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SCIENCE MEDICINES HEALTH

Antimicrobials: status update

Veterinary Medicines Info Day 2021

Presented by Ana Vidal on 25th March 2021
Veterinary Risk and Surveillance, Veterinary Medicines Division

AMR: a global public health threat

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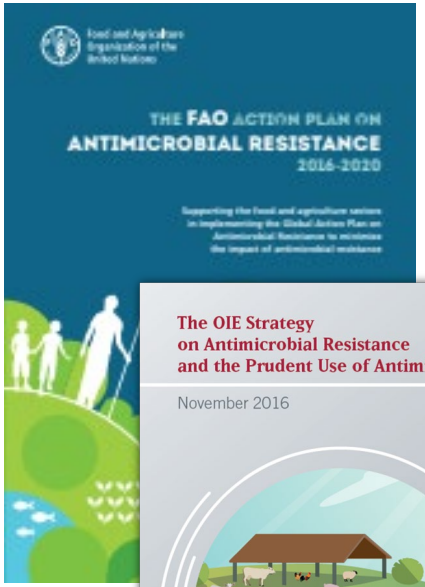

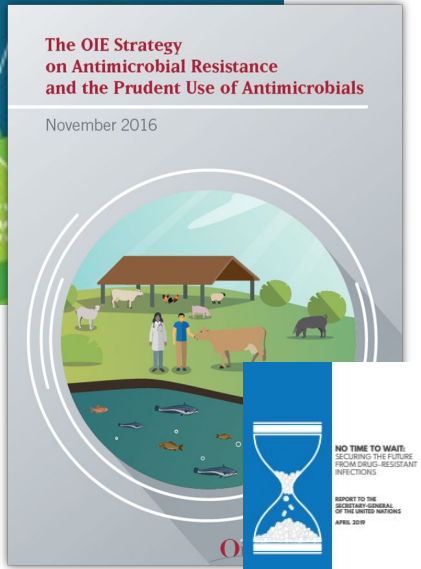

EMA’s role in the global response against AMR

EMA plays a vital role in the global response to AMR through a ‘One Health’ approach:

- contributing to **EU One Health Action Plan** against Antimicrobial Resistance
- supporting the development of **new medicines** and treatment approaches;
- promoting **responsible use** of existing antibiotics;
- **international cooperation** (e.g. ECDC, EFSA, EEA, ECHA, OIE, WHO, FDA, USDA, FAO, Health Canada, PMDA, and more)

European Surveillance of Veterinary Antimicrobial Consumption (ESVAC)

- Launched in 09/2009 by the EMA as a project mandated by the EC with 9 countries
- 2020: 10th report, 31 countries (EU 27 plus CH, IS, NO, UK)
- Between 2011 and 2018, sales have reduced by:
  - ↓ **34% for overall** sales;
  - ↓ 24% for third and fourth generation **cephalosporins;**
  - ↓ 70% for **polymyxins**;
  - ↓ 4% for **fluoroquinolones**;
  - ↓ 74% for other **quinolones**.
- Mixed picture across the EU, even increase over time in a few countries

Spatial distribution of overall sales of all antimicrobials for food-producing animals, in mg/PCU, for 31 countries, for 2018

New EU legislative landscape

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(EU) 2019/6: Veterinary Medicinal Products

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


Official Journal L 4
of the European Union
Legislation
EN

(EU) 2019/4: Medicated Feed

REGULATION (EU) 2019/4 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 11 December 2018

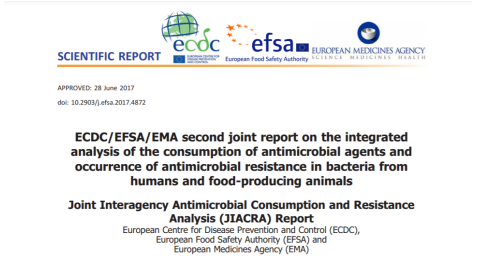
on the manufacture, placing on the market and use of medicated feed, amending Regulation (EC) No 183/2005 of the European Parliament and of the Council and repealing Council Directive 90/167/EEC

(EU) 2019/5: Community procedures for authorisation and regulation of MP for human and veterinary use

REGULATION (EU) 2019/5 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 11 December 2018

amending Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, Regulation (EC) No 1901/2006 on medicinal products for paediatric use and Directive 2001/83/EC on the Community code relating to medicinal products for human use


SCIENTIFIC REPORT

APPROVED: 28 June 2017

doi: 10.2903/j.efsa.2017.4872

ECDC/EFSA/EMA second joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals

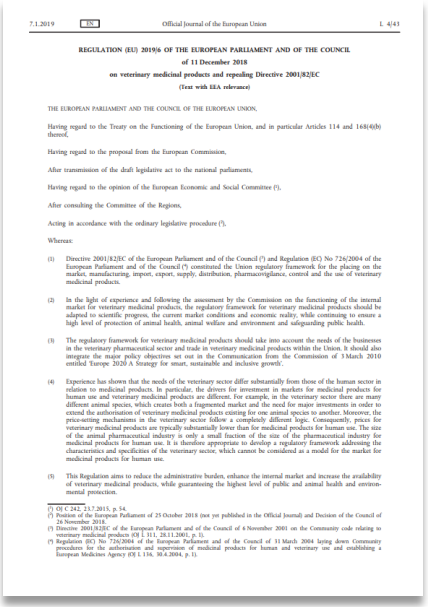
Joint Interagency Antimicrobial Consumption and Resistance Analysis (JIACRA) Report

European Centre for Disease Prevention and Control (ECDC), European Food Safety Authority (EFSA) and European Medicines Agency (EMA)

Regulation (EU) 2019/6 on veterinary medicinal products

Replaces Directive 2001/82/EC within the overall aim of **achieving 'Better Regulation' in the EU**

- provides for a modern, innovative and fit for purpose legal framework
- gives incentives to stimulate innovation
- gives incentives to increase the availability of veterinary medicines
- **strengthens the EU action against antimicrobial resistance**



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)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Articles 114 and 168(4)(b) thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinion of the European Economic and Social Committee (1),

After consulting the Committee of the Regions,

Acting in accordance with the ordinary legislative procedure (2),

Whereas:

(1) Directive 2001/82/EC of the European Parliament and of the Council (3) and Regulation (EC) No 726/2004 of the European Parliament and of the Council (4) constituted the Union regulatory framework for the placing on the market, manufacturing, import, export, supply, distribution, pharmacovigilance, control and the use of veterinary medicinal products.

(2) In the light of experience and following the assessment by the Commission on the functioning of the internal market for veterinary medicinal products, the regulatory framework for veterinary medicinal products should be adapted to scientific progress, the current market conditions and economic reality, while continuing to ensure a high level of protection of animal health, animal welfare and environment and safeguarding public health.

(3) The regulatory framework for veterinary medicinal products should take into account the needs of the businesses in the veterinary pharmaceutical sector and trade in veterinary medicinal products within the Union. It should also integrate the major policy objectives set out in the Communication from the Commission of 3 March 2010 entitled 'Europe 2020 A Strategy for smart, sustainable and inclusive growth'.

(4) Experience has shown that the needs of the veterinary sector differ substantially from those of the human sector in relation to medicinal products. In particular, the drivers for investment in markets for medicinal products for human use and veterinary medicinal products are different. For example, in the veterinary sector there are many different animal species, which creates both a fragmented market and the need for major investments in order to extend the authorisation of veterinary medicinal products existing for one animal species to another. Moreover, the price-setting mechanisms in the veterinary sector follow a completely different logic. Consequently, prices for veterinary medicinal products are typically substantially lower than for medicinal products for human use. The size of the animal pharmaceutical industry is only a small fraction of the size of the pharmaceutical industry for medicinal products for human use. It is therefore appropriate to develop a regulatory framework addressing the characteristics and specificities of the veterinary sector, which cannot be considered as a model for the market for medicinal products for human use.

(5) This Regulation aims to reduce the administrative burden, enhance the internal market and increase the availability of veterinary medicinal products, while guaranteeing the highest level of public and animal health and environmental protection.

(1) OJ C 242, 23.7.2015, p. 54.
(2) Position of the European Parliament of 25 October 2018 (not yet published in the Official Journal) and Decision of the Council of 26 November 2018.
(3) Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products (OJ L 311, 28.11.2001, p. 1).
(4) Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1).

Regulation (EU) 2019/6 – specific actions against AMR

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Measures applicable to **EU**

Mandatory collection of **data on sales and use** of antimicrobials

List of antimicrobials **reserved for human use**

Restriction of the use of specific antimicrobials

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

Other measures: **prudent** and responsible use

Measures applicable to imports of animal produce from **Third countries**

Regarding antimicrobials used as growth promotors

Regarding antimicrobials designated in the EU as for humans only

Delegated and Implementing Acts

3 Delegated Acts

- Criteria for the designation of antimicrobials for human use (**Art 37(4)**)
- Requirements for the collection of data on antimicrobials used in animals (**Art 57(3)**)
- Rules on imports from third countries (**Art 118**)

3 Implementing Acts

- List of antimicrobials reserved for human use (**Art 37(5)**)
- Format of the data to be collected on antimicrobials used in animals (**Art 57(4)**)
- List of antimicrobials not to be used outside the terms of MA or used subject to certain conditions (**Art 107(6)**)

Collection of data on antimicrobials used in animals – *Article 57*

- Mandatory collection of **comparable data** on the **volume of sales** and the **use** of **antimicrobials per animal species .**
- Under coordination of the Agency, **MSs responsible for collecting data** on the sales and use of antimicrobials used in animals **and sending them** to the Agency.
- The Agency is tasked to **analyse** those data and **publish** an annual report
- Building on existing EU data collection system for sales of antimicrobials in animals (ESVAC).
- **Aims:**
  - To **monitor trends** of sales and use (by animal species) of antimicrobials **overtime**
  - To facilitate **One Health integrated analysis** of AMC and AMR – JIACRA report
  - To monitor progress of the EU Farm-to-Fork strategy ('EU Green Deal') objective **to reduce the sales** of antimicrobials for farmed animals and aquaculture **by 50% by 2030**.

Collection and reporting of data on antimicrobials

Data requirements – Art 57(3)

- Requirements:
  - ✓ Types of antimicrobials
  - ✓ Data quality assurance
  - ✓ Rules on methods for data collection and reporting
    - Data sources (MAH data from UPD adjusted to account for movements of products; other sources possible)
    - Animal species, categories and stages
    - Timelines

* *Adopted by EC; Parliament and Council to accept/reject*

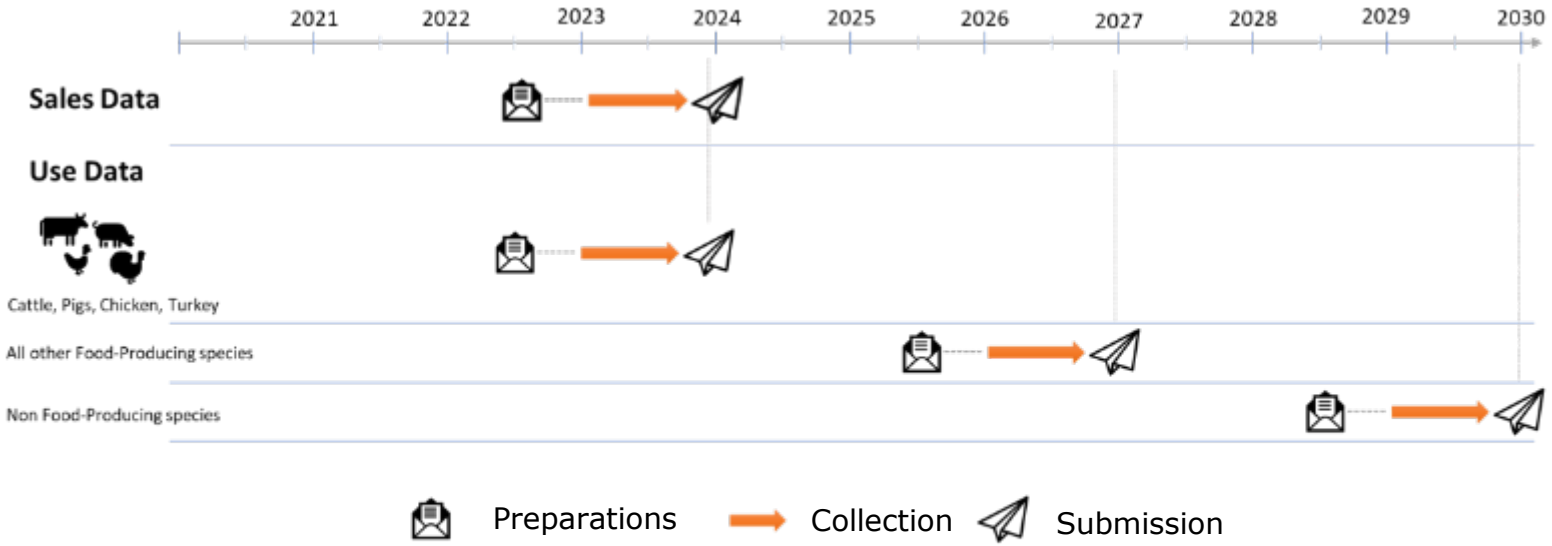
Format of data – Art 57(4)

- EMA scientific advice provided to EC
- Implementing Act being drafted

❑ *Guidance, manuals, data reporting protocols and templates to be developed after IA is published*

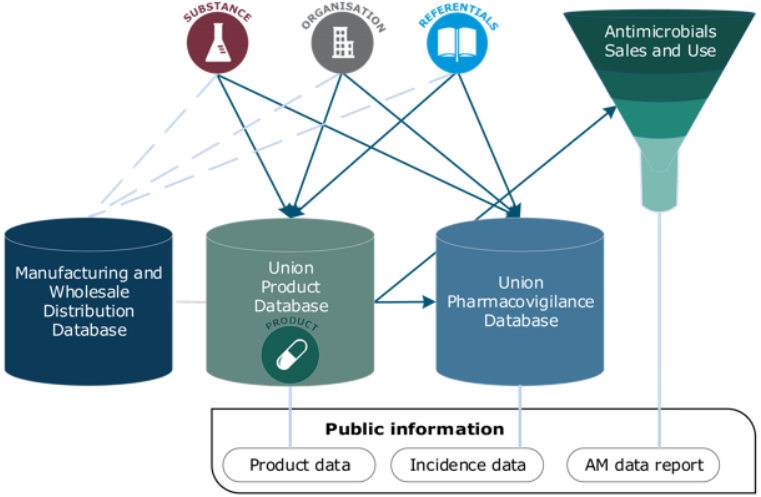
❑ *Considering international developments in this area*

High-level timeline – a stepwise approach



Antimicrobial data reporting – IT tool

- Project has started (Vet-Regulation programme)
- Aims:
  - To provide an environment for MSs to submit data in a standardised format
  - To support harmonisation and data quality
  - To facilitate integration with UPD re product information and avoid duplication
  - To provide interactive public database and support data analytics
- Leveraging existing capabilities for sales data collection



Criteria for the designation of antimicrobials for human use - *Art 37(4)*

Mandate from EC EMA → EMA scientific recommendations to EC → Delegated Act → Publication/ Entry into force

- Three **criteria** recommended:

1. High importance to human health
2. Risk of transfer of resistance
3. Low importance to animal health

- To be applied to new and already authorised products
- In collaboration with relevant **EU agencies** (e.g. EFSA and ECDC); considering work of relevant **international organisations** (e.g. OIE, WHO, FAO)

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31 October 2019
EMA/CVMP/158366/2019
Committee for Medicinal Products for Veterinary Use

Advice on implementing measures under Article 37(4) of Regulation (EU) 2019/6 on veterinary medicinal products – Criteria for the designation of antimicrobials to be reserved for treatment of certain infections in humans

List of antimicrobials reserved for human use - *Art 37(5)*

- Provide scientific advice to the EC on antimicrobials (antibiotics, antivirals, antifungals and anti-protozoals) reserved for treatment of certain infections in humans based on criteria established in the Delegated Act (Art 37(4)).
- Considering WHO, OIE and AMEG categorisations.
- EMA scientific recommendations to be delivered **after the delegated Act on the criteria (Art 37(4))** is published.
- The 'reserved list' will also apply to operators in **third countries** in respect to **animals** or **products of animal origin exported** to the Union (**Art 118**).

Regulation (EU) 2019/6 – specific actions against AMR

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List of antimicrobials, not to be used in accordance with Articles 112-114 ('cascade use') or to be used subject to certain conditions - *Art 107(6)*

Mandate from EC EMA → EMA scientific recommendations to EC → Delegated Act → Publication/ Entry into force

- Considers the associated **AMR risks to animal and public health,** balanced with **availability of treatments** for animals, and potential **impacts on aquaculture and farming**, if no treatment is available.
- Running in parallel to the 'Reserved List' advice
- EMA scientific recommendations **to be delivered soon after the advice on the reserved list** (Art 37(5)) is finalised

Provisions on Prophylaxis and metaphylaxis use - Art 107(3) & 107(4)

- ***Prophylaxis*** in **'exceptional cases' only**, for administration to an individual or a restricted number of animals, when risk of infection is high and consequences are likely to be severe (**Article 107(3)**).

- ***Metaphylaxis*** when the risk of spread of an infection or infectious disease in a group of animals is high and no appropriate alternatives are available. Guidelines to be elaborated at national level by MSs (**Article 107(4)**).

  - A **reflection paper** for determining **'exceptional cases'** when antimicrobial administration **for prophylaxis** would be accepted will be prepared (**January 2022**).

  - A procedure for **reviewing prophylaxis indications for existing** products will be elaborated **(January 2022**).

  - Existing guidelines will be **updated in line with the definitions** of the Regulation ('antimicrobial', 'antibiotic', 'metaphylaxis', 'prophylaxis') (Art 4) (**January 2022**).

Other provisions:

Article 8: Data to be submitted with the application

- Information on **direct or indirect risk to public or animal health or the environment** of use of the antimicrobial medicinal product in animals.
  - ➢ The draft **guideline on the risk assessment of antimicrobials** will be finalised following public consultation (**April 2021**).
- Information about **risk mitigation measures** to limit antimicrobial resistance development related to the use of the VMP.
  - ➢ Further guidance on risk management measures (to mitigate the risk of AMR) will be considered.

Other provisions:

Article 35: Summary of product characteristics

- **Special conditions for use**, including restrictions on the use of antimicrobials in order to limit the risk of development of resistance
  - **SPC guideline for antimicrobials** will be revised after public consultation; new definitions, risk management measures, aligned with QRD template (**June 2021**).

Article 36: Ensure on-going effectiveness of antimicrobials

- EC/EMA may request from MAH to conduct **post-authorisation studies** in order to ensure benefit-risk remains positive given the potential development of antimicrobial resistance (Article 36(2))
  - **Guidance** to be developed on the circumstances and requirements for post-authorisation studies (considered in the **CVMP strategy 2021-2025**).

Other provisions:

Article 39 & 40: Period of protection of technical documentation

- 14 years for antimicrobials for food producing animals (**Article 39(b)**)
- For **variations** involving a change to the **pharmaceutical form**, **administration route or dosage**, to have demonstrated (a) a reduction in the antimicrobial or antiparasitic resistance or (b) an improvement of the benefit-risk balance (**Art 40(5)**)

  ➢ For the purposes of the CVMP's reflection paper on Art 40(5)), elaborate scientific **criteria** that need to be satisfied to support a **reduction** in (the risk of) **AMR** to justify an additional period of **data protection** (Article 40(5)) (**ongoing**).

Other relevant activities

- *EMA Regulatory Science Strategy to 2025*
- *European Medicines Agency Network Strategy to 2025*
- *CVMP strategy on antimicrobials 2021-2025 (March 2021)*
  - *Use of **aminopenicillins** and their beta-lactamase inhibitor combinations in animals in the European Union: development of resistance and impact on human and animal health*
  - *Reflection paper on **AMR in the environment:** considerations for current and future risk assessment of veterinary medicinal products (March 2021)*
  - *Reflection paper on **dose optimisation** (January 2021)*
  - *Reflection paper on authorisation of **alternatives to antimicrobials** (consultation closed April 2020)*
- ***10th ESVAC report** (November 2020) & **3rd JIACRA report** (July 2021)*

Thank you for your attention

Further information

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