EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The past, present, and future of European surveillance of antimicrobial consumption in animals

AACTING Fourth International Conference 1 - 2 February 2024

Presented by Cristina Ribeiro-Silva
Veterinary Antimicrobial Monitoring and Resistance Service, EMA

Why do we care?

The golden era of antibiotics

1939
Penicillin developed as a drug
(N. Heatley, E. Chain, H. Florey)

1928
Penicillin (A. Flemming)
Difficulties growing the mold and purifying penicillin

1943
Mass production penicillin

The golden era of antibiotics

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Advertisement for penicillin production from Life magazine, United States, 14 August 1944
Science Museum London, CC BY 4.0

The golden era of antibiotics

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Mass production penicillin

1950
Antibiotics used to promote animal growth and prevent plant disease

1960
Antibiotics used in global food production

The golden era of antibiotics

1928
Penicillin (A. Flemming)
Difficulties growing the mold and purifying penicillin

1939
Penicillin developed as a drug (N. Heatley, E. Chain, H. Florey)

1940
First antibiotic resistance published

1943
Mass production penicillin

1950
Antibiotics used to promote animal growth and prevent plant disease

1960
Antibiotics used in global food production

Antibiotic resistance

The golden era of antibiotics

ALEXANDER FLEMING

Penicillin

Nobel Lecture, December 11, 1945

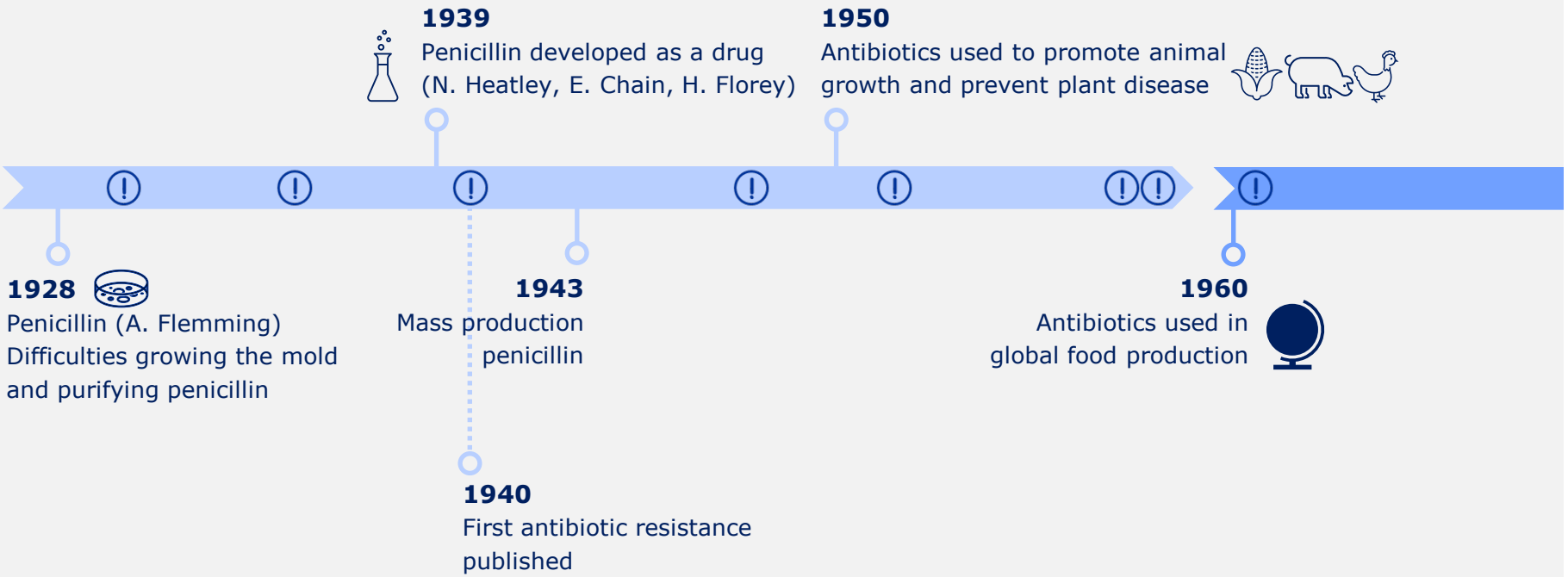
But I would like to sound one note of warning. Penicillin is to all intents and purposes non-poisonous so there is no need to worry about giving an overdose and poisoning the patient. There may be a danger, though, in underdosage. It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body.

The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant. Here is a hypothetical illustration. Mr. X. has a sore

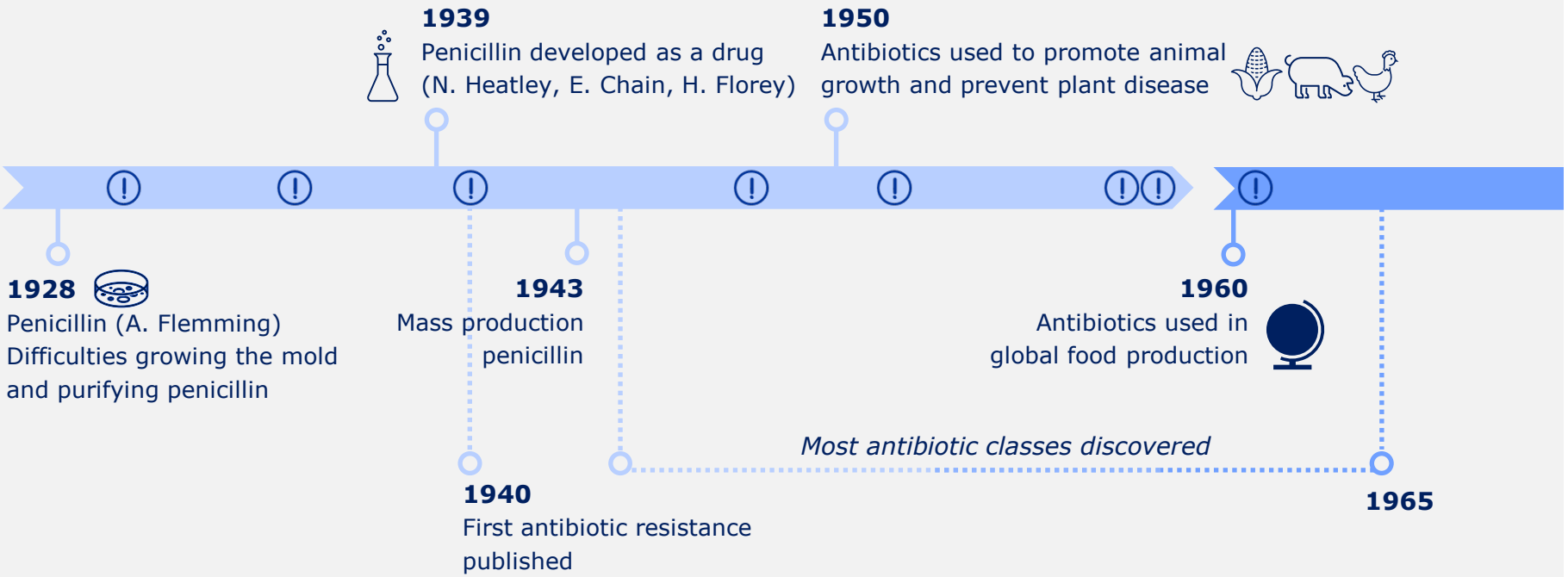
Fleming's Nobel acceptance speech warning:

https://www.nobelprize.org/uploads/2018/06/fleming-lecture.pdf

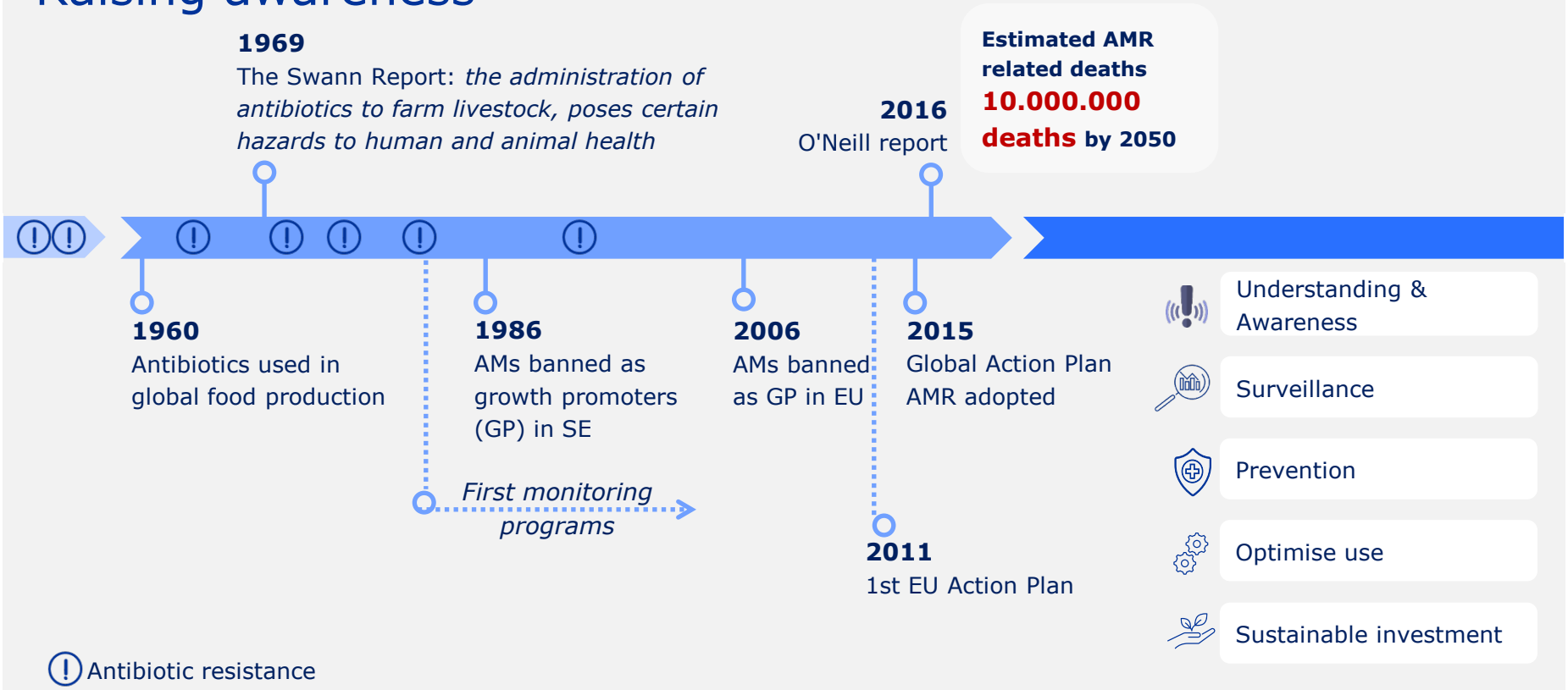
The golden era of antibiotics



The golden era of antibiotics



Raising awareness



AMR: a global One Health threat

We are losing treatment options. The number of people infected by antibiotic resistant bacteria in Europe keeps growing: **800 000 people in 2020.**

Impact in EU/EEA
Estimated AMR-related deaths:
35,000 per year (2020)
Estimated cost of AMR in EU/EEA:
1.1 billion € per year

https://www.consilium.europa.eu/en/infographics/antimicrobial-resistance/#environment

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1.1 billion € per year

AMR can only be tackled together

https://www.consilium.europa.eu/en/infographics/antimicrobial-resistance/#environment

What can we do?

Promote responsible use (keep AMs working)

Support developers (new AMs and alternative therapies)

Collect data

Cooperate

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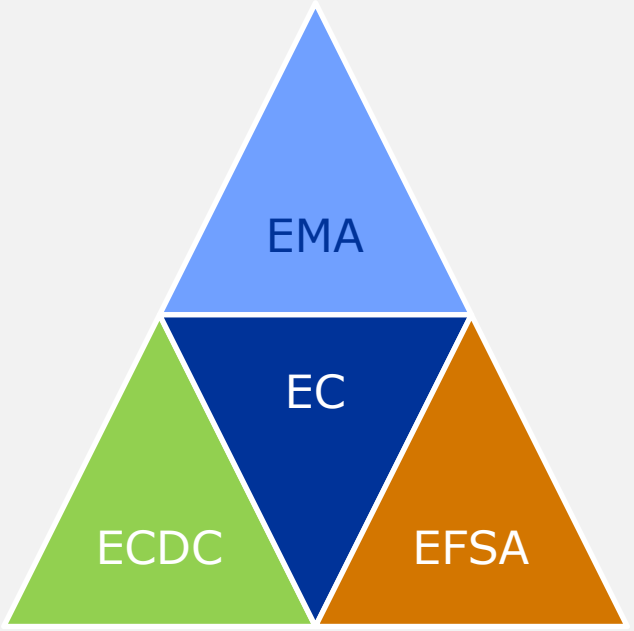

Intervention in EU

Intervention in EU

2009
Joint opinion AMR
(ECDC/EFSA/EMA/SCENIHR)
ESVAC (kick-off)

2011
1st EU Action Plan

2015
JIACRA I

European Antimicrobial Resistance Surveillance Network (**EARS-Net**)
European Surveillance of Antimicrobial Consumption Network (**ESAC-Net**)
Food- and Water-borne Diseases Network (**FWD-Net**)

European Food Safety Authority

Scientific Network on Zoonoses Monitoring Data

EU Summary Report on AMR in zoonotic and indicator bacteria from humans, animals and food

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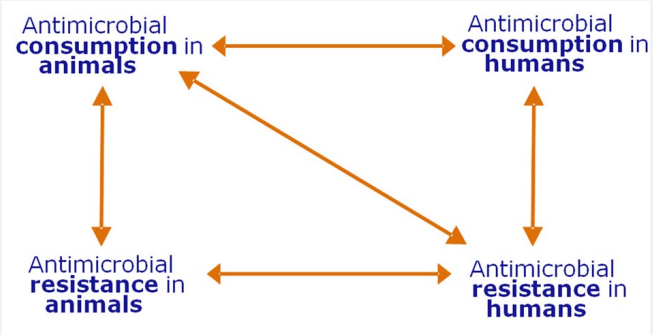
European Surveillance of Veterinary Antimicrobial Consumption
(ESVAC)



Reference:
The JIACRA reports

Intervention in EU

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JIACRA I

2016
EMA/CVMP/CHMP advice on colistin use in animals

Countries should reduce use of colistin in animals to decrease the risk of antimicrobial resistance Share

Press release 27/07/2016

Goal is to cut colistin sales by 65%

27 July 2016
EMA/CVMP/CHMP/231573/2016
Committee for Medicinal Products for Veterinary use (CVMP)
Committee for Medicinal Products for Human Use (CHMP)

Updated advice on the use of colistin products in animals within the European Union: development of resistance and possible impact on human and animal health

*"For the current "high and moderate consumers" the target and desirable levels are set **at 5 mg/PCU and 1 or below 1 mg/PCU**, respectively, based on the observations on the level of use in other countries."*

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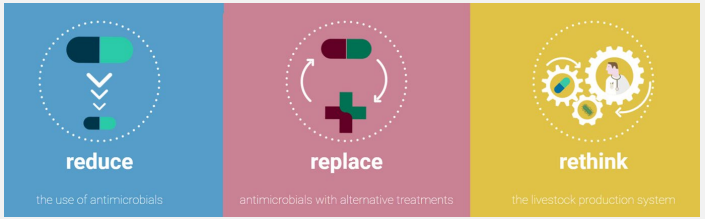
Outcome indicators
RONAFA
JIACRA II

ECDC, EFSA and EMA Joint Scientific Opinion on a list of outcome indicators as regards surveillance of antimicrobial resistance and antimicrobial consumption in humans and food-producing animals

RONAFA Scientific opinion (**R**eduction **O**f the **N**eed for **A**ntimicrobials in **F**ood-producing **A**nimals)



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2020
AMEG categorisation

ECDC, EFSA and EMA Joint Scientific Opinion on a list of outcome indicators as regards surveillance of antimicrobial resistance and antimicrobial consumption in humans and food-producing animals

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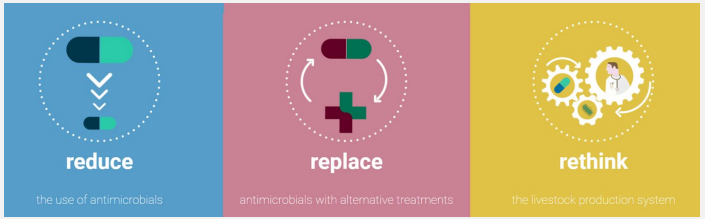
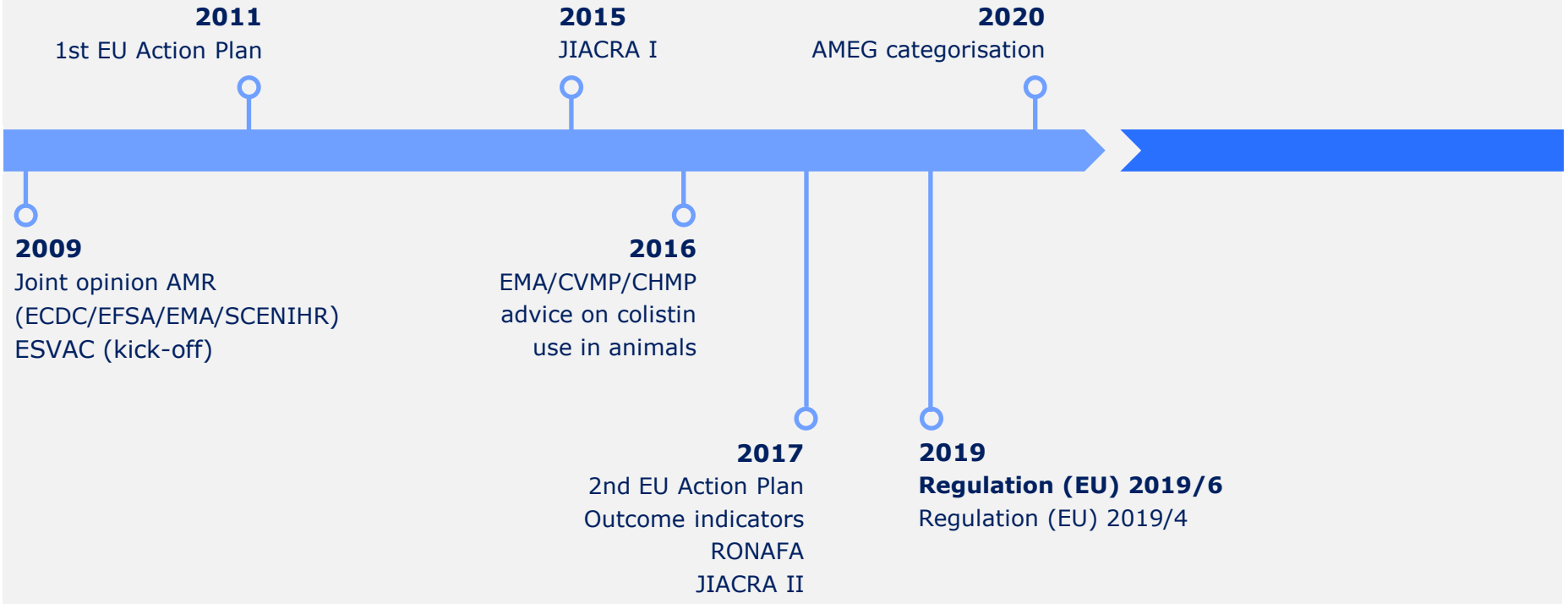


Intervention in EU



Intervention in EU

VMP-Reg specific actions against AMR

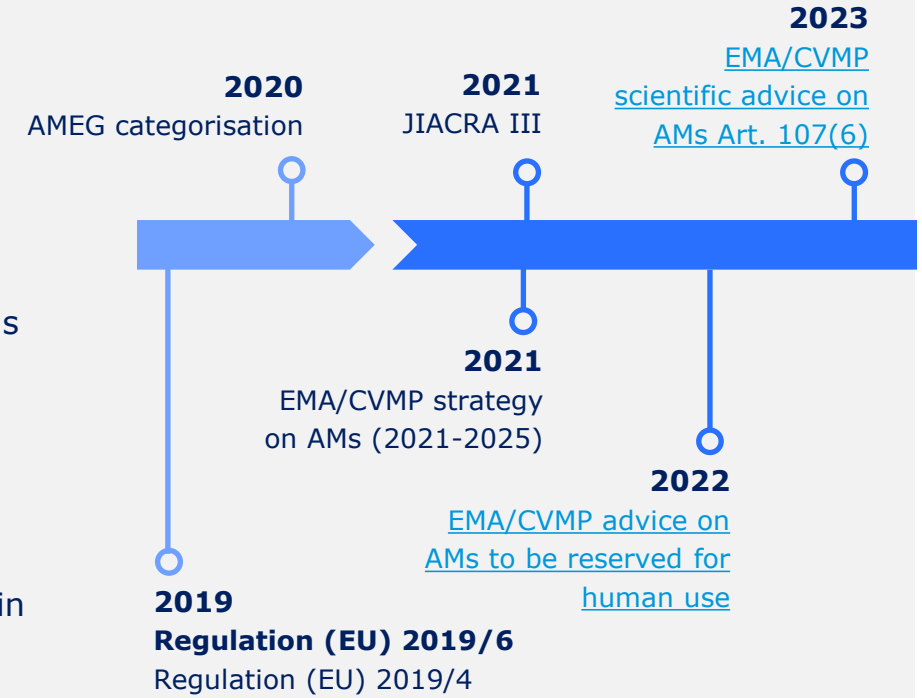
List of antimicrobials **reserved for human use**

Restriction of the use of specific antimicrobials

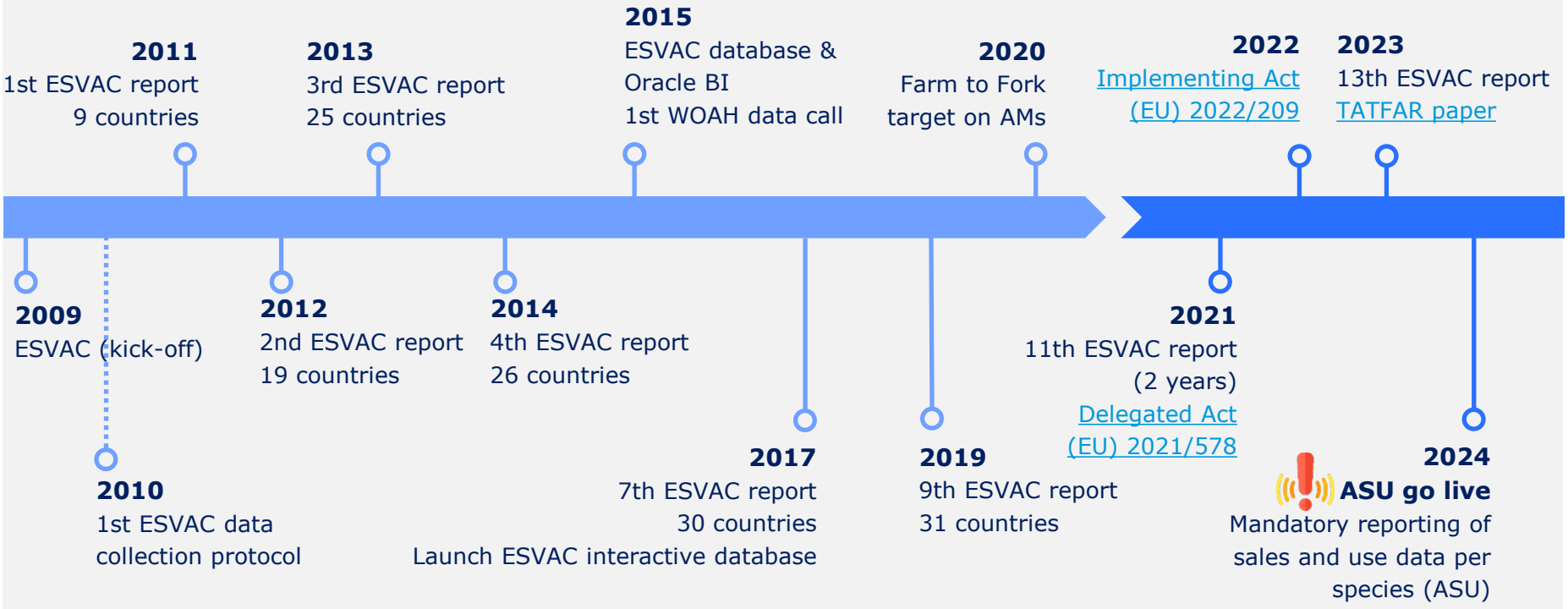
Promote **innovation** in the development of alternatives to antimicrobials

Collection of **data on use of antimicrobials** in animals

Extended collection of **antimicrobial sales data**



Surveillance of AMC in animals in EU



What have we learned?

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Mandate from EC to EMA: requests the EMA to take the lead in collecting data on the use of antimicrobials in animals.

Purpose of monitoring: obtain reliable data, document changes in antibacterial drug consumption, detecting patterns of use and trends to:

- understand the use of AMs in animals
- make recommendations based on data to improve use of AMs
- increase awareness

- assess impact of recommendations and interventions
- assist in the interpretation of AMR

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Agreed principles

Communicate purpose	Start simple	Develop progressively	Appropriate resources
Based on experience	Keep commercial confidentiality	Fit for purpose	Harmonisation

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Sales by VMP presentation

1. Pack size x strength = **quantity of antibiotic substance per package unit**

2. No. packages sold x amount of antibiotic substance per package unit = **quantity of antibiotic active substance sold**

Population correction Unit (PCU)

The PCU is calculated for each species, weight class or production type, as follows:

PCU domestic

- Number of animals slaughtered × estimated weight at treatment
- Number of livestock animals × estimated weight at treatment

PCU export

- Number of animals transported to another country for fattening or slaughter × estimated weight at treatment

PCU import

- Number of animals transported from another country for fattening or slaughter × estimated weight at treatment

Total PCU per country

- PCU = total $PCU_{Domestic}$ + total PCU_{Export} – total PCU_{Import}

1 PCU = 1 kg of animal biomass

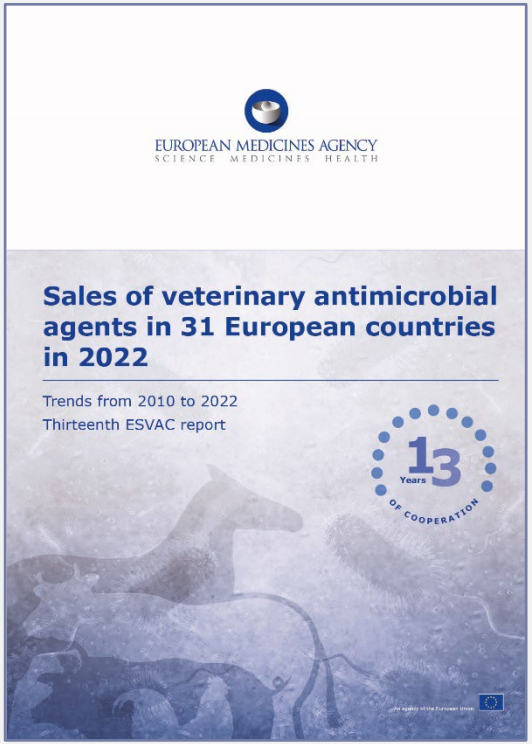
Standardised and harmonised data reporting: ESVAC Protocol

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Reporting data - indicator

$$\frac{\text{Quantity sold in tonnes} \times 10^9}{\text{PCU in kg}}$$

- Aggregated sales
- By antimicrobial class
- By product form

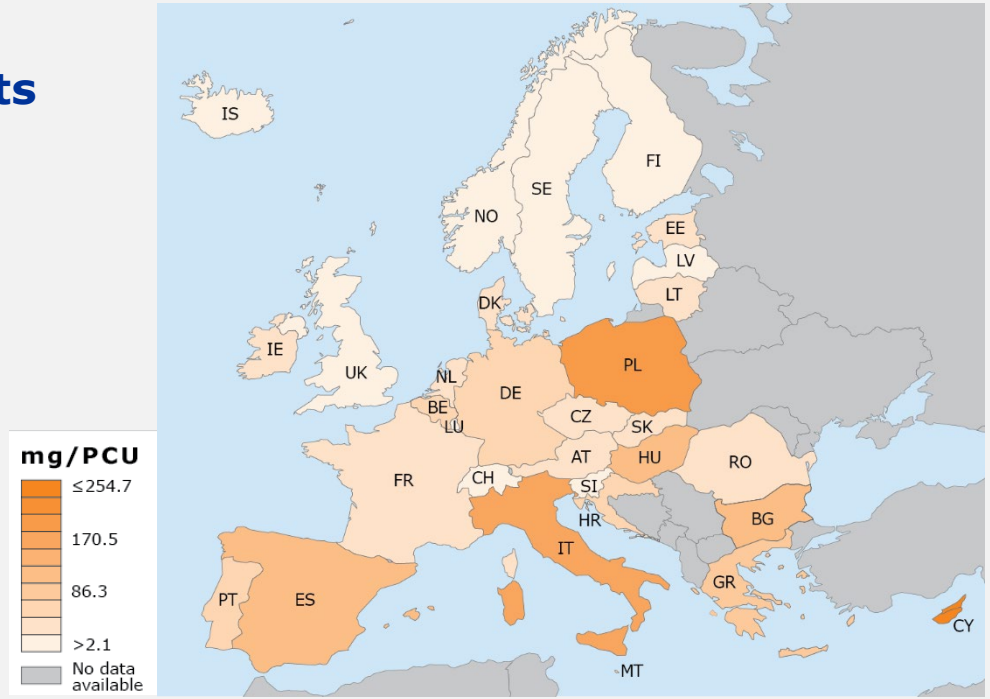


European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Indicators on surveillance of antimicrobial consumption in food-producing animals **were the lowest ever in 2022** (aggregated sales of 31 countries).

13% overall decrease compared to 2021

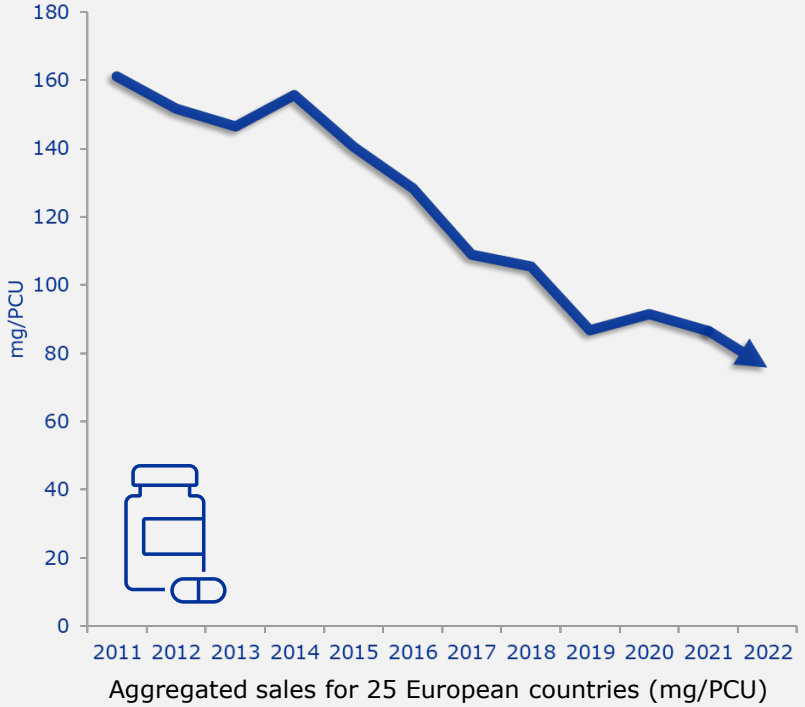


Total sales of antibiotic VMPs per country in 2022

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

53% overall decrease primary indicator (2011-2022)

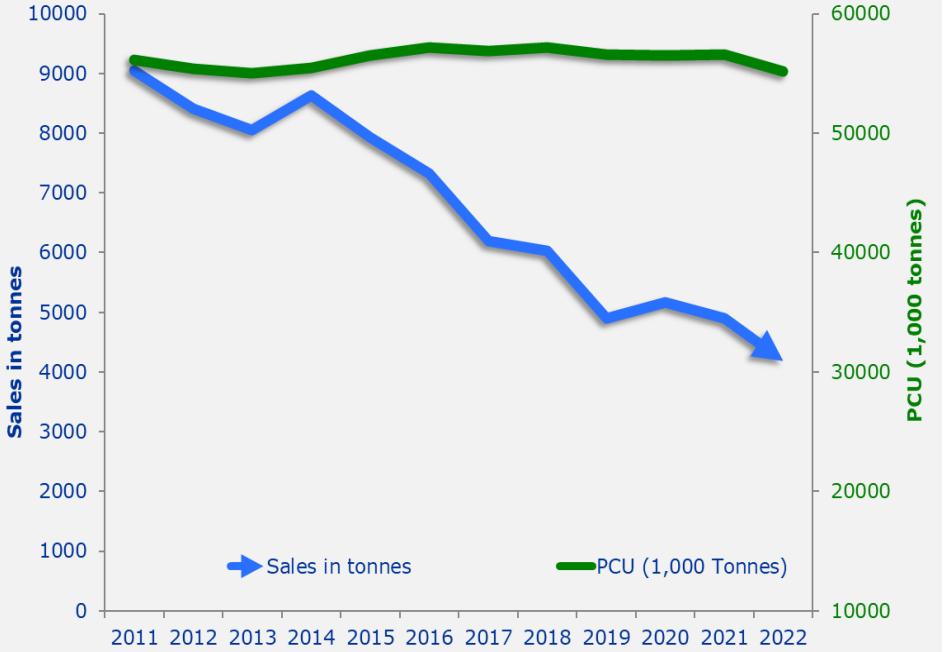


Aggregated sales for 25 European countries (mg/PCU)

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

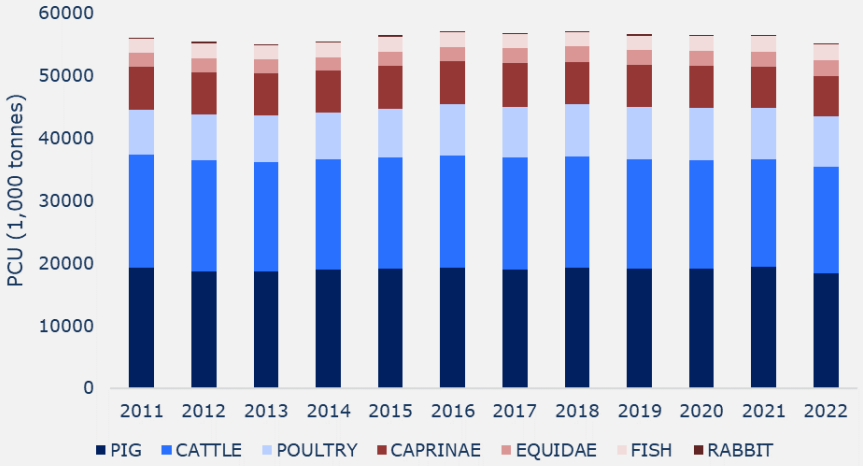
Sales in tonnes (not normalised) also decreased; aggregated PCU remained stable (-1.7%)



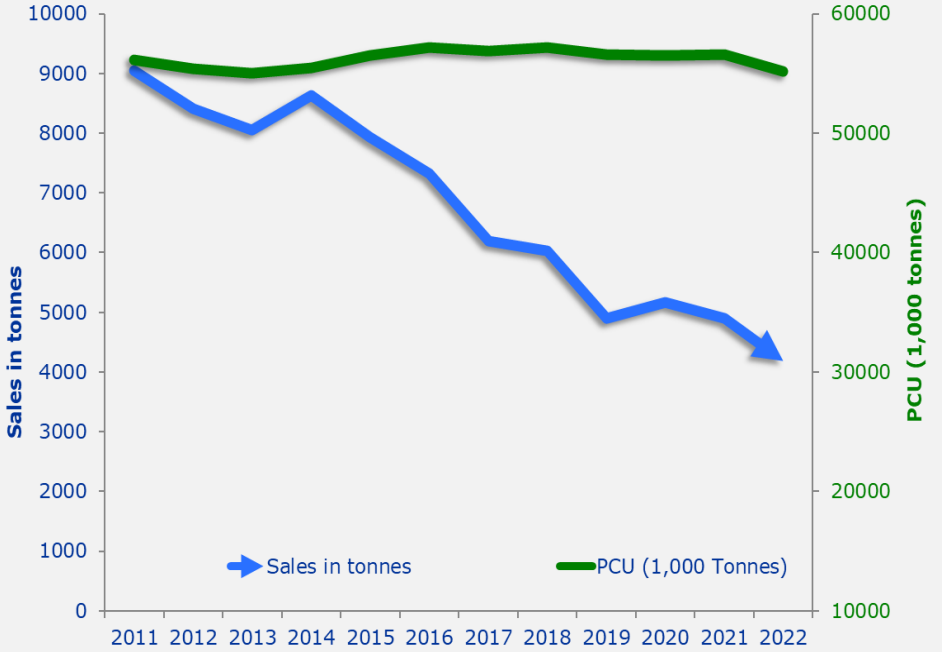
Aggregated sales (tonnes) and PCU for 25 European countries

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports



Aggregated data don't tell the full story



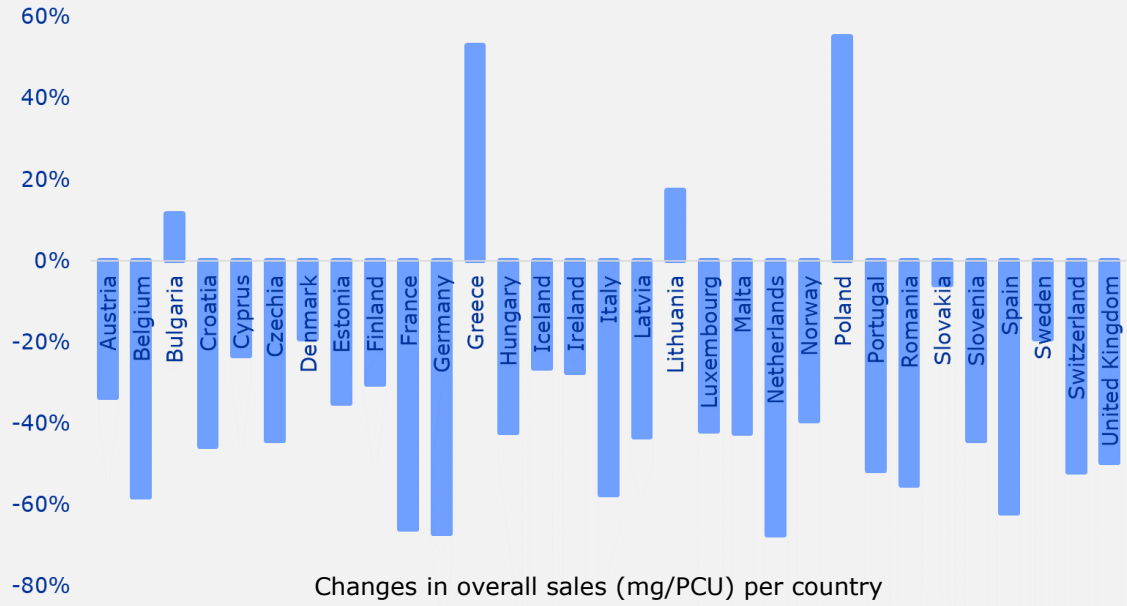
Aggregated sales (tonnes) and PCU for 25 European countries

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Change between 2011-2022
(or from first reporting year after 2011)

From 2012: Luxembourg
From 2014: Croatia, Romania, Switzerland
From 2015: Greece
From 2017: Malta

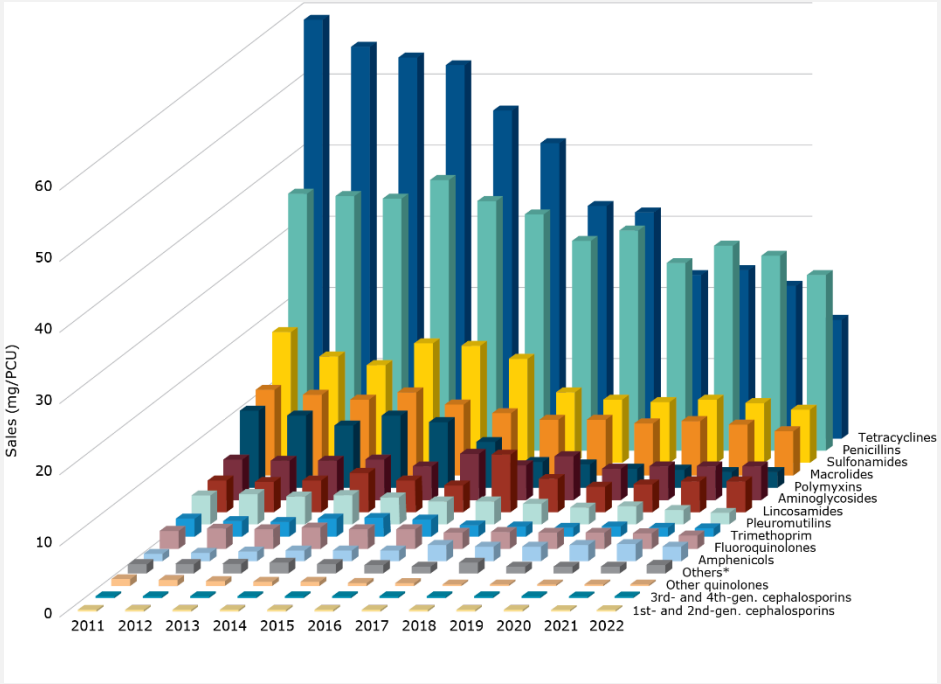


European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Highest selling antibiotic classes:

- Tetracyclines
- Penicillins (highest since 2019)
- Sulfonamides

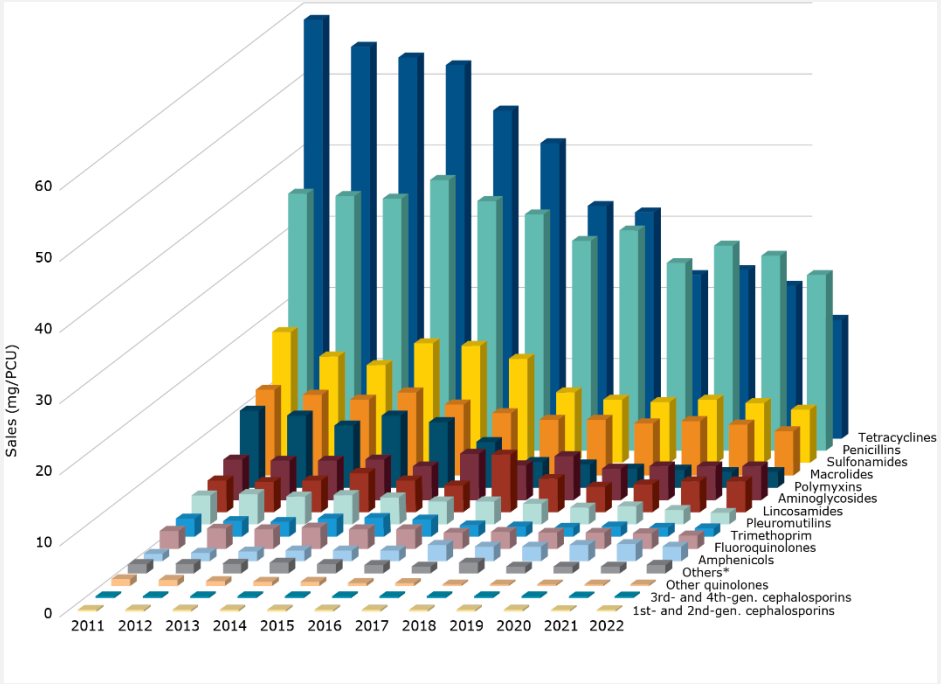


Sales trends per antibiotic class (mg/PCU) for 25 European countries

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Antibiotic class	Proportion total sales 2011	2022
Tetracyclines	**37%**	**23%**
Amphenicols	1%	3%
Penicillins	**23%**	**33%**
1st 2nd gen. cephalosporins	0.1%	0.2%
3rd 4h gen. cephalosporins	0.2%	0.2%
Sulfonamides	**12%**	**10%**
Trimethoprim	2%	2%
Macrolides	8%	8%
Lincosamides	3%	6%
Fluoroquinolones	2%	3%
Other quinolones	1%	0.1%
Aminoglycosides	4%	6%
Polymyxins	7%	3%
Pleuromutilins	3%	2%
Others	1%	2%



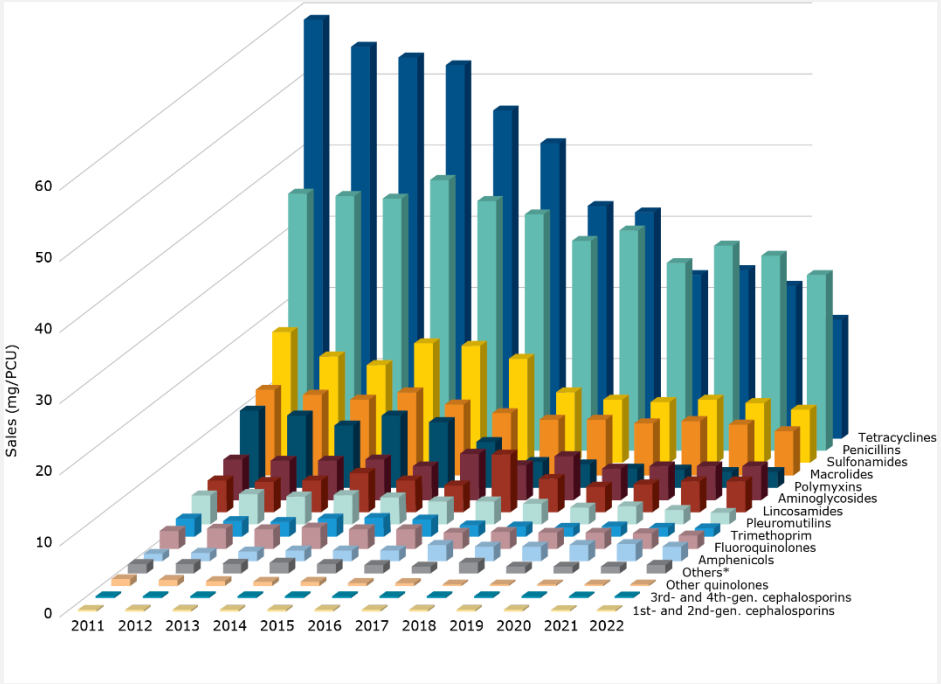
Sales trends per antibiotic class (mg/PCU) for 25 European countries

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Tetracyclines	Change 2011-2022	Relative proportion
Chlortetracycline	-76%	
Doxycycline	-37%	
Oxytetracycline	-82%	
Tetracycline	-96%	

Sales of all tetracyclines declined, but doxycycline represents a bigger slice of these sales in 2022



Sales trends per antibiotic class (mg/PCU) for 25 European countries

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Secondary indicators

Overall reduction sales of 3rd-and 4th-generation cephalosporins, polymyxins, fluoroquinolones and other quinolones

Reduction of AMEG Category B **contributed 12% to the overall reduction** in sales since 2011

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

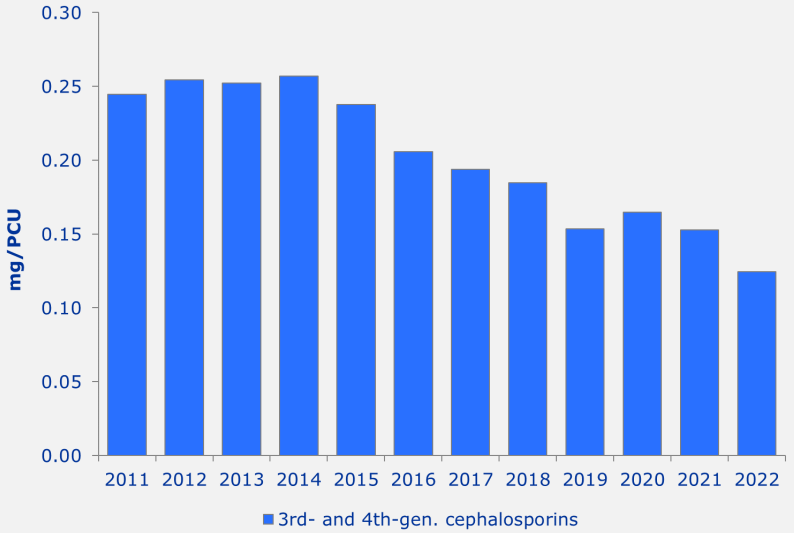
Data & figures from ESVAC reports

Secondary indicators

↓ **49%** for **3rd- and 4th-gen. cephalosporins**

3rd- and 4th-gen. cephalosporins	Change 2011-2022	Relative proportion
Cefoperazone	-90%	
Cefovecin	-34%	
Cefquinome	-66%	
Ceftiofur	-39%	

Sales for all substances decreased



3rd-and 4th-generation cephalosporins trends
25 European countries, 2011-2022

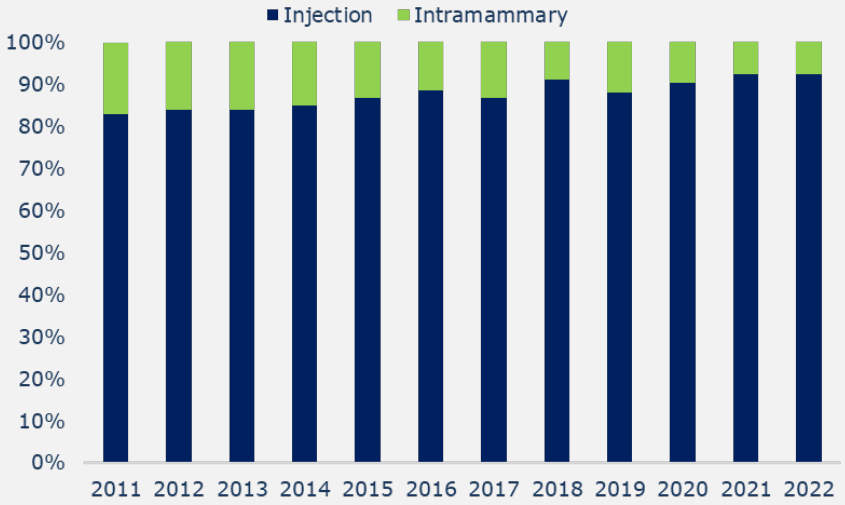
European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Secondary indicators

↓ **49%** for **3rd- and 4th-gen. cephalosporins**

Injection is the predominant product form at Europe level (also at country level)



Proportion of 3rd- and 4th-generation cephalosporins sales by product form (25 countries)

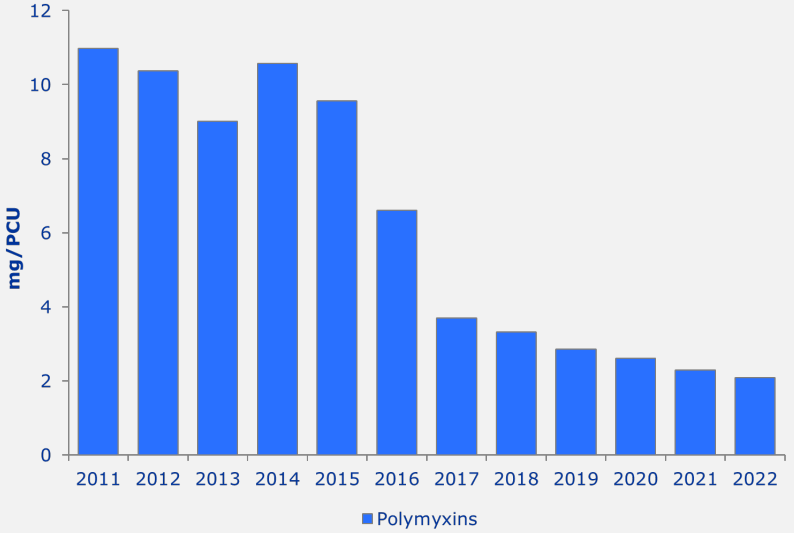
European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Secondary indicators

↓ **81%** for **polymyxins**

EMA/CVMP/CHMP advice 2016:
*"For the current "high and moderate consumers" the target and desirable levels are set **at 5 mg/PCU and 1 or below 1 mg/PCU**, respectively, based on the observations on the level of use in other countries."*



Polymyxins trends for 25 European countries, 2011-2022

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

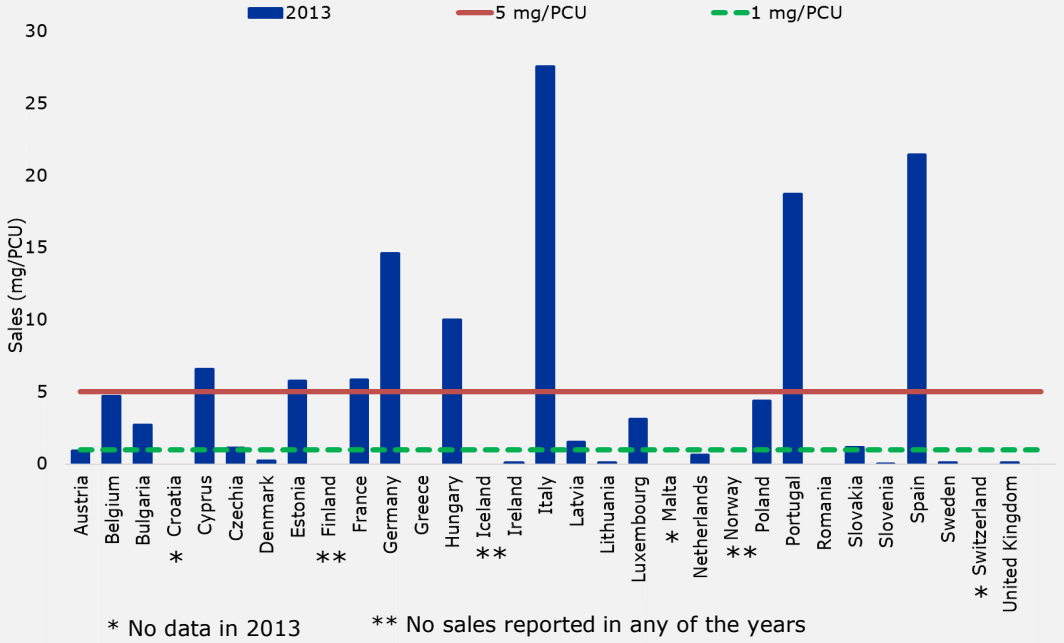
Secondary indicators

Polymyxins

In 2013 (26 countries):

11 countries have sales between 0-1 mg/PCU

8 countries have sales **>** 5 mg/PCU



* No data in 2013 ** No sales reported in any of the years

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Secondary indicators

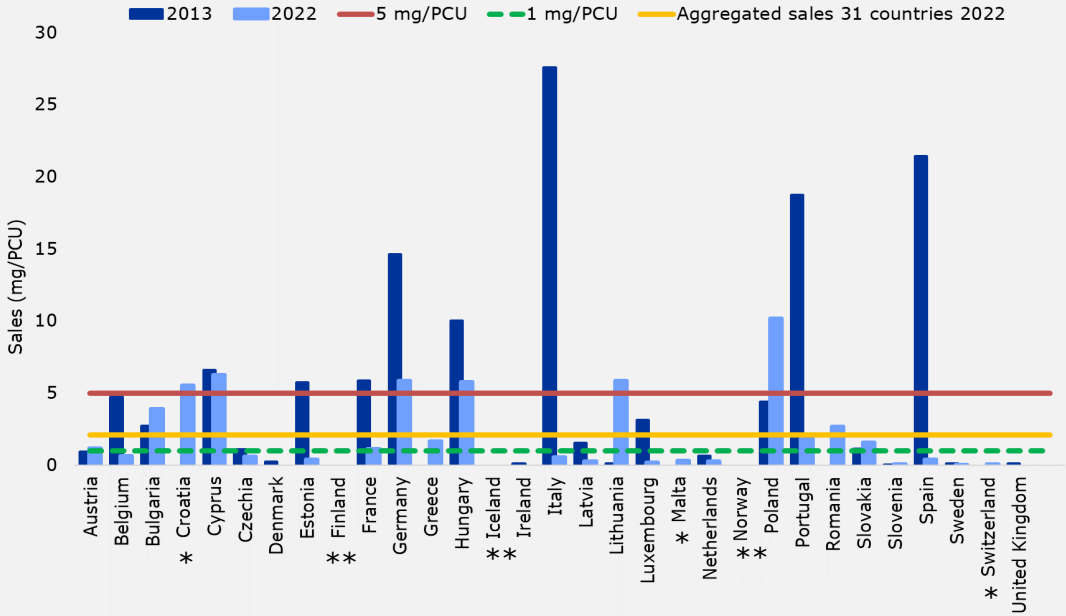
Polymyxins

In 2022 (31 countries):

18 countries have sales between 0-1 mg/PCU

6 countries have sales **>** 5 mg/PCU

2.1 mg/PCU aggregated sales



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** No sales reported in any of the years

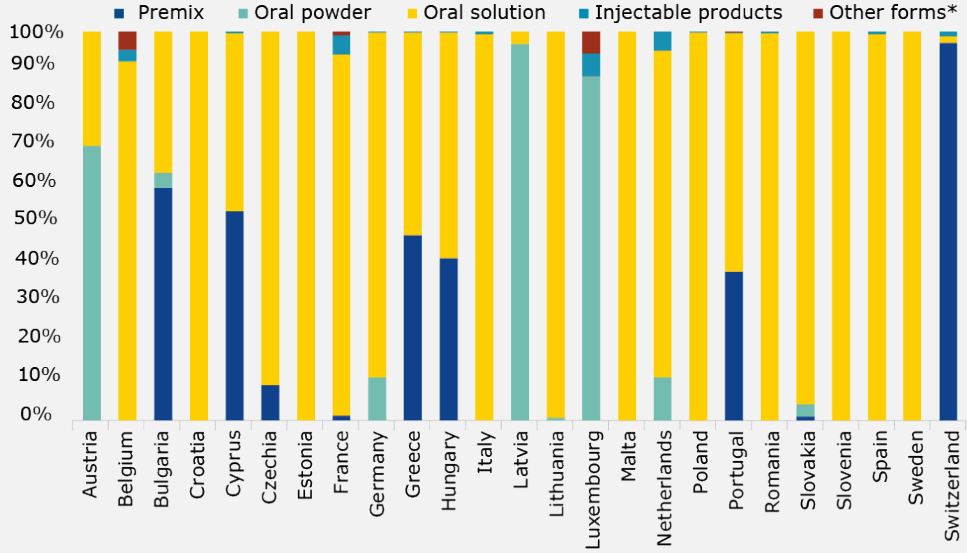
European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Secondary indicators

Polymyxins

Stratification **polymyxin** sales by product form varies between countries



Proportion of polymyxins sales by product form (25 countries)

No sales of polymyxins in Denmark, Finland, Iceland, Ireland, Norway and the United Kingdom.

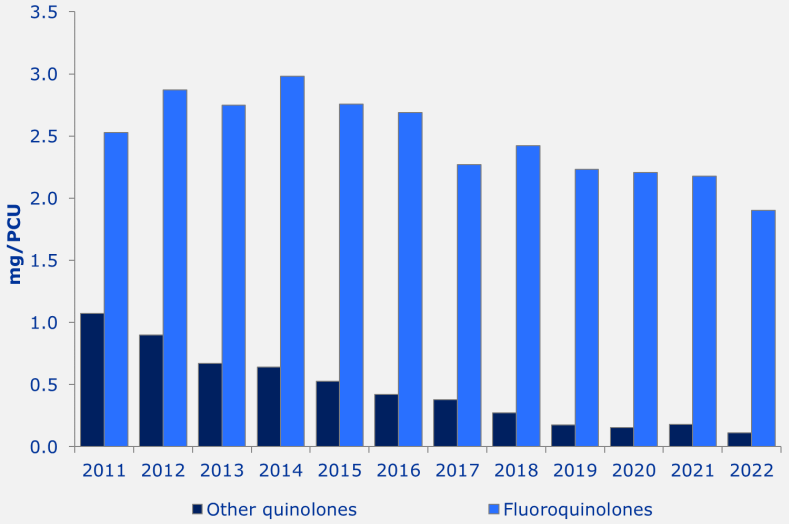
European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Secondary indicators

↓ **25%** for fluoroquinolones (FQ)
↓ **90%** for other quinolones (OQ)

Sales of OQ in only 13 countries in 2022



Quinolones trends for 25 European countries, 2011-2022

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

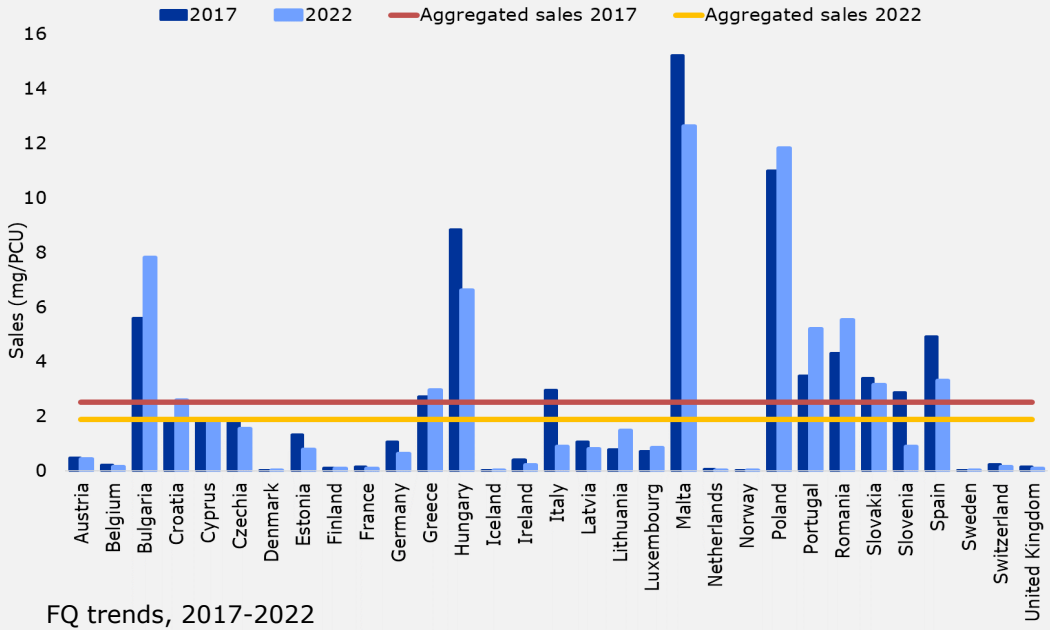
Data & figures from ESVAC reports

Secondary indicators

Fluoroquinolones

Despite overall decrease since 2011 (25%) and 2017 (16%), FQ sales have increased in a few countries.

FQs represented 2.8% of total sales in 2022.



FQ trends, 2017-2022

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

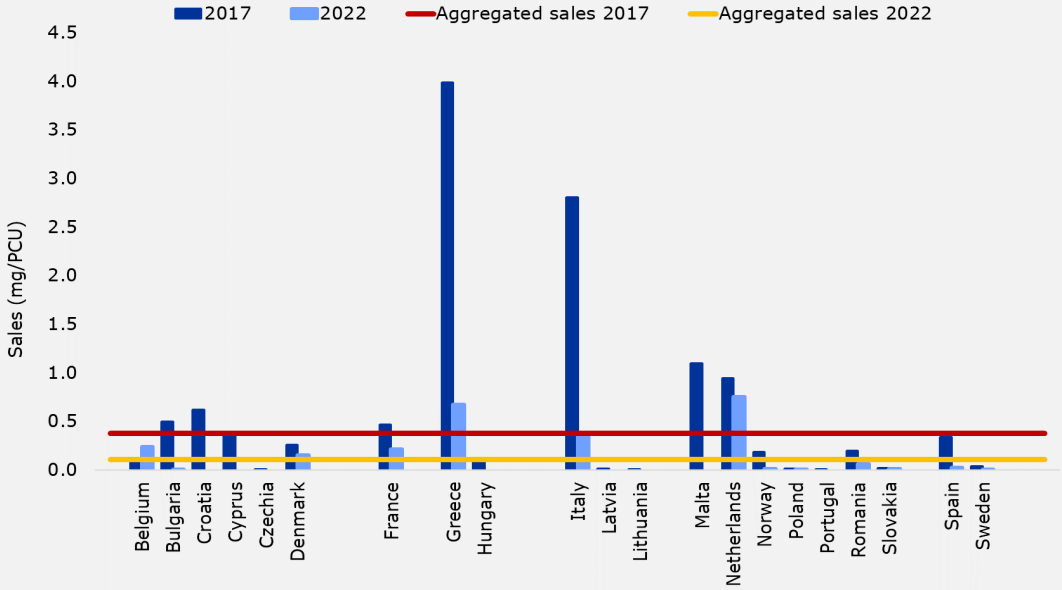
Data & figures from ESVAC reports

Secondary indicators

Other quinolones

Only 13 countries reported sales of other quinolones in 2022, against 21 in 2017.

OQ represented only 0.2% of total sales in 2022.



Other quinolones trends, 2017-2022

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

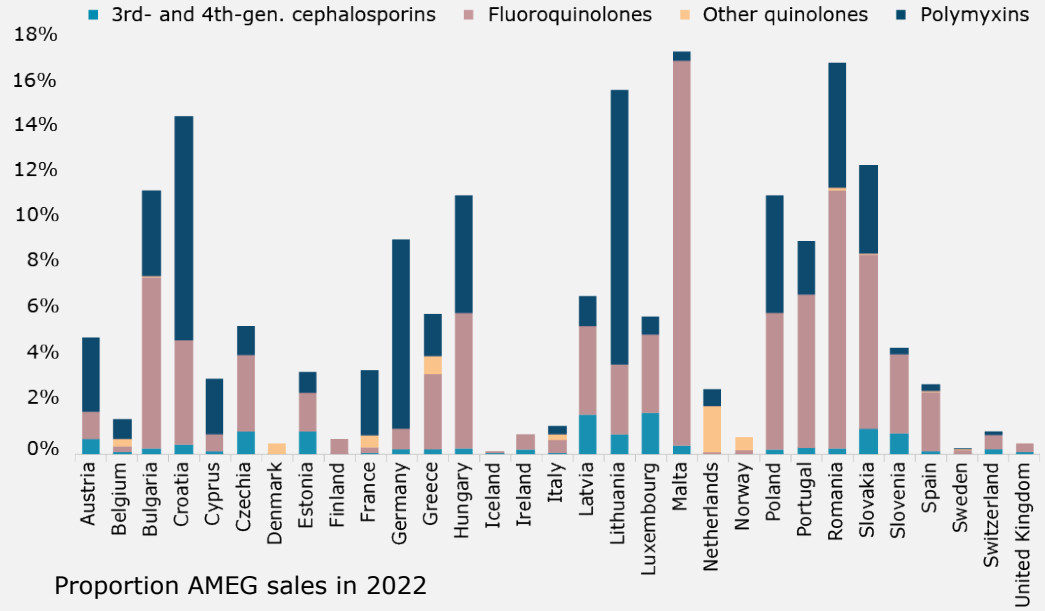
Data & figures from ESVAC reports

Secondary indicators

All

AMEG B substances still represent a significant portion of national sales in some countries (up to 18%)

Important differences remain across Europe in the extent of antibiotics used by country and choice of antibiotic class



Proportion AMEG sales in 2022

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

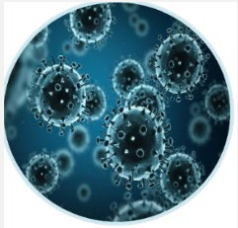
Data & figures from ESVAC reports

Farm to Fork Strategy

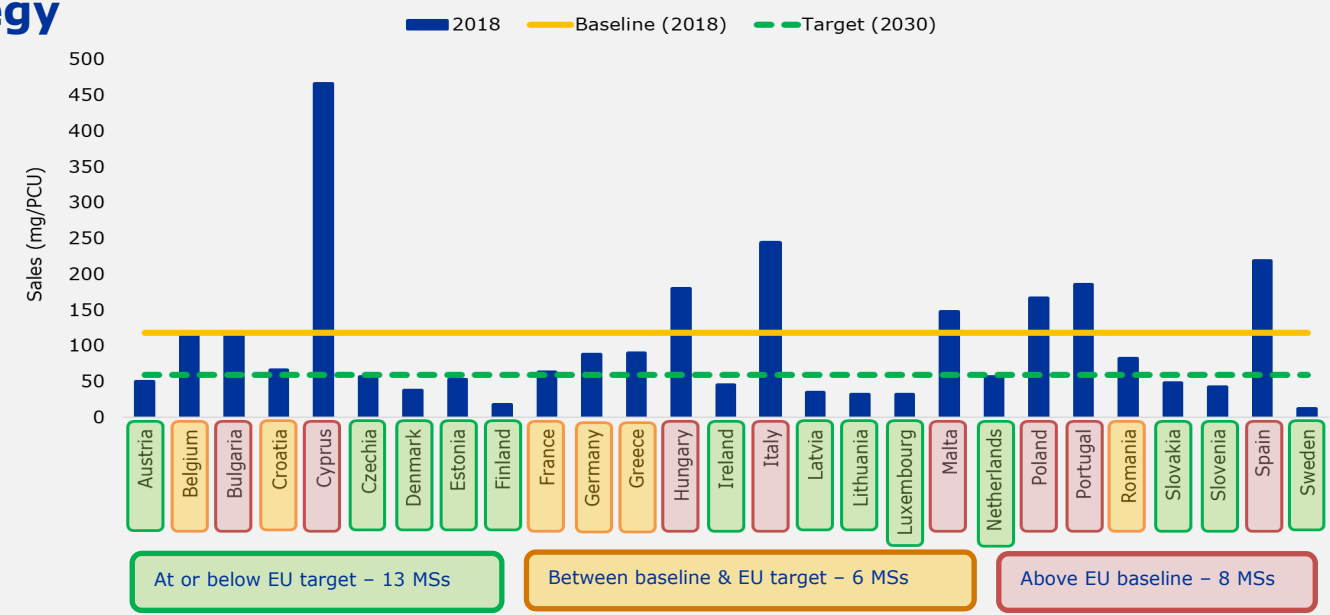
European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Farm to Fork Strategy



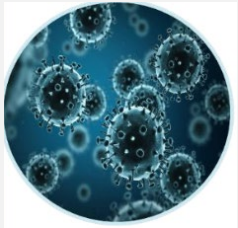
Reduce sales of **antimicrobials** for farmed animals and in aquaculture by 50%



European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

Data & figures from ESVAC reports

Farm to Fork Strategy



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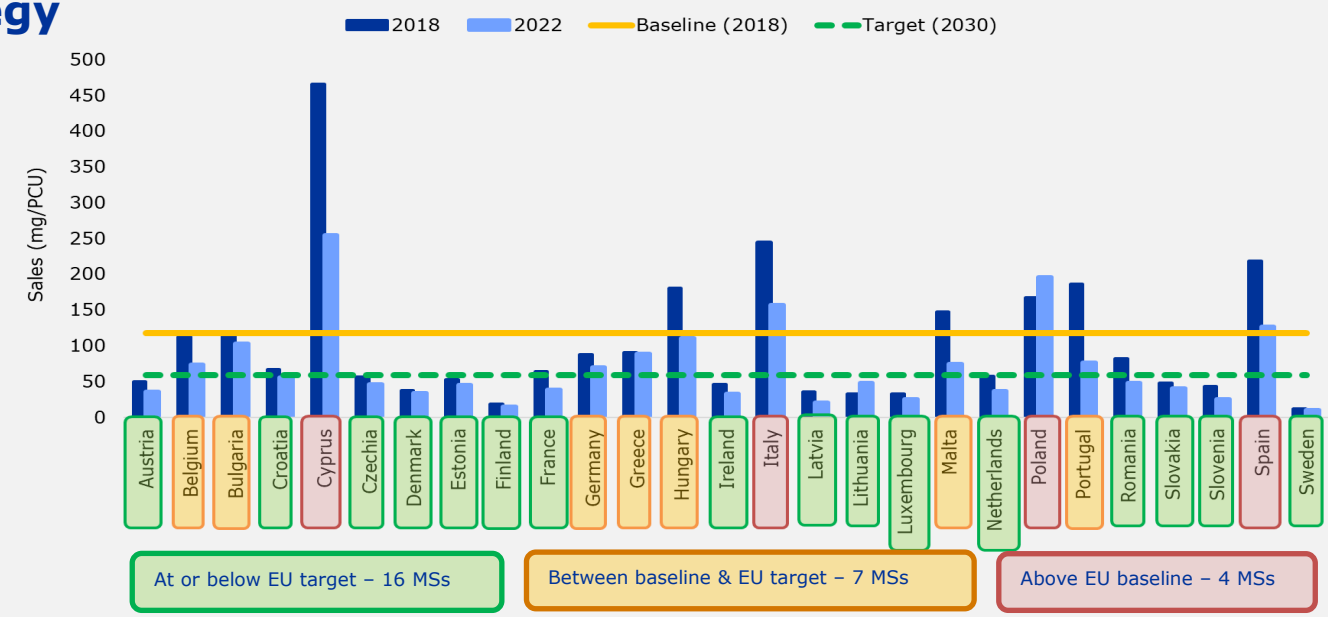


European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

ESVAC lessons

Voluntary and successful project	Progress towards responsible use of AMs in animals	A project and data with impact worldwide
Cooperative MSs and expert ESVAC Network	Collection reliable data on AMs sold for use in animals	Data used by policy makers, researchers, stakeholders
	Sales decrease, including in AMEG Category B	EU/EEA trends show effects national policies and interventions

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC): 2009-2023

What is the impact for the future?

ESVAC legacy

Delegated Regulation (EU) 2021/578

- **Mandatory** plus **voluntary** data collection based on ATC/ATCvet code
- Focus on **data quality**
- Establishment of **national data collection systems** and **IT tools** for automated or semi-automated reporting and analysis (use data)

Implementing Regulation (EU) 2022/209

- **Data collected at package level**
- **Data format**
- **Pre-filling of data entry** fields by the Agency with information available from the Union Product Database (UPD)

Next steps: what does the future look like?

Surveillance of AMC in animals in EU

2023
Final ESVAC report
ESUAvet WG

2024
ASU go live
Mandatory reporting of sales and use data per species (ASU)

2025
1st ASU report

2025
2nd ASU report, hereafter annual

2027
Mandatory reporting of sales and use data per species (ASU)

2030
F2F target:
50% reduction AMs sales

2030
Mandatory reporting of sales and use data per species (ASU)

ASU annual reports

Surveillance of AMC in animals in EU

Mandatory collection and reporting of data

New substances

Sales data

Antimicrobial Sales and Use (ASU) technical implementation protocol

New

Use data per species

Antimicrobial use data reporting per animal categories (numerator) - Manual for reporting the data to EMA

New methodology

Animal population data

Guideline on the reporting of antimicrobial sales and use in animals at the EU level – denominators and indicators

Surveillance of AMC in animals in EU

Mandatory collection and reporting of data

Guideline on the reporting of antimicrobial sales and use in animals at the EU level – denominators and indicators

Establishes a **new** animal biomass **denominator**

New animal population categories

New animal weights (pre slaughter)

Establishes relevant **sales** and **use** (**new**) **indicators**

mg/kg animal biomass: sales and use

Dose- and dose-course-based: **use**

Surveillance of AMC in animals in EU

ASU Platform

1

EUROPEAN MEDICINES AGENCY
UNION PRODUCT DATABASE

Home ASU Logout

Provides:

1. **Access to ASU**
2. **Product information**

2 **National data collection systems**

Provide:

1. **Data on sales and use of antimicrobials in animals**

ASU Platform

3 **PowerBI analytics tool**

Power BI

Provides:

1. **Data validation**
2. **Data analysis**
3. **Report preparation**
4. **Public access to data**

Surveillance of AMC in animals in EU

How does EMA support change?

Live support

- Change Liaison Meetings
- Webinars
- Data manager support sessions

Written guidance

- ASU protocols
- ASU User Guides
- Visual guides and checklists
- FAQs documents

Recorded materials

- Bite sized videos
- ASU reporting webinars on EU NTC
- ASU data quality series on EU NTC

Surveillance of AMC in animals in EU in 2024

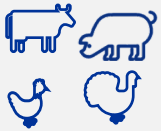
1st ASU reporting cycle

April
Sales and use data call open

30 June
Deadline sales and animal population data

30 September
Deadline use data

29 January
ASU go live



Preparation phase

Reporting to ASU phase

Annual report preparation

Take home messages

AMR remains a global threat that requires global action, despite global differences

AMR is a high priority for EMA, recognising specific nature of the human and vet sectors

EMA plays an important role in the AMR One Health approach

- Collecting antimicrobial consumption data to guide policy and research 
- Supporting the development of new medicines and treatment approaches 
- Promoting responsible use of existing antibiotics 
- Providing advice to the European Commission 
- Inter-agency and international cooperation 

Take home messages

Surveillance of antimicrobial consumption in animals is key

- Information on the use
- Identify opportunities for improvement
- Communication, improve awareness
- Effectiveness of efforts to reduce unnecessary use

Transition period from ESVAC to **mandatory** collection and reporting of sales **and use data** brings **new challenges**

Cooperate, liaise, manage expectations

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Barbara Freischem
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Scientific Officer

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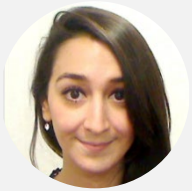
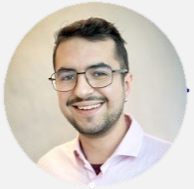
Project/Programme Officer

Cristina Ribeiro-Silva
Scientific Officer



Stephanie d'Angelo
Procedure Coordinator



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Thank you for your attention!

Further information

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