CODA - CERVA

Approaches for quality control testing of LSD vaccines

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EURL for diseases caused by Capripox viruses

CVMP and IWP Focus Group on Lumpy skin disease vaccines

European Medicines Agency, London, January 31, 2017

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LSD: Vaccination in Europe

Directive 92/119/EEC – art 19 :

However, by way of derogation the decision to introduce **emergency vaccination** may be taken by the **Member State** concerned following notification of the Commission, provided that the fundamental interests of the Community are not affected.

DIRECTIVE 2001/82/EC – art 8:

In the event of serious disease epidemic, **Member States** may **provisionally** allow the use of immunological veterinary medicinal products **without an authorization** for placing on the market, in the absence of a suitable medicinal product and after informing the Commission of the detailed conditions of use.

Decision to use LSD vaccine: Member State – CVO

LSD: Vaccination in Europe

Currently

-Infected countries have been able to limit the spread or eradicate LSD with vaccination

-Only live attenuated LSD vaccines are available

-Live attenuated vaccines provide good protection in case a homologous vaccine is used in combination with sufficient vaccination coverage (>80% needed) and a (re)vaccination policy of young animals and imported animals.

-None of the vaccines used in Europe has a marketing authorisation within the European Union or other European countries

-None of these vaccines is produced under GMP conditions

-None of these vaccines is produced with a QC system as described in the European Pharmacopoeia

LSD Vaccine QC needed?

LSD Vaccine: How much quality information or guarantees do you have now? -> Trust on Vaccine Manufacturer Information:

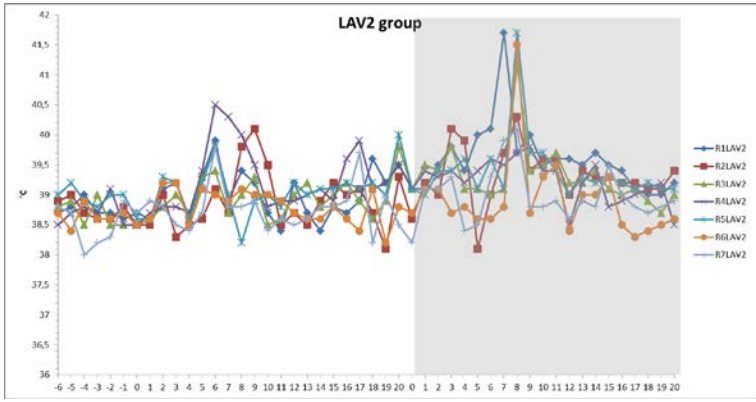
Dossier: License / Registration
Marketing Authorisation
Quality Control

LSD Vaccine: Registration Dossier available outside Europe?

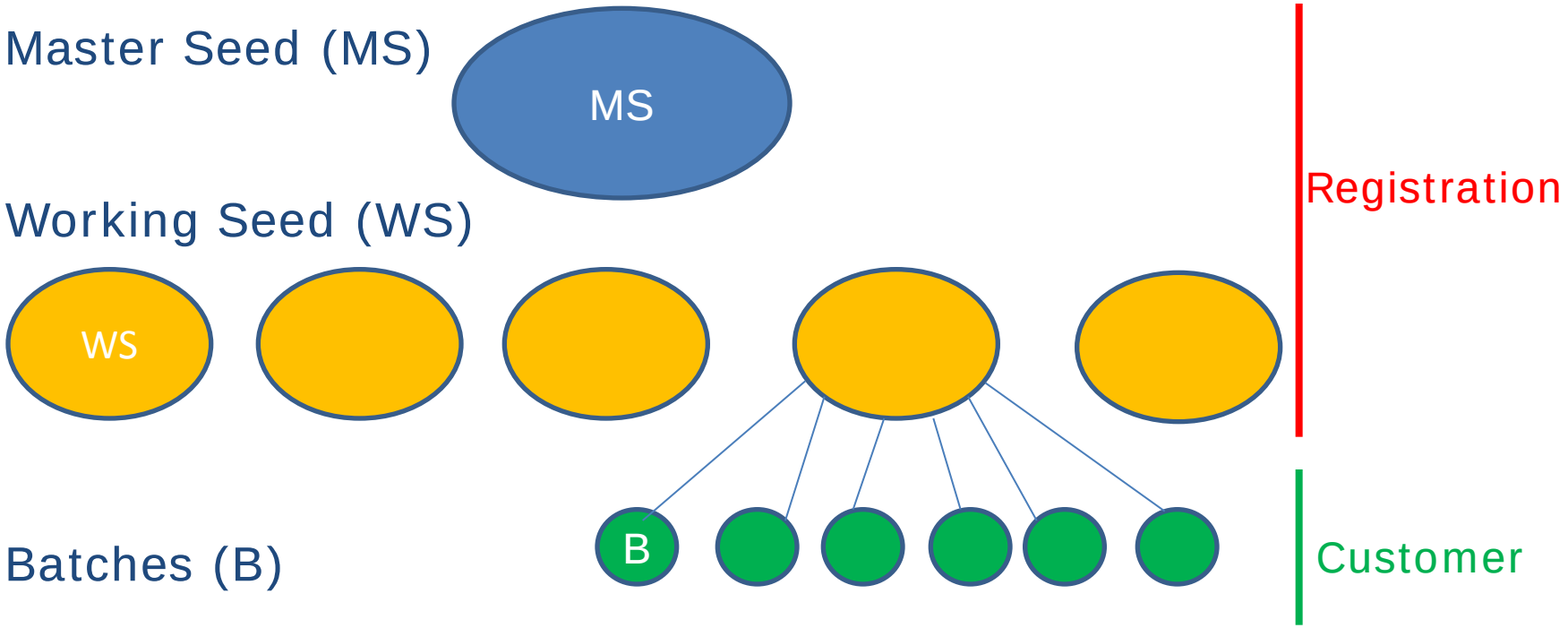
Tender for vaccine Purchase (EC/Country):
Quality criteria - Check criteria fulfilled? --> Needed?

Field information on secondary effects after vaccine campaigns:

- 'Neethling disease': <1% - 10%
- Milkdrop 6-9 dpv correlated with fever
- Detection and isolation of Bluetongue virus from commercial vaccine batches (Bumbarov et al., 2016)



Independent LSD Vaccine QC



1. Master and Working Seed Lot

1.1. Description of the production

- Identity of the vaccine strain

  Confusing Kenyavac from JOVAC: Kenyan SGPV O-240 and 180 strains despite the name the strain is LSDV (Tuppurainen et al., 2014; Vandenbussche et al., 2016)

- Substrates for seed culture preparation and for production
  - Sera, media, primary cells, cell cultures
  - Freedom from extraneous agents

1. Master and Working Seed Lot

1.2. Freedom from extraneous agents

-Evidence of absence of bacterial, fungal or mycoplasmal contaminants

-Evidence of absence of viral contaminants

e.g. BTV, EHDV, BVD, BDV, SPPX, GTPX, Lentiviruses (Maedi-visna virus, Bovine leucosis virus)

1. Master and Working Seed Lot

1.3. Evaluation of safety

-Laboratory studies using MS or WS of maximum titre

-Administration of one dose: ≥ eight animals per group

-One administration of an overdose: 10 doses, 8 young animals

-Reproductive Performance: use in pregnant animals

-Dissemination of vaccine strain in vaccinated animals

-Increase in virulence – Reversion to virulence – Spread of the vaccine strain

-Residues

-Abnormal toxicity

-Laboratory rodents

-Field study

1. Master and Working Seed Lot

1.4. Evaluation of efficacy

-Laboratory studies using WS of minimum titre expected at the end of the period of validity

-Efficacy tests are carried out in the target species to show at least efficacy in protection against LSD upon viral challenge: ≥ 12 animals

-Additional evidence must support all the claims being made, e.g.

-onset and duration of immunity

-onset and duration of protection

-influence of passively acquired immunity

1. Master and Working Seed Lot

1.5. Stability

-Period of validity (shelf-life): periodical re-titration

1.6. Pharmacovigilance

-Continuous monitoring of LSD vaccines used in the field

2. Batch controls

2.1. Description of the production

- Identity of the vaccine strain
- Substrates for batch preparation

2.2. Freedom from extraneous agents

- Evidence of absence of bacterial, fungal or mycoplasmal contaminants
- Evidence of absence of viral contaminants

2. Batch controls

2.3. Safety

- For each batch at least one
  - 'Administration of an overdose'
  - Abnormal toxicity in laboratory rodents

2.4. Efficacy

- Potency test
- Ascertain that virus titre per vaccine dose of the vaccine batch under control is higher than the minimum protective dose (virus titration)

2. Batch controls

2.5. Stability

-Period of validity (shelf-life): periodical re-titration

2.6. Pharmacovigilance

-Continuous monitoring of LSD vaccines used in the field

References

-European Pharmacopeia 04/2013:0062 Vaccines for Veterinary Use
-European Pharmacopeia 04/2013:50206 Evaluation of safety of veterinary vaccines and immunosera
-European Pharmacopeia 04/2008:50207 Evaluation of efficacy of veterinary vaccines and immunosera
-European Pharmacopeia 01/2008:50107 Viral safety
-European Pharmacopeia 01/2008:20609 Abnormal toxicity
-European Pharmacopeia 04/2011:20601 Sterility
-European Pharmacopeia 01/2016:50204 Cell cultures for the production of veterinary vaccines
-European Pharmacopeia 07/2009:50205 Substances of animal origin for the production of veterinary vaccines

-OIE Chapter 1.1.8 Principles of veterinary vaccine production. Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2016.
-OIE Chapter 1.1.9 Tests of biological materials for sterility and freedom from contamination. Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2016.
-OIE Chapter 2.4.13 Lumpy Skin disease (Version adopted in May 2016).Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2016.