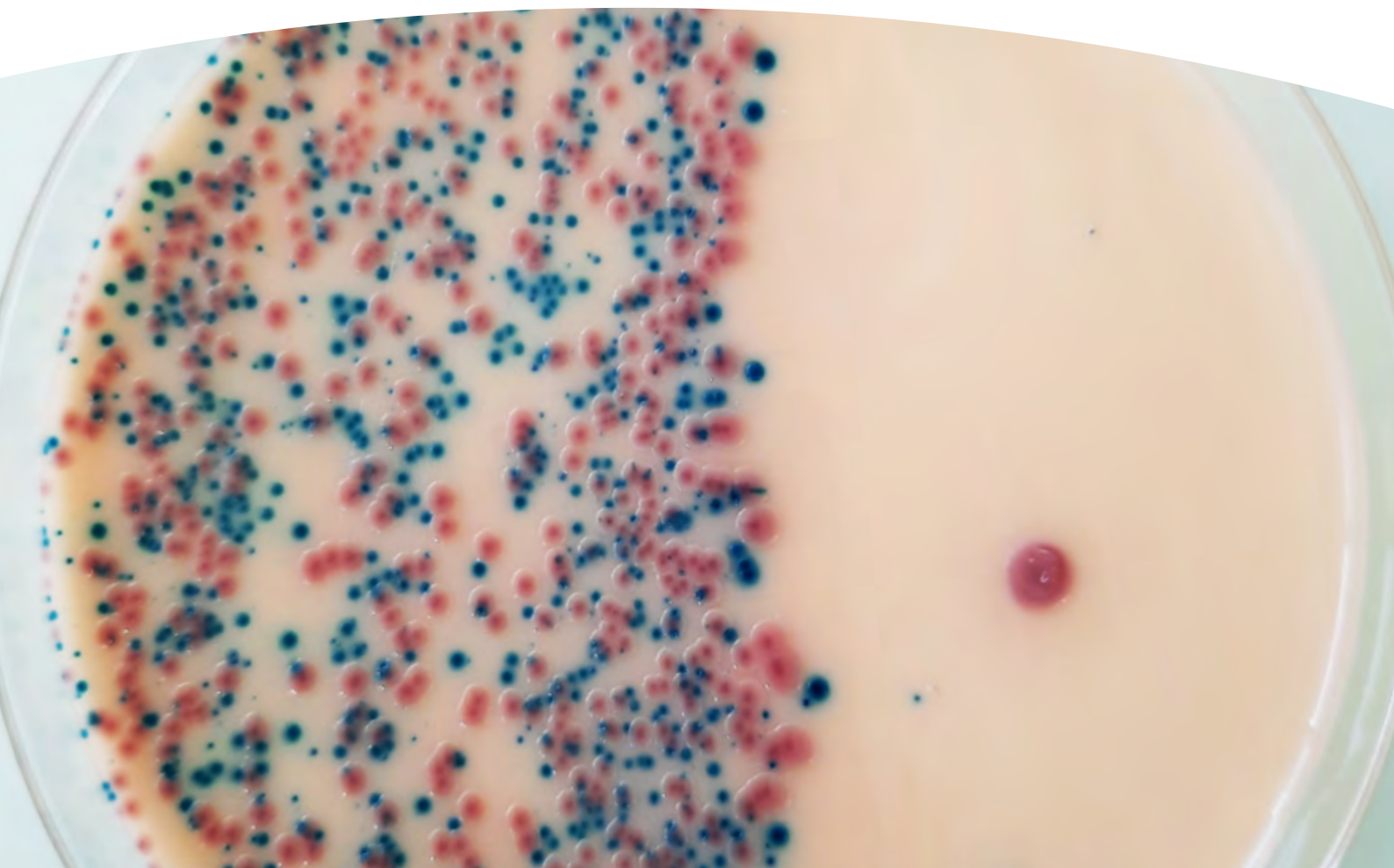


Resapath

French surveillance network
for antimicrobial resistance
in bacteria
from diseased animals

2021 Annual report

November 2022



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

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RESAPATH - HIGHLIGHTS 2021

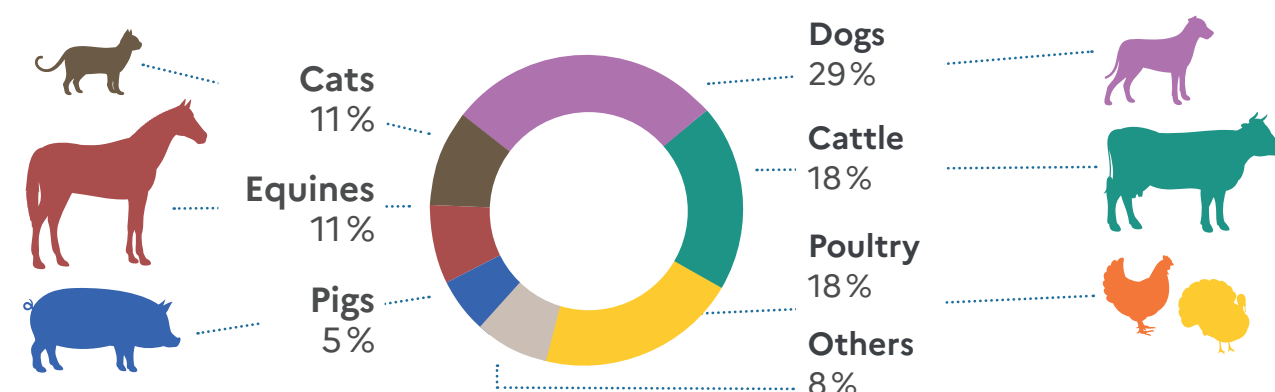
40TH

ANNIVERSARY OF THE RESAPATH

101

PARTICIPATING VETERINARY DIAGNOSTIC LABORATORIES

62,070 ANTIBIOGRAMS COLLECTED FROM



RESISTANCE TO CRITICALLY IMPORTANT ANTIBIOTICS ; EXTENDED-SPECTRUM CEPHALOSPORINS (ESC) AND FLUOROQUINOLONES (ESCHERICHIA COLI)

► Limited proportions of resistance (< 6-8% for all animal species)

RESISTANCE TO COLISTIN *E. COLI*

► Very limited proportions of resistance over the last 4 years (< 10% in pigs and cattle, < 4% in turkeys and < 2% in hens and chickens)

RESISTANCE TO CARBAPENEMS

► Emergence in companion animals (OXA-48)

RESISTANCE TO METHICILLIN

► Limited but depends on animal species for *Staphylococcus aureus* (MRSA)

► Frequent (15-20%) for *Staphylococcus pseudintermedius* (dogs, cats)

RESISTANCE TO OTHER ANTIBIOTICS (*E. COLI*)



► ALL ANIMALS:

All antibiotics : stability or decline EXCEPT

Amoxicillin: Increase or stability

Amoxicillin - clavulanic acid: Increase



► EQUINES:

Increase for trimethoprim-sulfonamide

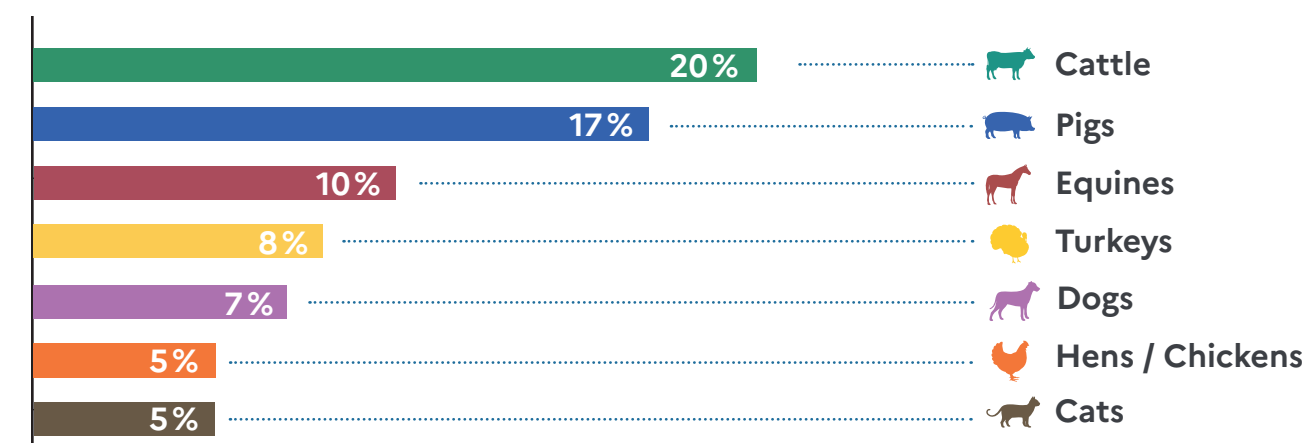
MULTIDRUG RESISTANCE AND MULTI-SUSCEPTIBILITY (*E. COLI*)

MULTIDRUG RESISTANCE: ACQUIRED RESISTANCE (PHENOTYPE I OR R) TO AT LEAST THREE ANTIBIOTICS AMONG THE FIVE TESTED FOR IN THE PANEL: (amoxicillin, gentamicin, tetracycline, trimethoprim-sulfonamides, nalidixic acid)

► Highly variable proportions of multidrug resistant strains from one animal species to another. Multidrug resistance highly depends on type of infections.

► An overall stable or downward trend in the proportions of multidrug resistant strains over the last 5 years, except in equines.

PROPORTIONS OF *E. COLI* MULTIRESTANT STRAINS IN 2021



MULTI-SUSCEPTIBILITY: SUSCEPTIBILITY TO ALL FIVE ANTIBIOTICS TESTED IN THE PANEL

► Around 20% of multi-susceptible *E. coli* in most animal species

► Lower proportions in cattle and pigs (around 10%)

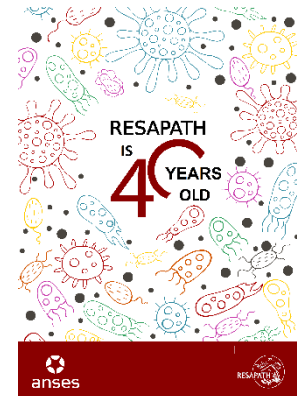
Abbreviations

Abbreviation	Explanation
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 – Antibigram Committee
CIA	critically-important antibiotics
CoNS	Coagulase negative staphylococci
CoPS	Coagulase positive staphylococci
CP-R	Carbapenem resistant
EARS-Net	European Antimicrobial Resistance Surveillance Network
EARS-Vet	European Antimicrobial Resistance Surveillance network in Veterinary medicine
EEA	European Economic Area
EFSA	European Food and Safety Authority
EQA	External quality assessment
ESBL	Extended-spectrum beta-lactamase
ESC	Extended-spectrum cephalosporins
EUCAST	European Committee on Antimicrobial Susceptibility Testing
EU-JAMRAI	European Joint Action on Antimicrobial Resistance and healthcare Associated Infections
FAO	Food and Agriculture Organization
FQ	Fluoroquinolones
IT	Information technology
JPI-AMR	Joint Programming Initiative on Antimicrobial Resistance
MDR	Multidrug resistance
MIC	Minimal inhibitory concentration
MLS_B	Macrolides-Lincosamides-Streptogramins B
MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
MRSP	Methicillin-resistant <i>Staphylococcus pseudintermedius</i>
MSSA	<i>Staphylococcus aureus</i> susceptible to methicillin
ONERBA	French National Observatory for Epidemiology of Bacterial Resistance to Antimicrobials
PRR	National Priority Research Programme on AMR
Resapath	French surveillance network for antimicrobial resistance in bacteria from diseased animals
SSTI	Skin and soft tissue infections
UE	European Union
UTI	Urinary tract infections
WHO	World Health Organization
WOAH	World Organization for Animal Health

Editorial

Created in 1982, the **Resapath network celebrates in 2022 its 40th anniversary** in the service of monitoring antibiotic resistance in animal pathogenic bacteria in France.

Initially created for the bovine sector, then progressively extended to other animal species, Resapath collects the results of antibiograms produced annually by the member laboratories and provides a scientific analysis useful for public policies (Ecoantibio, Interministerial Roadmap).



As a member of the National Observatory of the Epidemiology of Bacterial Resistance to Antibiotics (ONERBA), Resapath also interfaces animal data with those available in human medicine in a **One Health approach**. Also, beyond the resistance phenotypes, the molecular analyses conducted by the Resapath contribute to a better understanding of crossed issues in the three sectors: Human, animal and the environment.

Finally, Resapath's ambition is to monitor animal antibiotic resistance **beyond national borders**, by piloting the European network EARS-Vet set up within the framework of the EU-JAMRAI 1 joint action (2017-2021), and expected to be fully developed within the framework of the EU-JAMRAI 2 joint action (2023-2027).

The Resapath report presents useful raw data but also several in-depth analysis 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 scope 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 result 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 French surveillance programmes in animals, including the European AMR surveillance programme in commensal and zoonotic bacteria¹ from food-producing animals at slaughterhouse and food thereof, and the monitoring of sales and deliveries of antimicrobials for veterinary use² (*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) and EcoAntibio 2 (2017-2022), as well as the Interministerial roadmap for the control of AMR (2016).

Resapath also opens up many opportunities for molecular and genomic surveillance by setting up of 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 Centers, 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 also contributes to the comparisons of AMR data from the human and animal sector facilitated by the National Observatory of the Epidemiology of Bacterial Resistance to Antibiotics (ONERBA)³. 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 will 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 12 European countries and several EU bodies, an initiative that aims to develop a European AMR surveillance network in veterinary medicine (EARS-Vet)⁵.

¹ <https://multimedia.efsa.europa.eu/dataviz-2020/index.htm>

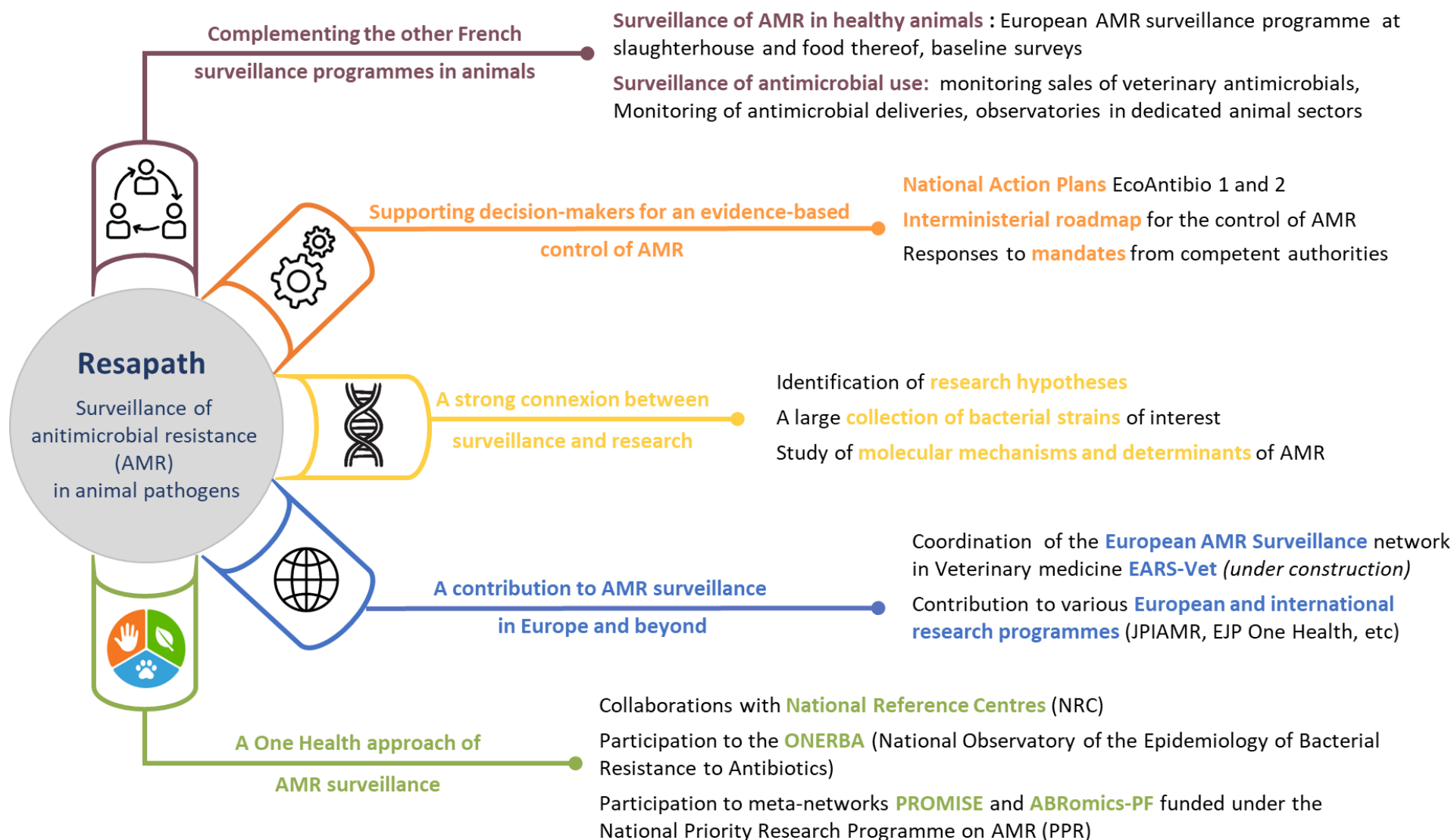
² ANSES 2021. Sales survey of veterinary medicinal products containing antimicrobials in France in 2020, Anses-ANMV, France, November 2021, report, 89 pp. <https://www.anses.fr/en/system/files/ANMV-Ra-Antibiotiques2020EN.pdf>

³ <http://onerba.org/>

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.

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



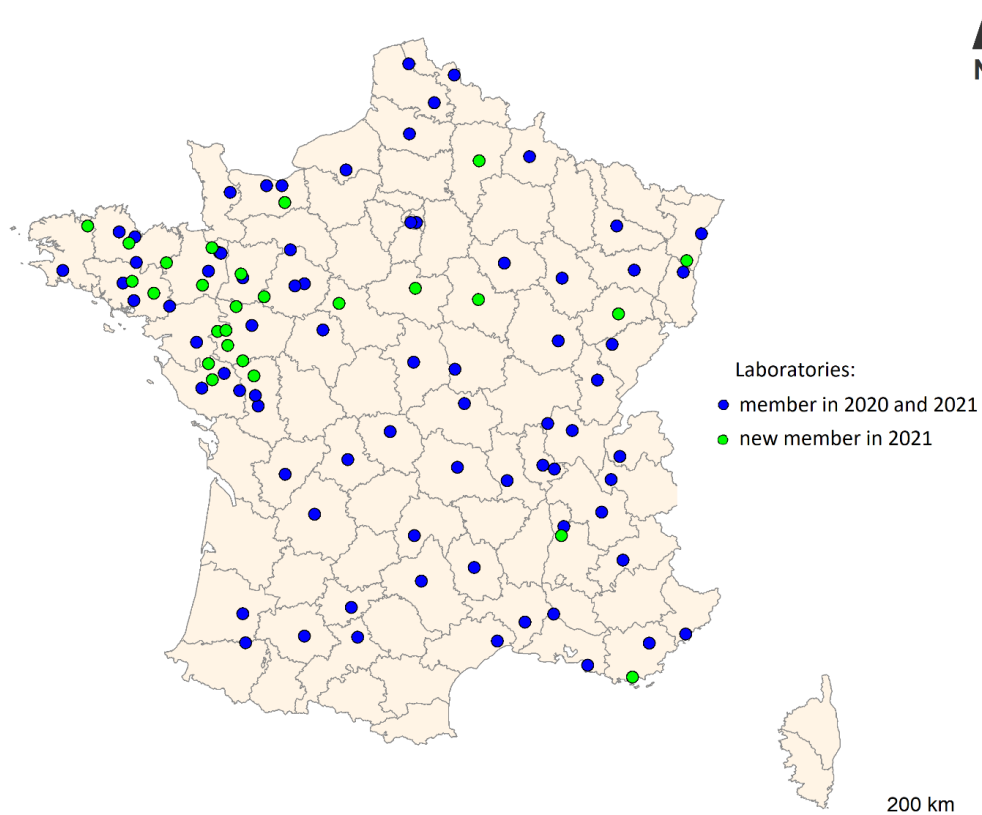
Network functioning and operations

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 101 contributing laboratories in 2021 spread over the metropolitan territory (*Appendix 1*). Major developments in the data management IT system have enabled the addition in 2021 of 26 new member laboratories (*Figure 2*).

Figure 2. Laboratories participating to Resapath in 2021



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, human medicine, the General Directorate for Food and ANSES (including both Laboratories and the Agency for Veterinary Medicinal Products).

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 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 methicillin-resistant *Staphylococcus aureus* (MRSA)), other antibiotics may also be tested (e.g. ceftiofur), which in no way reflects veterinary use of these antibiotics.

Collection of bacterial strains and molecular analyses

ANSES collects, via the Resapath, certain strains 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.

⁶ Comité de l'antibiogramme - Société française de microbiologie - <https://www.sfm-microbiologie.org>

⁷ The human version of the CA-SFM used here dates back from 2013. Since 2014, recommendations of the European referential 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 referential, now under development) to be launched

Figure 3. Resapath actors

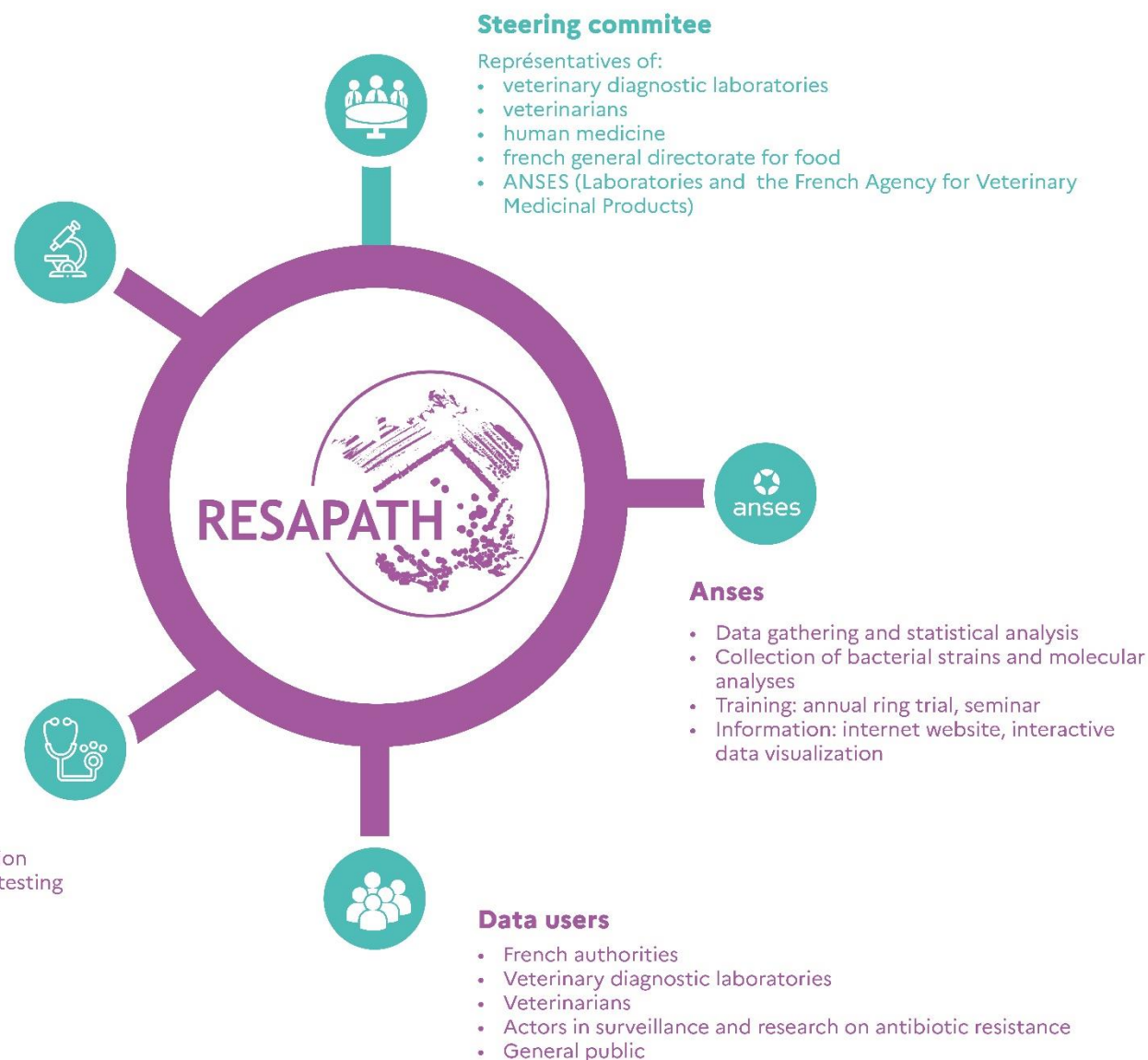
Resapath actors

Veterinary diagnostic laboratories

- Bacterial identification and antimicrobial susceptibility testing AFNOR NF U47-107
- Standards and breakpoints from the veterinarian CA-SFM
- Transmission of AST results to ANSES

Veterinarians

- Diseased animals sampling
- Request for bacterial identification and antimicrobial susceptibility testing
- Use of data to guide treatment

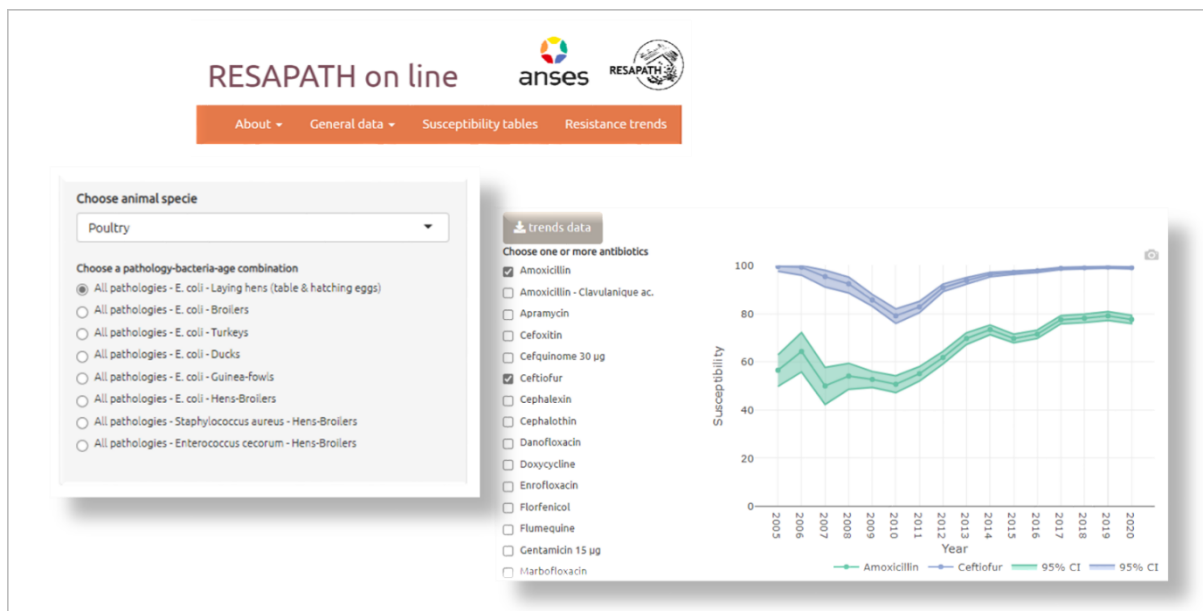


Data access

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

<https://shiny-public.anses.fr/ENresapath2/>

Figure 4. Screenshot from the Resapath open-access interface (RESAPATH on line)



This interface (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 three tabs:

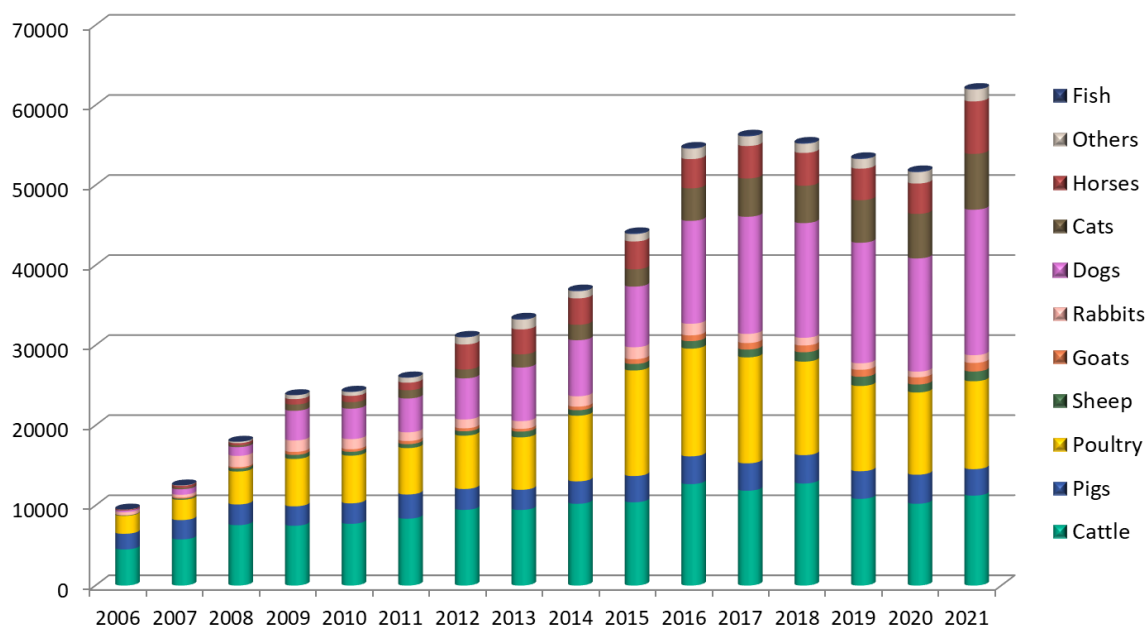
- General data: number of antibiograms;
- Antimicrobial susceptibility tables: proportion of susceptible strains;
- Trends: curves of temporal evolution of the proportions of susceptible isolates with their 95% confidence intervals.

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

Key figures

- 62,070 antibiograms collected in 2021

Figure 5. Annual number of antibiograms collected per animal sector



- Antibiograms per animal categories in 2021

Tableau 1. Number of antibiograms collected per animal categories in 2021

Animal categories	No of antibiograms	%
Dogs	18,167	29.3
Cattle	11,230	18.1
Poultry	10,982	17.7
Cats	6,972	11.2
Horses	6,561	10.6
Pigs	3,309	5.3
Others*	1,496	2.4
Sheep	1,212	2.0
Goats	1,079	1.7
Rabbits	966	1.6
Fish	96	0.2
Total	62,070	100.0

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

Part 2

Results by animal categories



CATTLE

COLLECTED DATA

- 10,230 antibiograms
- 80 contributing laboratories
- Samples from 85 departments (=local administrative unit)(Figure 6)
- Adults (36%), calves (43%), unknown age (21%)

Adults

- Main disease:
 - Mastitis (92%)
- Main bacteria:
 - *Escherichia coli* (31%)
 - *Streptococcus* spp. (28%)
 - Coagulase negative *Staphylococcus* (CoNS) (9%)
 - Coagulase positive *Staphylococcus* (CoPS) (9%)

Calves

- Main diseases:
 - Digestive (82%)
 - Respiratory (11%)
- Main bacteria:
 - *Escherichia coli* (85%)
 - *Pasteurella* spp. (5%)
 - *Mannheimia* spp. (3%)
 - *Salmonella* spp. (2%)

RESISTANCE DATA

Escherichia coli

- Isolates of digestive origin (neonatal gastroenteritis) are the most frequently resistant ones.
- Resistance are mostly found to amoxicillin, streptomycin and tetracyclines (>75%).
- Resistance to amoxicillin and amoxicillin-clavulanic acid is increasing in mastitis isolates (+7 % and +6 % in 2021, respectively).
- Resistance to 3GC/4GC and fluoroquinolones remains very low (<9%) (see dedicated focus section).

Pasteurella spp.

- Bovine *Pasteurella* spp. remain largely susceptible to all beta-lactams.
- Resistance to streptomycin and spectinomycin has significantly increased since 2016.

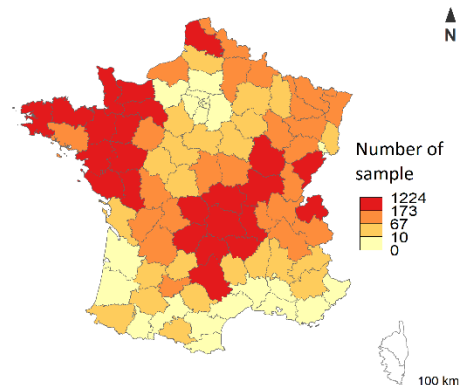
Staphylococcus spp.

- The majority of staphylococci (CoPS or CoNS) comes from mastitis (757/839, 90.2%).
- The most frequent resistance phenotype is resistance to penicillin G (17% in CoPS and 25% in CoNS).
- MRSA are still very rare in bovine (<5%).

Streptococcus spp.

- Nearly all bovine streptococci are susceptible to penicillin G and to gentamicin.
- 17% of *S. uberis* and *S. dysgalactiae* isolates are resistant to erythromycin, and thus cross-resistant to lincosamides (inducible or constitutive MLS_S phenotype).

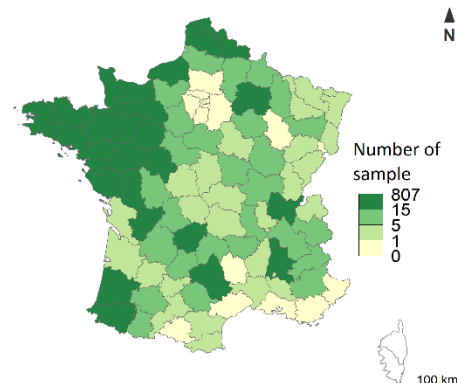
Figure 6. Origin of cattle samples





PIGS

Figure 7. Origin of pig samples



COLLECTED DATA

- 3,309 antibiograms
- 53 contributing laboratories (including 6 which represent 76% of the data)
- Samples from 78 departments (Figure 7)
- Piglets (52%), sow (10%), unknown age (38%)

- Main diseases:
 - Digestive (36%), mainly in piglets
 - Septicemia (14%)
 - Respiratory (11%)
- Main bacteria:
 - *Escherichia coli* (52%)
 - *Streptococcus suis* (16%)
 - *Actinobacillus pleuropneumoniae* (5%)
 - *Enterococcus hirae* (4%)
 - *Glaesserella parasuis* (4%)
 - *Pasteurella multocida* (4%)

RESISTANCE DATA

Escherichia coli

- Isolates are frequently resistant to amoxicillin (60%), but very rarely to ceftiofur (0.8%).
- 81% of isolates are susceptible to nalidixic acid, and 98% to fluoroquinolones.
- Between 92% and 94% of isolates are susceptible to gentamicin or apramycin.
- 51% of isolates are susceptible to the trimethoprim-sulfamethoxazole association, and 40% to tetracycline.

Pasteurella multocida, *Actinobacillus pleuropneumoniae* and *Glaesserella parasuis*

- *Pasteurella* spp are largely susceptible to amoxicillin (98% for *P. multocida* and *G. parasuis*; 90% for *A. pleuropneumoniae*).
- More than 94% of isolates are susceptible to fluoroquinolones.
- More than 99% of isolates are susceptible to ceftiofur or florfenicol.

Streptococcus suis

- 99.8% of isolates are susceptible to amoxicillin and 96% to oxacillin (marker of penicillin G).
- High-level resistance to aminoglycosides is scarce (synergy with beta-lactams is preserved).
- 17% of isolates are susceptible to tetracycline, 33-37% to macrolides-lincosamides.

Enterococcus hirae

- 98% of isolates are susceptible to amoxicillin.
- Few isolates (18%) are susceptible to erythromycin and very few to lincomycin (2%).



POULTRY

COLLECTED DATA

- 10,982 antibiograms
- 83 contributing laboratories
- Samples from 90 departments (Figure 8)
- Poultry species:

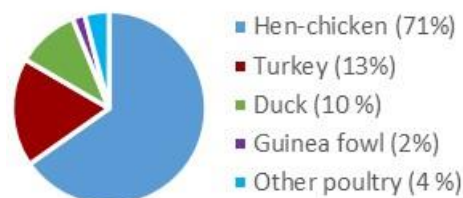
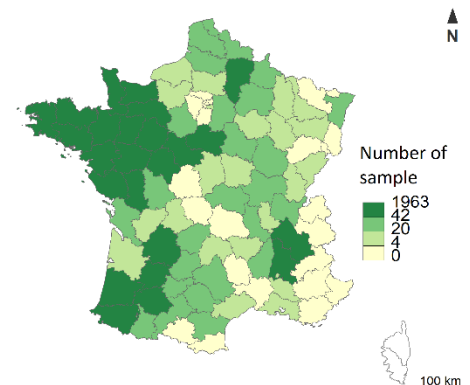


Figure 8. Origin of poultry samples



- Main diseases:
 - Septicemia (77%)
 - Arthritis (10%)
 - Respiratory (4%)
- Main bacteria:
 - *Escherichia coli* (77%)
 - *Enterococcus cecorum* (6%)
 - *Staphylococcus aureus* (4%)
 - *Enterococcus faecalis* (4%)
 - *Ornithobacterium rhinotracheale* (2%)
 - *Pasteurella multocida* (1%)

RESISTANCE DATA

Escherichia coli

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

- 41% (guinea fowl) to 67% (hens/broilers) of isolates are susceptible to amoxicillin, and more than 98% to ceftiofur.
- More than 95% of isolates are susceptible to gentamicin for all four animal species.
- 48% (ducks) to 74% (hens/broilers) of isolates are susceptible to tetracyclines, 77% (guinea fowl) to 85-86% (hens/broilers, turkeys and ducks) to the trimethoprim- sulfamethoxazole association.
- 97% to 99% of isolates are susceptible to enrofloxacin for all four animal species.

Staphylococcus aureus (hens and broilers)

- 92% to more than 99 % of isolates are susceptible to the most frequently tested antibiotics, with the exception of tetracycline, penicillin G and erythromycin (84% to 89%).
- 4% of isolates are resistant to ceftiofur, indicating a possible resistance to methicillin (MRSA).

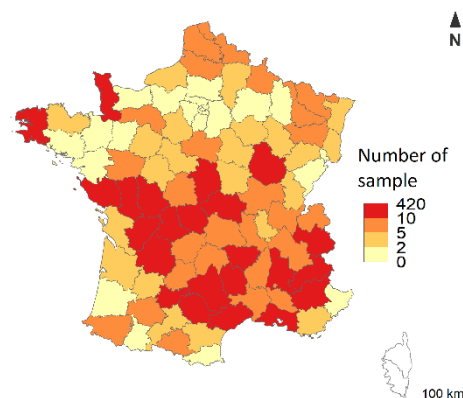
Enterococcus cecorum (hens and broilers)

- 99% of isolates are susceptible to amoxicillin.
- Susceptibility to erythromycin and lincomycin ranges between 69% and 70%.
- 48% of isolates are susceptible to the trimethoprim-sulfamethoxazole association, only 10% to tetracycline.



SHEEP

Figure 9. Origin of sheep samples



COLLECTED DATA

- 1,212 antibiograms
 - 63 laboratories (including 1 representing 40% of the data)
 - Samples from 75 departments (Figure 9)
 - Adults (23%), young (39%), unknown age (38%)
-
- | | |
|--|---|
| <ul style="list-style-type: none"> • Main diseases: <ul style="list-style-type: none"> – Respiratory (29%) – Digestive (34%) – Mastitis (11%) | <ul style="list-style-type: none"> • Main bacteria : <ul style="list-style-type: none"> – <i>Escherichia coli</i> (42%) – <i>Mannheimia haemolytica</i> (18%) – <i>Pasteurella multocida</i> (7%) – CoPS (7%) |
|--|---|

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.
 - present high resistance rates to commonly used antibiotics: tetracycline 56%, amoxicillin 52%, amoxicillin – clavulanic acid 43%.
 - present high resistance to streptomycin (55%), while resistance to gentamicin and kanamycin is low (5%).
 - present low levels of resistance to florfenicol (10%, stable over the last years).
 - remain globally susceptible to 3GC/4GC (>98%).

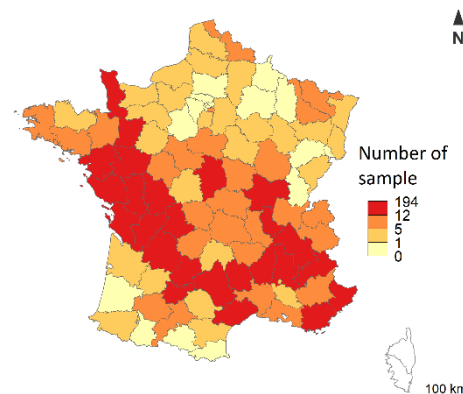
Mannheimia haemolytica

- Data concerning *M. haemolytica*, all pathologies included, show no specific resistance of interest.



GOATS

Figure 10. Origin of goat samples



COLLECTED DATA

- 1,079 antibiograms
- 74 laboratories
- Samples from 78 departments (Figure 10)
- Adults (34%), young (22%), unknown age (44%)

Adult sheep

- Main diseases:
 - Mastitis (73%)
 - Respiratory (10%)
- Main bacteria:
 - CoPS (25%)
 - CoNS (22%)
 - *Escherichia coli* (12%)

Young sheep

- Main diseases:
 - Digestive (49%)
 - Respiratory (27%)
- Main bacteria:
 - *Escherichia coli* (54%)
 - *Mannheimia* spp. (20%)
 - *Pasteurella* spp. (5%)

RESISTANCE DATA

Escherichia coli

- Resistance to 3GC/4GC remains low (2%).
- Resistance to enrofloxacin and marbofloxacin has increased (+10% between 2020 and 2021).
- High levels of resistance were reported for other antibiotics: tetracyclines (55 to 83%), amoxicillin (61%), and streptomycin (56%).

Pasteurella spp. and *Mannheimia* spp.

- No specific resistance phenotypes were observed for *Pasteurella* spp. and *Mannheimia* spp.

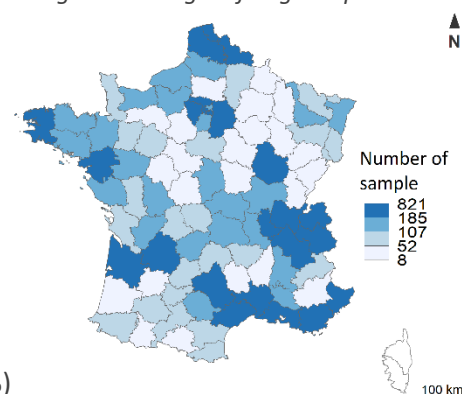


DOGS

COLLECTED DATA

- 18,167 antibiograms
- 82 laboratories*
- Samples from 98 departments (Figure 11)
- Adults (62%), young (4%), unknown age (34%)
- Main diseases:
 - Otitis (32%)
 - Kidney and urinary tract (24%)
 - Skin and soft tissue infection (13%)
- Main bacteria:
 - CoPS (27%)
 - *Escherichia coli* (20%)
 - *Pseudomonas* (10%)
 - *Proteus* spp. (9%)
 - *Streptococcus* spp. (7%)

Figure 11. Origin of dog samples



*Two laboratories account for 19% and 32% of the data, respectively. The geographical location of the laboratory does not necessarily indicate the origin of the animal. Indeed, numerous dogs suffering from severe conditions are visiting referral veterinary hospitals, sometimes far from where they live.

RESISTANCE DATA

Escherichia coli

- Resistance ranges from 5-9% to ceftiofur and from 5-12% to fluoroquinolones depending on the pathology.
- An increasing trend in resistance to amoxicillin and amoxicillin + clavulanic is observed over the past two years for UTI isolates. Tendencies are stable for isolates collected from otitis and SSTI.
- Resistance to ceftiofur is decreasing (15.7% in 2020; 8.8% in 2021) in isolates collected from SSTI.

Proteus spp.

- Resistance to 3GC is nearly absent in *P. mirabilis*.
- High proportions of resistance phenotypes were observed to streptomycin (24%) and fluoroquinolones (17% for enrofloxacin and marbofloxacin).

Staphylococcus spp.

- *S. aureus* isolates are frequently resistant to penicillin G (73-82% depending on the pathology).
- MRSA and MRSP represent around 10% of *S. aureus* and *S. pseudintermedius*, respectively.

Streptococcus spp.

- *Streptococcus* spp. are mostly isolated from otitis and are generally susceptible.
- The MLS_B phenotype (resistance to macrolides-lincosamides-streptogramins) is observed in 18% of isolates from otitis.

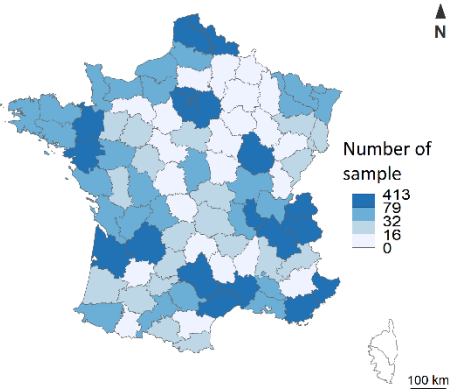


CATS

COLLECTED DATA

- 6,972 antibiograms
 - 73 laboratories (including two representing 42% and 19% of the data)
 - Samples from 95 departments (*Figure 12*)
 - Adults (63%), young (5%), unknown age (32%)
-
- | | |
|--|---|
| <ul style="list-style-type: none"> • Main diseases: <ul style="list-style-type: none"> – Kidney and urinary tract (42%) – Respiratory (12%) – Otitis (12%) – Digestive (4%) – Skin and soft tissue infection (6%) | <ul style="list-style-type: none"> • Main bacteria: <ul style="list-style-type: none"> – <i>Escherichia coli</i> (33%) – CoNS (13%) – CoPS (12%) – <i>Pasteurella</i> spp. (12%) – <i>Enterococcus</i> spp. (8%) |
|--|---|

Figure 12. Origin of cat samples



RESISTANCE DATA

Escherichia coli

- Resistance to critically important antibiotics (CIA) remains low (3GC, 4%; fluoroquinolones, 5-7%).
- Resistance to amoxicillin and amoxicillin + clavulanic seems to stabilize (46.6% and 35.5%) after a substantial increase in 2019 and 2020.

Staphylococcus spp.

- CoPS isolates are frequently resistant to penicillin G (55%) all pathologies included.
- Suspensions of MRSA exist for 13% of the isolates from UTI and 20% of the isolates from SSTI. This suspicion is much lower (6%) in isolates from otitis.



HORSES

COLLECTED DATA

- 6,561 antibiograms
- 60 laboratories (including two representing 42%* and 30% of the data)
- Samples from 96 departments
- Adults (32%), young (2%), unknown age (66%)
- Main diseases:
 - Reproduction (26%)
 - Respiratory (34%)
 - Skin and soft tissue infection (9%)
- Main bacteria :
 - *Streptococcus* spp. (30%)
 - *Escherichia coli* (14%)
 - *Pseudomonas* spp. (8%)
 - CoPS (9%) ou CoNS (7%)

* A unique laboratory collects 42 % of all equine antibiograms (mostly from top level sport horses). This laboratory also analyzes samples from horses that previously received one or two antibiotics therapies that failed.

RESISTANCE DATA

Escherichia coli

- Isolates are mostly resistant to amoxicillin, streptomycin and tetracycline.
- Resistance to the trimethoprim-sulfamethoxazole association is increasing (+10% in 10 years).
- Resistance to amoxicillin and amoxicillin + clavulanic acid is still increasing in isolates from the reproductive tract, while it is decreasing in isolates from the respiratory tract and from SSTI.
- Resistance to ceftiofur ranges from 3% to 6% depending on the pathology.

Enterobacterales

- Ceftiofur resistance is mainly carried by *Enterobacter* spp. (30%) and *Klebsiella pneumoniae* (12%).

Staphylococcus aureus

- *S. aureus* isolates are largely susceptible to all antibiotics tested.
- Resistance phenotypes to penicillin G (27%) and tetracycline (13%) are decreasing over the past two years.
- MRSA represent a little less than 13% of the isolates, most of which belong to the ST398 clone.

Streptococcus spp.

- *Streptococcus* spp. isolates are mostly susceptible to all antibiotics tested.
- The most frequent resistance phenotypes are to tetracycline and trimethoprim-sulfamethoxazole.
- Resistances to beta-lactams and aminoglycosides are very rare (hence, synergy is preserved).



RABBITS

COLLECTED DATA

- 966 antibiograms (food producing rabbits only)
- 60 laboratories
- Samples from 77 departments
- Main diseases:
 - Respiratory (28%)
 - Digestive (23%)
 - Septicemia (17%)
 - Skin and soft tissue infection (12%)
- Main bacteria:
 - *Escherichia coli* (34%)
 - *Pasteurella multocida* (17%)
 - *Staphylococcus aureus* (12%)
 - *Bordetella bronchiseptica* (4%)

RESISTANCE DATA

Escherichia coli

- 44% of isolates are susceptible to amoxicillin (not used in rabbits), 99% to ceftiofur.
- 86% of isolates are susceptible to nalidixic acid, and 97% to enrofloxacin.
- 90% of isolates are susceptible to apramycin or gentamicin.
- 37% of isolates are susceptible to the trimethoprim-sulfamethoxazole association, 18% to tetracycline.

Pasteurella multocida

- More than 90% of isolates are susceptible to most frequently tested antibiotics, except to nalidixic acid (59%) and flumequine (88%).

Staphylococcus aureus

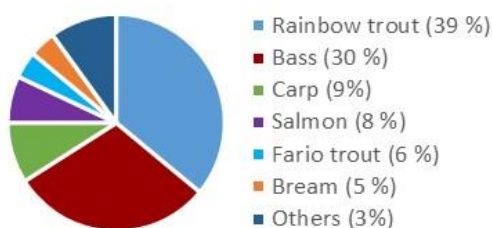
- 58% of isolates are susceptible to penicillin G.
- 8% of isolates are resistant to ceftiofur, indicating a possible resistance to methicillin (MRSA).
- Between 49% and 57% of isolates are resistant to tetracycline and macrolides-lincosamides.
- The vast majority of isolates is susceptible to gentamicin (80%) and enrofloxacin (94%).



FISH

COLLECTED DATA

- 96 antibiograms
- 3 laboratories (1 including 68% of the data)
- Samples from 5 departments (department unknown for 68% of the antibiograms)
- Mains fish species:



- Main diseases:
 - Septicemia (18%)
 - Unknown (82%)
- Main bacteria:
 - *Aeromonas* spp. (54%)
 - *Aeromonas salmonicida* (29%)
 - *Yersinia ruckeri* (20%)
 - *Vibrio* spp. (18%)

RESISTANCE DATA

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



OTHER SPECIES

COLLECTED DATA

- 1,496 antibiograms
- 61 laboratories
- Samples from 83 departments

Samples comes mainly from:

- Mammals (domestic rabbits, monkeys, dwarf rabbits, guinea pigs etc.) (70%)
- Birds (20%)
- Reptiles (8%)
- Aquarium fish (1%)
- Amphibians (1%)

RESISTANCE DATA

Due to the low numbers of antibiograms collected for each animal species and the multiplicity of pathologies 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, while their use in veterinary medicine is regulated by law. AMR rates to these two antibiotic classes are considered major indicators in the evaluation of national action plans against AMR.

Method

Ceftiofur and cefquinome in food-producing animals and horses, and ceftiofur in cats and dogs are the only three ESC molecules used in veterinary medicine.

ESC resistance (ESC-R) trends in *E. coli* have been estimated using values obtained for ceftiofur resistance. Despite slight differences with cefquinome or ceftiofur resistances, most likely resulting from differences in cephalosporin-hydrolyzing enzymes, resistance to ceftiofur is considered a reasonable proxy for all ESC-R.

Moreover, trends in resistances to enrofloxacin and marbofloxacin were considered representative of trends in all FQ-R.

Figure 13. Evolution of proportions (%) of *E. coli* isolates non-susceptible (R+I) to ceftiofur (2011-2021)

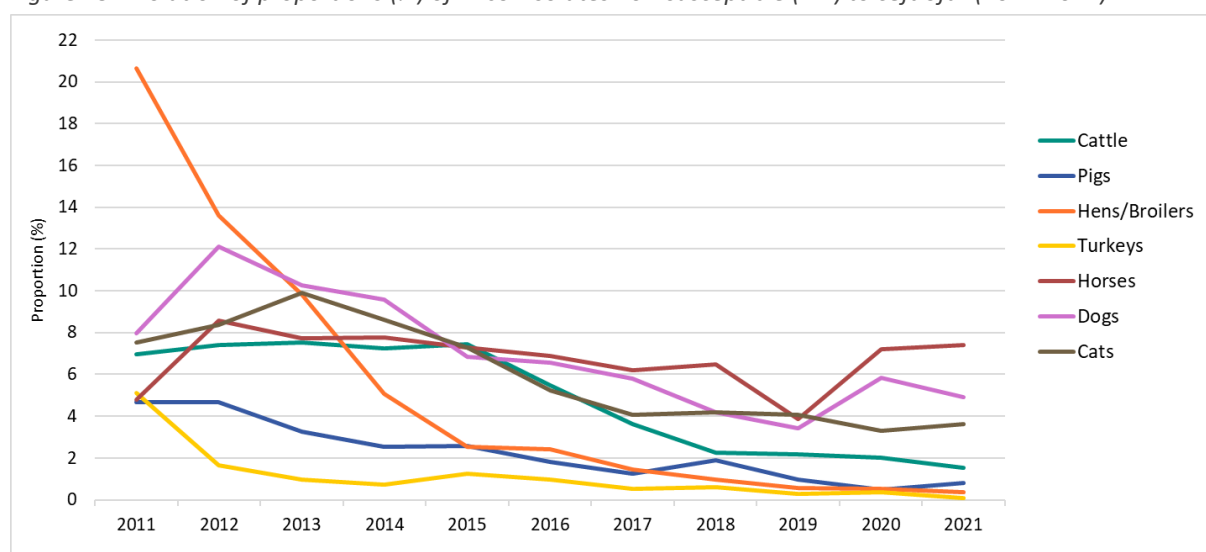


Figure 14. Evolution of proportions (%) of *E. coli* isolates non-susceptible (R+I) to ceftiofur in **cattle, adults and calves** (2011-2021)

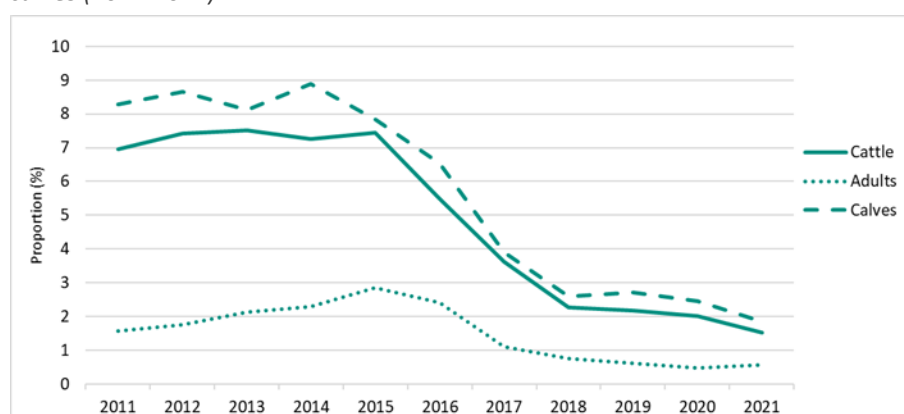


Figure 15. Evolution of proportions (%) of *E. coli* isolates non-susceptible (R+I) to enrofloxacin or marbofloxacin (2011-2021)

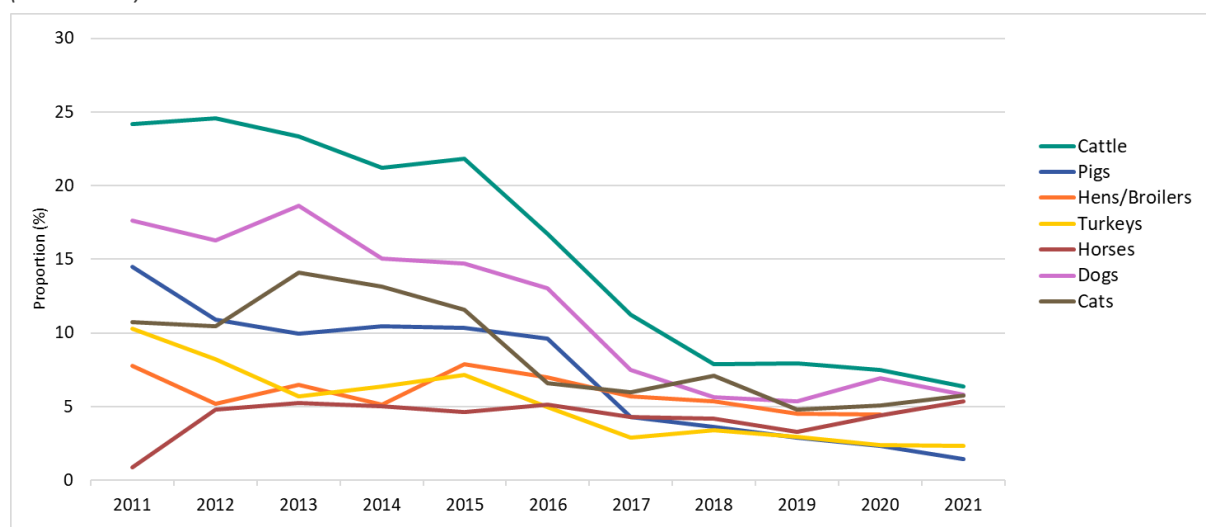
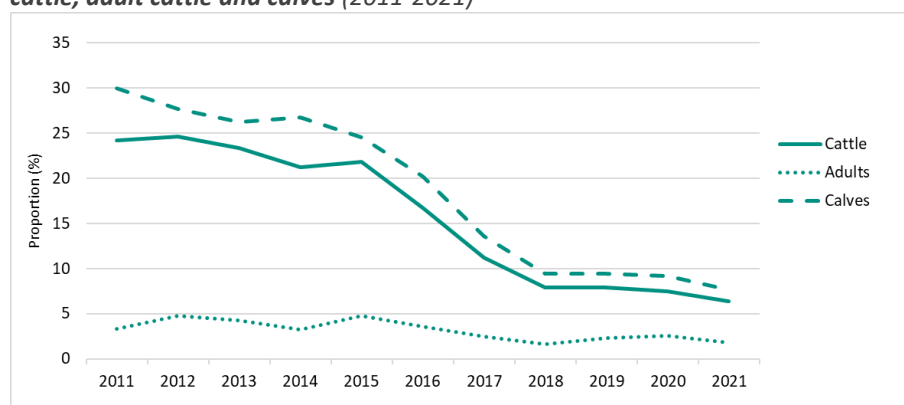


Figure 16. Evolution of proportions of *E. coli* isolates non-susceptible (R+I) to enrofloxacin or marbofloxacin in cattle, adult cattle and calves (2011-2021)



- ✓ Data in 2021 confirm observations from previous years highlighting low ESC- and FQ-R rates in *E. coli* isolates from all animal species (Figures 13 and 15).
- ✓ These trends reflect strong efforts from veterinarians to reduce antibiotic use and are consistent with a parallel substantial decrease in animal exposure to ESC and FQ⁸. In pigs and poultry, ESC- and FQ-R rates have been constantly low for several years. In cattle, a remarkable decrease in ESC- and FQ-R has been observed over the last years, although it is becoming more stable since 2018.
- ✓ An increase in 3GC/4GC-R in horses (from 3.9 to 7.4% between 2019 and 2021) is noted and should be closely monitored. Of note, the increase in 3GC/4GC-R observed in dogs in 2020 did not continue in 2021.
- ✓ For a given animal species, ESC- and FQ-R rates strongly depend on animal age and pathology. For instance in cattle, ESC- and FQ-R is more frequent in young animals (Figures 14 and 16).

⁸ ANSES 2021. Sales survey of veterinary medicinal products containing antimicrobials in France in 2020, Anses-ANMV, France, November 2021, report, 89 pp. <https://www.anses.fr/en/system/files/ANMV-Ra-Antibiotiques2020EN.pdf>

E. coli - Resistance trends for other antibiotics

Method

Resistance trends of *E. coli* to antibiotics other than fluoroquinolones and Extended-spectrum cephalosporins (ESC) were analyzed for cattle, pigs, poultry (chickens and turkeys separately), dogs, cats and horses.

Seven antibiotics representing five antibiotic classes were analyzed.

Data are displayed for the 2011-2021 period, except for dogs, cats, and horses for which the amount of data collected by the network before 2013 was insufficient.

In order to assess the significance of the changes observed, trend Chi2 values are calculated for the studied period and considered significant at the level of 5%.

Figure 17. Evolution of proportions (%) of *E. coli* isolates non-susceptible (R+I) to seven antimicrobials in **cattle** (2011-2021)

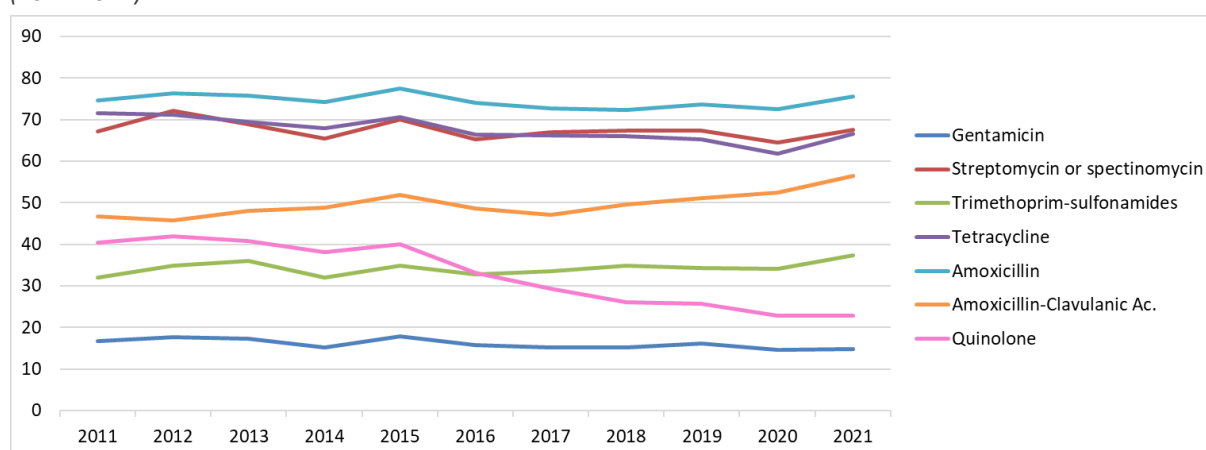


Figure 18. Evolution of proportions (%) of *E. coli* isolates non-susceptible (R+I) to seven antimicrobials in **pigs** (2011-2021)

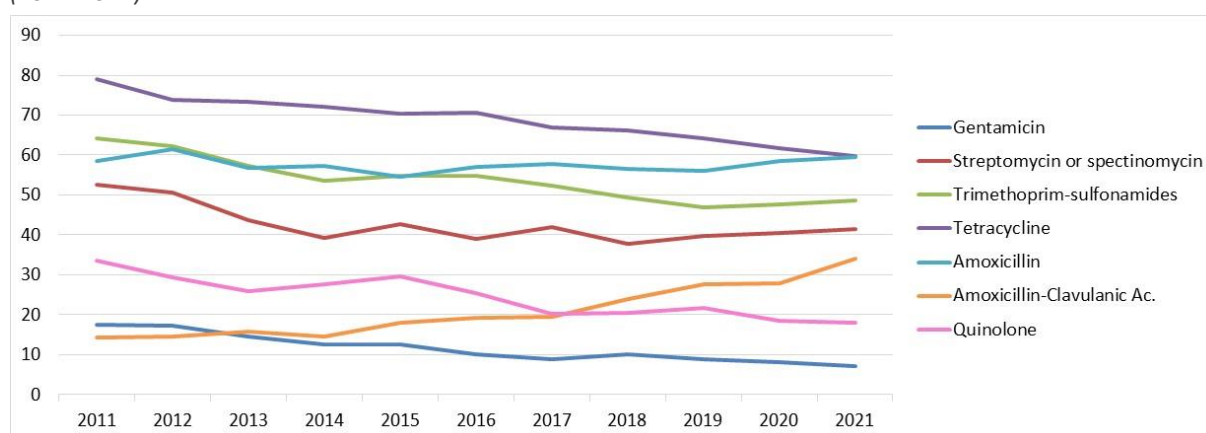


Figure 19. Evolution of proportions (%) of *E. coli* isolates non-susceptible (R+I) to seven antimicrobials in **hens and broilers** (2011-2021)

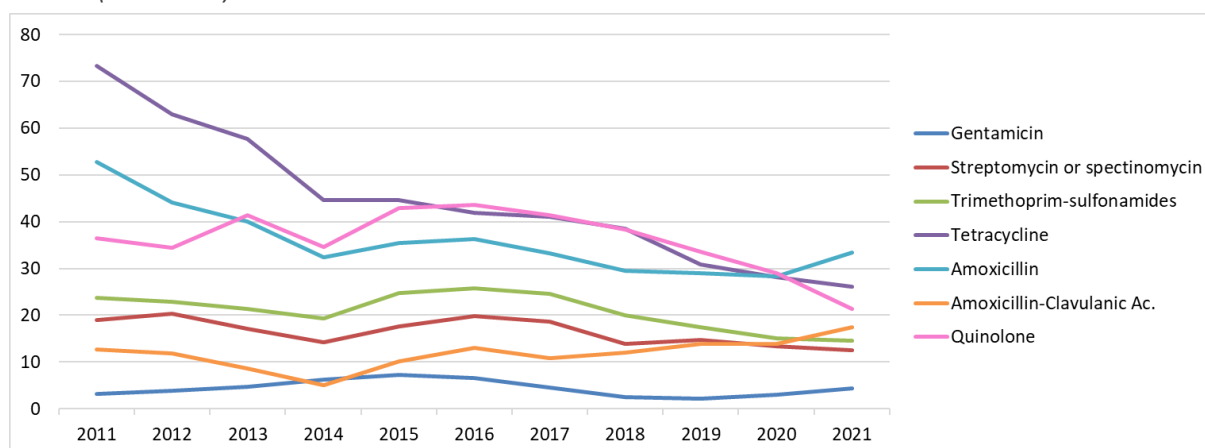


Figure 20. Evolution of proportions (%) of *E. coli* isolates non-susceptible (R+I) to seven antimicrobials in **turkeys** (2011-2021)

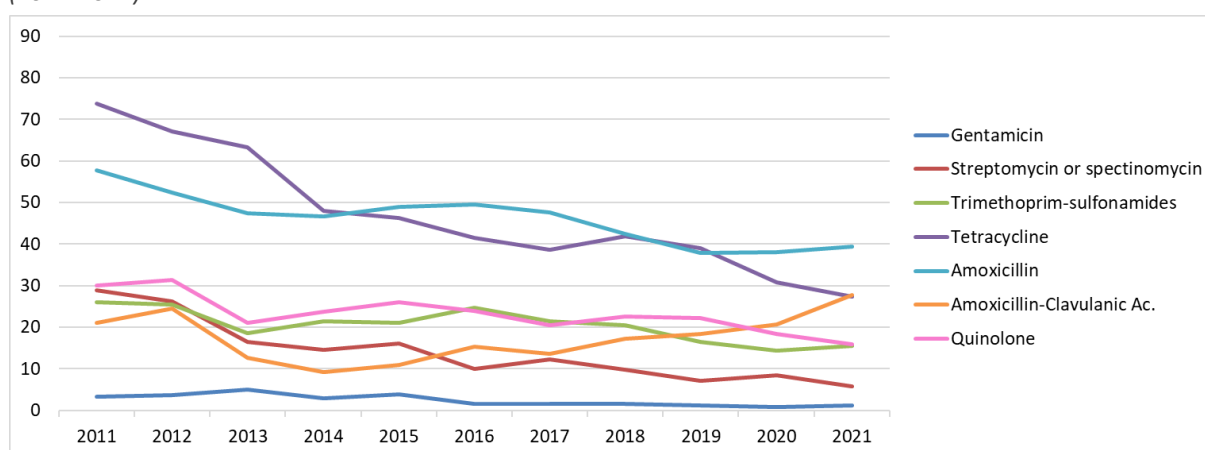


Figure 21. Evolution of proportions (%) of *E. coli* isolates non-susceptible (R+I) to seven antimicrobials in **dogs** (2013-2021)

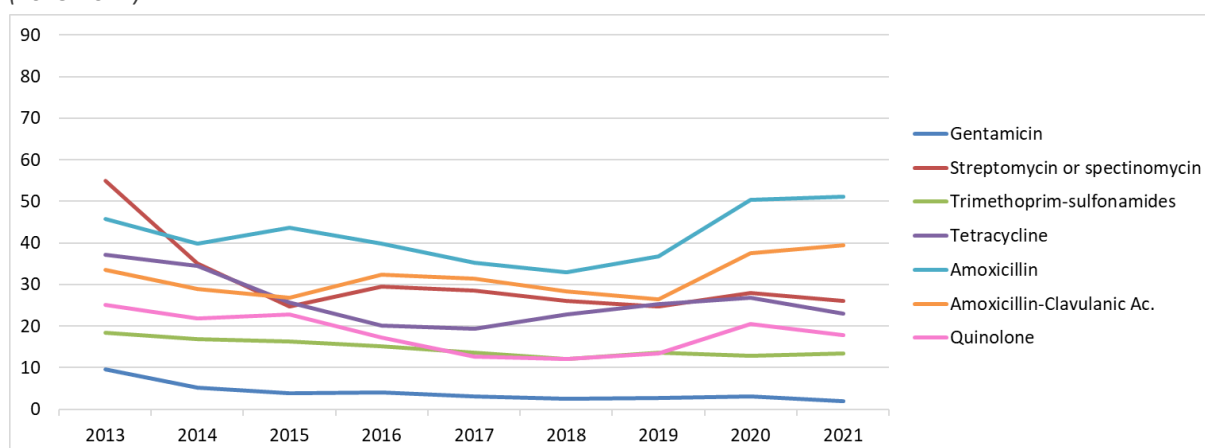


Figure 22. Evolution of proportions (%) of *E. coli* isolates non-susceptible (R+I) to seven antimicrobials in **cats** (2013-2021)

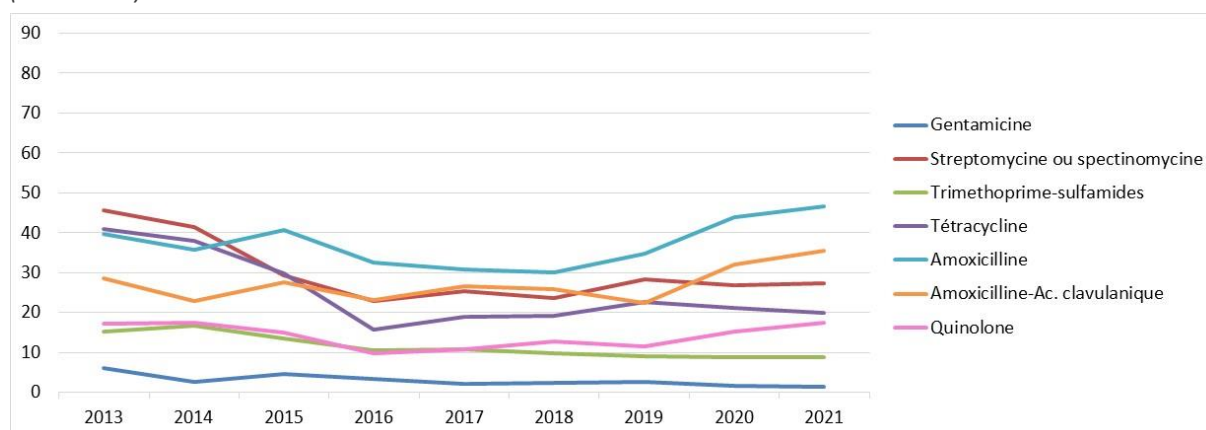
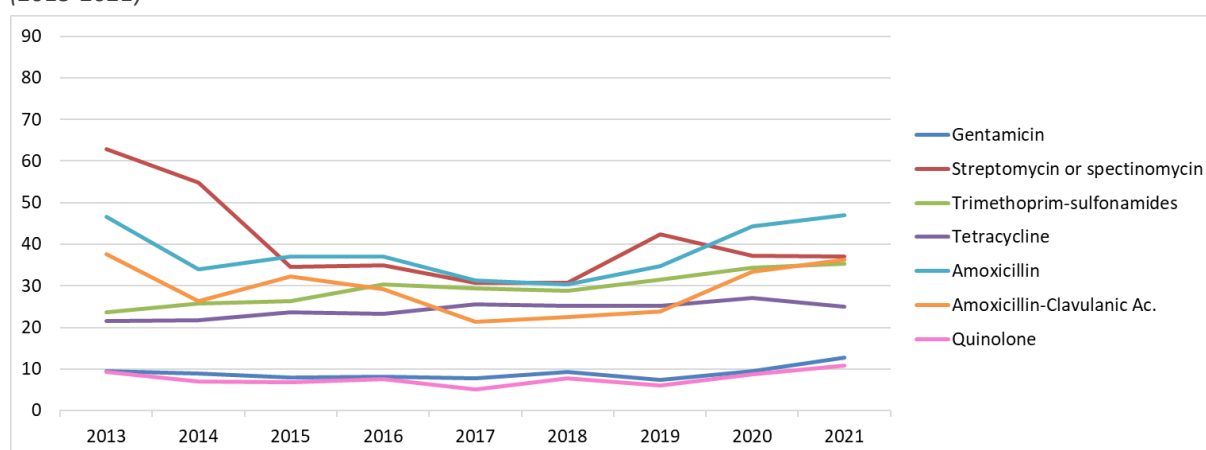


Figure 23. Evolution of proportions (%) of *E. coli* isolates non-susceptible (R+I) to seven antimicrobials in **horses** (2013-2021)



- ✓ Over the last ten years, the decrease in tetracycline resistance in poultry and pigs is the most striking phenomenon: turkeys (-46%), chicken (-47%), pigs (-19%) (Chi2, $p < 0.001$) (Figures 18, 19, 20).
- ✓ In cattle, resistances display stable or increasing trends for most antibiotics. In particular, resistance proportions remain very high (around 70%) for amoxicillin, tetracyclines and streptomycin/spectinomycin (Figure 17).
- ✓ For all animal sectors presented here, a reversal trend is observed (Chi2, $p < 0.01$) for amoxicillin and amoxicillin + clavulanic acid since 2018 with an increase in resistance proportions (I+R), excepted for turkeys and amoxicillin (stability).

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 analyzed 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. Hence, starting from this year (2021 data), 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 antimicrobials molecules among the following ones: amoxicillin, gentamicin, tetracycline, trimethoprim-sulfamethoxazole, nalidixic acid.

Multi-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 2011 and 2021.
- Number of resistances (none, 1, 2, 3, 4, or 5) for different animal and age categories.

Figure 24. Evolution between 2011 and 2021 of the proportions (%) of multi-drug resistant *E. coli* isolates

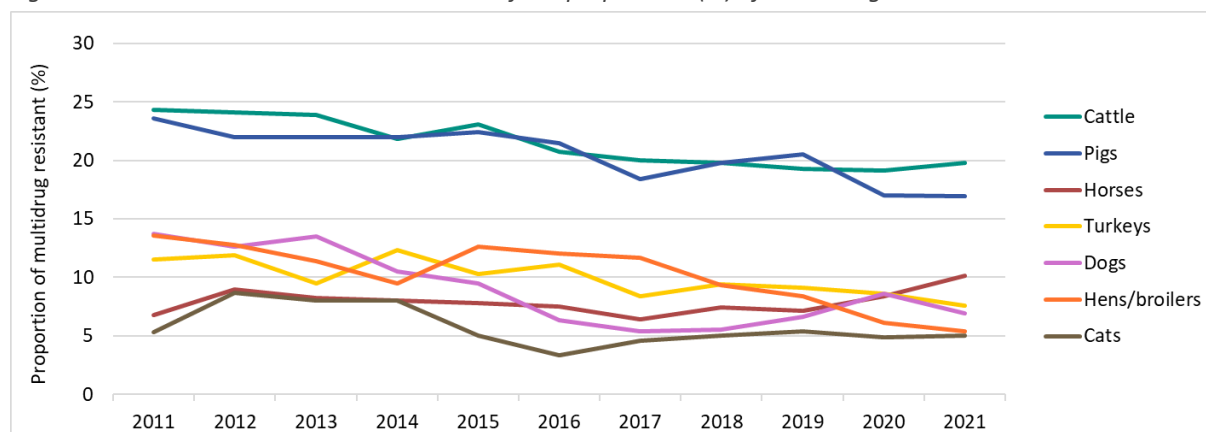
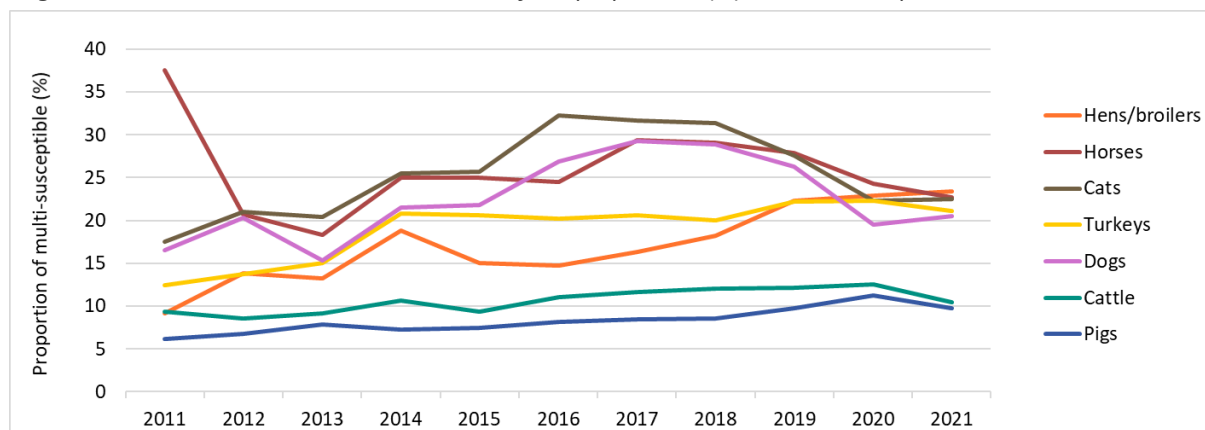


Figure 25. Evolution between 2011 and 2021 of the proportions (%) of multi-susceptible *E. coli* isolates



- ✓ The proportions of MDR strains are higher among isolates from bovines and pigs (18-20%) than among isolates from poultry, cats, dogs and horses (5-10%) (Figure 24).
- ✓ Results of MDR and multi-susceptibility are stable between 2020 and 2021. Overall, we observe (i) a rather positive evolution in livestock, with a decrease in proportions of MDR isolates and a concomitant increase in multi-susceptible isolates and (ii) mixed results in cats, dogs and horses where multi-susceptibility clearly decreased between 2017 and 2020 (Figures 24 et 25).
- ✓ The distribution of isolates according to their phenotype (susceptible to all 5 antimicrobials, carrying one, two, three, four or five resistances) highlights disparities between animal species (Figure 26). Disparities also exist in some cases depending on the pathological context within the same species. For example in cattle in 2021, 23% of the *E. coli* isolated were MDR among the strains isolated from digestive pathology versus only 3% for those isolated from mastitis.

Figure 26. Evolution in the proportions of *E. coli* strains resistant to none, 1, 2, 3, 4 or 5 of the antimicrobials tested, for various animal species and pathologies



Colistin resistance in veterinary medicine

Method

Analysis of data from the Resapath network allowed us to define a rule for interpreting diameters of inhibition zones for the colistin disk (50 µg) used in Enterobacterales.

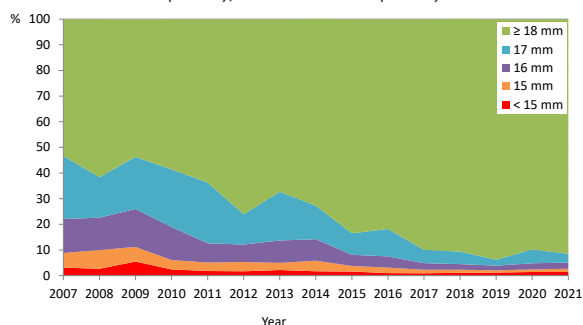
According to the current knowledge, diameters strictly < 15 mm correspond to MICs > 2 mg/L (resistance). Diameters of 15, 16 and 17 mm are considered uninterpretable and require confirmation by another validated method. Finally, a diameter ≥ 18 mm has a high probability of corresponding to a susceptible isolate.

Monitoring of colistin resistance is evaluated by observing the relative proportions of the different inhibition diameters over time for different animal species and pathologies. Trends are considered significant at the 5% level (Chi2 test).

Figure 27. Relative proportions of inhibition zone diameters measured at <15 mm, 15 mm, 16 mm, 17 mm and ≥18 mm around the colistin disk (50 µg) for *E. coli* isolates collected between 2007 and 2021 for various animal species and pathologies.

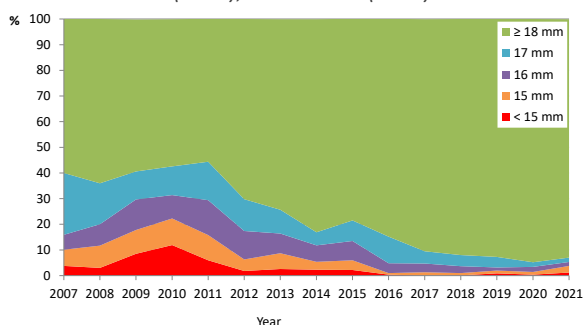
A / Digestive pathology in veal calves

n min.: 1 363 (2007); n max.: 4 219 (2016)



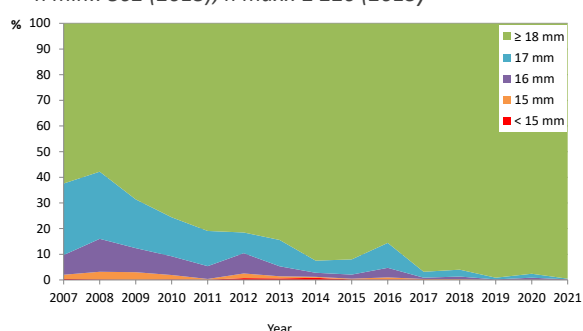
B / Digestive pathology in piglets

n min.: 385 (2007); n max.: 887 (2019)



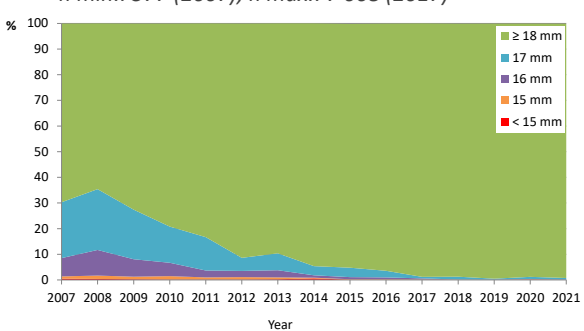
C / All pathologies in turkey

n min.: 862 (2013); n max.: 2 220 (2015)



D / All pathologies in laying hens and broilers

n min.: 577 (2007); n max.: 7 008 (2017)



- ✓ In all four animal categories studied, a significant (Chi2 trend, $p < 0.001$) increase in the proportion of susceptible isolates was observed between 2007 and 2021 (Figure 27). These data suggest the spread of pathogenic *E. coli* resistant to colistin is currently under control.

Phylogeny and resistome of the epidemic multidrug resistant ST25 *Acinetobacter baumannii* lineage

Acinetobacter baumannii ST25 lineage includes multidrug resistant isolates responsible for severe infections. In France, these isolates have been collected from humans (n=11) and animals (n=34) during 2010-2019. To provide an insight of this lineage, genomes of isolates collected in France were sequenced (Illumina) and a phylogenetic analysis (MrBayes) was conducted including all the ST25 genomes (n=103) available from NCBI (accessed on the 18/01/2022). The resistome was analyzed using ResFinder4.1. In total, 148 ST25 genomes were analyzed, which grouped into four clades (CI-CIV). Two clades, I and III, included genomes from South America, whereas geographical origin of genomes of clade II and IV, which included the French isolates, was more diverse. The phylogenetic analysis highlighted similarities between human and animal isolates. Genomes of clade CIV were the most recent and harbored a significantly higher amount of resistance genes, including genes coding for carbapenem-hydrolyzing enzymes, compared to the other clades. This suggests that clade IV is propagating and evolving. The ST25 *A. baumannii* lineage is widely distributed and includes multidrug resistant isolates that are able to colonize humans and animals overcoming host-related barrier.

Antimicrobial-resistant *Klebsiella pneumoniae*: from humans to animals and vice versa

Klebsiella pneumoniae resistant to last generation cephalosporins (ESC-R) and carbapenems (CP-R) are recognized by the WHO as one of the global priority pathogens. While many studies have characterized the clones circulating in humans, data are scarcer in companion animals. In the frame of the Resapath, 105 clinical strains of ESC-R and/or CP-R *K. pneumoniae* were isolated from pets between 2011 and 2018.⁹ Molecular microbiology approaches showed the emergence of the gene encoding the carbapenemase OXA-48, carried by a highly diffusible IncL plasmid, as well as the wide diffusion of those encoding the CTX-M-15 and DHA-1 enzymes, carried by IncF and IncR plasmids, respectively. Whole genome sequencing of all isolates showed the predominance (59/105) of three clones of major importance in humans (ST15, ST11 and ST307). Finally, the cross analysis of human and animal genomic data suggests both transfers from humans to animals, or vice versa, and adaptation to the animal host of a subgroup of ST11. These results show the importance of large-scale genomic analyses - still rare - for a better understanding of antimicrobial resistance routes of transmission and the evolution of multidrug resistant clones in a One Health context.

⁹ Garcia-Fierro R, Drapeau A, Dazas M, Saras E, Rodrigues C, Brisse S, Madec JY, Haenni M. Comparative phylogenomics of ESBL-, AmpC- and carbapenemase-producing *Klebsiella pneumoniae* originating from companion animals and humans. J Antimicrob Chemother. 2022 Apr 27;77(5):1263-1271. doi: 10.1093/jac/dkac041

Presence of the methicillin-susceptible ST398 clone in animals

The methicillin-resistant *S. aureus* ST398 clone (MRSA) was first identified in pigs in 2005, and then more widely in animals. In 2010, this same ST398 clone but susceptible to methicillin (MSSA) emerged as a human clone causing severe bacteremia. In France, the proportion of bacteremia due to ST398 MSSA increased from 3.6% in 2010 to 20.2% in 2017, and most strains belonged to the t517 *spa*-type. We searched for the presence of this "human" clone in animals in a collection of 275 *S. aureus* MSSA collected through the Resapath between 2014 and 2019.¹⁰ In total, 28 (10.2%) MSSAs belonged to CC398. The proportion of this clone was particularly high in cats (12/44, 27.3%) and dogs (8/55, 14.6%). Whole-genome sequencing of all CC398 isolates revealed that strains of animal origin are very similar to those of human origin, sharing the same *spa*-type (including t517) and the presence of an immune escape cluster allowing colonization of the human host. Our study shows that animals can contribute to the persistence (and possibly the dissemination) of this MSSA ST398 clone, which could therefore be less animal-independent than previously reported.

PROMISE : a national meta-network of professional actors engaged against antibiotic resistance

Funded under the National Priority Research Programme on AMR (1.4 million euros), the PROMISE meta-network launched in November 2021 aims to facilitate synergies and create a One Health community of actors engaged against antibiotic resistance in France. It involves 21 existing professional networks, including the Resapath, as well as 42 academic research teams from the animal, human and environmental sectors.

PROMISE activities are articulated around four transdisciplinary and intersectoral pillars: i) reinforcing synergies to improve One health surveillance of antibiotic resistance and antibiotic use, ii) data sharing to improve knowledge among the actors, iii) improvement of clinical research and iv) having an influence in Europe.

To achieve this, PROMISE is planning, among others, to create a data warehouse including surveillance data from the three sectors that will contribute to better evaluate the epidemic risk, and improve knowledge and skills of the meta-network actors. PROMISE will also facilitate the development of a new network dedicated to the surveillance of antibiotic resistance in the environment (AMR-Env), in collaboration with existing networks. PROMISE will contribute to the emergence of new networks and projects via an open discussion forum, and building bridges between several scientific communities. Additionally, PROMISE will participate to training and dissemination activities to reinforce One health practices and raise awareness about antibiotic resistance.

Overall, PROMISE aims to establish fruitful multisectoral collaborations between actors currently working in silo, and invite them to share best practices, expertise and methods in order to facilitate interdisciplinary and coordinated research on antibiotic resistance.

¹⁰ Tegegne HA, Madec JY, Haenni M. Is methicillin-susceptible *Staphylococcus aureus* (MSSA) CC398 a true animal-independent pathogen? J Glob Antimicrob Resist. 2022 Jun; 29:120-123. doi: 10.1016/j.jgar.2022.02.017. Epub 2022 Mar 1. PMID: 35240347.

EARS-Vet: Towards a European surveillance of AMR in veterinary medicine

The current European strategy for AMR surveillance in animals primarily focus on zoonotic and indicator bacteria isolated from food-producing animals at slaughter and food thereof (Directive 2003/99/CE and Implementing Decision 2020/1729/EU). While this surveillance provides useful evidence on human foodborne exposure to AMR, it also comes with a number of limitations, e.g. to formulate recommendations for good antimicrobial treatment practices in veterinary medicine. Hence, an important gap in the European strategy for AMR surveillance is AMR surveillance in veterinary medicine. As part of the EU Joint Action of AMR and Healthcare-associated infections (EU-JAMRAI), an initiative coordinated by ANSES has been launched to initiate a European AMR surveillance network in bacterial pathogens of animals. Paralleling the European network EARS-Net (surveillance of AMR in human clinical infections), this network is called EARS-Vet.

- A mapping of national surveillance systems of AMR in bacterial pathogens of animals across Europe¹¹ demonstrated that in 2020, approx. half of the EU/EEA countries (11 countries) had such a system in place. With 71 participating laboratories, the Resapath appeared as the largest system in Europe. The study showed that these systems were highly diverse and that collected data were not harmonized, with the use of various combinations of animal species-bacteria-antimicrobials of interest, and various standards for antimicrobial susceptibility techniques. Such a variability appears as a challenge for future joint data analyses across Europe.
- Nonetheless, the EU-JAMRAI activities kicked start a novel network of European scientists with a strong interest in collaborating and leveraging their national surveillance activities at a European level. A working group of approx. 30 experts proposed a vision and several objectives for the EARS-Vet network¹². Hence, EARS-Vet will aim to monitor trends and detect emergence among bacterial pathogens of animals, in order to *i)* support national and European decision-makers for the control of AMR, *ii)* contribute to define good antimicrobial treatment practices and *iii)* assess the risk of zoonotic transmission of AMR.
- A tentative EARS-Vet scope¹³ was also proposed. EARS-Vet will first target six animal species (cattle, pigs, broiler/laying hens, turkeys, dogs and cats), 11 bacterial species and 22 antimicrobial categories of interest to animal and human health. This scope will obviously evolve over time, e.g. considering changes in the AMR epidemiological situation, as well as recommendations from EU agencies (e.g. EFSA). Harmonisation of surveillance methods and standards will be achieved progressively, using preferably EUCAST standards where available.

A pilot phase of EARS-Vet was launched in 2022 including 11 partners from 9 European countries. It consisted in a first joint analysis of AMR data in animal pathogens across Europe, and will provide a proof-of-concept for a future joint programme for AMR surveillance in veterinary medicine in Europe. The EU-JAMRAI terminated in February 2021. Future funding of EARS-Vet could be obtained from a second joint action (EU-JAMRAI2) funded by the EU4Health programme, which is currently under preparation.

¹¹ Mader R, Muñoz Madero C, Aasmäe B, et al. (2021) "Review and analysis of national monitoring systems for antimicrobial resistance in animal bacterial pathogens in Europe: A basis for the development of the European Antimicrobial Resistance Surveillance Network in Veterinary Medicine (EARS-Vet)", <https://doi.org/10.5281/zenodo.5205371>

¹² 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

¹³ Mader R, on behalf of EU-JAMRAI, et al. (2021) "Defining the scope of the European Antimicrobial Resistance Surveillance network in Veterinary medicine (EARS-Vet): a bottom-up and One Health approach." *bioRxiv*, doi.org/10.1101/2021.03.09.434124

Contributions to the ANSES mandate as FAO Reference Centre for antimicrobial resistance

In November 2021, ANSES was appointed by FAO as a Reference Centre for antimicrobial resistance.¹⁴ Under this umbrella, ANSES provides expertise to FAO as part of various activities related to the implementation of the FAO Action Plan on Antimicrobial Resistance 2021–2025. Building on its expertise with Resapath, ANSES especially contributes to activities aiming at strengthening surveillance and research, which is one of the five objectives of the Action Plan.

In 2021, the Resapath coordination team contributed to the development of the FAO InFARM platform for surveillance of antibiotic resistance in animals.¹⁵ This platform aims to collect, at a global scale, surveillance data on antibiotic resistance in food producing animals (health or diseased animals). In a One Health and integrated approach of AMR surveillance, these data should in the future be jointly analysed with antibiotic sales data in animals from the WOAHA (previously OIE), as well as AMR and antibiotic consumption data in humans from WHO (GLASS system). These data will contribute to the Tripartite Integrated System for Surveillance on AMR and Antimicrobial Use (TISSA). Building on long-term experience with Resapath data management and analysis, and using a subset of Resapath data, ANSES contributed to pilot test and improve the InFARM template and tool for data collection, to be implemented on a full scale in 2023.

Capitalizing on its capacity to organize external quality assessment for antimicrobial susceptibility testing (EQA-AST), Resapath proposed in 2021 to organize EQA-AST among FAO partner laboratories. A simplified EQA-AST approach should be implemented in 2023 in several African countries, involving approximately 20 laboratories from the animal health sector. This project contributes to build capacity for antimicrobial susceptibility testing in African countries. It complements previous activities related to the evaluation of diagnostic laboratories capacities using the FAO ATLASS evaluation tool. This EQA-AST project in Africa is also funded via the French Ministry of Agriculture (EcoAntibio plan).

¹⁴ <https://www.fao.org/antimicrobial-resistance/resources/reference-centres/fr/>

¹⁵ <https://www.fao.org/documents/card/en/c/cc0822en>

Appendices

Appendix 1. Laboratories involved in Resapath (2021)

Laboratoire Départemental d'Analyses
Chemin de la Miche Cénord
01012 BOURG-EN-BRESSE CEDEX

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

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

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

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

ANSES laboratoire de pathologie équine de
Dozulé
RD 675
14430 GOUSTRANVILLE

Laboratoire Terana Cantal
100 rue de l'Egalité
15013 AURILLAC CEDEX

Laboratoire Départemental d'Analyses
de la Charente
496 route de Bordeaux
16000 ANGOULEME

Laboratoire Terana Cher
216 rue Louis Mallet
18000 BOURGES

Laboratoire Départemental de la Côte-d'Or
2 ter rue Hoche
CS 71778
21017 DIJON CEDEX

LABOCEA PLOUFRAGAN
5-7 rue du Sabot
22440 PLOUFRAGAN

LABOFARM
4 rue Théodore Botrel
BP 351
22600 LOUDEAC

VET&SPHERE Quintin
12 Rue de la Corderie
22800 QUINTIN

Laboratoire Départemental d'Analyses
42-44, route de Guéret
23380 AJAIN

Laboratoire Départemental d'Analyse et de
Recherche
161 Avenue Winston CHURCHILL
24660 COULOUNIEUX-CHAMIER

Laboratoire Vétérinaire Départemental
13 rue Gay-Lussac
BP 1981
25020 BESANCON CEDEX

AGRILAB 4A
5 Rue Gautier Lucet
ZA LES GOUVERNAUX
26120 CHABEUIL

LBAA
ZI allée du Lyonnais
26300 BOURG-DE-PEAGE

LABOCEA QUIMPER
22 Avenue de la plage des Gueux
ZA de Creach Gwen
CS 13031
29334 QUIMPER CEDEX

KER-VET
28 Avenue du Maréchal Leclerc
29610 PLOUIGNEAU

Laboratoire Départemental d'Analyses
970 route de St Gilles
ZAC mas des abeilles
30000 NIMES

SOCSA Analyse
11 Bis Rue Ariane
31240 L'UNION

Public labos site du Gers
824 Chemin de Naréoux
32020 AUCH CEDEX 9

Laboratoire Départemental Vétérinaire
306 rue de Croix Las Cazes
CS 69013
34967 MONTPELLIER CEDEX 2

Laboratoire Biovilaine Janzé
57 Rue Paul Painlevé
35150 JANZE

BIOCHENE VERT
Z.I. Bellevue II
Rue Blaise Pascal
35220 CHATEAUBOURG

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

LABOCEA - site de Fougères
BioAgroPolis
10 Rue Claude Bourgelat
JAVENE
CS 30616
35306 FOUGERES CEDEX

MC Vet Conseil - Velvet
47 Boulevard Leclerc
35460 SAINT-BRICE-EN-COGLES

BIOVILAINE
Z.A. des Chapelets
87 rue de la Chataigneraie
35600 REDON

INOVALYS TOURS
3 Rue de l'aviation
37210 PARCAY-MESLAY

Laboratoire Vétérinaire Départemental
20 avenue St Roch
38000 GRENOBLE

Laboratoire Départemental d'Analyses
59 rue du Vieil Hôpital
BP 40135
39802 POLIGNY CEDEX 2

Laboratoire des Pyrénées et des Landes
1 rue Marcel David
BP 219
40004 MONT-DE-MARSAN CEDEX

MC Vet Conseil - Naveil
9 Rue du Clos-Haut de la Bouchardièr
41100 NAVEIL

Laboratoire TERANA LOIRE
Zone Industrielle de Vaure
7 Avenue Louis Lépine
CS80207
42605 MONTBRISON CEDEX

LABOVET CONSEIL ANCENIS
125 Rue Georges Guynemer
ZAC de l'Aeropole
44150 ANCENIS

INOVALYS NANTES
Route de Gachet
BP 52703
44327 NANTES CEDEX 03

MC Vet Conseil - Quiers
8 Zone d'activités
45270 QUIERS-SUR-BEZONDE

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

Laboratoire Départemental d'Analyses
Rue du Gévaudan
BP 143
48005 MENDE CEDEX

INOVALYS ANGERS
18 bd Lavoisier
Square Emile Roux
BP 20943
49009 ANGERS CEDEX 01

YZIVET
ZA de la Charte Bouchère
49360 YZERNAVY

SARL ALVETYS
1 Rue Gillier
49500 SEGRE-EN-ANJOU-BLEU

LABOVET BEAUPREAU
130, Rue des forges
ZI EVRE ET LOIRE
49600 BEAUPREAU-EN-MAUGES

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
224 rue du Bas des Bois
BP 1427
53014 LAVAL CEDEX

MC Vet Conseil - Lab-elvet
1 Rue Charles Nicolle
53810 CHANGE

Laboratoire Vétérinaire et Alimentaire
Départemental
Domaine de Pixérécourt
BP 60029
54220 MALZEVILLE

SELARL VET&SPHERE Malestroix
Zone industrielle de Tirpen
56140 MALESTROIT

Laboratoire RESALAB BRETAGNE site Anibio
ZI du Douarin
56150 GUENIN

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

TERANA NIEVRE
Rue de la Fosse aux loups
58000 NEVERS

Laboratoire Départemental Public
Domaine du CERTIA
369 rue Jules Guesde
BP 20039
59651 VILLENEUVE-D'ASCQ CEDEX

LABEO ORNE
19 rue Candie
CS 60007
61001 ALENCON CEDEX

Laboratoire Départemental d'Analyses
Parc de Haute Technologie des Bonnettes
2 rue du Génévrier
62022 ARRAS CEDEX

AABIOVET
29 Quai du haut pont
62500 SAINT-OMER

TERANA Puy de Dôme
20 Rue Aimé Rudel
63370 LEMPDES

Laboratoire Alsacien d'Analyses (L2A)
2 place de l'Abattoir
67200 STRASBOURG

FILIAVET SELESTAT
67 Route de KINTZHEIM
67600 SELESTAT

Laboratoire Alsacien d'Analyses (L2A)
4 allée de Herrlisheim
CS 60030
68000 COLMAR

Laboratoire des Leptospires et analyses
vétérinaires (LAV)
Campus Vétérinaire
1,avenue Bourgelat
69280 MARCY-L'ETOILE

ORBIO LABORATOIRE
12 C Rue du 35è Régiment d'Aviation
69500 BRON

Laboratoire Départemental Vétérinaire et
d'Hydrologie
29 Rue Lafayette
70000 VESOUL

Laboratoire AGRIVALYS 71
Espace DUHESME
18 Rue de Flacé
71000 MACON

Laboratoire Val de Saône
159 Rue de Bourgogne
71680 CRECHE-SUR-SAONE

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

MC Vet Conseil - Sablé
152 Rue des Séguinières
72300 SABLE-SUR-SARTHE

Laboratoire Départemental d'Analyses
Vétérinaires
321 chemin des Moulins
73024 CHAMBERY CEDEX

Lidal - laboratoire vétérinaire
départemental
22 rue du Pré Fornet
SEYNOD, CS 70042
74600 ANNECY

Laboratoire Départemental d'Analyses
9 Avenue du Grand Cours, CS 51140
76175 ROUEN CEDEX

QUALYSE
ZAE MONTPLAISIR
79220 CHAMPDENIERS-SAINT-DENIS

FILIAVET BRESSUIRE
7 rue des artisans
Zone Alphaparc sud
79300 BRESSUIRE

Laboratoire Départemental d'Analyses
31 avenue Paul Claudel
CS 34415
80044 AMIENS CEDEX 1

Public Labos - Site de Tarn-et-Garonne
60 avenue Marcel Unal
82000 MONTAUBAN

Laboratoire Départemental d'Analyses du
VAR
375 rue Jean Aicard
83300 DRAGUIGNAN

VET'ANALYS
1128 Route de Toulon
Pôle d'activité Hyérois
83400 HYERES-LA-BAYORRE

Laboratoire Départemental d'Analyses
285 rue Raoul Follereau
BP 852
84082 AVIGNON CEDEX 2

Laboratoire de l'Environnement
et de l'Alimentation de la Vendée
Rond-Point Georges Duval
BP 802
85021 LA-ROCHE-SUR-YON CEDEX

ANI-MEDIC
52 Rue du Bourg Bâtard
85120 LA-TARDIERE

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
8 Rue Denis Papin
ZA de Mirville - Bellevue
BOUFFERE
85600 MONTAIGU-VENDEE

Laboratoire Vétérinaire Départemental
Avenue du Professeur J. Léobardy
BP 50165
87005 LIMOGES

Laboratoire Départemental
Vétérinaire Alimentaire
48 rue de la Bazaine
BP 1027
88050 EPINAL CEDEX 09

AUXAVIA
45 Route d'AUXERRE
89470 MONTEAU

VEBIO
41 bis avenue Aristide BRIAND
94117 ARCUEIL CEDEX

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 (PI) are quantitative tools for monitoring and verifying the proper functioning of an epidemiological surveillance network. The quality of the information produced is closely dependent on the quality of the network's operations. These indicators are essential tools to identify the weak points of an activity in order to adopt the optimal corrective measures. For Resapath, 16 indicators are being monitored (Table 1). They are grouped into four categories:

• Network operation:

In 2021, major upgrades to the IT data management system were implemented. They have greatly improved the performance of the system and have enabled the integration in the network of 26 new laboratories in 2021. The number of antibiograms collected has also increased by 20% (IP1a, IP1b). In 2021, one laboratory left the network following a cessation of activity and another one did not transmit its data (IP1c).

Two new operational indicators were calculated in 2021. The first one assesses the completeness of the data transmitted by the laboratories (IP1d). The objective of having 70% of descriptive data filled in and interpretable has not been reached in 2021 (60%). The second one assesses the frequency of data transmission by the laboratories. In 2021, 71% of laboratories transmitted their data at least quarterly, compared to an expected 80% (IP1e). Efforts from member laboratories have to be continued in these areas.

Despite the sharp increase in the number of data received, 74% of antibiograms were integrated into the ANSES database within four months upon the analysis by the laboratory (IP1f). The speed of data integration remains therefore highly satisfactory.

• Collection of strains of interest requested by Resapath from member laboratories:

Despite a significant increase in the quantities of strains requested in 2021 (+76% compared to 2020), the indicators remain very favorable, both for the number of strains transmitted (64% of the strains requested were transmitted to Resapath) and the rapidity of their transmission (80% of the strains were transmitted within 31 days upon request) (IP2a, IP2b).

• Coordination of the network and feedback to partners:

The Resapath steering committee met once a year as expected (IP3c) and the annual report presenting the main surveillance results was published. For the first time, this report was released simultaneously in French and English languages (IP3a).

The Resapath website is made available to members of the network and to Internet users. While, due to lack of time, it is not possible to provide regular updates of the website, it nevertheless remains a place for information exchange (IP3b). It is still regularly used to publish various documents online (key figures, list of member laboratories, annual reports, annual ring trial results, etc.).

• Scientific and technical support to partner laboratories:

In 2021, the response rate to questions from the laboratories within two weeks is highly satisfactory (89%) (IP4c). This result demonstrates the efforts implemented by the Resapath team to be available and responsive.

The results obtained by the laboratories in the annual ring trial organized by Resapath are highly satisfactory. All participating laboratories obtained a score above 31 out of 36 (IP4d, IP4e). In 2021, for the second year, the training and exchange day with the laboratories was held by videoconference. This operating mode did not allow the calculation of the exact number of participants (IP4a, IP4b).

Table 1 - Resapath performance indicators for the years 2017 to 2021

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

In pink: result lower than the expected value

Indicator				Expected value	2017	2018	2019	2020	2021
NETWORK OPERATIONS	IP1a	Number of collected antibiograms	Steady or increase	56 286	55 401	53 469	51 736	62 070	
	IP1b	Number of member laboratories (laboratory sites)	Steady or increase	72	74	75	77	102	
	IP1c	Proportion of laboratories having transmitted their antibiograms data	90%	99% (71/72)	100% (74/74)	100% (75/75)	100% (77/77)	99% (101/102)	
	IP1d	Completeness: proportion of antibiograms with fully documented and usable data ¹	70%	67%	71%	70%	67%	60%	
	IP1e	Proportion of laboratories transmitting their data at a rate consistent with the membership charter (at least quarterly)	80%	Not available					71% (72/101)
	IP1f	Proportion of antibiograms received at ANSES and included in the database within 4 months upon analysis of the sample	60%	82%	79%	79%	60%	74%	
STRAINS	IP2a	Proportion of strains requested by ANSES and actually received (excluding project mode)	50%	71% (1634/2294)	76% (1459/1917)	68% (650/958)	63% (477/757)	64% (851/1336)	
	IP2b	Proportion of strains received within 31 days upon request by ANSES	80%	82%	81%	80%	83%	80%	
COORDINATION	IP3a	Publication rate of annual reports (number of reports expected per year =1)	100%	100%	100%	100%	100%	100%	
	IP3b	Website update frequency (maximum 3-month period expected between two updates of the website)	100%	No regular update					
	IP3c	Completion rate of the steering committee meeting (number of meetings expected per year=1)	100%	100%	100%	100%	0%	100%	
SCIENTIFIC & TECHNICAL SUPPORT	IP4a	Completion rate of Resapath laboratories meeting (feedback, training and exchanges) (number of meetings expected per year=1)	100%	100%	100%	100%	100%	100%	
	IP4b	Participation rate of laboratories to the Resapath annual meeting	65%	62% (44/71)	54% (40/74)	45% (34/75)	Not available		
	IP4c	Rate of responses given within 15 days upon reception of the question from the member laboratories	60%	77% (64/83)	70% (35/50)	72% (50/69)	77% (34/44)	89% (42/47)	
	IP4d	Laboratories ² participation rate in the ring trial	90%	100% (71/71)	100% (74/74)	100% (75/75)	99% (76/77)	99% (83/84)	
	IP4e	Rate of laboratories having a score greater or equal to 31/36 to ring trial part ²	95%	96% (68/71)	97% (72/74)	99% (74/75)	99% (75/76)	100% (83/83)	

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

² Some laboratories with several laboratory sites carry out the annual ring trial in 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.

Appendix 3. Publications linked to Resapath activities (2021)

International peer-reviewed publications

Bastard J, Haenni M, Gay E, Glaser P, Madec J-Y, Temime L, Opatowski L (2021) Drivers of ESBL-producing *Escherichia coli* dynamics in calf fattening farms: A modelling study. *One Health*. 12:100238.

Bonnet R, Beyrouthy R, Haenni M, Nicolas-Chanoine M-H, Dalmasso G, Madec J-Y (2021) Host colonization as a major evolutionary force favoring the diversity and the emergence of the worldwide multidrug-resistant *Escherichia coli* ST131. *mBio*. 12(4):e0145121.

Mader R, Damborg P, Amat J-P, Bengtsson B, Bourély C, Broens EM, Busani L, Crespo-Robledo P, Filippitzi M-E, Fitzgerald W, Kaspar H, Madero CM, Norström M, Nykäsenoja S, Pedersen K, Pokludova L, Urdahl AM, Vatopoulos A, Zafeiridis C, Madec J-Y, Eu-Jamrai OB (2021) Building the European Antimicrobial Resistance Surveillance network in veterinary medicine (EARS-Vet). *Eurosurveillance*. 26(4):2001359.

Mader R, Jarrige N, Haenni M, Bourély C, Madec J-Y, Amat J-P (2021) OASIS evaluation of the French surveillance network for antimicrobial resistance in diseased animals (Resapath): success factors underpinning a well-performing voluntary system. *Epidemiology and Infection*. 149:e104.

Massot M, Châtre P, Condamine B, Métayer V, Clermont O, Madec J-Y, Denamur E, Haenni M (2021) Interplay between bacterial clones and plasmids in the spread of antibiotic resistance genes in the gut: lessons from a temporal study in veal calves. *Applied and Environmental Microbiology*. 87(24):e0135821.

Mesa-Varona O, Mader R, Velasova M, Madec J-Y, Granier SA, Perrin-Guyomard A, Norstrom M, Kaspar H, Grobbel M, Jouy E, Anjum MF, Tenhagen B-A (2021) Comparison of phenotypical antimicrobial resistance between clinical and non-clinical *E. coli* isolates from broilers, turkeys and calves in four european countries. *Microorganisms*. 9(4):678.

Valcek A, Sismova P, Nesporova K, Overballe-Petersen S, Bitar I, Jamborova I, Kant A, Hrabak J, Wagenaar J, Madec J-Y, Damborg P, Van Duinkerken E, Ewers C, Hordijk J, Hasman H, Brouwer M, Dolejska M (2021) Horsing Around: *Escherichia coli* ST1250 of Equine origin harboring epidemic IncHI1/ST9 Plasmid with bla_{CTX-M-1} and an operon for short-chain fructooligosaccharide metabolism. *Antimicrobial Agents and Chemotherapy*. 65(5):e02556-02520.

Verliat F, Hemonc A, Chouet S, Le Coz P, Liber M, Jouy E, Perrin-Guyomard A, Chevance A, Delzescaux D, Chauvin C (2021) An efficient cephalosporin stewardship programme in French swine production. *Veterinary Medicine and Science*. 7(2):432-439.

National publications

Bourély C, Jarrige N, Madec J-Y (2021) Que doit faire le praticien des données collectées par le Résapath ? *Bulletin des Groupements Techniques Vétérinaires*. Numéro Spécial 2020:15-20.

Madec J-Y, Jouy E, Haenni M (2021) Actualités sur la méthode d'antibiogramme en médecine vétérinaire. *Bulletin des Groupements Techniques Vétérinaires*. Numéro Spécial 2020:21-26.

Mader R, Jarrige N, Haenni M, Bourély C, Madec J-Y, Amat J-P (2021) Evaluation du réseau d'épidémiosurveillance de l'antibiorésistance des bactéries pathogènes animales (Résapath) par la méthode OASIS. *Bulletin Épidémiologique Santé Animale - Alimentation*. 95(Article 2):1-9.

Maugat S, Berger-Carbonne A, Jarrige N, Cazeau G, Madec J-Y, Al. (2021) Antibiotiques et résistance bactérienne : pistes d'actions pour ancrer les progrès de 2020. Saint-Maurice.13 p.
<https://www.santepubliquefrance.fr//rapport-synthese>

Oral communications and posters in congresses

Madec J-Y. (2021) Infections nosocomiales : le point de vue du bactériologiste. *Congrès annuel de l'AFVAC*. Bordeaux, France, 25 novembre. Communication orale sur invitation.

Madec J-Y. (2021) La résistance aux antibiotiques en 2021 chez les animaux de compagnie. *Congrès annuel de l'AFVAC*. Bordeaux, France, 25 novembre. Communication orale sur invitation.

Madec J-Y. (2021) Cinétique de l'antibiorésistance chez le veau de boucherie. *Les Matinales de la Recherche d'Interbev*. Paris, France, 16 novembre. Communication orale sur invitation.

Madec J-Y. (2021) The main AMR issues in a One Health approach. *11th GABRIEL International meeting*. Annecy, France., 9 novembre. Communication orale sur invitation.

Madec J-Y. (2021) Et si j'avais des bactéries résistantes dans ma clinique ? . *48èmes Journées annuelles de l'AVEF*. Marseille, France, 4 novembre. Communication orale sur invitation.

Madec J-Y. (2021) Sensibilité des staphylocoques dorés aux antibiotiques. *Journées Nationales des Groupements Techniques Vétérinaires*. Tours, France, 20 octobre. Communication orale sur invitation.

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