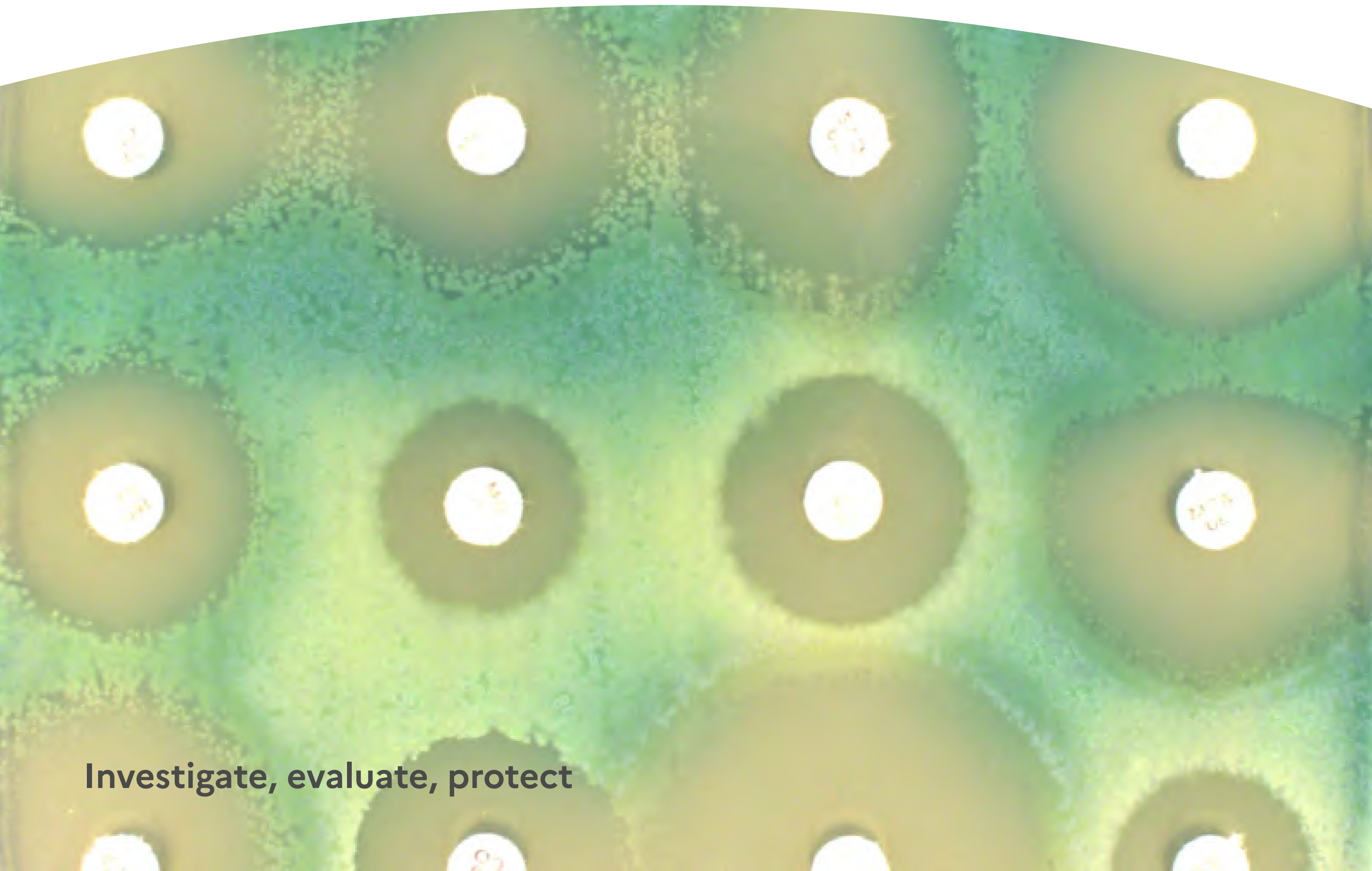
Resapath

French surveillance network for antimicrobial resistance in bacteria from diseased animals

2023 Annual report

November 2024



Investigate, evaluate, protect

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https://shiny-public.anses.fr/ENresapath2/ (English version)

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Key words

Antimicrobial resistance, antibiotics, bacteria, network, surveillance, animal

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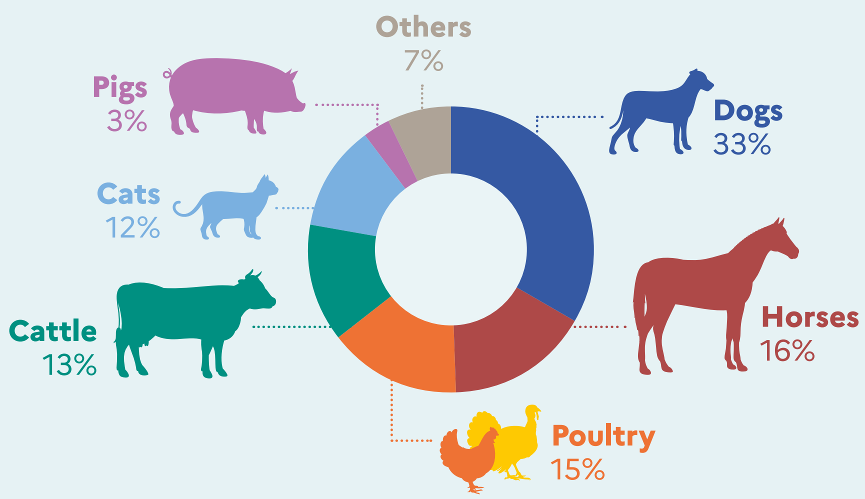
RESAPATH – HIGHLIGHTS 2023

105
contributing laboratories

93,285
antibiograms collected
↗ +32% compared to 2022

ORIGIN OF ANTIBIOGRAMS COLLECTED

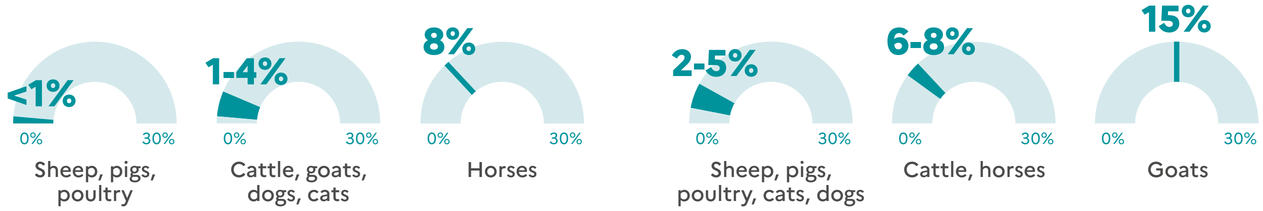


ANTIBIOTIC RESISTANCE, STILL ROOM FOR IMPROVEMENT!

PROPORTIONS OF *ESCHERICHIA COLI* RESISTANT STRAINS PER ANTIBIOTIC AND PER ANIMAL SPECIES IN 2023

Critically important antibiotics

For most animal species, resistance has stabilized at a low level, but it remains at a higher level for horses and goats.



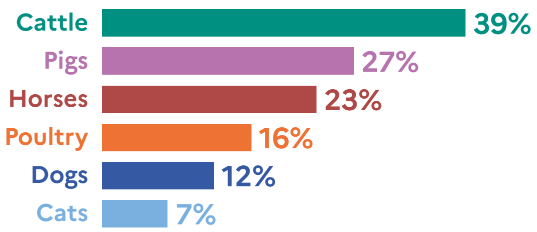
Other antibiotics

The results are variable depending on the animal species and the antibiotics.

DATA AVAILABLE ON **RESAPATH ONLINE**

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

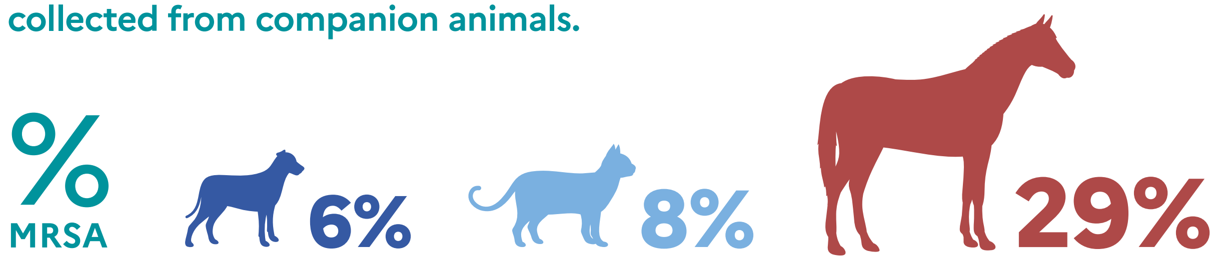
Panel: amoxicillin, gentamicin, tetracycline, trimethoprim-sulfonamides, nalidixic acid.



TWO RESAPATH-BASED STUDIES CONTRIBUTE TO THE CHARACTERIZATION OF EMERGING RESISTANCES

1 Methicillin-resistant *Staphylococcus aureus* (MRSA)

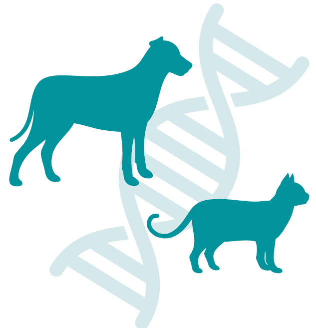
A genomic study conducted in 2023 on 500 isolates corroborates the phenotypic resistance data (antibiograms) collected from companion animals.



The emergence of a new clone (ST612) could explain the high proportion of MRSA in horses.

2 Carbapenem-resistant Enterobacterales

Carbapenem-resistant Enterobacterales have been emerging over the past 5 years in RESAPATH data (>20 isolates collected each year), despite the fact that the use of carbapenems is prohibited in animals.



- **Bacterial species:** mainly *Klebsiella pneumoniae*
- **Source of isolates:** always from dogs or cats
- **Gene responsible for resistance:** $bla_{\text{OXA-48}}$

According to an ANSES scientific opinion published in 2023, carbapenem-resistant Enterobacterales represent the top 1 priority among 11 bacteria/antibiotic combinations to be monitored in livestock and companion animals due to their major risk to human health. The emergence of carbapenem-resistant *K. pneumoniae* in RESAPATH data confirms the relevance of the network to characterize and monitor these strains.

TO LEARN MORE ABOUT THE **11 BACTERIA/ANTIBIOTIC COMBINATIONS TO BE MONITORED IN PRIORITY**

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Abbreviations

Abbreviation	Definition
3GC/4GC	Third- and fourth-generation cephalosporins
AFNOR	French organisation for standardisation
AMR	Antimicrobial resistance
ANSES	French Agency for Food, Environmental and Occupational Health & Safety
AST	Antimicrobial susceptibility testing
CA-SFM	Committee of the French Society of Microbiology – Antibiogram Committee
CIA	critically-important antibiotics
CoNS	Coagulase negative staphylococci
CoPS	Coagulase positive staphylococci
EARS-Vet	European Antimicrobial Resistance Surveillance network in Veterinary medicine
EFSA	European Food Safety Authority
EQA	External quality assessment
ESBL	Extended-spectrum beta-lactamase
EUCAST	European Committee on Antimicrobial Susceptibility Testing
EU-JAMRAI	European Joint Action on Antimicrobial Resistance and healthcare Associated Infections
FAO	Food and Agriculture Organization of the United Nations
FQ	Fluoroquinolones
IT	Information technology
JPI-AMR	Joint Programming Initiative on Antimicrobial Resistance
MDR	Multidrug resistance
MLS_B	Macrolides-Lincosamides-Streptogramins B
MRSA	Methicillin-resistant *Staphylococcus aureus*
MRSP	Methicillin-resistant *Staphylococcus pseudintermedius*
ONERBA	French National Observatory for Epidemiology of Bacterial Resistance to Antimicrobials
PRR	National Priority Research Programme on AMR
S-I-R	Susceptible - intermediate - resistant
SSTI	Skin and soft tissue infections
EU	European Union
UTI	Urinary tract infections

Editorial

Created in 1982, the **Resapath network** has been contributing to the monitoring of antimicrobial resistance (AMR) in animal pathogenic bacteria in France for more than 40 years.

Set up first for the bovine sector (Resabo), then progressively extended to all other animal species, Resapath collects antibiograms data produced annually by the member laboratories in France and analyses AMR trends, thereby contributing to assess the efficiency of the National Action Plan Ecoantibio.

Resapath interfaces animal data with those available in other sectors in a **One Health approach**, in particular within the frame of the Interministerial Roadmap. Also, beyond resistance phenotypes, genomic analyses conducted by Resapath contribute to a better understanding of crossed issues in the three sectors: human, animal and the environment.

Additionally, Resapath promotes AMR monitoring in diseased animals **beyond national borders**, with ANSES co- coordinating the European network EARS-Vet set up during the EU-JAMRAI 1 joint action (2017-2021), and currently being expanded in the EU-JAMRAI 2 joint action (2024-2027).

The Resapath report presents useful raw data (available online at https://shiny-public.anses.fr/ENresapath2/) but also several in-depth analyses on AMR in diseased animals in France.

Thanks to all contributors and enjoy reading!

The Resapath Team

Part 1

About the Resapath

Context

Resapath objectives

The Resapath is the French network for surveillance of antimicrobial resistance (AMR) in bacteria from diseased animals. Launched in 1982 for the study of AMR in cattle, it has over time extended its range and consolidated its legitimacy for surveillance of AMR in pigs and poultry (2001), as well as dogs, cats and horses (2007).

More specifically, the main objectives of Resapath are as follows:

- To monitor AMR in bacteria isolated from diseased animals in France,
- To provide member laboratories with scientific and technical support on antimicrobial susceptibility testing methods and results interpretation,
- To detect the emergence of new resistances and their dissemination within bacteria of animal origin,
- To contribute to the characterization of the molecular mechanisms responsible for resistance.

French and European context

The Resapath complements the data collected by other surveillance programmes including the European regulatory plans for monitoring antimicrobial resistance in zoonotic and commensal bacteria at abattoirs, retail outlets and border inspection points[1], the monitoring of sales of antimicrobials for veterinary use[2], and the monitoring of antimicrobial use by veterinarians and others entitled professionals– so called Calypso[3] (Figure 1). All these data contribute to the development, the implementation and the evaluation of intervention measures for the control of AMR in animals, including those that are part of the National Action Plans EcoAntibio 1 (2012-2016) 2 (2017-2022) and 3 (2023-2028), as well as the Interministerial roadmap for the control of AMR (2023-2033).

Resapath also opens up many opportunities for molecular and genomic surveillance by setting up a large collection of animal bacterial strains of interest. Beyond characterization of phenotypical trends of AMR, molecular studies are performed in parallel of the National Reference Centres, allowing to compare bacteria, clones or mechanisms of resistance between humans and animals. These comparisons are critical to better understand which hazards are common across sectors and which are not, which is an important aspect to support targeted and effective decision-making.

Acknowledging the importance of the One Health approach, Resapath is also a partner of the national meta-network of professional actors engaged against AMR (PROMISE), as well as the national platform of AMR multi-omics databases (ABRomics-PF)[4]. Those two networks were launched in 2021 as part of the National Priority Research Programme on AMR (PPR) and contribute to support and coordinate AMR surveillance and research at the human-animal-environment interface.

Lastly, Resapath works in close collaboration with its European and international counterparts. While AMR surveillance in animal pathogens is still not regulated nor harmonized in Europe so far, the Resapath currently coordinates, in collaboration with 18 European countries and several EU bodies, an initiative that aims to develop a European AMR surveillance network in veterinary medicine (EARS-Vet)[5].

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[1] EFSA & ECDC (2024). The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2021–2022. EFSA Journal, 22(2), e8583.

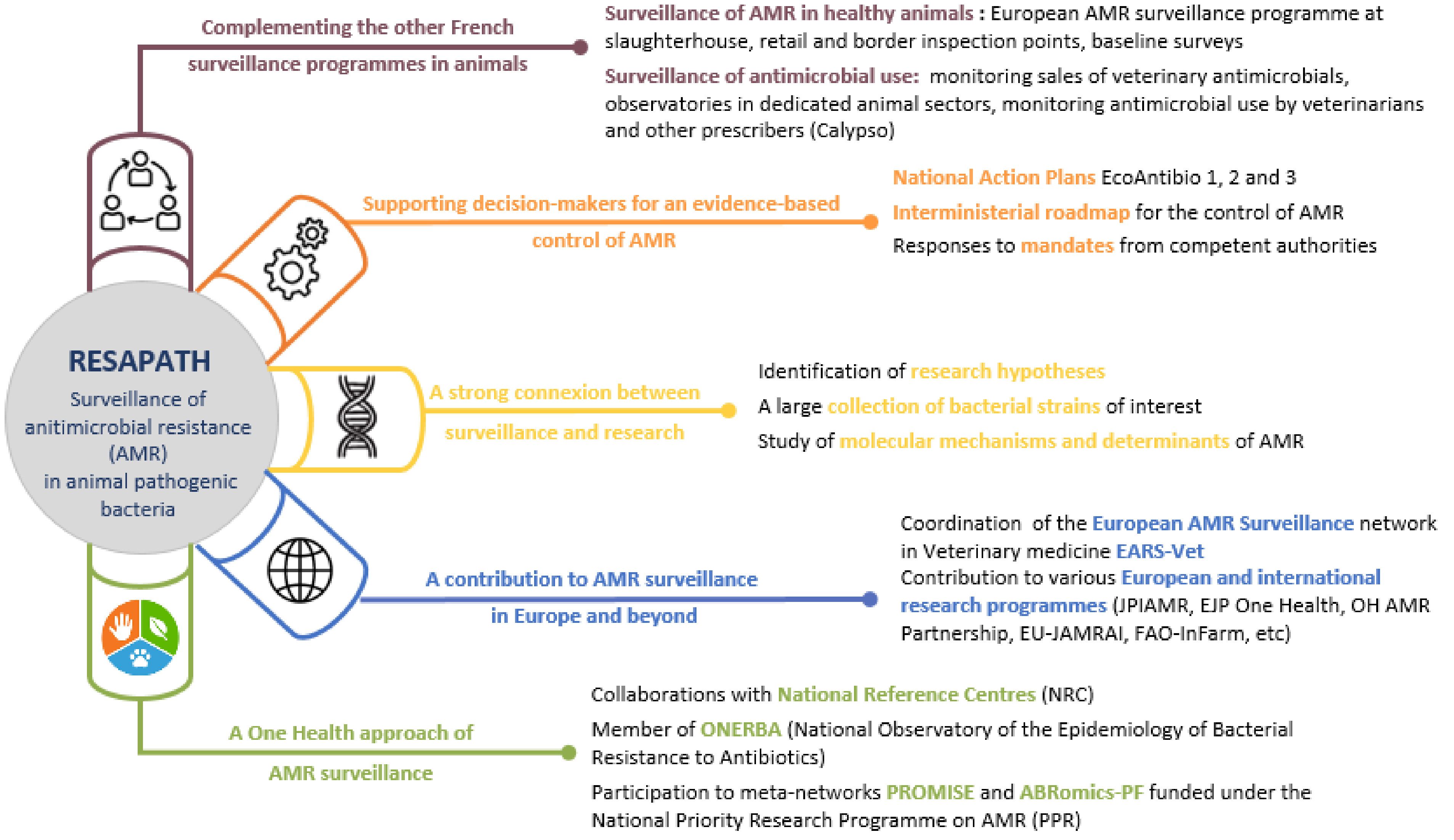
[2] ANSES. (2023). Sales of Veterinary Medicinal Products Containing Antimicrobials in France in 2022. Annual Report. ANSES-ANMV, 98 p. https://www.anses.fr/fr/system/files/ANMV-Ra-Antibiotiques2022EN.pdf

[3] https://www.anses.fr/fr/portails/1808/content/152856

[4] https://ppr-antibioresistance.inserm.fr/fr

[5] Mader R, Damborg P, Amat J-P, et al. (2021). Building the European Antimicrobial Resistance Surveillance network in veterinary medicine (EARS-Vet). Eurosurveillance, 26(4), 2001359. DOI: 10.2807/1560-7917.ES.2021.26.4.2001359

Figure 1. Contributions of Resapath to AMR surveillance in France and beyond



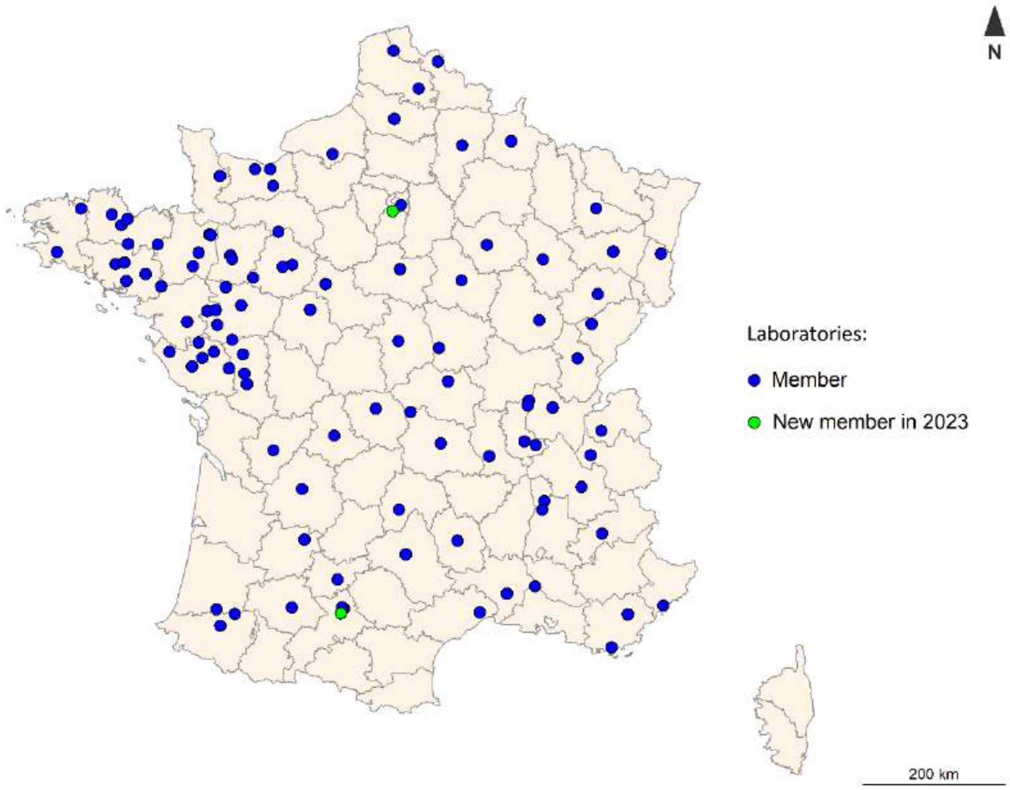
* *Calypso is an information system launched in 2023, facilitating health data to be exchanged between veterinarians, national authorities and other relevant stakeholders, including data on the prescription and deliveries of antimicrobials*

Network functioning and operations

Member laboratories

Resapath performs passive and phenotypical AMR surveillance. Coordinated by the French Agency for Food, Environmental and Occupational Health & Safety (ANSES), it brings together a large number of veterinary diagnostic laboratories in France (public or private).
The network had 105 contributing laboratories in 2023 spread over the metropolitan territory *(Appendix 1).* Major developments in the data management IT system have enabled the addition of 26 new member laboratories in 2021, 7 in 2022 and 2 in 2023 *(Figure 2).*

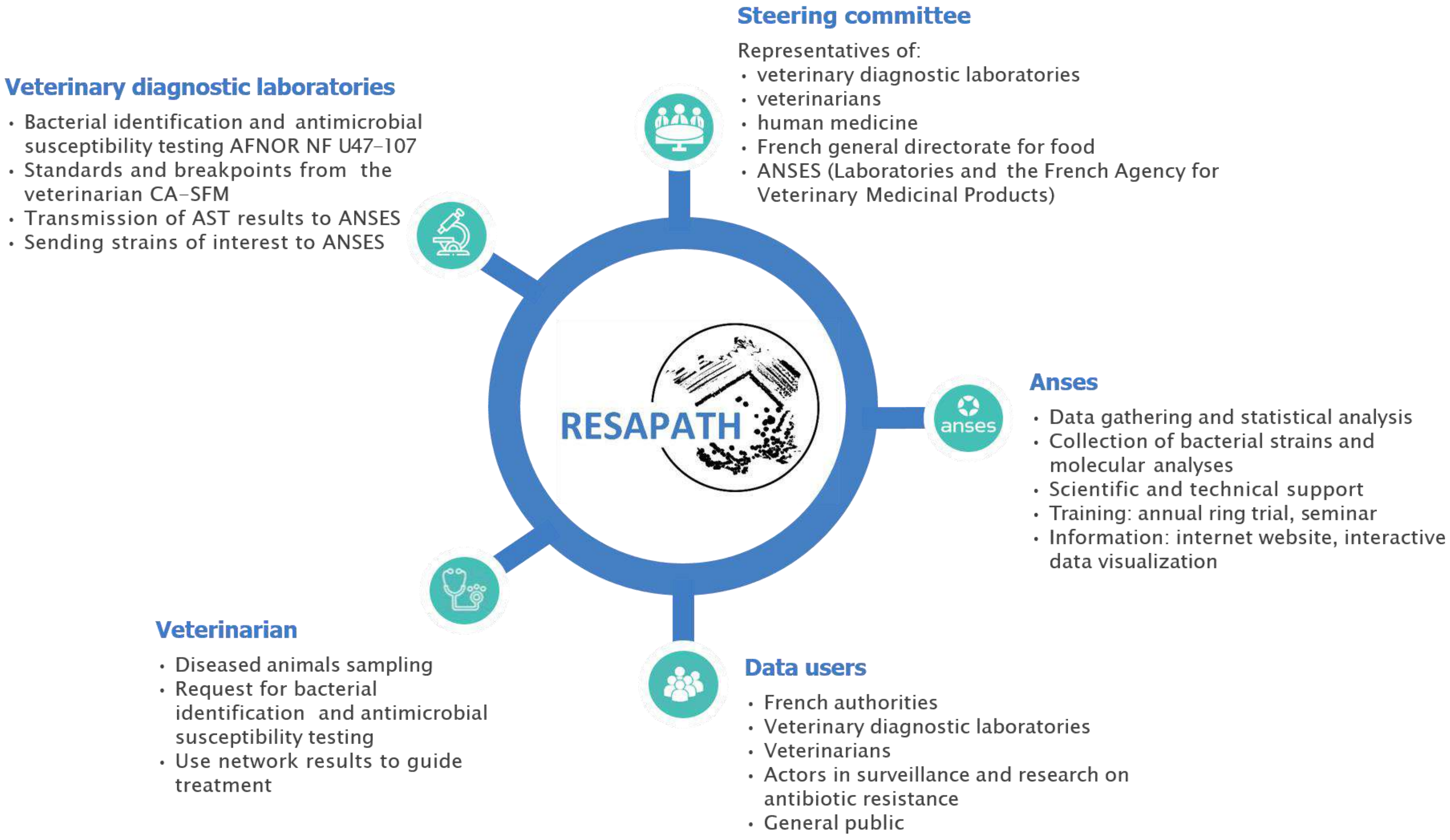
Figure 2. Laboratories participating to Resapath in 2023



Steering committee

Resapath is supervised by a steering committee that meets once a year *(Figure 3).* It is composed of representatives of diagnostic laboratories, veterinary practitioners, representatives of human medicine, the General Directorate for Food and ANSES (including both Laboratories and the Agency for Veterinary Medicinal Products).

Figure 3. RESAPATH actors



Collected data

The member laboratories, which are all volunteers, send to Resapath the results of antimicrobial susceptibility testing (antibiograms) carried out at the request of veterinary practitioners as part of their animal care activity.

For each antibiogram carried out in a member laboratory, Resapath collects data on the bacteria identified, the antibiotics tested, the inhibition zone diameters and the date of the analysis. Other epidemiological data are also collected (i.e. animal species, age category, pathology, type of sample and geographical location). Some data may be missing when they have not been transmitted by the veterinarian or by the laboratory. The network's operations and the quality of the data collected are assessed each year by calculating performance indicators (PI) *(Appendix 2).*

Susceptibility testing method

Antibiograms are performed by disk diffusion according to the recommendations from the veterinary section of the Antibiogram Committee of the French Society of Microbiology (CA-SFM) and the AFNOR NF U47-107 standards. Laboratories contributing to Resapath participate to an annual ring trial (Inter-laboratory proficiency testing). In addition, annual training sessions, technical support, on-site training and other training activities are also provided to the Resapath laboratories, as part of a continuous improvement process.

Standards and interpretation

From the inhibition zones diameters transmitted by the laboratories, Resapath categorizes bacteria strains as susceptible (S), intermediate (I) or resistant (R) according to the CA-SFM recommendations.[6,7] Should no established breakpoints be available, cut-off values provided by the antibiotic manufacturer are used.

The antibiotics tested by the Resapath laboratories are primarily those prescribed in veterinary medicine. To help characterize certain resistance profiles of major interest (e.g. extended spectrum beta-lactamase (ESBL)-producing Enterobacterales or meticillin-resistant *Staphylococcus aureus* (MRSA)), other antibiotics may also be tested (e.g. cefoxitin), which in no way reflect veterinary use of these antibiotics.

Collection of bacterial strains and molecular analyses

ANSES collects, via the Resapath, certain isolates whose AMR profile is of interest to be characterized at a molecular level. In-depth characterization of the molecular mechanisms involved makes it possible to more precisely document the evolutions and emergences observed in the field. Other strains are collected to document the distributions of inhibition zones diameters for certain bacteria / antibiotic combinations and contribute to update the interpretation criteria.

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[6] Antibiogram committee - French society of microbiology https://www.sfm-microbiologie.org/2023/06/15/casfm-veterinaire-2023

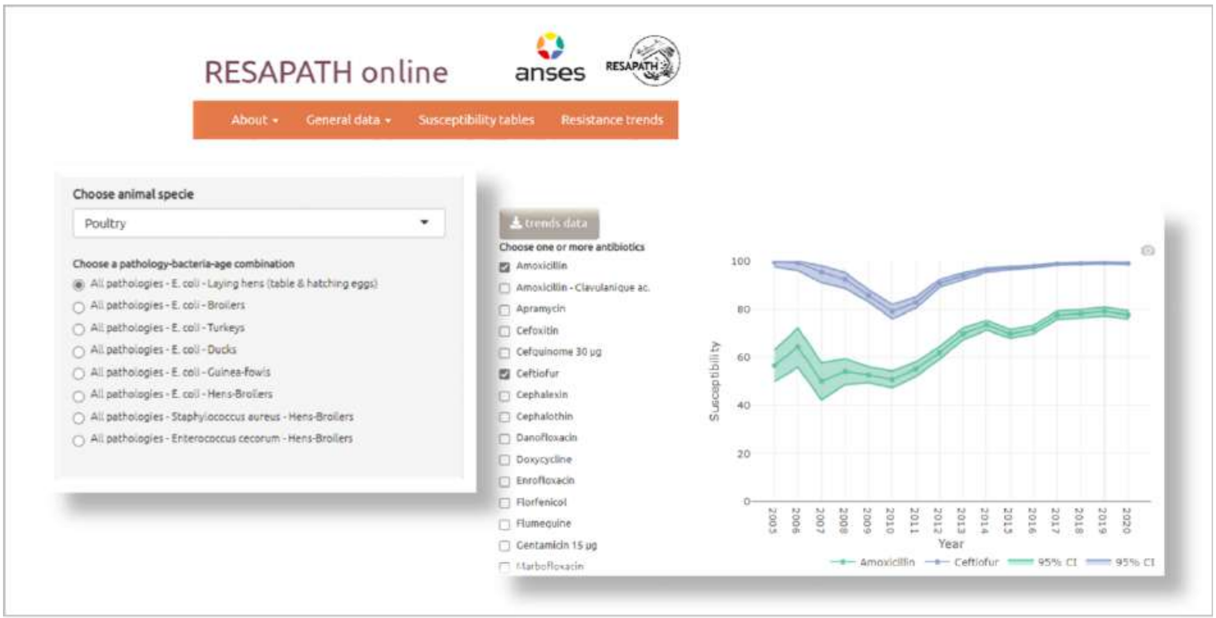
[7] The human version of the CA-SFM used here dates back from 2013. Since 2014, recommendations of the European standard EUCAST (www.eucast.org) were included to the CA-SFM, leading to methodological changes (incubation at 35°C and higher inoculum). Resapath decided not to use the CA-SFM/EUCAST version because of the paucity of veterinary molecules included, and is waiting for VetCast (veterinary European standards, now under development) to be launched

Data access

Resapath data are freely accessible via an interactive open-access dashboard:

RESAPATH online (https://shiny-public.anses.fr/ENresapath2/)

Figure 4. Screenshot from the Resapath open-access dashboard (RESAPATH online)



This dashboard *(Figure 4)* allows the visualization of data collected by Resapath, by selecting different combinations of interest (year/animal species/bacteria/pathology/antibiotic). Data are presented through four tabs:

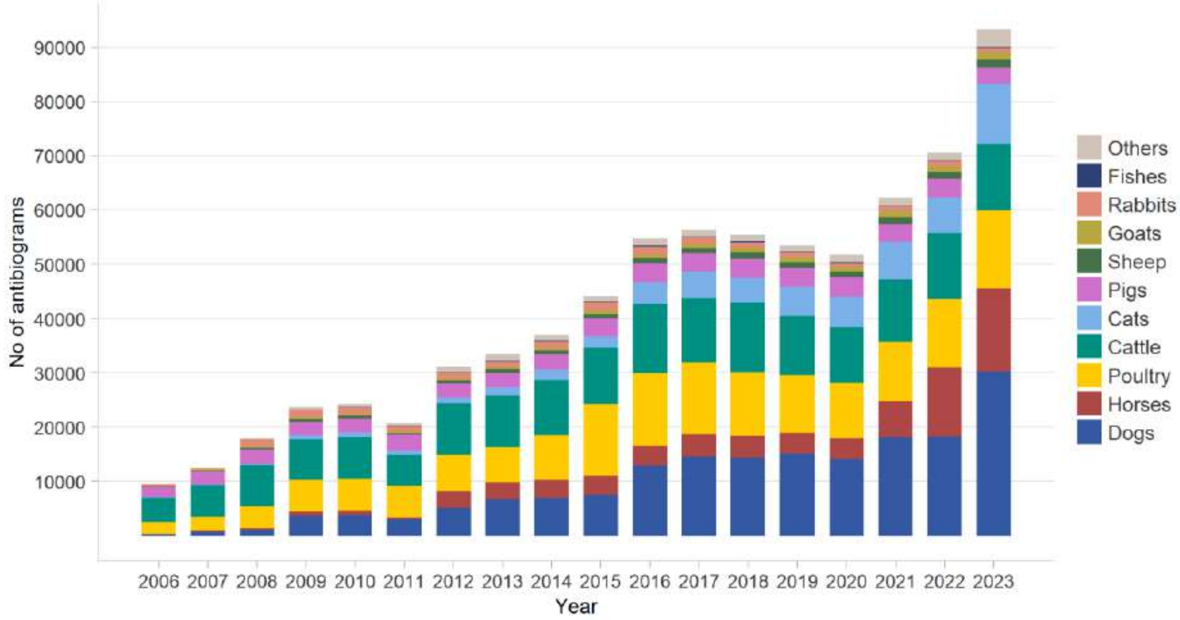
- General data: number of antibiotic susceptibility tests performed;
- Antimicrobial resistance tables: proportion of resistant isolates;
- Trends: temporal trends in the proportions of resistant isolates with their 95% confidence intervals.
- Resistance mapping: proportions of resistant isolates by French department.

All graphs are downloadable as images along with their associated data in Excel® format.

Key figures

- **93,285 antibiograms collected in 2023**

Figure 5. Annual number of antibiograms collected per animal sector



- **Antibiograms per animal categories in 2023**

***Tableau** 1. Number of antibiograms collected per animal categories in 2023*

Animal categories	No of antibiograms	%
Dogs	30,296	32.5
Horses	15,256	16.4
Poultry	14,364	15.4
Cattle	12,268	13.2
Cats	10,987	11.8
Pigs	3,128	3.4
Pet rabbits	1,743	1.9
Others*	1,477	1.6
Sheep	1,436	1.5
Goats	1,251	1.3
Farmed rabbits	904	1.0
Fishes	175	0.2
Total	93,285	100.0

** Birds, pet rodents, aquarium fish, monkeys, snakes...*

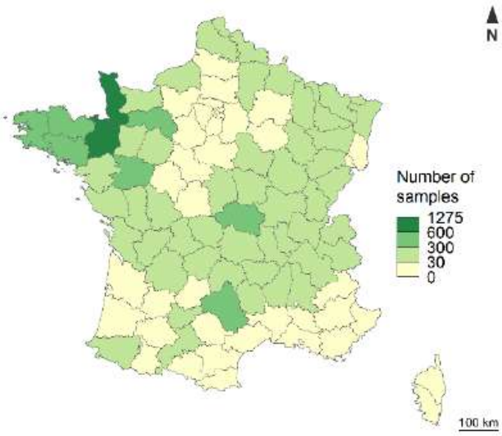
Part 2

Results
by animal categories

CATTLE

COLLECTED DATA

Figure 6. Origin of cattle samples



- 12,268 antibiograms
- 85 contributing laboratories
- Samples from 84 departments (local administrative unit) *(Figure 6)*
- Adults (42%), calves (40%), unknown age (18%)

Adults

- Main diseases:
  - Mastitis (94%)
- Main bacteria:
  - *Escherichia coli* (35%)
  - *Streptococcus* spp. (24%)
  - CoNS (9%)
  - CoPS (7%)

Calves

- Main diseases:
  - Digestive (79%)
  - Respiratory (13%)
- Main bacteria:
  - *Escherichia coli* (83%)
  - *Pasteurella* spp. (5%)
  - *Mannheimia* spp. (3%)
  - *Salmonella* spp. (2%)

RESISTANCE DATA

Escherichia coli

- Isolates from digestive diseases show the highest levels of resistance, particularly to amoxicillin, streptomycin, and sulfonamides (82-87%).
- Resistance to amoxicillin and amoxicillin + clavulanic acid in isolates from mastitis (52% and 31%) and digestive diseases (87% and 67%) remains stable compared to 2022.
- Resistance to 3GC/4GC (<2%) and fluoroquinolones (7%) remains low and stable (see dedicated focus).

Pasteurella spp.

- Bovine *Pasteurella* spp. remain largely susceptible to all beta-lactams.
- Resistance to streptomycin is high (73%), but a decrease was observed in 2022 (-6%).

CoPS and CoNS

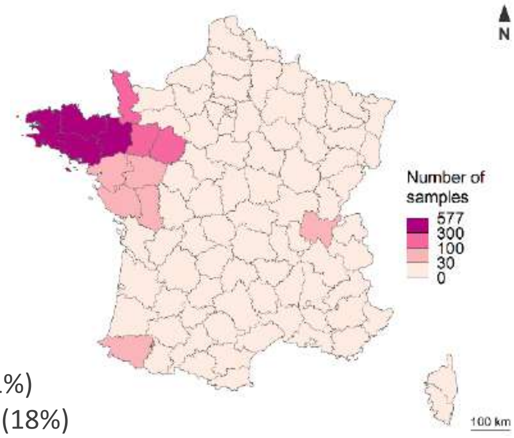
- The majority of staphylococci (CoPS or CoNS) comes from mastitis cases (90-92%).
- The most frequent resistance concerns penicillin G (22% in CoPS and 31% in CoNS). An increase (+5%) is observed in 2023 compared to 2022 for both CoPS and CoNS.

Streptococcus spp.

- Resistance to gentamicin remains very low in *S. uberis* (2%) while resistance to penicillin G is almost absent.
- There is an increase in erythromycin resistance (+6%) in *S. dysgalactiae* (20%) compared to 2022.

PIGS

Figure 7. Origin of pig samples



COLLECTED DATA

- 3,128 antibiograms
- 55 contributing laboratories
- Samples from 73 departments (4 providing 61% of the data) *(Figure 7)*
- Piglets (55%), sows (12%), unknown age (33%)

- Main diseases:
  - Digestive (40%), mainly in piglets
  - Respiratory (13%)
  - Septicemia (10%)

- Main bacteria:
  - *Escherichia coli* (51%)
  - *Streptococcus suis* (18%)
  - *Actinobacillus pleuropneumoniae* (5%)
  - *Enterococcus hirae* (3%)
  - *Glaesserella parasuis* (4%)
  - *Pasteurella multocida* (3%)
  - CoPS (3%)

RESISTANCE DATA

Escherichia coli

- 59% of isolates are resistant to amoxicillin, but less than 1% to ceftiofur.
- 14% of isolates are resistant to nalidixic acid and 2% to fluoroquinolones.
- 5% of isolates are resistant to apramycin or gentamicin.
- 38% of isolates are resistant to the trimethoprim-sulfamethoxazole combination, and 51% to tetracycline.
- Less than 5% of isolates are resistant to colistin.

Pasteurella multocida, Actinobacillus pleuropneumoniae and Glaesserella parasuis

- Less than 1% of *P. multocida* and *G. parasuis* isolates are resistant to amoxicillin, 6.5% for *A. pleuropneumoniae*.
- No isolates resistant to ceftiofur or florfenicol, and less than 1.5% to fluoroquinolones.

Streptococcus suis

- Resistance to amoxicillin is very rare (< 1%) and 4% of isolates are resistant to oxacillin (marker of penicillin G resistance).
- High-level resistance to aminoglycosides is scarce (synergy with beta-lactams is preserved).

Enterococcus hirae

- Resistance to amoxicillin concerns 8% of isolates.
- 85% are resistant to erythromycin and almost all to lincomycin (99%).

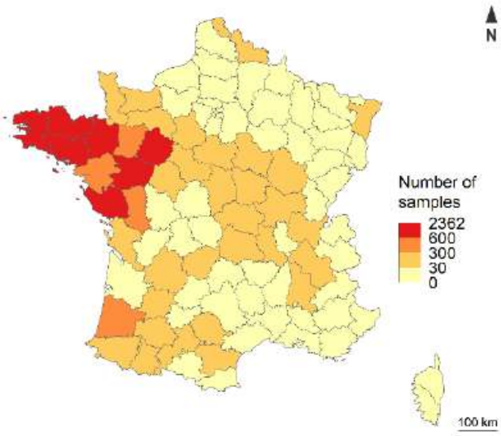
Staphylococcus aureus

- Among CoPS, 34% of *S. aureus* isolates (n= 38) were resistant to cefoxitin, suggesting the occurrence of MRSA phenotype.

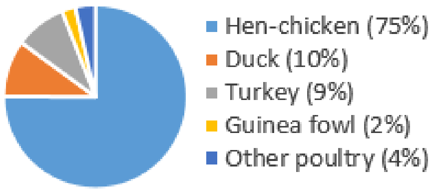
POULTRY

COLLECTED DATA

Figure 8. Origin of poultry samples



- 14,364 antibiograms
- 88 contributing laboratories
- Samples from 91 departments *(Figure 8)*
- Poultry species:



- Main diseases:
  - Septicemia (78%)
  - Arthritis (10%)
  - Respiratory (2%)
- Main bacteria:
  - *Escherichia coli* (77%)
  - *Enterococcus cecorum* (7%)
  - *Staphylococcus aureus* (3%)
  - *Enterococcus faecalis* (3%)

RESISTANCE DATA

Escherichia coli

In hens and broiler chickens, turkey, ducks and guinea fowls, depending on the species:

- A proportion of 47% (turkeys) to 68% (guinea fowls) of isolates are resistant to amoxicillin, and less than 1% to ceftiofur.
- 3% of isolates are resistant to enrofloxacin for broilers-hens and turkeys, less than 1% for ducks and guinea fowls.
- 1% (turkeys) to 11% (hens/broilers) are resistant to gentamicin.
- 23% (guinea fowls) to 38% (ducks) of isolates are resistant to tetracycline, and 11-14% to the trimethoprim-sulfamethoxazole combination for all four animal species.

Enterococcus cecorum (hens and broilers)

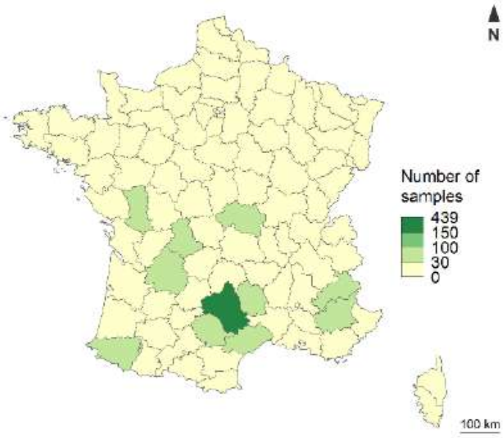
- 4% of isolates are resistant to amoxicillin.
- 27% of isolates are resistant to macrolides-lincosamides.
- 61% of isolates are resistant to the trimethoprim-sulfamethoxazole combination, and 90% to tetracycline.

Staphylococcus aureus (hens and broilers)

- Between 1% and 8% of isolates are resistant to the most frequently tested antibiotics, with the exception of erythromycin, lincomycin, tetracycline and penicillin G (11% to 23%).
- 8% of isolates are resistant to cefoxitin, indicating a possible resistance to methicillin (MRSA).

SHEEP

Figure 9. Origin of sheep samples



COLLECTED DATA

- 1,436 antibiograms
- 69 laboratories (1 providing 38% of the data)
- Samples from 80 departments *(Figure 9)*
- Adults (22%), young (46%), unknown age (32%)

Adults

- Main diseases:
  - Mastitis (42%)
  - Respiratory (19%)
- Main bacteria :
  - CoPS (24%)
  - *Mannheimia* spp. (13%)
  - *Escherichia coli* (12%)
  - *Pasteurella* spp. (9%)

Lambs

- Main diseases:
  - Respiratory (39%)
  - Digestive (36%)
- Main bacteria :
  - *Escherichia coli* (48%)
  - *Mannheimia* spp. (20%)
  - *Pasteurella* spp. (15%)

RESISTANCE DATA

Escherichia coli

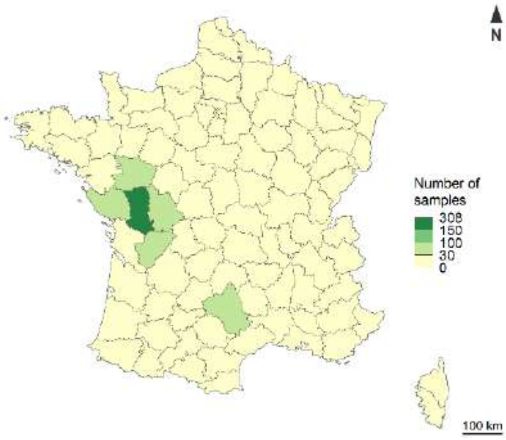
- *E. coli* isolates responsible for digestive tract infections in sheep present resistance proportions lower than those reported for bovine neonatal gastroenteritis, but nevertheless high to the following antibiotics: 57% to tetracycline, 62% to amoxicillin and 51% to amoxicillin+clavulanic acid.
- Resistance to streptomycin is high (53%), while resistance to gentamicin is low (4%).
- Resistances to 3GC/4GC and fluoroquinolones remain very low (<2%).

Mannheimia haemolytica

- *M. haemolytica* isolates collected from respiratory diseases present high proportions of resistance to penicillin G and sulfonamides (70%), as well as to aminoglycosides (56%).
- Resistances to 3GC/4GC (<1%) and fluoroquinolones (4%) remain low.

GOATS

Figure 10. Origin of goat samples



COLLECTED DATA

- 1,251 antibiograms
- 67 laboratories
- Samples from 74 departments *(Figure 10)*
- Adults (37%), young (30%), unknown age (33%)

Adults

- Main diseases:
  - Mastitis (75%)
  - Respiratory (11%)
- Main bacteria:
  - CoPS (23%)
  - CoNS (21%)
  - *Escherichia coli* (15%)

Young

- Main diseases:
  - Digestive (37%)
  - Respiratory (25%)
- Main bacteria:
  - *Escherichia coli* (54%)
  - *Mannheimia* spp. (18%)
  - *Pasteurella* spp. (6%)
  - *Clostridium* spp. (4%)
  - *Klebsiella* spp. (3%)

RESISTANCE DATA

Escherichia coli

- Resistance to fluoroquinolones is high (16% for enrofloxacin and marbofloxacin), while resistance to 3GC/4GC remains low (<3%).
- Resistance to amoxicillin (60%) and amoxicillin + clavulanic acid (46%) is high and on an increasing trend since 2018 (53% and 32% respectively at that time).

Pasteurella spp. and *Mannheimia spp.*

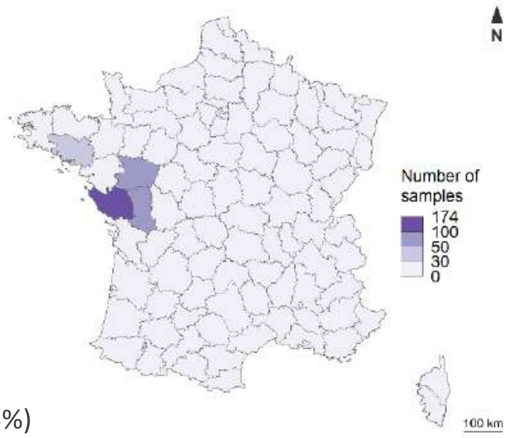
- Resistance to fluoroquinolones and 3GC/4GC remains low (<5%).

CoPS and CoNS

- Resistance to cefoxitin (marker of MRSA) reaches 11% for CoPS and 5% for CoNS.

FARMED RABBITS

Figure 11. Origin of rabbit samples



COLLECTED DATA

- 904 antibiograms
- 65 laboratories (3 providing 43% of the data)
- Samples from 56 departments *(Figure 11)*
- Adults (50%), young (5%), unspecified (45%)

- Main diseases:
  - Septicemia (23%)
  - Respiratory (22%)
  - Digestive (21%)
  - Skin and soft tissue infection (10%)
- Main bacteria:
  - *Escherichia coli* (33%)
  - *Pasteurella multocida* (17%)
  - CoPS (15%)
  - CoNS (5%)
  - *Bordetella bronchiseptica* (3%)

RESISTANCE DATA

Escherichia coli

- 73% of isolates are resistant to amoxicillin (not used in rabbits) but no resistance to ceftiofur.
- 10% of isolates are resistant to flumequine (-8% between 2022 and 2023), and 2% to enrofloxacin.
- Resistance to apramycin or gentamicin is around 7%.
- 53% of isolates are resistant to trimethoprim-sulfamethoxazole, 79% to tetracycline.
- Resistance to colistin is found in about 7% of the isolates.

Pasteurella multocida

- Between 0% and 8% of resistant isolates to the most frequently tested antibiotics, except for nalidixic acid (43%), flumequine (16%) and spectinomycin (13%).

Staphylococcus aureus

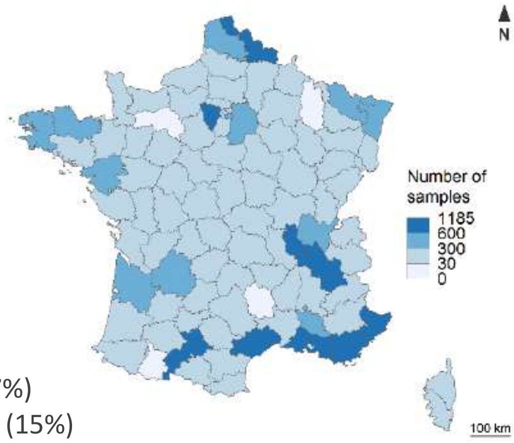
- 35% of isolates are resistant to penicillin G, +9% compared to 2022.
- 7% of isolates are suspected of being MRSA (resistance to cefoxitin).
- 5% of isolates are resistant to enrofloxacin.
- The rates of resistance to trimethoprim-sulfamethoxazole and to gentamicin are 21% and 17% respectively, in steady decline over the past 3-4 years.
- 46% of isolates are resistant to tetracycline and between 56% and 60% to macrolides-lincosamides.

DOGS

COLLECTED DATA

- 30,296 antibiograms
- 86 laboratories (3 providing 75% of the data)*
- Samples from 98 departments *(Figure 12)*
- Adults (60%), young (3%), unknown age (37%)

Figure 12. Origin of dog samples



Adults

- Main diseases:
  - Otitis (37%)
  - Kidney/urinary tract infection (26%)
  - Skin and soft tissue infection (10%)
- Main bacteria:
  - CoPS (27%)
  - *Escherichia coli* (17%)
  - *Pseudomonas* spp. (15%)
  - *Proteus* spp. (9%)
  - *Streptococcus* spp. (8%)

Young dogs

- Main diseases:
  - Kidney/urinary tract infection (31%)
  - Digestive (22%)
  - Otitis (7%)
  - Skin and soft tissue infection (7%)
  - Respiratory (4%)
- Main bacteria:
  - *Escherichia coli* (28%)
  - CoPS (16%)
  - *Campylobacter* spp. (10%)
  - *Proteus* spp. (8%)

**Because of the frequency of referral cases in veterinary medicine, the location of the laboratory does not predict the geographical origin of the animals.*

RESISTANCE DATA

Escherichia coli

- Between 2021 and 2023, resistance to ceftiofur is on a decreasing trend in skin and soft tissue infections (23% to 13%) and in otitis (8% to 2%), but stable in urinary tract infections (3-4%).
- Resistance to amoxicillin and amoxicillin+clavulanic acid is strongly decreasing in urinary tract infections (-15% and -10%) and in otitis (-24% for both antibiotics).

Proteus spp.

- Resistance to 3GC and cefoxitin (marker of AmpC phenotype) is stable around 3-4%.
- Resistance to fluoroquinolones is decreasing (-5% for enrofloxacin and marbofloxacin).

CoPS

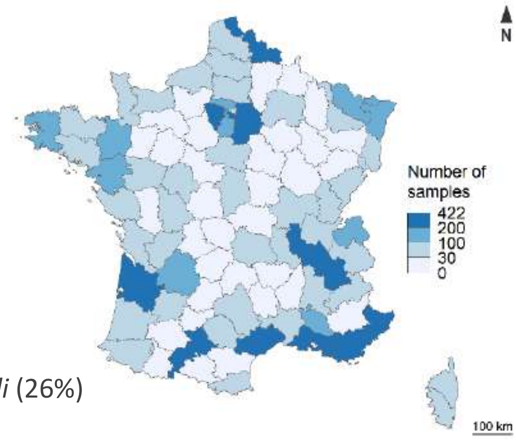
- 78% of *S. aureus* isolates and 82-86% of *S. pseudintermedius* isolates are resistant to penicillin G.
- 30% of *S. aureus* isolates and 26-37% of *S. pseudintermedius* isolates present an MLSb phenotype.
- MRSA are on a decreasing trend (11% in 2023, 20% in 2022), while MRSP represent 9-18% of *S. pseudintermedius* isolates depending on the pathology.

CATS

COLLECTED DATA

- 11,987 antibiograms
- 78 laboratories (2 providing 71% of the data)
- Samples from 98 departments *(Figure 13)*
- Adults (63%), young (4%), unknown age (33%)

Figure 13. Origin of cat samples



- Main diseases:
  - Kidney/ urinary tract infection (40%)*
  - Respiratory (12%)
  - Otitis (11%)
  - Skin and soft tissue infection (5%)
  - Digestive (4%)*
- Main bacteria:
  - *Escherichia coli* (26%)
  - CoPS (16%)
  - *Pasteurella* spp. (10%)
  - *Enterococcus* spp. (9%)
  - CoNS (6%)

**When the age of the animals was specified, most of the samples from urinary tract infections originated from adults (98%).*

RESISTANCE DATA

Escherichia coli

- Resistance to critically important antibiotics (CIA) remains low and stable (2% for 3GC/4GC and 4% for fluoroquinolones).
- Resistance to amoxicillin and amoxicillin+clavulanic acid is strongly decreasing (respectively -15% and -10% compared to 2022).

CoPS

- Resistance to penicillin G is on a decreasing trend (55% in 2022, 46% in 2023) all considered diseases.
- MRSA are on a decreasing trend (7-15% in 2022, 3-9% in 2023) all considered diseases.
- 24% of isolates are resistant to macrolides, 14% to lincomycin and 9% to fluoroquinolones.

Pasteurella spp.

- Resistance to amoxicillin (6%) and amoxicillin+clavulanic acid (3%) are on a decreasing trend.
- Resistance to tetracyclines is low (8%), while resistance to ceftiofur and florfenicol is very rare (1 - 2%).

HORSES

COLLECTED DATA

- 15,256 antibiograms
- 64 laboratories (1 providing 75% of the data)
- Samples from 96 departments*
- Adults (14%), young (1%), unknown age (85%)

- Main diseases**:
  - Respiratory (27%)
  - Reproduction (20%)
  - Skin and soft tissue infection (5%)
  - Ocular (4%)
- Main bacteria :
  - *Streptococcus* spp. (25%)
  - *Escherichia coli* (11%)
  - CoPS (9%) or CoNS (9%)
  - *Pseudomonas* spp. (7%)

** The department of origin is unknown for 76% of the samples, hence the map displaying the departments of origin could not be produced.*
*** The type of infection is unknown for 38% of the samples.*

RESISTANCE DATA

Escherichia coli

- Overall, resistance to ceftiofur reaches 8%.
- Resistance to amoxicillin (59%) and amoxicillin+clavulanic acid (50%) is still on an increasing trend when all diseases are considered, but is clearly decreasing in skin and soft tissue infections (respectively -18% and -14%).
- Resistance to amikacin is stable (2%) for all considered diseases.

Enterobacterales

- Resistance to ceftiofur is stable in *Enterobacter* spp. (38%) and *Klebsiella pneumoniae* (16%).
- Resistance to amikacin is stable at 5% in *Enterobacter* spp. and is emerging in *Klebsiella pneumoniae* (3%).

Streptococcus spp.

- *Streptococcus* spp. isolates are mostly susceptible to all antibiotics tested, with resistances mostly to tetracycline (21-45%) and trimethoprim-sulfamethoxazole (27-38%).
- Resistances to beta-lactams and aminoglycosides are very rare (hence, synergy is preserved).

Staphylococcus aureus

- Resistance to penicillin G (28%) is stable, while resistance to tetracycline is on increasing trend (13% in 2022, 22% in 2023).
- MRSA are found in 13% of the isolates.

PET RABBITS

COLLECTED DATA

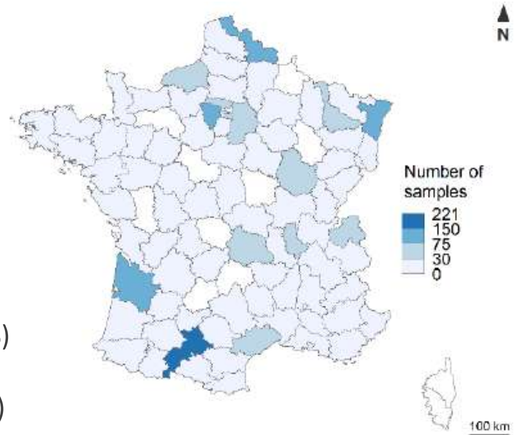
- 1,743 antibiograms
- 15 laboratories (2 providing 74% of the data)
- Samples from 88 departments *(Figure 14)*
- Age in unknown for almost all samples (97%)

- Main diseases*:
  - Respiratory (25%)
  - Otitis (10%)
  - Oral pathology (9%)

- Main bacteria:
  - *Pasteurella* multocida (11%)
  - *Pseudomonas* spp. (10%)
  - *Staphylococcus* aureus (8%)

**The disease is not reported in 49% of cases.*

Figure 14. Origin of pet rabbits samples



RESISTANCE DATA

Pasteurella multocida

- The majority of *Pasteurella* spp. isolates come from respiratory diseases.
- Less than 8% of isolates are resistant to the most frequently tested antibiotics, except for streptomycin (63%), nalidixic acid (33%), and neomycin (31%).

Pseudomonas spp.

- The majority of *Pseudomonas* spp. isolates come from respiratory diseases.
- *Pasteurella* in pet rabbits remain largely susceptible to beta-lactams.
- Resistance to streptomycin is high (67%); the decrease observed in 2022 continues in 2023 (-6%).

Staphylococcus aureus

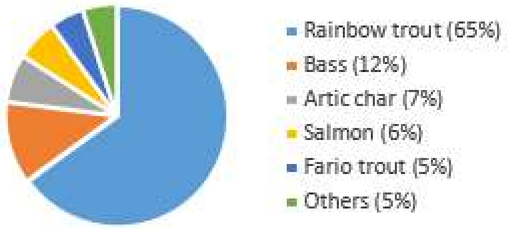
- The majority of *Staphylococcus aureus* isolates come from otitis cases.
- 60% of isolates are resistant to penicillin G.
- 14% of isolates are resistant to cefoxitin, indicating possible MRSA phenotype.
- 11% of isolates are resistant to tetracycline, and 12% to macrolides-lincosamides.
- 6% of isolates are resistant to trimethoprim-sulfonamides, and 3% to gentamicin.
- 13% of isolates are resistant to enrofloxacin.

FISHES

COLLECTED DATA

- 175 antibiograms
- 5 laboratories
- Samples from 5 departments (department unknown for 92% of the isolates)

- Mains fish species:



- Main diseases:
  - Septicemia (3%)
  - Skin and soft tissue infection (2%)
  - Unknown (95%)

- Main bacteria:
  - *Aeromonas salmonicida* (53%)
  - *Yersinia ruckeri* (14%)
  - *Vibrio* spp. (11%)

RESISTANCE DATA

The data collected do not currently allow for a detailed description of AMR results in fish. This is due to the small number of collected data, as well as the uncertainty in the representativeness and the methodology used to test certain bacteria such as *Aeromonas salmonicida*.

OTHER SPECIES

COLLECTED DATA

- 1,477 antibiograms
- 56 laboratories
- Samples from 78 departments

Samples come mainly from:

- Mammals (monkeys, dwarf rabbits, guinea pigs, etc.) (51%)
- Birds (31%)
- Reptiles (16%)
- Aquarium fishes (2%)

RESISTANCE DATA

Due to the low numbers of antibiograms collected for each animal species and the multiplicity of diseases and bacterial species, the detailed results of resistance levels concerning these animal species are not displayed in this report.

Part 3

Focuses

E. coli - Resistance trends for extended-spectrum cephalosporins and fluoroquinolones

Extended-spectrum cephalosporins (ESC) and fluoroquinolones (FQ) are critically-important antibiotics (CIA) for human health, thus their use in veterinary medicine is regulated by law, in France. Proportions of resistance to these two antibiotic classes are considered as major indicators in the evaluation of national action plans against AMR.

Method

Three 3GC/4GC molecules are used in veterinary medicine: ceftiofur and cefquinome in production animals and equines, and cefovecin in dogs and cats. Trends are analysed on the basis of ceftiofur and for *E. coli*, which is the most frequently identified species in the Resapath. This indicator is considered valid, although differences may be observed with cefquinome or cefovecin. These differences are due in particular to the nature of the enzymes hydrolyzing cephalosporins.
With regard to fluoroquinolones, enrofloxacin and marbofloxacin are the markers chosen to monitor the evolution of resistance to this antibiotic class.
In order to assess the significance of the trends observed, Chi2 trend tests are carried out for the period under consideration and deemed significant at a level of 5% (this applies to all the trends analysed in Part 3-Focus of this report).

Figure 15. Evolution of proportions (%) of E. coli isolates non-susceptible (R+I) to ceftiofur (2013-2023)

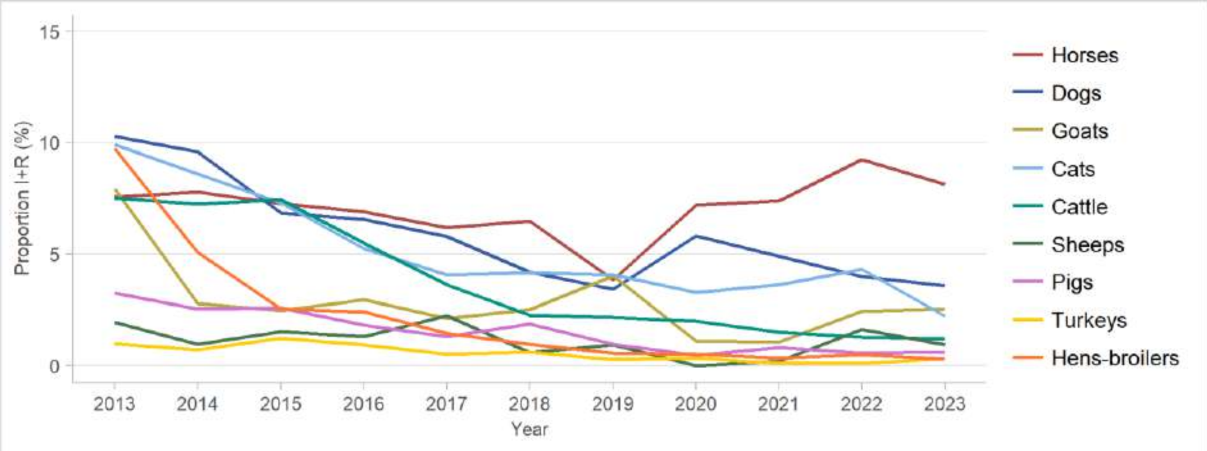


Figure 16. Evolution of proportions (%) of E. coli isolates non-susceptible (R+I) to enrofloxacin or marbofloxacin (2013-2023)

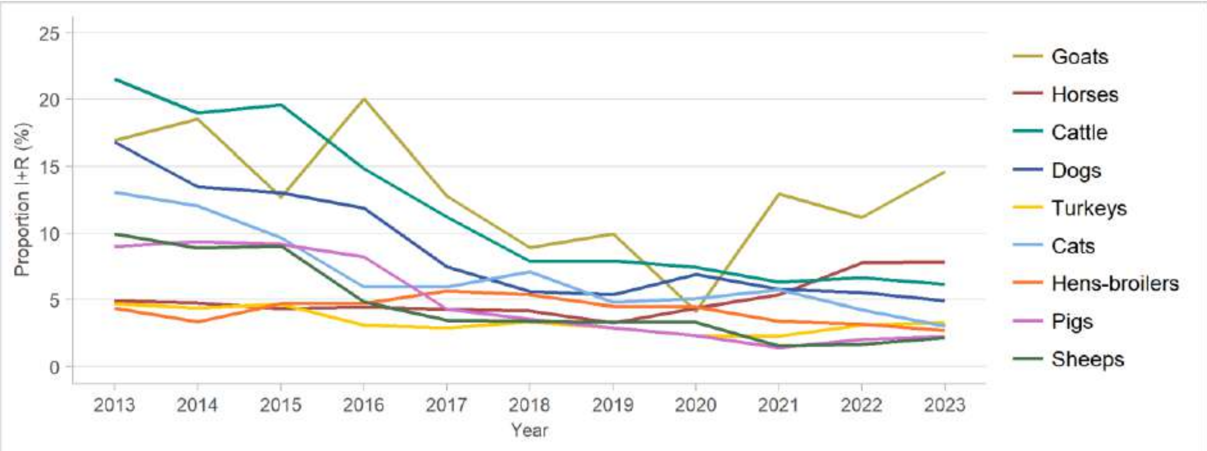
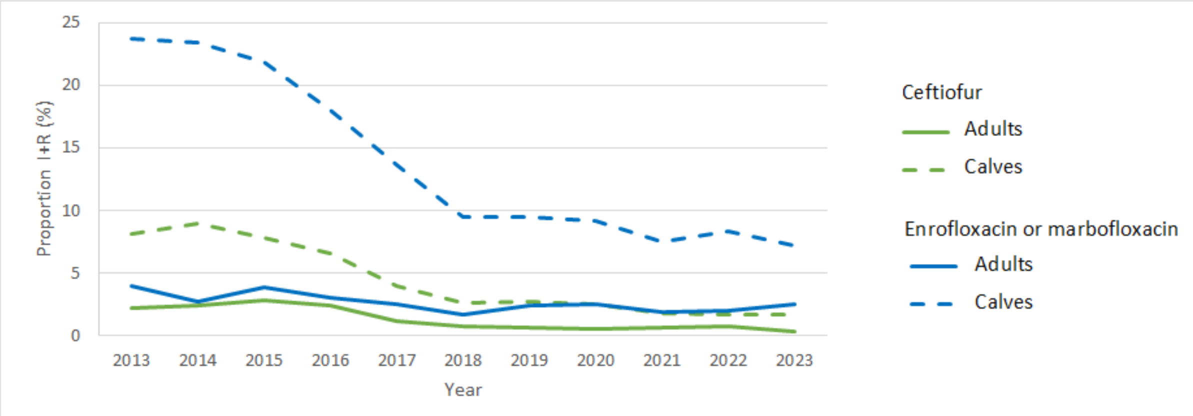


Figure 17. Evolution of proportions (%) of E. coli isolates non-susceptible (R+I) to ceftiofur, to enrofloxacin or marbofloxacin, for cattle according to their age (2013-2023)



- The trend in *E. coli* resistance is generally decreasing for 3GC/4GC with proportions less than or equal to 5%, except for horses (8%). For fluoroquinolones, proportions are less than 7%, except for goats (14.6%) for which an increase of 3.5% was observed compared to 2022 (*Figures 15 and 16*).

- These trends reflect the veterinary profession's efforts to reduce antibiotic use, and are consistent with the observed reductions of animal exposure. In all animal categories, except equines and goats, the proportions of resistance to 3GC/4GC and fluoroquinolones appear to be reaching a plateau.

- The increase in 3GC/4GC resistance in equines, which began between 2019 and 2022 (up from 4% to 9%), shows a slight inflexion in 2023 (-1.1% compared with 2022). For fluoroquinolones, a stagnation is observed compared to 2022 (*Figures 15 and 16*).

- For a given animal category, the burden of resistance may rely mostly on certain age classes. In cattle, for example, resistance to 3GC/4GC and fluoroquinolones mostly comes from young animals (*Figure 17*).

Resistance to 3GC/4GC and fluoroquinolones in *K. pneumoniae* and *Enterobacter* spp.

Resistance to 3rd and 4th generation cephalosporins (3GC/4GC) and fluoroquinolones can concern all Enterobacterales, of which *Klebsiella pneumoniae* and *Enterobacter* spp. (including mainly *Enterobacter hormaechei*) are major pathogens in animals. The mechanisms involved are broadly similar between *E. coli*, *K. pneumoniae* and *Enterobacter* spp. In human medicine, the latter two bacteria are known to be highly resistant to 3GC/4GC and fluoroquinolones.

The methodology applied here is identical to the one described above for *E. coli*. Only data concerning horses and dogs were large enough to be analysed and compared with the proportions of resistance observed in *E. coli*.

*Figure 18. Evolution of proportions (and 95% confidence intervals) of E. coli, K. pneumoniae and Enterobacter spp. isolates non-susceptible (R+I) to **ceftiofur** in **dogs** (2017-2023).*

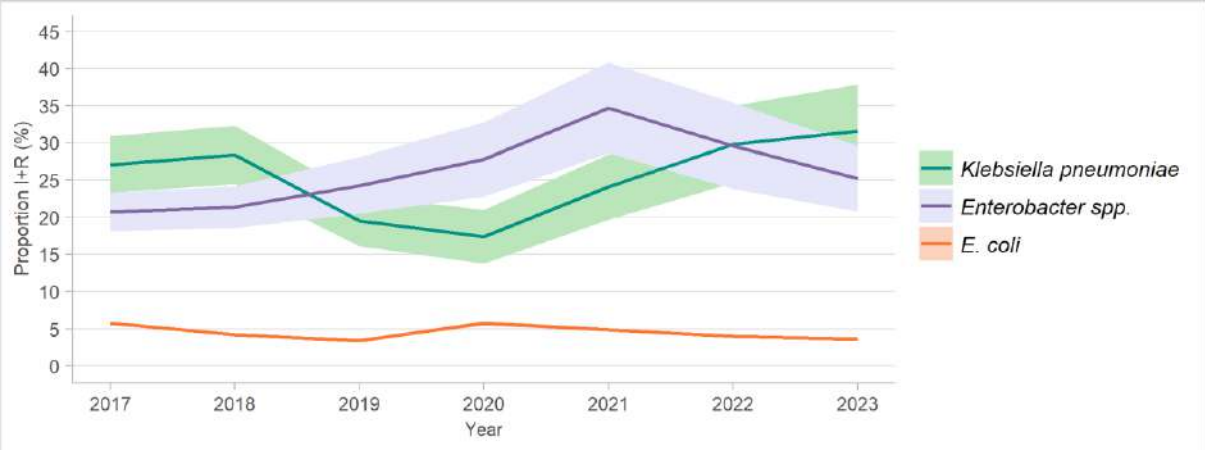


*Figure 19. Evolution of proportions (and 95% confidence intervals) of E. coli, K. pneumoniae and Enterobacter spp. isolates non-susceptible (R+I) to **ceftiofur** in **horses** (2017-2023).*

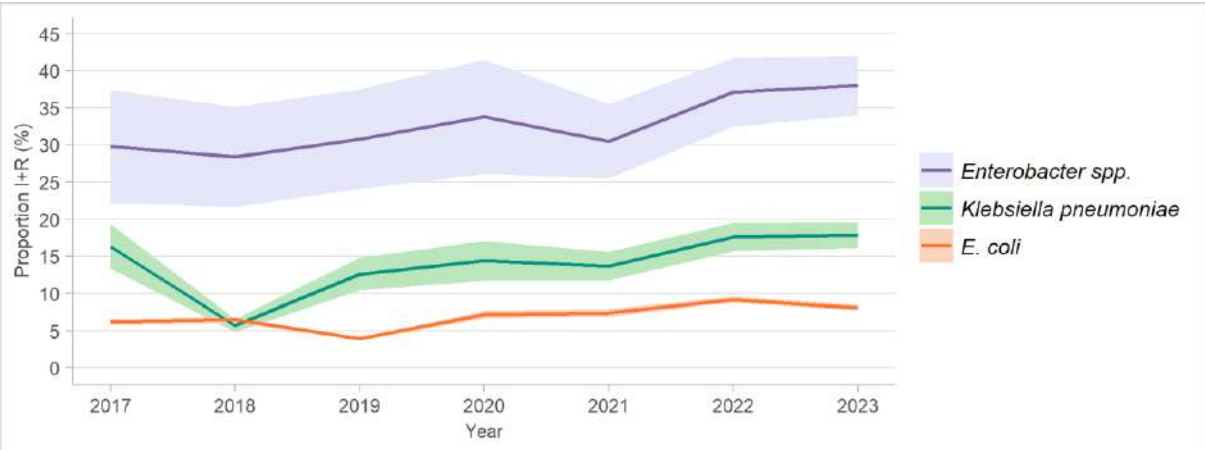


Figure 20. Evolution of proportions (and 95% confidence intervals set) of E. coli, K. pneumoniae and Enterobacter spp. isolates non-susceptible (R+I) to ***enrofloxacin or marbofloxacin*** *in* ***dogs*** *(2017-2023).*

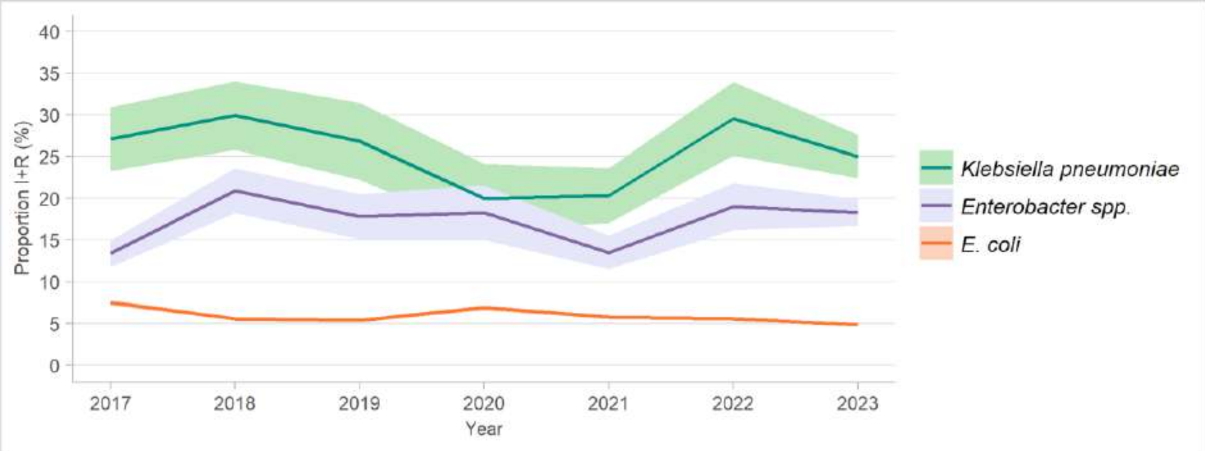
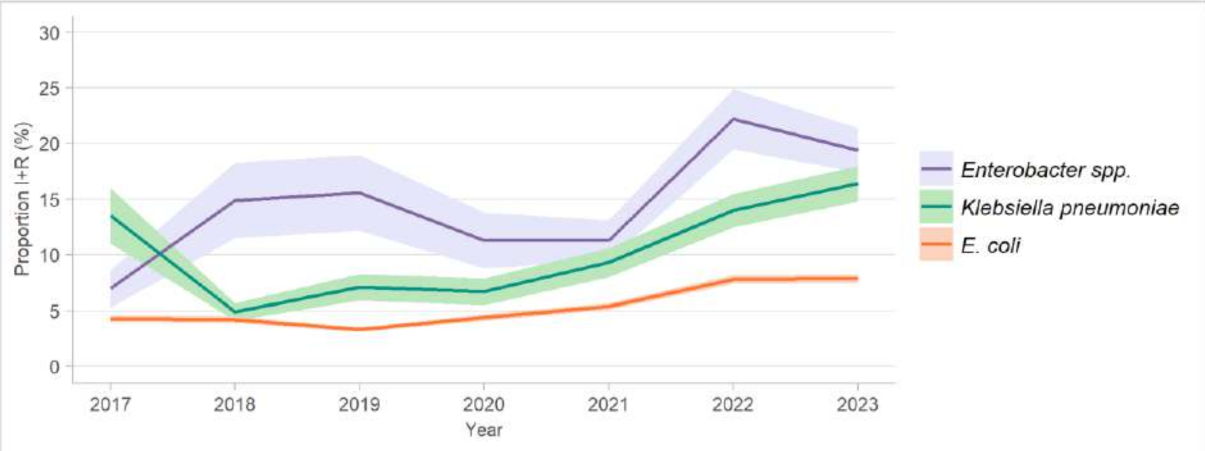


Figure 21. Evolution of proportions (and 95% confidence intervals) of E. coli, K. pneumoniae and Enterobacter spp. isolates non-susceptible (R+I) to ***enrofloxacin or marbofloxacin*** *in* ***horses*** *(2017-2023).*



- ✓ Resistance to 3GC/4GC and fluoroquinolones is systematically higher in *K. pneumoniae* and *Enterobacter* spp. than in *E. coli (Figures 18 to 21).*

- ✓ In dogs and equines in 2023, resistance to 3GC/4GC is 32% and 18% respectively for *K. pneumoniae*, and 25% and 38% for *Enterobacter* spp. *(Figures 18 and 19)*. Trends are stable, except for 3GC/4GC resistance in *Enterobacter* spp. isolated from dogs, which is on a decreasing trend since 2021.

- ✓ In dogs and equines in 2023, fluoroquinolone resistance is respectively 25% and 16% for *K. pneumoniae*, and 18% and 19% for *Enterobacter* spp. (*Figures 20 and 21*).

- ✓ The evolution of resistance in these two pathogens should be monitored, both for 3GC/4GC and fluoroquinolones, since the proportions observed are considerably higher than those seen in *E. coli*.

E. coli – Resistance trends for amoxicillin, amoxicillin + clavulanic acid and cephalexin

Method

Amoxicillin is a major antimicrobial, both in human and veterinary medicine. Trends in *E. coli* resistance to this molecule, alone or in combination with clavulanic acid, are studied here separately from other antimicrobials. Cephalexin, a first-generation cephalosporin, has been added to refine the interpretation of trends.

Trends in the proportions of intermediate and resistant strains are analysed separately.

Figure 22. Evolution of proportions (%) of E. coli intermediate or resistant to amoxicillin, amoxicillin + clavulanic acid or cephalexin in cattle (A) and pigs (B) (2016-2023)

(A) Cattle *(B) Pigs*

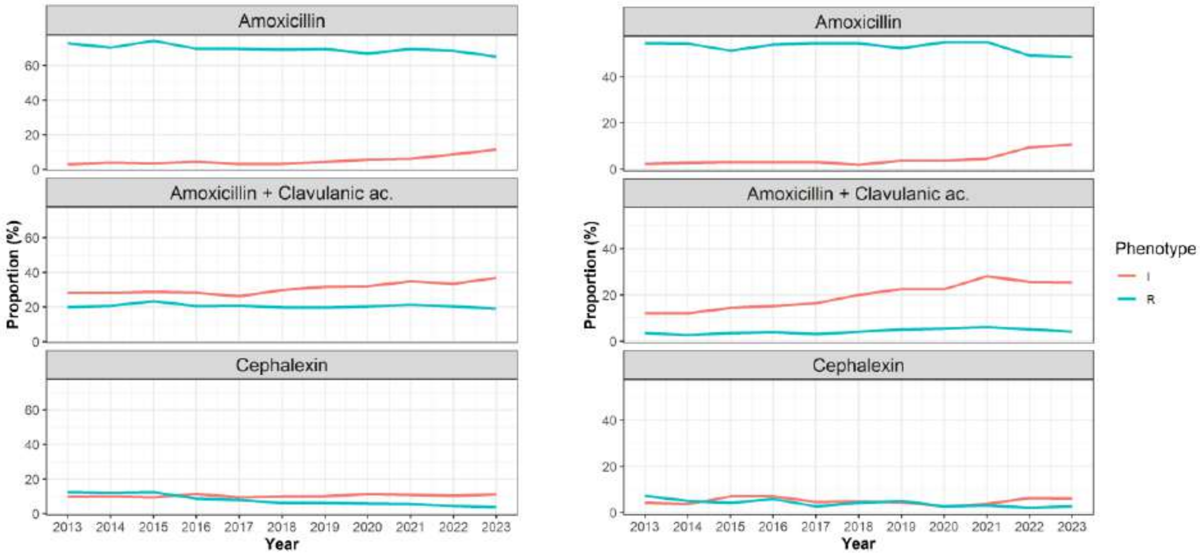


Figure 23. Evolution of proportions (%) of E. coli intermediate or resistant to amoxicillin, amoxicillin + clavulanic acid or cephalexin in hens-broilers (A) and turkeys (B) (2016-2023)

(A) Hens-broilers *(B) Turkeys*

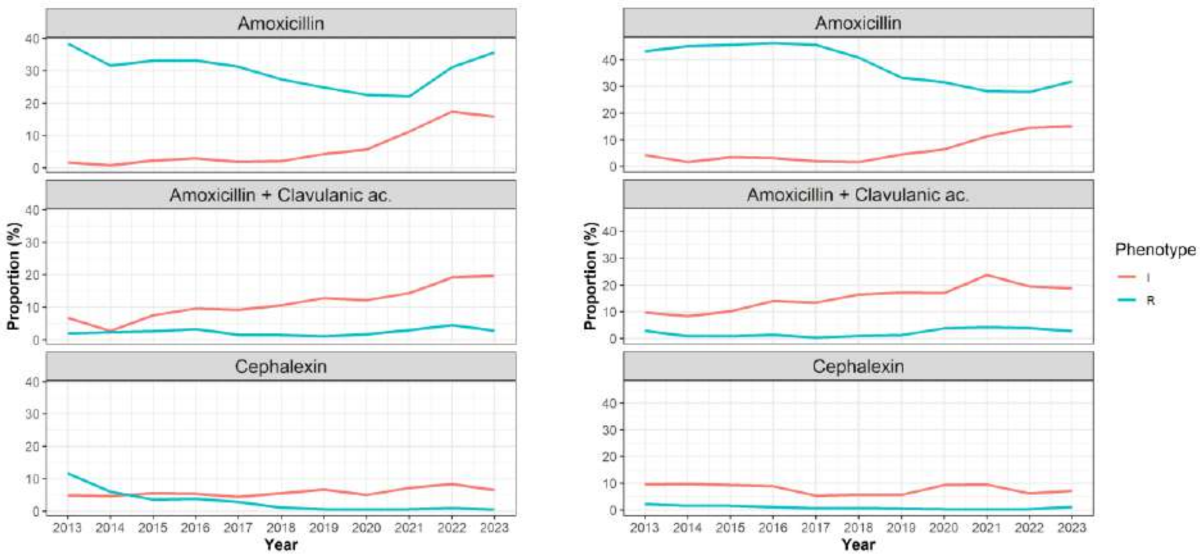
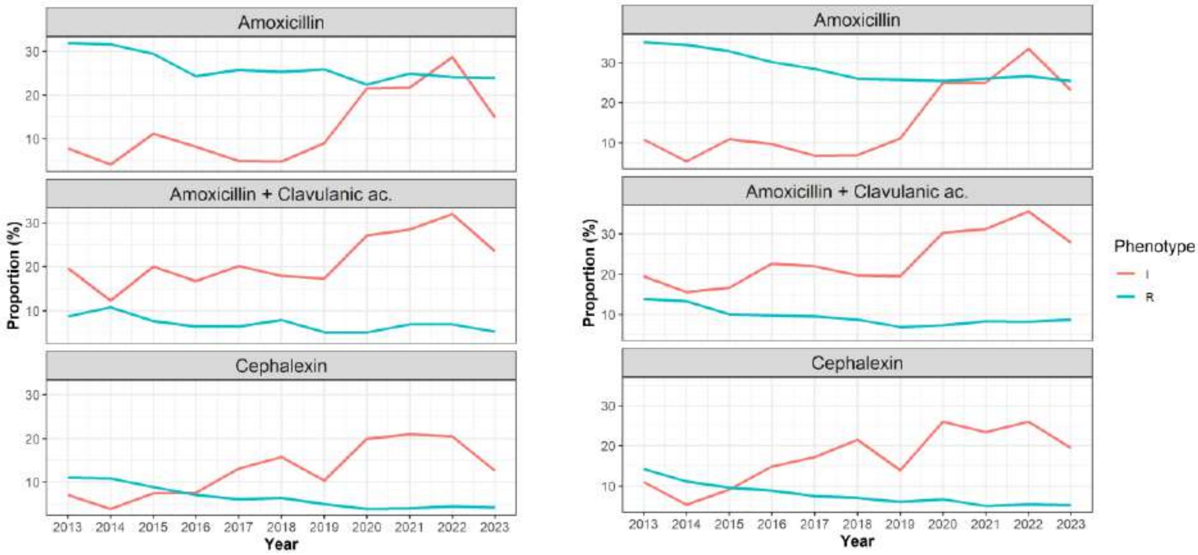


Figure 24. Evolution of proportions (%) of E. coli intermediate or resistant to amoxicillin, amoxicillin + clavulanic acid or cephalexin in cats (A) and dogs (B) (2016-2023)

(A) Cats *(B) Dogs*



- ✓ For all animal species presented here, an upward trend in the proportions of isolates categorised intermediate to amoxicillin and amoxicillin+clavulanic acid has been observed since 2016. *(Figures 22 to 24).*

- ✓ For cats and dogs, there is also an increase in the proportion of intermediate isolates to cephalexin over the same period. For these two animal species, the increase stopped in 2023 for all three antimicrobials. This break in evolution is enhanced by a significant increase of data (+65%) from a new laboratory in 2023 (Figure 24).
  The data for cephalexin, combined with those for amoxicillin (with or without clavulanic acid), suggest an increase in the rate of *E. coli* with their slightly de-repressed intrinsic cephalosporinase.

- ✓ However, for these antimicrobials, the switch from the category sensitive to the category intermediate for *E. coli* strains can also be influenced by variations in disc diffusion methodology used in France by the veterinary laboratories, especially the type of disc supplier.

- ✓ An increase in the proportions of resistant isolates to amoxicillin (excluding intermediate category) was noted for hens-broilers and turkeys, since 2021 and 2022, respectively *(figure 23).*

- ✓ Between 2016 and 2023, rates of amoxicillin resistant strains (excluding intermediate category) remain high in cattle (>60%) and pigs (>40%), although there has been a slight decline over the past two years *(Figure 22)*.

E. coli - Resistance trends to other antibiotics

Method

Resistance trends of *E. coli* to other antibiotics were analysed for cattle, pigs, poultry (hens-broilers and turkeys separately), dogs, cats and horses.
Six antibiotics representing five antibiotic classes were analysed.
Data are displayed for the 2013-2023 period.

*Figure 25. Evolution of proportions (%) of E. coli isolates non-susceptible (R+I) to six antimicrobials in **cattle** (2013-2023).*

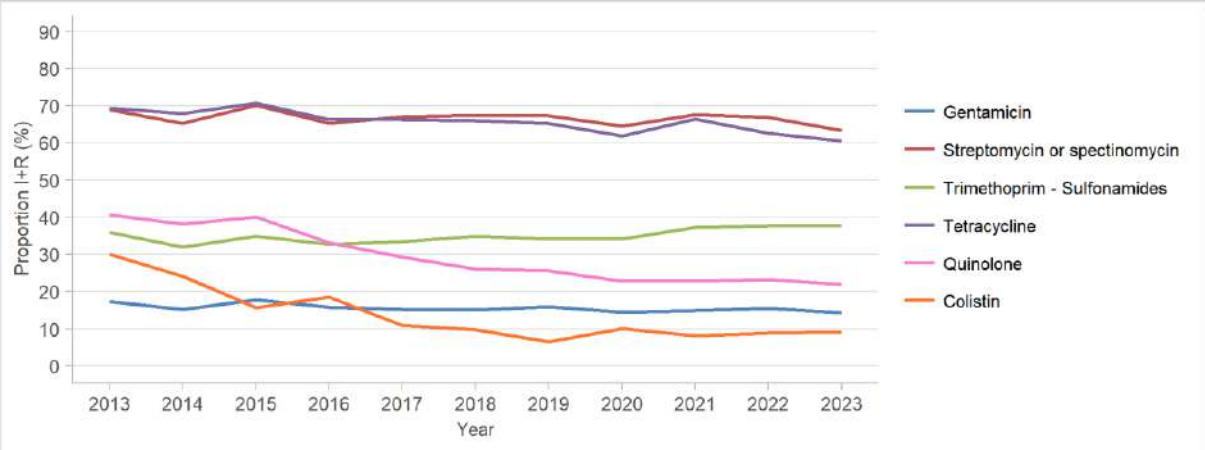


*Figure 26. Evolution of proportions (%) of E. coli isolates non-susceptible (R+I) to six antimicrobials in **pigs** (2013-2023).*

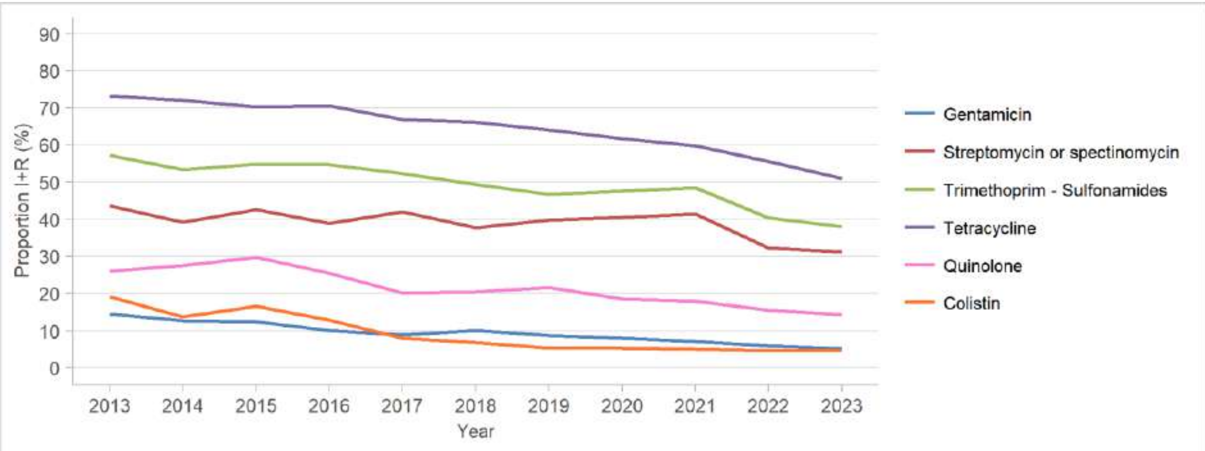


*Figure 27. Evolution of proportions (%) of E. coli isolates non-susceptible (R+I) to six antimicrobials in **hens and broilers** (2013-2023).*

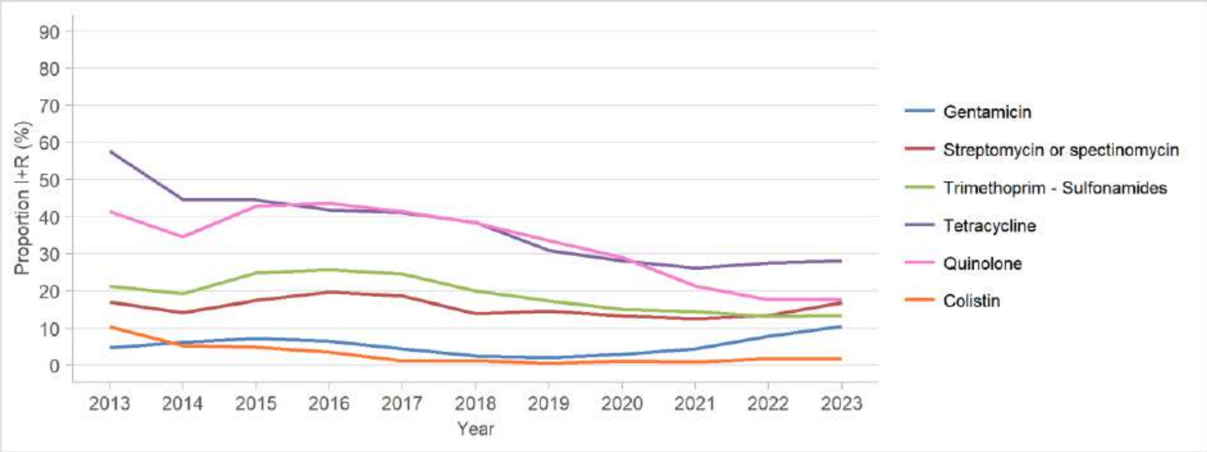


*Figure 28. Evolution of proportions (%) of E. coli isolates non-susceptible (R+I) to six antimicrobials in **turkeys** (2013-2023).*

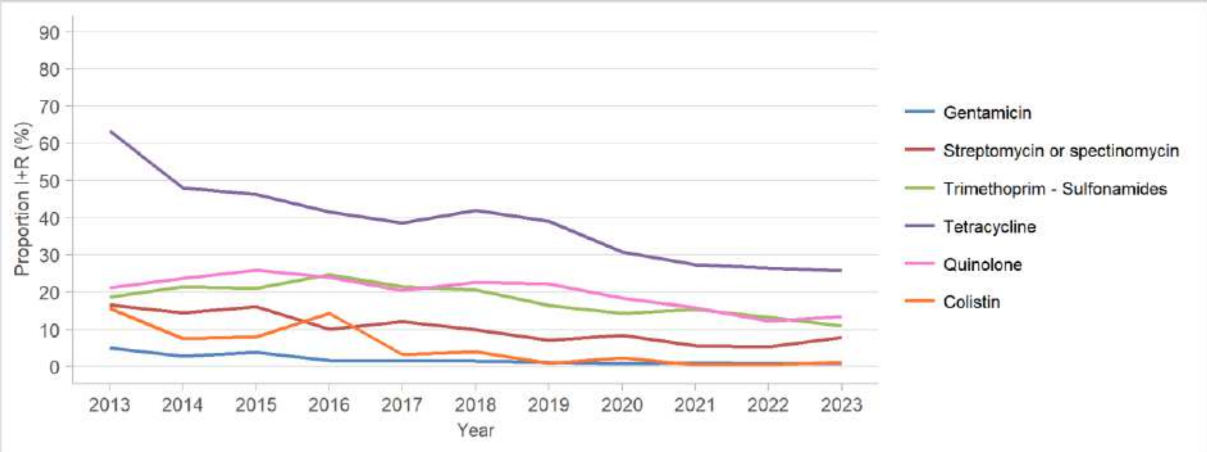


*Figure 29. Evolution of proportions (%) of E. coli isolates non-susceptible (R+I) to six antimicrobials in **dogs** (2013-2023).*

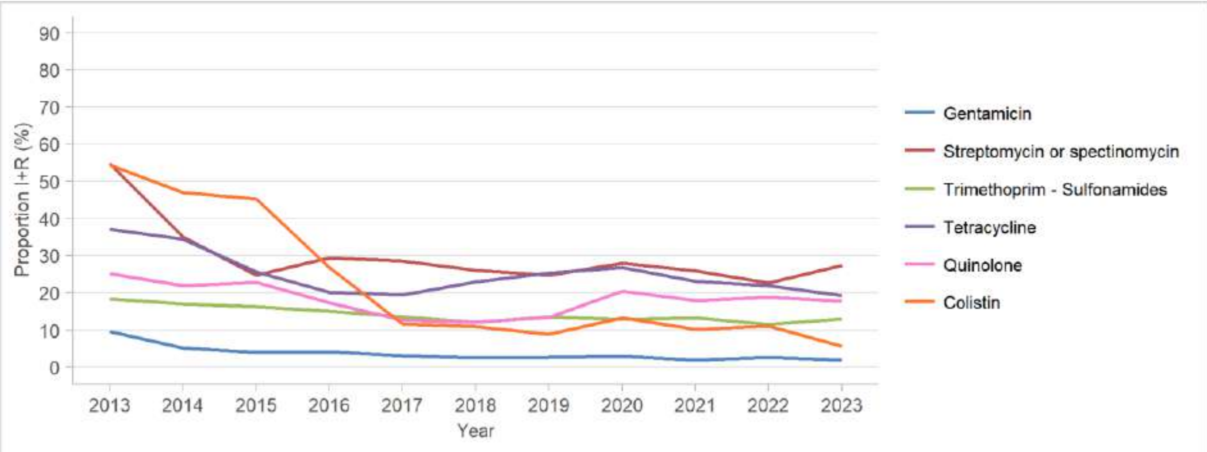


Figure 30. Evolution of proportions (%) of E. coli isolates non-susceptible (R+I) to six antimicrobials in ***cats*** *(2013-2023).*

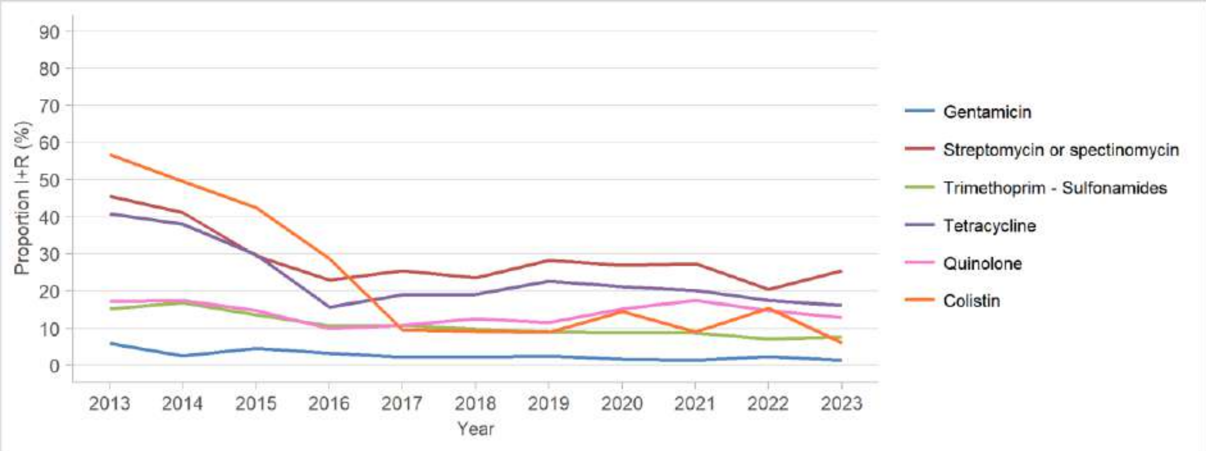
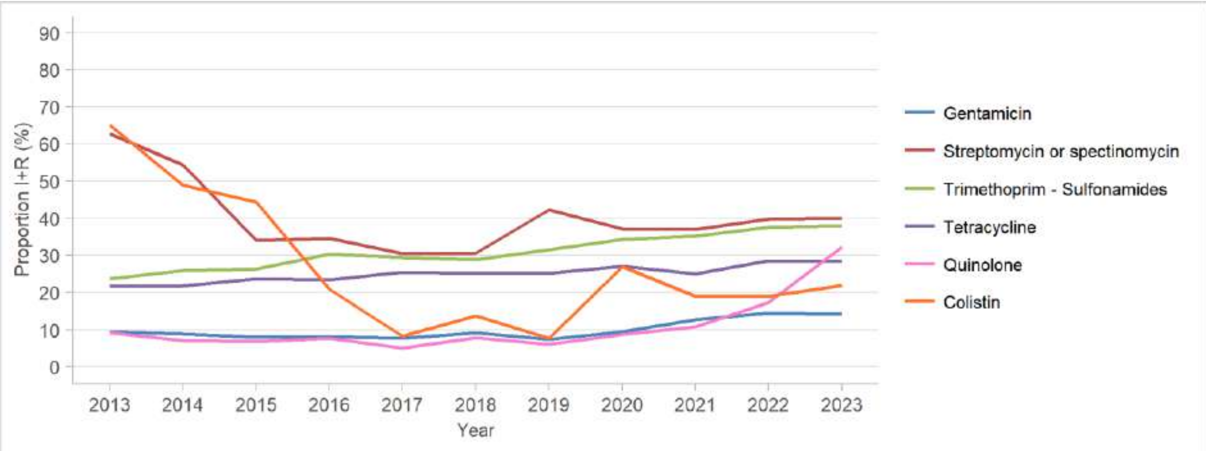


Figure 31. Evolution of proportions (%) of E. coli isolates non-susceptible (R+I) to six antimicrobials in ***horses*** *(2013-2023).*



- ✓ For all animal species considered, trends are generally decreasing or stabilizing for production animals (cattle, pigs, and poultry) *(Figures 25 to 31).*
- ✓ However, a trend reversal has been observed in recent years for gentamicin in the "hens and broilers" category *(Figure 27).*
- ✓ Resistance proportions are decreasing in dogs and cats, except for quinolones, which show a slight increase *(Figures 29 and 30).*
- ✓ Over the last ten years, resistance to colistin has significantly decreased in all animal species.
- ✓ A significant increase in resistance to quinolones is also observed in horses, and to a lesser extent, to gentamicin and the trimethoprim-sulfonamides combination *(Figure 31).*

E. coli - Multidrug resistance and multidrug susceptibility

The accumulation of resistance mechanisms in bacteria can lead to treatment failures. The evolution of the presence of multidrug resistant (MDR) *E. coli* strains is analysed annually using Resapath data. In the past, the indicator of multidrug resistance used by the Resapath included resistance to critically-important antimicrobials (3GC/4GC and fluoroquinolones). Considering that resistance to these antibiotic classes has substantially decreased over the past 10 years, the Resapath team has considered it was now less relevant to include them into the definition of multidrug resistance. Since 2021, the multidrug resistance definition has changed as follows.

Method

Multidrug resistance to antimicrobials (MDR) is defined here as acquired resistance (I or R phenotype) to three or more distinct antimicrobial substances among the following ones: amoxicillin, gentamicin, tetracycline, trimethoprim-sulfamethoxazole, nalidixic acid.
Multidrug susceptibility: susceptibility to all five antimicrobials.

Only *E. coli* tested for each of the five antimicrobials were included. Analyses were performed on:

- Evolution of proportions of MDR and multi-susceptible isolates collected between 2013 and 2023.
- Number of resistances (none, 1, 2, 3 4, or 5) for different animal species and age categories.

Figure 32. Evolution between 2013 and 2023 of the proportions (%) of multidrug resistant E. coli isolates

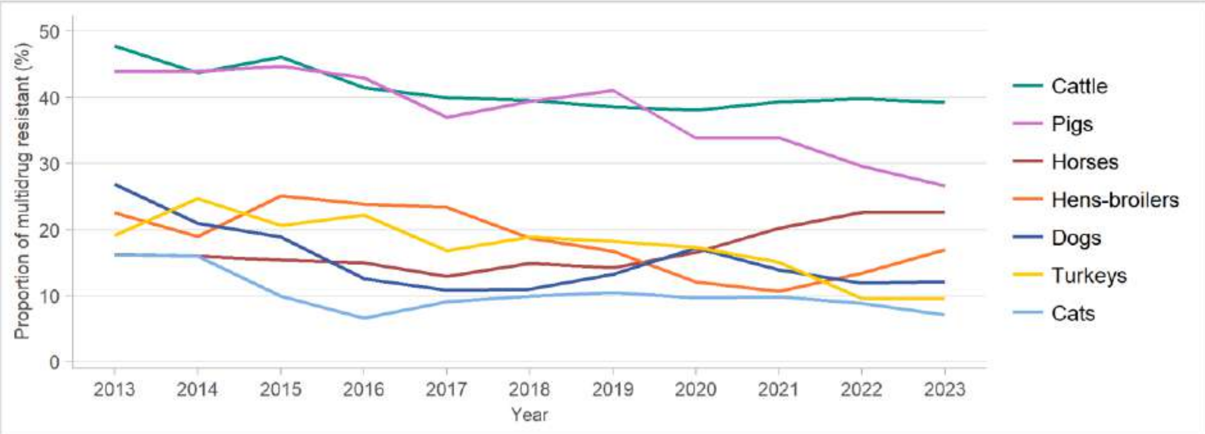
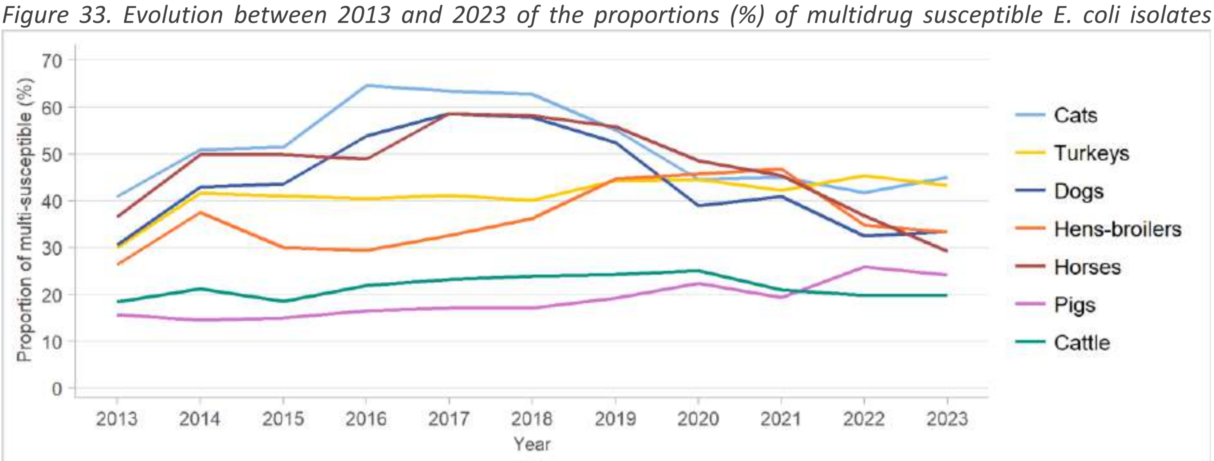


Figure 33. Evolution between 2013 and 2023 of the proportions (%) of multidrug susceptible E. coli isolates



Evolutions between 2022 and 2023 are broadly in line with those seen in recent years, with the following notable exceptions (*Figures 32 and 33*):

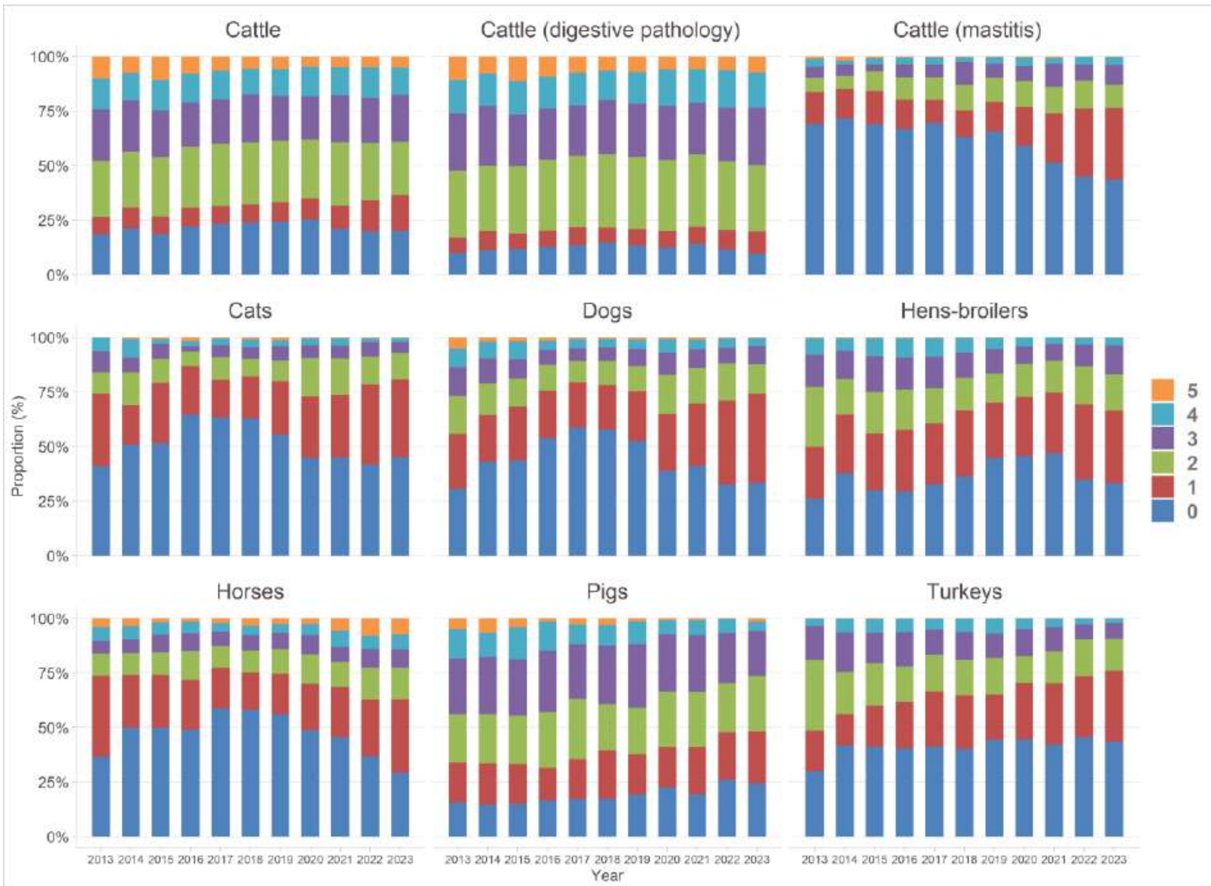
(i) in livestock, the trend over the last ten years has been positive for pigs and turkeys (MDR *E. coli* levels decreased (-39% and -50% respectively since 2013). On the other hand, the situation, which has shown little change over the past 10 years, is more worrying for cattle, with MDR *E. coli* proportions at around 40%, and multi-susceptible *E. coli* proportions around 20%. In hens-broilers, there has even been an increase in MDR *E. coli* (+59%) and a drop in multi-susceptible *E. coli* (-29%) since 2021.

(ii) in domestic cats and dogs, a fairly favorable situation is observed since 2020, with MDR *E. coli* proportions stabilized around 14% in dogs and 9% in cats, and multi-susceptible *E. coli* proportions stabilized around 36% in dogs and 44% in cats.

(iii) in horses, a rather unfavorable trend is observed since 2017, with an increase in MDR *E. coli* proportions (from 13% in 2017 to 23% in 2023) and a decrease in multi-susceptible *E. coli* (from 59% in 2017 to 29% in 2023).

The distribution profiles of strains according to their phenotype (multi-susceptible, carrying one, two, three, four or five joint resistances) show the disparities that exist between animal species (*Figure 34*). These disparities also exist, in certain cases, depending on the pathological context within the same species. For cattle in 2023, for example, 50% of *E. coli* isolates isolated from digestive infections are MDR, compared with 13% for isolates associated to mastitis.

Figure 34. Evolution in the proportions of E. coli *isolates resistant to none, 1, 2, 3, 4 or 5 of the antimicrobials tested, for various animal species and pathologies*



Limitations in the definition of MDR *E.coli*

The proportion of multi-resistant isolates in a given sector is a relatively accurate macro indicator of selection pressure in that sector. Indeed, the greater the overall exposure of animals to antibiotics, the higher the proportion of multi-resistant strains over time. A decreasing trend in this proportion thus globally reflects the efforts to reduce the use of antibiotics, and therefore the exposure of bacterial flora, in the sector under consideration.

The choice of antibiotics for this indicator is fairly straightforward in human medicine. It involves listing the five or six most representative molecules of antibiotic consumption in humans. In veterinary medicine, the construction of such an indicator is more difficult, due to the diversity of animal species and therefore the diversity of antibiotics used for each of them. To date, Resapath has chosen to define the same panel of five antibiotics (see above) for all animal species, with the aim of comparing the different sectors with a single indicator.

However, this type of indicator should also be useful to veterinary practitioners, enabling them to identify levers of action in terms of antibiotic use in the event of unfavorable resistance trends. For equines, for example, in which amoxicillin is not used, monitoring resistance to this antibiotic does not provide relevant information on the current practice. At the Resapath level, we are therefore considering the development of one or more indicators more closely linked to the use of antibiotics in specific animal species. The design of one or more indicators of this type is closely linked to the availability of antibiotic use data via the Calypso system (which is starting to collect data on antibiotic prescribing and dispensing in France since 2023), and must include antibiotics regularly tested by diagnostic laboratories, in order to maintain a sufficient number of isolates for multi-resistance analysis.

3GC/4GC and carbapenem resistance in *Enterobacter hormaechei* isolated from dogs, cats and horses

Enterobacter hormaechei is an important human and animal pathogen which, in addition to its intrinsic AmpC beta-lactamase, can acquire a wide variety of genes conferring resistance to extended-spectrum cephalosporins (ESCs) and carbapenems (CPs). In France, clinical outbreaks of *E. hormaechei* resistant to ESC or CP have recently been reported in humans. Since last year, we decided to have a special look at this pathogen, which we thus included in the focus of the Resapath report. To complement the network's phenotypic data and to understand the transmission routes of this pathogen, we performed a molecular study on *E. hormaechei* isolates collected from cats, dogs and horses and presenting a beta-lactam non-susceptible phenotype.

For this purpose, 114 *E. hormaechei* isolates were whole-genome sequenced using the Illumina technology and five isolates were long-read sequenced (MinION) to better characterize plasmids carrying ESC and CP resistance determinants. Phenotypes were characterized by antibiograms using disc diffusion.

A clear divergence in molecular epidemiology was observed depending on the host. In cats and dogs, most isolates had an overexpressed *ampC* gene or the $bla_{\text{CTX-M-15}}$ gene carried by an IncHI2 plasmid, and eight isolates (8/59, 14%) had a $bla_{\text{OXA-48}}$ carbapenemase. Thirty-two isolates (54%) belonged to the high-risk human clones ST78, ST114 and ST171. In horses, on the other hand, ESC resistance was mainly due to the $bla_{\text{SHV-12}}$ and $bla_{\text{CTX-M-15}}$ genes carried by an IncHI2 plasmid, and very few high-risk clones were identified (5/55, 9%).

The potential for selection through antibiotic use (which is increasing in France for cats, dogs and horses), the dissemination capacities of IncHI2 conjugative plasmids and occurrence of high-risk clones, and the possible transfer of resistant bacteria between humans and animals clearly indicate that *E. hormaechei* antibiotic resistance needs to be closely monitored from a One Health perspective.

Emergence of MRSA ST612 in horses and methicillin-susceptible *S. aureus* CC398 in cats

Staphylococcus aureus (SA) is an important zoonotic pathogen that has often been observed in animals through the prism of CC398 methicillin-resistant strains (MRSA) widely disseminated in asymptomatic pigs and humans in contact. In a context where the EFSA will be conducting a large-scale survey in 2025 on the prevalence of MRSA in pigs in Europe, we determined precisely the prevalence of this pathogen in cats, dogs and horses in France. Data from Resapath always involve a degree of uncertainty, since MRSA strains are categorized on the basis of phenotypic resistance to cefoxitin, and not on the basis of molecular detection of the *mecA* or *mecC* genes. We also took advantage of this large-scale study to document the presence of methicillin-susceptible SA (MSSA) belonging to the CC398 clone, which are pathogens causing severe bacteremia in humans.

In this study, 479 clinical *S. aureus* isolates from 143 dogs, 186 cats and 150 horses were characterized. Antibiograms were performed on all isolates, and those considered MRSA and MSSA CC398 were short-read sequenced (Illumina). Phylogenetic analyses based on core-genome MLST and Single Nucleotide Polymorphisms (SNPs) were also carried out.

Sixty-six MRSA were identified in 9 dogs (6%), 14 cats (8%), and 43 horses (29%). MRSA epidemiology in cats and dogs has remained stable since 2015, with the presence of CC398 and human-associated clones. On the contrary, in horses, a significant increase in MRSA (from 10% to 29%) was observed, potentially attributable to the emergence of the ST612 clone. At the same time, 68 MSSA CC398 were identified. This clone, usually described as animal-independent, was found in 24.2% of cat isolates.

This study, which paves the way for genomic surveillance of *S. aureus* in France, strongly suggests that MRSA clones ST612 and MSSA CC398 need to be closely monitored to prevent their zoonotic spread, and to understand their transmission dynamics between humans and animals.

Appendices

Appendix 1. Laboratories contributing to Resapath (2023)

Laboratoire Départemental d'Analyses
Chemin de la Miche Cénord
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Laboratoire Départemental d'Analyses et de Recherche
180 Rue Pierre Gilles de Gennes
ZA du Griffon
BARENTON BUGNY
02007 LAON CEDEX

Eurofins Laboratoire Coeur de France
Zone Industrielle de l'Etoile
Boulevard de Nomazy
BP 1707
03017 MOULINS CEDEX

SELARL VETALLIER
96 Grand Rue
03420 MARCILLAT-EN-COMBRAILLE

Laboratoire Départemental Vétérinaire et Hygiène Alimentaire
5 rue des Silos
BP 63
05002 GAP CEDEX

Laboratoire Vétérinaire Départemental
105 route des Chappes
06410 BIOT

Laboratoire Départemental d'Analyses
Rue du chateau
BP 2
08430 HAGNICOURT

Laboratoire d'Analyses Vétérinaires et Alimentaires du département
Chemin des Champs de la Loge
CS 70216
10006 TROYES CEDEX

Aveyron Labo
Parc d'activités de Bel Air
195 Rue des Artisans
12031 RODEZ CEDEX 9

Laboratoire Départemental d'Analyses
29 rue Jolliot Curie
Technopole de Château-Gombert
CS 60006
13455 MARSEILLE CEDEX 13

ANSES laboratoire de pathologie équine de Dozulé
RD 675
14430 GOUSTRANVILLE

LABEO Frank DUNCOMBE
1 route de Rosel
14053 SAINT-CONTEST CEDEX 4

VETODIAG
6 Route du Robillard
14170 SAINT-PIERRE-EN-AUGE

Laboratoire Terana Cantal
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15013 AURILLAC CEDEX

Laboratoire Départemental d'Analyses de la Charente
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16000 ANGOULEME

Laboratoire Terana Cher
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18000 BOURGES

Laboratoire Départemental de la Côte-d'Or
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CS 71778
21017 DIJON CEDEX

LABOCEA PLOUFRAGAN
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22440 PLOUFRAGAN

LABOFARM
4 rue Théodore Botrel
BP 351
22600 LOUDEAC

LABOFARM ARMOR
Kergré
22970 PLOUMAGOAR

VET&SPHERE Quintin
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22800 QUINTIN

TERANA Creuse
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23380 AJAIN

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Laboratoire Vétérinaire Départemental
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BP 1981
25020 BESANCON CEDEX

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26120 CHABEUIL

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26300 BOURG-DE-PEAGE

KER-VET
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29610 PLOUIGNEAU

LABOCEA QUIMPER
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ZA de Creach Gwen
CS 13031
29334 QUIMPER CEDEX

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ZAC mas des abeilles
30000 NIMES

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LD 31 EVA
76, chemin Boudou
31140 LAUNAGUET

SOCSA Analyse
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31240 L'UNION

Public labos site du Gers
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32020 AUCH CEDEX 9

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34967 MONTPELLIER CEDEX 2

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35220 CHATEAUBOURG

BIOVILAINE
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35600 REDON

Laboratoire Biovilaine Janzé
57 Rue Paul Painlevé
35150 JANZE

LABORATOIRE DE BROCELIANDE
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ZA du Maupas
35290 SAINT-MEEN-LE-GRAND

LABOCEA - site de Fougères
BioAgroPolis
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JAVENE
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35306 FOUGERES CEDEX

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44327 NANTES CEDEX 03

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ZAC de l'Aeropole
44150 ANCENIS SAINT GEREON

MC Vet Conseil - Quiers
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45270 QUIERS-SUR-BEZONDE

SOCSA ELEVAGE
SELARL de vétérinaires du Val Dadou
ZI Piquemil
47150 MONFLANQUIN

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18 bd Lavoisier
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49009 ANGERS CEDEX 01

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ZI Evre et Loire
49600 BEAUPREAU-EN-MAUGES

YZIVET
ZA de la Charte Bouchère
49360 YZERNAY

LABEO Manche
1352 Avenue de Paris
CS 33608
50008 SAINT-LO CEDEX

Laboratoire Départemental d'Analyse
Rue du Lycée Agricole
CHOIGNES
CS 32029
52901 CHAUMONT CEDEX 9

Laboratoire Départemental d'Analyses
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BP 1427
53014 LAVAL CEDEX

MC Vet Conseil - Lab-elvet
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53810 CHANGE

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Départemental
Domaine de Pixérécourt
BP 60029
54220 MALZEVILLE

LABOFARM MOREAC
ZA Du Bronut
56500 MOREAC

INOVALYS VANNES
5 rue Denis Papin
BP 20080
56892 SAINT-AVE CEDEX

Laboratoire RESALAB BRETAGNE
site Anibio
ZI du Douarin
56150 GUENIN

SELARL VET&SPHERE Malestroit
Zone industrielle de Tirpen
56140 MALESTROIT

TERANA NIEVRE
Rue de la Fosse aux loups
58000 NEVERS

Laboratoire Départemental Public
Domaine du CERTIA
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BP 20039
59651 VILLENEUVE-D'ASCQ CEDEX

LABEO ORNE
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CS 60007
61001 ALENCON CEDEX

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62500 SAINT-OMER

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62022 ARRAS CEDEX

TERANA Puy de Dôme
20 Rue Aimé Rudel
63370 LEMPDES

Bio-Chêne Vert Arzacq Arraziguet
Route de Samadet
64410 ARZACQ ARRAZIGUET

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Site de Lagor
64150 LAGOR

Laboratoire Alsacien d'Analyses (L2A)
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68000 COLMAR

Laboratoire des Leptospires et analyses vétérinaires (LAV)
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ORBIO LABORATOIRE
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69500 BRON

Laboratoire Départemental Vétérinaire et d'Hydrologie
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70000 VESOUL

Laboratoire AGRIVALYS 71
Espace DUHESME
18 Rue de Flacé
71000 MACON

Laboratoire Val de Saône
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71680 CRECHES-SUR-SAONE

Bio-Chêne Vert Saint-Mars
72470 SAINT MARS LA BRIERE

INOVALYS LE MANS
128 rue de la Beaugé
72018 LE-MANS CEDEX

MC Vet Conseil - Sablé
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72300 SABLE-SUR-SARTHE

Laboratoire Départemental d'Analyses Vétérinaires
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73024 CHAMBERY CEDEX

Lidal – laboratoire vétérinaire départemental
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SEYNOD
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74600 ANNECY

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76175 ROUEN CEDEX

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79130 SECONDIGNY

FILIAVET BRESSUIRE
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Zone Alphaparc sud
79300 BRESSUIRE

QUALYSE
ZAE Montplaisir
79220 CHAMPDENIERS

Laboratoire Départemental d'Analyses
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Laboratoire Départemental d'Analyses
du VAR
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Pôle d'activité Hyèrois
83400 HYERES

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85140 LES ESSARTS

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Parc des judices
85300 CHALLANS

LABOVET CONSEIL site des Essarts
28 rue des Sables
85140 ESSARTS-EN-BOCAGE

LABOVET
ZAC de la Buzenière
BP 539
85500 LES-HERBIERS

LCE, SELARL Mathon et Bonal
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ZA de Mirville - Bellevue
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87005 LIMOGES

Laboratoire Départemental Vétérinaire Alimentaire
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BP 1027
88050 EPINAL CEDEX 09

AUXAVIA
45 Route d'Auxerre
89470 MONETEAU

Laboratoire Cerba Vet
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91300 MASSY

Laboratoire de Bactériologie biopôle ALFORT
Ecole Nationale Vétérinaire d'Alfort
7 Avenue du Général De Gaulle
94704 MAISONS-ALFORT CEDEX

Appendix 2. Resapath performance indicators

Performance indicators are quantitative tools for monitoring the proper functioning and operations of an epidemiological surveillance network. These performance indicators are essential to identify the weak points of an activity and adopt the optimal corrective measures. For Resapath, fifteen indicators are being monitored. The results are presented for the period 2019-2023 and discussed for the year 2023 *(Table 1).*

Table 1 - Resapath performance indicators for the years 2019 to 2023

In green: result equal to or greater than the expected value | In pink: result lower than the expected value

	Indicator	Expected value	2019	2020	2021	2022	2023	Comments
NETWORK OPERATIONS	Number of collected antibiograms	*Steady or increase*	53,469	51,736	62,070	70,604	93,285	The number of antibiograms collected in 2023 is increasing sharply (+32% compared to 2022). This very positive development is linked to the integration of many laboratories in recent years, including two in 2023. Five laboratories left the network due to *i)* the cessation of their bacteriology activity, *ii)* merging with another laboratory, *iii)* a decision from the laboratory.
	Number of contributing laboratories (laboratory sites)	*Steady or increase*	75	77	101	108	105	
	Proportion of laboratories having transmitted their antibiograms data	*90%*	100%	100%	99%	100%	100%	
	Proportion of laboratories transmitting their data at a rate consistent with the membership charter (at least quarterly)	*80%*	*Not available*	*Not available*	71%	96%	97%	Laboratories are made aware throughout the year of the importance of regularly sending their data for the proper functioning of the system. The efforts made in 2022 continued in 2023: 97% of laboratories sent their data to ANSES at least quarterly.
	Proportion of antibiograms received at ANSES and included in the database within 4 months upon analysis of the sample	*60%*	79%	60%	74%	97%	93%	Despite the very sharp increase in the number of antibiograms transmitted to the network, the rate of data integration into the RESAPATH database remains at a very satisfactory level.
	Proportion of laboratories with a completeness rate of submitted data[1] higher than or equal to 70%	*75%*	71%	67%	74%	75%	77%	In 2023, ¾ of laboratories reach the level of completeness expected by the network, but only 53% of antibiograms are considered fully complete. For continuous improvement, since 2022, each laboratory has received an annual completeness report on its data transmitted to RESAPATH.

Indicator		Expected value	2019	2020	2021	2022	2023	Comments
COORDINATION	Publication rate of annual reports (number of reports expected per year =1)	*100%*	**100%**	**100%**	**100%**	**100%**	**100%**	The 2022 results have been published in French and English. The data are accessible via the electronic annual report presenting the main monitoring results and via the **RESAPATH online** application which provides detailed numerical data.
COORDINATION	Website update frequency (maximum 3-month period expected between two updates of the website)	*100%*	*No regular update*				**100%**	The website underwent a major content refresh in 2023. The site would require a more in-depth update on a regular basis.
COORDINATION	Completion rate of the steering committee meeting (number of meetings expected per year=1)	*100%*	**100%**	**0%**	**100%**	**100%**	**100%**	The steering committee met by videoconference on June 8, 2023. This later than usual schedule made it possible to present and discuss the data from the 2023 annual report ahead of its publication.
SCIENTIFIC & TECHNICALL SUPPORT	Completion rate of Resapath laboratories meeting (feedback, training and exchanges) (number of meetings expected per year=1)	*100%*	**100%**	**100%**	**100%**	**0%**	**100%**	The annual training and exchange day with laboratories, scheduled for December 2022, could not be held due to strike movements impacting the participants' travel. The day was postponed to March 2023 by videoconference.
SCIENTIFIC & TECHNICALL SUPPORT	Participation rate of laboratories to the Resapath annual meeting	*65%*	**45%**	*Not available*		*Not applicable*	*Not available*	
SCIENTIFIC & TECHNICALL SUPPORT	Rate of responses given within 15 days upon reception of the question from the member laboratories	*60%*	**72%** *(50/69)*	**77%** *(34/44)*	**89%** *(42/47)*	**79%** *(37/47)*	**74%** *(39/53)*	Nearly ¾ of the questions asked by member laboratories were answered by the RESAPATH team within a fortnight. This result demonstrates the efforts made by the RESAPATH team to commit to rapid response to participating laboratories

Indicator	Expected value	2019	2020	2021	2022	2023	Comments
Participation rate of laboratories in the ring trial[2]	*100%*	**100%** *(75/75)*	**100%** *(76/76)*	**100%** *(79/79)*	**99%** *(84/85)*	**98%** *(104/106)*	Almost all laboratories took part in the ring trial (Nov. 2022-Feb. 2023). Two laboratories left the network during this period and therefore did not participate.
Rate of laboratories scoring 40/48 or more to ring trial technical part[3]	*95%*	**97%** *(73/75)*	**99%** *(75/76)*	**99%** *(78/79)*	**100%** *(84/84)*	**99%** *(103/104)*	The annual ring trial was marked by the implementation of a new format related to aspects of anonymization and non-collusion between laboratories. The number of strains to be tested was increased from six to eight, covering two different bacterial species. The results were very satisfactory overall, both in terms of the implementation of the method itself, as well as the interpretation of phenotypes and the comments provided to veterinarians.
Rate of laboratories scoring 6/8 or more to ring trial interpretation part[3]	*95%*	**88%** *(66/75)*	**83%** *(63/76)*	**80%** *(63/79)*	**96%** *(81/84)*	**95%** *(99/104)*	

[1] The data used to estimate the completeness of the data are the sample department of origin, the age of the animal, the type of sample and/or the pathology.

[2] Some laboratories with several laboratory sites carry out the annual ring trial as a group and return a single result. Each site is counted as a participant and assigned a unique score. Only laboratories that were Resapath members at the time of the ring trial are counted in the denominator.

[3] Until 2022, the mark to be achieved was greater than or equal to 31/36 for the technical part and 5/6 for phenotypes interpretation.

Appendix 3. Publications linked to Resapath activities (2023)

International peer-reviewed publications

Azaiez S, Haenni M, Cheikh AB, *et al.* (2023) Healthcare Equipment and Personnel Reservoirs of Carbapenem-Resistant *Acinetobacter baumannii* Epidemic Clones in Intensive Care Units in a Tunisian Hospital. *Microorganisms.* 11(11):2637. DOI : 10.3390/microorganisms11112637

Babu Rajendran N, Arieti F, Mena-Benítez CA*, et al.* (2023) EPI-Net One Health reporting guideline for antimicrobial consumption and resistance surveillance data: a Delphi approach. *The Lancet Regional Health - Europe*. 26:100563. DOI :10.1016/j.lanepe.2022.100563

Bourély C, Rousset L, Colomb-Cotinat M, Collineau L (2023) How to move towards One Health surveillance? A qualitative study exploring the factors influencing collaborations between antimicrobial resistance surveillance programmes in France. *Frontiers Public Health.* 11:1123189. DOI: 10.3389/fpubh.2023.1010335

Collineau L, Bourély C, Rousset L*, et al.* (2023) Towards One Health surveillance of antibiotic resistance: characterisation and mapping of existing programmes in humans, animals, food and the environment in France, 2021*. Eurosurveillance.* 28(22):2200804. DOI : 10.2807/1560-7917.ES.2023.28.22.2200804

Coz E, Jouy E, Cazeau G*, et al.* (2023) Evolution of the proportion of colistin-resistant isolates in animal clinical *Escherichia coli* over time - a hierarchical mixture model approach. *Preventive Veterinary Medicine.* 213:105881. DOI : 10.1016/j.prevetmed.2023.105881

Delannoy S, Hoffer C, Tran M-L*, et al.* (2023) High throughput qPCR analyses suggest that Enterobacterales of French sheep and cow cheese rarely carry genes conferring resistances to critically important antibiotics for human medicine. *International Journal of Food Microbiology*. 403:110303. DOI : 10.1016/j.ijfoodmicro.2023.110303

Elankumuran P, Browning GF, Marenda MS*, et al.* (2023) Identification of genes influencing the evolution of *Escherichia coli* ST372 in dogs and humans. *Microbial Genomics.* 9(2):000930. https://doi.org/10.1099/mgen.0.000930

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