anses
French agency for food, environmental and occupational health safety

Investigate, evaluate, protect

Example of existing guidance on autogenous vaccines France - legal framework & EU perspectives

Kuala Lumpur, 14-16 January 2020

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Introduction

Place of autogenous vaccines

Alternative medecine to be used in particular and justified circumstances

. new disease

. Absence of authorised vaccines (minor species)

. Alternative to antibiotics

…

Definition of Autogenous vaccines in EU

- Reg 2019/6 – New vet regulation - art 2 (3) :

… **inactivated immunological** veterinary medicinal products which are manufactured from **pathogens and antigens obtained from an animal** or animals in an epidemiological unit and used **for the treatment of that animal** or those animals in the same epidemiological unit or for the treatment of an animal or animals in a unit **having a confirmed epidemiological link.**

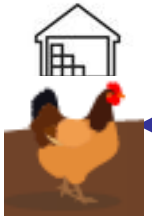
Consequence : harmonised european regulation

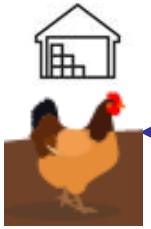
Enter into application 28th January 2022

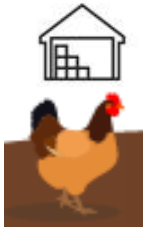
Definition of Autogenous vaccines in EU

Production

Epidemiological link







Other definition – CMDv recommendations

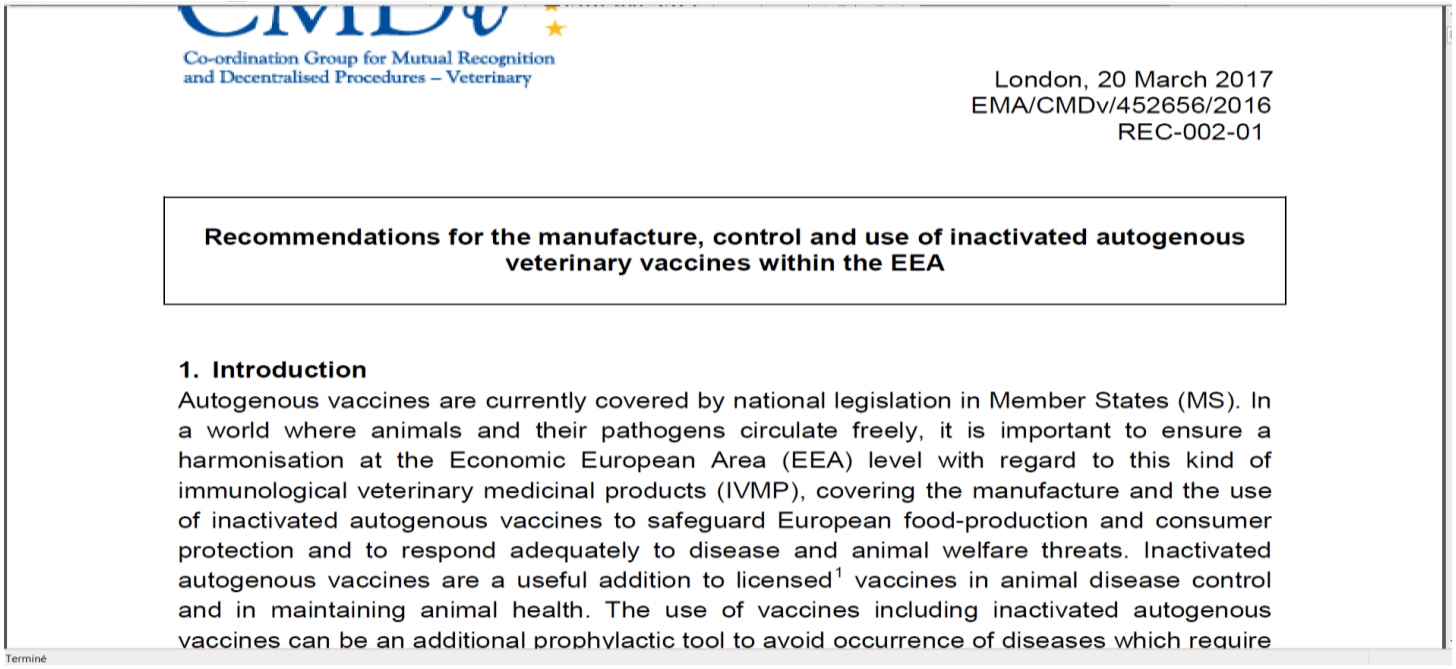
Definition

To fit with current practices and integrated concepts of breeding/rearing/production :

- Same locality : same and single rearing site / same farm where the pathogen is present or multiple rearing site/farm having an epidemiological link
- Epidemiological link : groups of animals having a link when one of them is to be put in contact with pathogens never met before but present in the other group of animals raised in another rearing site/farm. The movement of animals between, rearing sites/farms should be considered when establishing the epidemiological link

EU framework

- CMDv working group: adopted recommendations
  - http://www.hma.eu/fileadmin/dateien/Veterinary_medicines/CMDv_Website/Procedural_guidance/Miscellaneous/270317_Aut_vacc_recommendations.pdf



Co-ordination Group for Mutual Recognition and Decentralised Procedures – Veterinary

London, 20 March 2017
EMA/CMDv/452656/2016
REC-002-01

Recommendations for the manufacture, control and use of inactivated autogenous veterinary vaccines within the EEA

1. Introduction

Autogenous vaccines are currently covered by national legislation in Member States (MS). In a world where animals and their pathogens circulate freely, it is important to ensure a harmonisation at the Economic European Area (EEA) level with regard to this kind of immunological veterinary medicinal products (IVMP), covering the manufacture and the use of inactivated autogenous vaccines to safeguard European food-production and consumer protection and to respond adequately to disease and animal welfare threats. Inactivated autogenous vaccines are a useful addition to licensed[1] vaccines in animal disease control and in maintaining animal health. The use of vaccines including inactivated autogenous vaccines can be an additional prophylactic tool to avoid occurrence of diseases which require

Terminé

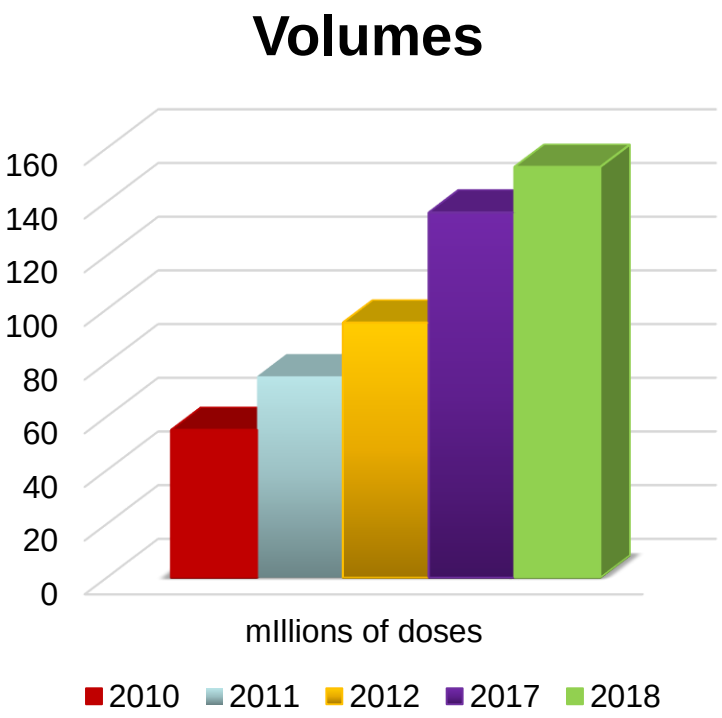
FR Legal framework

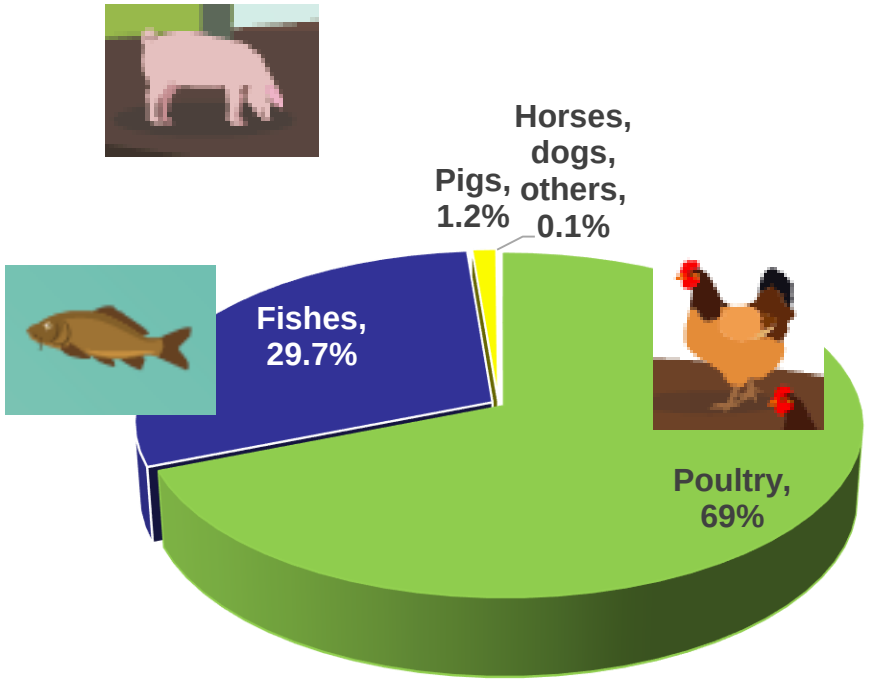
- Extemporaneous products = do not require a marketing autorisation
- Extemporaneous preparation after prescription of 1 veterinarian from a pathogen isolated from 1 breeding farm/locality and destinated to be administered in the same farm/locality.
- Limited to products prepared from inactivated bacteria,
- For viral antigen, high risk of contamination purification in compliance with Ph Eur

FR Legal framework

Current market

3 authorised sites





Autogenous Vaccines / Authorised Vacccines

Authorised vaccines

Full application

- Master seed :
  - (bacteria, viruses, activated or inactivated)
- *Quality :*
  - *control, batch release*
- *Safety :*
  - Analytical test
  - Extraneous agents
- *Efficacy :*
  - Field trial to attest efficacy, immunological

Post AMM

- Pharmacovigilance
- GMP certificate

Autogenous vaccines

No full dossier

- Inactivated
- Bacteria
- No test on quality
- No test on efficacy

Surveillance and control

- Pharmacovigilance
- GMP certificate

FR Legal framework- Manufacturing licence

Manufacturing Licence– « obligation of means and no obligation of results »

Location

licence is granted for 1 preparation site (establishment)

Technical dossier and inspection of the site

A qualified person

Preparation must be performed by a qualified person (veterinarian or pharmacist) mentioned in the authorisation

Positive list of bacteria and animal species

Listed in the appendix of the licence

Positive list of adjuvants

In compliance with MRL regulation

Qualified person

The authorisation is for 1 person in link with 1 preparation site

Qualified person : responsible for conformity of the autogenous vaccine with general regulation – autogenous vaccines, TSE, MRL, European Pharmacopoeia, pharmacovigilance, …

TO BE NOTED

The veterinary surgeon writer of the prescription is responsible for the delivery and administration of the products to animals

Pathogens and adjuvants

Pathogens/target species – examples

Dogs
Mycoplasma spp
Staphylococcus spp
…

Sea-bass
Listeria monocytogenes
Vibrio anguillarum (excepted serotypes 1 and 2)
…

Chickens – layers / reproduction
Bordetella spp
Haemophilus spp apart from *H. paragallinarum* A, B,C
Escherichia coli excepted antigens F11 and FT
Escherichia coli aerobactin positive O1, O2 and 078 spp (even if containing antigens F11 and FT)
…

Adjuvants used : Alumine, complex adjuvants, aqueous or oil

Pathogens and adjuvants

Pathogens/target species

→ Only **bacterial** autogenous vaccines
→ Only **inactivated** products
→ Only when vaccines with MA do not exist
→ Special restrictions for ruminants (TSE)

Ruminants

Considering risk management for TSE, preparation of autogenous vaccines for ruminants was forbidden until 12/2017.

Now

Authorised for bovines, ovines & caprines with special restrictions (matrices, passages of the isolate…)

Adjuvants

→ MRL regulation

Authorisation for preparation

- Anses-ANMV competent authority for delivering authorisation for preparation of autogenous vaccines
- Use is considered when :
  - no adequate authorised vaccines (with marketing autorisation) is available :
    - Shortages of authorised vaccines
    - Vaccines non suitable with regard to the need on the field
  - authorised vaccines have not provided adequate protection → Pharmacovigilance notification of lack of efficacy

Authorisation for preparation

Application

- Data on process of preparation
  - Isolation of pathogen, purification, raw material, control of extraneous agents
  - Process of inactivation
  - Batch release control, packaging and labelling
- No data required on safety and efficacy but requirement on Pharmacovigilance
- Veterinarian prescription : use restricted… to the same farm/locality

Inspection

Every 3 years by an inspector of ANSES-ANMV to verify the compliance with the specific GMP.

Autorisation for preparation

Rules

- Autorisation for preparation of autogenous products is granted by Anses-ANMV for 5 years and can be renewed (a new application has then to be submitted)
- Any change has to be declared (prior) [evolution in the production methods / changes of the annexes : new adjuvants – pathogens/species]
- Update of the positive list by Anses-ANMV in case a new vaccine with a MA becomes available (automatically)
- in case a MA becomes invalid (if a request for a new pathogen/species is proposed by the preparer)

Isolation of the pathogen agents

Requirements for isolation of the antigen :

- Importance of the diagnosis
- In the locality
- Collection by the vet
- No GMO or notifiable disease
- Importance of traceability
- Isolation and identification by a competent authorised site

Manufacturing site - Important requirement

– Requirements for manufacture and formulation :
  - Production : GMP compliance, Validation of critical operations like inactivation

– Requirements for controls :
  - Sterility
  - Complete inactivation
  - Endotoxin (bacterial)
  - Absence of extraneous agents (viral)

– Requirements for stability :
  - 6-12 months

– Requirements for labelling

Pharmacovigilance

- Qualified person : designation, qualification, attribution, duties & responsabilities : same requirements as for VMP with MA

- System : as for VMP with MA

Rapid notification (human cases, serious animal cases) within 15 days / annual report (all pharmacovigilance data, sales volumes, nb of treated animals, incidence, benefit/risk balance analysis)

Obligation for the vet

- Make the initial diagnosis and order the prescription
- Responsible for the administration
- Should report quality defects and suspected adverse reactions

Risks identified with regard to the use of autogenous vaccines

For livestock animals,

- risk of transmission of disease if inactivation not validated
- risk inherent in the use of adjuvants : local and/or general reactions →Choosing of adjuvants suitable for the target species
- risk of infection can result from the contamination of raw materials, specifically samples taken at the farm, or of the autogenous vaccine when it is being prepared.

For the user : risk is negligible, limited to accidental injection (importance of the adjuvant)

For the consumer : no risk, only adjuvants with MRL

CONCLUSION

- Autogenous vaccines are useful VMPs but less secure than an authorised vaccines with full dosssier
- Authorised vaccines shall be used as 1st choice
- Only Restricted Use for autogenous vaccines : adminstration to the animal of the same location or with epidemiological link
- Only inactivated vaccines
- Only bacteria
- Licence for manufacturing
- GMP compliance

Thank you for your attention