The tripartite initiative: France-Portugal-Spain

Challenges, opportunities and next steps to improve the availability of antimicrobials and their alternatives

ANMV (France)
DGAMV (Portugal)
PRAN (Spain)

CHALLENGES, OPPORTUNITIES AND NEXT STEPS

Plan Nacional Resistencia Antibióticos

01. INTRODUCTION

02. MEASURES AT EU LEVEL

03. MEASURES ADOPTED BY THE TRIPARTITE INITIATIVE

04. MEASURES AT NATIONAL LEVEL

05. RECOMMENDATIONS FOR STAKEHOLDERS

06. WHAT ELSE?

INTRODUCTION

Plan Nacional Resistencia Antibióticos

Lack of availability. WHO (2023) adapted

The unavailability of an antimicrobials/alternatives corresponds to:

- No antimicrobial/alternative available on the market, but available in other countries
- Antimic
  - .
  - .
- Antimic pharma should

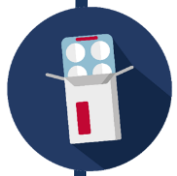
Most antibiotic-resistant infections would respond to antibiotics that have already been developed and approved for market, **but not all existing antibiotics are available for the potential species & indications and in all countries**

Additionally, **preventive/therapeutic gap:** Absence of therapeutic/alternative

MEASURES AT EU LEVEL: REGULATION (EU) 2019/6

Plan Nacional Resistencia Antibióticos

Provides for a modern, innovative and fit for purpose legal framework



Promotes and stimulates innovation

Offers incentives to overcome the lack of availability of veterinary medicines

Reinforces the EU action to fight antimicrobial resistance

Adapted from CVMP workplan for 2023 and beyond 16 February 2023

MEASURES AT EU LEVEL: REGULATION (EU) 2019/6

Plan Nacional Resistencia Antibióticos

UPD public website

- ✓ Allows to search and view up-to-date information on veterinary medicines authorised in the EU/EEA;
- ✓ Enables veterinarians to find out in which country a specific VMP is available, compare medicines or to find information on potential alternatives;
- ✓ It also includes [illegible] veterinary medicines and ve[illegible]

FULLY FUNCTIONAL IN Q1 2023

From EMA/FVE webinar on UPD public website 27 June 2022

MEASURES AT EU LEVEL: REGULATION (EU) 2019/6

Plan Nacional Resistencia Antibióticos

Prescription of medicines outside the terms of the MA

- ✓ Distinctio
  - Non
  - Food
  - Food
- ✓ New rule
  115 (unles
  summary
- ✓ The casca

The cascade is a **risk-based decision tree**. Prescribing decisions in accordance with the cascade should be made on a case-by-case basis

The prescription and use of the product is a veterinarian responsibility

When using a product under the cascade, the professional should balance the expected benefits to the animal with the risks of using a medicine under the cascade

Adapted from EMA/FVE webinar on UPD public website 27 June 2022

MEASURES AT EU LEVEL: REGULATION (EU) 2019/6

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Limited market

Art 4(29) A market for one of the following medicinal product types: (a) veterinary medicinal products for the treatment or prevention of diseases that occur infrequently or in limited geographical areas; (b) veterinary medicinal products for animal species other than cattle, sheep for meat production, pigs, chickens, dogs and cats;

Applications

Art. 23 The applicant shall not be required to provide the comprehensive safety or efficacy documentation required in accordance with Annex II, if all of the following conditions are met:

(a) the benefit of the availability on the market of the veterinary medicinal product to the animal or public health outweighs the risk inherent in the fact that certain documentation has not been provided AND

(b) the applicant provides the evidence that the veterinary medicinal product is intended for a limited market

MEASURES AT EU LEVEL: REGULATION (EU) 2019/6

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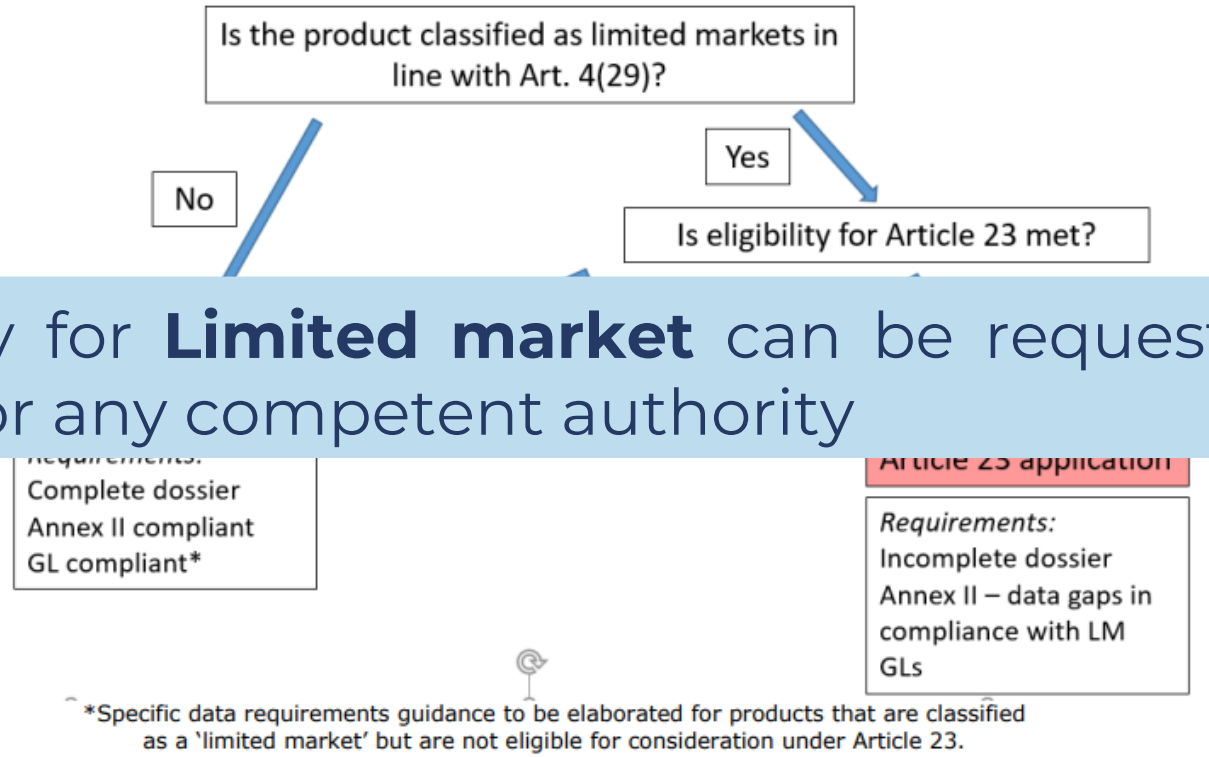
Limited market

Reflection paper on classification of a product as intended for a limited market according to Article 4(29) and/or eligibility for authorisation according to Article 23



Eligibility for **Limited market** can be requested to EMA or any competent authority

Development of guidance for limited market products not deemed eligible for Art. 23

Finalise Q2 2023

MEASURES AT EU LEVEL: REGULATION (EU) 2019/6

Plan Nacional Resistencia Antibióticos

Limited market

Outcome of Request for classifications limited market under article 4(29) and eligibility under article 23

- 15 products have been considered eligible under Article 23:
  - 3 chemicals
  - 12 biologicals (10 vaccines)

- 12 products have been classified as limited market according to art.4 (29) and not eligible under art.23:
  - 7 chemicals
  - 5 vaccines

From CVMP workplan for 2023 and beyond 16 February 2023

MEASURES AT EU LEVEL: REGULATION (EU) 2019/6

Plan Nacional Resistencia Antibióticos

Exceptional circumstances

Art. 25 “benefit of the immediate availability on the market of the veterinary medicinal product concerned to the animal or public health outweighs the risk inherent in the fact that certain quality, safety or efficacy documentation has not been provided”

Validity 1 year

Periods of the protection of technical documentation and additional periods Art. 39 & 40

For more than one animal species or extension of the marketing authorisation to another species (cattle, sheep for meat production, pigs, chickens, dogs and cats) **1 year**

For another species **4 years**

For the establishment of MRLs **5 years**

Prolongation and additional periods of the protection of technical documentation

Art. 40(5) If a variation to the terms of the marketing authorisation approved in accordance with Article 67 involves a change to the pharmaceutical form, administration route or dosage, which is assessed by the Agency or the competent authorities referred to in Article 66 to have demonstrated:

(a) a reduction in the antimicrobial or antiparasitic resistance; or

(b) an improvement of the benefit-risk balance of the veterinary medicinal product, the results of the concerned pre-clinical studies or clinical trials shall benefit from

4 years protection

- Reflection paper on the application of Article 40(5) of 5 Regulation (EU) 2019/6 for certain categories of variations

MEASURES AT EU LEVEL: REGULATION (EU) 2019/6

Plan Nacional Resistencia Antibióticos

Activities relating to antimicrobial resistance

- ✓ Dose review and adjustment (research – follow up of Pilot Project on the Harmonisation and Optimisation of Veterinary Antimicrobials) – establish a prioritised list of products
- ✓ Reflection paper on promoting the authorisation of alternatives to antimicrobial veterinary medicinal products in the EU

Other initiatives

- ✓ Expert group to provide scientific recommendations to the CVMP regarding the list of substances which are essential for the treatment of **equine species**.
- ✓ **Vet Big Data Hub**
- ✓ **SPOC (Single Point of Contact) task force**

Vaccines

- Guideline on plasmid **DNA vaccines** for veterinary use (Released for public consultation)
- Guideline on data requirements for **adjuvants** in vaccines for veterinary use
- Guideline on data requirements for authorisation of immunological veterinary medicinal products in **exceptional circumstances** - Scientific guideline
  Replaced CVMP related guidelines for vaccines agaisnt bluetongue and avian influenza
- Guideline on data requirements for **vaccine platform technology master files** (vPTMF)

Novel Theraphies

- **Monoclonal antibodies:** VICH Draft guideline on target animal safety evaluation for veterinary monoclonal antibody products. *Completion date: December 2023 (to be determined)*

- **Cell therapies:** Guideline on the development and data requirements of potency tests for cell-based veterinary therapy products and the relation to clinical efficacy. *Completion date: Q2 2023.*

- **Bacteriophages** Guideline on quality, safety and efficacy of veterinary medicinal products specifically designed for phage therapy. *Released for public consultation*
  EFSA: Safety and efficacy of a feed additive consisting of the bacteriophages PCM F/00069, PCM F/00070, PCM F/00071 and PCM F/00097 (Bafasal®) for all avian species (Proteon Pharmaceuticals S.A.)

- **Nanomedicines:** Guideline on the safety data requirements for the assessment of VMPs containing non-degradable nanomaterials. *Concept paper to be developed and released for public consultation (Q2 2023)*

MEASURES ADOPTED BY THE TRIPARTITE INITIATIVE

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- To identify the similarities of needs in our countries, esp. on minor species, in order to **communicate on such "extended" limited markets** and motivate more investment from pharmaceutical companies
- To list the requests for VMPs approved in one of our countries, in order to motivate MAH to **submit mutual recognition** for those VMPs
- To promote the interest of defining together some **good practices about early declaration and anticipation of any VMPs' abandon**, in order to better assess its possible negative impact and find out some possible alternatives
- To encourage the involvement of **other MMSS**

HPRA An tÚdarás Rialála Táirgí Sláinte Health Products Regulatory Authority

MEASURES AT NATIONAL LEVEL: SPAIN

Plan Nacional Resistencia Antibióticos

Ley 17/2022

Reduction of registration fees

For those veterinary VMPs intended exclusively for limited markets a **70% reduction** will be applied for:

- ✓ marketing authorization fees
- ✓ marketing authorization modifications requiring evaluation
- ✓ scientific advice
- ✓ products under veterinary clinical investigation, veterinary clinical trials, post-authorization studies
- ✓ official batch release certificates
- ✓ maintenance on the market of veterinary drugs authorized by national procedure, of mutual or decentralized recognition
- ✓ procedures for re-examination and harmonization of the summaries of SPC

MEASURES AT NATIONAL LEVEL: FRANCE

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Reduction of registration fees

- ✓ **80% reduction** for full dossier registered via national procedure or decentralised procedure with France as reference Member State
- ✓ **58% reduction** when France as concerned Member States
- ✓ For a generic or hybrid dossier, **75% reduction** with France as reference Member State, and **33% reduction** when France is a concerned Member States

RECOMMENDATIONS FOR STAKEHOLDERS

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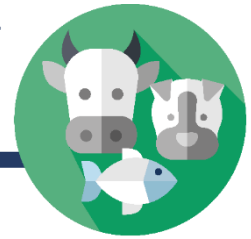
Veterinarians should report on the lack of efficacy in authorised antimicrobial VMPs when used either according to the label or off-label, via the pharmacovigilance system.



notifica VET

Pharmaceutical industry is expected to:

- Make use of the new regulatory tools available.
- Work collaboratively with the different groups and competent authorities to develop new VMPs
- Bring to the market new pharmaceutical forms, target species, etc. apart from new VMPs

WHAT ELSE?

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To improve the centralization the reporting and publish past and current shortages of veterinary medicines at the European level

To improve the procedure of allowing manufacturers to declare market withdrawal or their intention to withdrawal a marketing authorisation (to anticipate future situations and potential impact on the market)

To allow health care professionals to notify authorities not only perceived lack of availability of veterinary antibiotics (already in place) but also **lack of therapeutic/preventive tools** (*unmet medical needs*)

Generate evidence on the impact of new AMR legislation from a One Health perspective

European Commission's ***Pharmaceutical Strategy for Europe*** support public R&D in human medicine. Can a similar approach be adopted to have new VMPs for animal use?

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Many thanks!

www.resistenciaantibioticos.es

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agencia española de medicamentos y productos sanitarios