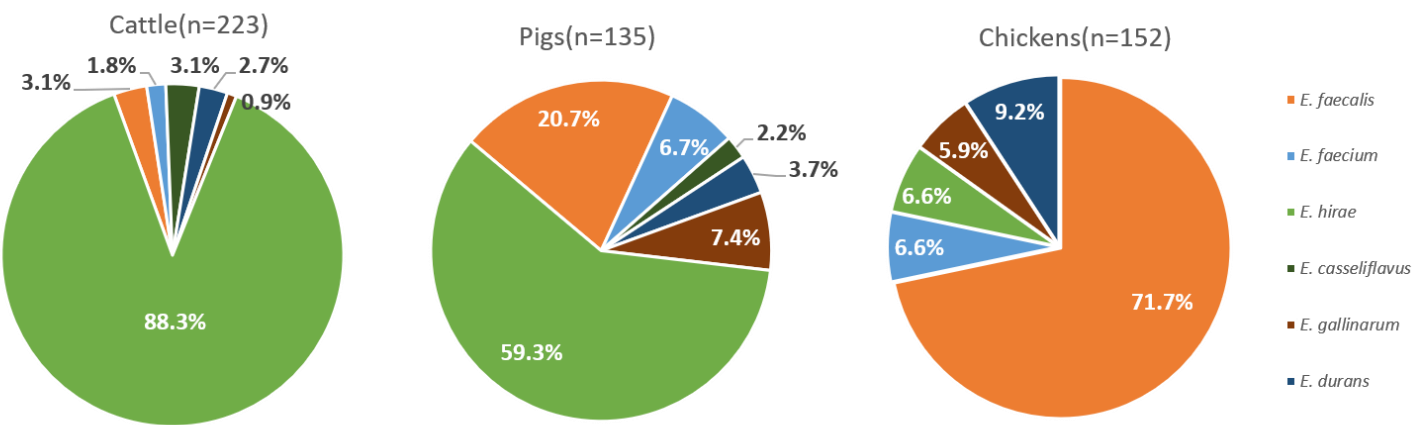


Fig. 3-I-8 Species distribution of *Enterococcus* spp. isolated at slaughterhouses and poultry slaughterhouses in 2023



3.1.1.3. *Campylobacter jejuni* (Cattle, Broilers), *C. coli* (Pigs)

Among *Campylobacter* spp., which are foodborne pathogens, antimicrobial susceptibility is examined in *C. jejuni*, the species predominantly isolated from cattle and broilers, and *C. coli*, the species predominantly isolated from pigs.

Among *C. jejuni* isolates from cattle, resistance rates to TC, NA, and CPFX were high, exceeding 50% (Figure 3-1-9). In 2023, the resistance rate to TC was significantly higher than those in 2014 and 2015, while the resistance rates to NA and CPFX were significantly higher than those recorded from 2014 to 2018, excluding 2017 (Figure 3-1-9).

Resistance rates to all tested antimicrobials among *C. coli* isolates from pigs remained higher than those among *C. jejuni* isolates from cattle and broilers. The resistance rate to SM among *C. coli* isolates from pigs was significantly higher than that in 2022. Continued monitoring is needed to determine whether this high resistance rate to SM is temporary. Resistance rates to the other antimicrobials among *C. coli* and *C. jejuni* isolates either remained stable or

fluctuated over time, with no consistent increasing or decreasing trends observed (Figures 3-1-9 to 3-1-11).

Fig. 3-1-9 Resistance rates to individual antimicrobials among *C. jejuni* isolates from cattle

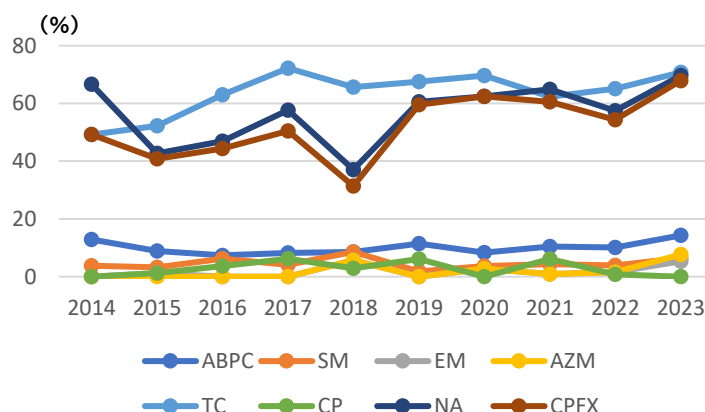


Fig. 3-1-10 Resistance rates among *C. coli* isolates from pigs

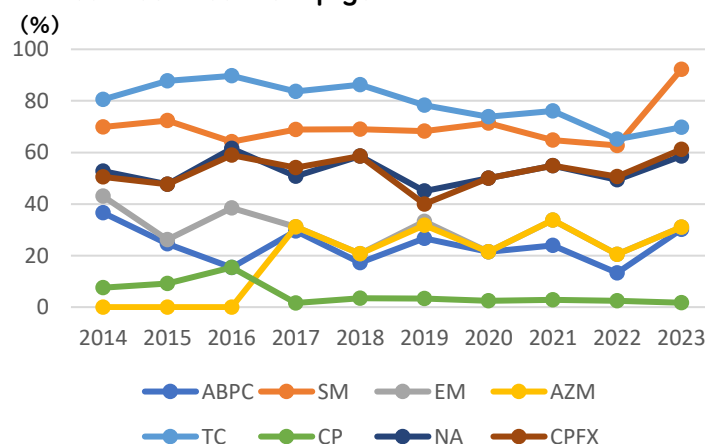
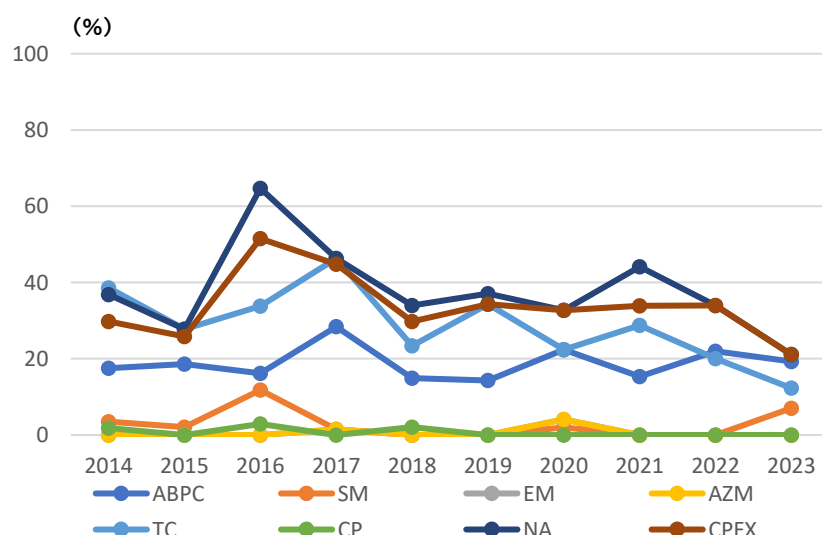


Fig. 3-1-11 Resistance rates among *C. jejuni* isolates from broilers



3.1.1.4. *Salmonella* spp. (Broilers)

Among healthy livestock in Japan, *Salmonella* spp. are rarely isolated from cattle or pigs but can be isolated from broilers. Therefore, antimicrobial susceptibility testing in the monitoring of healthy livestock is conducted on isolates obtained from broilers.

Among *Salmonella* isolates from poultry slaughterhouses, the proportions of the Infantis and Typhimurium serotypes decreased, whereas the proportion of Schwarzengrund increased annually, accounting for approximately 90% of the isolates in 2023. In contrast, Enteritidis, the most common serotype among isolates from human foodborne disease cases, was rarely isolated. Manhattan has also been isolated since 2020, and future changes in its prevalence should be monitored (Figure 3-1-12). Resistance rates to the second-line antimicrobials CL, CPFX, and CTX were low, while the resistance rate to MEPM, a carbapenem, was 0.0%. In contrast, although the resistance rate to TC remained high, it has shown a decreasing trend since 2014 and was 61.2% in 2023. The resistance rate to KM increased through 2017 and has since remained at approximately 70%. The increase in KM resistance may have been influenced by the co-administration of KM with in-egg vaccines to reduce chick mortality after hatching and for other purposes (Figure 3-1-13).

Fig. 3-1-12 Distribution of *Salmonella* serotypes

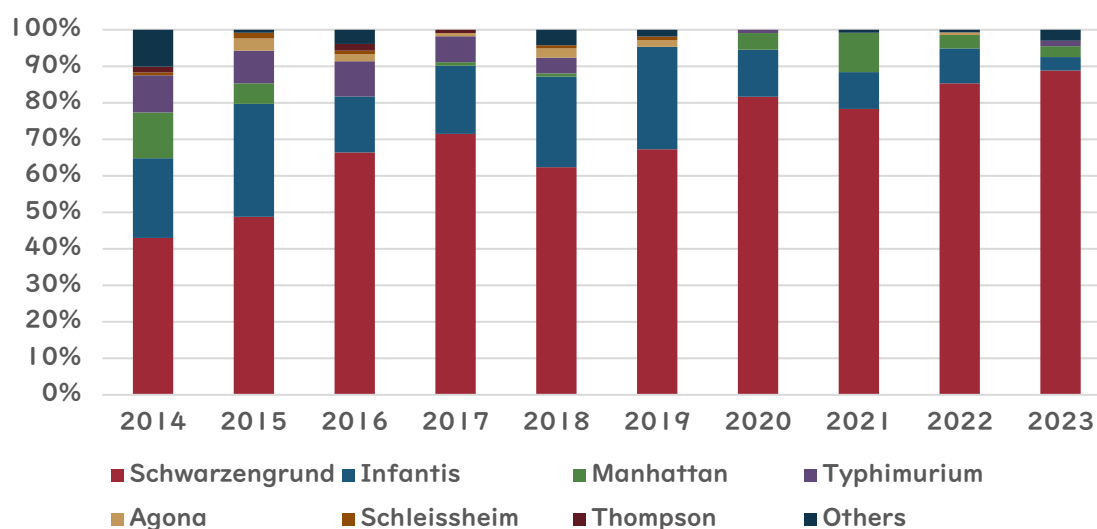
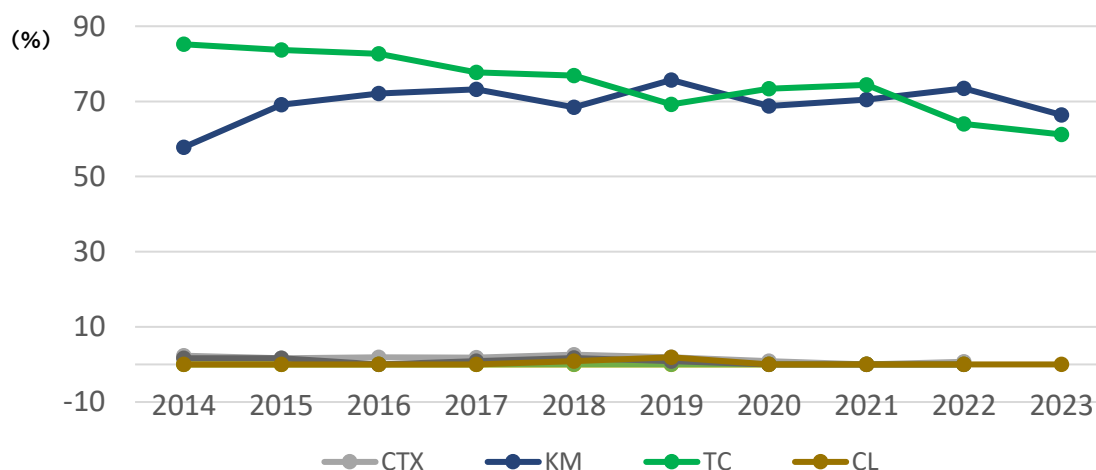


Fig. 3-1-13 Resistance rates of *Salmonella* spp.



3.1.2. Summary

Resistance rates of *Escherichia coli* to fluoroquinolones and third-generation cephalosporins, which are medically important antimicrobials designated as outcome indices in the new Action Plan, generally remained low, as indicated by the resistance rates to CPF and CTX. In addition, the resistance rate to CL, which is also critically important in human medicine, remained low. This was considered to reflect efforts by livestock farmers, veterinarians, and other stakeholders to ensure the prudent use of these antimicrobials as second-line antimicrobials. Furthermore, resistance rates to MEPM and VCM, which are not approved for veterinary use but are regarded as last-resort treatments for multidrug-resistant bacterial infections in human medicine, were 0.0%. In contrast, although sales volume of TC, which is the most widely used antimicrobial in the animal health sector and is designated as an outcome index in the Action Plan, showed a decreasing trend in pigs, the resistance rate remained stable and showed no decline. An analysis of antimicrobial resistance patterns among *E. coli* isolates from pigs in 2023 showed that only a small proportion of the isolates were resistant to TC alone, whereas many were resistant to TC as well as to other antimicrobials. These findings suggest that reducing the use of TC alone may not readily lead to a reduction in TC resistance.

What is required of all stakeholders is to take action, working together as one, to promote the establishment of livestock production systems that do not rely on antimicrobials. This should be achieved by thoroughly implementing the measures set out in the new Action Plan, including: (1) promoting the prevention of infectious diseases through appropriate livestock hygiene management and the use of vaccines; and (2) ensuring the prudent use of antimicrobials through the appropriate selection of antimicrobials, refraining from prophylactic administration, and other measures.

These efforts will help preserve antimicrobial susceptibility so that antimicrobials can continue to be used as therapeutic agents when needed in both veterinary and human medicine and will also help maintain consumer confidence in livestock products produced in Japan. The Ministry of Agriculture, Forestry and Fisheries will continue to conduct surveys on trends in antimicrobial resistance, disseminate information on related issues, and consider and implement more effective and concrete measures. We would like to further strengthen our collaboration with livestock farmers and veterinarians who are directly involved in livestock hygiene management and the use of antimicrobials at production sites, and would appreciate their continued understanding and cooperation.

Acknowledgements

We would like to express our sincere gratitude to all those who cooperated in this survey, including personnel at slaughterhouses and poultry slaughterhouses who assisted with

sample collection, and we would greatly appreciate their continued cooperation in monitoring surveys.

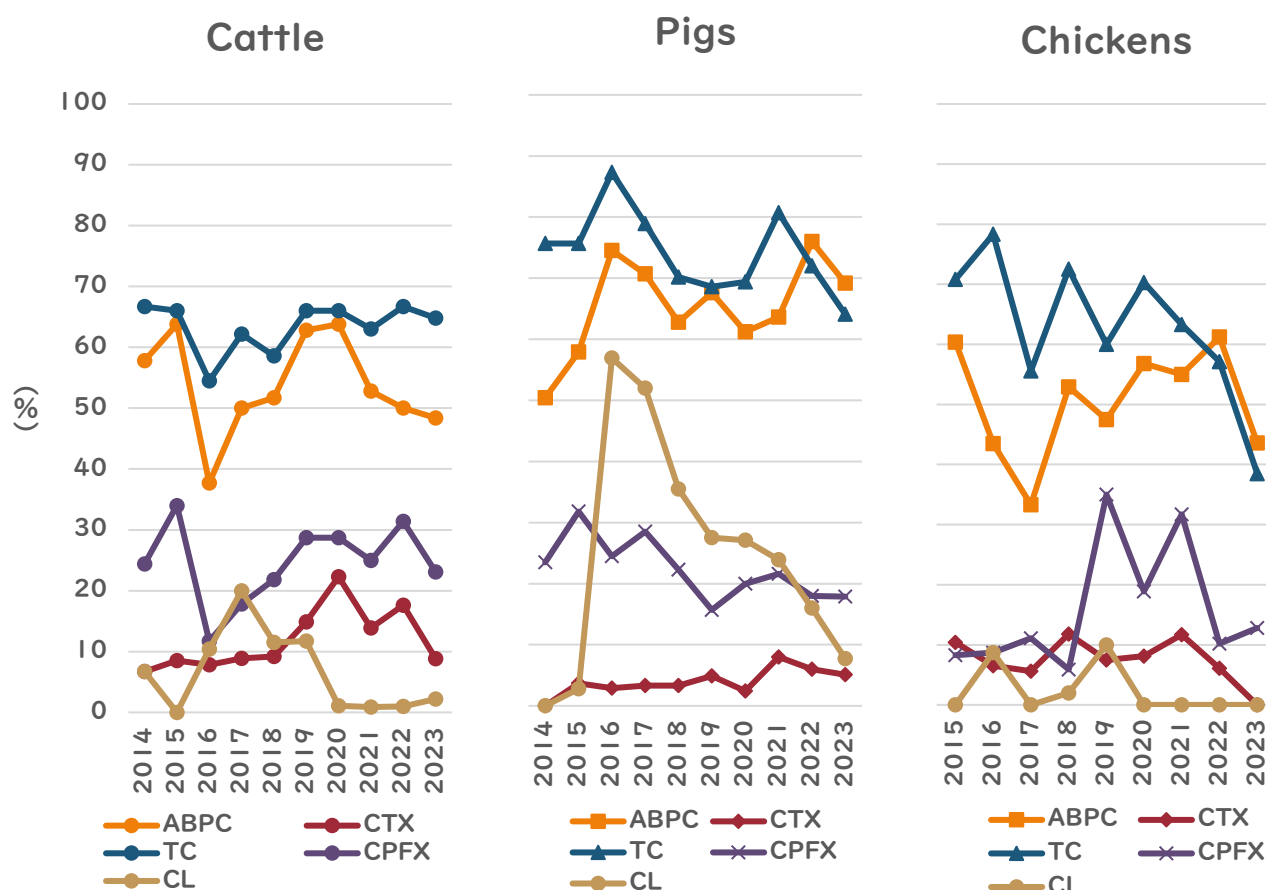
3.2. Diseased livestock: Clinical isolates

Escherichia coli isolates derived from diagnostic specimens and *Streptococcus* spp. isolates associated with mastitis were collected under the FY2023 Program for the Prevention of and Response to Adverse Events Associated with Veterinary Drugs. In addition, *Salmonella* spp. and *Staphylococcus aureus* isolates were collected through a survey on the occurrence of antimicrobial-resistant bacteria conducted as part of the FY2023 Veterinary Drug Risk Management Program. As part of JVARM, antimicrobial susceptibility test results were compiled for antimicrobials approved for the animal species from which each bacterial species was isolated, other antimicrobials in the same classes, antimicrobials important from a public health perspective, and antimicrobials subject to continuous monitoring. A summary of the results is provided below.

3.2.1. *Escherichia coli* (Cattle, Pigs, Chickens)

A total of 169 isolates were collected from 29 prefectures, comprising 91 isolates from cattle, 39 from pigs, and 39 from chickens. Resistance rates in each animal species from 2014 to 2023 are shown in Figure 3-2-1. Resistance rates for chicken-derived isolates in 2014 are not presented because fewer than 20 isolates were collected.

Fig. 3-2-1 Antimicrobial resistance rates among *Escherichia coli* isolates from diseased livestock



From 2014 to 2023, resistance rates to TC exceeded 50% among isolates from cattle and pigs. A similar trend was observed among isolates from chickens from 2015 to 2022, but the resistance rate decreased to 38.5% in 2023.

Among the antimicrobials other than TC, resistance rates to ABPC were 40% or higher in all livestock species in 2023. ABPC is used as a veterinary drug for indications including bacterial diarrhea caused by *E. coli* in cattle and pigs and colibacillosis in chickens. The results of this survey indicate that antimicrobial susceptibility should be confirmed before administration in clinical practice.

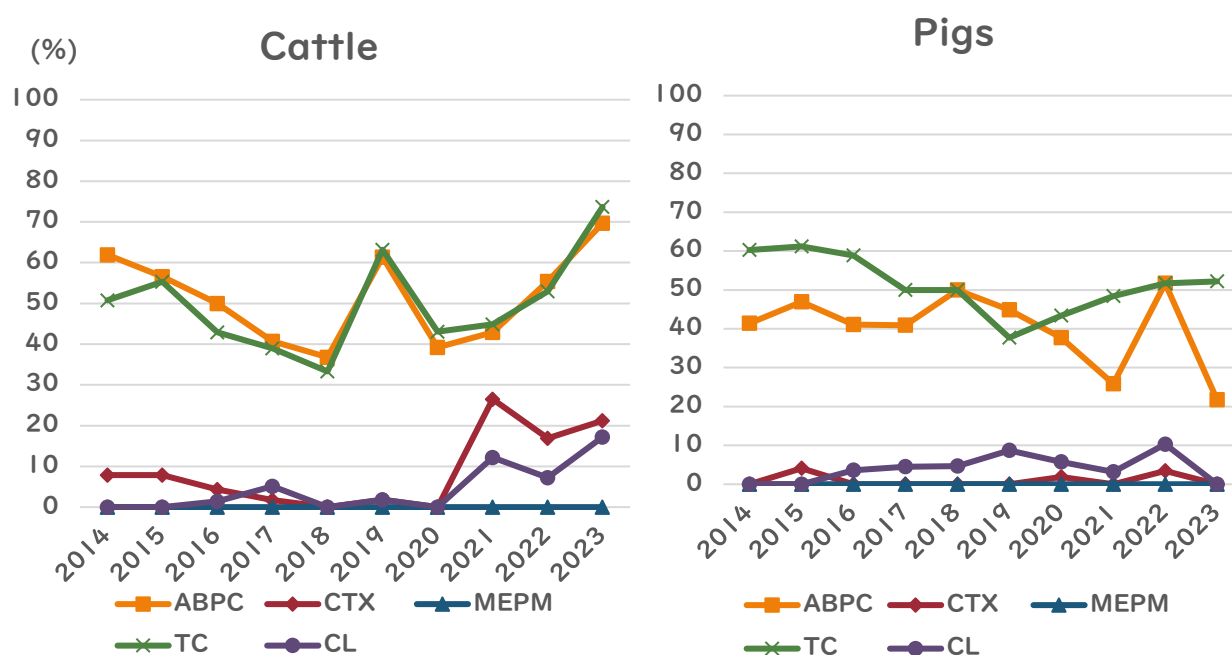
Resistance rates to CPF and CTX remained at or below 35% in all livestock species from 2014 to 2023, or from 2015 to 2023 for chickens. In 2023, resistance rates to CTX decreased from the previous year in all livestock species, including cattle, pigs, and chickens. In chickens, the resistance rate to CPF was 31.7% in 2021 but decreased to below 20% in 2022 and remained below this level thereafter.

The resistance rate to CL in pigs has continued to decline since 2017, when it was 52.0%, and decreased to 7.7% in 2023. CL was designated as a second-line antimicrobial in 2018. The breakpoint for CL was 4 µg/mL, compared with 16 µg/mL through 2015.

3.2.2. *Salmonella* spp. (Cattle, Pigs, Chickens)

A total of 136 isolates were collected from 25 prefectures, comprising 99 isolates from cattle, 23 from pigs, and 14 from chickens. The most common serotypes among isolates from cattle were 4:i:- (44 isolates), Dublin (17 isolates), and Typhimurium (15 isolates), in descending order. Typhimurium was the predominant serotype among isolates from pigs (14 isolates), while Schwarzengrund was predominant among isolates from chickens (11 isolates).

Fig. 3-2-2 Antimicrobial resistance rates among *Salmonella* spp. isolated from diseased cattle and pigs



Resistance rates of *Salmonella* spp. isolated from diseased livestock from 2014 to 2023 are shown in Figure 3-2-2. Resistance rates are not presented for chicken-derived isolates because fewer than 20 isolates were collected in each year since monitoring began, except in 2014 and 2018. Resistance rates to TC among isolates from cattle and pigs exceeded 30% throughout the study period. In cattle in particular, the resistance rate has shown an increasing trend since 2020.

The resistance rate to ABPC among isolates from cattle gradually increased from 42.9% in 2021 to 69.7% in 2023. In contrast, the resistance rate among isolates from pigs decreased from 51.7% in 2022 to 21.7% in 2023.

The resistance rate to CTX among isolates from pigs has remained at or below 5% since 2014. Among isolates from cattle, however, the resistance rate increased from 16.9% in 2022 to 21.2% in 2023. The CTX-resistant isolates detected in 2023 belonged to the Typhimurium and Dublin serotypes and were derived from cattle. Among the Dublin isolates, 16 of 21 were resistant to CTX.

The resistance rate to CL decreased from 10.3% to 0% among isolates from pigs but increased from 7.2% to 17.2% among isolates from cattle. The CL-resistant isolates detected in cattle in 2023 comprised 16 Dublin isolates and one 4:i:- isolate. Continued monitoring of the serotypes isolated and their resistance rates is necessary.

3.2.3. *Streptococcus* spp. associated with mastitis (Cattle)

The collection of *Streptococcus* spp. associated with bovine mastitis began in FY2022. In FY2023, 51 isolates were collected from 12 prefectures.

Streptococci that cause bovine mastitis include *Streptococcus agalactiae*, which causes contagious mastitis, and other *Streptococcus* spp. (OS), which cause environmental mastitis. Four bacterial species were isolated in 2023. As in the previous year, *S. uberis*, one of the species classified as OS, was the most frequently isolated species (Table 3-2-3).

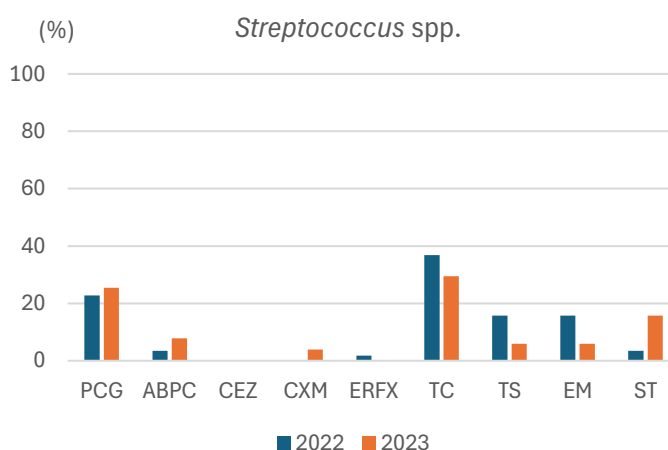
Figure 3-2-4 shows the resistance rates of *Streptococcus* spp. associated with bovine mastitis to PCG, ABPC, CEZ, CXM, ERFX, TC, TS, EM, and ST. These antimicrobials are among the drugs approved in Japan for the treatment of bovine mastitis. The highest resistance rate was 29.4% for TC. Susceptibility to the other antimicrobials was generally maintained, and the resistance rate to ERFX, a second-line antimicrobial, was 0.0%.

All isolates that were not susceptible to the penicillins PCG and ABPC were identified as *S. uberis*. Most isolates resistant to TC, TS, and EM were also *S. uberis*. In contrast, reduced susceptibility to ST was observed among bacterial species other than *S. uberis*.

Table 3-2-3 *Streptococcus* spp.
isolated from cases of bovine mastitis
(2022 and 2023)

Bacterial species	2022	2023
<i>S. uberis</i>	27	22
<i>S. infantarius</i>	15	15
<i>S. dysgalactiae</i>	10	9
<i>S. agalactiae</i>	2	0
<i>S. gallolyticus</i>	1	5
<i>S. parasuis</i>	1	0
<i>S. pluranimalium</i>	1	0
Total	57	51

Fig. 3-2-4 Resistance rates among
Streptococcus spp. isolated from



3.2.4. *Staphylococcus aureus* (Cattle, Pigs, Chickens)

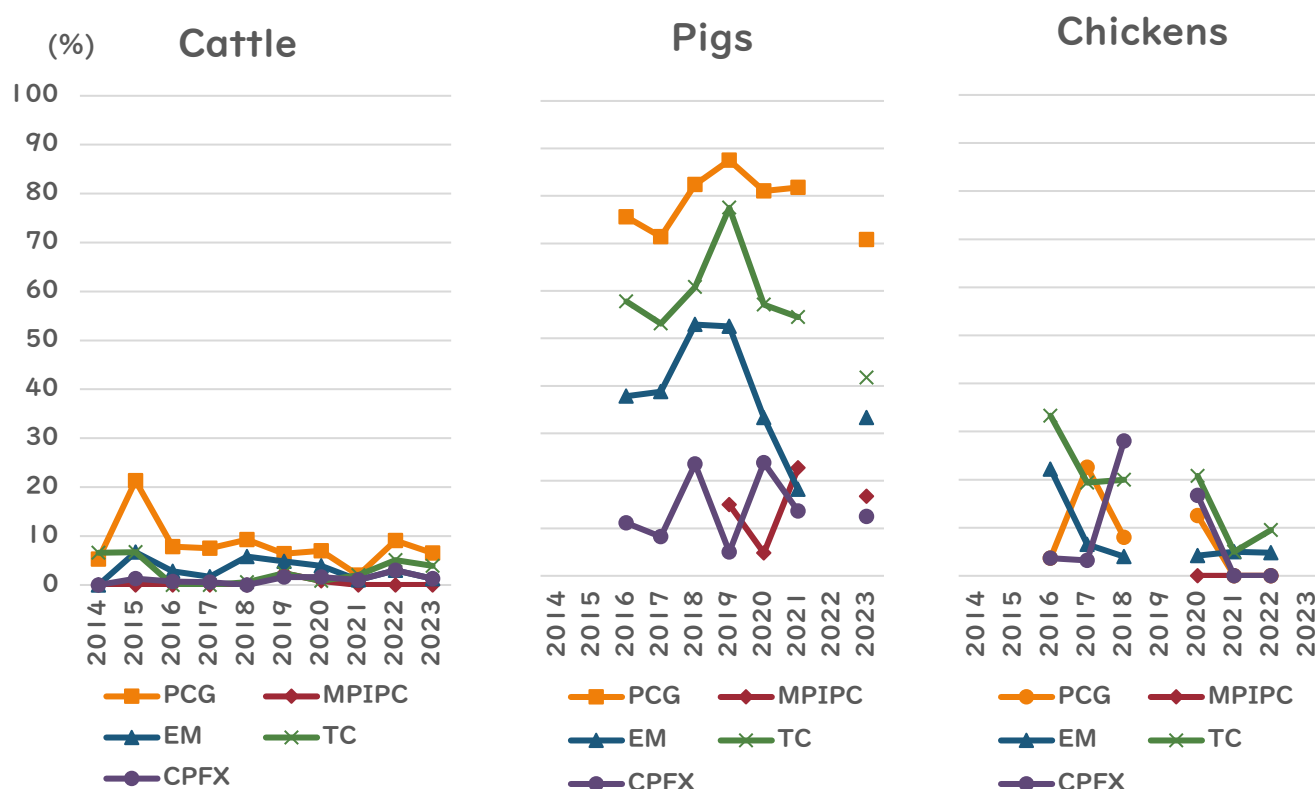
In FY2023, a total of 120 isolates were collected from 27 prefectures, comprising 77 isolates from cattle, 24 from pigs, and 19 from chickens.

Resistance rates of *Staphylococcus aureus* field isolates from diseased livestock from 2016 to 2023 are shown in Figure 3-2-5. Resistance rates are not presented for the pig-derived isolates collected in 2022 or the chicken-derived isolates collected in 2023 because fewer than 20 isolates were collected.

Among the cattle-derived isolates collected in 2023, resistance rates to all tested antimicrobials remained below 10%. In contrast, the pig-derived isolates showed particularly high resistance rates to PCG (70.8%) and TC (41.7%). Resistance rates to CPFX, a fluoroquinolone, were 1.3% among cattle-derived isolates and 12.5% among pig-derived isolates. As in the previous year, MIPIC-resistant, *mecA*-positive isolates were detected in pigs. The *mecA* gene was also detected in isolates from chickens. Because the number of pig-derived isolates was relatively small, caution is required when comparing resistance rates.

Fig. 3-2-5 Antimicrobial resistance rates of *Staphylococcus aureus* isolated from diseased livestock

Resistance rates are not presented for years in which fewer than 20 isolates were tested.



The five antimicrobials presented here are either approved veterinary drugs or have mechanisms of action similar to those of approved veterinary drugs. Susceptibility to these antimicrobials was generally maintained among isolates from cattle. In contrast, resistance

rates to PCG and TC were high among isolates from pigs, indicating a high likelihood that these antimicrobials may not achieve the desired therapeutic effect in clinical practice. Therefore, it is important to perform antimicrobial susceptibility testing before administration.

3.2.5. Summary

Among *Escherichia coli* isolates from cattle and pigs, resistance rates to TC remained high at over 50% from 2015 to 2023. A similar trend was observed among isolates from chickens, although the resistance rate decreased to 38.5% in 2023. Resistance rates to ABPC were also high, at 40% or higher in all livestock species in 2023. In contrast, resistance rates to CPFEX and CTX remained at or below 35% overall. In chickens in particular, the resistance rate to CPFEX decreased to below 20% in 2022 and remained below this level thereafter. Resistance to CL among isolates from pigs declined after CL was designated as a second-line antimicrobial, reaching 7.7% in 2023.

Among *Salmonella* spp. isolates from cattle and pigs, resistance rates to TC remained above 30% throughout the period from 2014 to 2023. In cattle in particular, the resistance rate increased sharply from 2020 onward, reaching 73.7% in 2023. The resistance rate to ABPC increased among isolates from cattle, reaching 69.7% in 2023, whereas it decreased to 21.7% among isolates from pigs. The resistance rate to CTX remained at or below 5% among isolates from pigs but increased among isolates from cattle in 2023, with the Dublin serotype accounting for most of the resistant isolates. The resistance rate to CL decreased to 0% among isolates from pigs but increased among isolates from cattle, indicating the need to monitor differences among serotypes.

Among *Streptococcus* spp. isolates associated with bovine mastitis, the highest resistance rate was 29.4% for TC, while susceptibility to the other antimicrobials was generally maintained.

Among *Staphylococcus aureus* isolates from cattle in 2023, resistance rates to all tested antimicrobials (PCG, MPIPC, EM, TC, and CPFEX) were below 10%. In contrast, isolates from pigs showed high resistance rates to PCG (70.8%) and TC (41.7%). As in the previous year, MPIPC-resistant, *mecA*-positive isolates were detected in pigs. The *mecA* gene was also detected in isolates from chickens.

Resistance to approved veterinary drugs was identified in all bacterial species isolated from diseased livestock. Although resistance rates to second-line antimicrobials were generally maintained at low levels, increasing trends were observed in some cases. Therefore, antimicrobial susceptibility testing should be performed before treatment, and an appropriate effective antimicrobial should be used only when truly necessary.

Acknowledgements

These findings are based on antimicrobial susceptibility test results for bacteria isolated from diagnostic specimens collected through the Survey on the Occurrence of Antimicrobial-Resistant Bacteria under the FY2023 Veterinary Drug Risk Management Program and the

FY2023 Program for the Prevention of and Response to Adverse Events Associated with Veterinary Drugs.

We would like to express our sincere gratitude to the staff of prefectural Livestock Hygiene Service Centers for their efforts in collecting, storing, and sending the isolates. We would greatly appreciate their continued cooperation in surveys of antimicrobial susceptibility in diseased livestock.

3.3. Healthy Companion Animals

Escherichia coli and *Enterococcus* spp., which are indicator bacteria, were isolated from healthy dogs and cats that visited veterinary clinics for medical checkups or vaccinations rather than for the treatment of disease. Antimicrobial susceptibility testing was then performed on the isolates. At the same time, interviews were conducted to collect information on the animal species, sex, housing conditions, and other characteristics. In 2023, samples were collected from 173 veterinary clinics throughout Japan that agreed to participate in the survey through the Japan Veterinary Medical Association. Swab samples and complete questionnaires were collected from 131 dogs and 131 cats. The bacterial species identified in the samples and the numbers of isolates are shown in Table 3-3-1.

Table 3-3-1 Bacterial species and numbers of isolates

	Dogs	Number of isolates	Cats	Number of isolates
<i>Escherichia coli</i>	<i>E. coli</i>	107	<i>E. coli</i>	107
	<i>E. faecalis</i>	72	<i>E. faecalis</i>	44
	<i>E. faecium</i>	8	<i>E. hirae</i>	6
	<i>E. hirae</i>	3	<i>E. faecium</i>	5
	<i>E. casseliflavus</i>	2	<i>E. gallinarum</i>	1
<i>Enterococcus</i> spp.	<i>E. durans</i>	2	<i>E. avium</i>	1
	<i>E. gallinarum</i>	2		
	<i>E. avium</i>	1		
	Total	90	Total	57

3.3.1. *Escherichia coli* (Dogs, Cats)

Trends in resistance rates among *E. coli* isolates from dogs and cats from the start of the survey in 2018 through 2023 are shown in Figures 3-3-1-1 and 3-3-1-2.

Fig. 3-3-1-1 Trends in resistance rates among *Escherichia coli* isolates from dogs

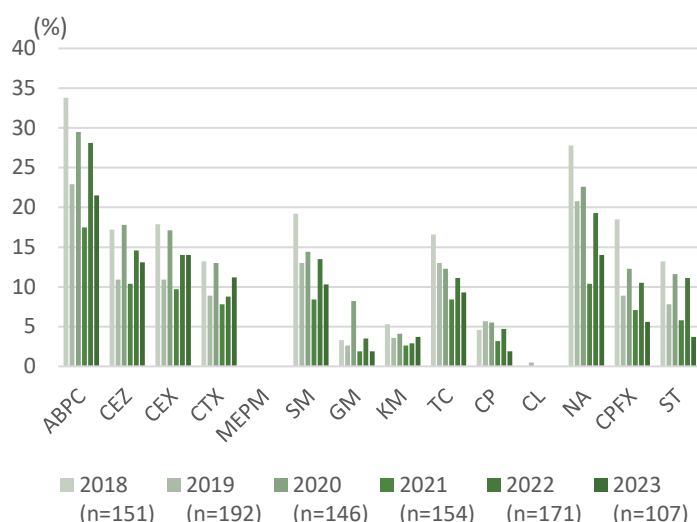
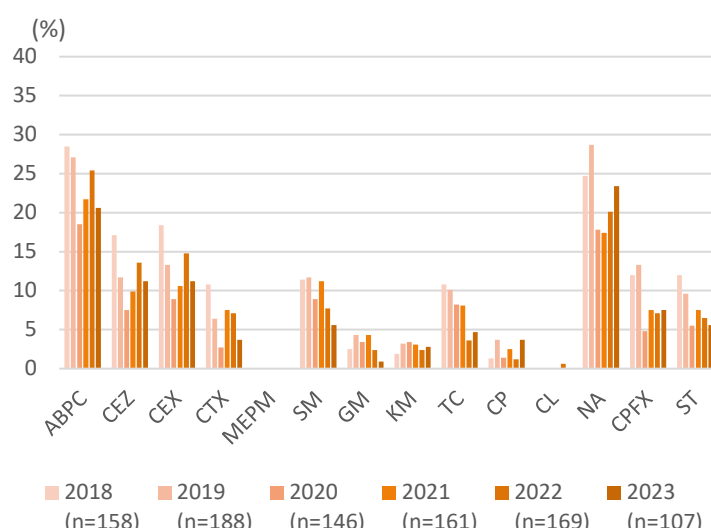


Fig. 3-3-1-2 Trends in resistance rates among *Escherichia coli* isolates from cats



Among the 107 *E. coli* isolates from dogs tested in 2023, the highest resistance rate was observed for ABPC, at 21.5%, while resistance rates to all other tested antimicrobials were below 20%. The resistance rates to CPMX, a fluoroquinolone, and CTX, a third-generation cephalosporin, were 5.6% and 11.2%, respectively. Resistance rates to MEPM, a carbapenem, and CL, a polypeptide, were both 0.0%. The resistance rate to ST was significantly lower than that among *E. coli* isolates from healthy dogs in 2022 (Figure 3-3-1-1). For antimicrobials to which resistant isolates were detected, resistance rates were significantly lower than those among *E. coli* isolates collected from diseased dogs, except for SM and KM (Figure 3-3-1-3).

Among the 107 *E. coli* isolates from cats subjected to antimicrobial susceptibility testing, resistance rates to all tested antimicrobials other than ABPC and NA were below 20%. The highest resistance rate was observed for NA, at 23.4%, followed by ABPC, at 20.6% (Figure 3-3-1-2). Resistance rates to CPMX and CTX, which are medically important antimicrobials, were 7.5% and 3.7%, respectively, while resistance rates to MEPM and CL were both 0.0%. No significant differences were observed between the 2023 results and those for *E. coli* isolates from healthy cats in 2022. For antimicrobials to which resistant isolates were detected, resistance rates were significantly lower than those among *E. coli* isolates collected from diseased cats in the same year, except for KM and CP (Figure 3-3-1-4).

Fig. 3-3-I-3 Resistance rates among *Escherichia coli* isolates from healthy and diseased dogs in 2023

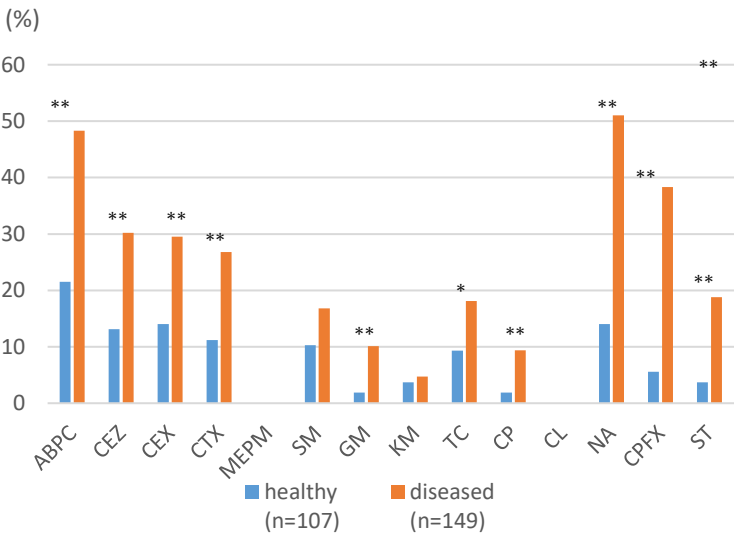
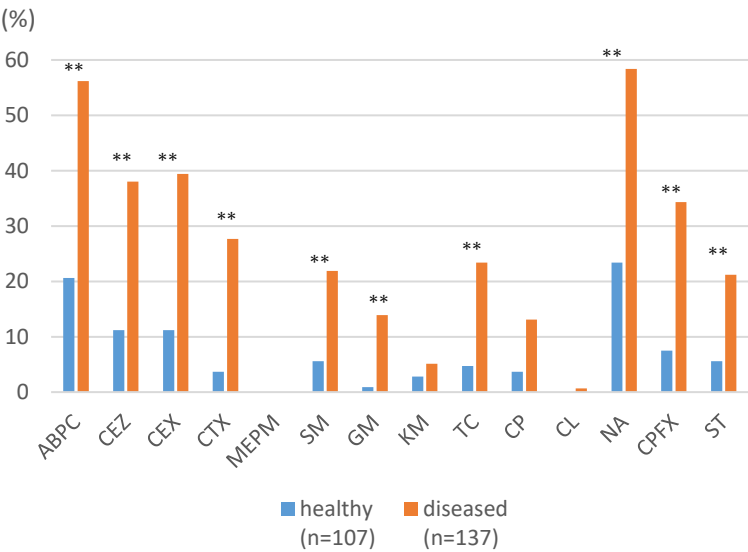


Fig. 3-3-I-4 Resistance rates among *Escherichia coli* isolates from healthy and diseased cats in 2023



** p<0.01, *p < 0.05 (Fisher's exact test)

3.3.2. *Enterococcus* spp. (Dogs, Cats)

Trends in resistance rates among *Enterococcus* spp. isolated from dogs and cats from the start of the survey in 2018 through 2023 are shown in Figures 3-3-2-1 and 3-3-2-2.

Fig. 3-3-2-1 Trends in resistance rates among *Enterococcus* spp. isolated from dogs

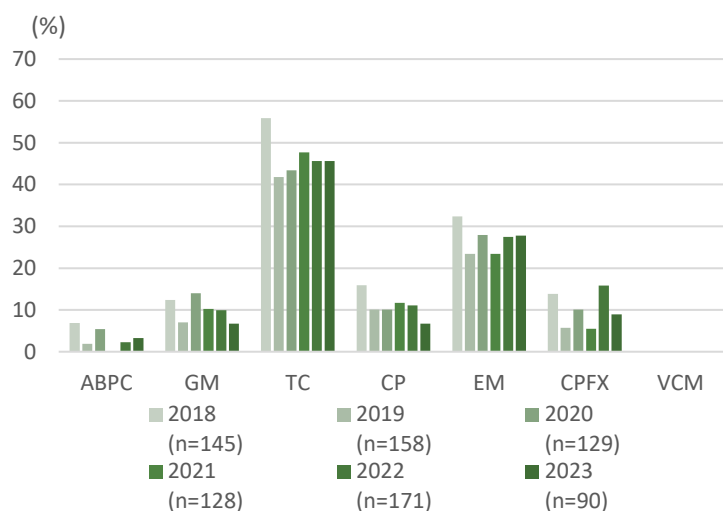
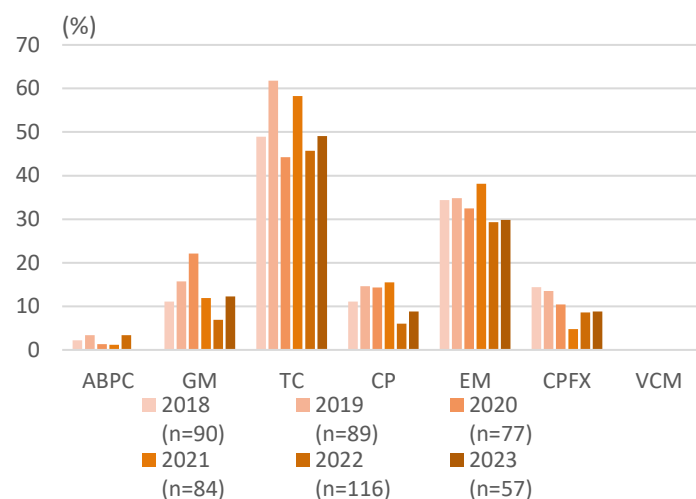


Fig. 3-3-2-2 Trends in resistance rates among *Enterococcus* spp. isolated from cats



Among the 90 isolates from dogs collected in 2023, resistance rates were highest for TC, followed by EM, while resistance rates to all other tested antimicrobials were below 20% (Figure 3-3-2-1). The resistance rate to CPFX was 8.9%, and that to VCM, which is an important antimicrobial in human medicine, was 0.0%. Compared with isolates collected from diseased dogs in the same year, isolates from healthy dogs showed significantly lower resistance rates to all tested antimicrobials except CP and EM (Figure 3-3-2-3).

Among the 57 isolates from cats, resistance rates were highest for TC, followed by EM, as observed in dogs, while resistance rates to all other tested antimicrobials were below 20% (Figure 3-3-2-2). Resistance patterns for the tested antimicrobials were similar between isolates from dogs and cats. The resistance rate to CPFX was 8.8%, while that to VCM was 0.0%. Compared with isolates collected from diseased cats in the same year, isolates from healthy cats showed significantly lower resistance rates to all tested antimicrobials except CP (Figure 3-3-2-4).

Fig. 3-3-2-3 Resistance rates among *Enterococcus* spp. isolated from healthy and diseased dogs in 2023

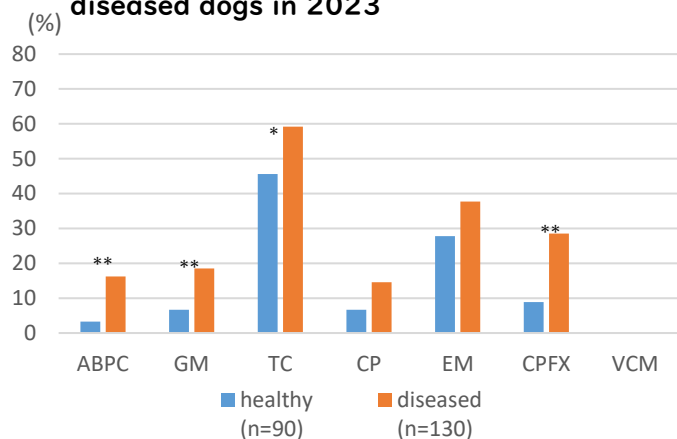
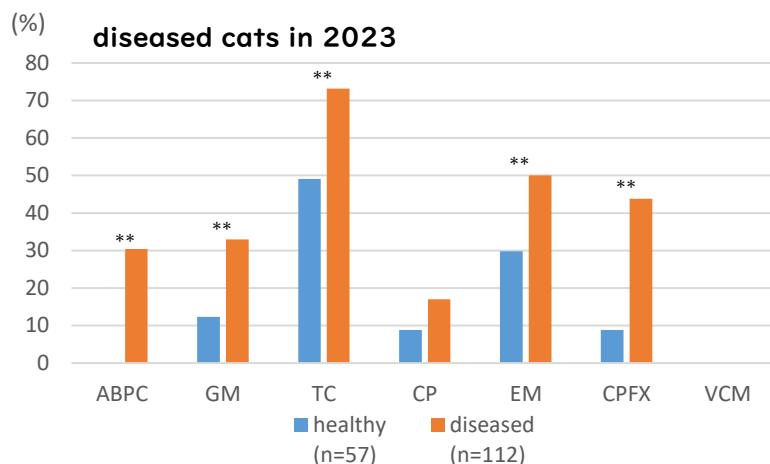


Fig. 3-3-2-4 Resistance rates among *Enterococcus* spp. isolated from healthy and diseased cats in 2023



** $p < 0.01$, * $p < 0.05$ (Fisher's exact test)

Figure 3-3-3 shows the species distribution of *Enterococcus* spp. isolated through JVARM in 2023 from healthy companion animals (dogs and cats) and livestock (cattle, pigs, and broilers). In chickens, as in dogs and cats, *E. faecalis* was the predominant species, accounting for approximately 70% of the isolates. In contrast, *E. hirae* accounted for a high proportion of the isolates from cattle and pigs, at approximately 90% and 60%, respectively, whereas *E. faecalis* accounted for approximately 3% of the isolates from cattle and 20% of those from pigs. These findings demonstrate that the species composition of *Enterococcus* spp. differs considerably among animal species.

Fig. 3-3-3 Species distribution of *Enterococcus* spp. isolated from healthy companion animals and livestock in 2023

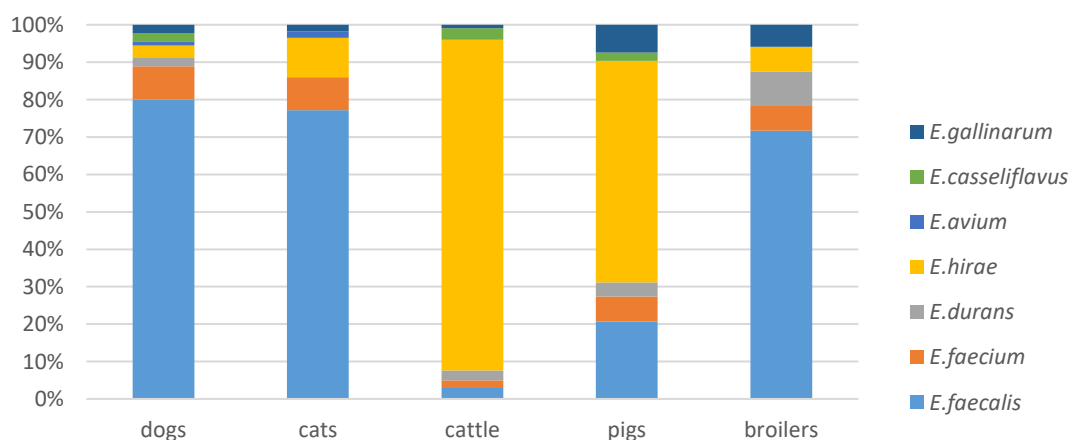
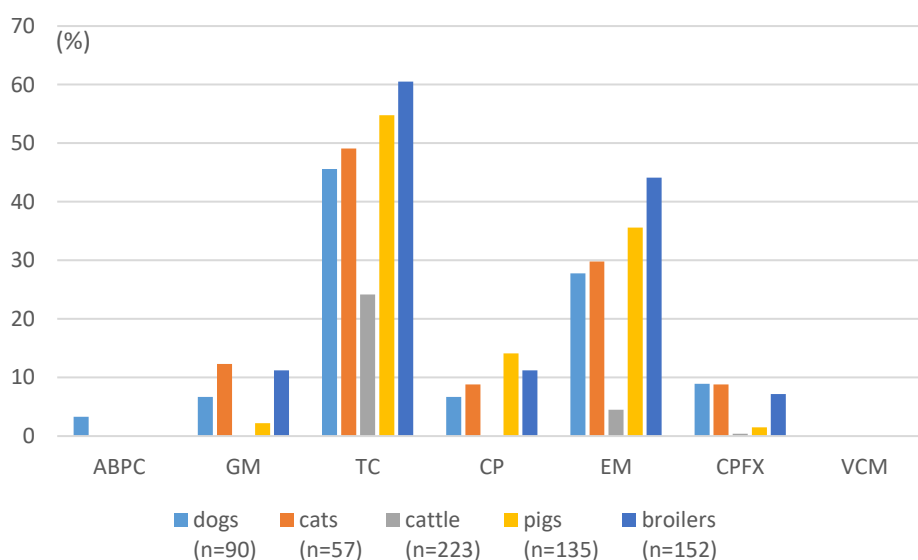


Figure 3-3-4 compares resistance rates among *Enterococcus* spp. isolated in 2023 from healthy companion animals and livestock. TC had the highest resistance rate in all animal species. This may be attributable to the propensity of *Enterococcus* spp. to acquire resistance to TC. In contrast, the resistance rate to TC among isolates from cattle was relatively low, at 24.2%. Although the reason for this is unclear, it may be related to the lower proportions of *E. faecalis* and *E. faecium* isolated from cattle compared with the other animal species.

Fig. 3-3-4 Comparison of resistance rates among *Enterococcus* spp. isolated from healthy companion animals and livestock in 2023



3.3.3. Results of Questionnaire

A questionnaire survey was administered to the owners of 131 dogs and 131 cats from which samples were collected at veterinary clinics in 2023. The results are presented on the following pages.

Although some respondents did not provide information on sex, the proportions of males and females were approximately equal for both dogs and cats. In both dogs and cats, animals aged six years or younger accounted for approximately 60% of the total. Approximately half of the dogs did not live with other dogs, whereas more than 60% of the cats lived with at least one other cat. The most common reason for visiting the veterinary clinic was a medical checkup for dogs and vaccination for cats.

Regarding the three months before sample collection, approximately 90% of both dogs and cats were usually kept indoors, excluding time spent walking or outside in the case of dogs.

Commercial pet food was the primary diet for nearly 80% of both dogs and cats, followed by prescription diets. These trends were similar to those observed in the previous year.

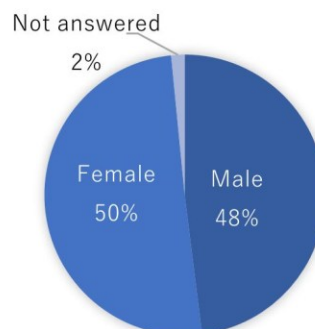
During the three months before sample collection, 16% of the dogs and 12% of the cats had received antimicrobials at a veterinary clinic. Oral administration was the most common route of administration in both dogs and cats. In addition, more than 90% of both dogs and cats had not been hospitalized during this period, and very few had contact with people who had an infectious disease or had been hospitalized.

Questionnaire results on dogs sampled in this survey in 2023 (number of responses 131)

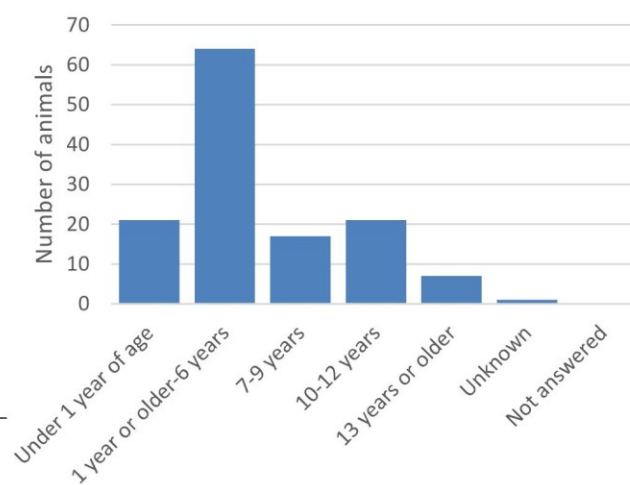
1. Species

Breed	Number of animals
Mongrel	30
Toy poodle	27
Chihuahua	9
Shiba dogs	7
Pomeranian	7
Dachshund	6
Golden Retriever	5
Labrador Retriever	5
Jack Russell Terrier	4
Yorkshire Terrier	4
Miniature Schnauzer	3
Beagle	3
Border Collie	3
Maltese	2
Pekingese	2
Bichon Frise	2
Scottish Terrier	2
Corgi	2
Other	7
No response	1
Total	131

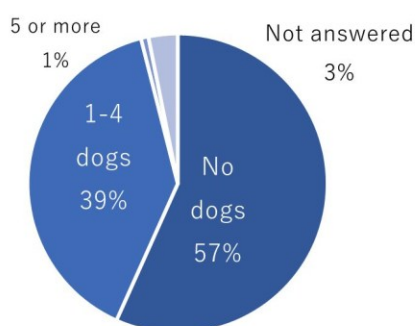
2. Sex



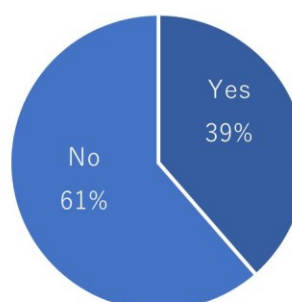
3. Age groups



4. Number of dogs living together



5. Cohabitation with animals other than dogs



6. Objective of the visit (multiple answers)



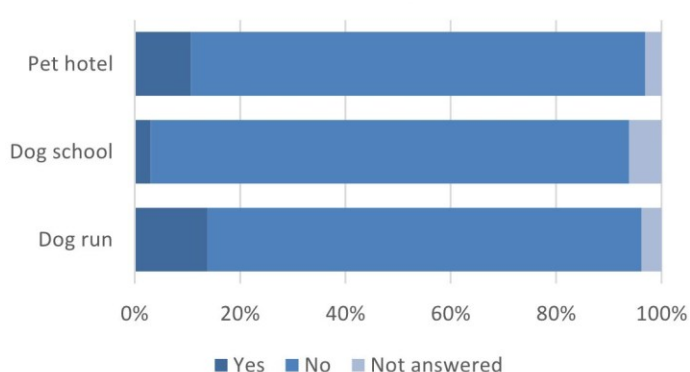
Objective	Number of animals	%
Vaccination	55	43
Medical checkup	39	30
Trimming	10	8
Pet hotel	4	3
Training class	3	2
Other	18	14

<Questionnaire results: 3 months before sample collection>

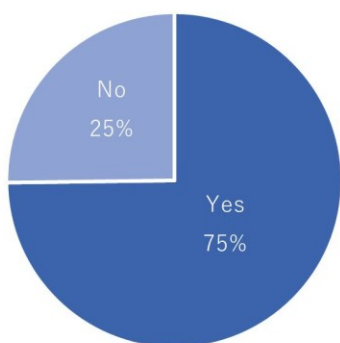
7. Where did you spend most of your time?



8. Have you used the following services?

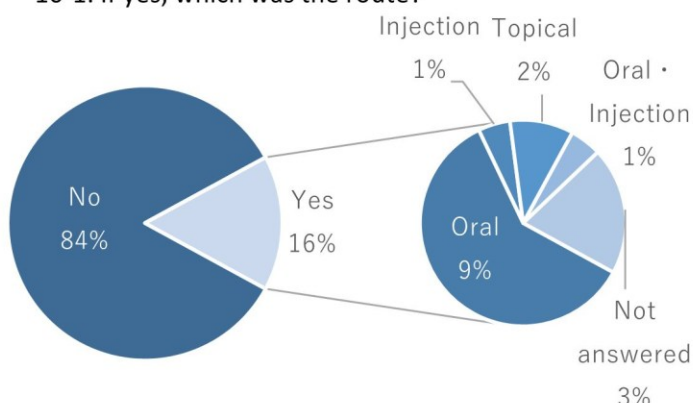


9. Have you visited animal clinic with a dog?
(For any purpose of the visit)

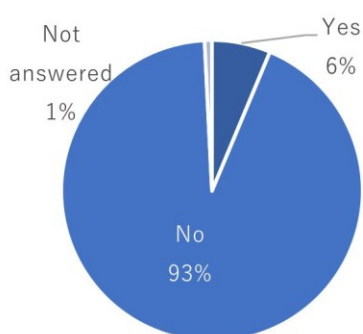


10. Has your dog administered antimicrobials?

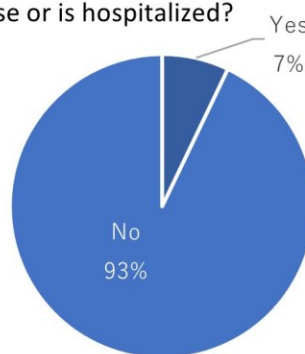
10-1. If yes, which was the route?



11. Has your dog been hospitalized?



12. Has your dog been in contact with anyone who has an infectious disease or is hospitalized?



13. What is the main diet?
(multiple answers)



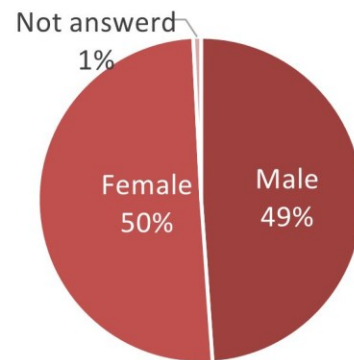
Diet	Number of animals	%
Commercial dry food	104	52.0
Commercial wet food	27	13.2
Commercially semi-dried dog food	11	5.4
Canine prescription diet	24	11.8
The same as a human diet	3	1.5
Cooked for dogs at home	16	7.8
Human meals leftover	2	1.0
Raw vegetables	13	6.4
Raw meat, bone	0	0.0

Questionnaire results on cats sampled in this survey in 2023 (number of responses 131)

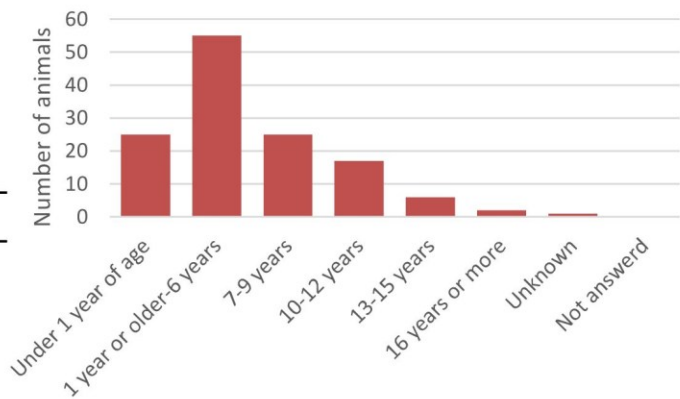
1. Species

Breed	Number of animals
Mixed breed (including mixed breeds, Japanese cats, domestic cats, and crossbreeds)	110
Abyssinian	3
Scottish Fold	2
American Shorthair	2
Ragdoll	2
Other	10
Unknown	1
Not answered	1
Total	131

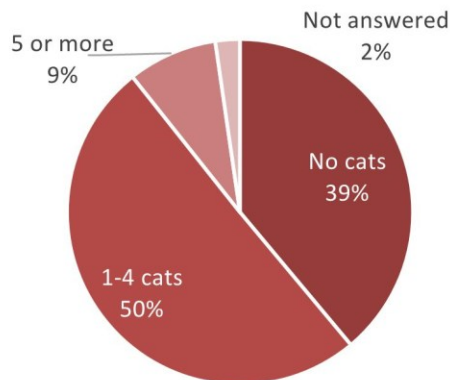
2. Sex



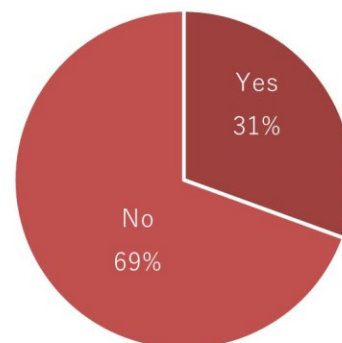
3. Age groups



4. Number of cats living together



5. Cohabitation with animals other than cats



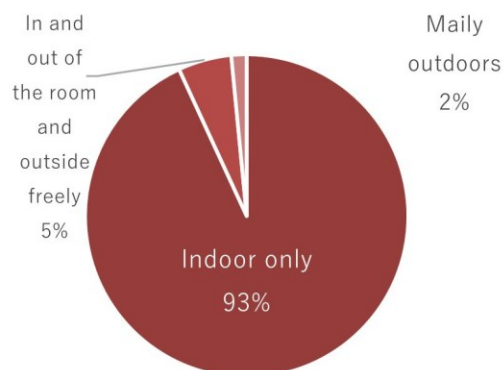
6. Objective of the visit (multiple answers)

	Number of animals	%
Medical checkup	52	38.0
Vaccination	40	29.2
Trimming	7	5.1
Pet hotel	6	4.4
Other	28	20.4
Not answered	4	2.9

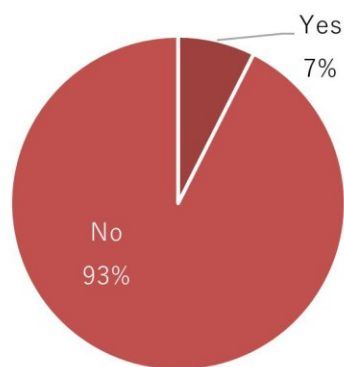


<Questionnaire results: 3 months before sample collection>

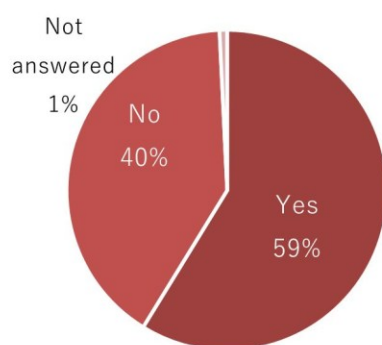
7. Where did you spend most of your time?



8. Did you use a pet hotel?

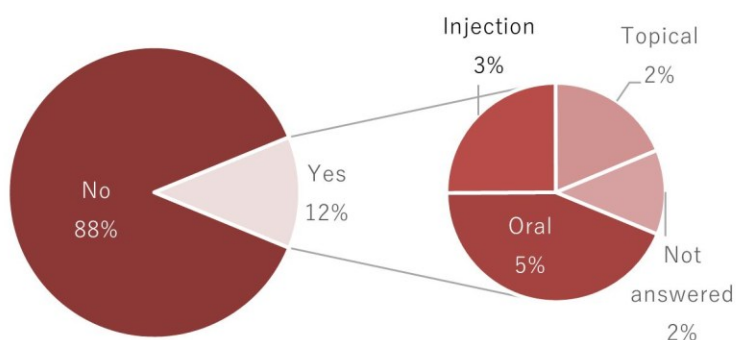


9. Have you visited animal clinic with a cat? (For any purpose of the visit)

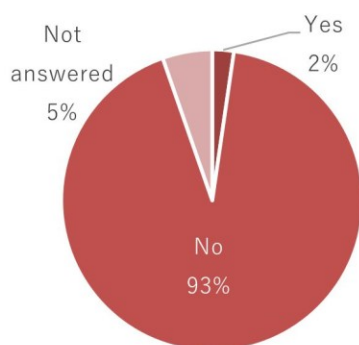


10. Has your cat administered antimicrobials?

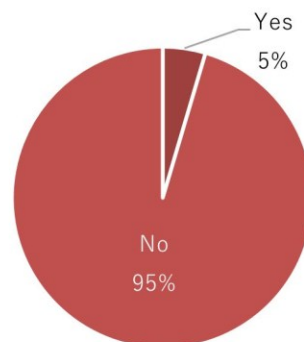
10-1. If yes, which was the route?



11. Has your cat been hospitalized?



12. Has your cat been in contact with anyone who has an infectious disease or is hospitalized?



13. What is the main diet? (multiple answers)



Diet	Number of animals	%
Commercial dry food	100	50.3
Commercial wet food	56	28.1
Commercially semi-dried dog food	4	2.0
Cat prescription diet	37	18.6
The same as a human diet	0	0.0
Cooked for cats at home	1	0.5
Human meals leftover	0	0.0
Raw vegetables	0	0.0
Raw meat	1	0.5

3.3.4. Summary

Companion animals have more opportunities for close contact with people, particularly their owners, than livestock, raising concerns about the transmission of antimicrobial-resistant bacteria from humans to animals or from animals to humans. In this survey, the resistance rate of *E. coli* to carbapenems, which are important last-resort treatments for multidrug-resistant bacterial infections, was 0.0%. The resistance rate of *Enterococcus* spp. to VCM, resistance to which poses a major concern in human medicine, particularly in relation to nosocomial infections, was also 0.0%.

Resistance rates to third-generation cephalosporins and fluoroquinolones, which are critically important antimicrobials in human medicine, were below 20% among both *E. coli* and *Enterococcus* spp. For many of the antimicrobials tested, bacteria isolated from healthy dogs and cats showed lower resistance rates than bacteria isolated from diseased dogs and cats. These findings confirmed that antimicrobial susceptibility has been well maintained in commensal bacteria carried by healthy dogs and cats.

The questionnaire results showed that approximately 60% of the healthy dogs and cats sampled in this survey were in the younger age groups and that more than 80% had not received antimicrobials during the three months before sample collection.

Acknowledgements

We would like to thank the veterinarians and staff at animal clinics throughout Japan who have cooperated in collecting the samples for this project, as well as the owners who have agreed to collecting samples, and dogs and cats who have provided samples. Additionally, the Japanese Veterinary Medical Association deserves special thanks for their devoted cooperation with our investigations.

3.4. Diseased Companion Animals

Bacterial isolates were collected from specimens obtained from diseased dogs and cats and submitted to clinical laboratories in 2023, and antimicrobial susceptibility testing was performed. The target bacterial species and sampling sites are shown in Table 3-4-1, and the numbers of isolates collected are shown in Table 3-4-2.

Table 3-4-1 Bacterial species and sampling sites collected in 2023

Bacterial Species	Sampling Site
<i>Escherichia coli</i> , <i>Klebsiella</i> spp.	Urine, Reproductive tract
Coagulase-positive <i>Staphylococcus</i> spp., <i>Acinetobacter</i> spp.	Urine, Skin
<i>Enterococcus</i> spp.	Urine, Ear
<i>Enterobacter</i> spp.	Urine

Table 3-4-2 Number of isolates

Bacterial Species	Dogs	Number of Isolates	Cats	Number of Isolates
<i>E. coli</i>	<i>E. coli</i>	149	<i>E. coli</i>	137
<i>Klebsiella</i> spp.	<i>K. pneumoniae</i>	63	<i>K. pneumoniae</i>	41
	<i>K. oxytoca</i>	13	<i>K. aerogenes</i>	7
	<i>K. aerogenes</i>	5	<i>K. oxytoca</i>	4
	Total	81	Total	52
<i>Enterobacter</i> spp.	<i>E. cloacae</i>	27	<i>E. cloacae</i>	38
<i>Acinetobacter</i> spp.	<i>A. pittii</i>	5	<i>A. baumannii</i>	7
	<i>A. baumannii</i>	4	<i>A. pittii</i>	3
	<i>A. ursingii</i>	3	<i>A. johnsonii</i>	2
	<i>A. calcoaceticus</i>	2	<i>A. courvalinii</i>	1
	<i>A. haemolyticus</i>	2	<i>A. guillouiae</i>	1
	<i>A. radioresistens</i>	2	<i>A. junii</i>	1
	<i>A. johnsonii</i>	1	<i>A. lwoffii</i>	1
	<i>A. junii</i>	1	<i>A. schindleri</i>	1
	<i>A. lwoffii</i>	1	<i>A. ursingii</i>	1
	Total	21	Total	18
Coagulase-positive <i>Staphylococcus</i> spp.	<i>S. pseudintermedius</i>	81	<i>S. pseudintermedius</i>	27
	<i>S. aureus</i>	2	<i>S. aureus</i>	31
	Total	83	Total	58
<i>Enterococcus</i> spp.	<i>E. faecalis</i>	93	<i>E. faecalis</i>	72
	<i>E. faecium</i>	20	<i>E. faecium</i>	22
	<i>E. gallinarum</i>	7	<i>E. gallinarum</i>	8
				37

<i>E. avium</i>	6	<i>E. casseliflavus</i>	6
<i>E. canintestini</i>	2	<i>E. canintestini</i>	1
<i>E. aquimarinus</i>	1	<i>E. durans</i>	1
<i>E. raffinosus</i>	1	<i>E. hirae</i>	1
		<i>E. raffinosus</i>	1
Total	130	Total	112

3.4.1. *Escherichia coli* (Dogs, Cats)

Among *Escherichia coli* isolates from dogs in 2023, resistance rates to the tested antimicrobials were highest for NA, followed by ABPC, CPFX, CEZ, and CEX. The antimicrobials showing high resistance rates were unchanged from 2022 (Figure 3-4-1-1). Among isolates from cats, resistance rates were highest for NA, followed by ABPC, CEX, CEZ, and CPFX, in the same order as in the previous year (Figure 3-4-1-2).

Resistance rates to CPFX, a fluoroquinolone, were 38.3% and 34.3% among isolates from dogs and cats, respectively. The corresponding resistance rates to CTX, a third-generation cephalosporin, were 26.8% and 27.7%, respectively. Resistance rates to MEPM, a carbapenem, were 0.0% among isolates from both dogs and cats. The resistance rate to CL, a polypeptide, was 0.0% among isolates from dogs. Among isolates from cats, one CL-resistant isolate was detected, corresponding to a resistance rate of 0.7%. This isolate did not carry a *mcr* gene.

Fig. 3-4-1-1 Resistance rates of *E. coli* from dogs

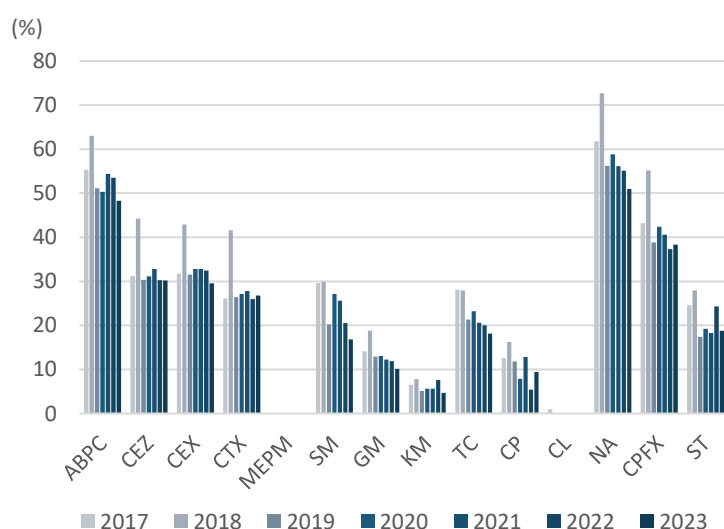
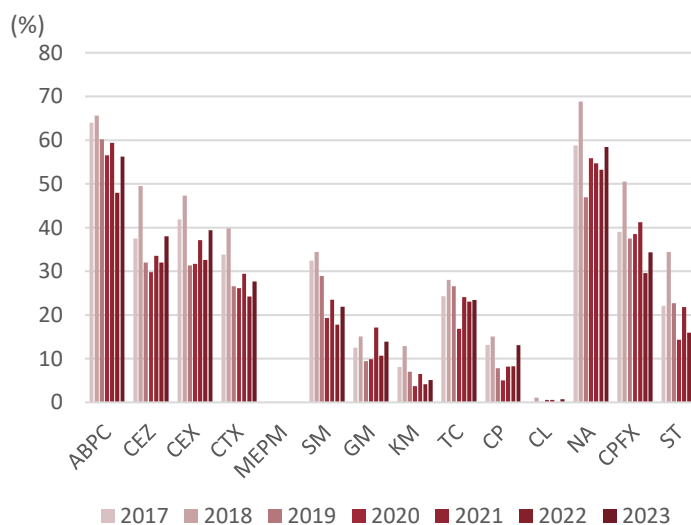


Fig. 3-4-1-2 Resistance rates of *E. coli* from cats



3.4.2. *Klebsiella* spp. (Dogs, Cats)

Among *Klebsiella* spp. isolated from dogs and cats in 2023, *Klebsiella pneumoniae* was the most frequently isolated species, followed by *K. oxytoca* in dogs and *K. aerogenes* in cats (Table 3-4-2).

Trends in resistance rates to the tested antimicrobials among *Klebsiella* spp. isolated from dogs and cats are shown in Figures 3-4-2-1 and 3-4-2-2. Among isolates from dogs, resistance rates tended to be high for CEZ and CEX. Compared with 2022, resistance rates to GM, SM, NA, and CPFX were significantly lower (Figure 3-4-2-1). Among isolates from cats, resistance rates were highest for CEZ, followed by CEX, CTX, NA, CPFX, ST, TC, SM, and GM, with no substantial changes from 2022 (Figure 3-4-2-2). Resistance rates generally tended to be higher among isolates from cats than among those from dogs. Resistance rates to CEZ, CEX, CTX, SM, GM, TC, CPFX, and ST were significantly higher among isolates from cats.

Resistance rates to CPFX, a fluoroquinolone, were 24.7% and 59.6% among isolates from dogs and cats, respectively. The resistance rates to CTX, a third-generation cephalosporin, were 23.5% and 65.4%, respectively. The resistance rate to MEPM, a carbapenem, was 0.0% among isolates from cats, whereas one resistant isolate was detected among those from dogs. Two isolates from dogs were resistant to CL, a polypeptide, but neither carried an *mcr* gene.

Fig. 3-4-2-1 Resistance rates of *Klebsiella* spp. from dogs

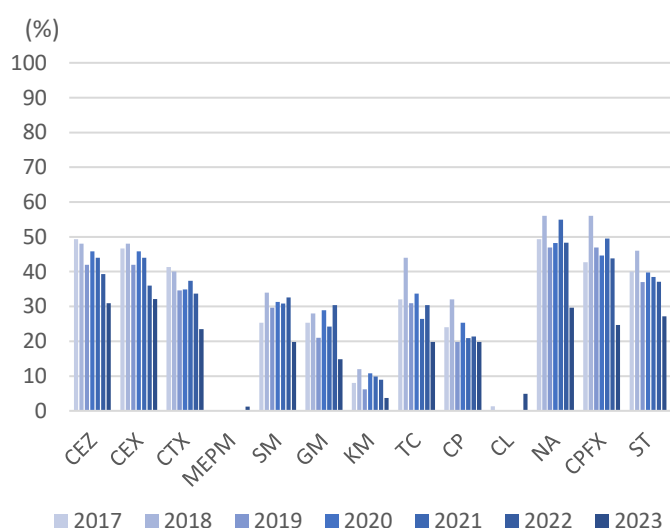
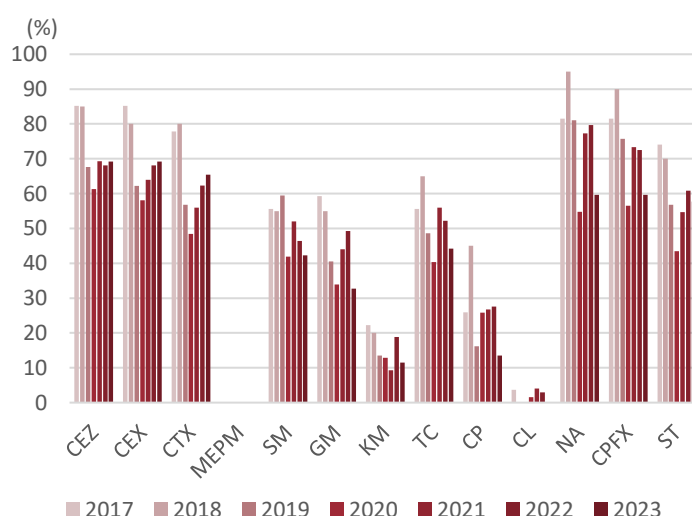


Fig. 3-4-2-2 Resistance rates of *Klebsiella* spp. from cats



3.4.3. *Enterobacter* spp. (Dogs, Cats)

Among *Enterobacter* spp. isolated from dogs and cats in 2023, *E. cloacae* was the only species identified in both animals. Although caution is required because of the small numbers of isolates collected in 2023, with 27 isolates from dogs and 38 from cats, resistance rates to GM and KM remained below 20% in both animals. In contrast, resistance rates of 50% or higher were observed for CTX, NA, and CPFX among isolates from dogs and for CTX, NA, and CPFX among isolates from cats. Resistance rates to CL, a polypeptide, were 11.1% among isolates from dogs and 31.6% among isolates from cats. Some *Enterobacter* spp. strains are known to exhibit resistance to CL independently of plasmid-borne *mcr* genes. Consistent with this characteristic, none of the CL-resistant isolates detected in this survey carried an *mcr* gene.

Fig. 3-4-3-1 Resistance rates among *Enterobacter* spp. isolated from dogs in 2020 and 2023

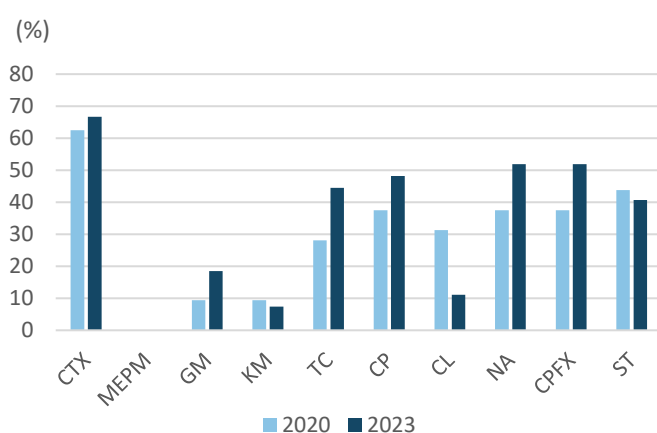
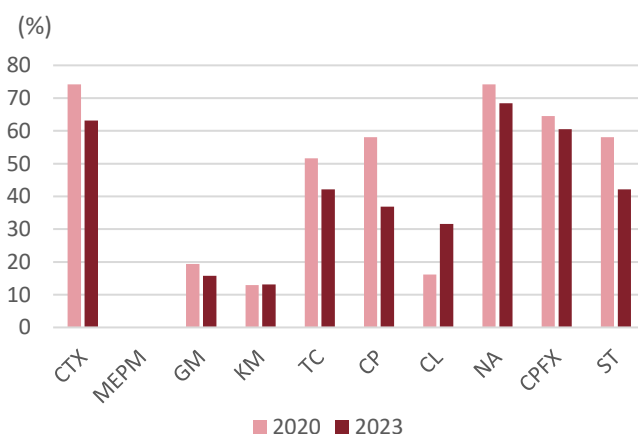


Fig. 3-4-3-2 Resistance rates among *Enterobacter* spp. isolated from cats in 2020 and 2023



3.4.4. *Acinetobacter* spp. (Dogs, Cats)

Nine species of *Acinetobacter* were isolated from each of dogs and cats in 2023. In both animals, *A. pittii* and *A. baumannii* were the two most frequently isolated species (Table 3-4-2).

Resistance rates among *Acinetobacter* spp. isolated from dogs in 2020, 2021, and 2023 are shown in Figure 3-4-4-1. Among isolates from dogs, resistance rates to all tested antimicrobials remained at or below 20%. Although caution is required because only 18 isolates were collected from cats, resistance rates to all tested antimicrobials were below 20% in 2023. Resistance rates are not presented for the cat-derived isolates collected in 2020 because only 11 isolates were available.

One isolate from a dog and two isolates from cats were resistant to MEPM, a carbapenem. Carbapenems are among the most important antimicrobials in human medicine and are regarded as last-resort treatments for multidrug-resistant bacterial infections. Trends in carbapenem-resistant bacteria therefore require continued close monitoring.

Fig. 3-4-4-1 Resistance rates among *Acinetobacter* spp. isolated from dogs in 2020, 2021, and 2023

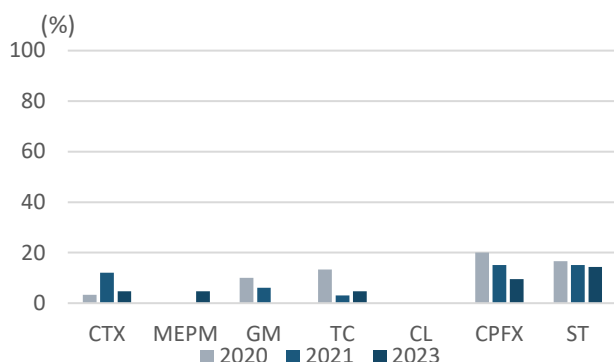
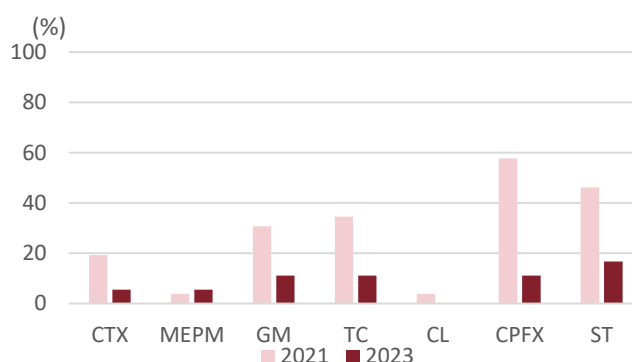


Fig. 3-4-4-2 Resistance rates among *Acinetobacter* spp. isolated from cats in 2021 and 2023



3.4.5. Coagulase-positive Staphylococci (Dogs, Cats)

Most coagulase-positive *Staphylococcus* spp. isolated from dogs in 2023 were *Staphylococcus pseudintermedius*, while only two isolates were identified as *S. aureus*. In contrast, *S. pseudintermedius* and *S. aureus* were isolated from cats in approximately equal proportions (Table 3-4-2). Because the breakpoints established by CLSI and EUCAST differ among *Staphylococcus* species, resistance rates were calculated separately by species and are presented for *S. pseudintermedius* isolated from dogs and cats and *S. aureus* isolated from cats (Figures 3-4-5-1 to 3-4-5-3).

Among *S. pseudintermedius* isolates from dogs in 2023, resistance rates were highest for PCG, followed by TC, EM, AZM, CPF, CP, MPIPC, and GM. Resistance rates to PCG, TC, EM, and AZM were particularly high, exceeding 80% (Figure 3-4-5-1). Among *S. pseudintermedius* isolates from cats, resistance rates were highest for CPF, followed by PCG, EM, AZM, MPIPC, TC, CP, and GM. The resistance rate to CPF was particularly high, at 100% (Figure 3-4-5-2). The trends observed in both dogs and cats were similar to those in 2022.

Among *S. aureus* isolates from cats, resistance rates were highest for PCG, followed by CPF, AZM, EM, CFX, CEZ, CEX, CTX, and MPIPC. Resistance rates to the other tested antimicrobials, namely SM, GM, TC, and CP, were below 30% (Figure 3-4-5-3). Because

only 17 isolates were collected in 2018, caution is required when comparing resistance rates for that year.

Fig. 3-4-5-1 Trends in resistance rates among *S. pseudintermedius* isolates from dogs

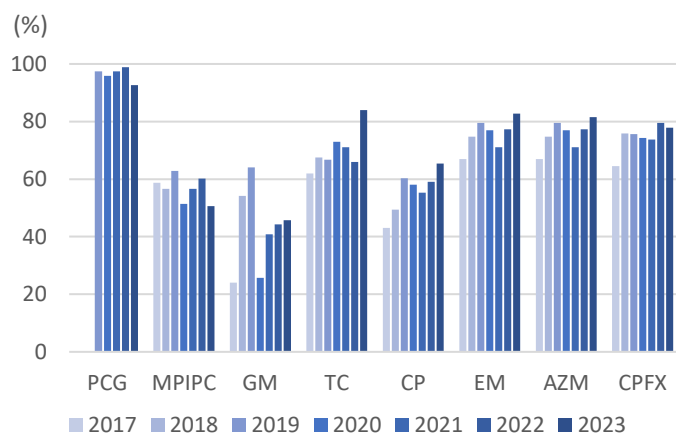
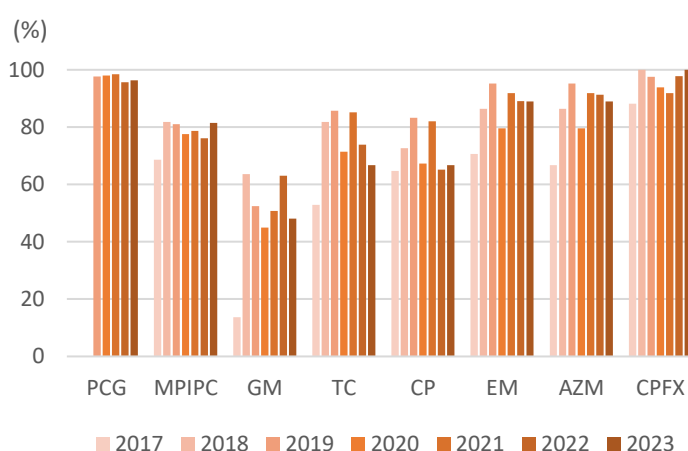


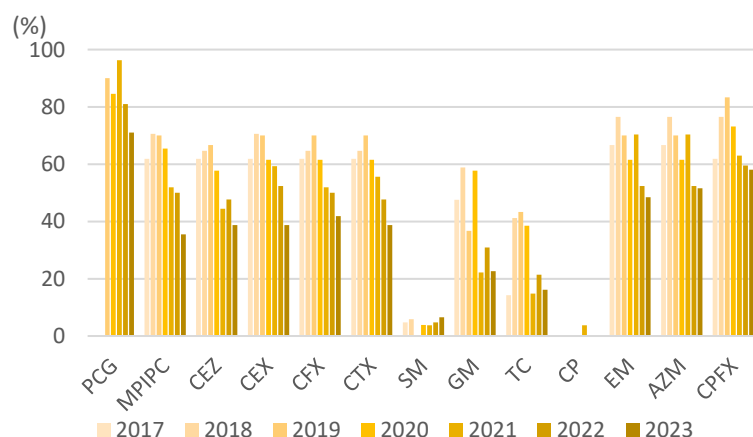
Fig. 3-4-5-2 Trends in resistance rates among *S. pseudintermedius* isolates from cats



Among *S. pseudintermedius* isolates, the resistance rate to TC was significantly higher in isolates from dogs than in those from cats, whereas resistance rates to MPIPC and CPFX were significantly higher in isolates from cats. Resistance rates to CPFX, a fluoroquinolone, were 77.8% and 100.0% among isolates from dogs and cats, respectively. Resistance rates to AZM, a 15-membered ring macrolide, were 81.5% and 88.9%, respectively.

Resistance rates to MPIPC were 50.6% among *S. pseudintermedius* isolates from dogs, 81.5% among *S. pseudintermedius* isolates from cats, and 35.5% among *S. aureus* isolates from cats.

Fig. 3-4-5-3 Trends in resistance rates among *S. aureus* isolates from cats



3.4.6. *Enterococcus* spp. (Dogs, Cats)

Among *Enterococcus* spp. isolated from dogs and cats in 2023, *Enterococcus faecalis* was the most frequently isolated species in both animals, followed by *E. faecium*. Other species isolated from dogs included *E. gallinarum*, *E. avium*, *E. canintestini*, *E. aquimarinus*, and *E. raffinosus*. Other species isolated from cats included *E. gallinarum*, *E. casseliflavus*, *E. canintestini*, *E. durans*, *E. hirae*, and *E. raffinosus* (Table 3-4-2).

In 2023, resistance rates to TC were the highest among isolates from both dogs and cats, at 59.2% and 73.2%, respectively. Resistance rates below 20% were observed for ABPC, GM, and CP among isolates from dogs and for CP among isolates from cats (Figures 3-4-6-1 and 3-4-6-2). Resistance rates to VCM were 0.0% among isolates from both dogs and cats.

For all tested antimicrobials except CP and VCM, resistance rates were significantly higher among isolates from cats than among those from dogs. Resistance rates to CPFX, a fluoroquinolone, were 28.5% and 43.8% among isolates from dogs and cats, respectively. In both dog- and cat-derived isolates, the resistance rate to VCM, resistance to which poses a major concern in human medicine, particularly in relation to nosocomial infections, was 0.0%.

Fig. 3-4-6-1 Trends in resistance rates among *Enterococcus* spp. isolated from dogs

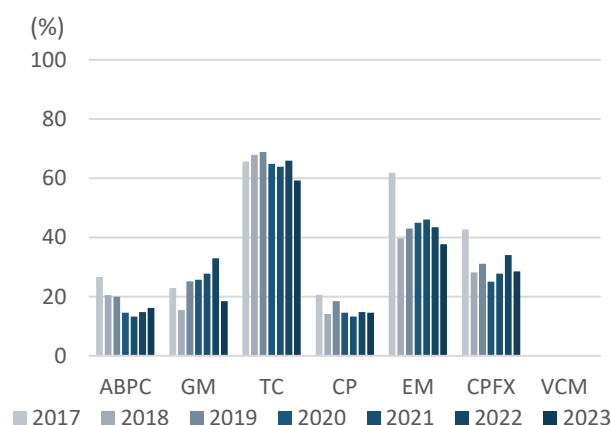
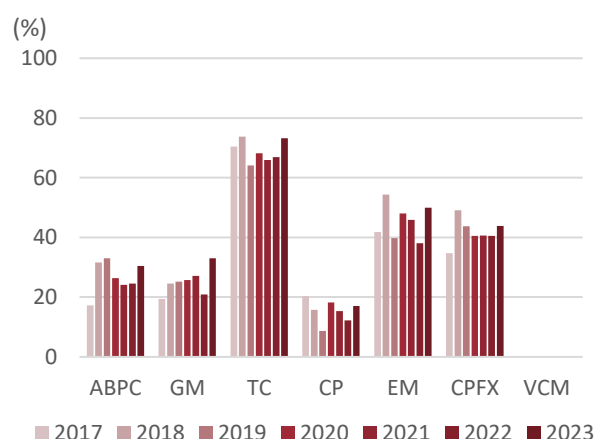


Fig. 3-4-6-2 Trends in resistance rates among *Enterococcus* spp. isolated from cats



Because resistance characteristics differ between *E. faecalis* and *E. faecium* (for example, *E. faecalis* is generally susceptible to ABPC, whereas *E. faecium* is often resistant), resistance rates are also presented by bacterial species for reference (Figures 3-4-6-3 to 3-4-6-6).

Among *E. faecalis* isolates from dogs, resistance rates tended to be high for TC and EM. The resistance rate to GM was significantly lower than that in 2022. Among isolates from cats, resistance rates also tended to be high for TC and EM, while trends for the other tested antimicrobials were similar to those observed in 2022.

Among *E. faecium* isolates from both dogs and cats, the resistance rate was highest for CPFX, and high resistance rates were also observed for ABPC, EM, TC, and GM. Because only 20 isolates from dogs and 22 isolates from cats were collected, these resistance rates are presented for reference only.

Fig. 3-4-6-3 Trends in resistance rates among *E. faecalis* isolates from dogs

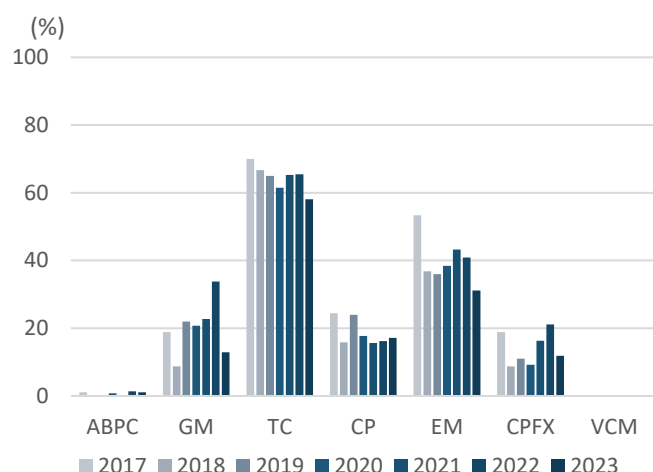


Fig. 3-4-6-4 Trends in resistance rates among *E. faecalis* isolates from cats

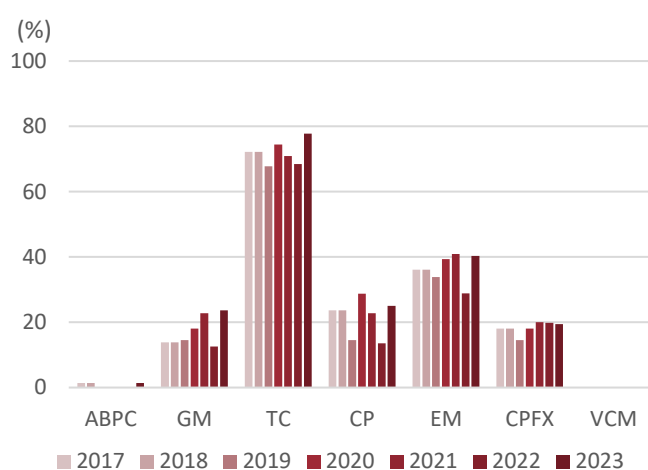


Fig. 3-4-6-5 Trends in resistance rates among *E. faecium* isolates from dogs

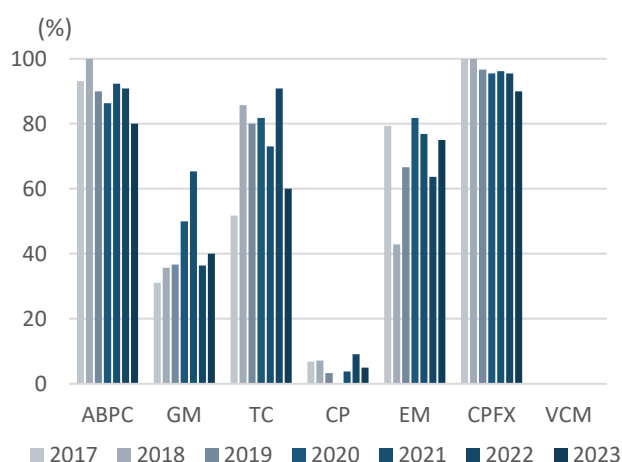
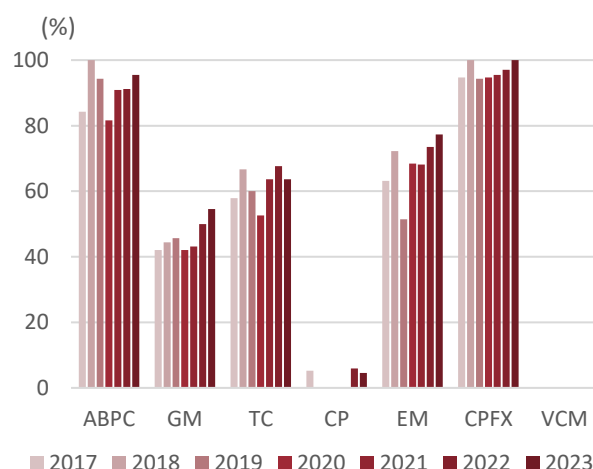


Fig. 3-4-6-6 Trends in resistance rates among *E. faecium* isolates from cats



3.4.7. Summary

For *E. coli*, *Klebsiella* spp., coagulase-positive *Staphylococcus* spp., and *Enterococcus* spp., which have been continuously collected since the survey began in 2017, the overall trends were similar to those observed previously. Among *Enterobacter* spp. collected in 2023, resistance rates to third-generation cephalosporins and fluoroquinolones tended to be high in isolates from both dogs and cats. In contrast, resistance rates to all tested antimicrobials among *Acinetobacter* spp. were below 20%.

Resistance to MEPM, a carbapenem that is not approved for veterinary use but is one of the most important antimicrobials in human medicine, was detected among *Klebsiella* spp. and *Acinetobacter* spp. Although the resistance rates were low, future trends require continued monitoring. The resistance rate to VCM among *Enterococcus* spp. was 0.0%. VCM resistance poses a major concern in human medicine, particularly in relation to nosocomial infections.

Third-generation cephalosporins, fluoroquinolones, 15-membered ring macrolides, and colistin are critically important antimicrobials in human medicine. Therefore, in the animal health sector, they are designated as second-line antimicrobials to be used when other antimicrobials are ineffective. In this survey, which also included bacterial species other than *E. coli*, resistance rates to CTX were high among *Enterobacter* spp., *Klebsiella* spp. isolated from cats, and *S. aureus*, but were 30% or lower among the other bacterial species. Resistance rates to CPFX varied widely, ranging from 11.1% to 100.0%. Resistance rates to AZM, a 15-membered ring macrolide, were 50% or higher among coagulase-positive *Staphylococcus* spp. CL-resistant isolates were uncommon, and no *mcr* genes were detected among the CL-resistant isolates collected in 2023.

This survey examined bacteria isolated from diseased dogs and cats, and the results were considered to have been influenced by factors such as antimicrobial treatment and the occurrence of disease. Some bacterial species showed high resistance rates to multiple antimicrobials. To preserve the effectiveness of antimicrobials for the future treatment of bacterial infections, it is essential to ensure their prudent use. This includes selecting effective antimicrobials based on susceptibility testing performed before treatment and considering alternatives to antimicrobial administration, such as cleansing and disinfection, for conditions such as dermatitis.

Acknowledgements

We would like to thank Sanritsu Zelkova Veterinary Laboratory, FUJIFILM VET Systems Co., Ltd., MIROKU Medical Laboratory, Inc., and IDEXX Laboratories, Inc. for their cooperation in providing strains for this project.

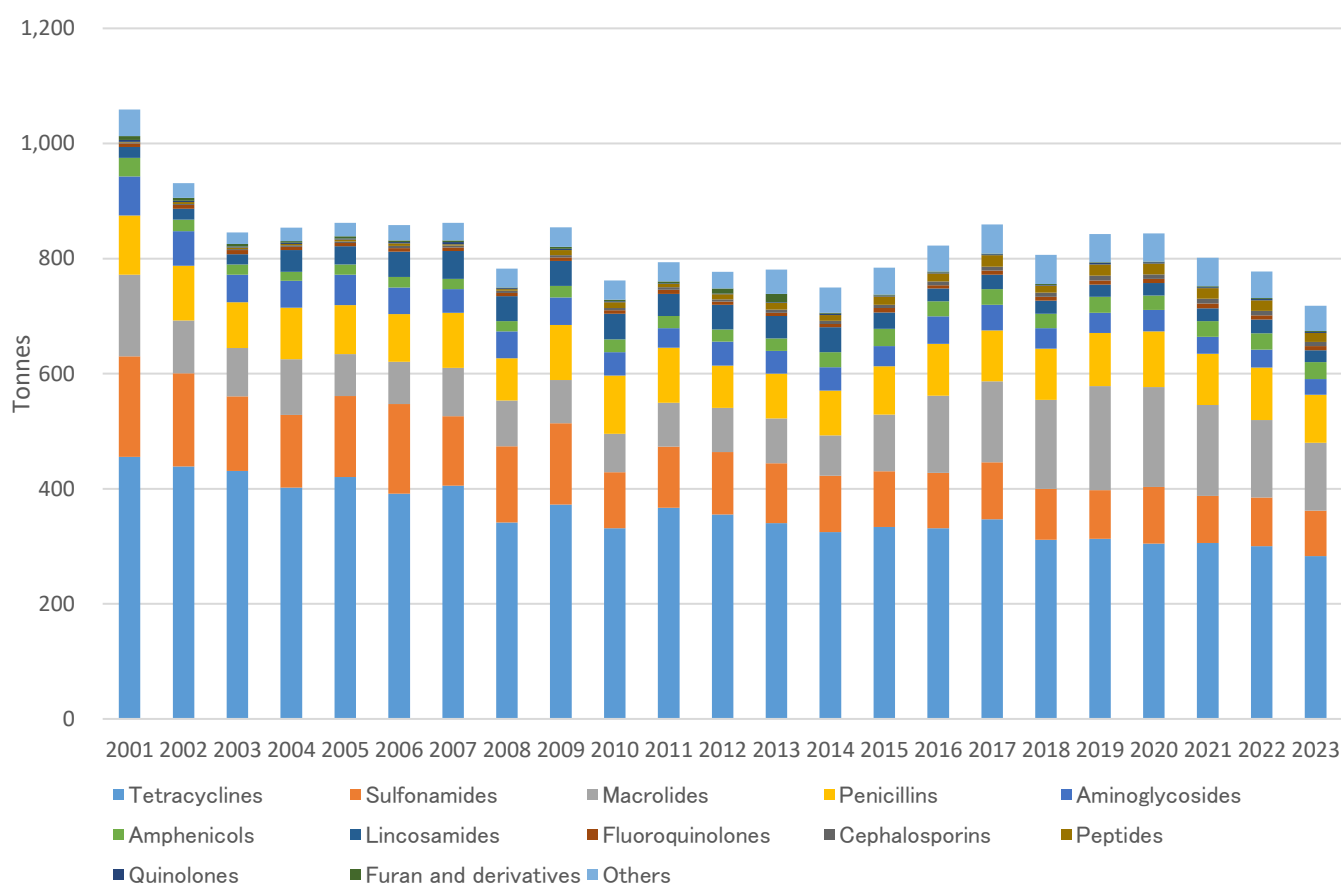
4. Monitoring Results of Antimicrobial Sales Volume

4.1. Veterinary Antimicrobials

4.1.1. Overview of Veterinary Antimicrobials Sales Volume

Trends in veterinary antimicrobial use are estimated based on sales volume. Sales volume of veterinary antimicrobials has decreased by approximately 30% since 2001 and has remained below 800 tons in recent years (Figure 4-1-1-1). By antimicrobial class, tetracyclines accounted for the largest sales volume. However, sales volume of tetracyclines has shown a decreasing trend, and their share of the total sales volume has remained below 40% since 2018.

Fig. 4-1-1-1 Trends in sales volume of veterinary antimicrobials (2001–2023)



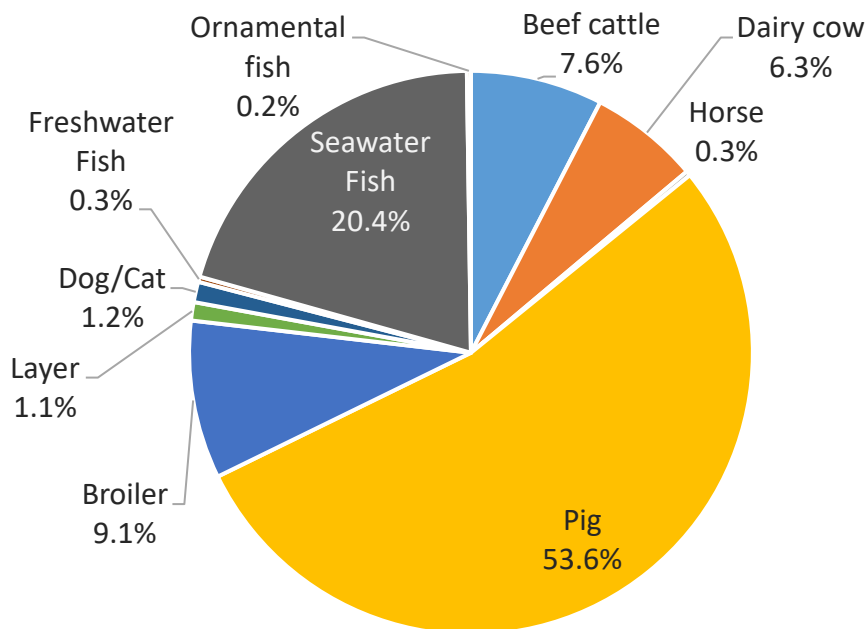
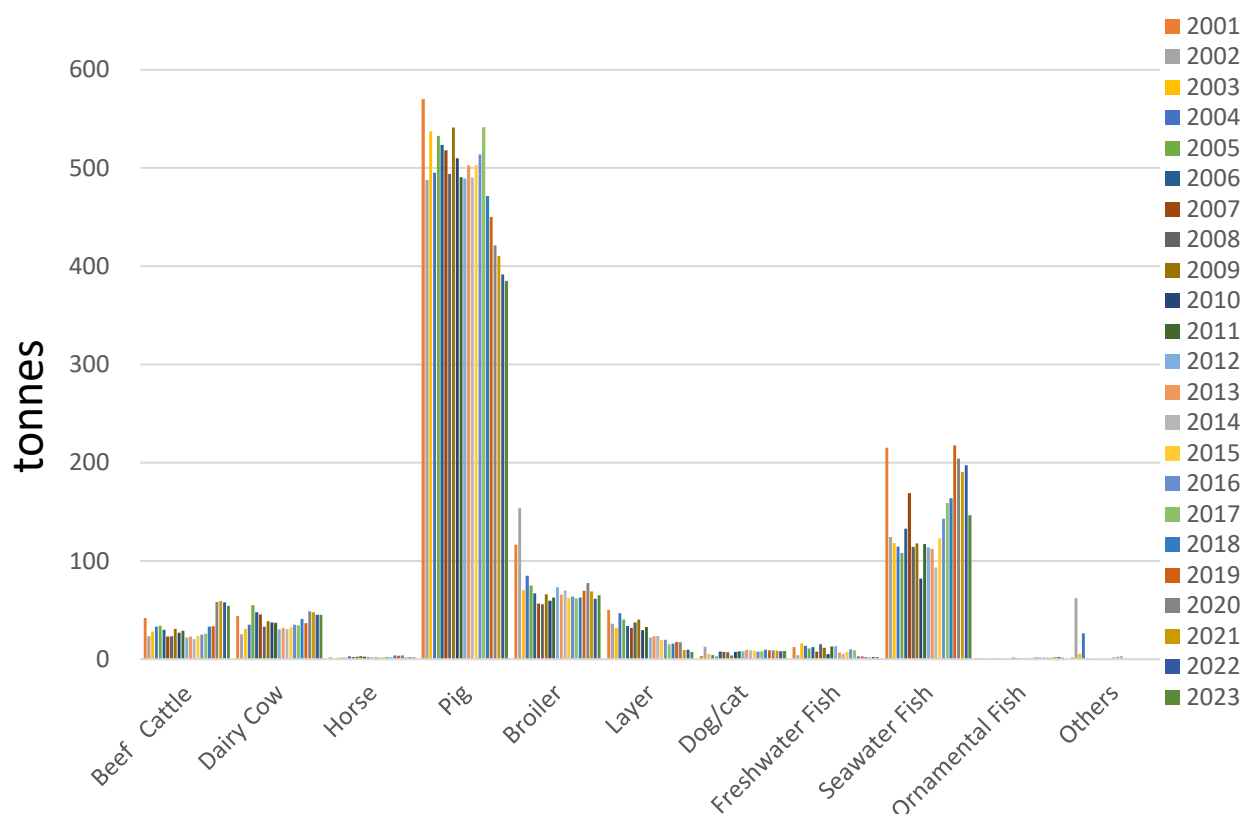


Fig. 4- I - I -2 Proportion of sales volume of veterinary antimicrobials by animal species (2023)

By estimated animal species, pigs accounted for the largest sales volume, followed by fisheries (seawater) (Figure 4- I - I -2).

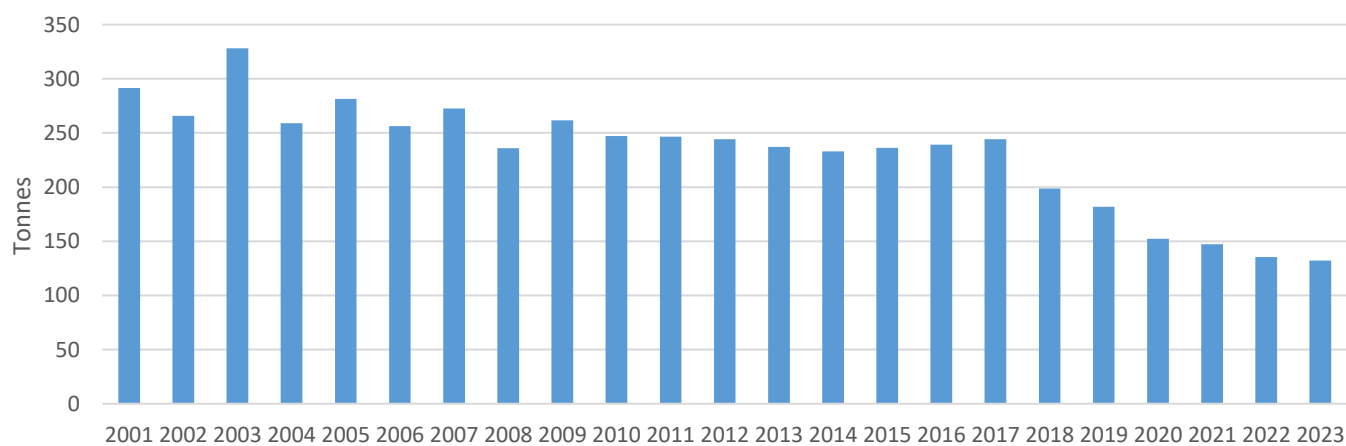
Trends by animal species are shown below (Figure 4- I - I -3).

Fig. 4- I - I -3 Sales volume of veterinary antimicrobials by animal species (2001-2023)



Sales volume for pigs, which accounted for the largest share, has shown a decreasing trend in recent years, mainly due to a decline in tetracycline sales. In 2023, the sales volume was half that recorded in 2001 (Figure 4- I - I -4).

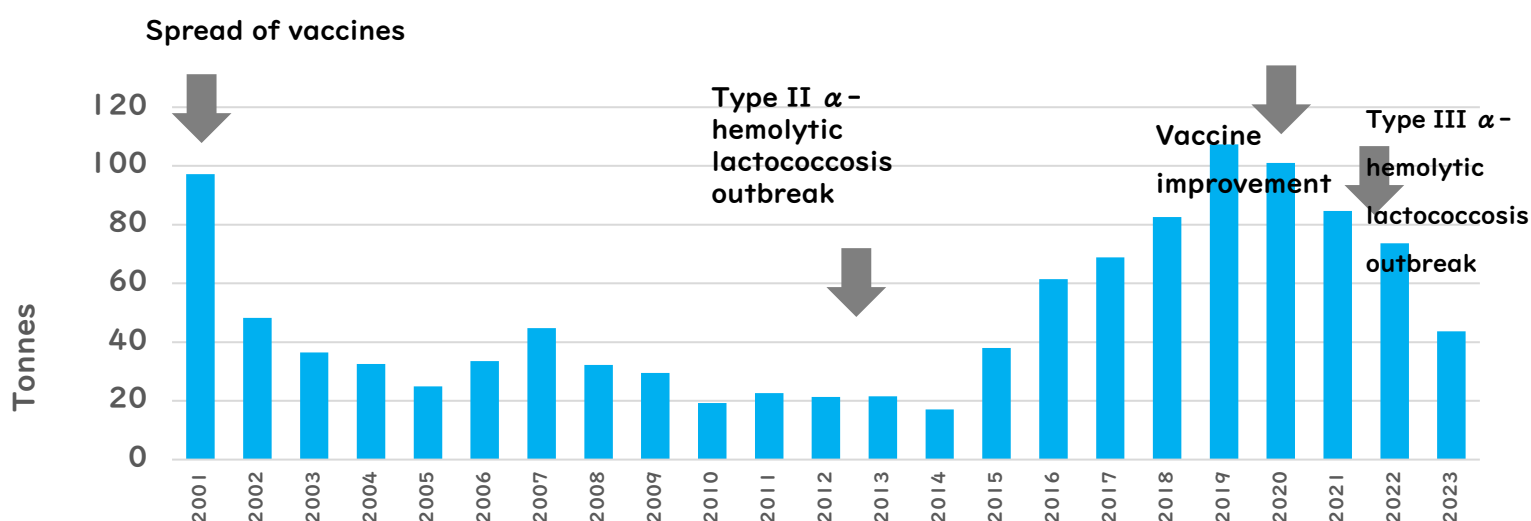
Fig. 4- I - I -4 Trends in tetracycline sales volume for pigs



Sales volume for seawater fish, which accounted for the second-largest volume after pigs, increased from 2015 to 2019, mainly due to an increase in sales of macrolides, particularly EM. This increase was considered to be associated with the treatment of type II α -hemolytic lactococcosis, which has been reported since around 2013. In 2020, the upward trend reversed, and sales began to decline, possibly because of improvements in vaccines

Fig. 4-1-1-5 Trends in EM sales volume in seawater fish and matters related to lactococcosis

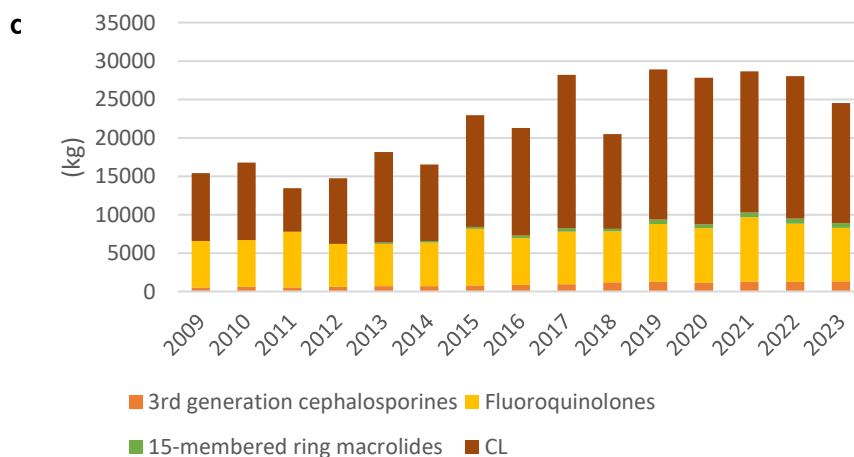
and other measures. However, cases of type III α -hemolytic lactococcosis have been reported since around 2021, and future trends require continued monitoring (Figure 4-1-1-5).



4.1.2. Sales Volume of Second-line Drugs

Antimicrobials that are important in human medicine and whose use is restricted to cases in which other antimicrobials are ineffective are referred to as second-line antimicrobials. These include fluoroquinolones, third-generation cephalosporins, 15-membered ring macrolides, and

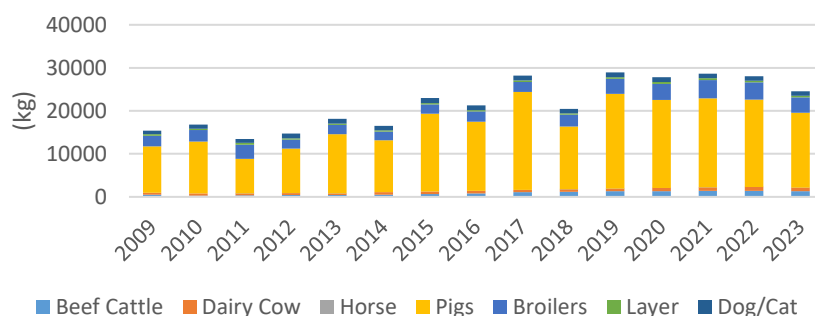
Fig. 4-1-2-1 Trends in sales volume of second-line



CL. Trends in sales volume by second-line antimicrobial are shown in Figure 4-1-2-1. CL had the largest sales volume, followed by fluoroquinolones.

By animal species (Figure 4-1-2-2), pigs accounted for the largest share of sales. CL accounted for approximately 80% of second-line antimicrobial sales for pigs, and its sales increased following the revocation of its approval as a feed additive in 2018. However, following the development of a vaccine against edema disease, for which CL is indicated, sales are expected to decrease in the future.

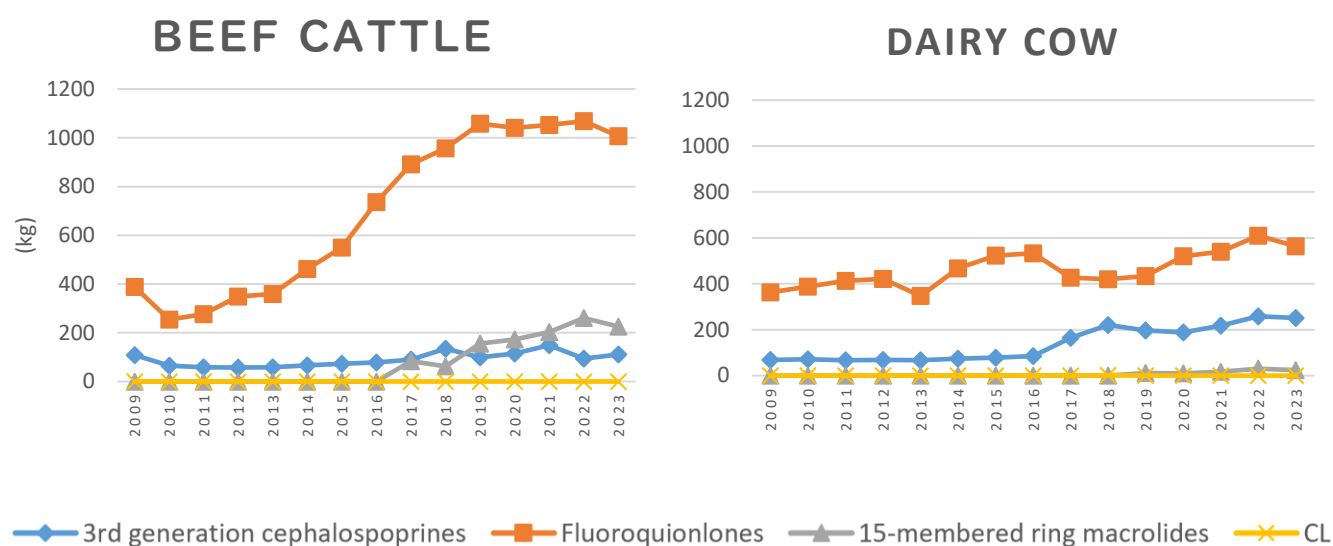
Fig. 4-1-2-2 Trends in sales volumes of second-line



Broilers accounted for the second-largest sales volume of second-line antimicrobials after pigs, with fluoroquinolones accounting for 66% of the volume. Sales volume of fluoroquinolones for broilers increased from 2018 to 2021 and began to decline in 2022. Nevertheless, future trends require continued monitoring in conjunction with resistance rates.

Sales volume of second-line antimicrobials for cattle, including beef and dairy cattle, was lower than that for pigs and broilers. However, sales of fluoroquinolones and 15-membered ring macrolides for beef cattle and third-generation cephalosporins and fluoroquinolones for dairy cattle have increased in recent years and remained at high levels (Figure 4-1-2-3). CL use in broilers has also increased, and this trend will continue to be monitored in conjunction with resistance rates.

Fig. 4-I-2-3 Trends in sales volume of second-line antimicrobials sold for beef cattle and dairy cattle (2009-2023)

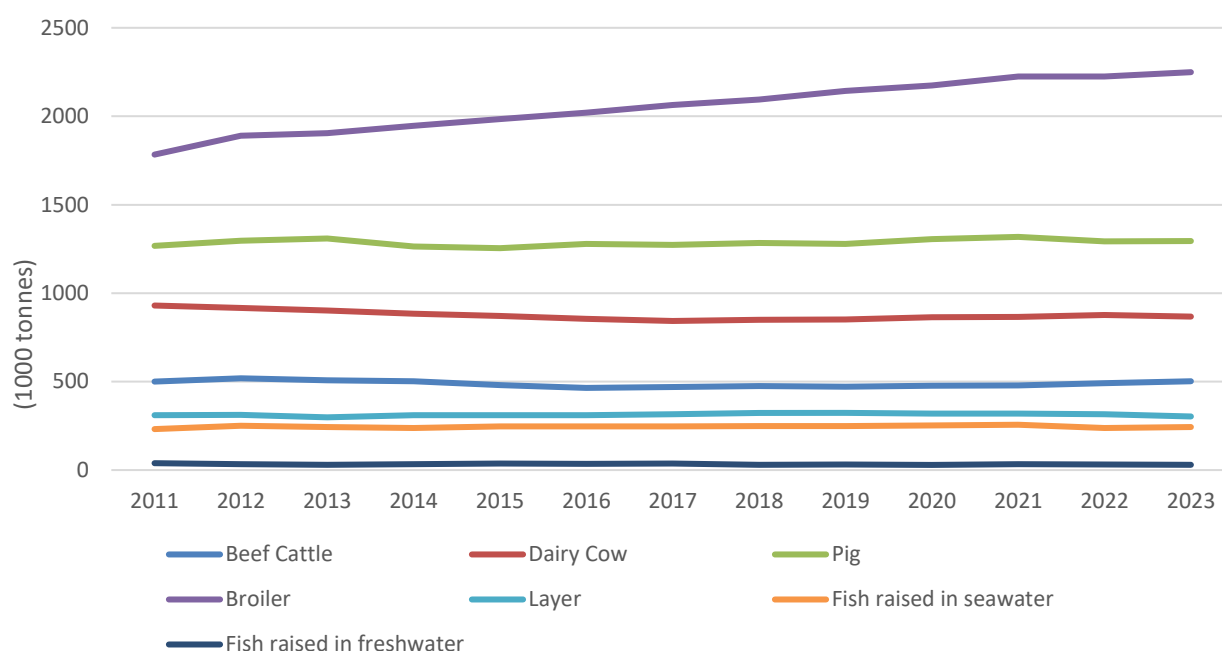


4.1.3. Veterinary Antimicrobials Sales Volume Adjusted by animal biomass

Sales volume of veterinary antimicrobials is influenced by the size of the animal population to which the antimicrobials are administered. In general, sales volume of antimicrobials would be expected to increase as the number of animals increases. Therefore, combining antimicrobial sales data with animal population estimates provides a more accurate assessment of changes in antimicrobial use within livestock production systems. Because the total weight of animals in Japan cannot be measured directly, animal weight (biomass) was estimated using statistical data, including carcass weights and livestock numbers. For details of the estimation methods, please refer to Section 5, Materials and Methods.

Because the available data differ among animal species, biomass was not calculated using the same criteria for all species. Therefore, biomass cannot be strictly compared across animal species. Nevertheless, the overall estimates indicated that broilers and pigs had relatively large biomasses (Figure 4-I-3-I). Broiler biomass showed an increasing trend from 2011 to 2023.

Fig. 4-1-3-1 Trends in biomass from 2011 to 2023

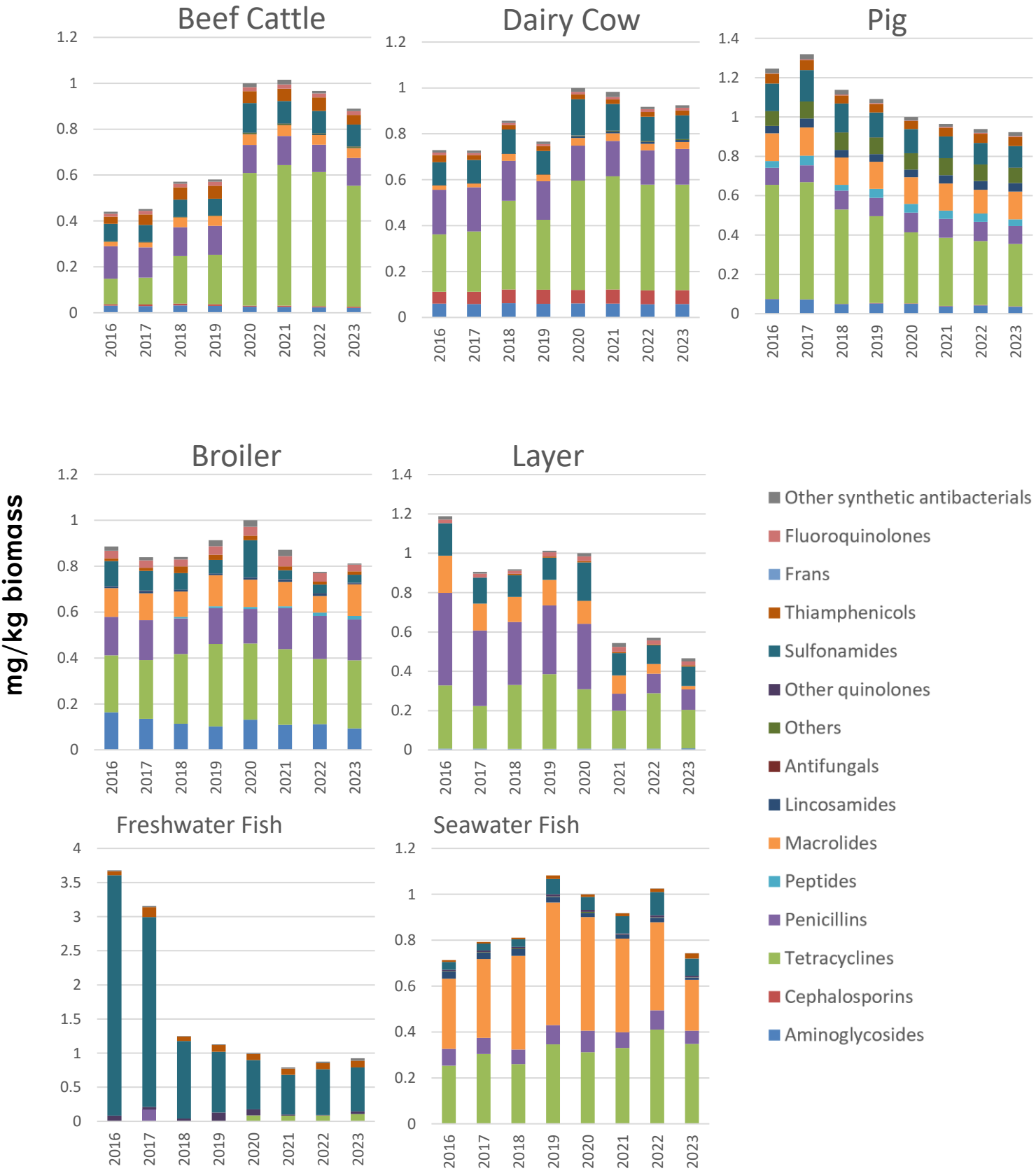


Dividing antimicrobial sales volume by the estimated biomass provides an indicator of antimicrobial use that takes changes in animal population size into account. For each animal species, the 2020 value was set to 1 and values for other years were calculated relative to this baseline. The year 2020 is the baseline year for the Action Plan outcome index concerning the reduction of antimicrobial use in the livestock sector. Trends from 2016, when Japan's first Action Plan was established, through 2023 are shown in Figure 4-1-3-2.

Decreasing trends were observed in layers, broilers, and freshwater fish, whereas increasing trends were observed in beef cattle, dairy cattle, and seawater fish. A decreasing trend was observed from 2018 onward in pigs and from 2022 onward in dairy cattle. Although the unadjusted antimicrobial sales volume for broilers did not show a decreasing trend (Figure 4-1-1-3), the biomass-adjusted sales volume showed a decreasing trend.

Several limitations of this biomass adjustment method should be noted. Because biomass is calculated using different methods for each animal species, the resulting values are not suitable for comparisons across species. In addition, the method does not account for the exact size of the animal population at the time the antimicrobials were administered. Nevertheless, because it can be calculated relatively simply from available statistical data without relying heavily on complex assumptions or models, it is useful as an indicator for the long-term assessment of changes in antimicrobial use within the same animal species while accounting for changes in population size over time.

Fig. 4-1-3-2 Biomass-adjusted antimicrobial sales volume relative to the 2020 value of 1, 2016–2023



4.1.4. Summary

The total sales volume of veterinary antimicrobials in 2023 was approximately 718 tons, representing a decrease of approximately 59 tons from 2022.

By antimicrobial class, sales of tetracyclines decreased by approximately 17 tons from the previous year, while sales of macrolides decreased by approximately 16 tons. In contrast, sales of thiamphenicols increased by approximately 1 ton.

By animal species, the largest decrease in antimicrobial sales volume in 2023 was observed for seawater fish, with a reduction of approximately 51 tons, followed by pigs and beef cattle, with reductions of approximately 7 tons and 4 tons, respectively. In contrast, sales for broilers increased by approximately 4 tons. The sharp increase in macrolide sales for seawater fish reversed in 2020 and has since declined. This was considered to reflect the development of vaccines against the disease responsible for the increase, together with improvements in vaccine administration methods.

Among second-line antimicrobials, CL had the largest sales volume. Because CL is used almost exclusively in pigs, sales for pigs accounted for the largest share. A further decrease is expected as vaccination becomes more widely adopted. Among all animal species, broilers accounted for the largest sales volume of fluoroquinolones. Sales of fluoroquinolones and 15-membered ring macrolides for beef cattle, third-generation cephalosporins and fluoroquinolones for dairy cattle, and CL for broilers have increased. These trends require continued monitoring.

Biomass-adjusted antimicrobial sales volume showed decreasing trends in layers, broilers, and freshwater fish, but increasing trends in beef cattle, dairy cattle, and seawater fish. In pigs, a decreasing trend has been observed since 2018.

4.2. Antimicrobial feed additives

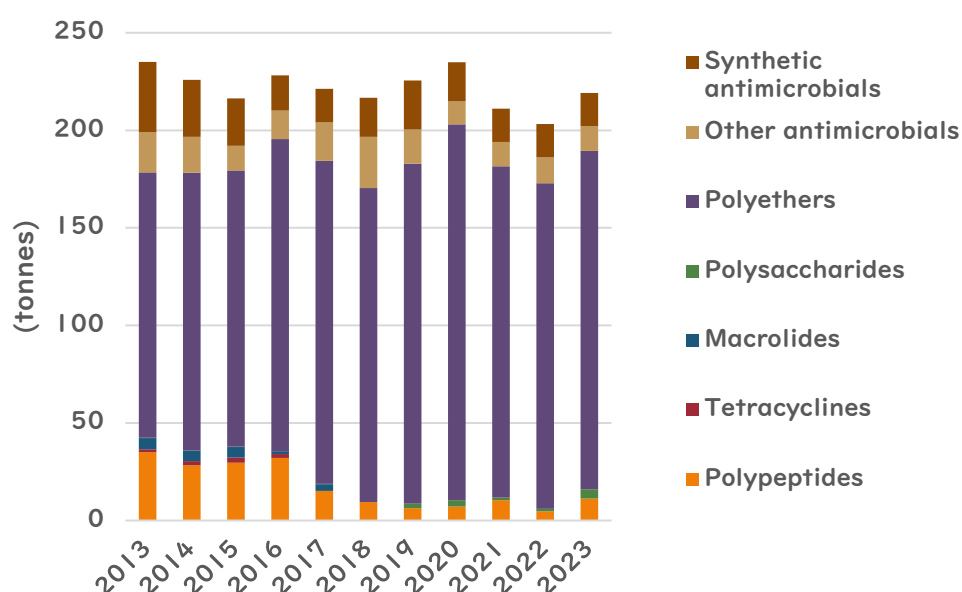
The distribution volume of antimicrobial feed additives, based on surveys conducted by the Food and Agricultural Materials Inspection Center (FAMIC) and the Japan Scientific Feeds Association, is shown in Figure 4-2. The distribution volume increased slightly from 203.3 tonnes in 2022 to 219.2 tonnes in 2023.

By antimicrobial class, polyethers, which accounted for most of the distribution volume and are not used in humans, showed an increasing trend. Their share of the total distribution volume increased from 57.8% in 2013 to 79.1% in 2023.

The designation of the polypeptide CL as a feed additive was revoked in July 2018, that of the macrolide TS in May 2019, and those of two tetracyclines in December 2019. Consequently, these antimicrobials have not been distributed as feed additives since their respective designations were revoked.

Data sources: Food and Agricultural Materials Inspection Center (FAMIC) and Japan Scientific Feeds Association.

Fig. 4-2 Trends in distribution volume of antimicrobial feed additives, 2013–2023



4.3. Antimicrobials for human use sold to animal clinics

The sales volume of antimicrobials approved as veterinary drugs (hereinafter referred to as “veterinary antimicrobials”) has been surveyed under JVARM since 2001. However, at clinics for companion animals, antimicrobials approved as human drugs (hereinafter referred to as “human antimicrobials”) are also used based on the judgment of veterinarians. Therefore, a survey has been conducted on the sales volume of human antimicrobials sold to veterinary clinics.

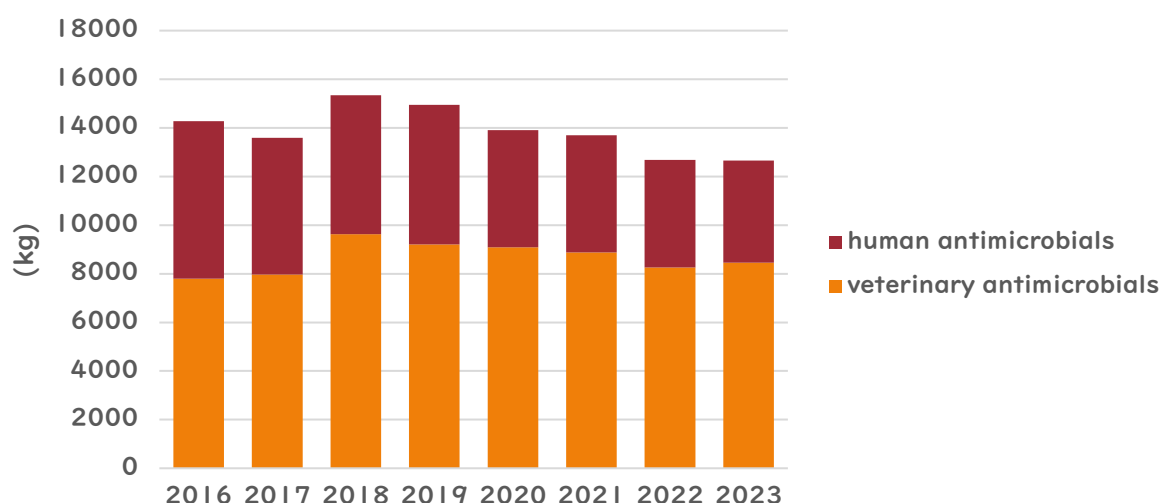
4.3.1. Survey Results

In 2023, the total annual sales volume of antimicrobials for human use sold to veterinary clinics was 4,948.4 kg, calculated as the amount of pure active substance. Of this amount, 84.9% (4,200.9 kg) was sold to companion animal clinics. The remaining 15.1% was sold to farm animal clinics, including equine clinics, and exhibition facilities such as zoos.

Sales volume to companion animal clinics in 2023 was lower than that in 2022, which had been the lowest since the survey began in 2016, and therefore reached a new record low. The combined sales volume of antimicrobials for human use and veterinary antimicrobials was 12,652.3 kg. Antimicrobials for human use accounted for 33.2% of the total sales volume of antimicrobials in the companion animal sector (Figure 4-3-1).

Surveys conducted since 2016 have shown no substantial changes in the proportions of individual antimicrobial classes or products within the total sales volume of antimicrobials for human use sold to companion animal clinics.

Fig. 4-3-1 Trends in sales volume of antimicrobials sold for companion animals

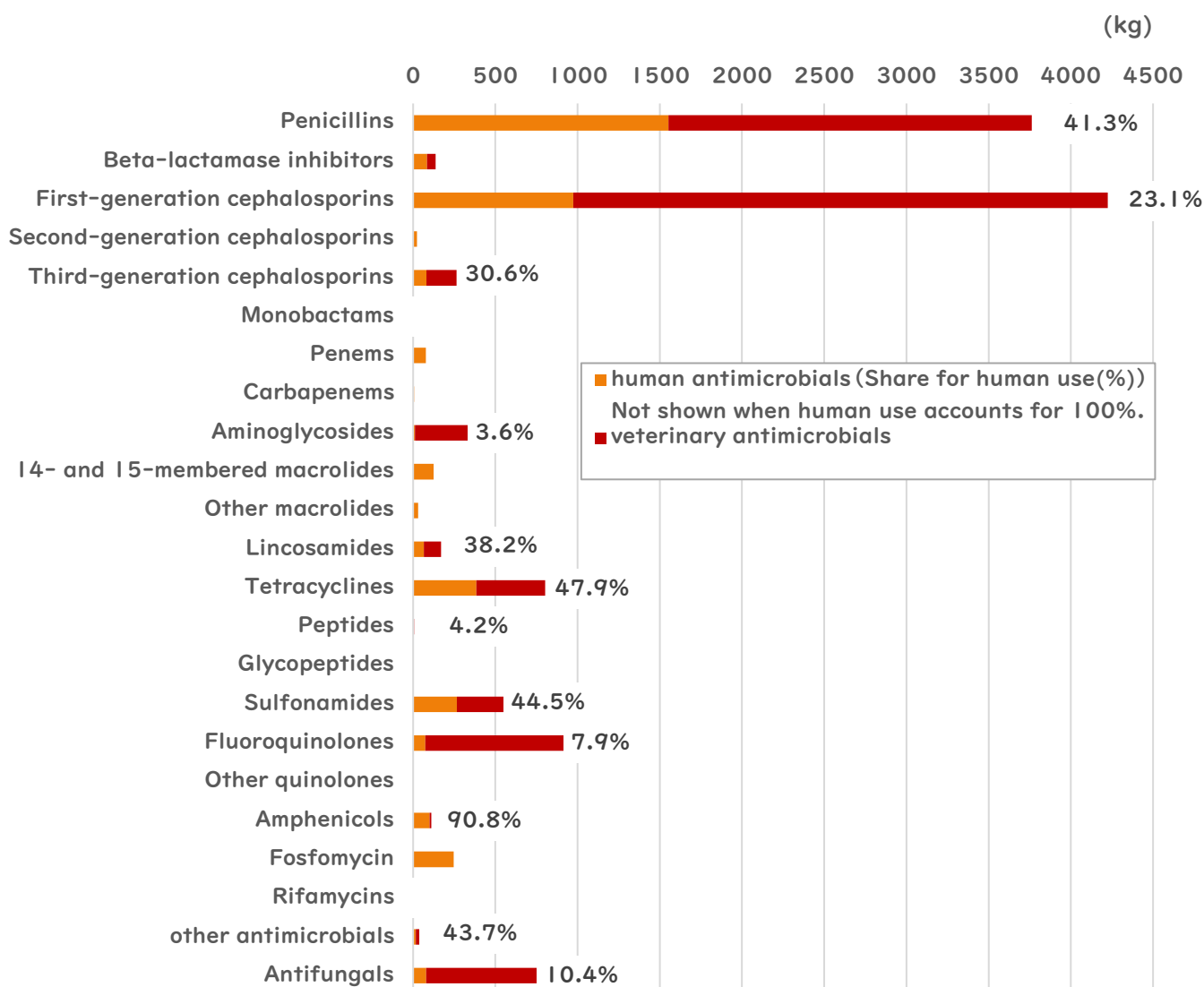


In 2023, penicillins and first-generation cephalosporins accounted for the largest shares of antimicrobials for human use sold to companion animal clinics, together representing 60.2% of the total. These were followed by tetracyclines, sulfonamides, and fosfomycin. The five leading antimicrobial classes accounted for 81.5% of the total. By active ingredients, amoxicillin, a penicillin, and CEX, a first-generation cephalosporin, ranked first and second, respectively. Together, these two antimicrobials accounted for 55.2% of the sales volume of antimicrobials for human use.

In contrast, fluoroquinolones, which are highest priority critically important antimicrobials in human medicine, accounted for 1.8% of the total. Third- and later-generation cephalosporins accounted for 1.9%, penems for 1.8%, carbapenems for 0.2%, and peptides and glycopeptides for 0.01% or less.

Of the combined sales volume of antimicrobials for human use surveyed and veterinary antimicrobials compiled under JVARM in 2023, antimicrobials for human use accounted for 23.1% of first-generation cephalosporins and 41.3% of penicillins. These proportions showed a decreasing trend compared with the 2022 survey results. Among antimicrobials important in human medicine, antimicrobials for human use accounted for 7.9% of fluoroquinolones and 30.6% of third- and later-generation cephalosporins, indicating that veterinary antimicrobials accounted for the larger shares of these classes (Figure 4-3-2).

Fig. 4-3-2 Sales volume of human and veterinary antimicrobials in companion animals by antimicrobial class



WHO has developed the “AWaRe classification”* as one of the tools to promote appropriate use, considering the impact on antimicrobial resistance and clinical importance. In this classification, antimicrobials are categorized into three groups: “Access,” which includes many antimicrobials used as first- or second-choice treatments for common infections and is considered to have fewer disadvantages than the other two groups if resistance develops; “Watch,” which should be used only for limited diseases or indications because treatment options are limited if resistance develops; and “Reserve,” which should be preserved as a last resort because very few options remain if resistance develops. In human medicine, WHO has set a target that at least 60% of antimicrobials used in each country should be classified as Access.

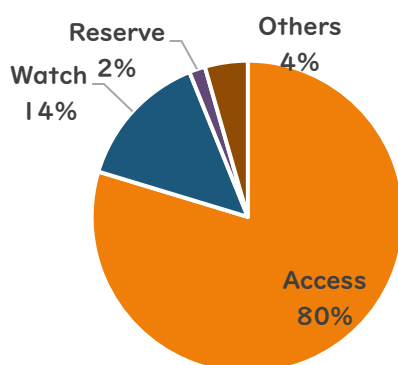
Based on the 2023 AWaRe classification, the proportions of antimicrobials sold to companion animal clinics in 2023 in each AWaRe group were unchanged from 2022. Antimicrobials in the Access group, including first-generation cephalosporins, accounted for the largest share, at 80% (Figure 4-3-3).

Salazosulfapyridine, although structurally classified as sulfonamide, is used as an antirheumatic drug and for conditions such as ulcerative colitis. Because it is not included in the AWaRe list, it was classified as “Others” in this analysis.

Antimicrobials in the Reserve group accounted for 2% of the sales volume in the companion animal sector, with faropenem accounting for 95% of this amount by active ingredient. In principle, the use of these antimicrobials should be avoided. It is essential not only to refrain from using them without careful consideration but also to ensure the prudent use of antimicrobials so that animals do not develop conditions that can only be treated with Reserve antimicrobials.

* <https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.04>

Fig. 4-3-3 Proportions of human antimicrobials sold for companion animals by WHO AWaRe classification



4.3.2. Summary

Since the first survey in 2016, approximately 90% of antimicrobials for human use sold to veterinary clinics have consistently been supplied to companion animal clinics. These antimicrobials accounted for approximately 40% of the combined sales volume of veterinary antimicrobials and antimicrobials for human use in the companion animal sector, although the proportion of antimicrobials for human use has shown a decreasing trend. Because antimicrobials for human use that are also approved for dogs and cats, such as amoxicillin, were widely sold, the lack of approved veterinary drugs was not considered to be the primary reason for the use of antimicrobials for human use.

It was also confirmed that antimicrobials that are neither approved nor marketed for dogs and cats and are classified as Reserve under the WHO AWaRe classification, meaning that they should be preserved as last-resort treatments for infections caused by multidrug-resistant bacteria and similar conditions, accounted for approximately 2% of the antimicrobials for human use sold to companion animal clinics. The use of these antimicrobials requires the utmost caution, and it should be recognized that, in principle, their use should be avoided.

In companion animal clinical practice, a guidebook such as the Guide for the Prudent Use of Antimicrobials in Companion Animals 2020* should be utilized. When drugs for companion animals have been approved and are commercially available as veterinary medicinal products, it is important to use these veterinary antimicrobials appropriately, as their efficacy and safety have been established, rather than using antimicrobials for human use. Further efforts should also be made to ensure the prudent use of antimicrobials.

* https://www.maff.go.jp/j/syouan/tikusui/yakuza/attach/pdf/240328_7-8.pdf (in Japanese)

Acknowledgements

We would like to express our sincere gratitude to the member companies of the Japan Veterinary Products Association and the Federation of Japan Pharmaceutical Wholesalers Associations for their extensive cooperation in conducting this survey.

5. Materials and Methods

5.1. Sampling Specimen and Target Species

5.1.1. Healthy Livestock: Strains from Slaughterhouses and Poultry Slaughterhouses

The animal species monitored as healthy livestock were cattle, pigs, and broilers. Samples were collected at slaughterhouses and poultry processing plants, which represent the stage closest to the final food products, to monitor antimicrobial resistance from a public health perspective.

Typically, rectal stool samples were collected from 1–3 cattle per farm and 4–6 pigs per farm, and cecal samples were collected from 10 broilers per farm at major slaughterhouses throughout the country. The homogenized samples were used to isolate the target bacterial species.

Bacterial species included the indicator bacteria (*E. coli* and *Enterococcus* spp.), which are the commensal bacteria of livestock, and foodborne pathogenic bacteria (*Campylobacter* spp. and *Salmonella* spp.), which are important public health concern. Since there is a bias in the isolation status of foodborne pathogenic bacteria in each animal species, the target species were restricted to each animal species as shown in “the list of bacteria collected in 2023”.

If multiple strains of the same target bacteria were isolated from the same farm, the first strain isolated was designated as “the farm representative strain”.

5.1.2. Diseased Livestock: Clinical Isolates (Farm-derived Strains)

Bacterial strains isolated and identified from samples for pathological appraisal by livestock hygiene service centers across the country were collected.

The organs of origin and disease name are varied among the target bacteria species, and were not restricted. The selection criteria for the number of strains are as follows:

- In principle, when multiple strains of the same species were isolated and identified from the same animal, one strain was selected.
- When multiple strains of the same species were isolated and identified from multiple animals on the same farm, in principle, two strains from different animals were selected (except for cases in which it was judged not to be epidemic due to the same

strain, such as when the sampling times for the two bacteria were significantly apart if the same strains are taken from the same farm).

The target bacterial species in 2023 were as follows:

Bacterial species		Animal	Sampling site
Gram-negative bacteria	<i>Escherichia coli</i>	Cattle, Pigs, Chickens	Various
	<i>Haemophilus (Glaesserella) parasuis</i>	Pigs	
	<i>Salmonella</i> spp.	Cattle, Pigs, Chickens	
Gram-positive bacteria	<i>Streptococcus</i> spp. associated with mastitis	Cattle	
	<i>Staphylococcus aureus</i>	Cattle, Pigs, Chickens	

5.1.3. Healthy Companion Animals

Rectal swab samples were collected from healthy dogs and cats that visited small animal clinics for medical check, vaccination and so on, instead of treatment of the disease, and the indicator bacteria were isolated. Sample numbers were allocated to small animal clinics in each prefecture to reduce the bias of the region. The Japan Veterinary Medical Association provided full cooperation for this survey and coordinated the participation of animal clinics. Before sampling, informed consent was given to the owners, and one sample from each dog and cat was collected per animal clinic. Information regarding species, sex, housing conditions, and so on were also obtained.

Bacterial species		Animal species	Isolation site
Gram-negative bacteria	<i>Escherichia coli</i>	Dogs, Cats	Rectal swab
Gram-positive bacteria	<i>Enterococcus</i> spp.		

5.1.4. Diseased Companion Animals

Strains isolated from diseased dogs and cats submitted to clinical laboratories were collected. Based on the review by the Working Group on Companion Animal Antimicrobial Resistance (AMR) Monitoring*, high-priority species, *Escherichia coli*, *Klebsiella* spp., Coagulase-positive *Staphylococcus* spp. and *Enterococcus* spp. were collected every year,

while other species were to be carried out every few years. In the collection, the number of animal clinics was considered for six blocks (Hokkaido and Tohoku, Kanto, Chubu, Kinki, Chugoku and Shikoku, and Kyushu and Okinawa), to reduce the bias of the area, it was collected by one clinic, one species, and one strain.

Species collected and sample isolation sites in 2023 are as follows:

Bacterial species		Isolation site
Gram-negative bacteria	<i>Escherichia coli</i>	Urine, Genital Tract
	<i>Klebsiella</i> spp.	
	<i>Enterobacter</i> spp.	Urine
	<i>Acinetobacter</i> spp.	Urine, Skin
Gram-positive bacteria	Coagulase-positive <i>Staphylococcus</i> spp.	Urine, Skin
	<i>Enterococcus</i> spp.	Urine, Ear

※https://www.maff.go.jp/nval/yakuzai/yakuzai_p3-4.html

5.2. Isolation and Identification of Bacteria

In each sample, isolation was performed by the following methods: For diseased livestock, each prefecture carried out the test based on the Disease Diagnosis Manual (*). For diseased companion animals, the strains isolated and identified by each laboratory's method were re-identified by the following methods:

※ https://www.naro.affrc.go.jp/org/niah/disease_byosei-kantei2016/index.html

5.2.1. *Escherichia coli*

Samples were inoculated directly onto deoxycholate-hydrogen sulfide lactose (DHL) agar or CHROMagar ECC medium, and suspect colonies were isolated and identified by morphological and biochemical characterization.

5.2.2. *Enterococcus* spp.

Samples were cultured using a direct method and with Azide Citrate (AC) medium, and suspect colonies were isolated using Enterococcosel Agar (ECS medium) and identified by morphological and biochemical characterization.

5.2.3. *Campylobacter* spp.

Samples were cultured using a direct method and Preston enrichment broth followed by Modified Charcoal Cefoperazone Deoxycholate Agar (mCCDA). Then identification was carried out by morphological and biochemical characteristic inspection as well as PCR methodology.

5.2.4. *Salmonella* spp.

Samples were cultured using direct and peptone-water followed by secondary enrichment with Rappaport-Vassiliadis medium and, then were inoculated onto novobiocin-containing DHL agar and CHROMagar *Salmonella* medium, respectively, for isolation and culture. Identification was carried out by morphological, biochemical properties inspection, and specific antiserum testing.

5.2.5. *Haemophilus (Glaesserella) parasuis*

Conducted following the Pathogenicity Diagnostic Manual (cited *).

5.2.6. *Streptococcus* spp. associated with mastitis (Cattle)

The *Streptococcus* spp. isolates associated with mastitis submitted by the prefectures were identified using MALDI-TOF MS (Bruker Daltonics).

5.2.7. *Klebsiella* spp.

Klebsiella spp. strains sent by clinical laboratories were re-identified by API20E (Biomérieux Japan). When it could not be identified by API20E, identification by MALDI-TOF-MS (Bruker Daltonics) was performed.

5.2.8. *Enterobacter* spp.

Enterobacter spp. isolates submitted by clinical laboratories were reidentified using API 20E (bioMérieux Japan). Isolates that could not be identified using API 20E were identified using MALDI-TOF MS (Bruker Daltonics).

5.2.9. *Acinetobacter* spp.

Acinetobacter spp. isolates submitted by clinical laboratories were reidentified using API 20NE (bioMérieux Japan). Isolates that could not be identified using API 20NE were identified using MALDI-TOF MS (Bruker Daltonics).

5.2.10. Coagulase-positive *Staphylococcus* spp.

Coagulase-positive staphylococcal strains sent by the clinical laboratory were re-identified by PCR (Sasaki et al., JCM, 2010 48 765-769). Isolates for which no PCR bands were detected were subjected to a coagulase test, and isolates confirmed to be coagulase positive were identified using MALDI-TOF-MS (Bruker Daltonics)

5.3. Antimicrobial Susceptibility Test

5.3.1. Tested Antimicrobials

In order to understand the trend of antimicrobial resistance of the approved veterinary medicinal products and medically important products (other than diseased food-producing animals), representative drugs were selected for each class and used for the test (see list of target bacteria and tested antimicrobials below)

5.3.2. Antimicrobial Susceptibility Test

The broth microdilution method*¹ proposed by the Clinical and Laboratory Standards Institute (CLSI) to determine the minimum inhibitory concentration (MIC) was performed. Breakpoints (BP)*²: the value provided by CLSI was adopted. If no BP was defined by CLSI, the epidemiological cut-off value (Epidemiological cut-off values, ECOFF) of the European Committee on the Study of Antimicrobial Susceptibility Testing (EUCAST) was used. When neither a breakpoint (BP) nor an epidemiological cut-off value (ECOFF) has been established, an epidemiological cut-off value (Epidemiological Cut-off Value, ECV) calculated from the JVARM MIC distribution was adopted*³. Strains with MIC equal to BP or higher were defined as resistant strains, and the percentage of resistant strains in the total number of strains (number of resistant strains/number of strains × 100) was used as the resistance rate.

*1 CLSI. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard M07, 12th ed. CLSI, Wayne, PA, USA. 2024.

*2 CLSI. Performance Standards for Antimicrobial Susceptibility Testing M100, 34th ed. CLSI, Wayne, PA, USA. 2024.

*3 Kumakawa, M., et al. (2025). “Establishing tentative cut-off values for disk diffusion method for *Pasteurella multocida* and *Mannheimia haemolytica* from livestock animals in Japan” Journal of Veterinary Medical Science, 87(4), 349–355.

<https://doi.org/10.1292/jvms.24-0474>

5.4. Sales Volume of Antimicrobials

5.4.1. Veterinary Antimicrobial Sales

The data for veterinary antimicrobial sales volume are collected annually from the marketing authorization holders in accordance with the Pharmaceutical and Medical Device Act 71-2 (Ministry of Agriculture, Forestry and Fisheries ordinance No. 107, 2004). The results show the amount of each active ingredient by administration route, as well as the estimated percentage of the antimicrobials for each animal species. The results have been published on the websites of the National Veterinary Assay Laboratory as "Annual Report of Sales Amount and Sales Volume of Antibiotics, Synthetic Antibacterials, Anthelmintics and Antiprotozoals". It has also been published in the One Health Report and the Antimicrobial Resistance (AMR) Platform.

5.4.2. Biomass

The biomass was estimated using the statistical data and calculation methods shown in the table below.

Animal species	Statistical data used	Biomass estimation method
Beef cattle	Farm Products Distribution Statistics (Ministry of Agriculture, Forestry and Fisheries) > Slaughterhouse Statistics Survey > Carcass production by prefecture > Total cattle	Carcass weight
Dairy cattle	① Livestock Statistics (Ministry of Agriculture, Forestry and Fisheries) > Dairy cattle > Number of farms and animals > Total number of female dairy cattle ② Summary of Dairy Herd Performance Test Results (Livestock Improvement Association of Japan, Inc) > Table 8: Number of animals by body-weight class and body-weight efficiency index > Overall mean body weight	① Number of dairy cattle × ② Mean body weight of dairy cattle
Pigs	Farm Products Distribution Statistics (Ministry of Agriculture, Forestry and Fisheries) > Slaughterhouse Statistics Survey > Carcass production by prefecture > Pigs	Carcass weight
Broilers	Farm Products Distribution Statistics (Ministry of Agriculture, Forestry and Fisheries) > Poultry Distribution Statistics > Number and weight of poultry processed > Young broilers > Weight	Live weights at time of slaughter
Layers	① Livestock Statistics (Ministry of Agriculture, Forestry and Fisheries) > Layers > Number of farms and birds by agricultural region and prefecture > Number of birds raised (layers + breeding chickens) ② Farm Products Distribution Statistics (Ministry of Agriculture, Forestry and Fisheries) > Poultry Distribution Statistics > Number and weight of	① Number of layers raised × ② Mean body weight of bird (weight/number of birds) ① Missing data for the World Census of Agriculture and Forestry

	poultry processed > Culled chickens > Number and weight	survey years were imputed using data from the preceding year.
Seawater fish	Survey on Marine Fishery Production (Ministry of Agriculture, Forestry and Fisheries) > Marine Aquaculture > Statistics by prefecture > Production weight by cultured fish species (excluding seed production) > Fish subtotal	Production volume
Freshwater fish	Survey on Marine Fishery Production (Ministry of Agriculture, Forestry and Fisheries) > Inland Water Fisheries and Aquaculture > Production weight from inland aquaculture by prefecture > Production weight by prefecture and fish species > Fish (trout, ayu sweetfish, carp, eel, and others)	Production volume

An analysis of antimicrobial sales volume and animal biomass in Japan has also been reported in the following article.

Hosoi, Y.; Matsuda, M.; Kawanishi, M.; Harada, S.; Kumakawa, M.; Sekiguchi, H.; Asai, T.; Sekiya, T. Antimicrobial Use in the Animal Sector in Japan from 2011 to 2022. *Antibiotics* 2024, 13, 1204. <https://doi.org/10.3390/antibiotics13121204>

5.4.3. Antimicrobials for Human Use Sold to Animal Clinics

In many countries, veterinarians are allowed to prescribe human medicines, including antimicrobials, for treatment of animals under their responsibility. Human medicines are considered for use mainly by veterinarians in companion animal clinics. The sales data of antimicrobials for human were provided by members of the Japan Animal Drug and Instrument Dealers Association and the Federation of Japan Pharmaceutical Wholesalers Association.

Table: List of target bacteria and tested antimicrobials

Animal species	Healthy/ Diseased	Species	ABPC	PCg	CEZ	CTX	CTF	CFX	CEX	CXM	GM	KM	SM	DSM	AZM	EM	CLDM	TC	OTC	NA	CPFX	ERFX	CL	BC	CP	TMP	ST	MEPM	MP1PC	FFC	TP	TMS	TS	LCM	VCM	SNM		
Livestock	Healthy	<i>Escherichia coli</i>	○		○	○					○	○	○					○		○	○		○		○		○	○										
		<i>Enterococcus</i> spp.	○									○	○	○		○	○		○		○	○			○	○							○	○	○	○		
		<i>Campylobacter</i> spp.	○									○		○		○	○		○		○	○			○													
		<i>Salmonella</i> spp.	○		○	○						○	○	○					○		○	○		○		○		○	○									
	Diseased	<i>Salmonella</i> spp.	○		○	○						○	○	○					○		○	○		○		○		○	○									
		<i>Escherichia coli</i>	○		○	○						○	○	○					○		○	○		○		○		○	○									
		<i>Staphylococcus aureus</i>		○	○							○		○		○	○	○	○			○				○					○							
		<i>Streptococcus</i> spp. associated with mastitis	○	○	○													○		○				○				○							○			
Companion animals	Haelthy	<i>Escherichia coli</i>	○		○	○			○		○	○	○					○		○	○		○		○		○	○										
		<i>Enterococcus</i> spp.	○									○					○		○			○				○										○		
	Diseased	<i>Escherichia coli</i>	○		○	○				○		○	○	○					○		○	○		○		○		○	○									
		<i>Klebsiella</i> spp.			○	○				○		○	○	○					○		○	○		○		○		○	○									
		<i>Enterobacter</i> spp.				○						○	○						○		○	○		○		○		○	○									
		<i>Acinetobacter</i> spp.				○						○							○			○		○				○	○									
		<i>Enterococcus</i> spp.	○									○					○		○			○				○										○		
		Coagulase-positive <i>Staphylococcus</i> spp.		○								○					○	○		○			○			○					○							

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