The tripartite initiative: France-Portugal-Spain

Introduction, methodology and results

Workshop on Veterinary Medicines: Improving the availability of antimicrobials and their alternatives

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

Plan Nacional Resistencia Antibióticos

01. INTRODUCTION

02. PRESENTATION OF THE WORKING GROUP

03. METHODOLOGY

04. PRIORITIES BY SPECIES

SPANISH NATIONAL ACTION PLAN (PRAN)

Plan Nacional Resistencia Antibióticos

IMPROVING THE AVAILABILITY OF ANTIMICROBIALS AND THEIR ALTERNATIVES

CONSUMPTION SURVEILLANCE

RESISTANCE SURVEILLANCE

PRAN 2022-2024

REDUCE GROUPS IN SPECIES

ANIMAL SECTOR: PARTICULARITIES

Huge diversity of species and production type (and breeds): Mammals, birds, fishes, insects. Differences in metabolism and biology

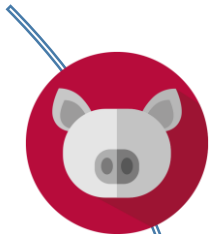
Major vs minor species, based on animal population threshold (except bees - minor species)

Cost sensitive : Markets weaker and more fragmented

- Limited markets >> human drugs market size
- Major investments to extend authorisations in other species

Complex veterinary formulations

ANIMAL SECTOR: PARTICULARITIES



Food producing animals: therapeutic, safety and environmental implications (Establish MRLs + withdrawal periods + ERA)

Restrictions to antibiotic use in veterinary medicine:

-NRV 2019/6

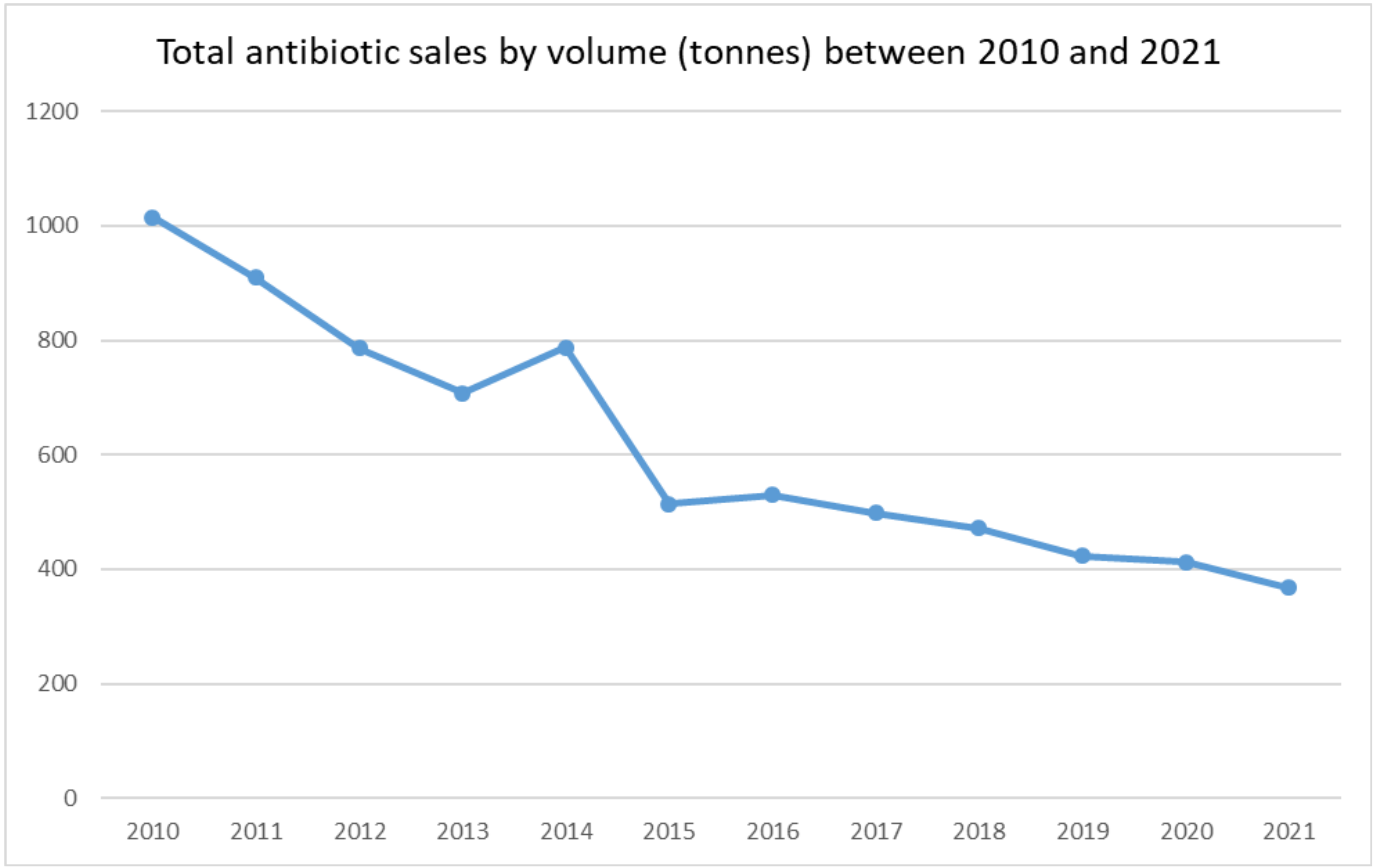
-Antimicrobial Advice Ad Hoc Expert Group categorization.

-Commission Implementing Regulation (EU) 2022/1255

-Antimicrobials reserved for the treatment of certain infections in humans

Only a few or no new antibiotics will be developed for use in veterinary medicine

EVOLUTION OF ANTIBIOTICS CONSUMPTION IN FRANCE



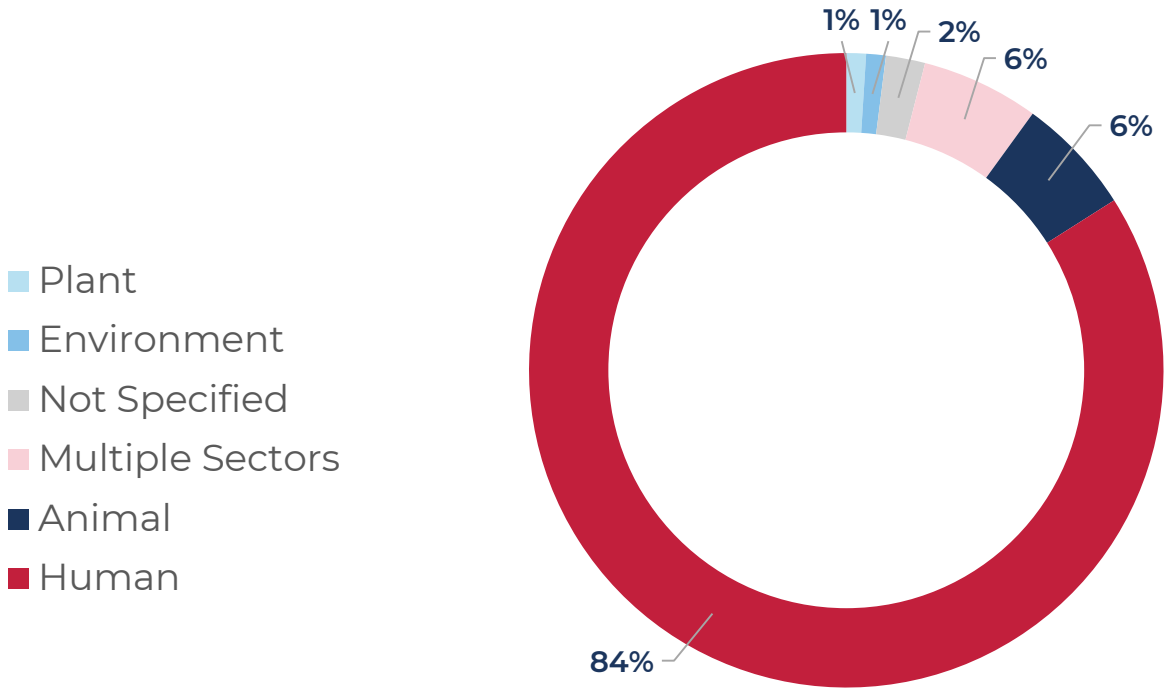
Anses-ANMV/ Market Surveillance and Pharmacovigilance Unit

A significant decrease in sales volume of 64% since 2010

-Ecoantibio plan

-Regulatory supervision of critical antibiotic use

ANIMAL SECTOR: INVESTMENT



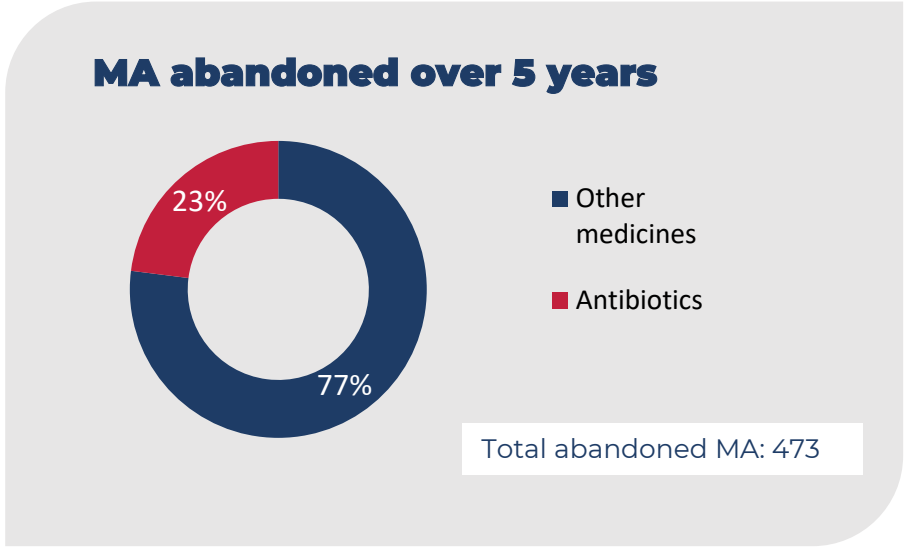
Investment by One Health sector as percentage of total funding volume. *Human, Animal, Plant and Environment health includes single sector projects only*

Global AMR R&D Hub (2021). Annual Report 2021: The Global AMR R&D Funding Landscape.

INDUSTRIAL INVESTMENT IN ANTIBIOTICS

- ✓ API manufacturers almost all in China/India, with serious implications in shortages (see GMP incident of a Chinese benzylpenicilin manufacturer (late 2015-2016-2017)
- ✓ Old APIs, small batches/human drugs, manufacturing costs and production capability
- ✓ No new Market Authorization dossier
- ✓ Abandonment of Market Authorization

Few profitable investments
High risk of discontinuation of marketing

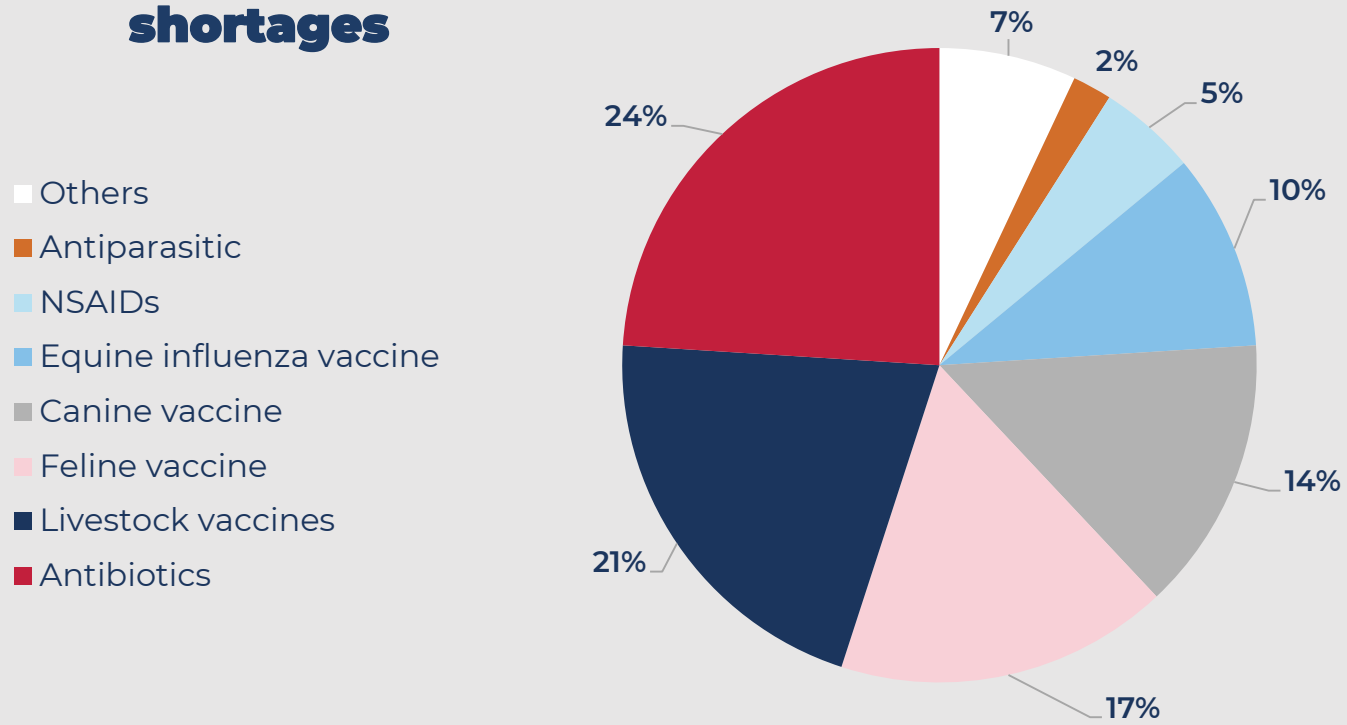


Anses-ANMV/ Market Surveillance and Pharmacovigilance Unit

ANIMAL SECTOR: VET PRACTICIONERS

Plan Nacional Resistencia Antibióticos

Medicines/vaccines shortages



FVE survey on medicine/vaccine shortages in Europe (2022)

Concerns

WHO survey : Industry consultation (2023)

- The market is being neglected in decline and constrained by **strong regulatory pressure**
- **Current and future innovations in veterinary antibiotics are rare**, meaning that there likely will be no new products coming on the market
- Antibiotics remain an **essential component** of the veterinary therapeutic arsenal for treating animals and therefore for their well-being
- **Societal expectations and health risks** (residues in food, antibiotic resistance) challenge the image of veterinary antibiotics

Plan Nacional Resistencia Antibióticos

Evolution

WHO survey : Industry consultation (2023)

- A risk for the future that there will be **no more investments** in this therapeutic class and that old MAs will be **abandoned**, thus reducing the number of available antibiotics on the market.
- **Reserving antibiotics for human health** to the detriment of animals poses a significant risk to animal health, animal welfare and public health.
- **Fewer industrial players** are involved in veterinary antibiotics.

WHAT INFLUENCES THE AVAILABILITY OF VETERINARY MEDICINES

Plan Nacional Resistencia Antibióticos

Shortages due to:

- Manufacturing defects
- Decline in production
- Withdrawls of MA

An **“uninteresting” market**:

- Small size
- Shipping costs (minor species-small quantity of VMPs and obligation of the supply via authorised distributor or MA holder (CZ-premixes))

- VMP
- Using cascade rules
- National legislation rules for permission to market authorised VMPs in a language other than national (CZ-EN, DE,...; same rules in FI)
- NNT

Available antibiotics by species and indicatios

Active substance (form)	Target Species	Bacterial diseases
Oxytetracycline	Salmonids, seabass, gilthead, turbot, eel, and carp	Lactococcosis Classical vibriosis Aeromonas infection
Florfenicol	Rainbow trout	Furunculosis
Flumequine	Salmonids, Trout Fish	Furunculosis Enteric red mouth disease Classical vibriosis
Oxolinic acid	Trout	Furunculosis Enteric red mouth disease

EXAMPLE FROM ANIMAL SECTOR

Plan Nacional Resistencia Antibióticos

RÉPUBLIQUE FRANÇAISE
Liberté Égalité Fraternité

anses

Working Group on Availability of AM Medicinal Products and Alternatives to their Use

Plan Nacional Resistencia Antibióticos

dgav
Direção Geral de Alimentação e Veterinária

DEFINITIONS

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
- Antimicrobial/alternative available but:
  - not approved for all relevant species
  - not approved for all relevant indications
- Antimicrobial/alternative available for the relevant species/indications but pharmaceutical form, dosage, treatment duration or other specifications should be be modified/updated

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

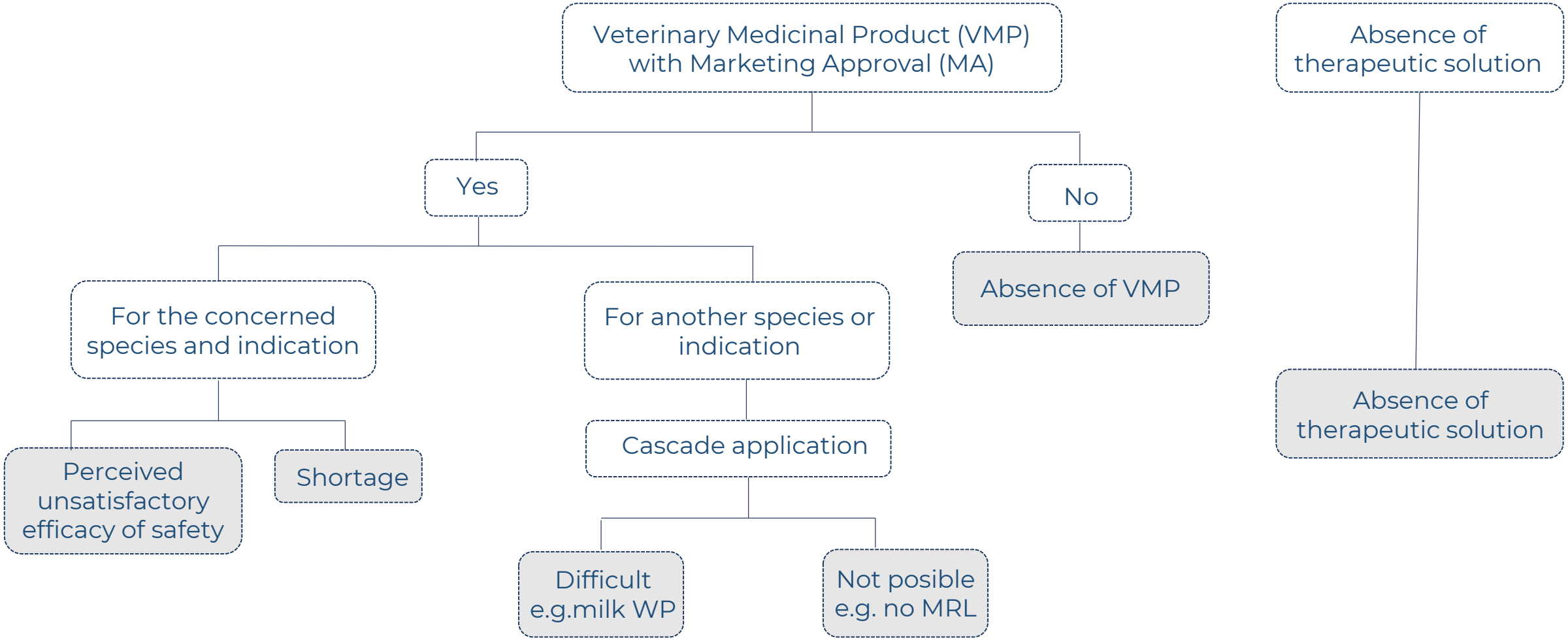
METHODOLOGY

Plan Nacional Resistencia Antibióticos

IDENTIFY & UPDATE GAPS

- **Identification of therapeutic gaps/availability issues**
  Listing of the field therapeutic gaps and other issues for each sector
- **Reasons** for those gaps/issues
- **A list (prioritisation) of therapeutic & alternative** to AMs gaps/issues
- **Action plan**, including possible ways of collaboration between the three countries (+ Ireland and others)

METHODOLOGY



IDENTIFICATION OF THE REASONS FOR THOSE GAPS OR PRESCRIPTIONS OUTSIDE THE MARKETING AUTHORISATION

Plan Nacional Resistencia Antibióticos

- Unsatisfactory effectiveness or safety
- Availability, shortage
- Regulatory issue: cascade application, withdrawal period, restricted access
- Absence of appropriate VMPs
- Absence of therapeutic solution

DATA SOURCES

Plan Nacional Resistencia Antibióticos

- Prescriptions outside the terms of the marketing authorisation (when available)
- Imports from outside the EU in 2021
- National reports on Therapeutic Gaps and other Priorities
- VMPs from other Member States
- VMPs for temporary use authorisation

Analysis

and

Expert Consultation

Plan Nacional Resistencia Antibióticos

RISK ANALYSIS

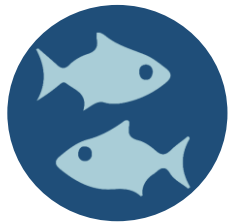
Biological hazard (animal & human)

Risk assessment

- ✓ Therapeutic impact
- ✓ Economic consequences

DEFINE 3-5 MAJOR PRIORITIES

PRIORITIES: FISH FARMING



DISEASE	ACTIVE SUBSTANCE	ROUTE	SPECIES
External parasitosis	formaldehyde	bath	Other species apart from gilthead and turbot
	others	bath	
Flavobacteriosis	oxytetracycline	premix	trout, rainbow trout
Furunculosis			gilthead, seabass, sole, trout, turbot,
Pasteurellosis			gilthead, meagre, seabass
Tenacibaculosis			gilthead, seabass, seriola, sole, turbot,
Vibriosis (not caused by *V. anguillarum*)			gilthead, meagre, seabass, seriola,sole, turbot

Other needs

Other antibiotics

Polyvalent vaccines

PRIORITIES: RABBIT FARMING

Plan Nacional Resistencia Antibióticos

Epizootic rabbit enteropathy

- ✓ Avilamycin (oral, premix) or others antibiotics
- ✓ Enzymes complex as feed additive

Coccidiosis: Other VMPs available

Staphylococcal mastitis: Long-acting penicillins (parenteral)

Myxomatosis: Review and update of available vaccines

Respiratory infections: Vaccines

Ringworn: Vaccines and VMPs

PRIORITIES: SMALL RUMINATS

Plan Nacional Resistencia Antibióticos

Sheep

Ovine respiratory disease complex

- ✓ Vaccine

Goats

Mycoplasmosis:

- ✓ Marbofloxacin as injectable form
- ✓ VMPs for mastitis

Coccidiosis:

- ✓ Diclazuril (oral forms)

Respiratory infections:

- ✓ Vaccines

PRIORITIES: SMALL RUMINATS

Plan Nacional Resistencia Antibióticos

Sheep & Goats

Cryptosporidiosis:
✓ Other VMPs available

Mastitis
✓ Intramammary VMPs such as **cloxacillin**

Anti-inflammatory drugs

PRIORITIES: CATTLE

Coccidiosis:
✓ Decoquinate for individual treatment

Respiratory infections:
✓ Pleuromutilins, injectable forms

Leptospirosis
✓ Vaccines (L. pomona)

Other needs

Tetracyclines: review and adjustment of the SPC

Alternatives to group B antibiotics for dairy cattle. Options with shorter withdrawal time in milk from group C and D

Topical antibiotic forms for ocular infections and teat injury

PRIORITIES: POULTRY

Plan Nacional Resistencia Antibióticos

Broilers and Turkeys

Salmonella, different serotypes
✓ In-ovo vaccines

Enteric and respiratory infections:
✓ Other antibiotics with shorter duration of treatments & withdrawal periods

Hemorrhagic enteritis (turkeys)
✓ Vaccine

Other needs

VMPs against Histomoniasis & Aspergillosis

In-ovo vaccines for other diseases

PRIORITIES: POULTRY

Plan Nacional Resistencia Antibióticos

Laying birds

Respiratory infections

- ✓ vaccines
- ✓ Bronchodilators, mucolytics
- ✓ Anti-inflammatory drugs

Red mite infestations

- ✓ vaccine
- ✓ antiparasitc drugs

Tapeworm infestations

- ✓ antiparasitic drugs

PRIORITIES: PIG FARMING

Plan Nacional Resistencia Antibióticos

Diarrhoea in piglets caused by Rotavirus

✓ Vaccine

Neonatal diarrhoea and post weaning colibacilosis

✓ VMPs and vaccines

Swine dysentery:

✓ Bacitracin methylene salicylate

✓ Vaccines

Other needs

Tetracyclines and florfenicol: review and adjustment of the SPC

PRIORITIES: BEES

Varroosis

✓Other VMPs available

PRIORITIES: EQUINES

Plan Nacional Resistencia Antibióticos

Theileriosis:
Buparvacuone

Sepsis:
Availability of antibiotics as intravenous forms, metronidazol and other antibiotics from group c and D

Other needs

Ectoparasiticides: availability of other VMPs

Antimicrobials for topic use

PRIORITIES: DOGS AND CATS

Plan Nacional Resistencia Antibióticos

DISEASE	ACTIVE SUBSTANCE	ROUTE
Sepsis	ampicillin/amoxicillin	intravenous
	cefazoline	intravenous
	metronidazol	intravenous
Viral eye infections	ganciclovir	eye drops (cats)
Bacterial eye infections	chloramphenicol	eye drops
	ciprofloxacin	eye ointment

Other needs/issues

VMPs for Kerotoconjunctivitis sicca

'Reserved' List

Antimicrobials for topic use

Plan Nacional
Resistencia
Antibióticos

¡Muchas gracias por tu interés!

www.resistenciaantibioticos.es

@PRANgob

MINISTERIO DE SANIDAD

agencia española de medicamentos y productos sanitarios