

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

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Introduction

Place of autogenous vaccines



Alternative medicine 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

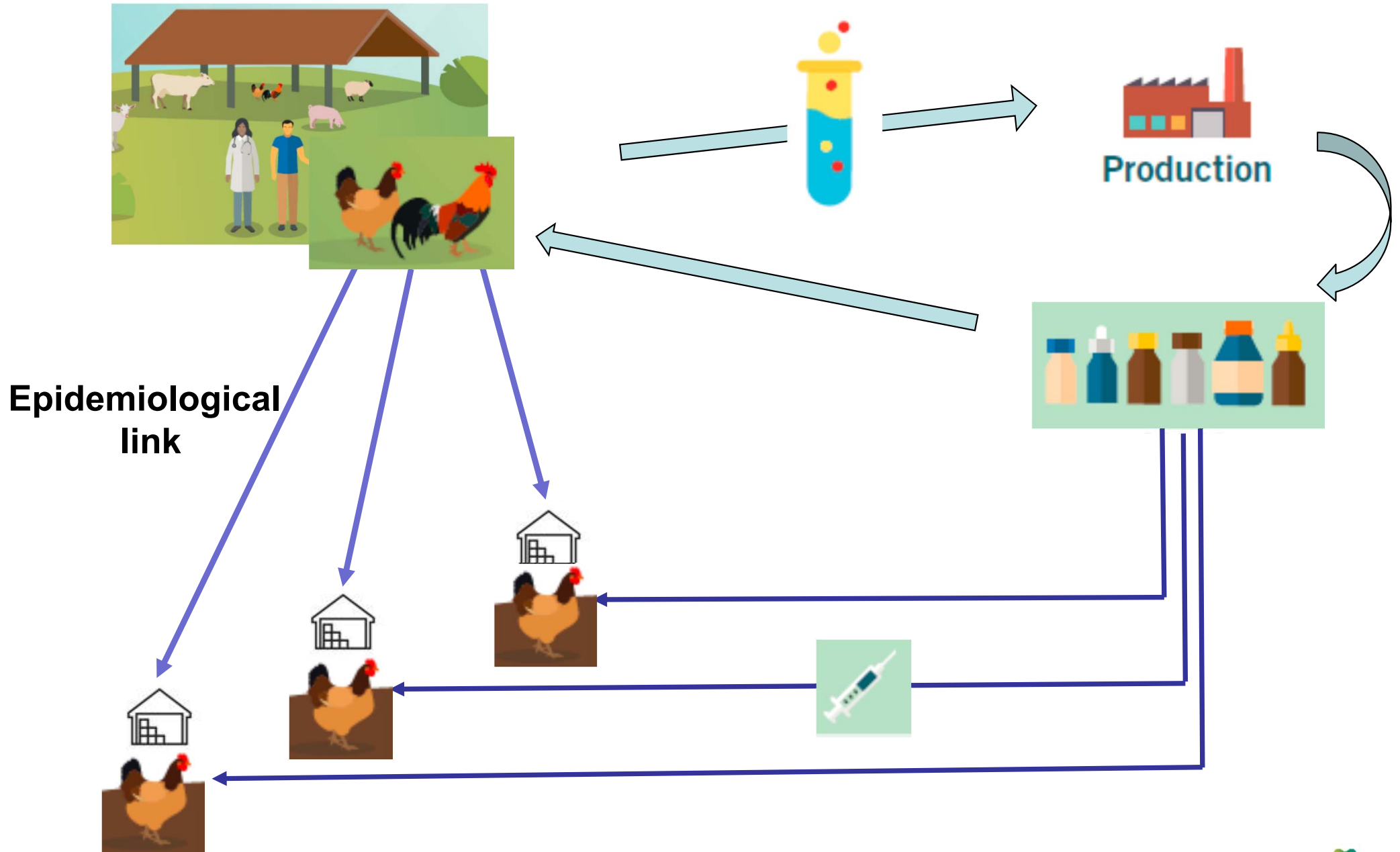
- **Reg 2019/6 – New vet regulation** - art 2 (3) :
... **inactivated immunological** veterinary medicinal products which are manufactured from **pathogens and antigens obtained from an animal** or animals in an epidemiological unit and used **for the treatment of that animal** or those animals in the 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



EU New Regulation

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

FR Legal framework

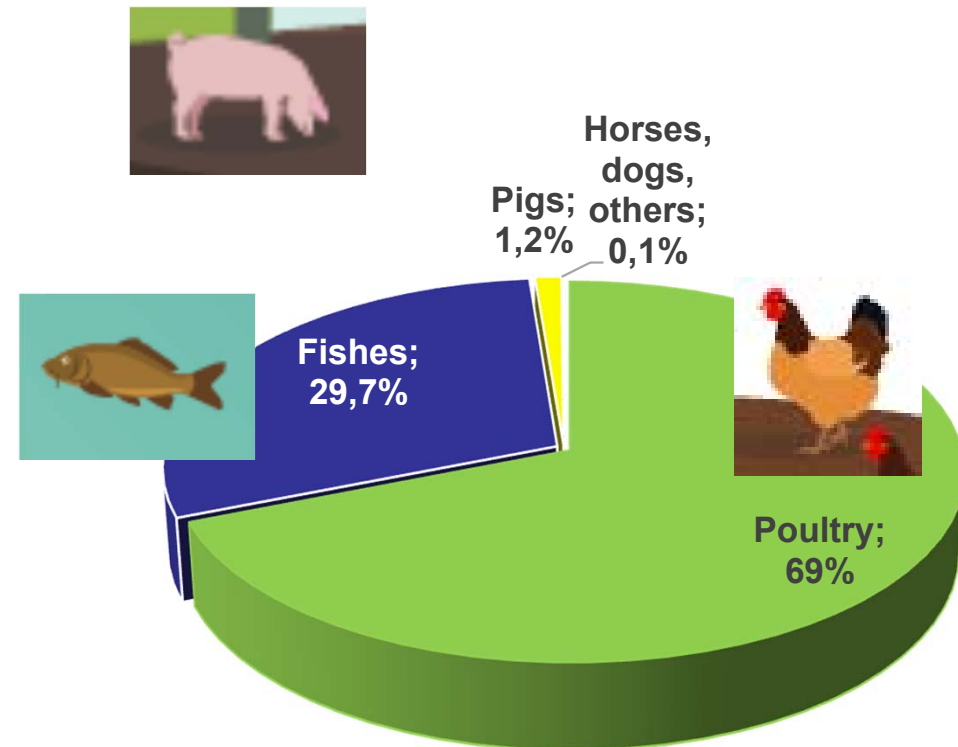
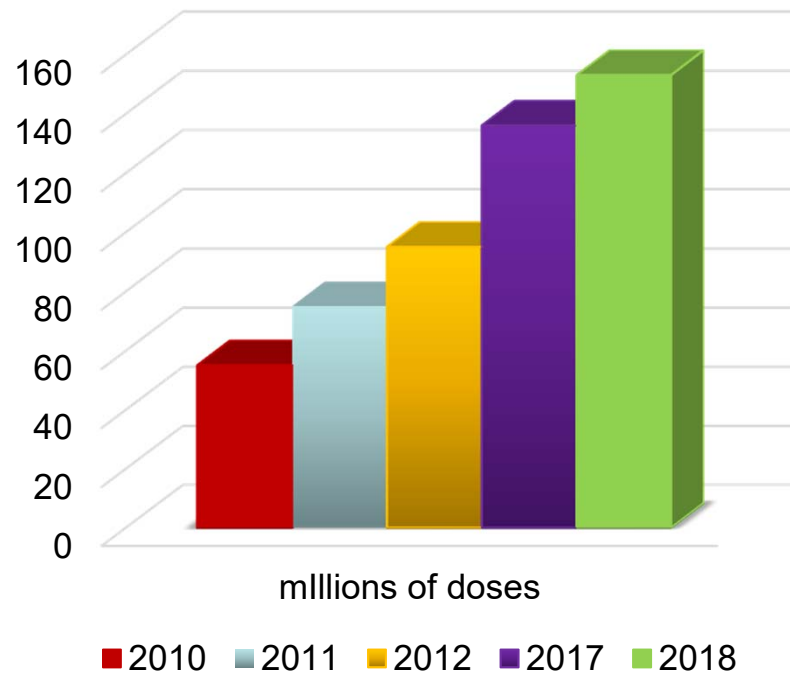
- Extemporaneous products = do not require a marketing autorisation
- Extemporaneous preparation after prescription of 1 veterinarian from a pathogen **isolated from 1 breeding farm/locality** and destined to be administered **in the same farm/locality**.
- Limited to products prepared from **inactivated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

FR Legal framework

Current market

3 authorised sites

Volumes



FR Legal framework

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 O78 spp (even if containing antigens F11 and FT)

...

Adjuvants used : Alumine, complex adjuvants, aqueous or oil

Autogenous Vaccines / Authorised Vaccines

Authorised vaccines

Full application

- Master seed :
 - (bacteria, viruses, activated or inactivated)
- *Quality*
- *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

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

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**

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

Manufacturing site - GMP

Good Preparation Practices

Ministerial order – based on GMP and takes into account GLP – document from 06/03/2008

- Ensure safety of the product (quality), avoid contamination, guarantee consistency & traceability
- Validation of critical operations **like inactivation**
- Takes into account specificity of these products : few pathogens handling, small batch sizes production & campaign basis...

Inspection

Every 3 years by an inspector of ANSES-ANMV to verify the compliance with the dossier and with the specific Good preparation practices

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

Manufacturing site - 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

Manufacturing licence

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)

Pharmacovigilance

- **Qualified person** : designation, qualification, attribution, duties & responsibilities : 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)

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

Obligation for the vet

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

CONCLUSION

- Autogenous vaccines are useful VMPs but less secure than an authorised vaccines with full dossier
- Authorised vaccines shall be used as 1st choice
- Only Restricted Use for autogenous vaccines : administration 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

