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EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

Funded by the European Union

EUROPEAN REGULATORY STANDARDS FOR HERBAL VETERINARY MEDICINAL PRODUCT

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MedPlant4Vet – WG 1
Training course
December 2025

1. Veterinary Medicinal Product – Regulatory standards for a marketing authorization

Definition of a VMP

- any substance or combination of substances presented as having properties for treating or preventing disease in animals;

- any substance or combination of substances that may be used in, or administered to, animals with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action;

- or to be used with a view of making a medical diagnosis;

- or to be used for euthanasia of animals

→ If a herbal product / plant extract / EO with therapeutic claim
→ = veterinary medicine

Legislation of herbal medicines

In Europe, European Directive 2001/82/EC: covers veterinary medicinal pro**ducts**, but only chemical, biological and homeopathic products.
Well-established use is mentioned in Article 13 bis;

➪ **No dedicated European reglementation for veterinary herbal medicines.**

- No specific scientific guidelines for these products, except for the quality part
- No specific committee on herbal products for the veterinary medicine

The life of a VMP

Research & Development

Authorities

Manufacturing & Marketing

Prescription & Use

benefit/risk balance

MRL establishment

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SCIENCE MEDICINES HEALTH

Marketing authorisation

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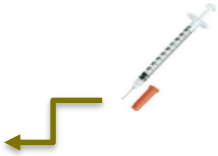

Consumption & Control

SCIENTIFIC ASSESSMENT

MANAGEMENT

DECISION

Benefits **Risks**

PROPOSAL

Assessment Report

Dossier of marketed autorisation of pharmaceutical VMP

Regulation (EU) 2019/6 and Commission delegated regulation (EU) 2021/805

Part 1

- Summary of the dossier

Part 2 : Quality documentation

- A - Product description
- B – Description of the manufactoring method
- C – Production and control of starting material
- D – Control tests carried out on isolated intermediates during the manufacturing process
- E – Control tests on the finished product
- F – Stability tests
- G – Other information

Dossier of marketed autorisation of pharmaceutical VMP

Regulation (EU) 2019/6 and Commission delegated regulation (EU) 2021/805

Part 3 : Safety documentation

- A – Safety tests
  - Toxicology
  - User safety
  - Environmental risk assessment
- B – Residues tests

Part 4 : Efficacy documentation

- A - Pre-clinical studies
  - Pharmacology
  - Resistance
  - Tolerance
- B – Clinical trials

2 - Consumer risk assessment

Maximum residue limit (MRL)

Dossier of marketed autorisation of pharmaceutical VMP

Regulation (EU) 2019/6 and Commission delegated regulation (EU) 2021/805

Part 3 : Safety documentation

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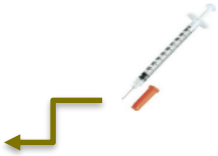
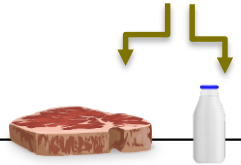




Consumption & Control

Maximum residue limit (MRL)

Food safety

Trade requirements

Regulation

European Regulations

(EC) 470/2009 of 06/05/09
(EU) 37/2010 of 22/12/09
(EU) 2017/12 of 06/01/17 (content of the application)
(EU) 2018/782 of 29/05/2018 (assessment & management)
(EU) 2017/880 of 23/05/2017 (extrapolation)
(EU) 2018/470 of 21/03/2018 (control & cascade)
(EU) 2019/2090 of 19/06/2019 (control: non compliance)
(EU) 2019/1871 of 07/11/2019 (control: reference value)

(EE) 2019/6 of 11/12/2018

VICH Guidelines

VICH GL 36 (microbiologic ADI)
VICH GL 46 (nature of residue)
VICH GL 47 (metabolisme comparatif)
VICH GL 48 (marker residue)
VICH GL 49 (analytical method)
VICH GL 56 (honey)
VICH GL 57 (aquatic species)

CVMP Guidelines

EMA/CVMP/516817/2009 (out of scope)

EMA/CVMP/SWP/591282/2021 (Biological substances)
EMA/CVMP/SWP/90250/2010 (Biocide)

EMA/ CVMP/SWP/355698/2006 (Pharmacological ADI)

EMEA/CVMP/SWP/345236/2020 (MRL Minor species)

EMA/CVMP/SWP/735325/2012 (meat & offal withdrawal period)
EMA/CVMP/473/98-Final (milk withdrawal period)
EMA/CVMP/520191/2007-Rev.1 (injection site)
EMA/CVMP/345237/2020 (article 23)
EMEA/CVMP/SWP/32027/2022 (MUMS article 8)

MRL - definitions

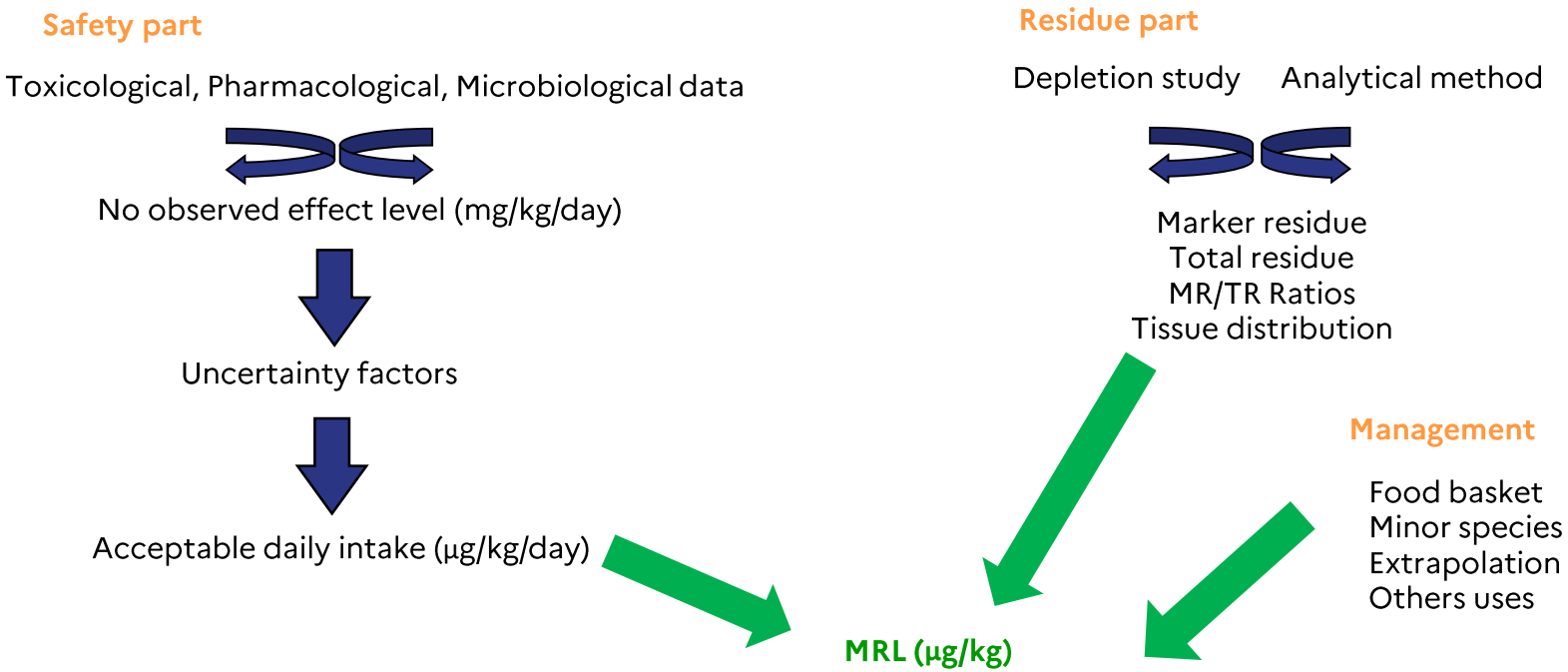
- Residues of pharmacologically active substances means all pharmacologically active substances, expressed in mg/kg or µg/kg on a fresh weight basis, whether active substances, excipients or degradation products, and their metabolites which remain in food obtained from animals.

- Food producing animals means animals bred, raised, kept, slaughtered or harvested for the purposes of producing food.

A **MRL** is established for

- a **pharmacologically active substance**
- per **animal species**
- and per **foodstuff** of animal origin (muscle, kidney, liver, fat, milk, egg, honey)

How is a MRL established?



Assessment of a MRL application

According to the data provided by the applicant

- The substance is included in the table 1 or table 2 of the European regulation (EU) 37/2010

Table 1: **allowed substances**
- MRL value ± restriction of use
- No MRL required ± restriction of use

Table 2: **prohibited substances**
- MRL cannot be established

- Or in the out of scope list for pharmacologically inactive substance

Table 1

Table 1: **allowed substances**

- MRL value ± restriction of use
- No MRL required ± restriction of use

Apramycin	Apramycin	Bovine	1 000 µg/kg 1 000 µg/kg 10 000 µg/kg 20 000 µg/kg	Muscle Fat Liver Kidney	Not for use in animals from which milk is produced for human consumption.	Anti-infectious agents/Antibiotics
	NOT APPLICABLE	Ovine, porcine, chicken, rabbit	No MRL required	NOT APPLICABLE	For oral use only. Not for use in animals from which milk or eggs are produced for human consumption.	

Table 1

Substance pharmacologiquement active	Résidu marqueur	Espèce animale	LMR	Denrées cibles	Autres disposition	Classification thérapeutique
Acide clavulanique	Acide clavulanique	Bovins, porcins	200 µg/kg 100 µg/kg 100 µg/kg 400 µg/kg	Foie Graisse muscle Rein	Pour les porcins la LMR graisse concerne peau et graisse dans des proportions naturelles	Médicaments anti-infectieux /antibiotiques
		Bovins	200 µg/kg	Lait		
Angelicae radix aetheroleum	Non applicable	Toutes les espèces productrices d'aliments	Aucune LMR requise	Non applicable	Néant	Néant
Cimifiguae racemosae rhizoma	Non applicable	Toutes les espèces productrices d'aliments	Aucune LMR requise	Non applicable	Ne pas utiliser chez les animaux produisant du lait destiné à la consommation humaine	Néant

Table 2

Table 2: **prohibited substances**

- MRL cannot be established

Pharmacologically active substances	MRL
Aristolochia spp et l'ensemble de ses préparations	No MRL can be establised
Chloramphénicol	No MRL can be establised
Chlorpromazine	No MRL can be establised
Colchicine	No MRL can be establised
Dapsone	No MRL can be establised
Dimétridazole	No MRL can be establised
Métronidazole	No MRL can be establised
Nitrofuranes (furazolidone incluse)	No MRL can be establised
Ronidazole	No MRL can be establised

Web sites

↳EMA : summary reports & European public MRL assessment report (EPMAR)
↳Out of scope list
http://www.ema.europa.eu

↳Consolidated version of tables 1 & 2 can be found at
http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02010R0037-20160324&from=DE

↳Anses-ANMV: MRL values
http://www.anses.fr

Rules of the veterinary drug practice: withdrawal period

- For food producing animal, a VMP can be use only if the substances are included in table 1 of 37/2010 or in « out of scope » list.

=> **withdrawal periods** should be determined….

21

Withdrawal period

Definition according to the European regulation (EU) 2019/6:

Withdrawal period means the minimum period between the last administration of a veterinary medicinal product to an animal and the production of foodstuffs from that animal which under normal conditions of use is necessary to ensure that **such foodstuffs do not contain residues in quantities harmful to public health.**

A **withdrawal period** is established for

- A veterinary medicinal product
- per animal species
- and per foodstuf of animal origin (meat & offal, milk, egg, honey)

Withdrawal period

A withdrawal period is determined

- From a depletion study : meat & offal, milk, eggs and honey
- With a validated analytical method
- By statistical or alternative approach

3 - Cascade

Cascade use - Definitions

According to the articles 112 to 115 of the European regulation 2019/6

Use of VMP outside the terms of the marketing autorisation

Where there is no authorised VMP in a Member State for an indication concerning an animal species, **the veterinarian responsible may, under his or her direct personal responsibility** and in particular to avoid causing unacceptable suffering, exceptionally treat the animals concerned

Non-food-producing animal species

Food-producing terrestrial animal species

Food-producing aquatic species

Antibiotic => list of not allowed antibiotics

Horses => list of substances which are essential for the treatment of equine species

Fish => list of allowed substances

Bees => the veterinarian shall determine the appropriate withdrawal period

Article 112 : non-food-producing animal species

Veterinary medicinal product authorised in the relevant Member State or in another Member State for use

in the same species or another animal species

for the same indication or for another indication

Human medicinal product

Veterinary medicinal product prepared extemporaneously

Animals of the equine species shall be declared as not being intended for slaughter for human consumption in the single lifetime identification document.

Article 113 : food-producing terrestrial animal species

Veterinary medicinal product authorised in the relevant Member State or in another Member State for use
in the same species or another food-producing terrestrial animal species
for the same indication or for another indication

Veterinary medicinal product authorised in the relevant Member State for use
in a non-food-producing animal species
for the same indication

Human medicinal product

Veterinary medicinal product prepared extemporaneously

Active substance of Table 1

! Others provisions!

Article 114 : food-producing aquatic species

Veterinary medicinal product authorised in the relevant Member State or in another Member State for use
for the same indication or for another indication
in the same species or another food-producing aquatic species

Veterinary medicinal product authorised in the relevant Member State or in another Member State for use
in a food-producing terrestrial animal species

Human medicinal product

Veterinary medicinal product prepared extemporaneously

List of allowed substances

Article 115 : withdrawal periods

« Meat & offal » withdrawal period of food-producing mammals, poultry & farmed game birds

The longest « meat and offal » WP x 1.5
28 days if the medicinal product is not authorised for food-producing animals
1 day if the WP is zero days and is used in a different taxonomic familly

« Milk » withdrawal period

The longest « milk » WP x 1.5
7 days if the medicinal product is not authorised for animals producing milk for human consumption
1 day if the WP is zero days

Article 115 : withdrawal periods

minimum

« Eggs » withdrawal period

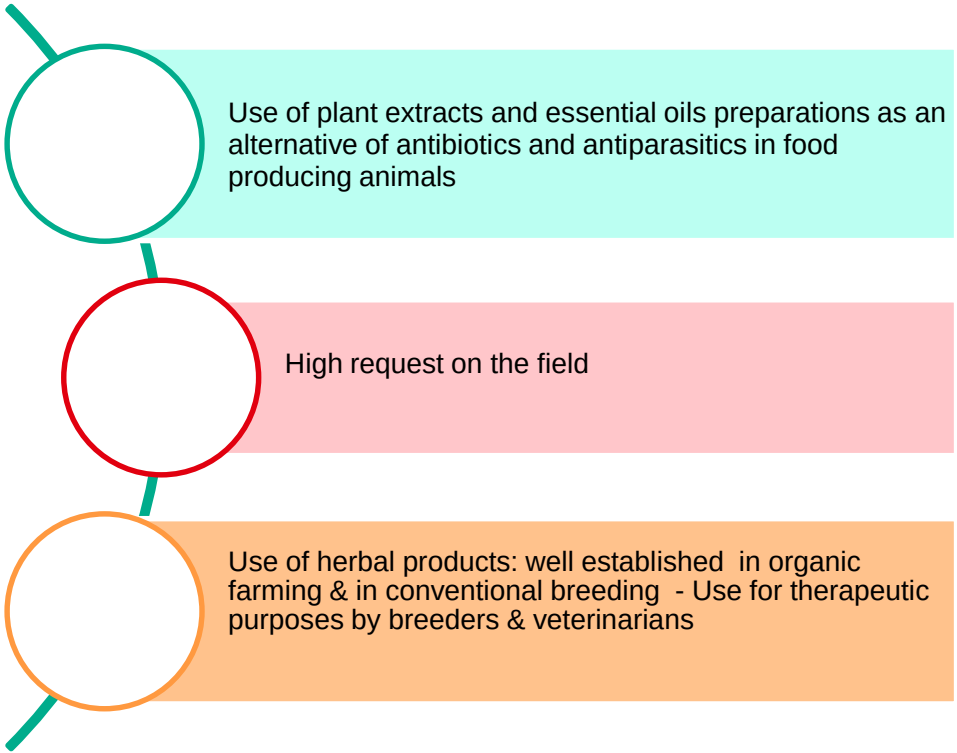
The longest « eggs » WP x 1.5
10 days if the medicinal product is not authorised for animals producing eggs for human consumption

« Meat » withdrawal period for aquatic species

The longest WP for aquatic species x 1.5
The longest WP for food-producing terrestrial animal species x 50 (but < 500 degree.days
500 degree.days if medicinal product is not authorised for food-producing
25 degree.days if the highest WP is zero days

4 – Impacts on herbal veterinary medicinal products (HVMP)

Background of the use of plants in France



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- or to be used with a view of making a medical diagnosis;

- or to be used for euthanasia of animals

→ If a herbal product / plant extract / EO with therapeutic claim
→ = veterinary medicine

Herbal medicines in France

- Several homeopathic products have a marketing autorisation and include herbal drugs.

- Few « old » veterinary chemical medicines include herbal drugs:
  For example the following products:

  . **Phytophale** including Lespedeza capitata , Artichoke ,and Java tea (all dry extracts)

  . **Apilife var** including Thymol, Eucalyptus (oil), Camphor, Levomenthol
  . Cothivet including essential oils and tinctures

Cothivet: Solution for cutaneous application with Cupressis EO, Lavandulae EO, Rosmarini EO, Thymi EO, Carlina acaulis tincture, Centell asiatica tincture, Alfala tincture and Chestnut tincture.

The life of a VMP

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Prescription & Use

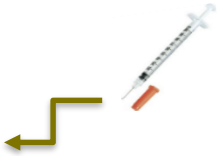
MRL establishment

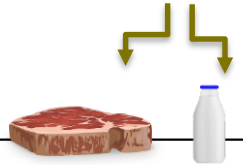
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

benefit/risk balance

Marketing authorisation

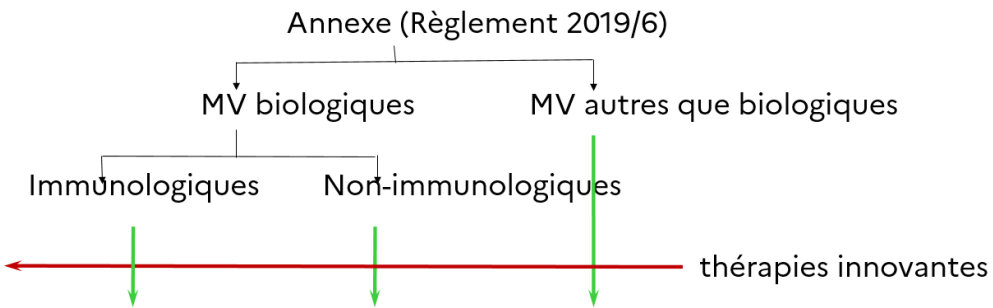
anses





Consumption & Control

Regulation (EU) 2019/6 and Annex II - NEW

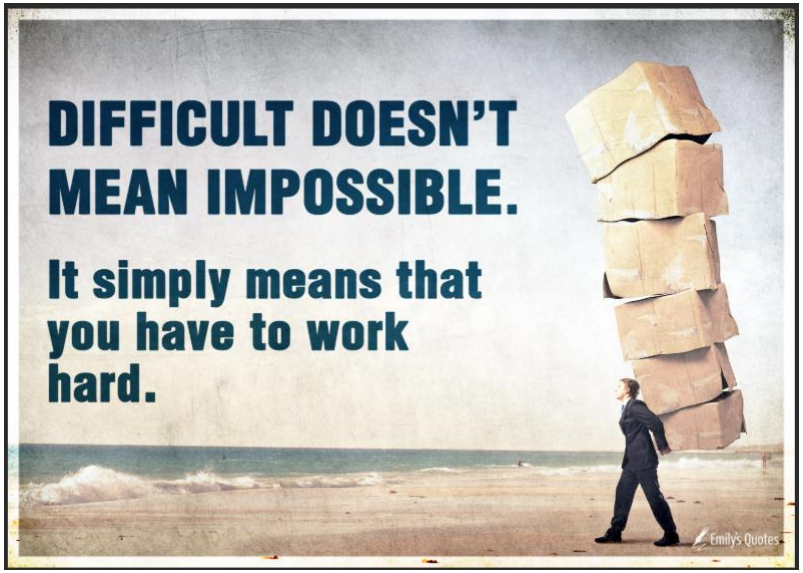


(43) 'novel therapy veterinary medicinal product' means:

(a) a veterinary medicinal product specifically designed for gene therapy, regenerative medicine, tissue engineering, blood product therapy, phage therapy;

(b) a veterinary medicinal product issued from nanotechnologies; or

(c) any other therapy which is considered as a nascent field in veterinary medicine;


DIFFICULT DOESN'T MEAN IMPOSSIBLE.
It simply means that you have to work hard.
Emily's Quotes

Cascade use - Definitions

According to the articles 112 to 115 of the European regulation 2019/6

Use of VMP outside the terms of the marketing autorisation

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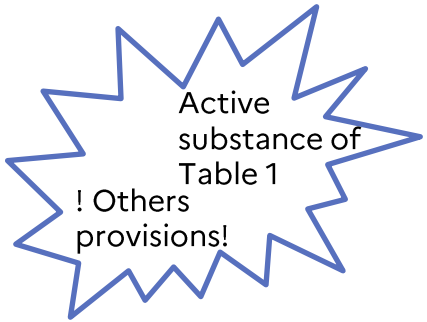


Only 120 herbal substances of the 300 plants commonly used in food-producing animals are included in Table 1 of Regulation UE 37/2010, half of which are reserved for homeopathic or topical use

Une substance « plante » est inscrite dans le tableau 2 (usage interdit)
Aristolochia spp. et l'ensemble de ses préparations

Aucune sur la liste « biological substances »

Les substances « plantes » inscrites sur la liste « out of scope » (usage autorisé) sont les suivantes
Amidon normalement trouvé dans l'alimentation et l'amidon de qualité alimentaire
Avena (oats)
Carboxyméthyle amidon sodique
Céréales
Coffea arabica
Huile d'olive
Huile de cacahouète = huile d'arachide
Huile de sésame
Huile de soja incluant huile de soja époxidée
Huile de graine de coton
Huile de mais = huile de blé
Huile de coco
Matériel fibreux d'origine végétale
Plantes légumineuses
Petroselium crispum
Soja (moulu & décortiqué)
Sciure de pin, pour abeille
Squalane, comme composant d'un adjuvant
Vanilline

Les substances « plantes » inscrites au tableau 1 (usage autorisé) sont présentées ci-dessous par ordre alphabétique.
Ces données sont extraites du tableau 1 publié dans le RÈGLEMENT (UE) N° 37/2010 DE LA COMMISSION du 22 décembre 2009 relatif aux substances pharmacologiquement actives et à leur classification en ce qui concerne les limites maximales de résidus dans les aliments d'origine animale.

N = 125
21 huiles essentielles
41 substances pour usage homéopathique
124 avec « aucune LMR requise » dont 1 avec une DJA
1 avec des LMR chiffrées

Angelica radix aetheroleum	Eucalypti aetheroleum
Anisi aetheroleum	Foeniculi aetheroleum
Carvi aetheroleum	Lauri folii aetheroleum
Caryophylli aetheroleum	Lavandulae aetheroleum Pour usage topique uniquement
Cinnamoni cassiae aetheroleum	Melissae aetheroleum
Cinnamoni ceylanici aetheroleum	Menthae arvensis aetheroleum
Citri aetheroleum	Menthae piperitae aetheroleum
Citronellae aetheroleum	Myristicae aetheroleum A n'utiliser que sur l'animal nouveau-né
Coriandri aetheroleum	Rosmarini aetheroleum
Cupressi aetheroleum Pour usage topique uniquement	Terebinthinae aetheroleum rectificatum Pour usage topique uniquement
	Thymi aetheroleum

MRL

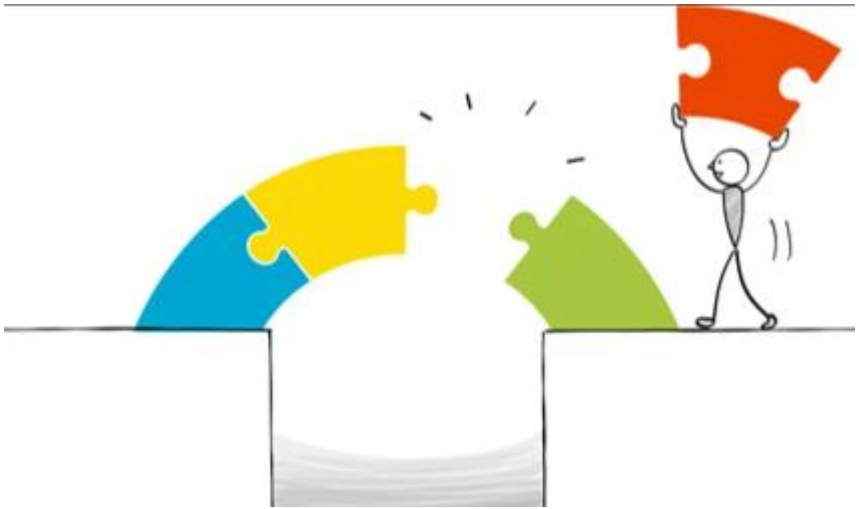
- The maximum allowed concentration of residue in a food product obtained from an animal that has received a veterinary medicine
- Defined for a given substance, species and tissue or commodity
- Aim to ensure a safe level of exposure for the consumer

European regulation on MRL			
Substances classification			
Out of scope	Biological substances	Table 1	Table 2
Not concerned by MRL = No risk	Not needing an assessment	Authorised +/- restrictions on use and/or species	Prohibited

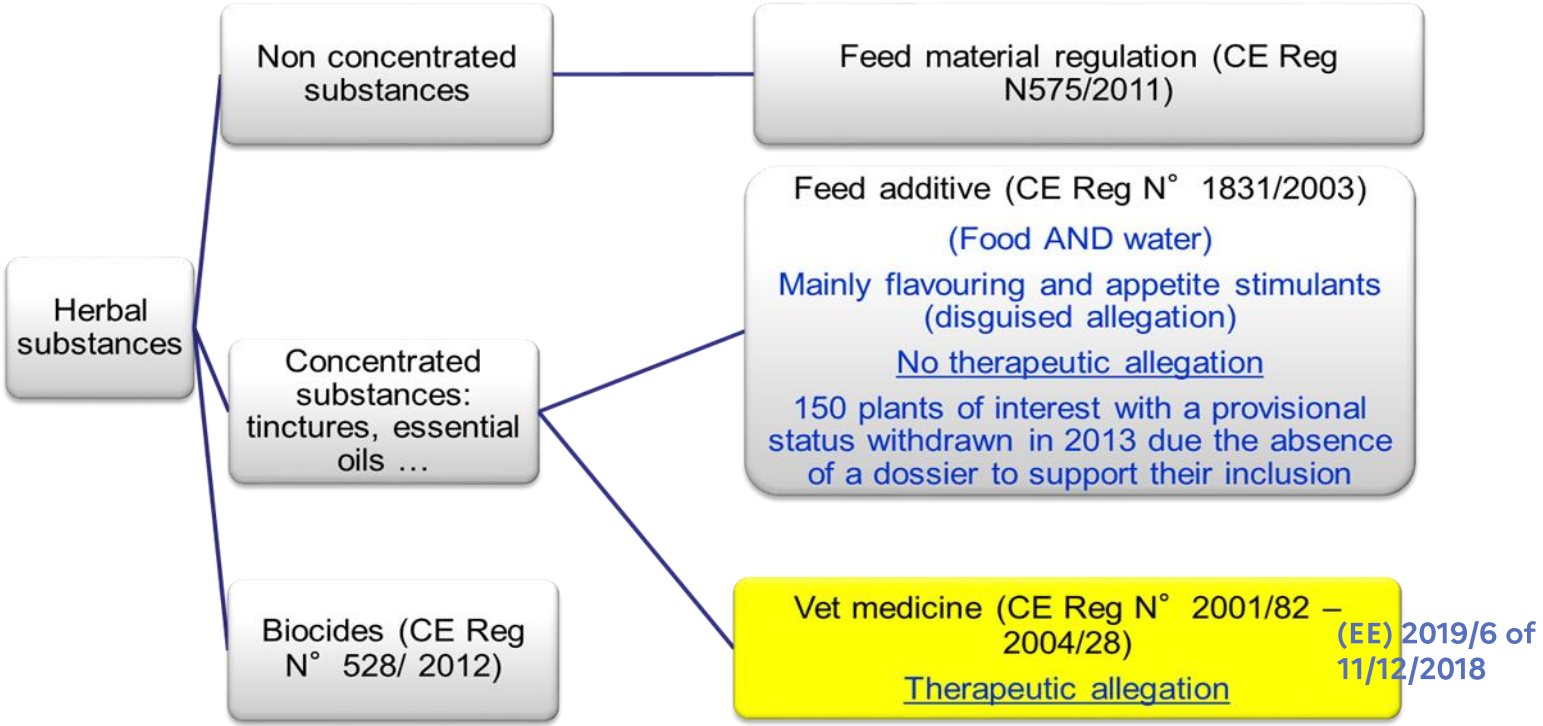
→Most EOs and plants currently used in VM
Not listed in Table 1 or in the out of scope and biological substances lists

Herbal specialities administered to food producing animals = complementary feedstuffs

Reason: MRL approach not adapted to the complex and variable composition of plants, plant preparation or EOs



Herbal substance regulatory status



Herbal products most frequently used

Essential oils

Plants

Complementary feed

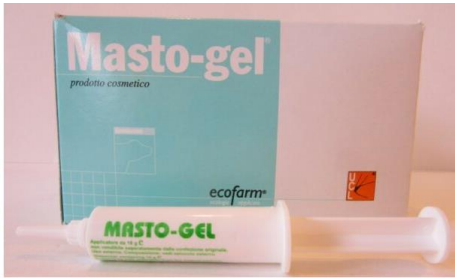
Hygiene products

Example of herbal products available on the veterinary market

COMPOSITION: Allium Sativum, Oregano Oil, Microcrystalline Cellulose, Salts of Fatty Acids, Gelatin.

Features of the Maycillin Bolus:

- Zero milk withdrawal
- No paperwork required
- Two boluses per cow
- Reduces SCC in cows
- No risk of contamination
- For subclinical & clinical mastitis
- Feed additive
- Bolus gun sold seperately



DESCRIPTION

Preparation for the care and prevention of udder in dairy cows.

Can be helpful with udder and teat health care and prevention

Properties

It prevents the teats from drying out by moisturizing and maintaining the proper pH of the skin
Possible effect on reducing the number of microorganisms on the teat surface
Strengthen the protective barrier of the teat canal by maintaining the integrity of the keratin litter
Protection of the udder gland from contamination

Additional description

Properly combined active extracts improve the functioning of the udder gland, deeply moisturize and soften it, maint
Both long-term and continuous use does not cause any skin irritation. In addition, the presence of natural factors witl
milking and the next thanks to the protective layer, protects the udder gland from contamination.

Description of ingredients: water extract of propolis, herbal extracts, urea

Composition
Vinaigre de cidre, Macérés de rose rouge (*rosa gallica*), de thym blanc (*thymus vulgare*), de verge d'or (*solidago virga aurea*), origan (*origanum vulgare*).

Composition
eucalyptol, cajeput EO, tea tree EO, nutmeg EO, cedar EO, camphor, menthol, laurel oil, colorant: chlorophylle

een one


NO
WAY!

5. CONCLUSION

Conclusion

- Herbal veterinary medicinal products are interesting alternatives to limit/reduce the use of antibiotics and the risk of antimicrobial resistance;

- Already widely used in France especially essential oils, by farmers on all target species and/or prescribed by vets on pets, at least in France and other EU MS and other countries,

- Used for treatment and/or prevention of disease, without MA, and MRL status in most of cases

Conclusion

- No guarantee about quality, safety **especially consumer safety and animal safety and efficacy**

- Some risks to use plants or derived plant products even if natural substances:

- ✓ Known toxicity: for example for several essential oils as Basil oil,
- ✓ Free access of the plant / essential oils on the field :
  - No guarantee of quality: no traceability, variability of the plants, …
  - No use of raw material for pharmaceutical use: well-controlled

Conclusion

- EC encourages the use of phytotherapy for organic production but in fact there is almost no products or substances assessed and authorized neither in the feed additive list nor in our veterinary market

- The status of this type of products should be considered in a number of cases as veterinary medicines

- Many of plants and preparations used as vet medicines have no MRL status and may represent a safety issue for the consumer. (Eg: basil essential oils)

→ There is a need to determine which plants and preparations can be used with no consumer safety risk → Need for MRL dossiers

Conclusion

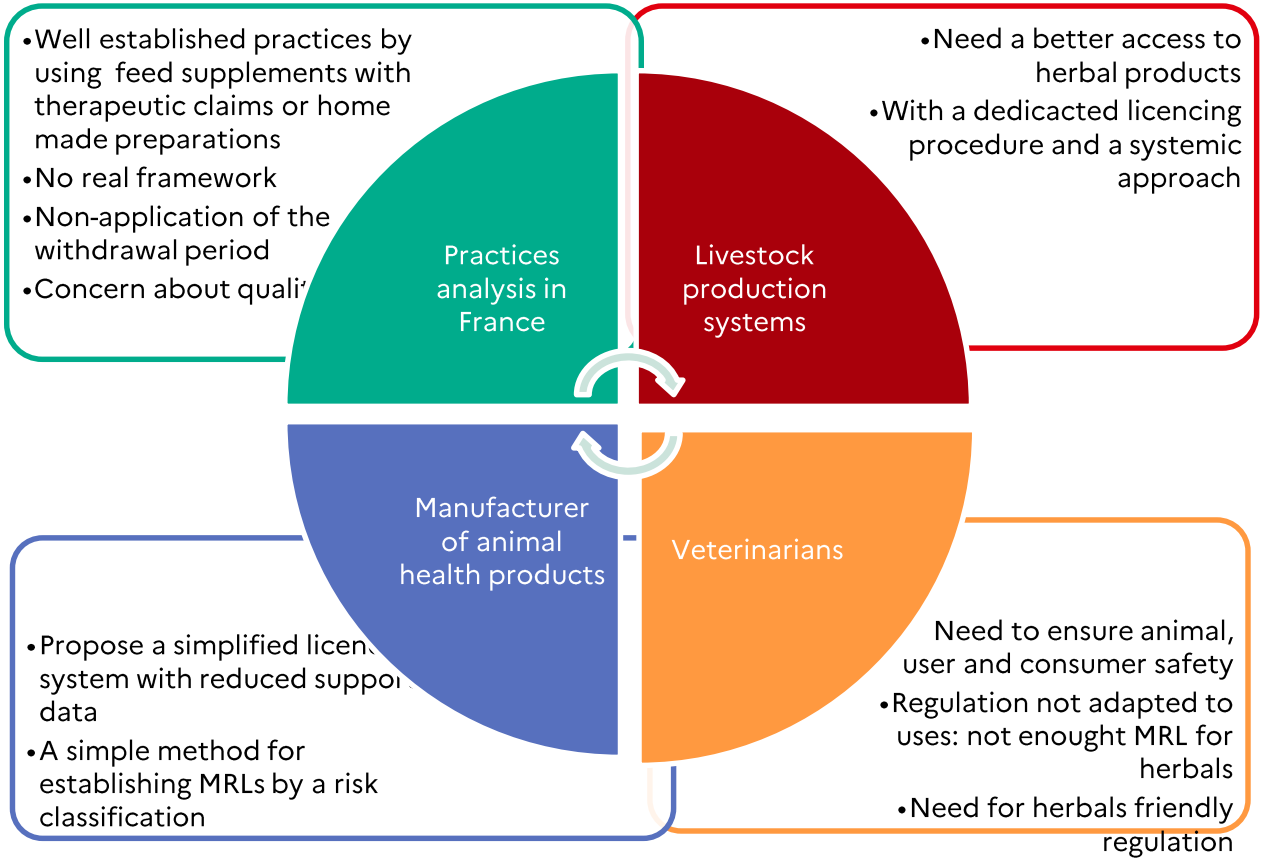
- To support this use, it is important to establish MRL status for numerous herbal substances

- The way to promote the MRL dossiers submission should always be discussed

- Always the need for an evolution of the european regulation on veterinary herbal medicines

- Furthermore, the quality of the herbal drugs and herbal preparations used on the field is also an other important point to monitor.

Needs and proposals



EU Regulation 2019/6… and now

Preamble 12:

There is **insufficient information** to date on traditional herbal products used to treat animals in order to allow the setting up of a **simplified system**. Therefore, the possibility of introducing such a simplified system should be examined by the Commission based on the information provided by the Member States on the use of such products on their territory.

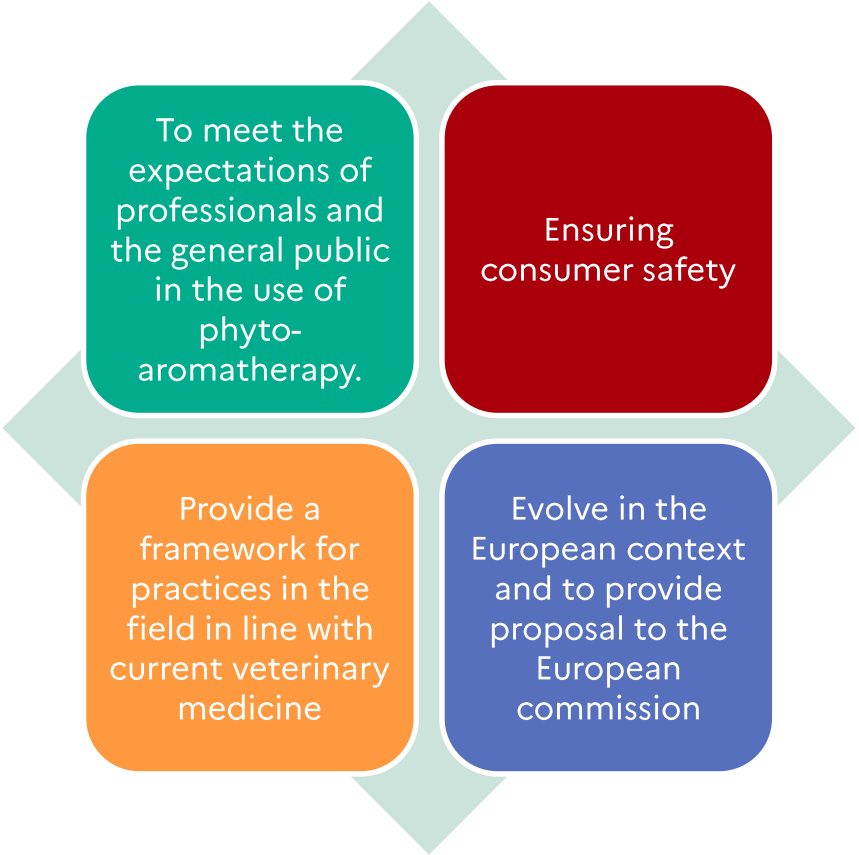
Article 157:

Commission report on traditional herbal products used to treat animals

The Commission shall report to the European Parliament and to the Council by **29 January 2027**, on traditional herbal products used to treat animals in the Union. If appropriate, the Commission shall make a legislative proposal in order to introduce a **simplified system for registering traditional herbal products used to treat animals**.

The Member States shall provide information to the Commission on such traditional herbal products within their territories.

As objectives



Thank you for your attention

MedPlants 4Vet

cost EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

Funded by the European Union

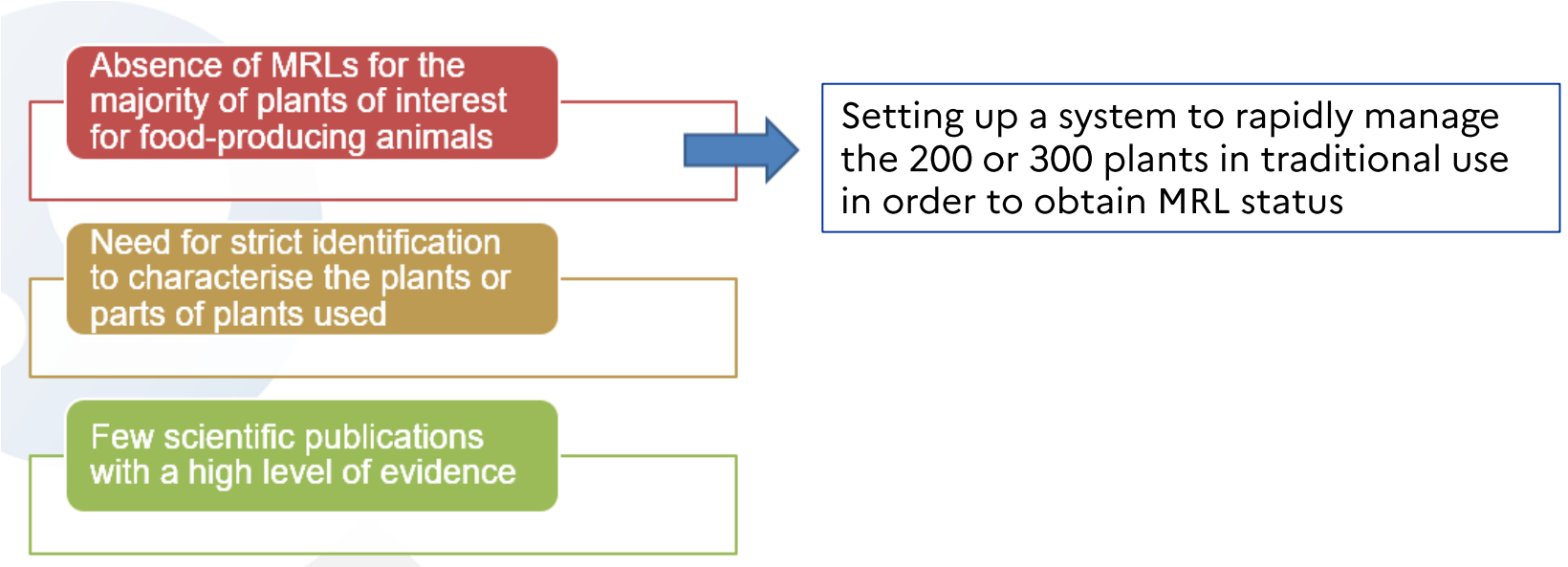
Promote the submission of MA applications for HVMP

Proposed amendments

Quality section	Safety section	Efficacy section
• Possible choice of a tracer substance to ensure the quality and concentration range present in the plant drug and in the finished product. • Possibility to provide a Pharmacopoeia certificate (as for chemical drug).	• Toxicological profile: possible reference to literature, in case of old or traditional use (except for genotoxicity: at least 1 in vitro test) • User safety minimum requirements with focus on exposure • Tolerance: a study with finished product and if necessary restriction(s)	• Possible reference to literature, for pharmacodynamic and pharmacokinetic effects (unless no data in any species or model) • Clinical trials not required if well established use demonstrated

Promote the submission of MA applications for HVMP

Major concerns



Human side

Two possibilities in Europe for herbal medicines:

- A simple registration if the herbal drug or the herbal preparation justifies a traditional use for 30 years of which at least 15 years in the European Community, proving its safety and making its efficacy plausible (European Directive 2004/24/EC);

- A marketing autorisation if the herbal drug or herbal preparation justifies of a well-established use of 10 years in the European Community (European Directive 2001/83/EC);

Legislation of herbal medicines

Human side

A Committee on Herbal Medicinal Products (HMPC) establishing EU standards to help the submission of dossiers:

Establishing EU monographs covering the therapeutic uses and safe conditions of well-established and/or traditional use for herbal substances and preparations :

European Union herbal monograph on Valeriana officinalis L., aetheroleum

Drafting a EU list of herbal substances, preparations and combinations for use in traditional herbal medicinal products;

Establishing scientific guidelines on herbal medicinal products on quality, safety, and efficacy