Standing Group of Experts on Lumpy Skin Disease in Europe under the GF-TADs umbrella

Third meeting (LSD3)
Istanbul, Turkey, 12-13 December 2016

LSD: Vaccine Quality

LSD Experts: Dr Kris De Clercq and Dr Annebel De Vleeschauwer
EU Ref Lab Capripox viruses
LSD Vaccine Quality
General Notes (Pro)

- Currently infected countries have been able to limit the spread or eradicate LSD with vaccination!

- Only live attenuated LSD vaccines are currently 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 currently 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: Vaccination

An emergency vaccination in accordance with Article 19 of Directive 92/119/EEC may therefore only be carried out in accordance with Article 8 of Directive 2001/82/EC of the European Parliament and of the Council, which permits Member States to provisionally allow the use of immunological veterinary medicinal products without a marketing authorisation in the event of a serious epizootic disease.

Decision to use LSD vaccine: Member State – CVO
LSD Vaccine Quality

Decision to use LSD vaccine: Member State – CVO

Who is responsible for the Quality and Quality Control (QC) of the LSD vaccines used?
Vaccines In Europe
Who is responsible for the Quality and Quality Control (QC) of the vaccines?

EMA - European Medicines Agency
Committee for Medicinal Products for Veterinary Use (CVMP)

EDQM - European Directorate for the Quality of Medicines
The European Pharmacopoeia (Ph. Eur.)
Vaccines In Europe
Who is responsible for the Quality and Quality Control (QC) of the vaccines?

Member States
Belgium: Federal Agency for Medicines and Health Products

OIE: Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
LSD Vaccines In Europe
Who is responsible for the Quality and Quality Control (QC) of the vaccines?

In case of LSD vaccines

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LSD Vaccine Quality Information

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?
LSD Vaccine Quality Control Needed?

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

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 Quality Control

How?

- 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

LSD Vaccine Quality Control

Production:
- Pilot batches: development, evaluation, improvements
- Master Seed (MS)
- Working Seeds (WS)
- Vaccine Batches

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Independent LSD Vaccine Quality Control

1. Master Seed Lot and Working Seed Lot

1.1. Description of the production

1.1.1. Identity of the vaccine strain

Confusing Kenyavac from JOVAC: Kenyan SGPV 0-240 and 180 strains despite the name the strain is LSDV (Tuppurainen et al., 2014; Vandenbussche et al., 2016)

1.1.2. Substrates for seed culture preparation and for production

- sera, media, primary cells, cell cultures
- freedom from extraneous agents
1. Master Seed Lot 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)
Independent LSD Vaccine Quality Control

1. Master Seed Lot and Working Seed Lot

1.3. Evaluation of safety

1.3.1 Laboratory studies using Master of Working seed lot of maximum titre

- Administration of one dose: at least 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
Independent LSD Vaccine Quality Control

1. Master Seed Lot and Working Seed Lot

1.4. Evaluation of **efficacy** using Working seed lot 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: a least 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
Independent LSD Vaccine Quality Control

1. Master Seed Lot 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

2.1.1. Identity of the vaccine strain

2.1.2. 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
Independent LSD Vaccine Quality Control

2. Batch controls

2.3. Safety

- For each batch at least one ‘Administration of an overdose’
- For each batch at least one Abnormal Toxicity test in mice

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)
Independent LSD Vaccine Quality Control

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
LSD Vaccine Quality

Thank you

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