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Monitoring of antimicrobial resistance in animal health and the sale of antibiotics for veterinary use: 2023 review

Antimicrobial resistance concerns us all

Antibiotics – and antimicrobials more broadly – are essential for safeguarding human health, animal health and food safety. However, their use encourages the spread of micro-organisms capable of resisting them. To preserve the effectiveness of antimicrobials, the first strategy is to reduce their use. This is what has been done with antibiotics in animals for over a decade now. The drastic fall in their use does not seem to have been associated with any increase in livestock mortality, showing that some of these uses were potentially superfluous.

Instead, it has led to a reduction in the resistance of bacteria carried by animals. Similar work is now under way for other antimicrobials: antivirals, antiparasitics and antifungals. Resistance to antimicrobials has long been dominated by bacterial resistance, but scientific studies are increasingly revealing the magnitude of the challenge it represents.

The second strategy is to work on non-drug alternatives. A great deal of progress has been made in preventing microbes from entering farms and in building clean, healthy farming environments. However, the problem of antimicrobial resistance is not just a matter for specialists in animal or human health: it affects society as a whole. It requires a rethink of our practices and our relationship with medicines, animals, farming systems and the environment. Because bacteria and their resistance genes know no borders, antimicrobial resistance needs a real One Health dimension.

It is essential to consider antibiotics as a common good, where human health and animal health are no longer set against each other.

Jean-Yves Madec, Scientific Director of the "Antimicrobial resistance" cross-functional theme at ANSES
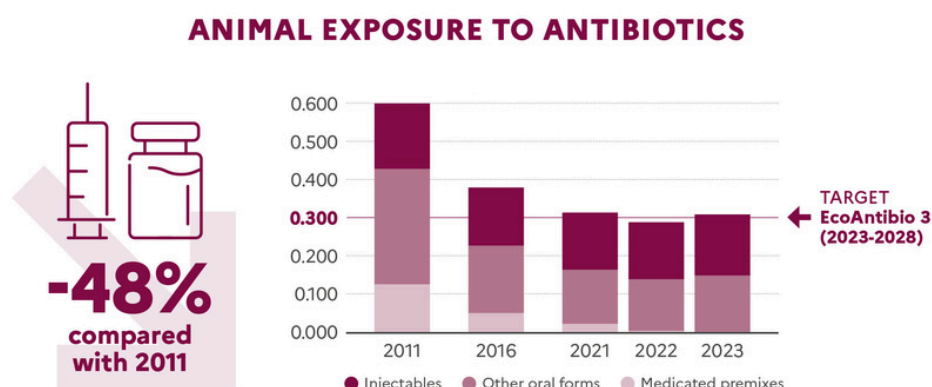
Find out the main results from the 2023 monitoring of the sale and use of antimicrobial medicines and resistant bacteria in animals.

A pivotal year in the monitoring of animal exposure to antimicrobials

Concerning the monitoring of exposure of livestock animals and pets to antimicrobials, 2023 seems to have been a pivotal year. Firstly, the new system for monitoring antibiotic uses (introduced in April 2023) now supplements the monitoring of sales, which has been in place since 1999. Secondly, 2023 marked a new step in the exposure trend: after a 48% fall in animal exposure to antibiotics between 2011 and 2022, the uptick observed in 2023 could indicate a levelling-off.

Moderate increase in animal exposure to non-critical antibiotics in 2023

ANIMAL EXPOSURE TO ANTIBIOTICS

-48% compared with 2011

TARGET EcoAntibio 3 (2023-2028)

● Injectables ● Other oral forms ● Medicated premixes

Animal exposure to antibiotics is calculated as the ratio between the body weight treated, estimated on the basis of the quantity of medicines sold and the recommended dosage for each one, and the total body weight, estimated from the animal population census.

The animal level of exposure to antibiotics (ALEA) in 2023, all animal species combined, **increased by 6.5% compared with 2022**. This moderate increase followed a 9% fall between 2021 and 2022

Exposure in 2023 was therefore still below the level observed in 2021. This ALEA value of 0.309 remains **close to the 0.3 set by the EcoAntibio 3** plan for the period 2023-2028.

Several assumptions may explain the rise observed in 2023, including possible health phenomena requiring the use of more antibiotics, or a slight underestimation of exposure in 2022 due to stocks of medicines purchased in previous years being reduced.

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This destocking in 2022 is thought to be due to the entry into force at the beginning of the year of new regulations on veterinary medicinal products and medicated feedingstuffs, which have brought tight restrictions on the use of antimicrobials for preventive purposes.

It is possible that the level of exposure **has reached a plateau** and that fluctuations around the 0.3 threshold will now be observed. This assumption will need to be confirmed in 2024. However, continued vigilance is needed to avoid a general upward trend in certain sectors.

Stable, limited animal exposure to critical antibiotics

For so-called critical antibiotics (fluoroquinolones and third- and fourth-generation cephalosporins), whose continued efficacy is crucial for human medicine, exposure levels remain very low. Exposure to colistin, across all species, appears to be levelling off after years of decline.

Increase in sales of antibiotics for cats and dogs

The method used to count cat and dog populations in France has changed, leading to a large increase in the estimated animal population in 2023. The change in the ALEA exposure indicator, which shows **a 5.0% decrease over the last year**, should therefore be **interpreted with caution** for these animals.

In 2023, **the body weight treated for these pets increased by 6%** compared with 2022. The quantity of antibiotics sold for cats and dogs has also increased in recent years. Vigilance is therefore needed to achieve the objective of the EcoAntibio 3 plan, which aims to reduce antibiotic exposure in these species by 15% over five years.

EXPOSURE OF CATS AND DOGS TO ANTIBIOTICS

In 2023

ECOANTIBIO 3 OBJECTIVE
-15%
in 5 years

More animals treated
↗ 6% increase in animal biomass treated in 1 year

47%
of exposure comes from tablets of **amoxicillin combined with clavulanic acid**

Reporting of data on the use of antimicrobials by veterinary care facilities should be stepped up

The European regulations on veterinary medicinal products, which came into force in 2022, provide for the gradual introduction of the collection of data on antimicrobial **use by animal species and category** by 2029. This concerns not only antibiotics, but also antivirals, antifungals and antiprotozoals. In France, these usage data are reported by veterinarians, pharmacists and manufacturers and distributors of medicated feedingstuffs via the CalypsoVet platform.

Declarations on this platform of the quantity of antibiotics used in 2023 accounted for just **17% of the tonnage sold** as reported by marketing authorisation holders. This low level of data reporting was due to the gradual roll-out of the system over the year.

A new feature enabling antimicrobial use data to be transmitted automatically has gradually been **incorporated into the prescribing and management software** used by veterinary practices. By the end of 2024, the vast majority of software packages will offer this feature. Increased reporting on uses has been noted in recent months, with more than 100,000 reports per month. Veterinary care facilities that have not yet done so are invited to update their software and start transmitting their data. The first data on sales of antimicrobials by pharmacists were collected in the summer of 2024.

More accurate data on the use of antimicrobials could help more effectively target which actions to take to combat antimicrobial resistance, in particular with the use of temporal analyses by animal species or category.

Read the report entitled "Monitoring sales and use of antimicrobial drugs in animals for 2023" (in French)

Resistant bacteria: differences persist according to the antibiotics and animal species

ANSES monitors antibiotic resistance in animals through two schemes. Firstly, the French surveillance network for antimicrobial resistance in pathogenic bacteria of animal origin (Resapath) monitors changes in resistance to antibiotics in bacteria responsible for infections in animals. Secondly, the National Reference Laboratory for antimicrobial resistance, run by ANSES, implements annual monitoring plans as part of the European surveillance scheme for antimicrobial resistance. This scheme, led by the Directorate General for Food (DGAL) in France, measures antibiotic resistance of bacteria collected from healthy food-producing animals and their products.
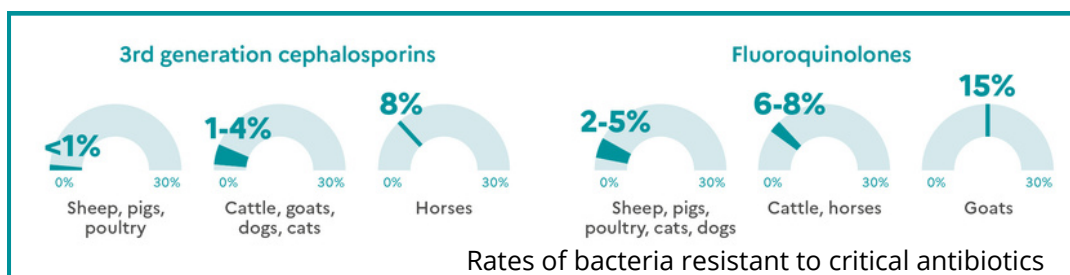
Resapath's review of 2023

More and more antibiograms provided

Veterinary testing laboratories send Resapath the results of the antibiotic resistance tests (antibiograms) they carry out at the request of veterinarians, on bacteria isolated from sick animals. In 2023, **93,285 antibiograms** were collected, a 32% increase over the previous year. This increase, due to laboratories carrying out a large number of antibiograms joining the network, gives a more comprehensive picture of antimicrobial resistance in pathogenic bacteria of animal origin in France.

Resistance to critical antibiotics remains low

Certain antibiotics are considered critically important because their efficacy is crucial in treating serious infections in humans. Their use in veterinary medicine is therefore regulated. Resistance of Escherichia coli to these antibiotics has reached a low point in most animal species, but remains higher in horses and goats.

3rd generation cephalosporins

<1% — Sheep, pigs, poultry (0% – 30%)
1-4% — Cattle, goats, dogs, cats (0% – 30%)
8% — Horses (0% – 30%)

Fluoroquinolones

2-5% — Sheep, pigs, poultry, cats, dogs (0% – 30%)
6-8% — Cattle, horses (0% – 30%)
15% — Goats (0% – 30%)

Rates of bacteria resistant to critical antibiotics

Multi-drug resistant *E. coli:* trends in line with previous years

The level of multi-drug resistant *Escherichia coli*, i.e. resistant to at least three of the five classes of antibiotics tested, continues the trend seen in previous years. The frequency of multi-drug resistant *E. coli* in cats and dogs is fairly low. It continues to fall in pigs and turkeys, while it has stagnated at a high level in cattle and is increasing in hens and chickens, as well as in horses.

Multidrug resistance: resistance to at least 3 antibiotics out of 5 tested

Panel: amoxicillin, gentamicin, tetracycline, trimethoprim-sulfonamides, nalidixic acid.

Cattle	39%
Pigs	27%
Horses	23%
Poultry	16%
Dogs	12%
Cats	7%
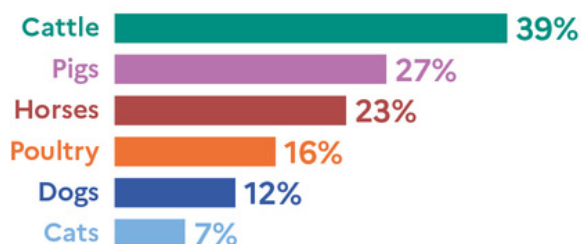
Enterobacterales resistant to an antibiotic prohibited in veterinary medicine

Enterobacterales is an order of bacteria that includes *Escherichia coli*, *Klebsiella pneumoniae* and *Enterobacter hormaechei.* For the past five years, Enterobacterales resistant to carbapenem antibiotics have been regularly detected in dogs and cats. Most of them belong to the species *K. pneumoniae*. Because the use of carbapenems in animals is banned, it is likely that this resistance developed in humans before being passed on to pets.

Enterobacter hormaechei resistant to critically important antibiotics: different resistance genes in horses and in dogs and cats

Enterobacter hormaechei is an important pathogen for humans and animals, and can be resistant to newer-generation cephalosporins and carbapenems, antibiotics of critical importance to humans. Resapath data show that this resistance is also circulating in dogs, cats and horses. The ANSES scientists responsible for coordinating Resapath genetically characterised the *E. hormaechei* strains resistant to newer-generation cephalosporins that had been isolated from these animals. This analysis showed that **the genes responsible for this resistance differed between dogs and cats on the one hand, and horses on the other.** These genes were mainly located on the chromosomal DNA of bacteria sampled from domestic carnivores, whereas they were mainly carried by plasmid DNA in bacteria sampled from horses. In addition, carbapenem resistance has only been observed in strains from dogs and cats. These divergences could be related to differences in antibiotic use.

Increase in methicillin-resistant *Staphylococcus aureus* in horses

Staphylococcus aureus is a bacterium that mainly affects humans, but animals can also be carriers. In particular, it can be resistant to methicillin (MRSA), making it resistant to all antibiotics of the beta-lactam class. Resapath data on resistance to methicillin in *Staphylococcus aureus* contain a degree of uncertainty, because the resistance test is based on a marker (cefoxitin) that tends to overestimate resistance.

To determine precisely the proportion of MRSA circulating in dogs, cats and horses, almost 500 strains were analysed. In dogs and cats, the proportion of MRSA has remained stable at around 7%. On the other hand, **it has increased in horses: 10% of staphylococci were resistant to methicillin in 2015, and this had risen to 29% by 2023.** This increase in MRSA could be linked to the emergence of a new clone, called ST612. In addition, another clone, usually considered to be typically human, was detected in 24.2% of samples taken from cats. The transmission of these two clones between humans and animals therefore needs to be monitored.

Read the Resapath 2023 report (in French)

Review of the scheme for monitoring antimicrobial resistance in France

The animal species monitored by the European surveillance scheme for antimicrobial resistance alternate every other year. In 2023, this monitoring concerned pigs and calves (cattle under one year of age). Samples were taken from caecal contents, i.e. the intestines of animals at the slaughterhouse, and from meat at distribution. All the monitoring results will be published in France in the DGAL's report on its monitoring and control plans. At European level, they will be covered in a report by the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC).

Salmonella: situation differs according to the sub-group

The level of resistance in *Salmonella* collected from pigs at the slaughterhouse **varied according to the serovar**, which defines sub-groups of strains. In 2023, 85 strains of Salmonella were collected from pigs at the slaughterhouse.

The most common serovar was Salmonella Derby: 59.4% of these were susceptible (i.e. not resistant) to all the antibiotics tested. Only 12 strains were resistant to one or two classes of antibiotics, and only one strain was multi-resistant to three classes of antibiotics.

In contrast, 71% of *Salmonella* strains belonging to the other two most common serovars (monophasic variant of Typhimurium and Typhimurium) were resistant to at least three classes of antibiotics. Salmonella were rare in calves: only three strains were isolated.

All sectors combined, **none of the *Salmonella* strains collected were resistant to antibiotics of critical importance** to human health, whether quinolones, cephalosporins or colistin.

Campylobacter: differences between strains taken from pigs and calves

Since 2005, bacteria of the genus *Campylobacter* have been the leading reported cause of human gastrointestinal infections of bacterial origin in Europe. The two species of bacteria most regularly implicated are, in order, *Campylobacter jejuni* and *Campylobacter coli.*

Nearly **90% of *Campylobacter* strains collected from calves and pigs were resistant** to at least one antibiotic, most often from the tetracycline class. The most frequent co-resistance was with tetracyclines and fluoroquinolones, even though the use of these antibiotic classes in animals has decreased.

In general, antibiotic resistance was greater in *C. coli* than in *C. jejuni*. Within *C. coli*, bacteria taken from calves were more resistant than those sampled from pigs.

Campylobacter resistance to two critically important antibiotics, erythromycin and ciprofloxacin, was also tested. No strain of *C. jejuni* was resistant to both antibiotics at the same time. *Campylobacter coli* simultaneously resistant to these antibiotics accounted for 7% of the strains in pigs and 27% in calves.

The level of erythromycin resistance of C. coli bacteria collected from pigs has been falling steadily since 2011: it was 45% in 2011 compared with 11% in 2023.

E. coli: declining resistance

Between 2021 and 2023, the susceptibility of *Escherichia coli* to all the antibiotics tested increased:

- **Pigs**: 44% of E. coli susceptible in 2021, 47.4% in 2023
- **Calves**: 35.7% of E. coli susceptible in 2021, 37.0% in 2023

No carbapenem-resistant strains of *E. coli* were detected among the strains taken from animals or their meat. This was also the case for *Salmonella*. Lastly, the number of *E. coli* producing enzymes responsible for cephalosporin resistance was the same for calves (5.5%) and had declined for pigs (2.1%), compared with 2021.

Research to improve knowledge of changes in resistance

A project to break down barriers to the monitoring of antimicrobial resistance

Together with Santé Publique France and the French Ministry of Agriculture, ANSES carried out the **Surv1Health project**, which aimed to improve cross-disciplinary surveillance of antimicrobial resistance in France, encompassing animals, humans, food and the environment. This project, funded by the EcoAntibio 2 plan, ran from 2020 to 2023. It highlighted the **broad range of existing schemes and the lack of coordination between them.** Moreover, certain aspects, such as the presence and spread of resistant bacteria in the environment, are monitored very little compared with antimicrobial resistance in human or animal health.

Organising networks of professionals working on antimicrobial resistance is one of the objectives of the **PROMISE network**, which was set up in 2021. ANSES is an active participant in this network, coordinated by Inserm, which is also aiming to set up a national scheme for monitoring resistant bacteria in the environment, particularly surface water, and to ensure its links with other antimicrobial resistance surveillance schemes. **Read the news update**

Klebsiella pneumoniae: increase in multi-drug resistance in horses

The *Klebsiella pneumoniae* bacterium is a major concern for both human and equine health. Scientists from ANSES, the Dynamicure joint research unit (Inserm/Universities of Caen and Rouen) and Caen University Hospital have joined forces to study this bacterium, and in particular the risk of transmission between humans and horses. They showed that the strains in the study taken from horses were specific to this species and showed great diversity.

Scientists tested strains of *Klebsiella pneumoniae* taken from horses over a period of almost 30 years for resistance to antibiotics used in human and veterinary medicine: **39% of these strains were multi-drug resistant**. This proportion has increased over time: 18.8% of strains taken from necropsies carried out between 1996 and 2007 were resistant, compared with 39.1% between 2008 and 2020. This increase is probably due to the growth in the use of antibiotics in the horse-breeding sector over the same period.
Read the news update

ANSES, French Agency for Food, Environmental and Occupational Health & Safety

The French Agency for Food, Environmental and Occupational Health & Safety (ANSES) provides public decision-makers with the scientific benchmarks needed to protect humans and the environment from health risks. It studies, assesses and monitors all the chemical, microbiological and physical risks to which humans, animals and plants are exposed, thereby helping the public authorities take the necessary measures, including in the event of a health crisis.

A national agency working in the public interest, ANSES comes under the responsibility of the French Ministries of Health, the Environment, Agriculture, Labour and Consumer Affairs.