Frequently Asked Questions (FAQ) on lumpy skin disease (LSD)

Contents

Section 1: General information on LSD

1. What is lumpy skin disease (LSD)?

Lumpy skin disease (LSD) is caused by lumpy skin disease virus (LSDV), a virus from the family *Poxviridae*, genus *Capripoxvirus*. Sheeppox virus and goatpox virus are the two other virus species in this genus.

2. What domestic animals may be affected by LSD?

LSDV is highly host specific and causes disease only in cattle (*Bos indicus* and *B. taurus*) and water buffalo (*Bubalus bubalis*). There is evidence from a study in Ethiopia of differential breed susceptibility to LSD, with Holstein Friesian or crossbred cattle exhibiting higher morbidity and mortality due to LSD when compared with local zebu cattle.

LSDV is not zoonotic, so humans cannot get affected by the disease.

3. Are there any recent LSD cases in sheep and goat?

There are no reports of LSD in sheep and goats or of their epidemiological involvement in the disease despite being kept in close proximity to cattle.

4. What is the risk of LSD in wildlife?

Recent findings indicate that several game species could be susceptible and evidence is growing of the susceptibility of southern Asian species including deer and antelope.

In wildlife, the presence of the virus has been reported in springbok (*Antidorcas marsupialis*) and in asymptomatic eland (*Taurotragus oryx*) in Namibia; oryx (Oryx gazelle) in South Africa; Arabian oryx (*Oryx leucoryx*) in Saudi Arabia; and in Guar (*Bos gaurus),* Mainland serow *(Capricornis sumtraensis)* and Banteng *(Bos javanicus)* in Thailand in 2021. The susceptibility of wild and captive wild ruminants (e.g. zoo ruminants) is not well-known and their possible role in the epidemiology of LSD is still under investigation.

5. How is LSD transmitted?

The disease can spread rapidly, and principal means of transmission is believed to be by arthropod vectors. Mechanical LSDV transmission leading to clinical disease in recipient cattle under experimental conditions has been shown for *Aedes aegypti* mosquitoes and *Stomoxys calcitrans* and *Haematopota spp*. biting flies. It is highly likely that several other mosquitoes (e.g. *Culex mirificens* and *Aedes natrionus*), biting flies (e.g. *Biomyia fasciata*), *Culicoides* and male ticks (*Riphicephalus appendiculatus* and *Amblyomma hebraeum*) could play a role in the transmission of the virus under field conditions. The relevance of different arthropod vectors is likely to vary in different areas depending on the abundance and feeding behaviour of the vector.

Direct contact with an infected animal is considered to play a minor role in the transmission of the virus. It is not known if transmission can occur via fomites, for example ingestion of feed and water contaminated with infected saliva, but the occurrence of newly detected recombinant field strains suggests these routes may be at play.

Infected bulls can shed the virus in their semen and transmission of LSD via infected semen has been demonstrated. There has been one report of placental transmission of LSD.

6. Where can LSD be found?

LSD is endemic in most African countries. Since 2012 it has spread rapidly through the Middle East, south-east Europe and West and Central Asia. Since 2019, several outbreaks of LSD have been reported by Members in Asia, and recently, south-east Asia.

For more recent and detailed information on the global occurrence of LSD, see the WOAH World Animal Health Information Database (WAHID) Interface.

7. What are the clinical signs of LSD?

The morbidity rates for LSD during outbreaks vary between 10 and 20% although it has been reported in some places to be as high as 45%, and mortality rates of 1 to 5% are considered usual. LSD does not cause chronic disease. It does not exhibit latency, and recrudescence of disease does not occur.

The clinical signs of LSD range from inapparent to severe disease.

- Fever that may exceed 41°C
- Marked reduction in milk yield in lactating cattle
- Depression, anorexia and emaciation
- Rhinitis, conjunctivitis and excessive salivation
- Enlarged superficial lymph nodes
- Cutaneous nodules of 2–5 cm in diameter develop, particularly on the head, neck, limbs, udder, genitalia and perineum within 48 hours of onset of the febrile reaction. These nodules are circumscribed, firm, round and raised, and involve the skin, subcutaneous tissue and sometimes even the underlying muscles
- Large nodules may become necrotic and eventually fibrotic and persist for several months ("sit-fasts"); the scars may remain indefinitely. Small nodules may resolve spontaneously without consequences
- Myiasis of the nodules may occur
- Pox lesions, erosions and ulcers may develop in the mucous membranes of the mouth and alimentary tract and in the trachea and lungs
- Limbs and other ventral parts of the body, such as the dewlap, brisket, scrotum and vulva, may be oedematous, causing the animal to be reluctant to move
- Bulls may become permanently or temporarily infertile
- Pregnant cows may abort and be in anoestrus for several months
- Recovery from severe infection is slow due to emaciation, secondary pneumonia, mastitis, and necrotic skin plugs, which are subject to fly strike and shed leaving deep holes in the hide.

There is no current evidence of variation in virulence regarding the different LSDV strains.

8. What are the differential diagnoses for LSD?

Severe LSD is highly characteristic, but milder forms can be confused with:

- Bovine herpes mammillitis (bovine herpesvirus 2) (sometimes known as pseudo-lumpy skin disease)
- Bovine papular stomatitis (parapoxvirus)
- Pseudocowpox (parapoxvirus)
- Vaccinia virus and Cowpox virus (orthopoxviruses) – uncommon and not generalised infections
- Dermatophilosis
- Demodicosis
- Insect or tick bites
- Besnoitiosis
- Rinderpest
- Hypoderma bovis infection
- Photosensitisation
- Urticaria
- Cutaneous tuberculosis
- Onchocercosis.

9. Do recovered animals become carriers for LSD?

There is no known carrier state.

Once an animal has recovered, it is well protected and cannot be the source of infection for other animals. In infected animals that do not show clinical signs, the virus may remain in blood for a few weeks and eventually disappear.

10. How can LSD be diagnosed?

For detailed information regarding laboratory diagnostic methodologies, please refer to the chapter on LSD in the latest edition of the WOAH *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* under the heading "B. Diagnostic Techniques".

Skin nodules, scabs and crusts contain relatively high amounts of LSDV. Virus can be isolated from this material for up to 35 days and likely for longer. LSDV can also be isolated from blood, saliva, ocular and nasal discharge, and semen.

LSDV is found in the blood (viraemia) intermittently from approximately 7 to 21 days post-infection at lower levels than present in skin nodules. Shedding in semen may be prolonged; LSDV has been isolated from the semen of an experimentally infected bull 42 days post-inoculation.

Tests for the detection of agent

- Conventional polymerase chain reaction (PCR) is the least expensive and quickest method for detection of LSDV. Skin nodules and scabs, saliva, nasal secretions, and blood are suitable samples for PCR detection of LSDV.
- Real-time PCR methods are available for detection of capripoxvirus; species-specific PCR methods are available to differentiate between LSDV, sheeppox virus and goatpox virus, and DIVA PCR methods have been published to differentiate a homologous vaccine virus from virulent field strain*.
- Virus isolation has the advantage of demonstrating the presence of live virus in the sample.
- Immunohistochemistry can be used to identify presence of virus to the genus level.
- Electron microscopy can be used to identify the classic poxvirus virion but cannot differentiate to genus or species level.
- Sequencing (partial or whole-genome) provides the most information relating to cluster grouping (classical field, vaccine-like or, more recently, field recombinant strains).

**Note that when using DIVA tests in regions where recombinant field strains are circulating, the recombinant strains may be undetected by DIVA PCR methods, or could be classified as vaccine strains and provide false negative results.*

Detection of immune responses

It is not possible to distinguish the three viruses in the *Capripoxvirus* genus (sheeppox virus, goatpox virus and LSDV) using serological techniques.

- Virus neutralisation: this is currently the gold standard test for the detection of antibodies raised against capripoxviruses.
- Western blot: highly sensitive and specific but expensive and difficult to perform.
- Capripoxvirus antibody enzyme-linked immunosorbent assay (ELISA): commercial kits for detection of capripoxvirus antibodies are on the market.

A virus specific immunoperoxidase monoloayer assay (IPMA) has also been developed for the detection of antibodies against LSDV but is yet to be validated as a standard by the WOAH Biological Standards Commission.

11. What measures may be taken to prevent and control LSD?

Evidence from the recent LSD epidemic in Europe and western Asia has revealed that successful control and eradication of LSD relies on early detection of the index case, followed by a rapid and widespread vaccination campaign. It is unlikely that total stamping-out (killing all clinically affected cattle and unaffected herd-mates) and partial stamping-out (killing only clinically affected cattle) alone, in the absence of vaccination, can eradicate LSD.

In a practical example, LSD was controlled in some Balkan countries within one to three months with a vaccination coverage higher than 80%, when supported by other measures such as early detection, zoning and movement controls, and total or partial stamping-out.

In unaffected countries or zones, it is also important to prepare any preventive vaccination or emergency vaccination plans (see point 17).

Sanitary prophylaxis

- Free countries:
  - Import measures on domestic cattle and water buffaloes, and selected products from these animals in accordance with the recommendations in the chapter on LSD in the WOAH *Terrestrial Animal Health Code*.
  - Surveillance measures to detect LSD are recommended over a distance of at least 20 kilometres from an infected country or zone, in reference to recommendations in the chapter on LSD in the WOAH *Terrestrial Animal Health Code*.

- Infected countries:
    - Control of LSD depends on restriction of movement of cattle and associated animal products in infected regions, removal of clinically affected animals, and vaccination. Movement restrictions and removal of affected animals alone without vaccination are usually not effective.
    - Proper disposal of dead animals and inactivation of at-risk animal products (e.g. incineration), and cleaning and disinfection of premises are recommended for LSD.
    - There is currently no evidence of the efficacy of vector control in preventing disease.
    - See WOAH *Terrestrial Animal Health Code* for recommendations on the recovery of LSD-free status of a country or zone, including recommendations on surveillance and waiting periods.

Medical prophylaxis

- LSDV live attenuated vaccine strain, for example 'Neethling' LSD strain.
- Sheeppox or goatpox virus live attenuated vaccine strain against LSDV if used at a higher dose than for prevention of sheeppox or goatpox.
- Vaccine side-effects such as a local skin reaction at the inoculation site or small generalised skin nodules, as well as fever and reduction in milk yield, may follow vaccination with homologous vaccine, more rarely after vaccination with sheeppox vaccine.
- Currently, no new generation recombinant capripox vaccines are commercially available.

For more detailed information regarding safe international trade in terrestrial animals and their products, please refer to the chapter on LSD in the latest edition of the WOAH *Terrestrial Animal Health Code*.

For further information on vaccination, refer to Section 2 of this FAQ.

Section 2: Vaccination for LSD

A. Benefits, availability, access and vaccine types

12. What are the benefits of LSD vaccination?

Vaccination:

- is the most effective tool for LSD control and potential eradication
- is easier to implement and more effective than other measures (i.e. stamping out) and, in most cases, is less costly
- reduces the total number of susceptible animals within the population, thus preventing entry (in the case of preventive vaccination) and spread of the disease
- protects the animals from getting infected with LSD thus preventing direct and indirect economic losses.

13. What type of LSD vaccines are available commercially and what do you mean by homologous and heterologous LSD vaccines?

Chapter 3.4.12. of the WOAH *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (Terrestrial Manual)* sets out the requirements for the vaccines to be used for LSD control. An appropriate vaccine to control LSD should provide good immunity for cattle against LSD, be safe to use for all cattle breeds, ages, and pregnant animals, and be correctly labelled. Live attenuated strains of capripoxvirus have been used as vaccines to control LSD. The capripoxviruses are cross-reactive within the genus and consequently, it is possible to protect cattle against LSD using strains of capripoxvirus derived from cattle as well as from sheep or goats.

'Homologous vaccine' refers to a vaccine that contains live attenuated Neethling-type LSDV as a vaccine seed. 'Heterologous vaccine' refers to a vaccine that contains either live attenuated sheep pox virus or goat pox virus and the vaccine is used to protect cattle against LSDV. For clarity, we will refer here to the virus used in the vaccine rather than to heterologous/homogenous denomination. Sheep pox virus- or goat pox virus-based vaccines may be used as an alternative vaccine in those countries where both LSD and sheep pox and goat pox occur or for those countries that already have manufacturing capacity for these vaccines. However, if a sheep/goat pox virus vaccine is selected for use in cattle, the vaccine product should be well characterised and the dose adjusted to cattle. Protection provided by the vaccines against LSD should be evaluated using a vaccine challenge trial.

There is no 'Differentiating Infected from Vaccinated Animals' (DIVA) vaccine available in the market, but PCR-based DIVA assays exist for discrimination between classical field and current vaccine virus strains. However, one should be

careful when using DIVA tests in regions where recombinant field strains are circulating, as recombinant strains might be classified as vaccine strains or go undetected by the currently described DIVA PCR tests.

Several live-attenuated vaccines (LSD and sheep/goat pox vaccines) are commercially available. While inactivated LSD vaccines are not yet described in the *Terrestrial Manual*, some manufacturers have developed inactivated vaccines against LSD. Inactivated vaccines may be preferred in LSD-free countries when there is risk of LSD introduction from neighbouring countries. Inactivated vaccines generate a shorter duration of immunity than live attenuated vaccines. Therefore, initial vaccinations comprise two vaccinations that are one month apart, followed by revaccination every six months to maintain immunity.

14. Does the WOAH have an emergency LSD vaccine bank?

The WOAH does not have a vaccine bank for LSD. Countries are invited to launch a national procurement process to buy LSD vaccines. The time needed for this process should be taken into account to prepare the call for tender as early as possible to ensure timely access to the vaccines.

For vaccine quality control, the WOAH can facilitate contact with WOAH Reference Laboratories in South Africa and UK and a Collaborating Centre in Belgium (Validation, Quality Assessment and Quality Control of Diagnostic Assays and Vaccine for Vesicular Diseases in Europe).

B. LSD vaccination programme

15. When and how should cattle be vaccinated against LSD?

The recommendations of the vaccine manufacturer should always be followed for those countries using LSD vaccination. For most of the vaccines:

- Annual vaccination of the adult cattle will protect animals from LSD.
- Calves from vaccinated animals or naturally infected mothers should be vaccinated usually at the age of 3 to 6 months, depending on the vaccine. Calves from unvaccinated dams can be vaccinated at any age.
- Newly purchased animals should be vaccinated 28 days before the introduction to the herd.
- Animals should be vaccinated 28 days before the transport or movement to another place.
- Same dosage and protocol should be applied to domestic buffaloes as for cattle.
- Pregnant, healthy cows or heifer can be safely vaccinated.
- When using an inactivated vaccine against LSD, the animals should be vaccinated twice before the transport or movement to another place.

16. How many doses of LSD vaccine does it require to provide full protection to susceptible animals, and how long does the protection last?

Please follow the recommendations from the vaccine manufacturer.

In most cases, a single dose of live attenuated LSD vaccine should confer adequate protection to the vaccinated animals after three weeks of vaccination and for at least one year. Annual vaccination is recommended in affected countries, and harmonized vaccination campaigns across regions provide the best protection.

Inactivated vaccines generate a shorter duration of immunity than live attenuated vaccines. Therefore, initial vaccinations generally comprise two vaccinations that are one month apart, followed by revaccination every six months for the maintenance of immunity.

17. In which context is preventive vaccination recommended in an LSD-free country?

In accordance with Article 11.9.3. of the WOAH *Terrestrial Animal Health Code*, a country or zone practising vaccination is not considered as an LSD-free country or zone. Therefore, a country or zone carrying out LSD vaccination will have to trade in compliance with the provisions for countries or zones not free from LSD, such as the provisions of Article 11.9.6. for live bovines and water buffaloes.

Notwithstanding, if LSD is widely present in a neighbouring country that presents a risk of LSD incursion to the LSD-free country, the latter country may consider setting up a protection zone(s) in accordance with Chapter 4.4. and Article 4.4.6. of the WOAH *Terrestrial Animal Health Code* where within the protection zone, vaccination may or may not be implemented. If vaccination is implemented, the LSD-free status of the protection zone will be lost, but the rest of the

country may still be considered free from LSD. In addition, the introduction of LSD into the protection zone would not affect the LSD-free status of the areas outside the protection zone. Naturally, the implementation of such a protection zone would require strict measures to be in place, including a clear identification of animals from within the protection zone, strict movement control of animals and products from the protection zone to the other parts of the country, enhanced surveillance in accordance with Article 11.9.15 and intensified biosecurity.

Therefore, the use of preventive vaccination should be considered after an evaluation of the specific country situation and local context. If successfully implemented, it may prevent the introduction of LSD in the country. For example, Croatia implemented preventive vaccination, and successfully prevented LSD from being introduced to the country and stopped its further spread in Europe.

A vaccination programme to prevent or control LSD will make a serologically based surveillance programme to detect disease outbreaks more difficult, as vaccinated cattle may be serologically positive. There are currently no serological tests that will differentiate vaccinated from infected animals. It is of utmost importance that LSD vaccination is accompanied by the implementation of appropriate active and passive LSD surveillance to ensure early detection of LSD. Active surveillance should include at least periodical clinical visits in holdings and could include serological testing of non-immune animals.

A successful post-vaccination surveillance relies heavily on correct timing (refer to point 19) and knowledge of the vaccination status of cattle. Therefore, a cattle identification (ID) system and/or database, comprising cattle ID, vaccination, health and movement records should be in place. Vaccinated animals may also be marked using a permanent marker to know which animals are vaccinated.

18. Can animals be administered the LSD and FMD vaccine at the same time?

There are limited scientific publications available on this matter. However, the administration of two different vaccines at the same time in the same animal has been practiced for many years, for practical and logistical reasons. The immune system of a healthy animal can respond to two antigens at the same time. However, it is critical not to mix the vaccines in the same syringe (except when specified otherwise by the manufacturer).

Israël has conducted combined LSD and FMD vaccination, in accordance with the following guidance: LSD and FMD vaccines are not mixed at any stage; separate syringes and needles are used; vaccines are injected into the neck, but far from each other and preferably on different sides of the neck. From this practical experience, an WOAH LSD Expert indicated that there was no report of vaccination failure that could be linked to this combined vaccination.

C. Immune responses and vaccine efficacy

19. How can you monitor the efficacy of LSD vaccination or herd immunity post-vaccination?

Active clinical surveillance is a very effective tool to assess the efficacy of a vaccination campaign. Due to the highly characteristic clinical manifestation of LSD, a thorough physical examination carried out by trained veterinarians is considered as an effective tool for active clinical surveillance. Passive surveillance provides an additional support if LSD awareness levels to identify typical LSD clinical signs are high, and the farmers, field vets and others who come into contact with cattle are willing to report any suspicious cases.

Antibody ELISA can be used for post-vaccination monitoring 2 to 3 months after vaccination, taking into account that antibody levels in some animals may be low and not detected by the ELISA.

20. Can a live-attenuated vaccine be used safely on infected animals (with or without any clinical signs)?

Most of the vaccine manufacturers recommend vaccination only of healthy animals with a live vaccine.

Clinically infected animals will be naturally immunised. Once these animals recover from disease, it is recommended that they receive an annual vaccination booster as the duration of natural immunity is as yet unknown.

Non-clinical animals: There is no evidence that vaccination of preclinically infected or sub-clinically infected animals would lead to severe disease. Due to the risk of spread of LSDV via needles used on non-clinical animals, it is critical to only use single-use needles.

21. Can live attenuated vaccine regain its virulence or lead to recombination with field virus?

Experiences obtained during LSD outbreaks in Europe and following vaccination campaigns between 2016 and 2020 using three live attenuated LSD vaccines did not indicate any evidence of return to virulence of the LSD vaccine strain, or recombination with field virus. A Croatian study reported that after passage of the vaccine virus in cattle, the genome of vaccine virus remained totally attenuated with 100% similarity to the original vaccine virus. A recombination of vaccine and field viruses has also been reported. There is still much we do not understand about how and when these events are occurring, therefore more detailed studies are required to investigate the importance of these findings. Nevertheless, it is important to conduct quality control of vaccines to assure their safety and efficacy.

The Neethling-type strain vaccine has been used for more than 60 years, vaccinating millions of animals, and there are NO reports of vaccine virus regaining virulence.

22. Can vaccinated animals still get LSD infection?

Development of full protection from the vaccine takes approximately three weeks. During this time, cattle may still be infected by the field virus, and may show clinical signs despite being vaccinated. Some animals may also be incubating the virus when vaccinated, and in such cases clinical signs are detected in less than ten days after vaccination.

In some exceptional cases, the vaccination may not provide adequate protection, resulting in a clinical disease. There may be a number of reasons for the vaccination failure which may be associated with either the vaccine itself (the level of attenuation is too low or high, low titre of vaccine seed virus or contaminated vaccine batch), host response (vaccine may be administered correctly but the animal may fail to mount an appropriate immune response), and due to lapses in delivery of vaccines (route of administration or dosage, timing, and cold chain maintenance during the storage and transport of vaccines). Clinical signs may also be due to other disease, caused by bovine herpesvirus 2, also called pseudo-LSD. Vaccination failure has therefore to be properly investigated to identify its source and cause.

D. Side effects and negative impact of LSD vaccination

23. What are the common side effects of LSD vaccination?

Live attenuated LSD vaccines may cause mild adverse reactions in cattle. Local reaction at the vaccination site is common. Other common adverse reactions include temporary fever and a brief drop in milk yield. Some animals may show a mild generalised reaction called Neethling response. This is rare and usually involves appearance of superficial and smaller skin lesions, different from those caused by the fully virulent field strain. They disappear within 2-3 weeks without converting into necrotic scabs or ulcers. Side effects are only seen when animals are vaccinated with LSD vaccine for the first time and are hardly seen after the revaccination. Adverse reactions and side effects of LSD vaccination should be well explained to farmers in advance to prevent their reticence to have their animals vaccinated and to prevent loss of trust if this happens.

E. Exit strategy

24. When can an LSD vaccination programme be stopped?

The FAO *Guide to develop lumpy skin disease emergency vaccination plan* provides guidance to countries on how to plan and implement emergency LSD vaccination as a response to LSD outbreaks within the national territory, as well as when outbreaks are detected in the neighbouring countries. A country that wishes to regain freedom from LSD (for the entire territory or a zone) should cease vaccination and forbid further LSD vaccination in the country. LSD vaccination withdrawal decision and approaches would depend on individual country situation and risk (estimated through specific risk assessment).

The important criteria/ discussion points should be:

- Was the virus circulation stopped after emergency vaccination?
- Is the likelihood of introduction or re-introduction of LSD sufficiently reduced, based on the situation in neighbouring countries?
- Is the sensitivity of surveillance (early detection) high enough to detect re-emergence?
- Is the level of preparedness adequate in case of re-emergence (contingency plan, early response), with special attention on containing disease, maintaining a vaccine stock, and carrying out emergency vaccination?

25. How to regain LSD-free status following effective LSD control, including vaccination?

The ideal outcome of the control strategy in affected countries is to eventually gain/regain LSD freedom in the country (or zone). The requirements to gain/re-gain freedom of LSD are described in the WOAH *Terrestrial Animal Health Code*.

The timeline for recovery would depend on whether a stamping-out policy was implemented and on the surveillance in place. If a stamping out policy was implemented, recommendations (and timelines) from Article 11.9.4 should be followed; if a stamping-out policy was not applied, recommendations (and timelines) from Article 11.9.3. should be followed.

The specific case of a country having conducted a preventive vaccination campaign without having detected the presence of LSD in its territory is also covered in Article 11.9.4.

26. How can WOAH Members self-declare freedom from LSD?

Upon fulfilling the requirement of the relevant articles (as described above) of WOAH *Terrestrial Animal Health Code*, countries may wish to self-declare freedom from LSD (as a country or for a zone). Countries should document compliance of their Veterinary Services with the provisions of Chapters 1.1., 3.2., 3.3. and 11.9. of the *Terrestrial Code* and Chapter 3.4.12. of the *Terrestrial Manual*.

WOAH Members may request the WOAH to publish this self-declaration to give it more visibility. To do so, they should follow the dedicated Standard Operating Procedures. The responsibility contained in a self-declaration lies entirely with the WOAH Delegate of the Member concerned and does not reflect the official opinion of the WOAH.