



# 1st GF-TADs Regional Conference in the European region

Lumpy skin disease: update from the EU/WOAH reference laboratory







Funded by

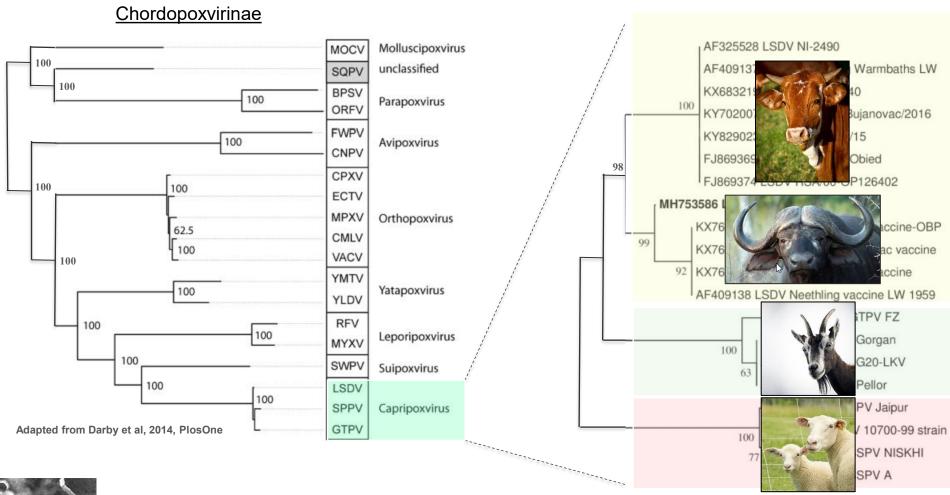
the European Union

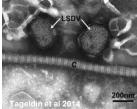


#### **OUTLINE**

- Introduction: virus, clinical signs, epidemiology
- EU/WOAH RL tasks
- Policy supporting studies and knowledge gaps

# **Capripox viruses**

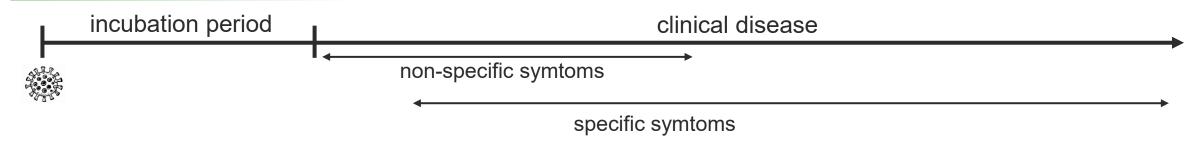




Adapted from Sprygin et al, 2018, PlosOne

• Not-segmented dsDNA genome, 150.000 bp

### LSDV incubation period and clinical signs



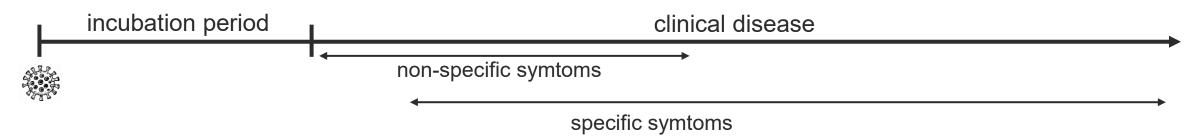
- Incubation period: 4 to 15d after experimental inoculation
   1 to 5 weeks after infection by vectors (experimental and field)
- Clinical signs
- Fever: can be higher than 41°C
- Enlarged lymph nodes
- Depression
- Decreased milk production
- · Ocular and nasal discharge
- Nodules on the skin (Lumps) → scabs → scars body, head, udder, genitalia
- Lesions in the mouth, pharynx, digestive tract, respiratory tract, surface of internal organs





Pictures: Dr. Stefano Cappai, IZS Sardinia

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### LSDV clinical signs

Disease severity varies between animals

severe LSDV cases - mild LSDV cases - subclinical animals - animals without productive infection





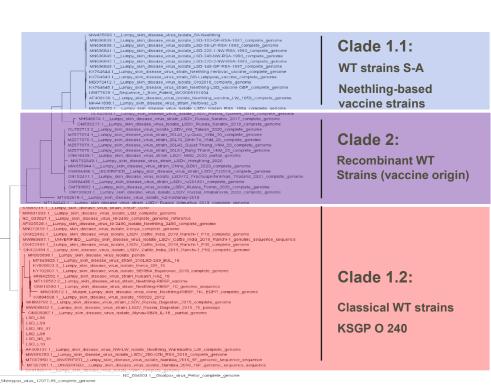
- Subclinical animals can be source of onwards transmission
- 30 to 50% of inoculated cattle develop clinical disease in experimental settings
- Field data: mortality: 1-5%; morbidity 10-45%
- Self limiting disease, no carrier status

# Most recent reported LSDV outbreaks (2021 - 07/2025)

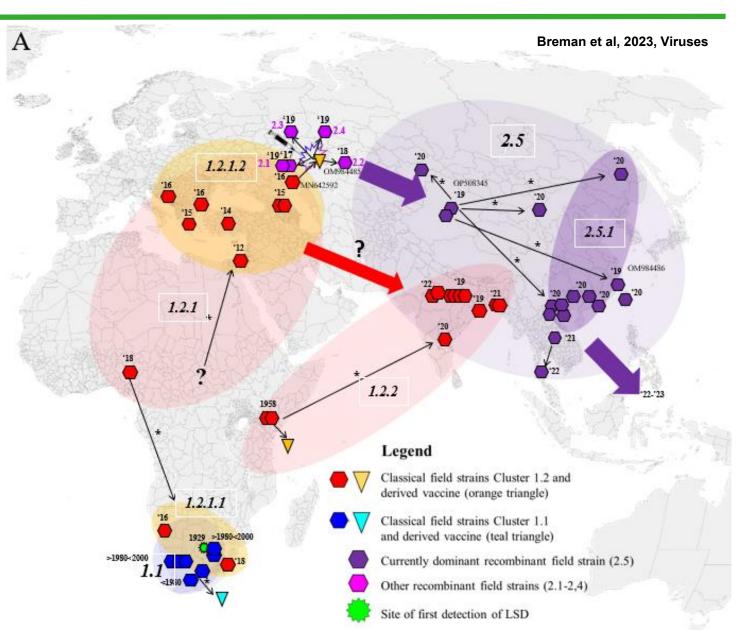
Data extracted from WOAH-WAHIS database



# LSDV spread and phylogeny

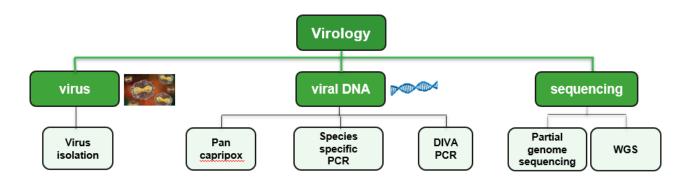


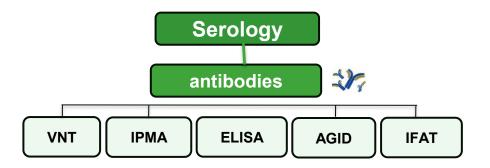
Impact on virulence?
Impact on diagnostics?
Impact on transmission?
Impact on vaccination?



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- Molecular tests are fit-for-purpose
- ISO17025
- SOPs available
- Improvement WGS methodology
- Importance of sample selection
  - Scabs or biopts of nodules when present



Oral/nasal swabs – EDTA blood

- Serological tests are available
- ISO17025
- SOPs available
- VNT IPMA sensitive but low-throughput
- ELISA high-throughput but lack of sensitivity
- Optimization/evaluation IGRA testing
- No DIVA vaccines and DIVA diagnostic tests

Organisation of proficiency tests for capripox virus – ISO17043 accreditation





- EURL for European NRLs
- NRL and WOAH RL: laboratories worldwide
- Report and advice how to improve diagnostic testing
- Reference material

- Sharing of SOPs
- Provision of training (in collaboration with many partners: EC, IAEA, FAO, EU-FMD, Gates Foundation)
  - ✓ Theoretical training courses
    - ➤ IAEA LSDV Croatia, 2022
    - > FAO VLC LSDV Africa, 2022
    - ➤ EU-FMD VLC LSDV Belgium, 2023
    - ➤ EU-FMD VLC LSDV North-Africa, 2024
    - ➤ EC BTSF training SPPV, 2024



- ➤ EC technicians Romania, 2020
- ➤ IAEA technicians Algeria, 2023
- ➤ EC technicians North-Macedonia, 2024
- > Gates foundation technicians Ethiopia, 2025
- ➤ EU-FMD, planned 2026
- > EC, planned 2026



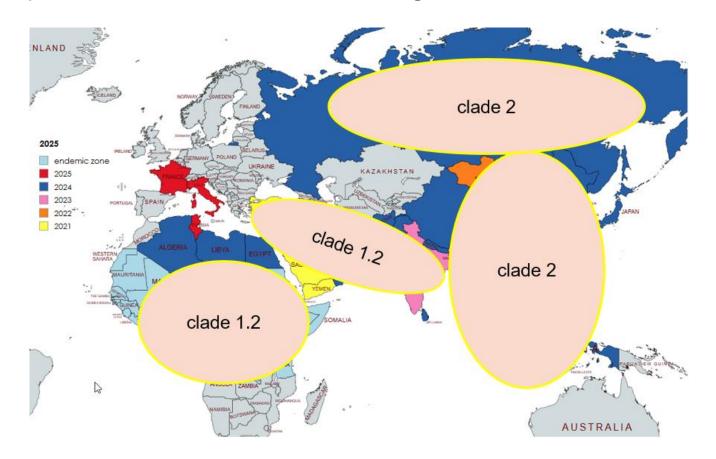


- Annual meeting of the EURL for capripox viruses
  - ✓ 2024: Montpellier, France



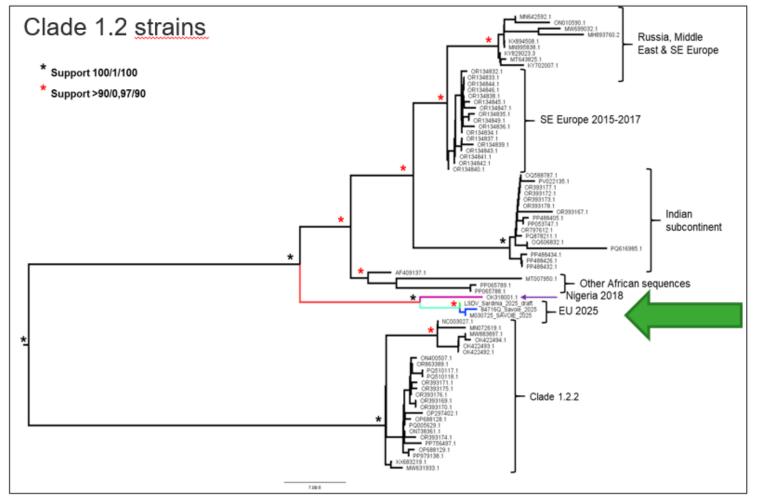
✓ 2025: Antwerp, Belgium

- Confirmatory diagnostics strain identification phylogenetic analysis
- Recent examples: LSDV Pakistan 2024, LSDV Nigeria 2024, LSDV Tunesia ongoing



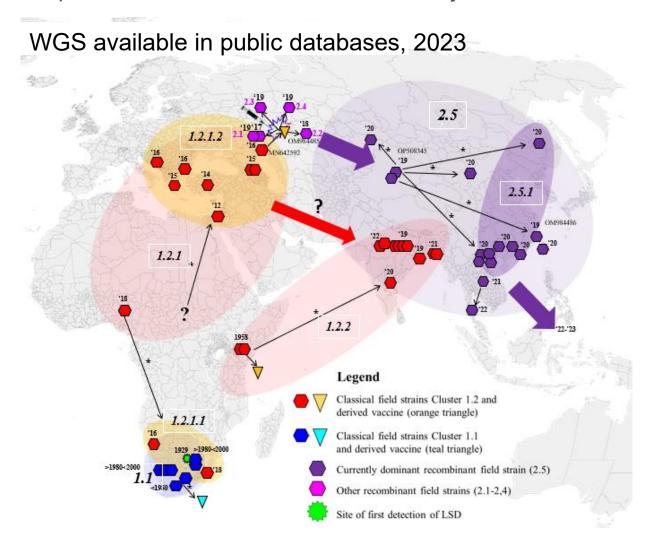
- Sample sharing became extremely challenging: Nagoya protocol, MTAs, shipment cost
- Assistance from international organisations is necessary

- Confirmatory diagnostics strain identification phylogenetic analysis
- LSDV outbreak Europe 2025 collaboration with NRL Italy and NRL France

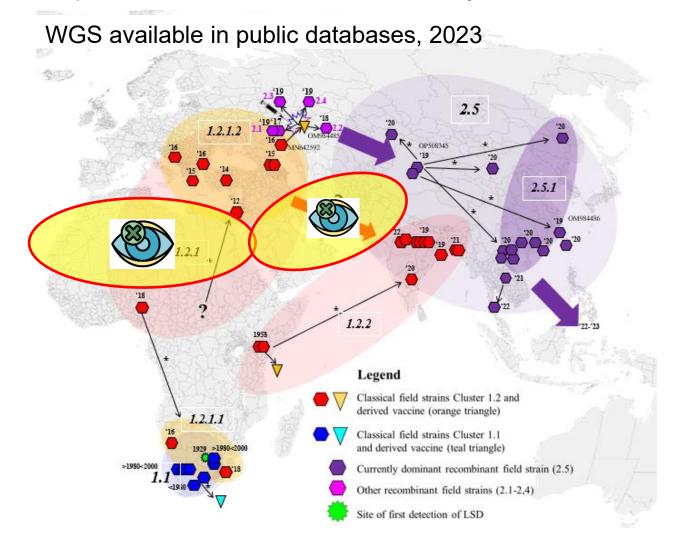


- Clade 1.2 strain
- Italian vs French strain: >99.9% similar,
   5 small INDEL in poly A/T regions,
   2 substitutions (p23509 T(It) vs N(Fr);
   p116346 T (It) vs A (Fr))
- Same LSDV strain responsible for outbreak in Italy and France
- Available diagnostic tests should be fit-for-purpose
- Neethling based vaccines are expected to provide protection
- Vector-borne transmission
- Origin and route of introduction?

- Confirmatory diagnostics strain identification phylogenetic analysis
- LSDV outbreak Europe 2025 collaboration with NRL Italy and NRL France



- Confirmatory diagnostics strain identification phylogenetic analysis
- LSDV outbreak Europe 2025 collaboration with NRL Italy and NRL France



- Vaccine batch quality control
  - Lumpivax (Kevevapi): marketed as Neethling strain based vaccine

PCR control of strain purity – PCR – partial genome sequencing – whole genome sequencing



- Neethling like LSDV vaccine strain
- KSGP-like LSDV vaccine strain
- Sudan-like GTPV strain
- Multiple recombinant strains (almost) identical to recently described recombinant vaccine-like strains

Haegeman et al, 2022, Vaccines - Vandenbussche et al, 2023, Viruses

One specific badly produced and insufficiently controlled LSDV vaccine was responsible for the release of recombinant LSDV strains in the field

Independent batch quality control recommended: identity and purity of vaccine strain, vaccine titer,
 freedom from extraneous agents

- Expert advice at international meetings (EC, GFTAD, WOAH, FAO, EU-FMD)
  - ✓ EuFMD : Online meeting du réseau d'épidémiologie Afrique du Nord LSDV outbreaks (Online, 18 July 2024)
  - ✓ FAO: Vaccines against emerging TADs (Rome, 23-24 September 2024)
  - ✓ WOAH SEA: LSDV update meeting (Online, 19 december 2024)
  - ✓ EuFMD SEE meeting: update epidemiology and control LSDV (Online, 30 January 2025)
  - ✓ GFTAD SGE LSDV: Latest activities on LSDV and update on diagnosis (Online, 05 March 2025)
  - ✓ GFTAD: webinar on PPR and LSDV in Europe (Online, 03 July 2025)
  - ✓ WOAH Asia and the Pacific: regional workshop on LSD control in Asia and the Pacific (Manila, 8-10 July 2025)
  - ✓ EuFMD: LSDV in Europe Emergency preparedness and response (Online, 17 July 2025)
  - ✓ ESVV conference: factors determining LSDV control strategy (Portoroz, 2-5 September 2025)



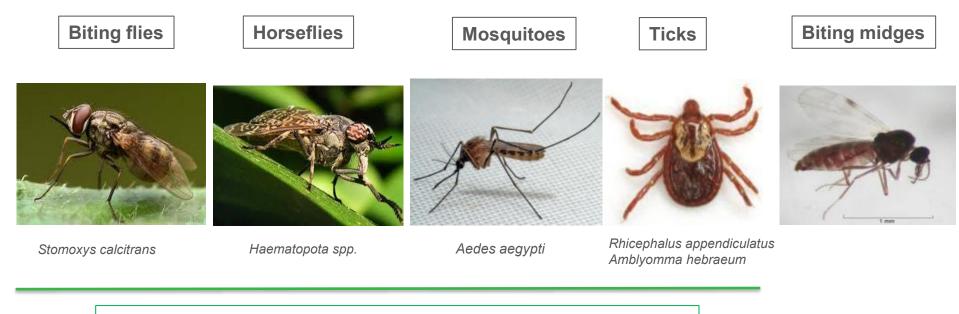
WOAH Asia and the Pacific: Towards LSDV free in 2030

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#### LSDV transmission

- LSDV is a vector-borne disease
- LSDV spreads mostly during the hot and humid seasons highest vector abundance



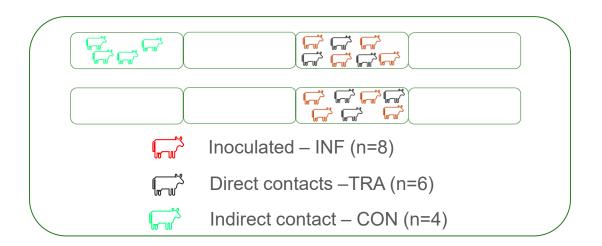
- Proven mechanical vectors based on animal experiments
- Based on epidemiological data, biting flies seem to be most important vector for LSDV
- Limited number of stable flies are sufficient to transmit LSDV
- Stable flies can spread LSDV after biting subclinical infected cattle

# **Mode of LSDV transmission**

Vector		Aedes aegypti	- Aedes aegypti - Cx tritaeniorhynchus - Cx quinquefasciatus
Strain	Clade 1.2	Clade 1.2	Clade 2
Result	10 30 32 34 36 38 40 40 42 2 h 6 h 24 h 48 h 72 h 120 h 1 d 2 d 3d 5 d  # positive —mean CP	Species   Day post infectious blood meal   QPCR (head)   No. positive/no. tested   QPCR (body)	LSDV detection in saliva  B  Dose  103,7/ml  Dose  104,7/ml  Ae. aegypti  Cx. tritaeniorhynchus  Cx. quinquefasciatus
	Haegeman et al, unpublished	Paslaru et al, 2022, Med Vet Entomol	Riana et al, 2024, Acta Tropica
Conclusion	Mechanical transmission	Mechanical transmission	Biological transmission

#### Non-vector-borne LSDV transmission of clade 2 strains

- LSDV transmission during winter (clade 2.1 strain; Shumilova et al, 2022, TBED)
- LSDV infection via spiked feed (clade 2.1 strain; Shumilova et al, 2022, Pathogens)
- Direct (clade 2.1; Kononov et al, 2020, Sci Rep) and indirect (clade 2.2; Nesterov et al, 2022, Front Vet Sci)
  contact transmission between cattle
- Efficient direct and indirect contact transmission of a clade 2.5 strain was shown at Sciensano



#### LSDV control measures

- Complete stamping out of infected farms
- Biosafe disposal of carcasses
- Cleaning and disinfection of infected premises
- Implementation of protection (20km) and surveillance zones (50km)
- Stop/restrict animal mouvement in surveillance zone
- Epidemiological investigation tracing of animals movements
- Clinical surveillance in protection and surveillance zone; clinical surveillance in all farms which
  received animals linked to the outbreak zones; where necessary complemented with
  laboratory surveillance
- Awareness campaigns for veterinarians, farmers, general public
- Vaccination

COMMISSION DELEGATED REGULATION (EU) 2020/687

of 17 December 2019

supplementing Regulation (EU) 2016/429 of the European Parliament and the Council, as regards rules for the prevention and control of certain listed diseases



### LSDV vaccine safety/efficacy

- LSDV outbreak Israel 2012-2013 (Ben-Gera & Klement, 2015, Vaccine)
- LSDV outbreak Balkan 2015-2017 (Tuppurainen et al, 2020, Prev Vet Med)
- LSDV vaccine safety/efficacy testing at Sciensano: standardized challenge model

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

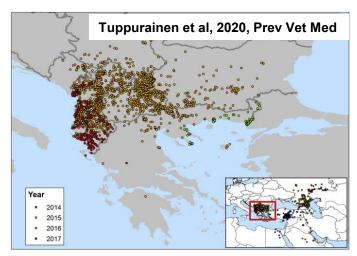
- Six homologous Neethling based LAV protected against clade 1.2 strain challenge
- Three homologous Neethling based LAV protected against clade 2.5 strain challenge
- One vaccine dose provides protection 3 weeks after vaccination
- Duration of immunity of 18 months
- Negative safety aspects found for certain live attenuated LSDV vaccines:
  - strong local reaction
  - fever
  - temporary drop in milk production
  - Neethling response in limited % of vaccinated cattle



- Despite use of millions of doses, no recombination with wild type strains reported under field conditions
- Independent vaccine quality control recommended
- No DIVA vaccines available

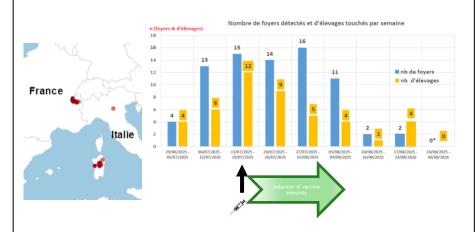
### LSDV control and remaining questions

>7000 outbreaks: 2015-2017



- EU policy <2015: no vaccination
- No vaccine bank
- Preventive vaccination in Bulgaria, Serbia and Croatia stopped northwards spread of LSDV

133 outbreaks: 2025 (until 16/09)



- Vaccination as control measure in the AHL
- EU vaccine bank
- Vaccination started <1 month in 50km surveillance zone (France)
- 55% vaccination coverage in Sardinia at 08 September

Knowledge gaps and problems identified by scientists, affected countries, international organisations

- ✓ LSDV presence and inactivation in milk
- ✓ Role of raw milk products in disease transmission
- ✓ Risks of LSDV spread via sperm, embryos, skeletal muscle
- ✓ Strain-dependent mechanical vs biological transmission by different vectors
- ✓ Epidemiological importance of non-vector transmission
- ✓ Stamping out policy in context of vaccination
- ✓ More sensitive ELISA needed, post vaccination monitoring
- ✓ DIVA vaccine and diagnostic tests

### Acknowledgements





National reference laboratories for LSDV



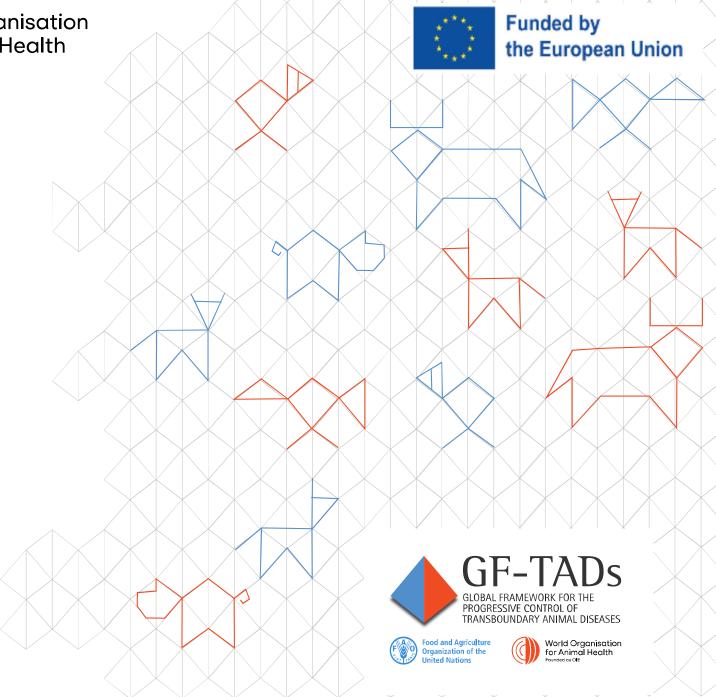
BILL& MELINDA GATES foundation







# THANK YOU





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