

# RECOMMENDATIONS FOR LSDV VACCINES FROM SAFETY AND EFFICACY STUDIES

Nick De Regge

Online meeting - WOAHA central Asia

13 December 2023

# LSDV vaccine quality control

- Chapter 3.4.12: Lumpy skin disease – part C: requirements for vaccines

Post market studies

Vaccine development/  
manufacturing

Quality assurance (GLP – GMP)

- master seed virus
- working seed virus
- master cell stock

Outline of production


- identity of vaccine (species – strain)
- purity: sterility/absence of contaminants (viruses, bacteria, fungi, mycoplasma, ...)

Safety testing

- One dose/repeat dose test
  - local reactions at inoculation site
  - fever
  - effect on milk production
  - Neethling response
- Breed/age effect
- Overdose test
- Non-reversion to virulence
- Environmental risks
  - Vaccine viremia
  - Vaccine spread
  - Environmental persistence
- Effect in pregnant cattle

Efficacy testing

- protect against clinical symptoms
- induce strong immune responses (humoral/cellular)
- protect against viremia
- protect against excretion
- absence of virus in organs/skin

In vitro batch  
quality control 

- identity of vaccine (species – strain)
- purity: sterility/absence of contaminants (viruses, bacteria, fungi, mycoplasma, ...)
- potency/dose

# LSDV vaccine safety/efficacy testing @sciensano

Challenge model in BSL3 animal facilities:



- Israel field isolate (cluster 1.2) / Vietnam field isolated (cluster 2.5)
- Titer  $10^{5-6}$  TCID<sub>50</sub>/ml
- 5ml intravenous
- 4x0,25ml intradermal

↓ 21 dpi monitoring

Clinical monitoring:

- Fever
- Swelling inoculation side
- Lnn swelling
- General health status
- Feed intake
- # noduli

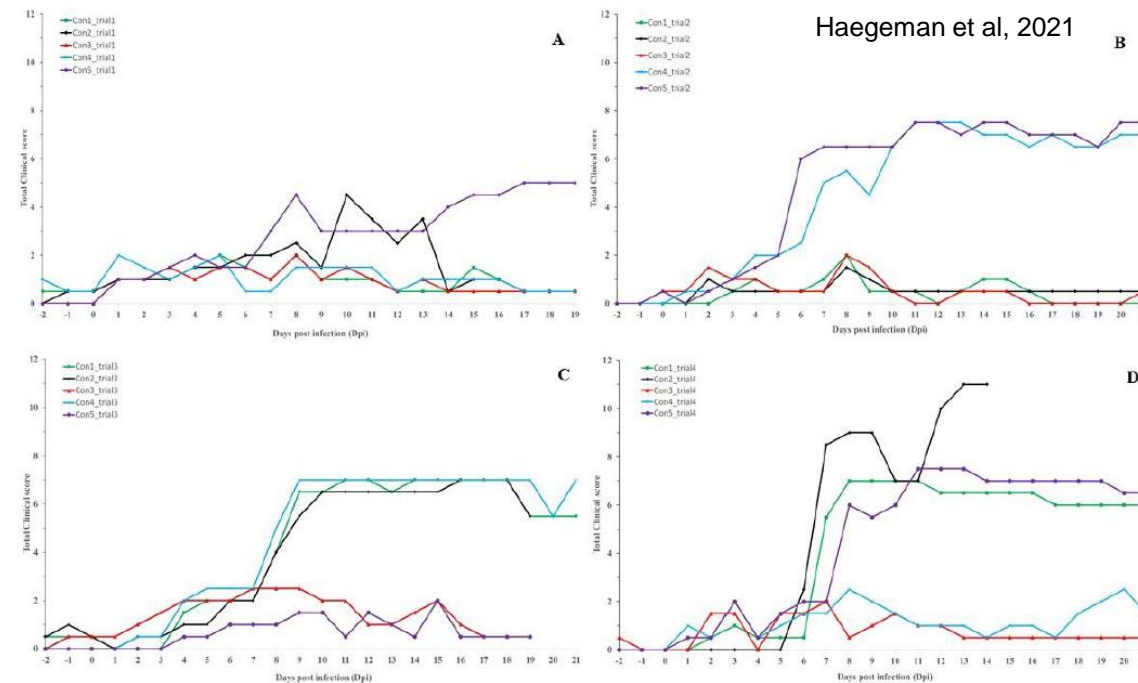
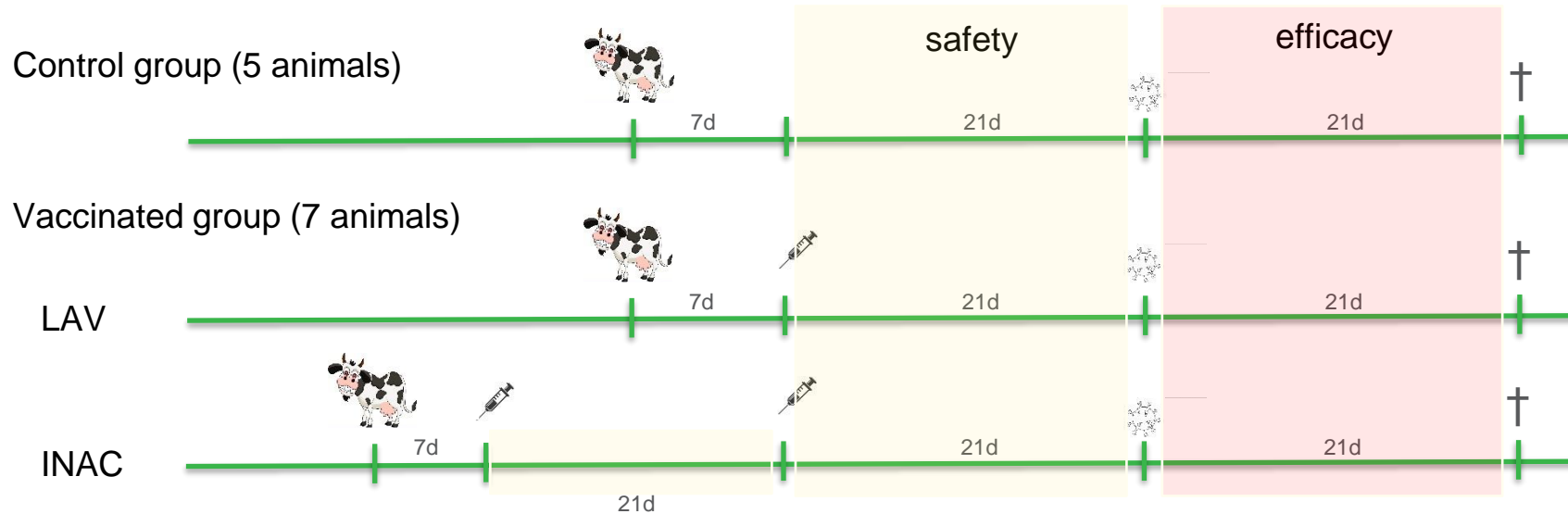


Figure 2. Total clinical score of the control animals. Infected at 0 dpi; (A): Trial 1; (B): Trial 2; (C): Trial 3; (D): Trial 4.

➡ +/-50% of inoculated animals develop clinical disease

# LSDV vaccine safety/efficacy testing @sciensano

## Vaccination – challenge experiments:



- Clinical scoring/monitoring: fever, Inn swelling, local reactions, nodule development, feed uptake,...  
→ adverse vaccine reactions/prevent clinical disease
- Intermediate sampling: - EDTA blood, swabs (PCR, isolation) → viremia and excretion (vaccine / challenge virus)  
- heparine blood (IFN $\gamma$  testing) → cellular immune response  
- serum (IPMA, VNT, ELISA) → humoral immune response
- Autopsy: biopts, organs (PCR, isolation) → persistence of vaccine / challenge virus

# LSDV vaccine safety/efficacy testing @ sciensano

	type	strain	Vaccin	Company	clinical signs		IPMA		IFNgamma	viremia		swabs	organs
					post V	post C	post V	post C	post V	post V	post C	post C	post C
homologous LAV		LSDV	Lumpy Skin Dis Vac	OBP									
		LSDV	LumpyVax	MSD Animal health									
		LSDV	KenyaVac	JOVAC									
		LSDV	Herbivac	Deltamune									
		LSDV	Neethling O	MCI									
		LSDV	Lumpivax	Kevevapi									
heterologous LAV		SPPV	Abic (10x)	Phibro									
		SPPV	JoviVac	JOVAC									
		SPPV	Penpox-M (3x)	Pendik									
		SPPV	Romania (10x)	MCI									
		GTPV	CapriVac (10x)	JOVAC									
homol/heterol INAC		LSDV	Bovivax (?)	MCI									
		SPPV	Romania	MCI									

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	LSDV	KenyaVac	JOVAC	A++	A++	+	++	+++	A++	A+++	not tested	P-	
	LSDV	Herbivac	Deltamune	P-	A+++	++	+	+++	P--	A+++	P-	P--	
	LSDV	Neethling O	MCI	P--	A++	++	++	+++	A++	A+++	A++	P-	
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heterologous LAV	SPPV	Abic (10x)	Phibro										
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- All homologous LAV protected against clinical signs upon challenge
- Important negative safety aspects found for certain live attenuated LSDV vaccins:
  - strong local reaction
  - prolonged fever
  - Neethling respons in multiple animals
  - vaccine viremia

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homologous LAV	LSDV	Lumpy Skin Dis Vac	OBP	 <p>Contents lists available at ScienceDirect Preventive Veterinary Medicine journal homepage: <a href="http://www.elsevier.com/locate/prevetmed">www.elsevier.com/locate/prevetmed</a></p> <p>Neethling vaccine proved highly effective in controlling lumpy skin disease epidemics in the Balkans</p>	A+++	not tested	P-						
	LSDV	LumpyVax	MSD Anir		A+++	not tested	P-						
	LSDV	KenyaVac	JOVAC		A+++	not tested	P-						
	LSDV	Herbivac	Deltamun		A+++	P-	P--						
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**PLOS ONE**

RESEARCH ARTICLE

Lumpy skin disease outbreaks in Egypt during 2017-2018 among sheeppox vaccinated cattle: Epidemiological, pathological, and molecular findings

Sherin R. Rouby<sup>1\*</sup>, Nesreen M. Safwat<sup>2</sup>, Khaled H. Hussein<sup>1</sup>, Aml M. Abdel-Ra'ouf<sup>2</sup>, Bahaa S. Madkour<sup>2</sup>, Ahmed S. Abdel-Moneim<sup>3</sup>, Hosenin I. Hosenin<sup>1</sup>

Contents lists available at ScienceDirect

**Veterinary Microbiology**

journal homepage: [www.elsevier.com/locate/vetmic](http://www.elsevier.com/locate/vetmic)

Goatpox virus (G20-LKV) vaccine strain elicits a protective response in cattle against lumpy skin disease at challenge with lumpy skin disease virulent field strain in a comparative study

K. Zhugunissov<sup>1,2\*</sup>, Ye. Bulatov<sup>3</sup>, M. Orynbayev<sup>3</sup>, L. Kutumbetov<sup>3</sup>, Ye. Abduraimov<sup>3</sup>, Ye. Shayakhmetov<sup>3</sup>, D. Taranov<sup>3</sup>, Zh. Amanova<sup>3</sup>, M. Mambetaliyev<sup>3</sup>, Zh. Absatova<sup>3</sup>, M. Azanbekova<sup>3</sup>, B. Khairullin<sup>3</sup>, K. Zakarya<sup>3</sup>, E. Tuppurainen<sup>1,2\*</sup>

<sup>1</sup> Research Institute for Biological Safety Problems, Gurevskiy, Kazakhstan  
<sup>2</sup> Institut für Internationale Tiergesundheit / One Health, Friedrich-Loeffler Institut, Stahfer 10, 17493 Greifswald, Insel Riems, Germany

VIRULENCE

2023, VOL. 14, NO. 1, 2190647

<https://doi.org/10.1080/21505594.2023.2190647>

Taylor & Francis  
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS

Check for updates

**Evaluation of the safety, immunogenicity and efficacy of a new live-attenuated lumpy skin disease vaccine in India**

[9,17–21]. These discrepancies in the use of heterologous vaccines in the past, together with the poor efficacy of goatpox vaccine in India, prompted us to develop a homologous vaccine which confers solid immunity against LSD

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- INAC SPPV based vaccines were safe, but lack efficacy as they did not protect against clinical disease in all vaccinated animals
- INAC LSDV vaccines showed good safety and efficacy
- Two initial doses of INAC vaccines are needed; booster after 6 months

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homol/heterol INAC												



Development and Evaluation of an Inactivated Lumpy Skin Disease Vaccine for Cattle

Jihane Hamdi<sup>a,b,\*</sup>, Zineb Boumart<sup>a</sup>, Samira Daouam<sup>a</sup>, Amal El Arkam<sup>a</sup>, Zahra Bamouh<sup>a</sup>, Mohamed Jazouli<sup>a</sup>, Khalid Omari Tadlaoui<sup>a</sup>, Ouafaa Fassi Fihri<sup>b</sup>, Boris Gavrilov<sup>c</sup>, Mehdi El Harrak<sup>a</sup>



Article

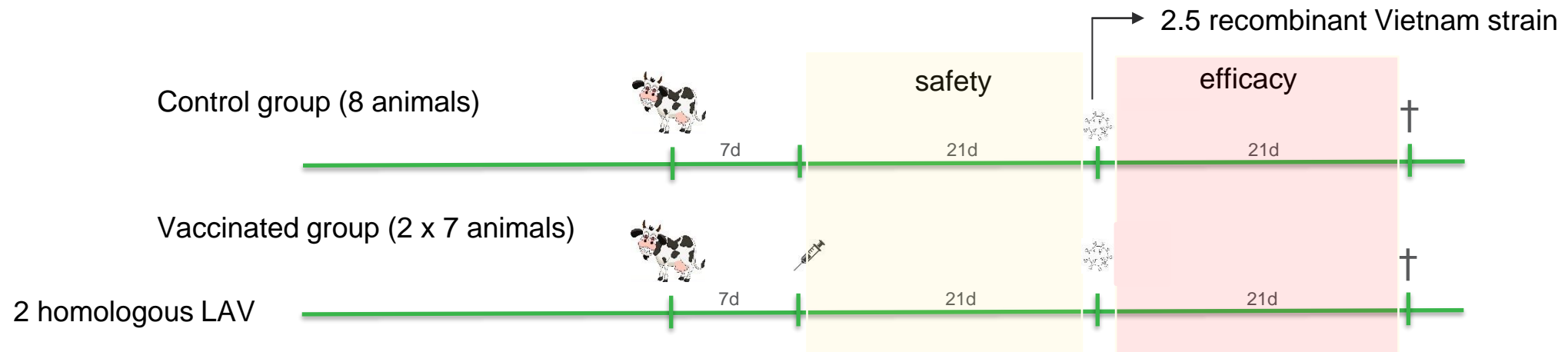
**Development of a Safe and Highly Efficient Inactivated Vaccine Candidate against Lumpy Skin Disease Virus**

Janika Wolff , Tom Moritz, Kore S. Jlottau, Donata Hoffmann , Martin Beer and Bernd Hoffmann <sup>\*</sup>

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# Homologous LAV protect against recombinant strain

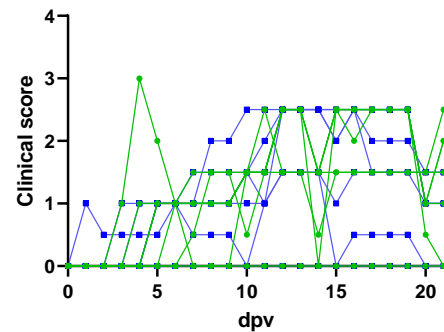
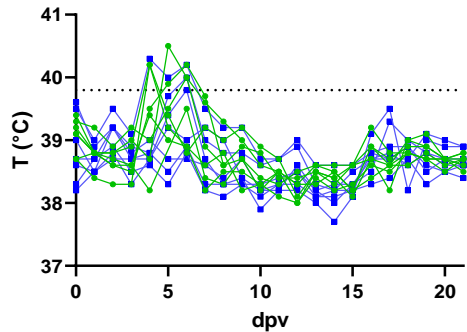
# Animals	Vaccine	Purpose
7	MSD (Lumpyvax)	Vaccine evaluation
7	OBP	Vaccine evaluation
8	N/A	Control Vaccine and infection model



# Homologous LAV protect against recombinant strain

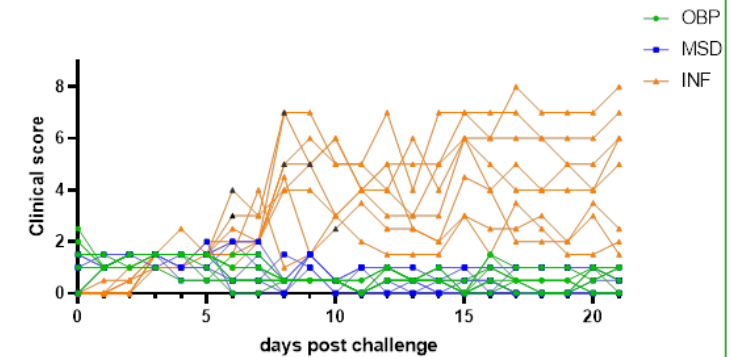
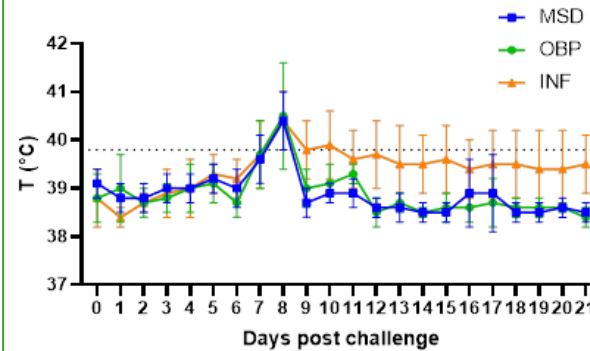
## Post vaccination

Clinical sign	Vaccinated animals
Fever	5-7 dpv
Local reaction	Limited
Nodules	No
Other	No vaccine viremia



## Post challenge

Clinical sign	Control animals	Vaccinated
Fever	Prolonged	7-8 dpv
Local reaction	Strong (75%)	Limited
Nodules	- 6 skin - 1 lung	No
Other	Wide variety	No



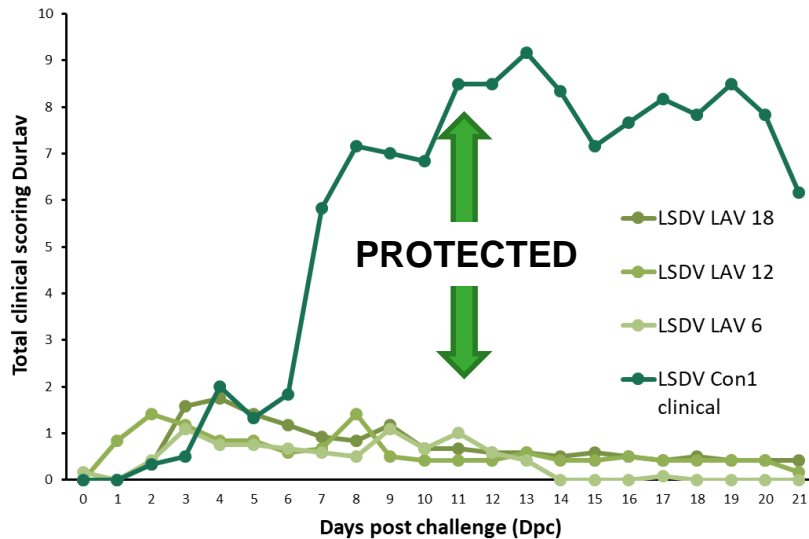
- Homologous live attenuated neethling-based strains provide protection against recombinant (clade 2.5) LSDV strains
- Efficacy of heterologous and inactivated LSDV vaccines remains to be evaluated

# LSDV vaccines – duration of immunity

## Live attenuated vaccine

Total clinical scoring

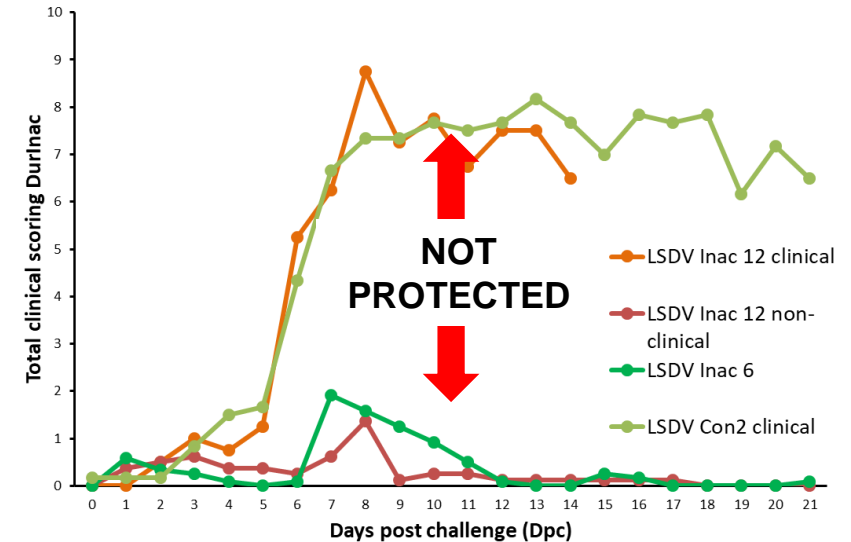
- Almost no clinical scoring
- No nodule formation



- Only 1 vaccination necessary
- Limited side effects upon vaccination
- Complete protection for at least 1,5 years

## Inactivated vaccine

- Clinical scoring in 2 animals LSDV Inac 12
- Nodule formation in LSDV Inac 12 (2/6)



- Prime/boost vaccination necessary
- Almost no side effects upon vaccination
- Complete protection up to six month, but not after one year

# LSDV vaccines - conclusions

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- Safe and efficacious LSDV vaccines are available against classical and recombinant LSDV strains
- Even for the best vaccines, limited, short lasting side-effects might be noticed (swelling at the inoculation site, temporary fever, brief drop in milk production, Neethling disease in rare cases)
- Duration of immunity: > 18 months for homologous LAV; 6 months for INAC
- A proper vaccine batch quality control needs to be performed

## Future work:

- DIVA vaccine, allowing preventive vaccination
- methods for post-vaccination monitoring



# Acknowledgements

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EUROPEAN  
COMMISSION



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SANTÉ PUBLIQUE,  
SECURITE DE LA CHAÎNE ALIMENTAIRE  
ET ENVIRONNEMENT



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VOLKSGEZONDHEID,  
VEILIGHEID VAN DE VOEDSELKETEN  
EN LEEFMILIEU

## Contact

Nick De Regge • [nick.deregge@sciensano.be](mailto:nick.deregge@sciensano.be) • +32 2 379 06 27