EFSA ACTIVITIES TO STRENGTHEN INTERSECTORAL COOPERATION IN MONITORING AND RISK ASSESSMENT OF AMR

Dr. Ernesto Liebana, BIOHAZ Team Leader and AMR coordinator

Cross-Sectoral One Health Conference on Antimicrobial Resistance. 7th December 2023. Riga Stradins University, Latvia

efsa
EUROPEAN FOOD SAFETY AUTHORITY

THE ONE HEALTH RESPONSE TO AMR

EU AMR One-Health Network

(i) trans-sectoral and integrated approach
- enhance MSs discussions
- exchange information and sharing of best practices

2017 EU AMR 'One Health' Action Plan

Council of the European Union

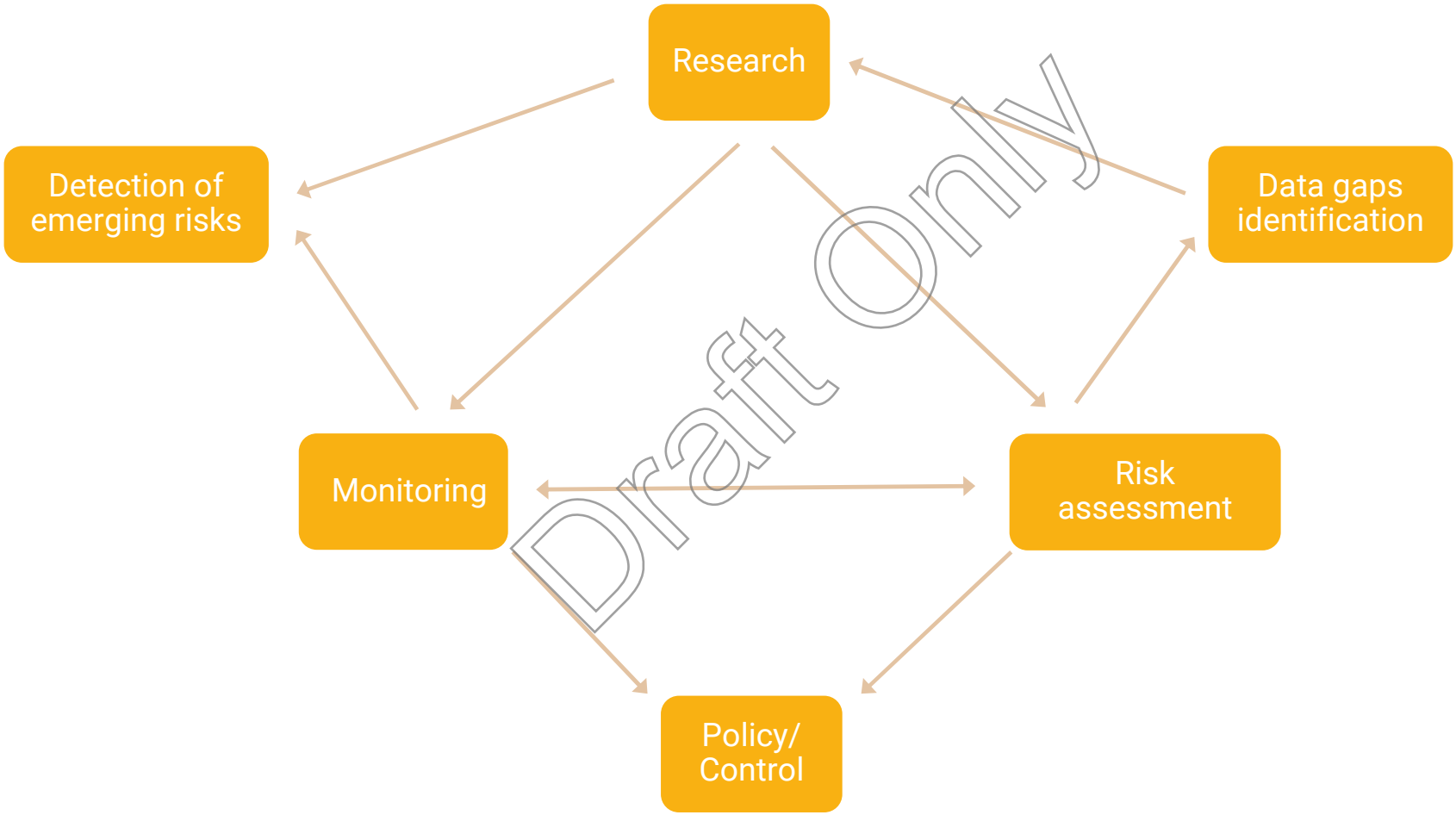
A common approach from the EU MSs in implementing actions against AMR:

(i) possible targets for AMR

(iii) how to design impactful 'one health' national action plans against AMR

(v) improvements in surveillance of AMR

EFSA BRIDGING AMR RESEARCH, MONITORING, RISK ASSESSMENT AND POLICY



AMR MONITORING FOOD CHAIN: EFSA/ECDC EU SUMMARY REPORT ON AMR

SCIENTIFIC REPORT

JOURNAL

The European Union Summary Report on Antimicrobial Resistance in zoonotic and indicator bacteria from humans, animals and food in 2020/2021

European Food Safety Authority (EFSA) and
European Centre for Disease Prevention and Control (ECDC)

Abstract

Antimicrobial resistance (AMR) data on zoonotic and indicator bacteria from humans, animals and food are collected annually by the EU Member States (MSs) and reporting countries, jointly analysed by EFSA and ECDC and presented in a yearly EU Summary Report. This report provides an overview of the main findings of the 2020–2021 harmonised AMR monitoring in *Salmonella* spp., *Campylobacter jejuni* and *C. coli* in humans and food-producing animals (broilers, laying hens and turkeys, fattening pigs and bovines under 1 year of age) and relevant meat thereof. For animals and meat thereof, indicator *E. coli* data on the occurrence of AMR and presumptive Extended spectrum β-lactamases (ESBL)-/AmpC β-lactamases (AmpC)-/carbapenemases (CP)-producers, as well as the occurrence of methicillin-resistant *Staphylococcus aureus* are also analysed. In 2021, MSs submitted for the first time AMR data on *E. coli* isolates from meat sampled at border control posts. Where available, monitoring data from humans, food producing animals and meat thereof were combined and compared at the EU level, with emphasis on multidrug resistance, complete susceptibility and combined resistance patterns to selected and critically important antimicrobials, as well as *Salmonella* and *E. coli* isolates exhibiting ESBL-/AmpC-/carbapenemase- phenotypes. Resistance was frequently found to commonly used antimicrobials in *Salmonella* spp. and *Campylobacter* isolates from humans and animals. Combined resistance to critically important antimicrobials was mainly observed at low levels except in some *Salmonella* serotypes and in *C. coli* in some countries. The reporting of a number of CP-producing *E. coli* isolates (harbouring bla_{OXA-48}, $bla_{VIM-1/-2/-4}$ and bla_{NDM-1} genes) in pigs, bovines and meat thereof by a limited number of MSs (4) in 2021, requests a thorough follow-up. The temporal trend analyses in both key outcome indicators (rate of complete susceptibility and prevalence of ESBL-/AmpC-producers) showed that encouraging progress have been registered in reducing AMR in food-producing animals in several EU MSs over the last years.

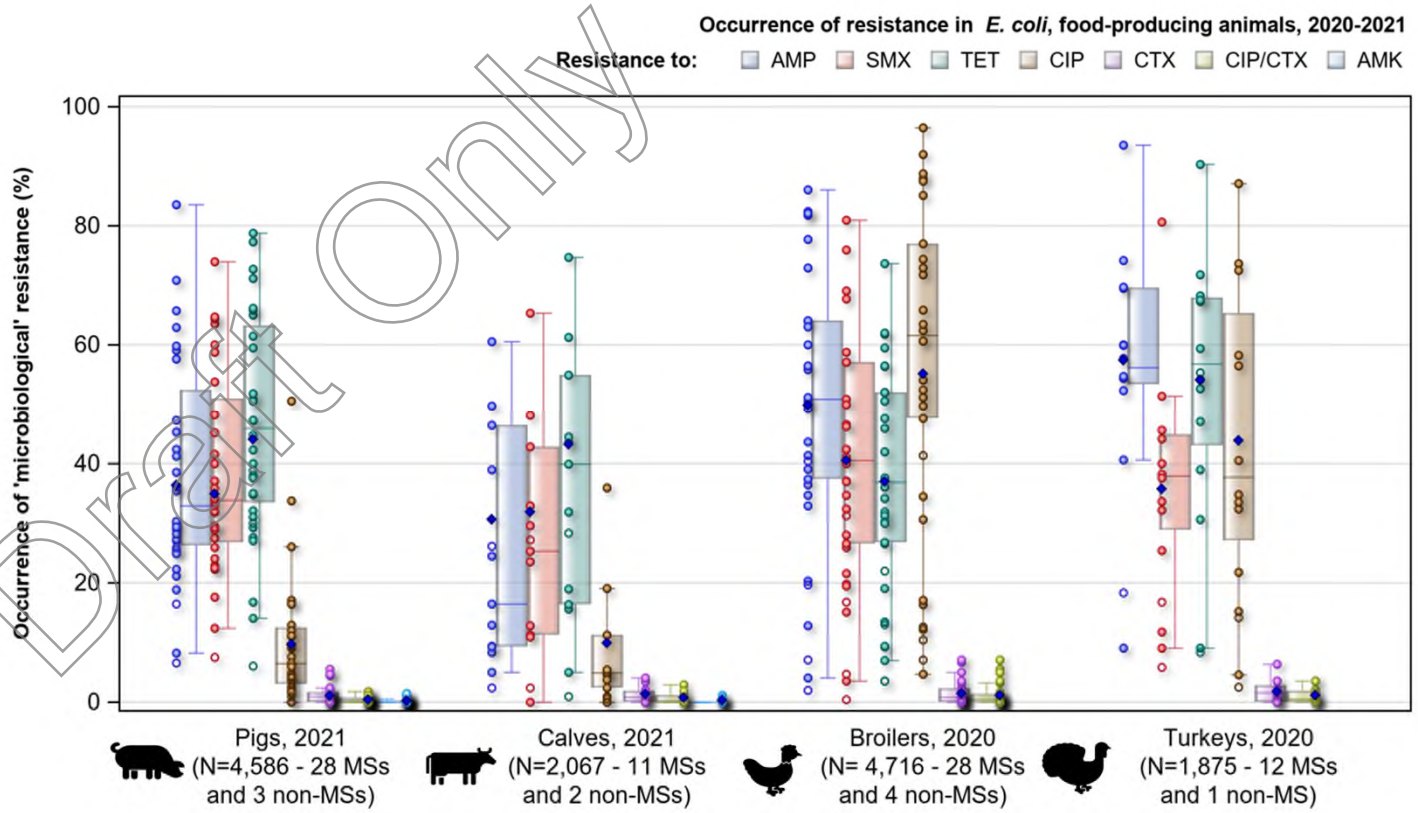
Keywords: antimicrobial resistance; zoonotic bacteria; indicator bacteria; ESBL; MRSA

Requestor: European Commission
Question number: EFSA-Q-2021-00768
Correspondence: zoonosis@efsa.europa.eu (EFSA); FWD@ecdc.europa.eu (ECDC)

- Understanding of the **development** and **spread** of resistance
- Follow up **temporal trends** in occurrence of AMR
- Provides **reliable indicators** for evaluating interventions
- Identification of **emerging** specific resistance patterns

REPORTING AMR IN THE EU - INDICATOR E. COLI

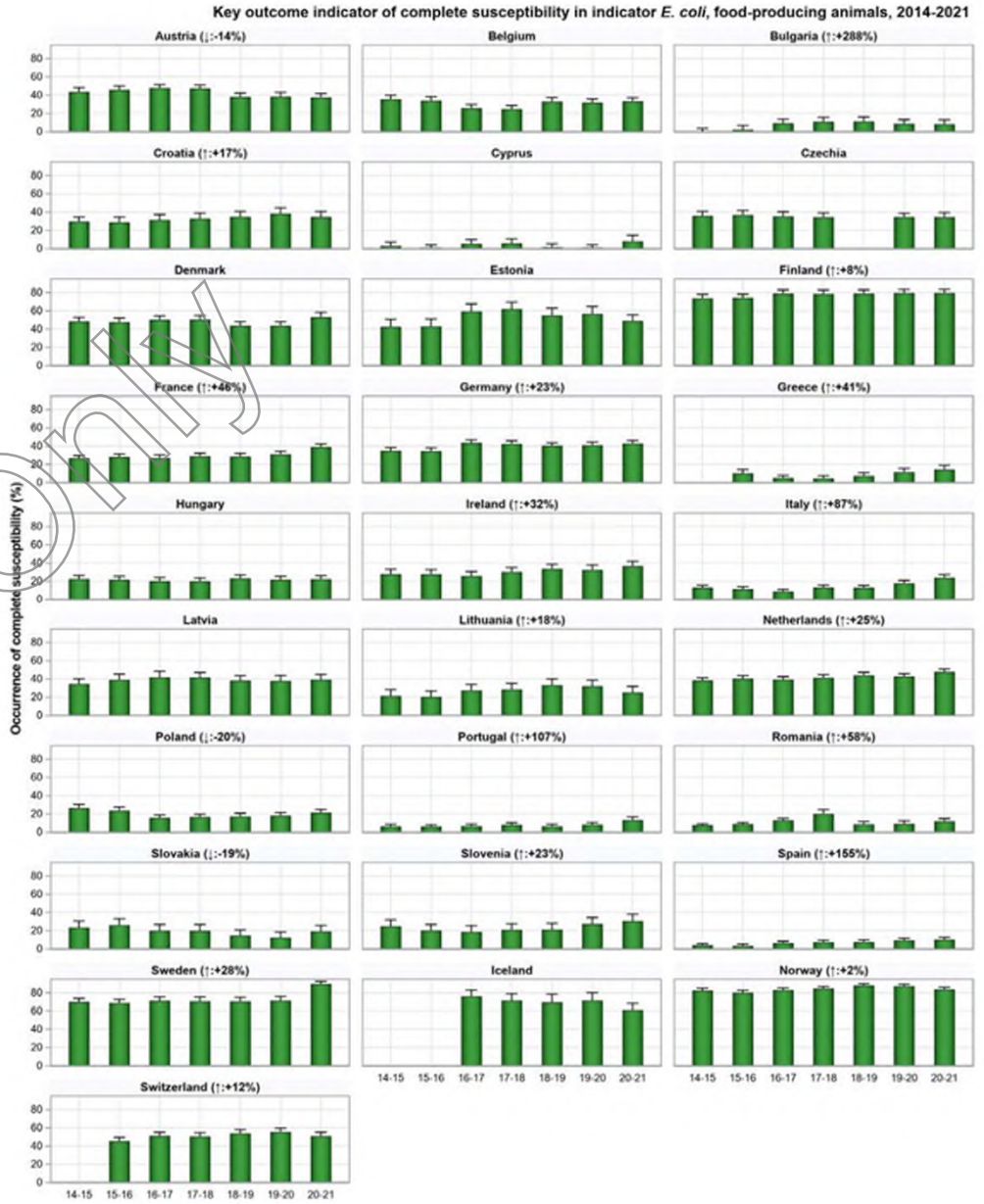
- **High** levels of R to commonly used antimicrobials (AMP, SMX, TET)
- **Important** R to fluoroquinolones (**CIP**) in broilers and turkeys
- **Low** R to cefotaxime (**CTX**)
- **Uncommon** combined R to third-generation cephalosporins and fluoroquinolones (***CIP/CTX***) in all animal categories.
- **Very low** levels of R to amikacin (**AMK**)



KEY OUTCOME INDICATOR COMPLETE SUSCEPTIBILITY IN INDICATOR *E. COLI*

Marked variations among reporting countries

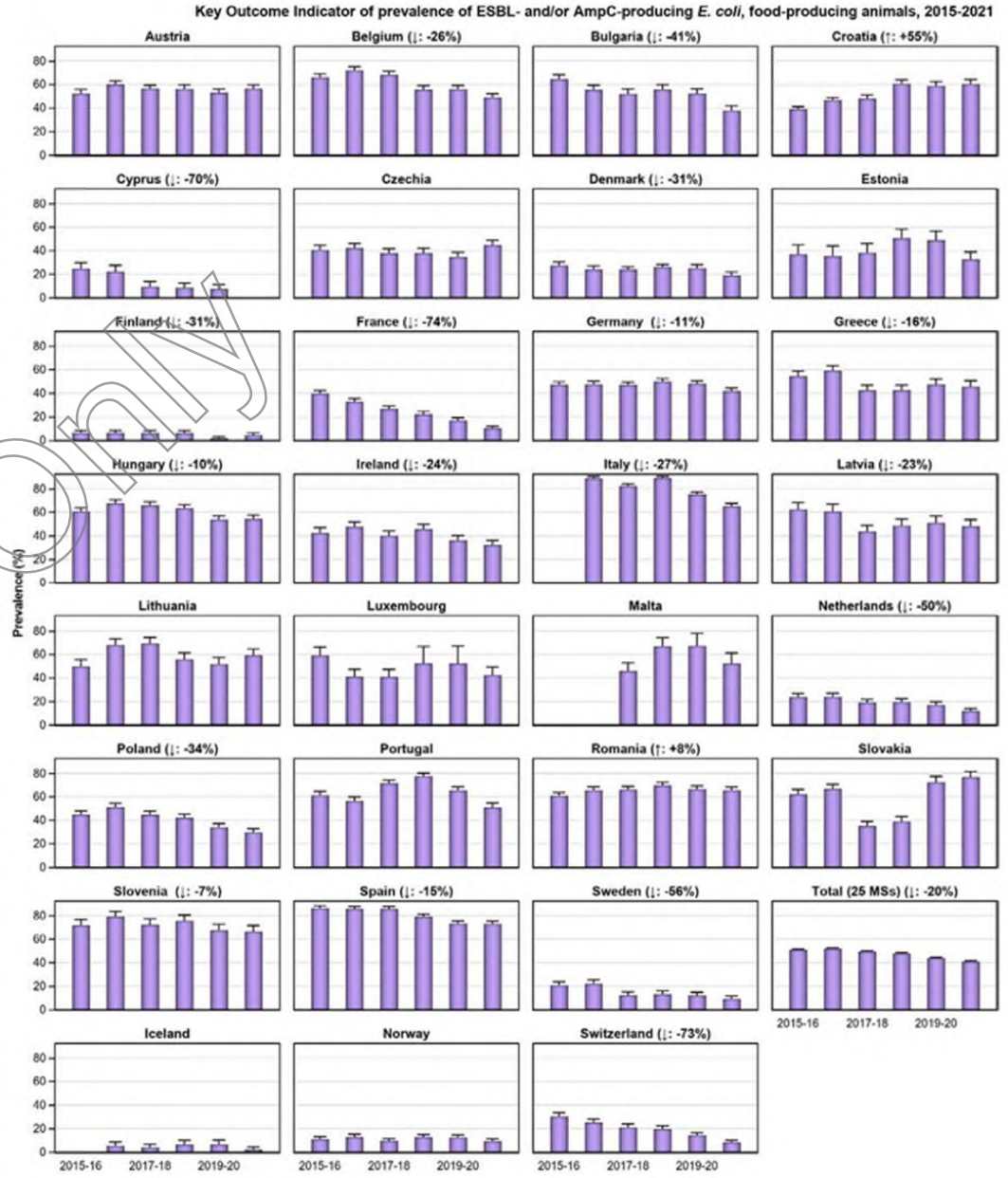
Statistically significant **increasing trends** (from 2014-2021) registered **in 55% of the MSs** (15 MSs) and **2 additional** reporting countries (CH, NO)



KEY OUTCOME INDICATOR PREVALENCE OF ESBL- AND/OR AMPC-PRODUCING *E. COLI*

Marked variations among reporting countries

Statistically significant **decreasing trends** (from 2015-2021) have been observed in **63% of the MSs** (17 MSs) **and 1 additional** reporting countries (CH)



DETECTING EMRGING SIGNALS: CARBAPENEM RESISTANCE AND THE FOOD CHAIN

- Paramount Importance of carbapenems in human medicine
- Monitoring identified emerging R (still uncommon) in bacteria from food-producing animals
- Further detailed investigations on origin and dissemination needed (spill over events from humans to animals ?)
- Risk that the problem becomes endemic in food-producing animals if nothing done.

2020 and before

2020, Austria: broilers (*bla*VIM-1)

2019, Germany: pigs (*bla*VIM, *bla*OXA-48 and *bla*GES-5)

2018, no CP-resistance *E. coli* were detected

2016, Romania: broilers (*bla*OXA-162)

2021

Hungary: bovine meat and pig meat (*bla*NDM-5).

Spain: pigs (*bla*OXA-48)

Italy: pigs and bovines.
Czechia: pigs

*bla*OXA-181
*bla*OXA-48
*bla*NDM-5

2022

Italy: turkey (*bla*OXA-181), broiler (*bla*VIM-1)

Austria: broilers (*bla*VIM-1)

2023 (preliminary data)

Norway: cattle (*bla*NDM-5)

Czechia: pigs (*bla*VNDM-5)

Others to come ??

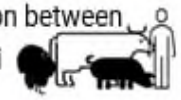
CARBACAMP PROJECT

CarbaCamp
GP/EFSA/BIOHAW/2023/04
enters into force on **14.09.2023**

- Beneficiary - DTU
- Subcontractor - EDL
- Budget - 357.000 €
- Duration – 24 months

Purpose of the study

wild-type distribution between C. jejuni and C. coli



ECOFF values

the comparability between the EUCAST and CLSI recommended media for MIC determination of Campylobacter.

Monitoring of Campylobacter ?
- Ertapenem
- Imipenem
- Meropenem

genomic diversity (clustering) of susceptible and non-susceptible C. jejuni and C. coli

resistance phenomenon, role of blaOXA genes

WGS IN AMR SURVEILLANCE: STEP BY STEP IMPLEMENTATION

✓ EURL-AR protocol


DTU Food
National Food Institute

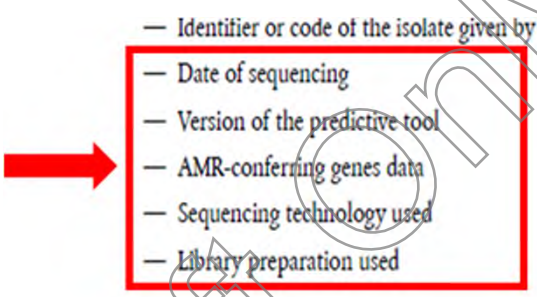
PROTOCOL FOR WHOLE GENOME SEQUENCING AND BIOINFORMATIC ANALYSIS OF BACTERIAL ISOLATES RELATED TO THE EU MONITORING OF ANTIMICROBIAL RESISTANCE

AUTHORED BY THE EURL-AR
VERSION 2.2 - DECEMBER 2021

RENE S. HENDRIKSEN & JETTE S. KJELDGAARD

https://www.eurl-ar.eu/wgs.aspx

✓ EFSA reporting guidelines


— Identifier or code of the isolate given by the l
— Date of sequencing
— Version of the predictive tool
— AMR-conferring genes data
— Sequencing technology used
— Library preparation used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Technical report | Open Access

Manual for reporting 2022 antimicrobial resistance data within the framework of Directive 2003/99/EC and Decision 2020/1729/EU

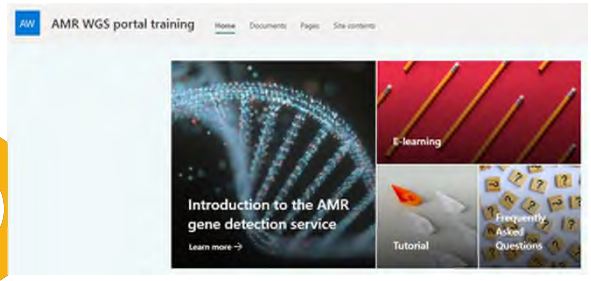
European Food Safety Authority (EFSA), Giusi Amore, Pierre-Alexandre Beloeil, Raquel Garcia Fierro, Beatriz Guerra, Alexandra Papanikolaou, Valentina Rizzi, Anca-Violeta Stoicescu

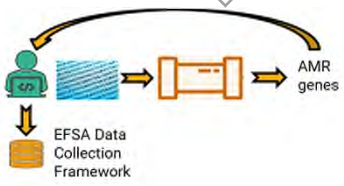
First published: 30 January 2023 | https://doi.org/10.2903/sp.efsa.2023.EN-7826

Requestor: European Commission
Question number: EFSA-Q-2023-00011

PDF TOOLS SHARE

✓ EFSA bioinformatics portal





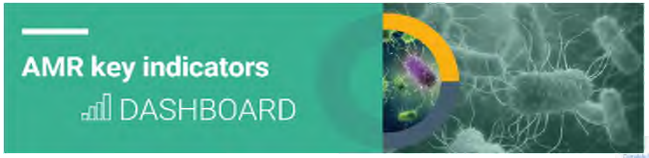
Genotypic data reported

2021 ➡ Provided by 4 MSs
2022 ➡ Provided by 7 MSs

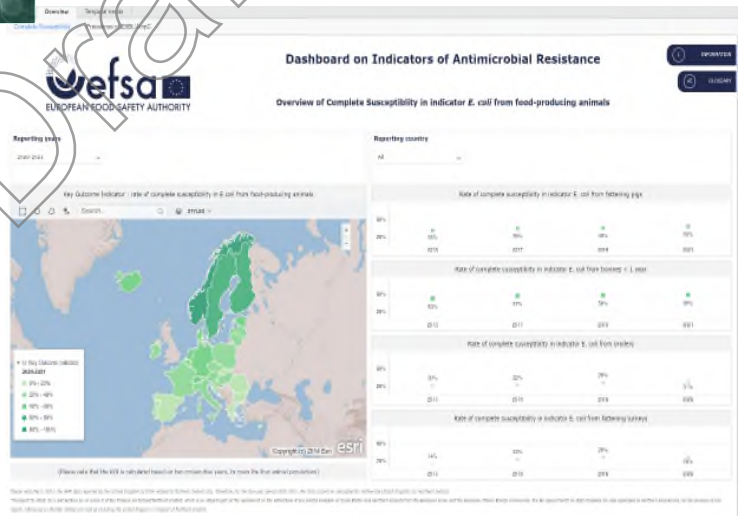
AMR MONITORING IN ANIMALS AND FOOD IN THE EU MODERNISATION - ONLINE VISUALISATION TOOLS: DASHBOARDS & STORY MAPS

[Monitoring antimicrobial resistance (arcgis.com)]

[Monitoring AMR in Escherichia coli (arcgis.com)]



[Dashboard on Indicators of Antimicrobial Resistance | EFSA (europa.eu)]



- KOI_{CS}
- KOI_{ESBL}

Data VIZ

[Antimicrobial resistance in Europe (europa.eu)]

RONAFA: REDUCING ABS NEES IN FOOD-PRODUCING ANIMALS

efsa
European Food Safety Authority

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH


SCIENTIFIC OPINION

EUROPEAN MEDICINES AGENCY

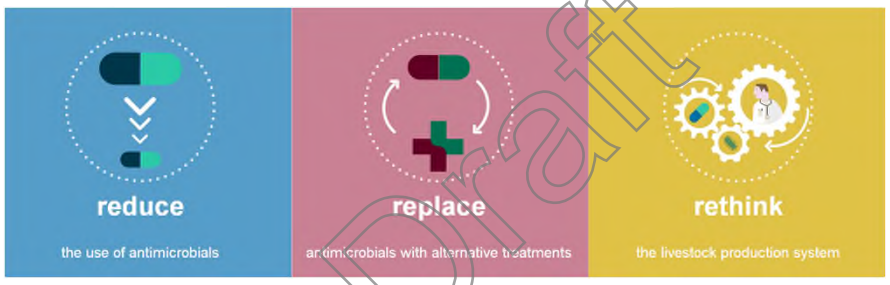
EFSA Journal

ADOPTED: 1 December 2016 (EFSA BIOHAZ Panel), 8 December 2016 (EMA CVMP)

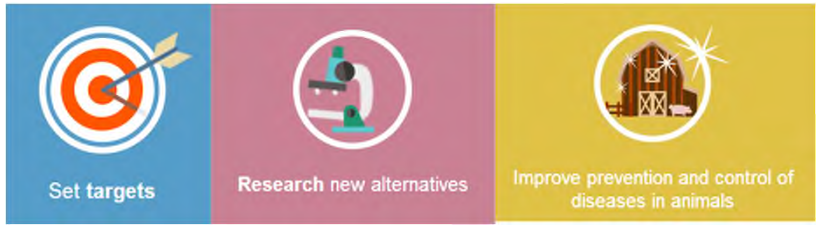
doi: 10.2903/j.efsa.2017.4666

EMA and EFSA Joint Scientific Opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety (RONAFA)

EMA Committee for Medicinal Products for Veterinary Use (CVMP) and EFSA Panel on Biological Hazards (BIOHAZ),



Some recommended control options:

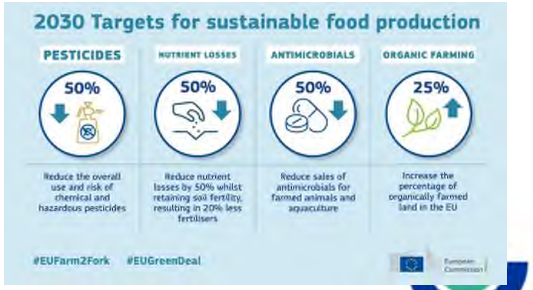


EC Legislation, Veterinary Medicinal Products, Regulation 2019/6

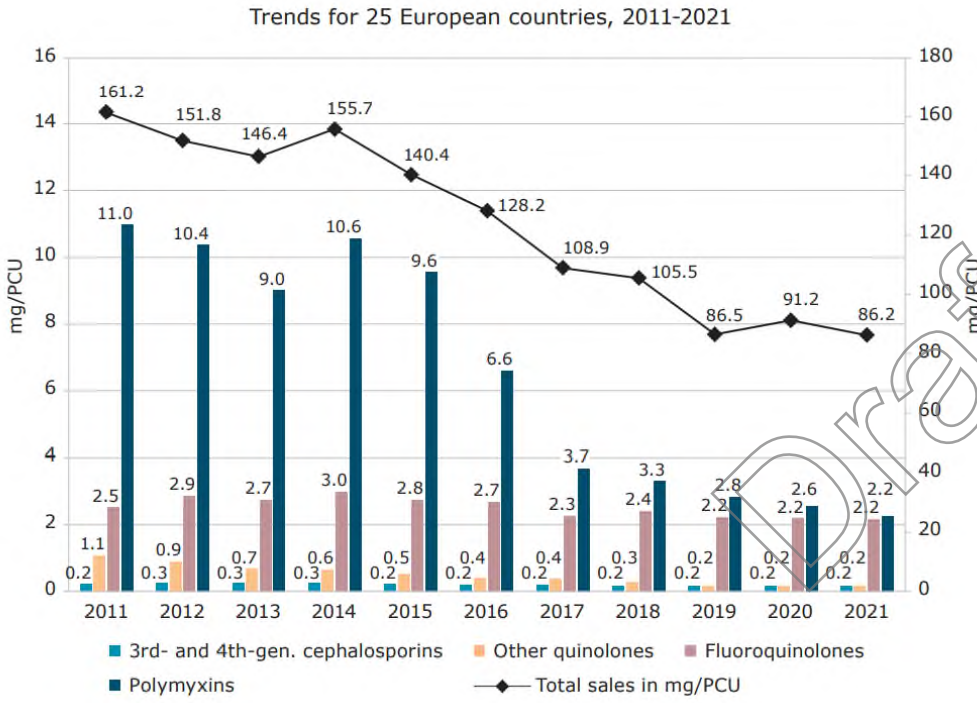

7.1.2019 EN Official Journal of the European Union L 4/43

REGULATION (EU) 2019/6 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 11 December 2018
on veterinary medicinal products and repealing Directive 2001/82/EC
(Text with EEA relevance)

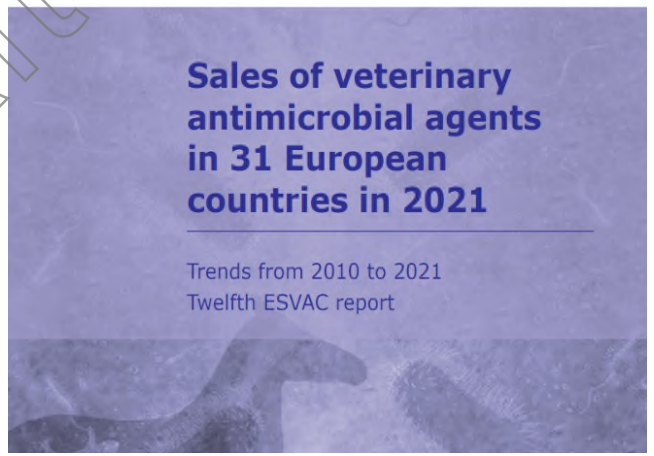
EU Green deal, F2F



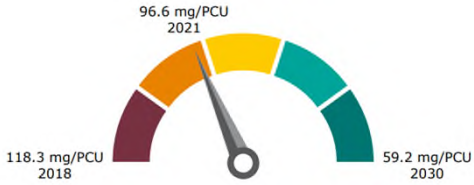
CONSUMPTION IN ANIMALS



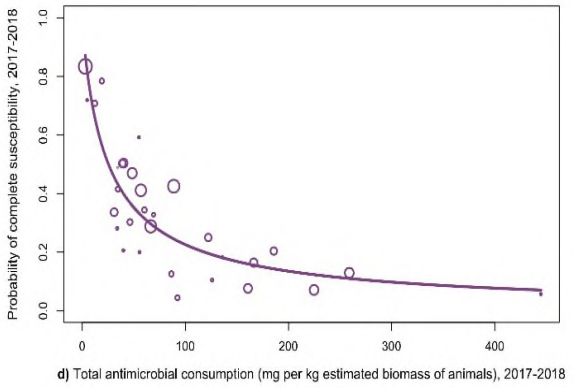
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH



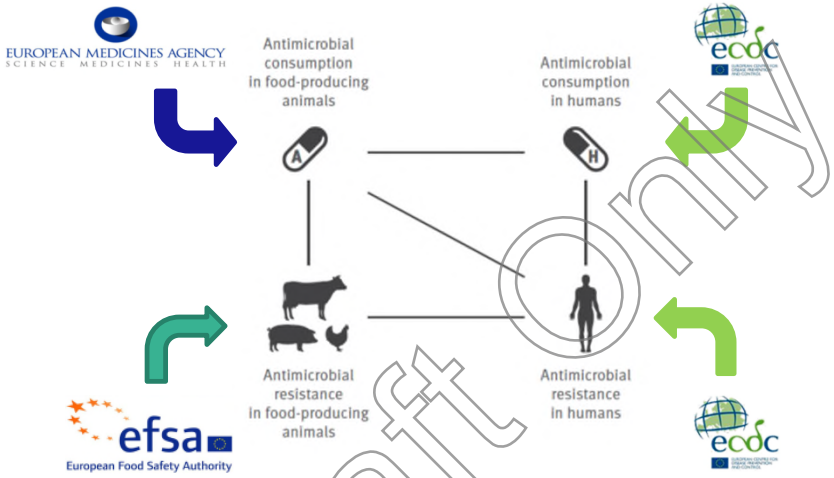
Farm-to-Fork goal: reduce EU sales of antimicrobials for farmed animals + aquaculture by 50% by 2030

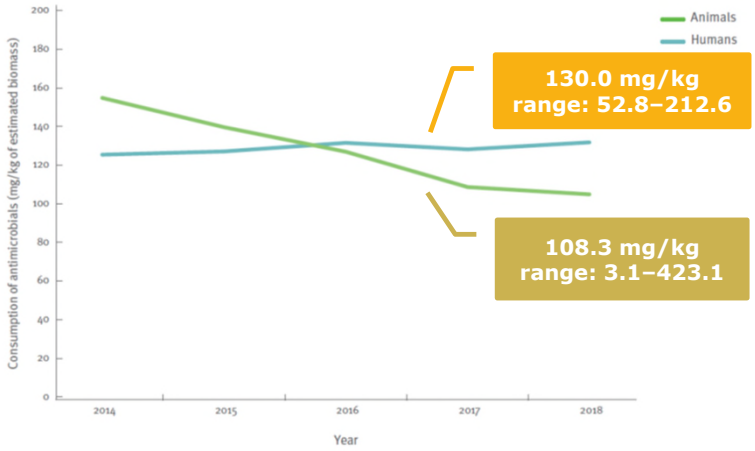


JIACRA: INTEGRATED ANALYSIS OF AB CONSUMPTION & AMR



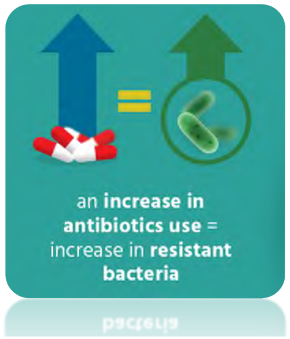
A consistently **lower probability** of detecting completely susceptible indicator *E. coli* in animals when AMC was higher





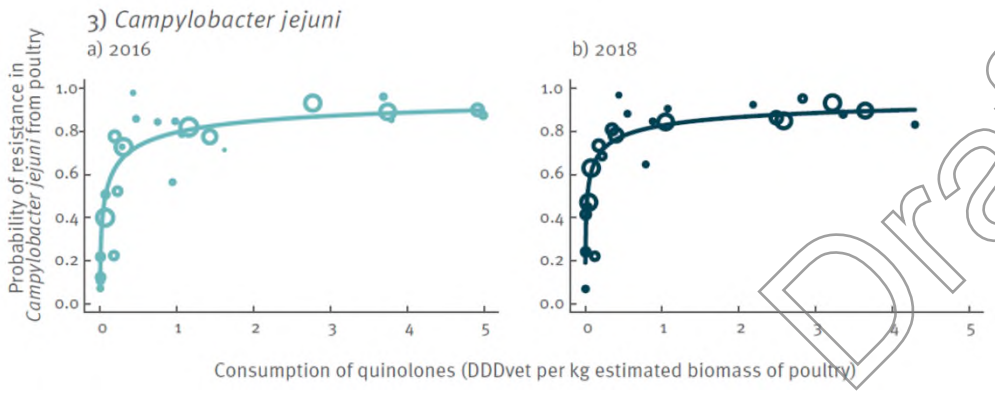
Overall Conclusions

- Interventions to **reduce AMC** will have a **beneficial impact** on **AMR**
- Need to promote, in both humans and food-producing animals:
  - ✓ **prudent use** of antimicrobial agents
  - ✓ **infection prevention and control**
- High levels of AMC and AMR still reported: **interventions to be reinforced**

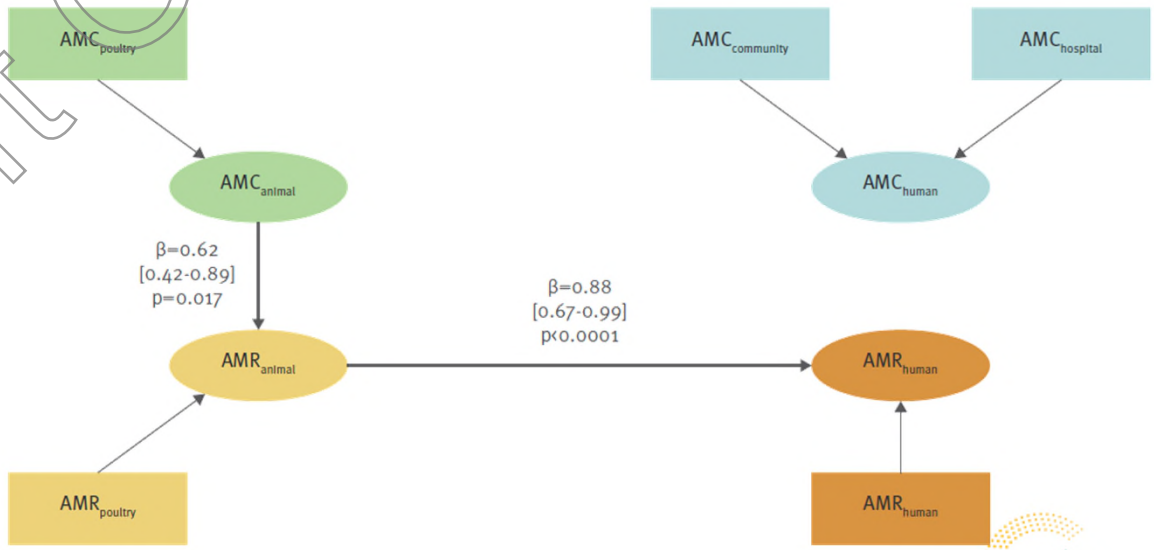


COMPARING AMC AND AMR: *C. JEJUNI* AND QUINOLONES

Association between **consumption** and **resistance** "within sector" (animal)



Association between **consumption** in **animals** and **resistance** in bacteria from **animals** and as well from **humans**



No goodness of fit estimate; R^2 AMRanimal = 0.39 [95% CI: 0.17–0.80]; R^2 AMRhuman = 0.78 [0.45–0.98].

AMR ENVIRONMENT

SCIENTIFIC OPINION

EFSA Journal

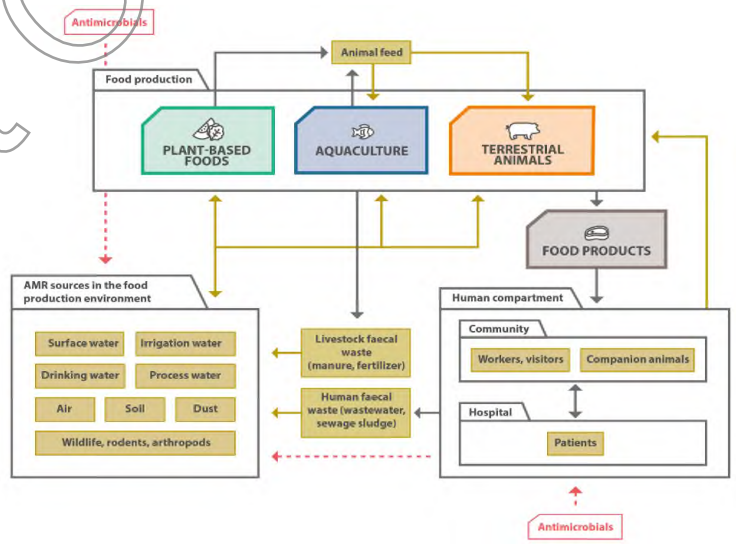
ADOPTED: 29 April 2021

doi: 10.2903/j.efsa.2021.6651

Role played by the environment in the emergence and spread of antimicrobial resistance (AMR) through the food chain

EFSA Panel on Biological Hazards (BIOHAZ),
Konstantinos Koutsoumanis, Ana Allende, Avelino Alvarez-Ordonez, Declan Bolton, Sara Bover-Cid, Marianne Chemaly, Robert Davies, Alessandra De Cesare, Lieve Herman, Friederike Hilbert, Roland Lindqvist, Maarten Nauta, Giuseppe Ru, Marion Simmons, Panagiotis Skandamis, Elisabetta Suffredini, Hector Arguello, Thomas Berendonk, Lina Maria Cavaco, William Gaze, Heike Schmitt, Ed Topp, Beatriz Guerra, Ernesto Liebana, Pietro Stella and Luisa Peixe

Sources and transmission routes



- Faecal matter (fertilisation and irrigation water)
- Feed, and humans
- Water (with human and animal faecal material)

AMR ENVIRONMENT

Mitigation strategies

- Reducing bacterial content of manure, sewage and irrigation/aquaculture water.
- Preventing transmission from other animals, dust, feed, or surface run-off water.
- Cleaning/disinfection, hygienic procedures for workers.
- Water treatment: a multiple barrier approach: low impact approaches together with advanced wastewater treatment technologies.

Knowledge gaps, research needs

- Large number of gaps
- Most detailed studies not within the EU.
- Lack of systematic studies (similar sampling, detection methodologies, etc).
- Insufficient data to support assessment of quantitative impact on public health.

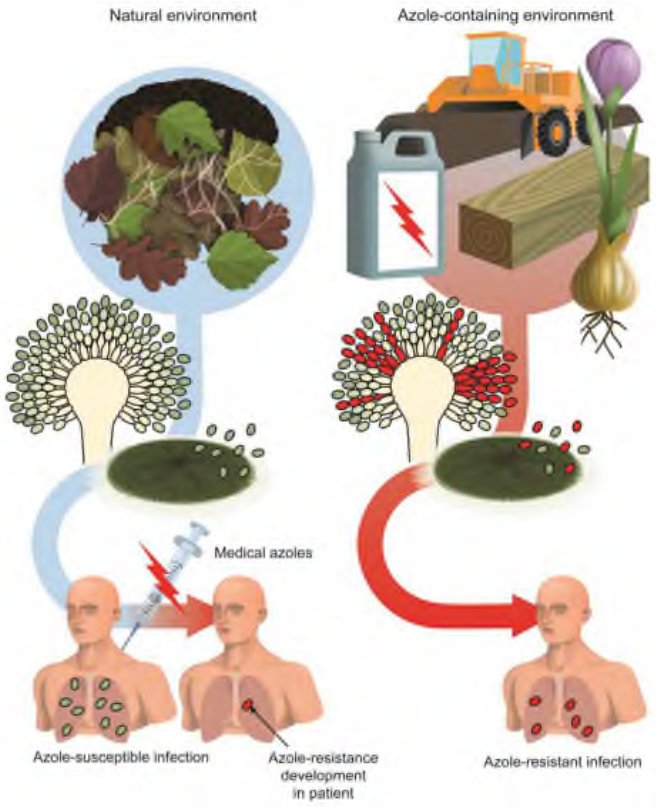
AZOLE FUNGICIDES

- Health issue: infection in human with *Aspergillus* spp. resistant to treatment with azoles
- Resistance may develop following:

  i) therapeutic treatment

  ii) environmental exposure (for which there is growing evidence)

- Use of azole fungicides in the environment, 4 regulatory regimes:
  - ➢Plant protection products (EFSA)
  - ➢Biocides (ECHA)
  - ➢Industrial chemicals (ECHA), e.g. wood preservatives, cosmetics
  - ➢Veterinary medicines (EMA)



source: Verweij et al., 2020

AZOLE FUNGICIDES

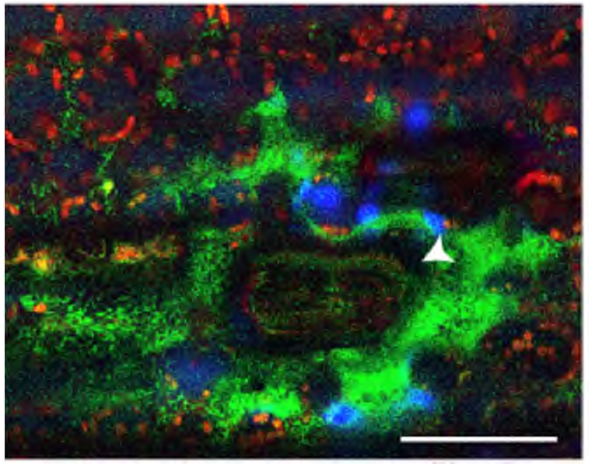
Joint EC Mandate (overall coordination by EFSA)

- ✓ Collect data on use in all domains other than human medicines
- ✓ Identify causative link between environmental use and R development and describe epidemiology
- ✓ Assess risks
- ✓ Identify risk factors and control options
- ✓ Identify type of studies to be provided by applicants for approval of azoles for different uses (affecting applications to ECHA, EFSA, EMA)
- ✓ Identify data gaps and research needs

Deadline for the interagency report: **July 2024**

ANTIBIOTIC AND PLANT PATHOGENIC BACTERIA

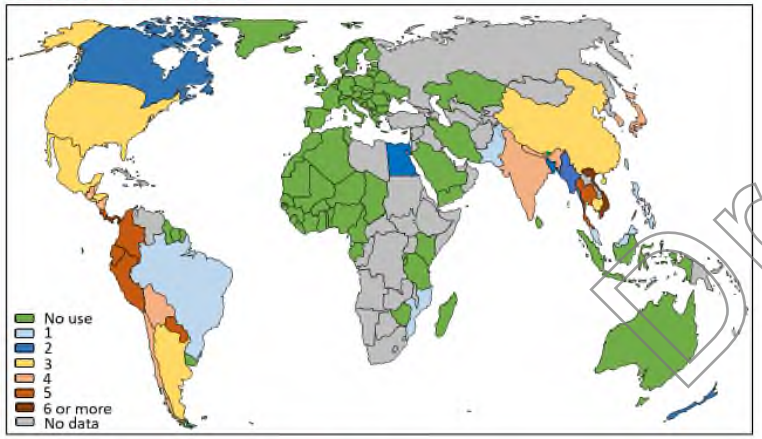
- PPB responsible for major losses to crops worldwide (estimated over one billion dollars / year)
- Increasing trend in Emerging infectious plant diseases linked to bacteria (also of AMR in plant pathogenic bacteria)
- Antibiotic use in crop cultivation is **considered** as very low in comparison to use in both veterinary and medical fields (FAO and WHO, 2019)
- Recent review (Taylor and Reeder in 2020) suggested that the use for crop protection is much more widespread than thought



EFSA COMMISSIONED THE PLANTIBIO PROJECT

- PPB responsible for major losses to crops worldwide
- Increasing trend in plant diseases linked to bacteria (also of AMR in PPB)
- Antibiotic use in crop cultivation is **not allowed in the EU**
- Recent evidence suggests that the use for crop protection is more widespread than thought

Antibiotics used for PPB control



More than 30 countries are reported to use antibiotics on crops

Difficulty to list countries authorizing the use of antibiotics as plant protection products worldwide

Collection, analysis and synthesis of data about...

Antibiotic use for control of PPB

Antibiotic resistance in PPB

Alternatives and innovative treatments for control of PPB

UCLouvain

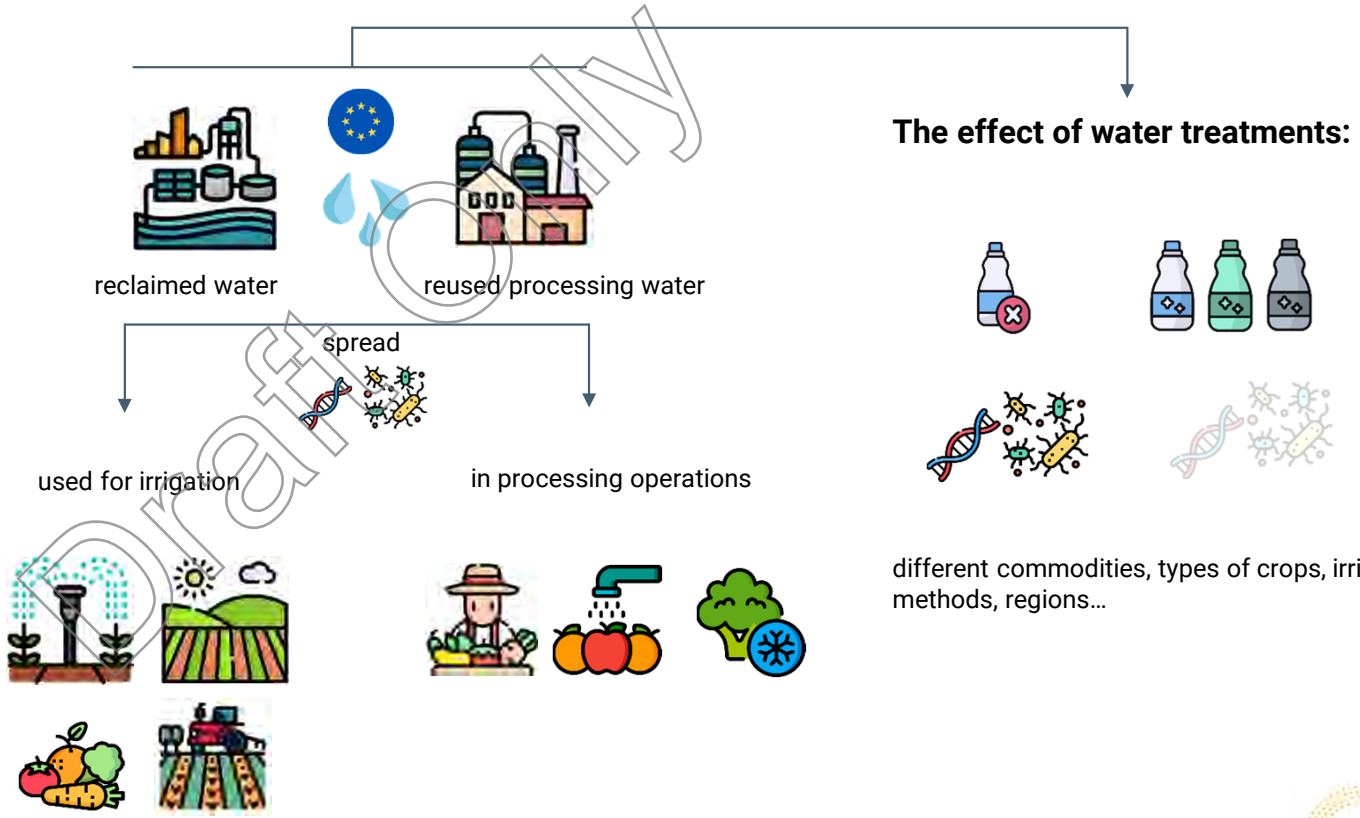
NEW EFSA PROCUREMENT: ROLE OF WATER IN THE SPREAD OF AMR TO FRUITS/VEGETABLES/ HERBS

Objective 1: Optimize detection methods: culture, PCR-based, metagenomics.

Objective 2: Occurrence in reclaimed water for irrigation

Objective 3: Occurrence in recycled water during handling/processing

3 Years Project (starting Jan 2024)



Icons from www.flaticon.com

AN UP-COMING BASELINE SURVEY (BLS) ON AMR IN AQUACULTURE ANIMALS

- A mandate from the European Commission
- The EC intends to undertake a BLS on AMR in bacteria from aquaculture animals, to assess the epidemiological situation in the aquaculture sector, and from a public health perspective.
- EFSA to provide report with technical specifications by June 2024.

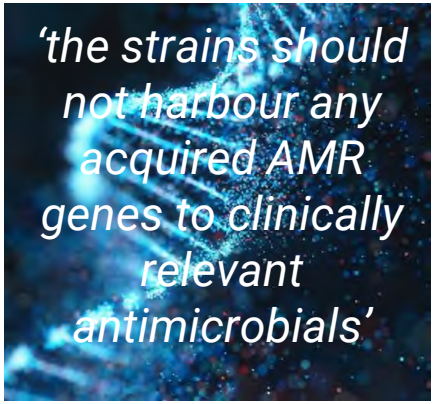
QPS AMR STATEMENT

BIOHAZ Panel Statement on "*How to interpret the Qualified Pressumption of Safety qualification on 'Acquired antimicrobial resistance genes'*"

- relevant for the EFSA safety assessment in regulated products
- the use of a QPS microorganism, viable/inactivated, or its product(s) should not add to the pool of AMR genes, nor increase the spread of AMR

Main conclusions:

- *The terms 'intrinsic' and 'acquired' AMR genes were defined for EFSA's risk assessments*
- *A bioinformatic approach is proposed for demonstrating the 'intrinsic'/'acquired' nature of an AMR gene.*
- *Genes identified as responsible for 'intrinsic' resistance could be considered as being of no concern*
- *'Acquired' AMR genes resulting in a resistant phenotype should be considered as a concern.*
- *If the presence of the 'acquired' AMR gene is not leading to phenotypic resistance, further case-by-case assessment is necessary.*



Public consultation

OTHER ACTIVITIES RELATED TO ANIMAL HEALTH AND WELFARE

LISTING AND CATEGORISATION OF AMR BACTERIA WITHIN THE FRAMEWORK OF THE EU 'ANIMAL HEALTH LAW'

8 'most relevant' antimicrobial-resistant (AMR) bacteria in the EU:

Dogs and cats 	Horses 	Swine 	Poultry 	Cattle 	Sheep and goats 
Escherichia coli	*Escherichia coli*	*Escherichia coli*	*Escherichia coli*	*Escherichia coli*	*Escherichia coli*
	Staphylococcus aureus			*Staphylococcus aureus*	
Pseudomonas aeruginosa	*Rhodococcus equi*	*Brachyspira hyodysenteriae*	*Enterococcus cecorum*		
Staphylococcus pseudintermedius			*Enterococcus faecalis*		

AMR ANIMAL PATHOGENS: EFSA OUTPUTS

8 Scientific Opinions:

0–33%	33–66%	66–100%
Not listed	Uncertainty about listing	Listed
Any probability range that crosses into the 33–66% zone		

From recent Council Recommendations: "Continue to assess, on the basis of follow-up to several recent scientific opinions EFSA, animal diseases caused by bacteria resistant to antimicrobials, to ascertain if it is needed to list any of those diseases in Regulation (EU) 2016/429 ('Animal Health Law') with a view to categorise them for any regulatory surveillance, control or other management measures."

Antimicrobial-resistant bacterium	Animal species	Link	Date published	Outcome of the assessment on listing (probability range)
Staphylococcus pseudintermedius	Dogs and cats	https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2022.7080	01/02/2022	**Uncertain** (33–90%)
Rhodococcus equi	Horses	https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2022.7081	02/02/2022	**Uncertain** (10–66%)
Enterococcus faecalis	Poultry	https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2022.7127	21/02/2022	**Uncertain** (33–66%)
Enterococcus cecorum	Poultry	https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2022.7126	25/02/2022	**Uncertain** (33–75%)
Brachyspira hyodysenteriae	Swine	https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2022.7124	15/03/2022	**Uncertain** (33–66%)
Pseudomonas aeruginosa	Dogs and cats	https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2022.7310	03/05/2022	**Uncertain** (33–90%)
Escherichia coli	Dogs and cats, horses, swine, poultry, cattle, sheep and goats	https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2022.7311	10/05/2022	**Uncertain** (33–66%)
Staphylococcus aureus	Cattle and horses	https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2022.7312	10/05/2022	**Uncertain** (60–90%)

AMR AND ANIMAL TRANSPORT

European Parliament


SCIENTIFIC OPINION

Transmission of antimicrobial resistance (AMR) during animal transport

EFSA Panel on Biological Hazards (BIOHAZ)

Abstract

CHECK OUT

OUR STORY

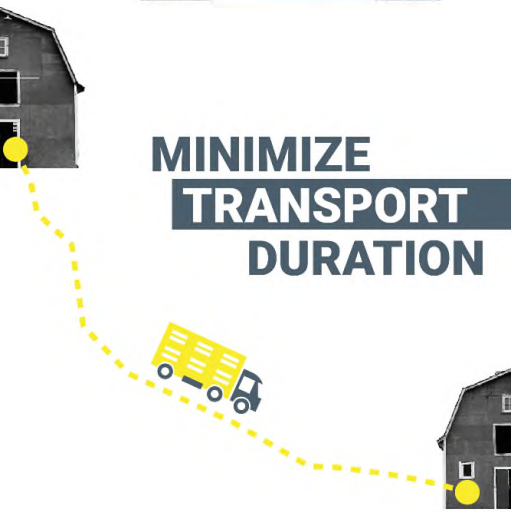
describing additional mitigation measures, main risk factors, and data gaps

HOW TO PREVENT the spread of RESISTANT BACTERIA during our TRANSPORT

CATTLE

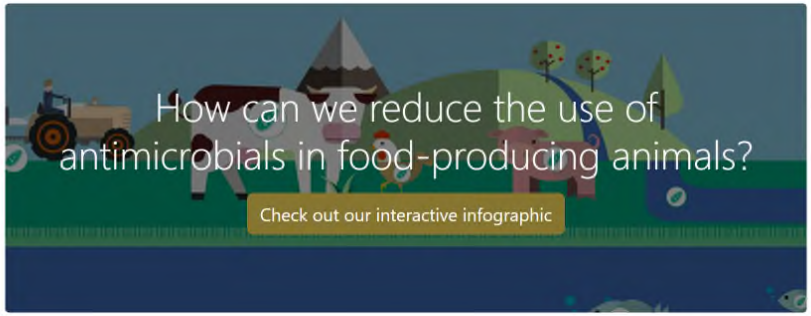
PIGS

POULTRY



CLEAN AND DESINFECT VEHICLES and equipment

IMPROVING AMR COMMUNICATION, EDUCATION AND STAKEHOLDER ENGAGEMENT



FINAL REMARKS

- Working with a **One health approach** is essential: power of integrated, timely and actionable surveillance and risk assessments.
- Importance of **partnership** between EFSA and EU MSs, with research funding bodies, and between risk managers and risk assessors.
- EFSA applies the latest findings and **new technologies** in the fight against AMR. Genomic techniques will help us to identify more effectively where AMR emerges and how it spreads across the food chain.

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