



# GF-TADs

GLOBAL FRAMEWORK FOR THE  
PROGRESSIVE CONTROL OF  
TRANSBOUNDARY ANIMAL DISEASES



**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**



**CODA - CERVA**

# 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.



# LSD Vaccine Quality

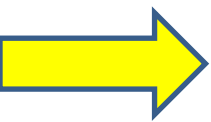
## General Notes (Con)

- ▶ 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.

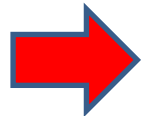


Decision to use LSD vaccine: Member State – CVO



# 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

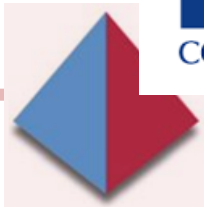
## Who is responsible for the Quality and Quality Control (QC) of the vaccines?

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.)



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# Vaccines In Europe

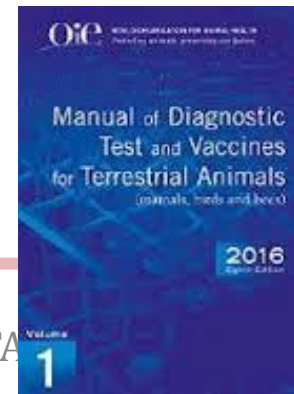
## Who is responsible for the Quality and Quality Control (QC) of the vaccines?

### Member States

Belgium: Federal Agency for Medicines and Health Products



OIE: Manual of Diagnostic Tests and Vaccines for Terrestrial Animals



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# 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?

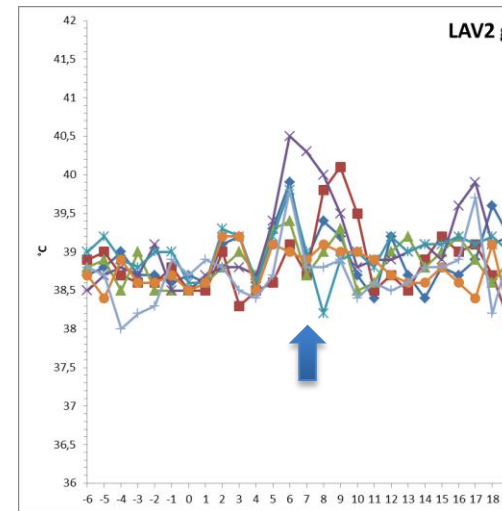
Trust on Vaccine Manufacturer Information:

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

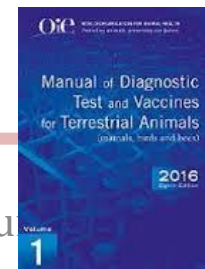
(Bumbarov et al., 2016)



# 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
- 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



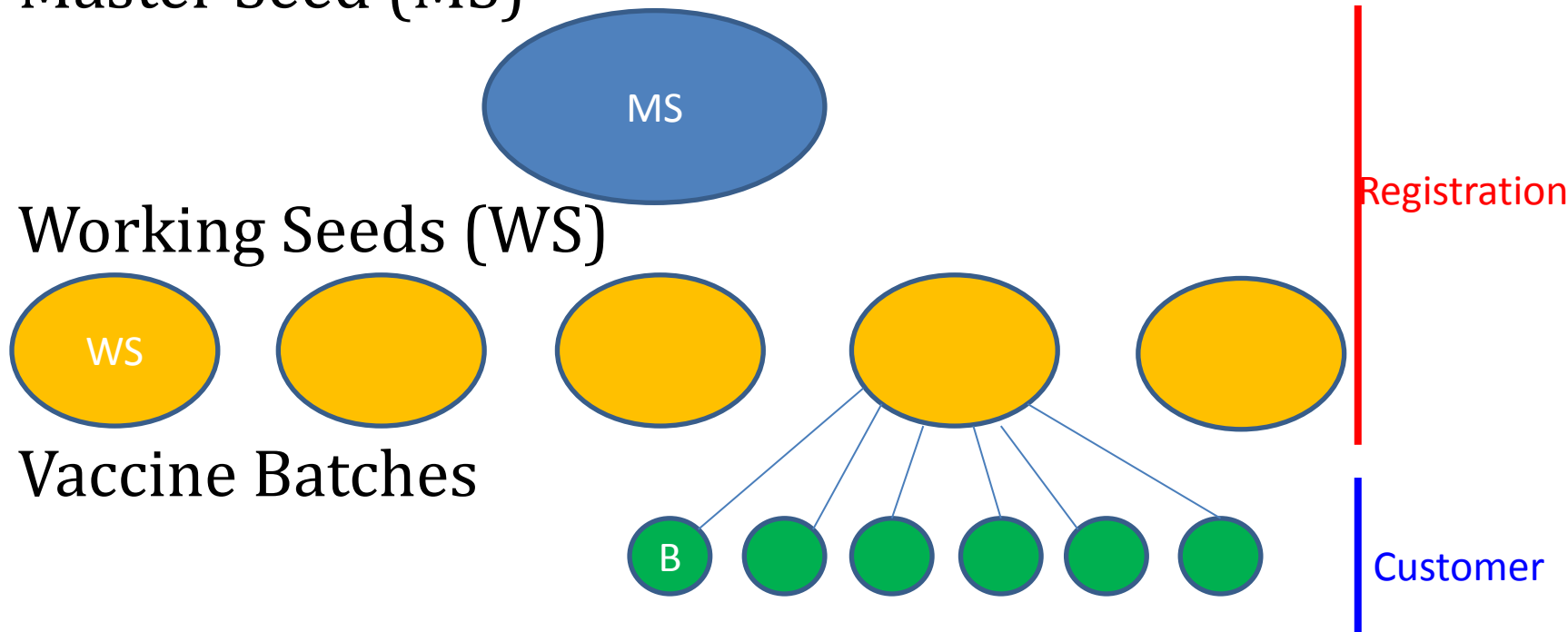
# LSD Vaccine Quality Control

Production:

- Pilot batches: development, evaluation, improvements
- Master Seed (MS)

- Working Seeds (WS)

- Vaccine Batches



# 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 O-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



# Independent LSD Vaccine Quality Control

## 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



# Independent LSD Vaccine Quality Control

## 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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