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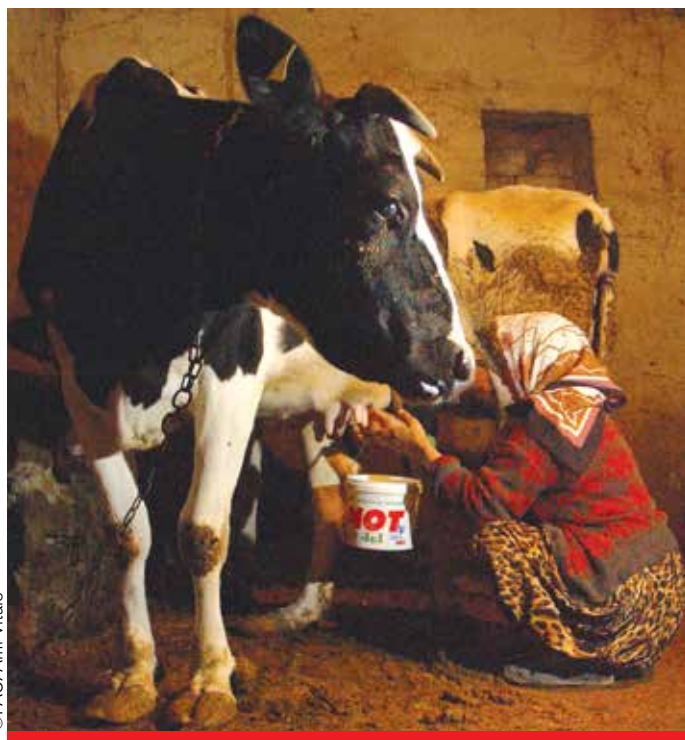


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**LUMPY SKIN DISEASE  
SPECIAL ISSUE**

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\* This designation is without prejudice to positions on status, and is in line with United Nations Security Council Resolution 1244 and the International Court of Justice opinion on the Kosovo Declaration of Independence, throughout empres360 v47.



## Lumpy Skin Disease: New tools to tackle new challenges

Contributor: Bernard Van Goethem<sup>1</sup>

In an ever changing global environment, under the pressure of climate change and movements of people and goods over long distances, the invasion of new, emerging animal diseases, in areas where they never occurred before, is no longer an exceptional event.

Vector-borne diseases, in particular, hold a prominent place in the list of these “newcomers”. Their mode of transmission (arthropods) greatly reduces our potential for intervention.

Lumpy Skin Disease (LSD) is a typical example of such an “exotic” disease that entered continental Europe for the first time in 2015. Within less than a year, it turned into a regional crisis involving many countries in the Balkan Peninsula.

There are several lessons learnt from the incursion of LSD in Europe.

The first sign of Lumpy Skin Disease in Greece, in 2015, was a warning sign for all. For our part, in the European Commission's Directorate-General for Health and Food Safety (DG SANTE), we soon realised that we needed to swiftly adopt new policies, such as for vaccination, and activate new tools, such as the European Union LSD vaccine bank. This was essential to stand any chance against this disease.

The events that followed in 2016 confirmed our concerns in the most spectacular and dramatic way. LSD spread quickly, between April and July, to seven different countries across the Balkan Peninsula. Channels of communication were swiftly established with all affected and at risk countries in the area. And it soon became clear that mass vaccination was the only promising control measure to contain the disease. This was confirmed, shortly afterwards, by the European Food Safety Authority (EFSA)<sup>2</sup> who issued an urgent opinion to this effect.

Information was exchanged between the EU and all countries concerned and the concept of a coordinated vaccination policy against LSD, supported by the EU in various ways, was quickly embraced by veterinary authorities in the region. An LSD Ministerial Conference in Sofia in September 2016 further consolidated this approach and provided the opportunity for an actual LSD regional control policy for Lumpy Skin Disease in South East Europe to be adopted.

Within a few days of the conclusion of the above conference, EU Member States voted in favour of a new set of sophisticated LSD measures adapted to the epidemiological situation on the basis of available information on the disease. These measures were instrumental in introducing for the first time, the concept of “LSD free zones with vaccination”.

At the same time, Croatia - an EU Member State not affected by LSD - became the first country in the region to implement preventive vaccination against the disease. This bold innovation further paved the way for the adoption of similar measures by other countries at risk of LSD.

The situation today shows that the vaccination policy in the area has delivered very promising results. There has been no further spread of LSD to the north or west of the affected area as of October 2016 and virtually no new outbreaks have occurred in those affected countries which have chosen to implement full vaccination.



A small dairy farm in Europe

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<sup>2</sup> <https://www.efsa.europa.eu/en/efsajournal/pub/4573>



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Dairy cow grazing in Eastern Europe

While these results are very promising, there is no place for complacency.

The possibility of disease recurrence in the months to come and the unfavourable epidemiological situation in the surrounding areas has made preparedness for LSD an integral part of our 2017 work programme.

Thanks to the *Standing Group of Experts on Lumpy Skin Disease in South-East Europe*, established in July 2016 under the umbrella of the FAO/OIE GF-TADs for Europe, we now have a platform that brings together all countries in the area. Together with renowned LSD experts, the OIE, the FAO and the European Commission, this group will continue to discuss, exchange information and plan their actions to contain the disease based on the best available scientific advice. The results of our latest meeting in Istanbul in December 2016 bear testimony to these facts.<sup>3</sup>

LSD is not the first, and in all likelihood, will not be the last, emerging animal disease crisis.

The fight to contain it may well be long and intense. However, it is also a useful reminder that when dealing with transboundary animal diseases, we must always be prepared for the unexpected, never

forgetting that a given disease may behave in a completely different manner when entering a 'new' area. Furthermore we should be ready to review our policies, as and when needed, to control emerging diseases using a flexible and open-minded approach.

The management of LSD in South-East Europe in the years 2015 and 2016 has been intense and demanding: for everyone involved, everywhere and at all levels. A lot of hard work and many innovations had to come together, in a very short time, often under strenuous and stressful conditions. I am confident that this work has contributed in no small way to the protection of the farming sector in our countries. It is indeed this that should be our biggest reward and our strongest incentive to continue our efforts, not solely against LSD but against any other emerging animal disease. Regional coordination and close cooperation between the countries involved will certainly be our biggest weapon in this common fight.

In conclusion, I would like to take this opportunity to thank colleagues from all the veterinary services in all countries of South-East Europe that stood side by side in this battle against LSD. I have been touched by their openness, their commitment and their unfailing efforts to battle this disease. <sup>360</sup>

**“ I am confident that this work has contributed in no small way to the protection of the farming sector in our countries ”**

<sup>3</sup> [http://web.oie.int/RR-Europe/eng/Regprog/en\\_GF\\_TADS%20-%20Standing%20Group%20LSD.htm#LSD1](http://web.oie.int/RR-Europe/eng/Regprog/en_GF_TADS%20-%20Standing%20Group%20LSD.htm#LSD1)



## THE DISEASE

## Epidemiology of Lumpy Skin Disease

Contributor: Eeva S.M. Tuppurainen<sup>1</sup>

Outbreaks of lumpy skin disease (LSD) typically occur as epidemics separated by several years (Davies, 1991). It is not known where the virus resides between epidemics. Outbreaks are usually seasonal, but they are not restricted to warm and humid seasons with abundance of blood-feeding vectors: in many of the regions affected there is no completely vector-free season, so year-round outbreaks can occur. Morbidity varies between 2 percent and 45 percent; mortality is usually less than 10 percent (Coetzer, 2004). The susceptibility of host animals depends on immune status, age and breed rather than the virulence of the virus. European high-producing cattle breeds are generally more susceptible than indigenous African and Asian breeds (Tageldin *et al.*, 2014); cows at the peak of milk production are usually the most severely affected.

Asymptomatic but viraemic cattle are commonly detected in the field and among experimentally infected animals (Annandale *et al.*, 2013; Osuagwu *et al.*, 2007; Tuppurainen *et al.*, 2005; Weiss, 1968). There are frequent references in the literature to so-called “natural resistance” against lumpy skin disease virus (LSDV) in cattle (Weiss 1968), but more studies based on sensitive molecular methods are needed to establish whether such animals are in fact sub-clinically infected. Halting the spread of the disease requires recognition of the possible presence in an affected herd of viraemic animals that do not show skin lesions but can transmit the virus via blood-feeding vectors. Movements of unvaccinated cattle from infected regions constitute a major risk of spreading the disease.

Affected animals with skin lesions shed virus-containing crusts into the environment. In contaminated premises, thorough cleaning – removal of dirt, dung and loose surface material – is therefore required before disinfection, and the disinfectant used must be able to penetrate organic material

without losing its efficacy. Instructions on decontamination are given in the FAO Animal Health Manual (FAO, 2001).

Infected cattle will eventually become clear of infection; no carrier stage is known to occur in cattle. Animals that recover from natural infection are resistant to reinfection, but more research is required into the completeness of this protection and to determine whether cattle are protected only from severe disease. Calves born to naturally infected or vaccinated cows are protected by passive maternal immunity; in practice, such calves are vaccinated between three and six months of age. In an outbreak, calves born of naïve mothers can be safely vaccinated at any age. More studies are needed to investigate the duration of maternal immunity and to establish whether calves vaccinated at less than three months of age need boosters.

Domestic cattle and Asian water buffalo are affected by LSDV (El-Nahas *et al.*, 2011), and some strains may replicate in sheep and goats. Although mixed herds of cattle, sheep and goats are common, there is to date no epidemiological evidence that small ruminants constitute a reservoir for LSDV. The role of wildlife in the epidemiology of LSD is not well understood either: wild ruminants such as springbok (*Antidorcas marsupialis*) are known to be infected (Lamien *et al.*, 2011) and the susceptibility of impala (*Aepyceros melampus*) and giraffe (*Giraffa*

*camelopardalis*) has been demonstrated experimentally (Young *et al.*, 1970); African buffalo (*Syncaerus caffer*) have been found to be seropositive (Davies, 1982; Fagbo *et al.*, 2014) and antibodies have been detected in wild ruminants such as blue wildebeest (*Connochaetes taurinus*), eland (*Taurotragus oryx*) and greater kudu (*Tragelaphus strepsiceros*) (Barnard, 1997).

Transmission of LSDV generally occurs mechanically biting as blood-sucking insect and tick vectors feed on cattle and change host frequently. The major vector is likely to vary between regions depending on climate, season, temperature, humidity and vegetation.

The common stable fly (*Stomoxys calcitrans*) is one suspected vector for LSDV: laboratory experiments have shown that it transmits sheep pox and goat pox viruses, which are closely related (Kitching and Mellor, 1986). In a recent study, high relative abundance of *S. calcitrans* was associated with LSD outbreaks in dairy farms in Israel (Kahana-Sutin *et al.*, 2016). Experimental transmission of LSDV by female *Aedes aegypti* mosquitoes was reported in Chihota *et al.* (2001).

The vector competence for LSDV of some African tick species has been described: interrupted feeding is a natural behaviour of male ticks of the African species *Rhipicephalus appendiculatus* (brown ear tick) and *Amblyomma hebraeum* (African



A herd of African buffalo grazing in a national park

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bont tick). In an experimental setting, *R. appendiculatus* males were capable of mechanical transmission of LSDV from infected to naïve hosts (Tuppurainen *et al.*, 2013a). There is less evidence with regard to *Amblyomma hebraeum* males (Lubinga *et al.*, 2015; Tuppurainen *et al.*, 2011), but it is likely that they are equally important mechanical vectors for LSDV. Infected African blue tick (*R. [Boophilus] decoloratus*) females have been shown to transfer the virus via eggs to subsequent larvae, which were in turn able to infect naïve recipient cattle (Tuppurainen *et al.*, 2013b); this mode of transmission can also occur mechanically during venereal transmission.

Investigation is needed to establish the vector competence of local insect and tick species in newly affected regions and to address a major epidemiological knowledge gap – whether biological transmission occurs in arthropod vectors. Because the LSDV is transmitted by vectors, it is clear that vaccination is the most effective control measure.

Transmission of LSDV by direct contact is considered to be relatively ineffective. Infected cattle excrete the virus in saliva and nasal discharges, which may contaminate common feeding or watering sites (Weiss, 1968). It is also known that LSDV persists in the semen of infected bulls: natural mating or artificial insemination may hence be a source of infection for cows and heifers (Annandale *et al.*, 2013). In the field, infected pregnant cows are known to give birth to calves with skin lesions (Rouby and Abouloud, 2016). Iatrogenic intra-herd or inter-herd transmission occurs when infected herds are vaccinated or injections are administered without changing needles between animals. The potential role of air currents in long-distance transport of LSDV has been investigated by Klausner *et al.* (2015). It

is possible that birds could disseminate of the virus by carrying infected insects and ticks, but this would be difficult to investigate. <sup>360</sup>

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Dairy farm in Eastern Europe



## THE DISEASE

# Diagnostic assays for the detection of Lumpy Skin Disease virus and antibodies

Contributor: Eeva S.M. Tuppurainen<sup>1</sup>

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The control and eradication of lumpy skin disease (LSD) requires that national reference laboratories have full diagnostic capacity, competent personnel and adequate equipment, materials, reagents and funding. Various virological, molecular and serological diagnostic tools are available for the identification and characterisation of lumpy skin disease virus (LSDV): it is recommended that methods used be accredited by appropriate quality assurance systems and that processing, testing of samples and reporting of test results be carried out in accordance with good laboratory practice (ISO 17025).

Virus isolation is the method used to investigate the viability of the virus in the samples. LSDV can be propagated in a variety of primary cells or cell lines of bovine, ovine or caprine origin. It grows slowly on cell cultures, and the first cytopathic effect changes can usually be detected four to six days after inoculation. Because the cytopathic effect may take up to two weeks to appear and may require several passages, polymerase chain reaction (PCR) assays have replaced virus isolation as a primary diagnostic assay. Electron microscopy can also be used to detect the virus in the samples.

In most reference laboratories the basic tests for LSDV diagnosis comprise molecular methods for generic detection of a Capripox virus (CaPV) – Bowden *et al.* (2008), Stubbs *et al.* (2012), Ireland and Binepal (1998), Haegeman *et al.* (2013), Tuppurainen *et al.* (2005) and Balinsky *et al.* (2008) – but these methods do not differentiate between LSDV, sheep pox virus and goat pox virus. The conventional CaPV PCR method is not so fast as real-time PCR, but it is reliable and sensitive and is a valuable back-up if laboratory computer systems are disrupted.

Several species-specific molecular assays have been published – Lamien *et al.* (2011a and 2011b), Le Goff *et al.* (2009) and Gelaye *et al.* (2009). These methods are of value when clinical signs of LSD are detected in a herd vaccinated with a sheep pox virus or goat



Free grazing beef cow in Southern Europe

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pox virus vaccine, or if characteristic clinical signs of LSD are detected in wild ruminants or if all three CaPV diseases are present in the country concerned.

If cattle affected by LSD are detected in a herd vaccinated with an attenuated LSDV vaccine, a molecular assay that differentiates between a virulent LSD field virus from the attenuated vaccine strain can be used (Menasherow *et al.*, 2014; Menasherow *et al.*, 2016). An alternative but more time-consuming method is to sequence the appropriate parts of the LSDV genome (Gelaye *et al.*, 2015). Publication of validated PCR methods for differentiating attenuated LSDV from field strains is forthcoming.

Although the clinical signs of LSD are highly characteristic, a simple, easy and affordable pen-side test is needed. The first PCR method suitable for a portable thermocycler is described in Armson *et al.* (2015), but it has the disadvantages that trained field personnel and expensive portable equipment, reagents and materials are needed, and that it may be unaffordable in countries with limited resources and widespread disease. Two loop-mediated isothermal amplification assays for LSDV published by Murray *et al.* (2013) and Das *et al.* (2012) have the great advantage that they can be developed into a lateral-flow device type assays (pen-side kits) that can be easily administered by field personnel.

In vaccinated and naturally infected animals, antibodies remain at levels detectable by traditional serological tools such as serum/virus neutralization test (SNT) for three to six months after infection or vaccination, after which cell-mediated immunity is likely to become the major element in protection. Further studies using more experimental animals and novel, more sensitive serological methods are required to investigate more accurately the long-term duration of LSDV antibodies following infection and vaccination. Because no differentiating infected from vaccinated animals vaccines exist for LSDV, and because the members of CaPV genus cross-react, serological assays are suitable for investigating recent outbreaks only in unvaccinated population. Sero-surveillance can be used to demonstrate the disease-free status of a country, however, provided that it is combined with active and passive clinical surveillance.

SNT is an accurate gold standard assay, but it requires live virus and cell cultures and hence cannot be used in national reference laboratories operating in low-level bio-containment facilities. To increase the number of samples tested on a single plate and to reduce the time needed to interpret the results, the serum/virus neutralization test can be modified to use only the two lowest dilutions of the test serum and a fluorescent marked LSDV (Wallace *et al.*, 2007).

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Veterinarians vaccinating a calf in Burkina Faso

Other serological tools include an immune-peroxidase monolayer assay described by Haegeman *et al.* (2015) and an indirect fluorescent antibody test described by Gari *et al.* (2008). Several enzyme-linked immunosorbent assays (ELISA) have been published, including indirect ELISAs based on killed whole virus, recombinant antigens or synthetic peptides (Babiuk *et al.*, 2009; Bhanot *et al.*, 2009; Bowden *et al.*, 2009; Tian *et al.*, 2010). Novel ELISA for the detection of antibodies against LSD have recently become commercially available. The new ELISA is suitable for large-scale testing and also for use in laboratories operating in lower biosecurity levels.

Although serology cannot be used to detect virus circulation in vaccinated populations, it is useful for monitoring antibody responses to vaccines or to demonstrate unnoticed or unreported outbreaks in high-risk regions in disease-free countries. It is important to note that if outbreaks have occurred more than six months previously, antibody levels may be at undetectable levels and cattle may consequently be sero-negative: this will be so even if the cattle were naturally infected or vaccinated, in which case immunity is mainly cell-mediated. <sup>360</sup>

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## THE DISEASE

# Current Knowledge about Vaccination against Lumpy Skin Disease

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The main prerequisites of a good vaccine are its safety and protection from infection. The safety of a vaccine is determined by the frequency and severity of the adverse reactions it might cause, by the probability of reversion to virulence and by its purity. The protection provided by a vaccine depends on the specific immunologic response it elicits; it can be measured in terms of its efficacy or effectiveness. The efficacy of a vaccine is shown by the percentage of morbidity prevented by vaccination, which is calculated by the following equation:

$$1 - R_v / R_c$$

where  $R_v$  is the incidence of the disease in vaccinated animals and  $R_c$  is the incidence in non-vaccinated animals. Efficacy can be calculated from the results of randomized field vaccine trials in which animals in the field are allocated to vaccination or non-vaccination groups, between which the incidence of natural infection is compared. Such studies require the occurrence of natural infection in the field, and involve vaccination of hundreds or even thousands of animals with subsequent monitoring in time intervals related to the nature of disease occurrence (I would suggest monitoring of every three days for lumpy skin disease).

Alternatively, vaccine efficacy can be measured in challenge studies in which vaccinated and non-vaccinated animals are inoculated with a certain amount of virus. Such studies involve small numbers of animals and enable perfect control of the amount of virus in the challenge dose (For LSD a challenge dose of  $2 \times 10^5$ - $10^6$  TCID was previously used (Ngichabe *et al.*, 1997, Gari *et al.*, 2015)). They do not, however, represent the effects obtained under conditions of natural infection. When a vaccine is used in the field its effectiveness can be measured in the same way as efficacy. It is based on incidence rates measured in real-life conditions, however, with no prior experimental design. In such studies, evaluation of the reduction of disease by

the vaccine is performed across a non-randomized application of vaccine in different groups of animals vaccinated at different times by different people. This may provide the most realistic results, but on the other hand it might involve bias because allocation of vaccination is not random.

This short article is a review of the available literature on vaccines used to prevent lumpy skin disease (LSD). The PubMed and Google Scholar databases were searched for challenge studies, efficacy or effectiveness studies in relation to these vaccines and for reports of vaccine use and vaccine safety in the field.

All the vaccines used to prevent LSD are currently based on live attenuated viruses. These vaccines can be roughly divided into two classes: i) homologous vaccines; and ii) heterologous vaccines. The homologous vaccines are based on attenuated LSD viruses (LSDV), whereas the heterologous vaccines are based on attenuated sheep pox or goat pox viruses.

## HOMOLOGOUS VACCINES

Data on safety and efficacy exist for two homologous virus strains: the Neethling strain and the Kenyan goat and sheep pox (KGSP) strain, which was recently revealed to be a strain of LSDV (Tuppurainen *et al.*, 2014).

## NEETHLING STRAIN BASED VACCINES

The most extensive and reliable data are available on the Neethling strain based vaccines, which are based on cell-adapted viruses of the original Neethling LSDV (Tuppurainen *et al.*, 2015). These vaccines are currently manufactured in South Africa by two producers. Before 2013 there were no reliable data from a controlled study that tested the effectiveness or efficacy of these vaccines. In a study carried out in 2013 during a large LSD epidemic in Israel, a commercial Neethling based vaccine was compared to a sheep pox (RM-65) live attenuated vaccine – Jovivac®, Jordan – administered at the same dose. Both vaccines were randomly and simultaneously administered



LSD affected cattle

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to 4 694 cows in 15 dairy herds. The Neethling vaccine was four times more effective than the sheep-pox vaccine for preventing a laboratory confirmed disease – that is, its relative vaccine effectiveness was 77 percent. No data could be recovered from this study as to the effectiveness of the sheep pox vaccine because there were no placebo controls.

Of the cows vaccinated with the attenuated Neethling vaccine, 0.38 percent developed an adverse effect as a result of the vaccination; this was mostly very mild and was characterized by the appearance of small lumps over the body. This effect resembled a very mild form of LSD, and was probably caused by infection and multiplication of the vaccine virus. All the cases of this adverse event occurred in the first two weeks after vaccination (Ben-Gera *et al.*, 2015).

The findings of this study were later reinforced by an analysis of data from an outbreak that occurred in Greece during 2016. Because reactive vaccination in the region of Serres was conducted during the advance of the outbreak, it was possible to compare the morbidity in vaccinated and non-vaccinated herds. The analysis revealed that at two weeks after vaccination the effectiveness of the vaccine reached 62.5 percent and one month after vaccination it reached 80 percent (AHAW [EFSA Panel on Animal Health and Welfare], 2016).

In a small-scale study in Ethiopia, a Neethling strain vaccine manufactured by the National Ethiopian Veterinary Institute failed to protect calves from challenge by a virulent LSDV strain. The disagreement between the results of this study and the two mentioned above and between much larger studies raises concerns about the quality of the vaccine used in the

Ethiopian trial and the possibility that it might have been over-attenuated (Gari *et al.*, 2015).

During the use of the Neethling vaccine in Israel there was an occasion on which contamination of a vaccine batch by bluetongue virus was detected by the Israeli Kimron Veterinary Institute (Bumbarov *et al.*, 2016).

## KENYAN GOAT AND SHEEP POX VACCINES

The KSGP-180 and KSGP-240 viruses were collected from infected sheep and goats during outbreaks of sheep and goat pox in Kenya in the 1970s. The former was attenuated by 18 passages in bovine foetal muscle cells; the latter was only passaged six times in cell cultures. KS-1 is a virus derived from attenuated KSGP-240; it was also used as a vaccine against LSD (Tuppurainen *et al.*, 2014). KSGP – and hence KS-1 – was shown to be a strain of LSDV (Tuppurainen *et al.*, 2014). There are no large-scale studies testing the effectiveness of these vaccines, and there are contradictory data regarding the effectiveness of the Kenyan strains for protection against LSDV. Two retrospective studies in Ethiopia report that the KS-1 vaccine was ineffective for protection against LSDV (Ayelet *et al.*, 2013 and 2014), but there are field reports from Kenya that the KGSP-180 vaccine is safe and protective (Davies and Mbugwa, 1985). Information about the manufacturer of these vaccines is lacking in the reports. A mixture of two recombinant KS-1 vaccines expressing either the haemagglutinin or fusion proteins of rinderpest virus did not elicit adverse effects and showed protection from challenge with a virulent Neethling strain of LSDV in 5/5 zebu cattle six months after vaccination, in 4/5 after 12 months, in 4/4 after

two years and 2/5 after three years (Ngichabe *et al.*, 1997 and 2002).

Vaccination of dairy cattle in Israel during 1992 with the KSGP-240 caused a high rate of vaccine-associated adverse effects. These were characterized by typical generalized LSD intradermal skin lesions, fever, eye and nose secretions, enlarged lymph nodes, anorexia and a clear decline in milk yield (Yeruham *et al.*, 1994). It can hence be concluded that although the KSGP vaccine might protect from infection by LSDV, there is not enough data from controlled studies with regard to their safety and effectiveness.

## ATTENUATED GOAT POX VACCINES

Several studies have shown the efficacy of goat-pox strains for protecting cattle from challenge by LSDV. The Kedong and Isiolo strains were isolated from sheep in Kenya during the 1950s, and were later shown to be goat pox viruses (Tuppurainen *et al.*, 2014). Both were shown to protect cattle from LSDV challenge (Capstick and Cocackley, 1961). In a recent study a commercial vaccine based on an attenuated Gorgon strain of goat pox virus isolated in Iran was administered at two doses to ten calves, five in each dose group. All calves were completely protected from challenge by a wild Ethiopian strain of LSDV. No adverse effects were observed in the vaccinated calves (Gari *et al.*, 2015). Attenuated goat pox vaccines currently seem to be a good alternative to vaccination by homologous vaccines. There is a need, however, for more extensive data from the field and for larger-scale clinical trials to ensure the efficacy and safety of these vaccines.



A herd of cattle, Ethiopia



## SHEEP POX VACCINES

Currently there is not enough evidence confirming efficacy of for sheep pox based vaccines, though until recently it was believed that vaccination by sheep pox vaccines could provide protection from infection by LSDV. This probably wrong concept was based on the genetic similarity between the different capripox viruses.

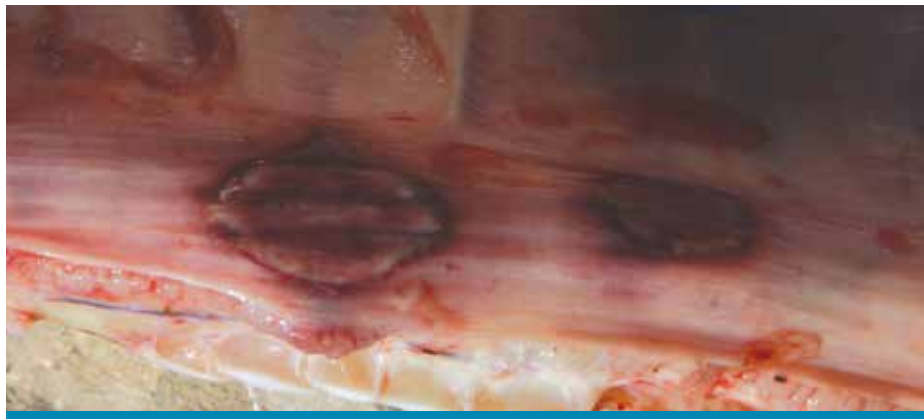
Earlier studies using thought-to-be sheep pox strains provided protection from challenge by LSDV, increased the confidence that such cross-protection in fact exists. But these were later shown as actually LSDV or goat pox strains (Tuppurainen *et al.*, 2014). To date, the sheep pox strains that have been used most to vaccinate against LSDV include the Romanian strain, the Yugoslavian RM-65 strain and the Bakirköy strain used in Turkey. The Romanian sheep pox virus strain was also used in Egypt (Tuppurainen *et al.*, 2015) and although it was claimed that it immunized cattle (Davies, 1991) and that it provided protection from challenge (Michael *et al.*, 1997), there is no report of a large-scale controlled study examining the efficacy of this vaccine for prevention of infection by LSDV. The disease remains endemic in Egypt despite the use of this vaccine, but this might be a result of low vaccine coverage and reduced efficacy.

The RM-65 vaccine was used in Israel after LSD outbreaks in 1989, 2006 and 2007 in a dose ten times lower than the dose of the homologous Neethling vaccine. During 2007, several herds that were vaccinated once, twice or three times with this low dose vaccine developed disease. In some of these herds incidence of 44 percent was observed (AHAW, 2015). The vaccine was shown to be ineffective in controlling the outbreak of LSD in Israel during 2012. The dose was therefore increased by a factor of ten. At this dose, however, the vaccine was demonstrated to be still significantly inferior to a Neethling vaccine used at the same dose (Ben-Gera *et al.*, 2015).

The Bakirköy vaccine was used during the LSD outbreak in Turkey. No significant differences in disease incidence were demonstrated between cattle vaccinated with this vaccine and non-vaccinated cattle (Sevik and Dogan, 2016). Although the vaccine was extensively used in Turkey, the disease has persisted in the country since 2013.

## CONCLUSIONS

The largest amount of information regarding safety and efficacy currently exists for the Neethling vaccine. The effectiveness of this vaccine seems to be about 75 percent in terms of preventing LSDV at the herd and the individual animal level. Full protection is provided by this vaccine about one month after vaccination, though there is evidence



LSD lesions, multifocal, 1.5-2.5 cm diameter, well-demarcated, ulceration of the tracheal mucosa

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that it is effective in certain individuals at two weeks as well. This vaccine might cause a mild adverse effect characterized by multiple small lumps on the skin, similar to the lesions formed during LSD. Detection of contamination of batches of Neethling and RM-65 vaccines emphasizes the importance of producing these vaccines under good manufacturing practice conditions.

In a recent urgent advisory provided by EFSA, different strategies of vaccination and stamping out were simulated. The simulation demonstrated that pre-emptive vaccination with the Neethling vaccine is significantly superior to reactive vaccination. Given the performance of pre-emptive vaccination, total stamping out has almost no advantage for disease control over modified stamping out, which means stamping out only generalized clinical cases (AHAW, 2016). <sup>360</sup>

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## SITUATION

## Lumpy Skin Disease: Situation, surveillance and control activities in Turkey

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**L**umpy skin disease (LSD) is an acute cattle disease caused by lumpy skin disease virus, also known as Neethling virus. LSD virus (LSDV) belongs to the genus *Capripox* in the *Poxviridae* family (Tuppurainen and Oura, 2012). The disease is of economic importance as it can cause a temporary reduction in milk production, temporary or permanent sterility in bulls, damage to hides and death as a result of secondary bacterial infections (OIE, 2010). LSD is a notifiable disease in Turkey and to the World Organization for Animal Health (OIE). LSD was first recorded in Zambia in 1929. In 1940s the disease spread to other southern African countries. Today only four African countries – Algeria, Libya, Morocco and Tunisia – declare that they are LSD-free. The disease was reported in Egypt for first time in May 1988, and in 1989 it crossed from Africa and spread into the Middle East where it was first diagnosed in Israel in 1989 (Tuppurainen and Oura, 2012). In the following years cases were reported in Bahrain, Jordan, Kuwait, Lebanon, Oman and Yemen (OIE Reports). After an absence of 17 years, LSD was again reported in Egypt in 2006, and despite a comprehensive vaccination campaign the disease spread rapidly throughout the country (Tuppurainen and Oura, 2012). Although LSD was observed only in the south of Israel

in 1989, 2006 and 2007, it also appeared in the north of Israel in July 2012 and in the neighbouring areas of Syria and Lebanon (OIE Report, 2012; Sharir, 2012). The outbreak occurred in July 2012 and was resolved by September 2013 (OIE Report, 2013). The first notification from Turkey to OIE was in September 2013, in which year the disease was reported by Jordan in April, by Palestine in May and by Iraq in August.

### LSD IN TURKEY

The first report to OIE of LSD in Turkey was made on 17 September 2013. The first clinically suspected cattle were seen in Kahramanmaraş province in August 2013. At that time, eight samples of skin lesions, blood samples and nasal discharge were examined by polymerase chain reaction (PCR) test at the LSD in accordance with the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* (2010).

After the first confirmation of the disease, epidemiological investigations were conducted in two villages in Elbistan district in Kahramanmaraş province and in one village in Gerçüş district in Batman province. The method of assessment was a combination of active disease follow-up, laboratory examination of samples collected from diseased and animals suspected of

infection and questionnaire data collected from five dairy farms involving 235 animals. The questionnaire format covered husbandry systems, animal movements, climate and season, presence of watercourses, factors that might cause an increase in populations of blood-feeding arthropods and insect vector populations, communal grazing and presence of an animal market, biosafety measures, veterinary services and LSD vaccination history.

Of the 235 animals tested, only 30 were found to be positive for LSDV. The number of sick, exposed and dead animals and the morbidity and mortality rates for five dairy farms are listed in Table 1.

In Turkey, LSD outbreaks emerged at the same time in different dairy herds in different villages and even different provinces – Kahramanmaraş and Batman. Although there was no movement of animals between these herds, the outbreaks emerged at the same time. According to the herd owners, all herds were located near bodies of water and there was communal grazing. For this reason it was concluded that LSD virus was transmitted by vectors in the first outbreak in Kahramanmaraş. The virus probably entered the country as a result of uncontrolled movement of livestock, and the presence of competent vectors enabled it to establish.

**Table 1:** Clinical and laboratory diagnosis of LSD in cattle in the first outbreaks in Turkey

Province	District	Village	Number of Cattle	Number of the clinical cases	Number of Dead Cattle	Morbidity (%)	Mortality (%)
Kahramanmaraş	Elbistan	Çatova	17	10	4	58.8	23.5
Kahramanmaraş	Elbistan	Çatova	6	1	0	16.7	0.0
Kahramanmaraş	Elbistan	Çatova	15	5	0	33.3	0.0
Kahramanmaraş	Elbistan	Kalealtı	7	1	0	14.3	0.0
Batman	Gerçüş	Karalan	190	13	8	6.8	4.2

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## LSD CONTROL STRATEGY IN TURKEY FROM 2013 TO 2016

According to the Turkish Statistical Institute there were 14 million cattle in Turkey in 2016. The total cattle population includes 45.8 percent pure breed, 41.2 percent hybrid breed and 12.9 percent native breed. There are 1.5 million registered dairy and meat business in Turkey.

The LSD control strategy is based on the veterinary services and Plant Health, Food and Feed Law no. 5996, and is in compliance with Council Directive 92/119/EEC apart from modification of the directions for stamping out. LSD is a compulsorily notifiable disease in Turkey, and control measures include laboratory confirmation of disease, destruction of infected animals, ring vaccination, control of animal movements, quarantine of outbreak premises and insect control. Cleaning and disinfection are also among the controls against the disease in the outbreak areas.

Because of antigenic homology and cross-protection between sheep pox, goat pox and LSDV, any of these viruses can be used as a vaccine strain to protect cattle against LSD (Kitching, 1983). There are several commercially available live attenuated vaccines that are based on LSDV or the other capripox viruses – sheep pox or goat pox (Brenner *et al.*, 2009; OIE, 2010; Tuppurainen and Oura, 2012). Four live attenuated capripox virus strains are currently used for vaccine production: i) Kenyan sheep pox; ii) Yugoslav RM 65 sheep pox; iii) Romanian sheep pox; and iv) South African Neethling LSD strains (OIE, 2010). A major neutralizing site of the capripox virus is shared by all four strains, so they have all been used in vaccinations of cattle to protect against LSD infection in different parts of the world (Brenner *et al.*, 2009; OIE, 2010).

Although the vaccine strains are characterized, there is no vaccine available that has met the safety and efficacy standards set by the European Union. Live attenuated vaccines are commercially available, but problems with poor vaccine efficacy have been reported in some countries (Yeruham *et al.*, 1994; Brenner *et al.*, 2006 and 2009, Ayelet *et al.*, 2013; Abutarbush, 2014; Abutarbush *et al.*, 2014). Some countries have produced vaccines by using local field strains, but these vaccines are reported by EFSA to be unsafe and they do not satisfy all the OIE criteria for safe vaccine production (OIE, 2015). Some researchers report that using sheep and goat pox virus vaccine to protect cattle herds from LSD was ineffective (Brenner *et al.*, 2009; Ayelet *et al.*, 2013). This lack of immunity may be a result of the vaccine strain chosen, over-attenuation of the seed virus, general

lack of quality of the vaccine, the dose of vaccine used and different application methods.

In 1975 a sheep pox and goat pox virus epidemic occurred in the Bakırköy district of Istanbul. The local virus strain – called the Bakırköy strain – was isolated from the outbreak by the Pendik Veterinary Control Institute. After 65 passages in primary lamb kidney cell cultures the virus was attenuated and stock was lyophilized for vaccine. The Bakırköy sheep and goat poxvirus strain vaccine – Penpox – M – contains at least  $10^{2.5}$  TCID<sub>50</sub> per dose, and it is still in use for sheep pox and goat pox disease control in Turkey.

When LSD was first observed in Turkey in 2013, the Commission of the Food, Agriculture and Livestock Ministry decided on the use of Penpox-M against LSD. One dose  $10^{2.5}$  TCID<sub>50</sub> of vaccine was used, as suggested by the OIE Manual. Observations from the field indicate that Penpox-M was effective in inducing protection against LSD

**“ In 2015 the LSD control strategy was revised in the light of experience in 2014. All provinces in Turkey were included in the vaccination campaign ”**

and that no serious side-effects were seen. Research at the national reference laboratory, however, suggests that three sheep doses of Penpox-M vaccine are required to protect against LSD. More scientific studies are therefore necessary to determine the efficacy, effective dose and duration of immunity of Penpox-M administered to large ruminants. There is also a need to research the molecular characterization of circulating field virus and the reliability, efficacy, immunity and side-effects of available commercial homologous LSD vaccines (Tuppurainen and Oura, 2012; Tuppurainen *et al.*, 2014a; Gari *et al.*, 2015). The national reference laboratory has isolated and identified LSDV from field samples, and has started to develop a homologous vaccine for LSD.

By the end of 2013 a total of 18 outbreaks had been detected in seven provinces in Turkey involving 158 infected animals. The disease control programme in 2014 and the 2013 protection and control strategy added LSD to the list of animal diseases for which compensation can be claimed. A positive

laboratory result and clinically affected animals in an outbreak zone entitle the owners to compensation at 50 percent of the market value of the animals.

In August 2014 it was observed that LSD was spreading rapidly, and that the transmission of the virus was faster than the vaccination programme. The Ministry of Food, Agriculture and Livestock then decided to implement a vaccination programme immediately in any outbreak area and in neighbouring areas. In spite of the vaccination programme, 3 109 cattle were detected with LSD in 784 outbreaks in 43 provinces at the end of 2014. Some outbreaks continued through the winter of 2013 and 2014. It was also noteworthy that up to September 2014 the epidemic spread to areas that were geographically contiguous with previous outbreaks, but after this point there was significant jumping of the epidemic to non-contiguous provinces.

Although movement controls were put in place, there were numerous animal movements each year before the Kurban festival, which falls in August or September, and consequently in 2014 most of the outbreaks occurred in August. In this situation animals that showed no signs of LSD were allowed to move from control zones to other parts of the country. It is now considered that this allowed virus transmission to more distant provinces, because some animals show no signs of disease after infection. When experimentally induced LSD, only 40 percent to 50 percent of the infected cattle developed generalized skin lesions. The remaining animals either developed localized and circumscribed painful swelling at the inoculation site of LSDV or showed no clinical signs apart from a fever reaction (EFSA, 2015).

The country-wide observations and consultations with official veterinarians led to the conclusion that some vaccinated animals were sick after vaccination. This might have been a reaction to the live vaccine as a result of predisposing factors such as lactation, pregnancy or weak physical condition, or because the animals were in the incubation period of the disease when vaccinated, or that the intensity of the outbreaks in the region overwhelmed the immunity conferred by vaccination. In 2014 a total of 4.1 million cattle were vaccinated in 43 provinces. The movement of animals was restricted for 28 days following vaccination, and in outbreak areas movements were completely restricted until the disease was no longer evident after 28 days.

In 2015 the LSD control strategy was revised in the light of experience in 2014. All provinces in Turkey were included in the vaccination campaign. The vaccination time was determined by each local authority

because of the differences between their climatic conditions, geographical status and husbandry system. The Penpox-M vaccine dose was increased to three times the sheep pox/goat pox dose, and the vaccination campaign was planned for all cattle older than three months and under nine months pregnant. The compensation rate was raised from 50 percent to 100 percent, and animal movements were not allowed until the vaccination campaign had been completed. According to the 2015 LSD control strategy, 8.3 million cattle were vaccinated in the whole country. Animal movements were restricted for 28 days following vaccination, and in outbreak areas movements were completely restricted until the disease had been eliminated.

In 2016 Turkey's LSD controls continued, with movement restrictions, quarantine, ring vaccination, sampling, diagnosis and vector control. An LSD homologous local strain vaccine study was initiated at the beginning of 2015 by the national reference laboratory.

Animal movements are strictly controlled in this context, vaccinated animals are allowed to move 28 days after vaccination, and only animals younger than three months are

**“ The compensation rate was raised from 50 percent to 100 percent, and animal movements were not allowed until the vaccination campaign had been completed ”**

allowed to move unvaccinated. A vaccine efficacy study is being conducted by the CODA-CERVA Veterinary and Agrochemical Research Centre in Belgium. A total of

10.2 million cattle were vaccinated in 2016, and 11.4 million cattle were vaccinated in 2017 (as of end of July), when animal movement conditions are the same as in 2015 (see Figure 3).

An evaluation of the three-year period of the LSD outbreaks in Turkey shows that they reached their highest level in August 2014, but declined after that time (see Figure 1). Because of the intensity of animal movements and vectors the disease has spread rapidly from east to west in Turkey, and it continues to spread to provinces that have not seen LSD before. This spread to new areas is continuing to maintain the disease in Turkey.

The number of LSD outbreaks has fallen considerably since 2014 following mass vaccination and the introduction of strict movement controls. The number of outbreaks in 2015 and 2016 decreased compared with the previous year (784 outbreaks occurred in 2014, 510 in 2015 and 221 in 2016). The increase in awareness, strategy

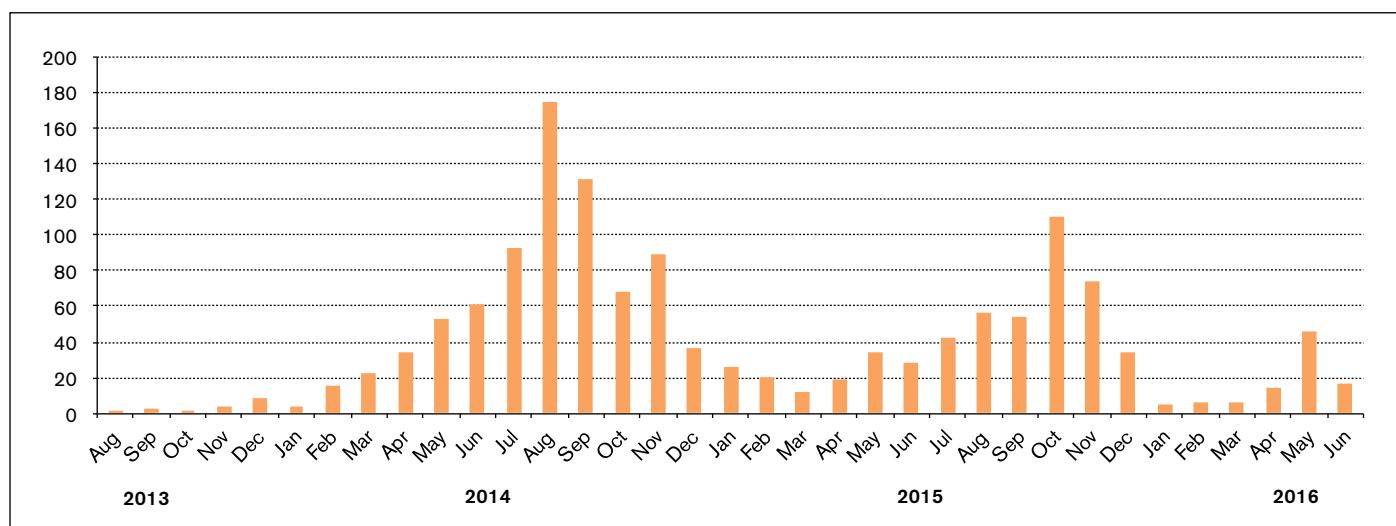


Figure 1: Monthly LSD reports, 2013–2016 in Turkey

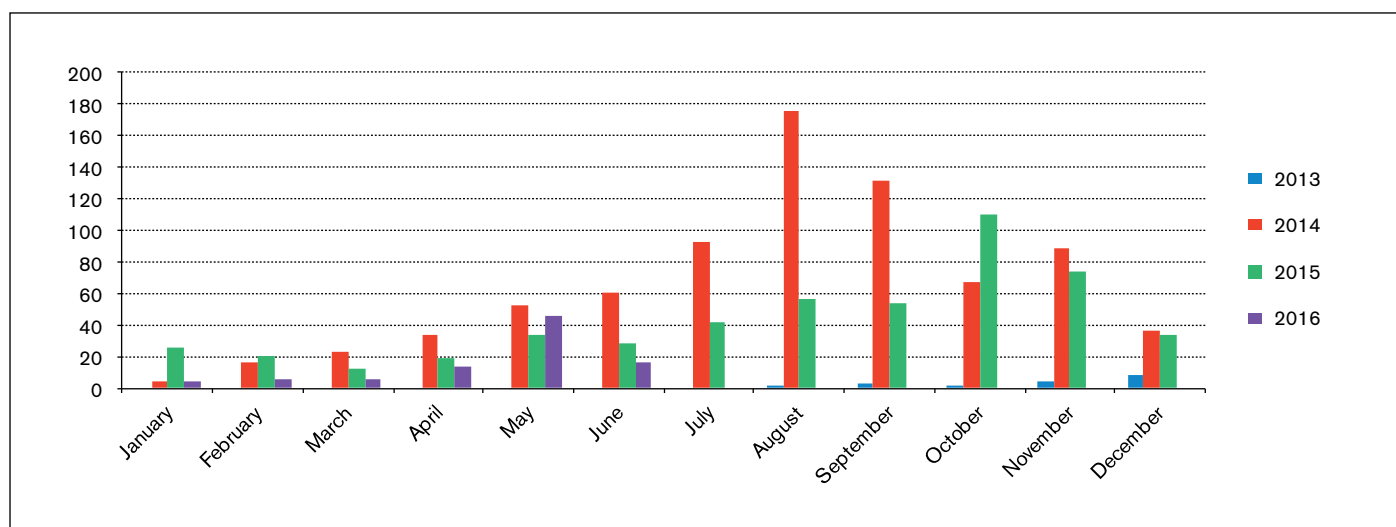
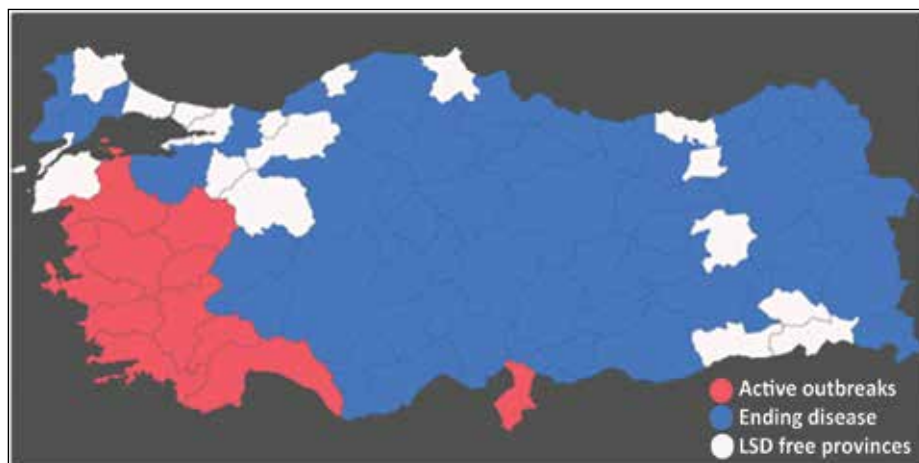


Figure 2: LSD outbreaks per month, 2013–2016 in Turkey





**Figure 3:** Active and finished outbreaks in Turkey as at 30 June 2016

revisions, increased herd immunity as a result of subclinical infections and reduced susceptibility of offspring born to vaccinated mothers also had positive effects on the disease-control programme. The cause of the increase in October 2015 was the intensity of animal movements before the Kurban festival, as was the case in August 2014 (see Figure 2).

## CONCLUSIONS

Confirmation of disease in the European part of Turkey in June 2015 was followed by confirmations from European countries. In June 2015, Greece reported the first outbreak to OIE. In 2016 the disease was observed successively in Bulgaria, the former Yugoslav Republic of Macedonia, Serbia, Kosovo, Albania and Montenegro. It is currently agreed that LSDV is transmitted mechanically via arthropod vectors. Recent published evidence shows a possible role for hard ticks in the transmission of LSDV with trans-stadial and trans-ovarial transmission occurring. In general, the outbreaks in Turkey were associated with wet and warm weather conditions with an abundance of blood feeding arthropods populations. It is noteworthy, however, that in the winters of 2013 and 2014 a small number of outbreaks occurred and that these were at altitudes ranging from 50 m to 1 300 m. This could be evidence that LSDV can be transmitted by a biological vector that can survive in the environment for a long time.

The control measures implemented in the affected areas were restriction of animal movements, vaccination, slaughter of affected animals, application of a protection and quarantine zone round infected premises, and vector control. Three years of experience suggests that movements of subclinically infected animals has the most important role of transfer of LSDV to new areas where there are naive animal populations. It has been determined that subclinically infected cattle are the source of virus for vectors in disease free-

areas. The rate of vaccination – 80 percent to 90 percent is required for effective control – and the timing of vaccination are important in controlling the disease.

Various difficulties have emerged in the fight against LSD, particularly in conducting vaccination programmes in a large animal population in different husbandry systems, and in a large number of holdings that have small numbers of animals that may be widely dispersed and grazing communally, and challenging geographical status in locations such as forested areas or situations such as free grazing at high altitude where access is difficult. <sup>360</sup>

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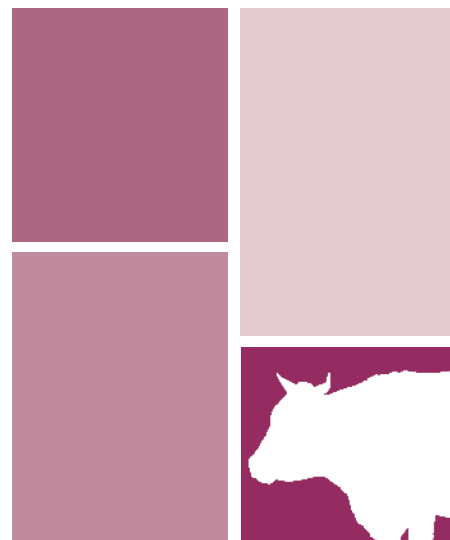
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## SITUATION

# Lumpy Skin Disease in Greece: A European approach to management of the disease

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## INTRODUCTION

Lumpy Skin Disease (LSD) entered the European Union (EU) on 20 August 2015 with the first outbreaks confirmed in East Macedonia and Thrace Region in Greece, close to the borders with Turkey (ADNS, 2015/16; Antoniou *et al.*, 2016; Antoniou and Dile, 2016; Tasioudi *et al.*, 2016). The disease spread westwards initially and subsequently to the south; it evolved in two waves: August to December 2015 and April to November 2016 (Antoniou and Dile, 2016). Until then, LSD had been considered as an exotic disease in the EU.

State veterinary authorities of the Ministry of Rural Development and Food and of the regions and Regional Units (RUs) were responsible for controlling the disease. The measures implemented and the activities undertaken were in accordance with European and national legislation and the National Contingency Plan.

## OCCURRENCE AND GEOGRAPHICAL DISTRIBUTION OF LSD IN GREECE

The first LSD outbreaks were confirmed in Evros RU and concerned two free-grazing beef cattle herds, in the delta of the Evros River, which forms the natural border between Greece and Turkey (Antoniou *et al.*, 2016; Antoniou and Dile, 2016; Tasioudi *et al.*, 2015). The delta



**Figure 1:** Map of Greece showing Regional Units and the outbreaks confirmed during 2015 (red pins) and 2016 (purple pins)  
Source: Department of Topography, Hellenic Ministry of Rural Development and Food

is a protected area and an important national wetland that hosts a variety of wildlife. Measures implemented by the Greek veterinary authorities kept the disease restricted into the Evros RU for five weeks from the start of the epizootic, during which 56 outbreaks were confirmed. From 25 September 2015, the sixth week of the epizootic, the disease moved west to other RUs. By the end of December 2015, LSD had spread to the west of northern Greece,

towards Central Macedonia and to the island of Limnos, affecting seven RUs (See Figure 1 and Figure 2). This first wave from 20 August to 15 December 2015 lasted for 17 weeks. In total, 117 outbreaks were confirmed and approximately 6 000 animals were culled (see Table 1) (Antoniou *et al.*, 2016; Antoniou and Dile, 2016; Tasioudi *et al.*, 2015).

There was a four-month interval from 16 December 2015 to 4 April 2016 without any new outbreaks – more than four incubation periods – while the vaccination campaign was already in progress (see Figure 2). Nonetheless, on 6 April 2016 the disease re-emerged in Greece in the Serres RU in the Central Macedonia Region, where vaccination coverage was low at only 40 percent of the bovine population because of restricted availability of vaccines at that time. In all cases except for a single herd it affected herds that

were unvaccinated or vaccinated during the incubation period of the disease (Antoniou *et al.*, 2016). During the following weeks, a few sporadic outbreaks emerged in neighbouring RUs with high vaccination coverage, close to 100 percent. The affected animals were unvaccinated and held in backyard, family or free grazing herds (Antoniou *et al.*, 2016). The disease then crossed the highly vaccinated areas and entered to unaffected areas

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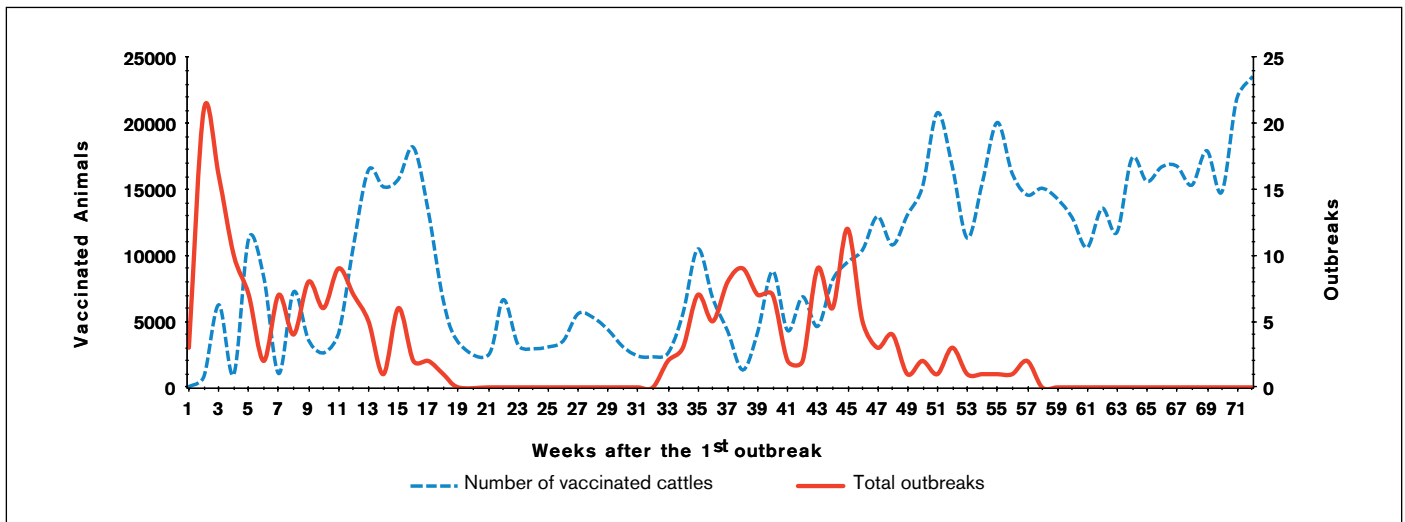
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**Figure 2:** Diagram presenting the number of outbreaks (red line) in relation to the number of vaccinations (blue line) during the weeks since the beginning of the epizootic until the end of 2016

Source: MRDF

(in the western part of southern Greece), where vaccination coverage was low at the time (see Figure 1 and Figure 2). During this second wave of 34 weeks from 6 April to 25 November 2016, 104 outbreaks were confirmed in 15 RUs (see Table 2). Approximately 6 000 bovines were culled (Antoniou *et al.*, 2016).

### CLINICAL SIGNS AND LESIONS

The main clinical signs observed included: fever at 40.0°C, depression, loss of appetite, localized or generalized subcutaneous nodules, salivation, nasal, ophthalmic and oral discharge, lameness, oedema of the legs, and ulcers on mucus membranes of the eyes and mouth (see Figure 3, Figure 4 and Figure 5). In one case where the skin was removed, nodules were observed on the inner surface of the skin and circular lesions were identified on the subcutaneous fat and on the meat (see Figure 6).

In advanced cases, ulcerated nodules and diarrhea were also observed and, depending on the severity of the clinical disease, some animals died (Antoniou *et al.*, 2016; Antoniou and Dile, 2016; Tasioudi *et al.*, 2015).

In some cases, early clinical signs observed even before the appearance of nodules, were lameness and oedema of the legs (Antoniou *et al.*, 2016). At the onset of the disease the skin nodules were not always obvious, and could be identified only by palpation.

Morbidity in the affected herds was estimated at 9 percent in 2015 and 7 percent in 2016; mortality was estimated at 0.7 percent in 2015 and 1.5 percent in 2016. Total culling of all animals in a herd, in the event of a positive LSD virus (LSDV) diagnosis, stopped the spread of the disease, and hence affected the range of clinical signs observed and the morbidity and mortality rates.

**Table 1:** First wave of LSD in Greece, August to December 2015

RUs	Number of outbreaks	Date of confirmation of first outbreak	Date of confirmation of last outbreak	Duration of outbreaks (day of first confirmation – day of last confirmation)
Evros	64	20/08/2015	23/10/2015	65 days
Kavala	1	01/10/2015	01/10/2015	-
Limnos	1	07/10/2015	07/10/2015	-
Xanthi	18	25/09/2015	09/11/2015	46 days
Chalkidiki	21	14/10/2015	14/12/2015	62 days
Rodopi	9	14/10/2015	15/12/2015	63 days
Thessaloniki	3	11/11/2015	09/12/2015	29 days
<b>Greek Territory</b>	<b>117</b>	<b>20/08/2015</b>	<b>15/12/2015</b>	<b>118 days</b>

**Table 2:** Second wave of LSD in Greece, April 2016 to November 2016

RUs	Number of outbreaks	Date of confirmation of first outbreak	Date of confirmation of last outbreak	Duration of outbreaks (day of first confirmation – day of last confirmation)
Serres	44	06/04/2016	27/05/2016	52 days
Thessaloniki	5	18/05/2016	23/11/2016	190 days
Kavala	3	18/05/2016	23/06/2016	37 days
Pella	18	23/05/2016	08/08/2016	78 days
Kilkis	1	26/05/2016	-	-
Drama	3	01/06/2016	14/06/2016	14 days
Imathia	14	16/06/2016	03/08/2016	49 days
Florina	4	30/06/2016	03/08/2016	35 days
Limnos	3	13/06/2016	22/07/2016	40 days
Achaia	1	15/07/2016	-	-
Kozani	1	26/08/2016	-	-
Larissa	3	26/08/2016	15/09/2016	21 days
Pieria	1	03/10/2016	-	-
Evros	2	19/10/2016	09/11/2016	22 days
Preveza	1	25/11/2016	-	-
<b>Greek territory</b>	<b>104</b>	<b>06/04/2016</b>	<b>25/11/2016</b>	<b>234 days</b>



**Figure 3:** a. Ulcerated skin nodules on the teats, b. Nodules on the teats (Serres RU)

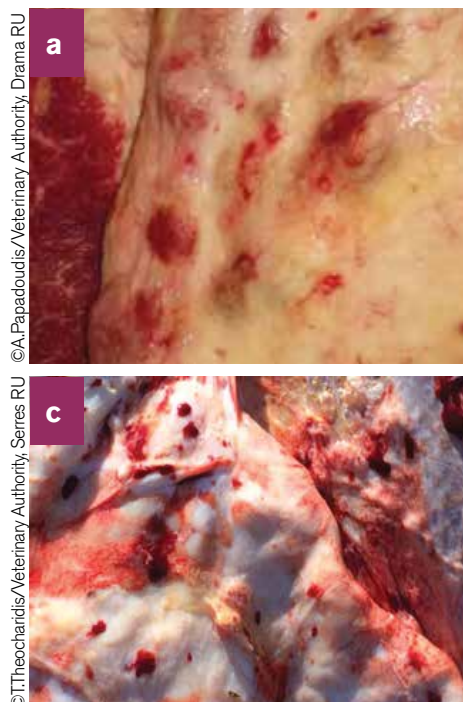


**Figure 4:** Clinical Signs of LSD seen in affected cattle in Greece: a. Ulcerations around the eyes b. Nasal discharge, c. Ophthalmic discharge, d. Oedema in front left leg, e. Skin Nodules and enlarged lymph nodes (Serres and Evros RUs)





**Figure 5:** Cows with skin nodules all over the body in Serres and Evros RUs



**Figure 6:** Lesions identified on the carcass: a and b haemorrhagic circular lesions on the external surface of the carcass on subcutaneous fat; c nodules observed on the inner surface of the skin (Serres and Drama RUs)

**Table 3:** Samples tested for LSDV by the Greek National Reference Laboratory in 2015 and 2016 in the framework of LSD surveillance

Year	Number of RUs	Number of Animals tested	Number of samples	Skin	EDTA blood	Nasal swabs	Ocular swabs	Saliva swabs	Other	Total***
2015	11	200	Tested	130	76	12	-	-	3	221
			Positives	113	47	10	-	-	1**	171
2016	22	523	Tested	94	465*	4	5	1	-	569
			Positives	68	141	1	2	1	-	213
2015-2016	23	723	Total tested	224	541	16	5	1	3	790
			Total positives	181	188	11	2	1	1	384

\* 215 EDTA blood samples come from one farm during surveillance to investigate the presence of viraemia

\*\* The positive sample was lymph node

\*\*\* More than one type of sample may be tested for each animal

## LABORATORY ANALYSIS

All samples were collected by the state veterinarians. Skin lesions were the sample of choice; ethylenediamine tetra-acetic acid (EDTA) blood samples, saliva, and ocular and nasal swabs were also dispatched to the Greek National Reference Laboratory for Capripoxviruses (NRL) of the Ministry of Rural Development and Food. During 2015 and 2016, 224 skin samples, 541 EDTA blood samples, 22 swabs (nasal, ocular and saliva) and three samples of lymph node, liver and kidney, were tested by the NRL (see Table 3).

The samples were examined by a Capripox virus (CaPV)-specific real-time polymerase chain reaction (PCR) previously described in Bowden *et al.* (2008). A gel-based PCR method was also used for differentiation of Sheep pox virus (SPPV) and Goat pox virus (GTPV)/ LSDV isolates (Lamien *et al.*, 2011). A Capripox virus detection method recommended by the World Organisation

for Animal Health (OIE) (Ireland and Binepal, 1998) and an LSDV-specific gel-based PCR were also applied, to confirm the presence of LSDV genome (Ireland and Binepal, 1998; Stram *et al.*, 2008).

The LSDV strains were characterized by sequencing and phylogenetic analysis of three virus genomic regions, : i) the RPO30 gene – RNA polymerase subunit 30 kD gene ; ii) the GPCR gene – G-protein-coupled chemokine receptor gene; and iii) the LSDV126 EEV – extracellular enveloped virus (EEV) glycoprotein gene and LSDV127 hypothetical glycoprotein gene (Agianniotaki *et al.*, 2017).

In analysed samples wild type LSDV differentiated from live attenuated vaccine strains used in Greece by sequencing analysis of the GPCR gene, and subsequently by applying a novel real-time PCR. The development and validation of the method was a result of collaboration among the National Reference Laboratory,

the Diagnostic Laboratory of the School of Veterinary Medicine at Aristotle University of Thessaloniki, and the EU reference laboratory for Capripox-viruses (CODA-CERVA).

Finally, virus isolation of the first two laboratory confirmed LSD strains was carried out in lamb testis cell-line cultures at the Greek National Reference Laboratory (Tasioudi *et al.*, 2016; Agianniotaki *et al.*, 2017).

## CONTROL MEASURES AND ACTIVITIES

Council Directive 92/119/EEC of 17 December 1992 defined the general control measures to be applied in the event of an outbreak of LSD. They included mainly zoning, total stamping out, movement restrictions, cleaning and disinfection of premises and vehicles, epidemiological investigation, sampling, periodic visits to holdings and clinical examination of animals, vector control and emergency vaccination.

Restrictions were also imposed through European Commission Implementing Decisions on vaccinated animals, their products and animal by-products – milk and dairy products, fresh meat, meat products, bovine semen, ova and embryos, and raw hides and skins – with severe negative effects on trade (European Commission Implementing Decisions: 2015/2055; 2015/1500; 2015/1423).

In the light of the European Food Safety Authority (EFSA) scientific opinion (EFSA, 2016) and of the experience gained all these period, several of the restrictions were lifted according to the European Commission Implementing Decision, and since August 2016, preventive vaccination has been permitted in non-affected countries that are at high risk of LSD expansion.

### PREPARATORY ACTIVITIES

In view of its proximity with Turkey, where LSD has been endemic since 2013, Greece started its preparations in mid-2014, focusing on prevention and on improving the capacity for early detection of the disease. Official veterinarians attended a series of training workshops on LSD: i) a laboratory workshop in August 2014 in Istanbul, supported by the European Commission for the Control of Foot-and-Mouth Disease (EuFMD); ii) LSD training in the field in February 2015 in Adana, Turkey, supported by EuFMD; and iii) an LSD training workshop in March 2014 in Alexandroupolis, Greece, organized by Greek veterinary authorities. Posters and leaflets were distributed to stakeholders (see Figure 7). Meetings with farmers and information campaigns took place mainly in high-risk areas. The Ministry of Rural Development and Food webpage available to the public was also updated with information about LSD.

In response to the outbreaks in Turkey, notified in June 2015, an enhanced safeguard zone of 10 km along the Greek-Turkish border in the Evros RU was established (see Figure 8). Within it, all cattle holdings were regularly visited by official veterinarians, and all bovines were clinically examined. Thorough clinical examination by an official veterinarian was also required before any dispatch of bovines was allowed. Enforcement of biosecurity measures was strongly recommended by the

Ministry of Rural Development and Food, and awareness campaigns were implemented. The same practices were implemented later at the borders with the former Yugoslav Republic of Macedonia and Albania.

### STAMPING-OUT POLICY AND DESTRUCTION OF CARCASSES

In accordance with Council Directive 92/119/EEC, total stamping out was implemented in the infected herds in order to eradicate LSD. Even if only one animal was LSDV positive, all susceptible animals in the herd were culled immediately after the laboratory confirmation of the virus. In some cases, depending on the epidemiological situation, animals were culled pre-emptively on the basis of clinical signs, before the laboratory confirmation, to minimize the risk of virus transmission. During 2015, pre-emptive culling was implemented in 16 percent of the outbreaks.

The interval between the date of suspicion and the date of depopulation was 4 days (median) (25th percentile: 3 days; 75th percentile: 7 days) in 2015; and 13 days (median) (25th percentile: 7 days; 75th percentile: 21 days) in 2016.

All animals of the infected herds were killed on the spot and on-site sanitary burial of

their carcasses was implemented. Although they were necessary, these actions resulted in a large number of carcasses, and they compromised milk and meat production, damaged the local rural economy and raised public, economic and environmental concerns.

### ZONING AROUND THE OUTBREAKS

A protection zone of at least 3 km radius lasting for 28 days and a surveillance zone of at least 10 km radius lasting for at least 56 days were initially established around the outbreaks (Council Directive 92/119/EEC). Passive and active surveillance were increased in all herds in these zones. On the recommendation of the Ministry of Rural Development and Food, the surveillance zone was subsequently extended to a radius of at least 25 km with a view to matching the potential radius of vector activity. Inside the protection zones bovine movements were not allowed, even to slaughterhouses; in the surveillance zones, however, animals were allowed to move to private pastures and directly to slaughterhouses in the zone. In addition and in accordance with the National Contingency Plan, bovines were not allowed to be dispatched to another Greek region outside the RU, whether that region was affected, or not, even for immediate slaughter.

Zoning extended the negative impacts of LSD not only to the infected herds but also to other herds in an RU, and to live animal traders, abattoirs, meat and milk plants and animal by-product establishments.

### VACCINATION POLICY

Emergency vaccination with homologous live attenuated virus vaccines was decided for the first time in EU by Greek Veterinary Authorities in cooperation with the European Commission soon after the beginning of the epizootic in 2015. The main reasons were the need for drastic reduction of the spread caused by the involvement of vectors and the elimination of negative effects on local economies.

The Greek veterinary authorities nonetheless had to deal with legal limitations with regard to the facts that: i) preventive vaccination for LSD was not allowed in EU Member States at that time; and ii) the available vaccines were produced only in non-EU countries, and had no marketing authorization granted by a Member State



Figure 7: Poster for LSD by the veterinary services of East Macedonia and Thrace



(Council Directive 92/119/EEC; European Parliament and Council Directive, 2001/82/EC).

Only exceptionally in the event of a serious epizootic disease such as LSD and in the absence of a suitable medical product could a Member State provisionally allow the use of immunological veterinary medicinal products without a marketing authorization in EU, but authorized under the legislation of a non-EU country and after informing the European Commission (European Parliament and Council Directive, 2001/82/EC). The Greek National Organization for Medicines (EOF) approved the import of the vaccines at the request of the Animal Health Directorate of the Ministry for Rural Development and Food. Two homologous live attenuated virus vaccines – Lumpy Skin Disease Vaccine for Cattle

made by Onderstepoort Biological Products, and Lumpyvax made by MSD in South Africa – were approved for import and use.

The vaccination of susceptible cattle and buffalo is compulsory. The conditions for setting out emergency vaccination were included in European Commission Implementing Decisions 2016/2008, 2015/2055 and 2015/1500 and in the guidelines of the Greek National Disease Control Centre. All the procedures regarding vaccination – import, delivery, storage, implementation, registration, and management of residual quantities – were under the official control of the Greek veterinary authorities and the National Organization for Medicines. An online application was developed at the Ministry of Rural Development and Food for the registration of vaccinated animals and holdings.

A 28-day standstill of vaccinated animals followed vaccination. According to the manufacturer's instructions, for calves born from unvaccinated mothers, vaccination starts at the age of one day, an annual booster vaccination is considered necessary and the withdrawal period is seven days. In accordance with in European Commission Implementing Decision 2016/2008, calves born of vaccinated cows, should be vaccinated at the age of four months.

The vaccination campaign started in the Evros RU on 5 September 2015 and gradually extended to other RUs (see Figure 2). The initial plan was to implement vaccination in all RUs where LSD was confirmed. Vaccination priorities were initially protection zones, surveillance zones and high-risk areas close to wetlands with high-



**Figure 8:** Map of the Safeguard Zone of 10 km along the borders with Turkey

Source: Presentation by Greece at the Standing Committee on Plants, Animals, Food and Feed, Brussels 9–10 September 2015

density bovine populations, and then the rest of the RU. In November 2015 vaccination was extended to LSD-free RUs, in an attempt to prevent the spread of the disease. By the end of 2015 the vaccination campaign had covered 146 000 bovine animals.

After the re-emergence of LSD in Greece in April 2016, and in view of the epidemiological situation in other Balkan countries, the decision was made to expand vaccination to the entire Greek mainland firstly, and then to the islands depending on the availability of the vaccine. During the 2016 campaign approximately 590 000 bovine animals were vaccinated. Of the total vaccinations, 66 percent were conducted by state veterinarians and the remaining 34 percent by private veterinarians.

The main difficulties with regard to vaccination faced by the Greek veterinary authorities were: i) short supply of vaccines and limitations imposed by financial and legal procedures; ii) vaccination of the large cattle population in the limited time of two months, especially in free-grazing beef herds; iii) restrictions imposed on vaccinated animals and their products which made it difficult to convince farmers of the benefits of vaccination; iv) lack of scientific knowledge regarding the immune response to vaccination, especially for calves, the duration of immunity and viraemia in vaccinated animals; v) lack of a real-time PCR until recently, which could differentiate the vaccine from the field strain – the differentiation of infected from vaccinated animals (DIVA) test (Agianniotaki *et al.*, 2017); vi) lack of inactivated vaccines; and vii) the duration of the vaccination campaigns.

## MEASURES IMPLEMENTED IN THE ENTIRE GREEK TERRITORY

In addition to the measures implemented in RUs affected by LSD, horizontal measures were implemented across the entire country. Initially local disease control centers were formed in each RU to optimize preparation, and a range of biosafety measures was enforced. Bovines were allowed to be dispatched only to the nearest slaughterhouse and for a period of one month a total standstill of all bovine animals was enforced by the Ministry of Rural Development and Food, except for dispatches to slaughterhouses. Passive and active surveillance were implemented, including:

i) clinical examination of bovines in the protection and the surveillance zones; ii) clinical examination of bovines before vaccination against LSD and during the implementation of other eradication and control programs;

and iii) laboratory investigation of suspected cases. A quarantine of 28 days was mandatory for all animals that had transited through the protection and surveillance zones.

Training programs were conducted for veterinarians, and information campaigns were continued throughout this period.

## TRANSBOUNDARY INITIATIVES AND ACTIVITIES

Given the fact that LSD is a disease that has recently affected several countries in three continents, the need for a global approach to policies is evident: initiatives and activities have accordingly been undertaken by European and international bodies.

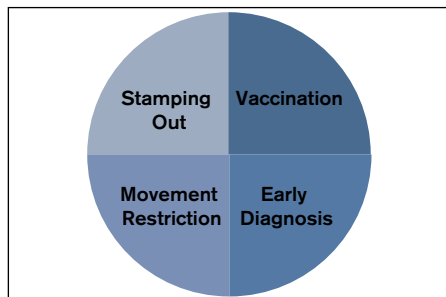
The Community Veterinary Emergency Team (CVET) of experts provides on-the-spot technical, managerial and scientific assistance for diagnostic methods and epidemiological investigations for the EU Member States and non-EU countries, especially in times of crises. In Greece, CVET carried out two missions in November 2015 and April 2016 at the request of the Greek veterinary authorities.

In 2016 the European Commission created the European Bank of Vaccines for LSD to support Member States and non-EU countries at the onset of the disease or in case vaccines are unavailable. Greece has already received 150 000 doses in three dispatches of 50 000 in April, July and December 2016.

To verify the effectiveness of the measures and their compliance with EU legislation, the Directorate-General of Health and Food Safety carried out an audit in Greece from 30 November to 4 December 2015.

Training in relation to LSD was also organized through the European Commission Better Training for Safer Food (BTSF) programme. Four seminars were carried out in Greece, one in Alexandroupolis and three in Thessaloniki.

The Ministerial Conference on Lumpy Skin Disease took place in Sofia on 8–9 September 2016. Ministers from EU Member States and non-EU countries in the Balkan region affected by, previously affected by and at risk of LSD participated with a view to reinforcing and harmonizing the regional policy for control of the disease.



**Figure 9:** Four pillars of Greek policy on the control of LSD

## CONCLUSIONS

Early diagnosis, stamping out, simultaneous vaccination of large number of bovines and restrictions on animal movements – the four pillars of Greek policy on control of the disease – seem to be effective (see Figures 2, and 9). Since September 2016, only six sporadic new outbreaks have been reported, and since November 2016 no new outbreak has occurred (see Figure 2). The evolution of LSD in Greece followed a best-case scenario, taking into consideration the EFSA models of the spread of the disease.

Vaccination was an effective measure in controlling the spread of LSD. In areas where it was implemented before the disease appeared and where there was high vaccination coverage, only a few sporadic outbreaks occurred in unvaccinated animals.

In geographical terms, most of the LSD outbreaks occurred in areas of wetland – rivers, seashores, lakes, lagoons, and ponds – or close to them. The places where the outbreaks were mainly confirmed were the river Evros and the wetland of its delta, the Visthonia lake and lagoon, the river Nestos and its delta, lake Volvi, the delta of the rivers Axios and Pinios and coastal areas (see Figure 1). The special conditions favoring the activity of vectors probably contributed to the distribution of LSD. More research is needed to increase understanding of the epidemiology of the disease.

The LSD epizootic in Greece also revealed legislative limitations, especially regarding preventive vaccination under emergency

circumstances. Legislation governing the control of rapidly spreading epizootics, should be continually adapted to incorporate current scientific knowledge and epidemiological information.

The next challenge for the veterinary community is the establishment of epidemiological and the legislative procedures to avoid the need for total stamping out in cases of sporadic LSDV of positive animals in a vaccinated population with high vaccination coverage.

To control LSD and put in place the most effective prevention and control measures each time it appears, thorough knowledge of different aspects of the disease is essential. Future studies should focus on the mechanism of transmission, the role of vectors, the immunity response of vaccinated animals, the role of subclinical cases in disease transmission, and the development of new inactivated vaccines.

Lumpy Skin Disease knows no boundaries or legislative limitations. Cooperation and exchanges of experience among countries must be continuous to control such a devastating epizootic.

## ACKNOWLEDGEMENTS

Using this opportunity we express our profound gratitude to the veterinarians of Greek Veterinary Authorities who gave a tough fight against the disease. We are also thankful to the European Commission, the EURL for Capripox-viruses; the European Food Safety Authority and the International Atomic Energy Agency for their assistance. <sup>360</sup>

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## SITUATION

# Emergence of Lumpy Skin Disease in Bulgaria: epidemiological situation, control and eradication

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## INTRODUCTION

The first report of lumpy skin disease (LSD) in Bulgaria was made on 13 April 2016, and within three months the disease had spread throughout the country. The national strategy for limiting and controlling the spread of LSD included early detection, prompt implementation of the total stamping out policy and vaccination. In view of the several transmission pathways, strict controls of cattle movements, intensified clinical surveillance, vector control and disinfection were also applied, supported by education and awareness campaigns.

## METHODS AND RESULTS

Bulgaria was the second European Union member country to be affected by LSD after Greece, which was first observed on 13 April 2016 in two cattle farms about 5 km apart in the Haskovo region 80 km from the border with Greece and Turkey: in all, 217 outbreaks were recorded in 17 of Bulgaria's 28 regions and confirmed by the National Reference Laboratory for Capripox viruses using real-time and conventional PCR laboratory diagnostic techniques (see chapter 2.4.13 of the *OIE Terrestrial Manual* and the standard operating procedures (SOPs) of the *OIE Reference Laboratory on Capripoxviruses* published by the Pirbright Institute in the United Kingdom of Great Britain and Northern Ireland (UK)). The virus was also studied and sequenced in the Kimron Veterinary Institute in Israel and classified as an Egypt/Middle East strain.

Following the incursion of LSD into Greece in 2015, the livestock population in Bulgaria was subjected to intensified surveillance. Because it was considered that these index cases had been detected relatively early, the probable time of arrival of the LSD vector was taken to be the second half of March. The epidemiological investigation indicated that the source of infection was vector transmission, but it did not rule out illegal introduction of infected animals.



*Bulgarian landscape and cattle*



**Figure 1:** Geographical distribution of LSD outbreaks in Bulgaria in 2016

Source: BFSА

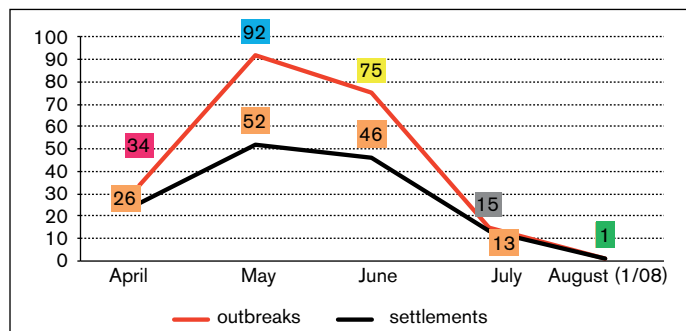
Clinical signs observed in the primary outbreaks were generally confined to high body temperature and skin nodules. Most of the outbreaks were detected in the south-western regions bordering Greece, the former Yugoslav Republic of Macedonia and

Serbia. The problem peaked in May, with 92 outbreaks of LSD in 52 villages, after which there was a gradual decline to the end of June, when vaccination coverage had reached 80 percent; the last outbreak was confirmed on 1 August. Figures 1, 2 and 3 show the

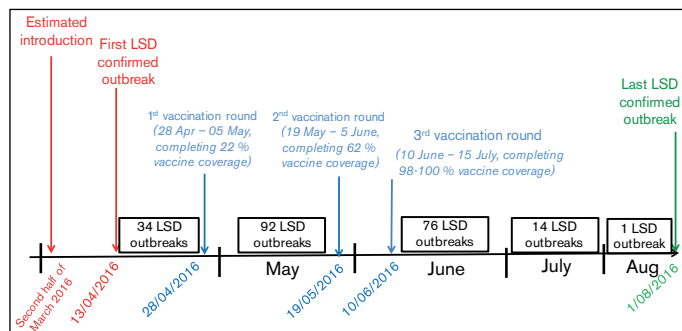
<sup>1</sup> Bulgarian Food Safety Agency (BFSА)

<sup>2</sup> National Reference Laboratory for Capripox viruses, National Diagnostic and Research Veterinary Medical Institute, Bulgaria





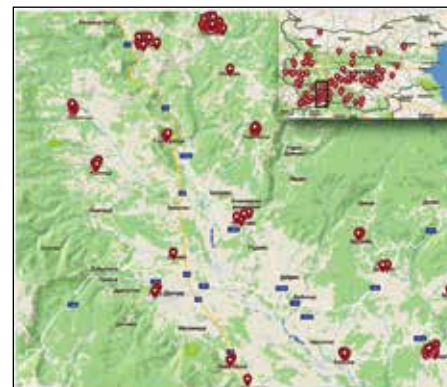
**Figure 2:** Number of LSD outbreaks and affected villages, per month in Bulgaria



**Figure 3:** Timetable of LSD situation in Bulgaria



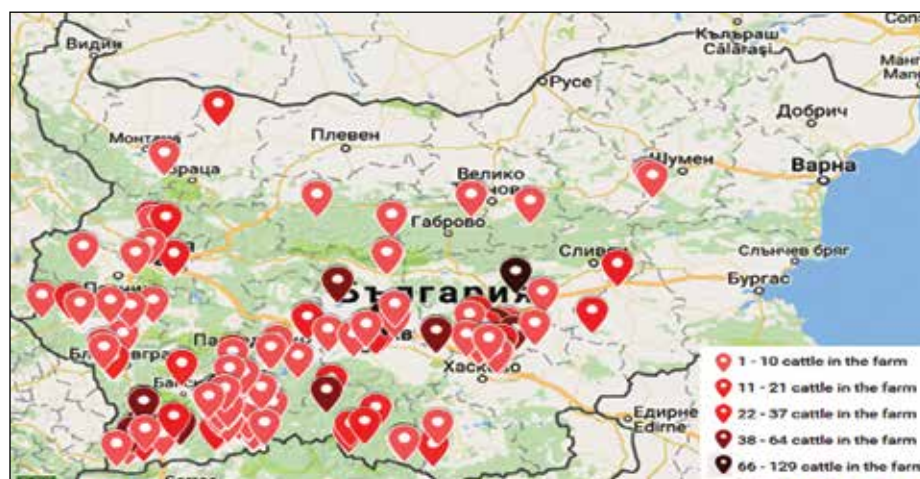
**Figure 4:** Intensity of LSD outbreaks in Plovdiv, Stara Zagora and Haskovo regions near the Maritsa River, Bulgaria



**Figure 5:** Intensity of LSD outbreaks in Blagoevgrad region near the Mesta River, Bulgaria



**Figure 6:** Severe large skin nodules of the head, neck, udders and tail area around the perineum; genital and ocular discharges



**Figure 7:** Geographic distribution of LSD outbreaks in Bulgaria, by herd size

distribution of cases, the LSD outbreak curve and the timetable of the outbreak in Bulgaria.

The highest intensity of LSD was observed in holdings in areas with high abundance of vectors along major rivers and watercourses in Bulgaria. Animals were infected in locations up to 5 km away from these (see Figures 4 and 5).

There were 2 814 head of cattle in the affected herds, of which 366 were observed with clinical signs of LSD. The estimated population infection rate was 0.41 percent of the total cattle population. The morbidity rate was 13 percent with a mortality rate of less than 1 percent among the susceptible animals in each outbreak. These rates were observed before immediate stamping out was implemented. Of the affected herds, 53 percent were dairy, 29 percent were mixed dairy and beef, and 18 percent were beef only.

As the outbreak progressed, the clinical signs observed in cattle affected by LSD were lethargy and weakness, reduced milk production, high temperature, skin nodules, nasal discharges and salivation; in a few cases ulceration and scabs were observed (see Figure 6).

The units affected by LSD were mainly small farms of the "backyard" type, where one to ten animals were kept in conditions of low biosecurity (see Figures 7 and 8). In the region of Blagoevgrad, for example, 114 of the 217 outbreaks were detected, of which 81 percent occurred in small farms with five cattle or fewer.



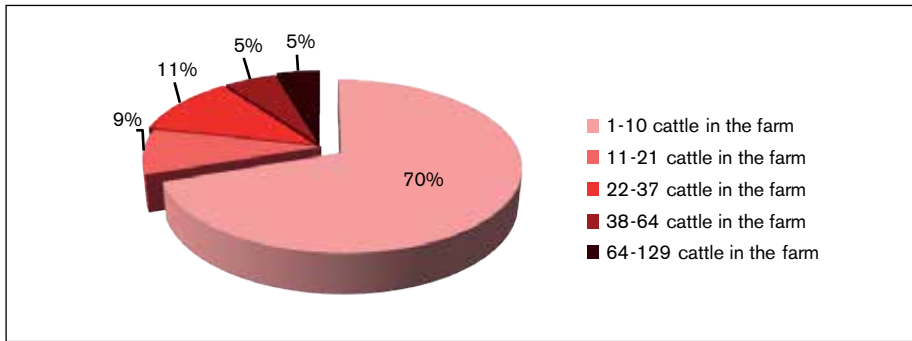


Figure 8: LSD outbreaks in Bulgaria by herd size

## CONTROL AND ERADICATION MEASURES

The Bulgarian Food Safety Agency (BFSA) correctly notified OIE and the European Union of the outbreaks, and managed the disease according to EU Council Directive 92/119/EEC, followed by Commission Implementing Decisions 2016/645 and 2016/1183, which set out the safeguard measures for LSD in Bulgaria and the vaccination programme. The total stamping out strategy was implemented in every laboratory-confirmed outbreak, and the carcasses were immediately buried on-site. Stamping out was completed within one week of laboratory confirmation in 96 percent of the outbreaks. Other control measures included restrictions on the movement of susceptible livestock, including small ruminants in the case of mixed farming, enforced biosecurity measures on the farms, and intensified clinical surveillance over the entire country. In addition to the measures to eliminate vectors on cattle farms, the BFSA initiated an insect-control programme over 2,790,125 ha along major rivers and in valleys and paddy fields considered to be risk areas.

A vaccination programme was implemented in conjunction with the control and eradication measures. First, ring vaccination was implemented in 20 km zones around each outbreak and in regions considered to be at risk; this was subsequently extended to blanket vaccination of the whole cattle population in Bulgaria in view of the spread of the disease in the Balkan Peninsula. Vaccination was conducted in three rounds in two and a half months, using live homologous vaccines. The Neethling strain of LSD vaccine produced by Onderstepoort Biological Products (OBP) was used for the first and third ring vaccination programmes; the Lumpyvax (SIS type) vaccine made by MSD Animal Health, Intervet, South Africa was utilized for the second vaccination round, as set out below and in Figure 9:

- First round of vaccination – 18 April to 5 May: 150 000 doses of OBP from the EU bank (Neethling strain) administered in the areas round the LSD outbreaks at that time.
- Second round of vaccination – 19 May to 5 June: 275 000 doses of Intervet (SIS-type) covering the rest of the southern areas and the north-western areas.

- Third round of vaccination – 10 June to 15 July: 350 000 doses of OBP used in the rest of the country; 100 percent vaccine coverage.

Of the laboratory-confirmed cases, 21 percent of the animals developed typical LSD clinical signs between 3 and 21 days after vaccination. These were regarded as field cases that had been infected prior to vaccination.

To protect wildlife, non-invasive sampling and surveillance for LSD were carried out in areas where the disease had been confirmed in domestic cattle. There is no evidence so far that the LSD virus has affected red and fallow deer.

Awareness and education were particularly important aspects of LSD prevention and control. Working groups, seminars and “cascade” training sessions have contributed to the high level of preparedness and commitment among Bulgarian veterinarians working to prevent LSD and conducting surveillance. Various training materials and leaflets were used to raise awareness among farmers, and a dedicated web link and emergency phone number were set up to enable daily communication with farmers and other stakeholders.

## CONCLUSIONS

- Transmission and long-distance spread of the LSD virus could be minimized through surveillance, rapid laboratory confirmation, prompt implementation of total stamping out, safe destruction of infected animals and enforced control and movement restrictions.

- The disease is controlled by coupling the total stamping out strategy with mass vaccination covering at least 85 percent of all herds.
- Further field monitoring is required to investigate quality, safety and adverse reactions after administration of the SIS-type and Neethling strain vaccines.
- Enhanced preparedness and capacities among veterinarians, awareness campaigns and daily communication with farmers and stakeholders are essential aspects of an LSD warning and early detection system.
- Because Bulgaria is known for its wildlife, the study of the mechanical transmission of the LSD virus and the role of wild animals as potential reservoirs of the virus should be continued. <sup>360</sup>

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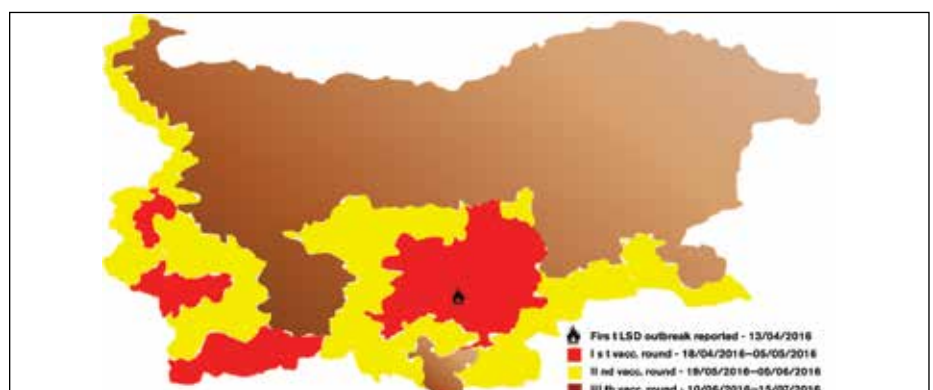
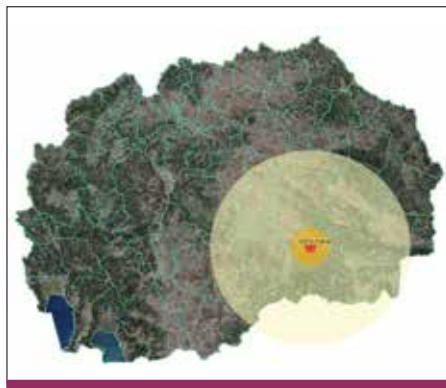


Figure 9: Map of Bulgaria showing the areas covered and timetable for each vaccination round



## SITUATION

# Experience of the veterinary service of the former Yugoslav Republic of Macedonia with the occurrence of Lumpy Skin Disease in 2016

Contributors: Blagojcho Tabakovski,<sup>1</sup> Kiril Krstevski<sup>2</sup> and Srgjan eshterovikj<sup>3</sup>

## SUMMARY

Veterinary services in the Balkan Peninsula will remember 2016 for the occurrence and rapid spread of Lumpy Skin Disease (LSD): the former Yugoslav Republic of Macedonia was one of the countries affected by the incursion. The disease was suspected in Vardar region on 18 April 2016 and officially confirmed on 21 April 2016. The initial outbreak occurred eight days after the first outbreak in the Haskovo region of the Republic of Bulgaria and nine days after the last outbreaks in 2016 in the Serres region of the Republic of Greece.

The strategies applied for control and eradication of the disease in the former Yugoslav Republic of Macedonia were adjusted to the situation in the field. The initial control measure was total stamping out of the affected epidemiological units – holdings – but with the arrival of vaccine contributed by the European Union (EU) the measure was replaced by culling of clinical cases and vaccination of the rest of the cattle population.

Vaccination was conducted in two phases, with 46 370 animals vaccinated in May and 165 783 in July 2016. After July, an additional 3 033 animals were vaccinated, mainly newborn calves, imported animals and animals omitted during the first two phases of vaccination. A total of 1 535 outbreaks was reported in the veterinary information system of the Macedonian Food and Veterinary Agency; of these, 1 464 were confirmed and 71 were not confirmed. Of these 1 464 confirmed outbreaks vaccination was carried out by private veterinary practitioners at 1 373 holdings; on 91 holdings there were no vaccinations. From the 1 373 holdings where vaccination took place, 942 holdings were reported at least one day after the vaccination. The last occurrence of LSD in 2016 was in December; three new outbreaks were reported up to May 2017.



**Figure 1:** The first case of LSD in the former Yugoslav Republic of Macedonia (in Demir Kapija)

## ACTIVITIES PRECEDING DISEASE OCCURRENCE

The Macedonian veterinary service monitored the progress of LSD in the region, particularly in neighbouring countries. The disease was detected in Greece in 2014, with sporadic outbreaks that were managed by the veterinary service in accordance with EU legislation then in force. In 2015, LSD was still present in Greece and was detected in several outbreaks. It appeared that the disease could be managed with the available control measures, and the prediction was for very slow spread. It was generally concluded that LSD did not pose a serious threat, although knowledge about the disease under European conditions was scarce. At this time, experience was available from two countries in the region, Greece and Turkey, had applied different control approaches. The only recommended strategic approach was early detection and stamping out at affected epidemiological units.

The Macedonian Government was informed about the threat of LSD and the possible effects of an outbreak in the country and accordingly implemented several sets of activities to increase preparedness and to control the disease. In December 2015 a one-day seminar was organized for the contracted private veterinary practitioners on the clinical signs of

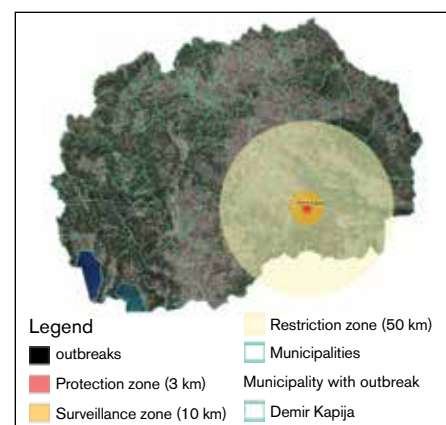
LSD. All private veterinary practitioners active in the regions bordering with Bulgaria and Greece were informed, and an administrative order was issued mandating regular visits to cattle establishments near these borders. Posters and information materials in various media were disseminated to private veterinary practitioners to inform livestock owners. The entire veterinary service was alerted and prepared to recognize, report and control the disease.

One of the biosecurity measures applied in the former Yugoslav Republic of Macedonia was a ban on imports of live cattle and associated products from affected countries and regions.

## DISEASE OCCURRENCE AND SPREAD

The first outbreak occurred in the middle of April 2016 in Demir Kapija, and the suspicion was notified on 18 April to the local official veterinarian. One of the five animals on the holding had exhibited typical clinical signs of LSD, but because the disease has not been present in the country the case could only be officially confirmed after a positive laboratory result was obtained from the National Reference Laboratory at the Animal Health Institute in Skopje. The affected animal is shown in Figure 1; the control zones for the first outbreak are shown in Figure 2.

Given the early detection and notification of LSD and the prompt response of the



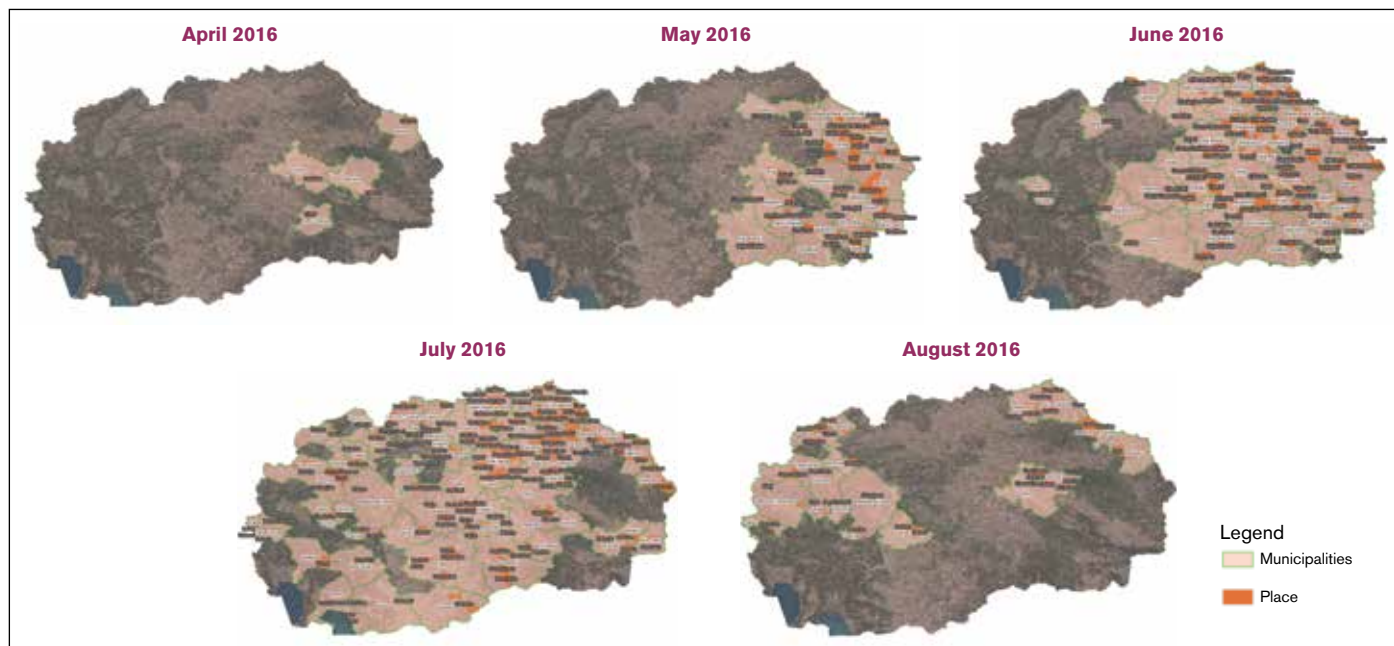
**Figure 2:** Restricted zones after the detection of the first case

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**Figure 3:** Incidence of LSD by month in the former Yugoslav Republic of Macedonia

veterinary service, which had all possible control measures in place, and considering the information on the “slow” spread of the disease in Turkey and Greece, there was initially a hope that the disease could be contained in this single outbreak. Unfortunately, this was not the case, and the veterinary service received a salutary lesson. After the outbreaks of foot-and-mouth disease in 1996, this was the most serious occurrence of an infectious animal disease in the country. The animal husbandry system in the former Yugoslav Republic of Macedonia had addressed the problem of bluetongue in 2014, and relevant legislation was in force based on extensive knowledge, with validated vaccines available. But this was not the case with LSD. At that time only countries that had experienced LSD were in possession of some reliable data for controlling it.

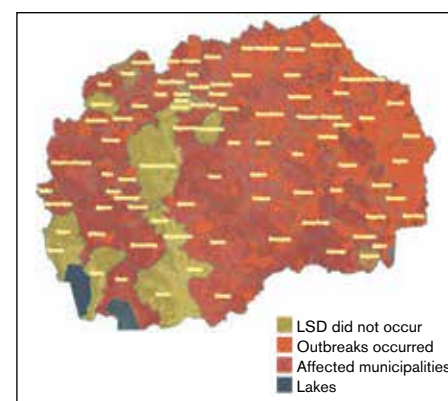
The first suspicion of LSD outbreak was reported by a private veterinary practitioner, who notified the official veterinarian on 26 April about an animal with clinical signs. In the next two days two new suspicions were reported, and reports of new outbreaks increased as time passed. The incidence of new outbreaks in the following months is shown in Figure 3.

Figure 4 provides a map with all outbreaks registered up to 31 December 2016. The places where the outbreaks occurred are shown in orange, affected municipalities are shown in dark red and municipalities where LSD did not occur are shown in dark green.

Of the 1 535 cases reported in the veterinary information system of the Food and Veterinary Agency, 1 464 were confirmed as shown in Table 1.

Of the total of 1 464 outbreaks, two thirds were recorded at least one day after

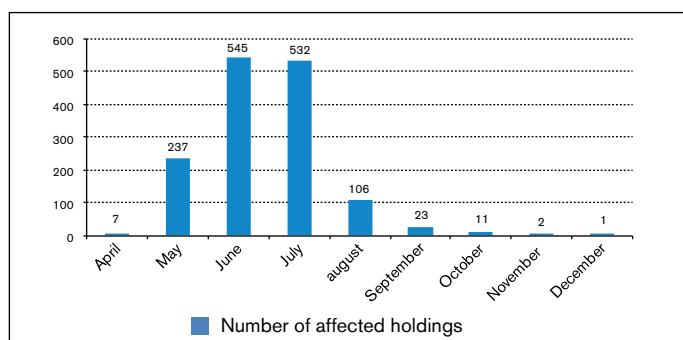
vaccination. A number of outbreaks required additional scrutiny because some had not been confirmed by laboratory results. Because the disease occurred on an epizootic scale, a significant number of outbreaks were confirmed on the basis of clinical signs and/or the epidemiological situation. Figure 5 shows the number of holdings affected by month; Figure 6 shows the percentage of holdings



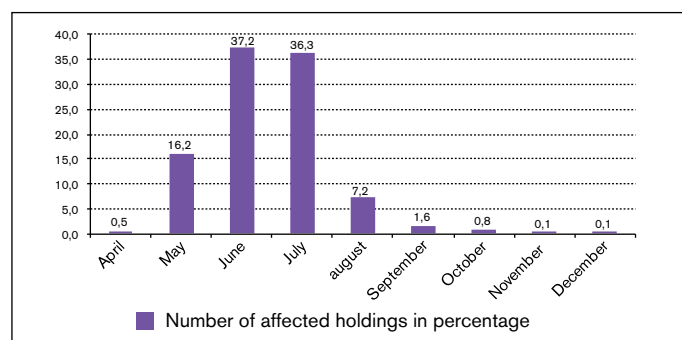
**Figure 4:** Distribution of LSD on 31 December 2016 in the former Yugoslav Republic of Macedonia

**Table 1:** Overview of affected, culled and dead animals resulting from outbreaks of LSD in the former Yugoslav Republic of Macedonia in 2016

Number of outbreaks	Number of animals on affected holdings	Culled animals	Dead animals
1 464	30 480	3 925	313



**Figure 5:** Number of LSD affected Macedonian holdings by month



**Figure 6:** Percentage of LSD affected Macedonian holdings by month

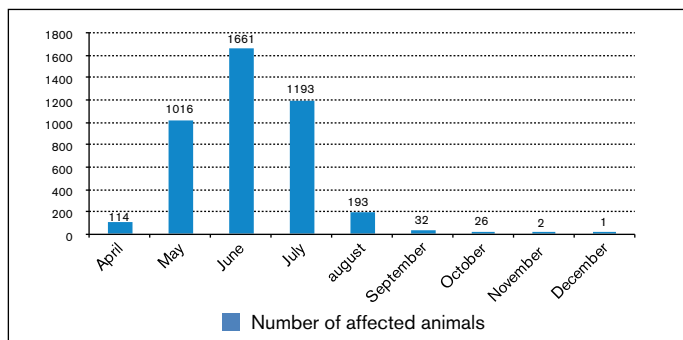


Figure 7: Number of LSD affected Macedonian animals by month

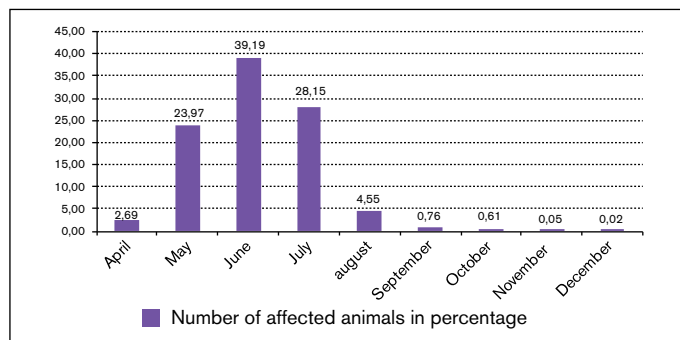


Figure 8: Percentage of LSD affected Macedonian animals by month

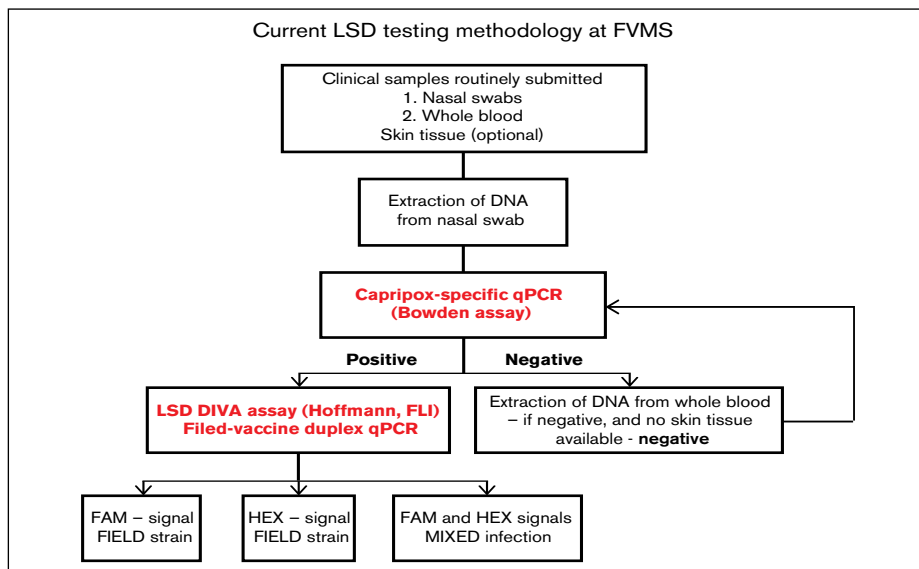


Figure 9: LSD laboratory testing methodology in the former Yugoslav Republic of Macedonia

affected by month; Figure 7 shows the number of animals affected by month; and Figure 8 shows the percentage of animals affected by month.

### SAMPLING, LABORATORY CAPACITY AND DETECTION METHODS APPLIED

The disease was diagnosed by the Veterinary Institute of the Laboratory for Diagnosis of Animal Disease at the Faculty of Veterinary Medicine, University of Skopje. For diagnosis of the disease, whole blood and nasal swabs were submitted to the laboratory; the samples were collected by private veterinary practitioners in the presence of the official veterinarian. If on the basis of the clinical findings it was clear that infection had been present at a holding for the first seven days, the private veterinary practitioners collected blood and swab samples: this was done because it was observed that the virus could not be reliably detected in blood if the incubation period had been exceeded. In such cases the swabs were positive and more suitable for detecting the disease. If the disease was detected at an early stage, the blood samples were suitable for detection.

Real-time polymerase chain reaction assay (PCR) was the method used by the laboratory to detect the virus, using several different kits. When vaccination started the laboratory applied an in-house DIVA protocol to determine the wild type from the vaccine strain. The work of the laboratory was reliable at the time and provided the necessary support to the veterinary service for decision-making and planning of further steps. When DIVA was applied, the diagnostic test steps presented in Figure 9 were followed.

### APPLIED STRATEGIES FOR CONTROL AND ERADICATION OF THE DISEASE

After the first several cases, and considering new developments in neighbouring countries, it was evident that the disease would continue to spread rapidly through the unprotected naive animal population. Many factors favoured the spread of LSD. The threat of the disease came from two directions – Bulgaria and Greece – with almost equal intensity, though both countries were implementing stamping out at affected holdings. The weather conditions were favouring the vectors, and cattle were out

grazing on pastures, particularly in the Eastern Region of the country. Additionally, the country was facing another refugee crisis at the border that further complicated the availability of the resources usually utilized in such cases such as the army and police and their engineering units.

The initial strategy used by the officials was stamping out of all animals on affected holdings, but it soon became clear that the disease could not be controlled only by this approach. Experience in other countries with LSD supported this conclusion. It emerged that the only effective solution that could be applied to contain the disease was emergency vaccination of the entire national population of bovine animals.

Fortunately, the spread of the LSD was recognized by the EU as a regional problem, and it was addressed with high levels of interest. The affected countries met several times and discussed emergency vaccination and the possible use of the only vaccines available at the time, which were produced in South Africa. With the donation of vaccine from EU stocks, it was decided to vaccinate immediately in the Eastern Region where the disease was present and also to tender for procurement of the doses of vaccine required to launch a vaccination programme for the rest of the bovine population. The first vaccine was delivered at the end of May 2016 and procurement was completed at the end of June, hence vaccination was implemented in two separate phases.

The first phase of vaccination started on 25 May 2016 in the eastern part of the country. A total of 46 370 animals were vaccinated in a period of three weeks. Vaccination was conducted in accordance with the plan drafted by the veterinary service, with emphasis on the mandatory biosecurity measures. The vaccination plan was drafted in accordance with EU Decision 2015/2055. The vaccine used was the live attenuated virus vaccine against LSD – the Neethling strain lumpy skin disease vaccine for cattle made by Onderstepoort Biological Products, South Africa.

As noted earlier, before the first phase the strategy applied to control LSD was



stamping out of all animals at affected holdings. With the start of the vaccination programme only confirmed cases were culled and disposed safely; the remaining animals were vaccinated. The restrictive measures in EU Directive 92/119 and EU Decision 2016/645 currently remain in force.

The second phase of vaccination started on 24 June 2016 and covered the rest of the country. A total of 165 783 animals were vaccinated in a period of one month. Vaccination was conducted in accordance with the plan drafted by the veterinary service. As in the first phase, the vaccination plan was in accordance with EU Decision 2015/2055. In the second phase, however, the vaccine used was live attenuated virus vaccine against LSD – SIS type Lumpyvax made in South Africa by MSD Animal Health, Intervet.

Both phases in total, 212 153 animals were vaccinated up to 31 July 2016 in 25 053 holdings. An additional 3 033 animals were vaccinated after 31 July aiming at covering any omitted animals, calves and imported animals. The operation was conducted by 129 private veterinary practitioners contracted by the veterinary service.

The policy of healthy animal vaccination and culling and safe disposal of confirmed cases remains in force in the former Yugoslav Republic of Macedonia.

## VECTOR MONITORING

At present, scientific data on the transmission of LSD remain scarce. The rapid spread of the disease with no epidemiological connection between outbreaks is a good indication that LSD is mainly transmitted by vectors. The scientific literature shows that the virus can be transmitted by other means, but it appears that vectors remain the most significant source of infection. Our presentation of the data on the monitoring of *Culicoides* in 2016 should not be understood as suggesting anything in this respect, but should be seen as a possible field for further scientific research. Nevertheless, data from the monitoring of *Culicoides* in 2016 indicated a peak of this particular arthropod in the month of June. Traps were placed in all seven epidemiological regions, and counting was conducted by the laboratory at the Veterinary Institute. The data on vector monitoring are presented in Figure 10.

## EXPENDITURES AND DIRECT LOSSES

Pending more comprehensive analysis of expenditures and cost-benefit ratios, farmers' direct losses and the expenditures on controlling LSD paid through the budget of the veterinary service are presented in Table 2. The table does not include vaccines

contributed by the EU, farmers' indirect losses, expenditures for burial and safe disposal of carcasses, indirect losses caused by the ban on movements of animals, their products and by-products, or the cost of resources for awareness and information campaigns for stakeholders.

## REGIONAL INITIATIVES AND COLLABORATION

The regional approach was necessary to control LSD and prevent its spread in the Balkan Peninsula. All affected countries were unanimous in agreement when the strategies to prevent the disease were in question. The authors are, therefore, grateful to the initiatives implemented through the Global Framework for the Progressive Control of Transboundary Animal Diseases (GF-TADs) and the European Commission for their support, and to the strong participation of all countries in the region in addressing the single goal of preventing LSD. We firmly support the vaccination approach and the measures agreed at the meetings and ministerial conferences in 2016. The actions implemented by the former Yugoslav Republic of Macedonia have been recognized and appreciated by all parties. The experience gained in controlling LSD under the regional approach must be reflected in future whenever eradication of transboundary animal diseases is in question.

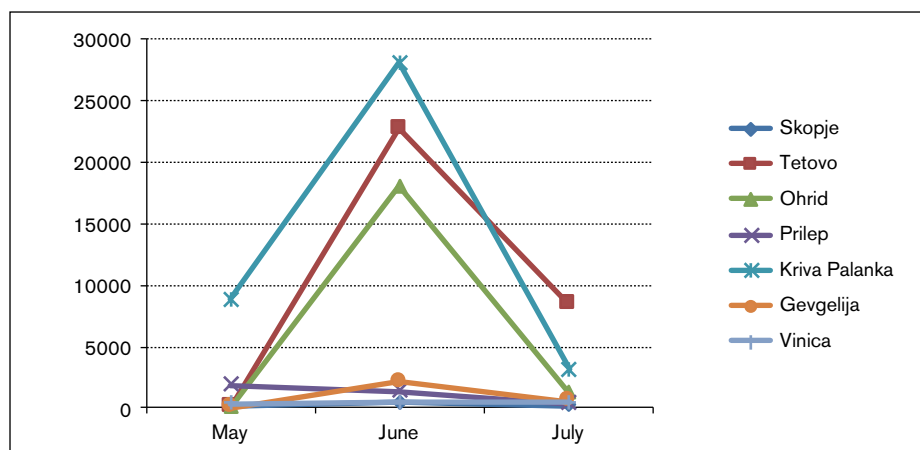


Figure 10: Results of the monitoring of *Culicoides* in May, June and July 2016

## CURRENT SITUATION

As of 31 May 2017, three new outbreaks were reported: in the municipality of Gostivar in January, in Kochani in April and in Kriva Palanka in May. All these cases appeared in vaccinated animals. The three outbreaks strongly indicate that the virus still circulates in the country. The animals were culled and safely disposed. Samples were collected from other animals in the affected holdings, with negative results. The distribution of the outbreaks is shown in Figure 11.

All the measures that were in place in 2016 are being implemented to address the new outbreaks in 2017, and to cover the



Figure 11: Distribution of LSD outbreaks in 2017 in the former Yugoslav Republic of Macedonia (as of May 2017)

Table 2: Direct expenditures required to address the LSD crisis in the former Yugoslav Republic of Macedonia

Intervention	Cost (€)
Materials for sampling and protective equipment	17 690
Vaccine used in 2016	340 376
Application of the vaccine	383 922
Disinfestation and disinfection	436 932
Farmers' direct losses	2 759 356
Laboratory testing	134 500
Total	4 072 776

rest of the territory. The provisions of the Book of Rules on animal health measures in animals for controlling LSD were put in place. The Book of Rules, which was adopted on 28 April 2016, is in effect a transposition of EU Decision 2016/2008.

With the purchase in 2016 of the remaining vaccines, the first phase of vaccination started on 1 April 2017. The procedure for purchasing an additional 175 000 doses of LSD vaccines has been completed, and the second phase of vaccination started in second half of June. The vaccine was used to vaccinate newborn calves and to re-vaccinate the cattle population in 2017. Vaccination started as recommended within one year of the first vaccination and in accordance with the adopted vaccination plan drafted in compliance with the rules laid down in EU Decisions 2015/2055 and 2016/1183.

## LESSONS LEARNED

Considering the circumstances, the former Yugoslav Republic of Macedonia is among the countries in the region that managed the LSD crisis most efficiently and in coordination

with other affected countries. The Food and Veterinary Agency participated in all activities supporting the regional approach for controlling LSD and preventing its spread. The fact that LSD is a vector-borne disease means that its spread is difficult to

**“ LSD is a vector-borne disease means that its spread is difficult to predict and manage; the best solution for the protection of animals is vaccination ”**

predict and manage; the best solution for the protection of animals is vaccination.

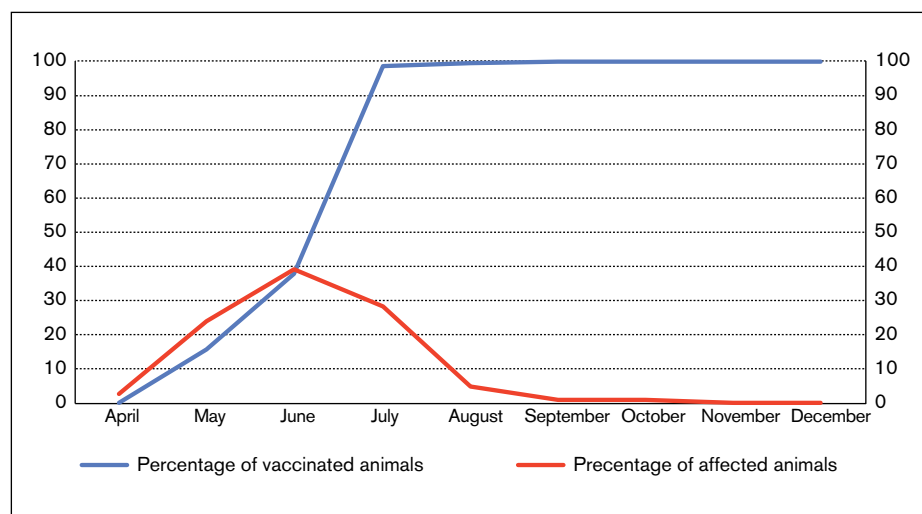
Current legislation does not allow vaccination unless LSD has emerged and is spreading, hence vaccination was inevitable for the disease control. In 2016 there was no vaccine bank apart from the vaccine purchased

by the European Commission. The process of purchasing vaccines, vaccination and the onset of immunity prolonged the spread of the virus through the former Yugoslav Republic of Macedonia. The “wait and vaccinate” policy applied in the affected countries proved to be less successful than the “preventive vaccination” carried out in Croatia.

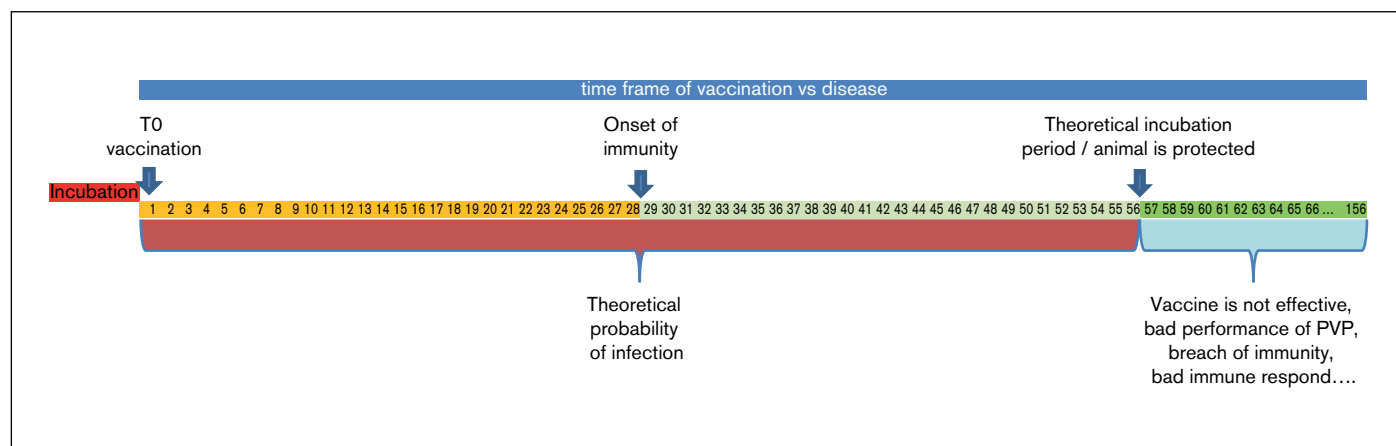
The strategy applied in the former Yugoslav Republic of Macedonia after receipt of the vaccines – culling of animals with clinical signs or confirmed by laboratory result only – was considered by EFSA and compared with the stamping-out policy applied in affected EU Member States: its report did not find any significant differences in the strategies that supported the Macedonian veterinary service. The EFSA findings are based on experience gained in Bulgaria and Greece.

The former Yugoslav Republic of Macedonia has reported more outbreaks than any other affected country in the region, and LSD has spread through almost its entire territory. This epidemiological situation was analysed using the data on LSD collected in 2016 and other circumstances that could influence the spread of the disease. The overall findings show that the evidence of the effectiveness of the vaccine is indisputable: as the number of vaccinated animals increased, the number of new reported outbreaks decreased. The results of the vaccination campaign are shown in Figure 12. It is worth emphasizing once more that the June vaccination campaign took place only in the eastern part of the country.

Analysis of the incidence of LSD as shown in Figure 3 also speaks in favour of vaccination. Vaccination started at the end of May 2016 and was implemented in the eastern part of the country during June 2016; the disease then moved from the eastern part of the country to the central area in July and then to western areas in August. As indicated in Figure 12, when vaccination of the entire cattle population reached 50 percent the

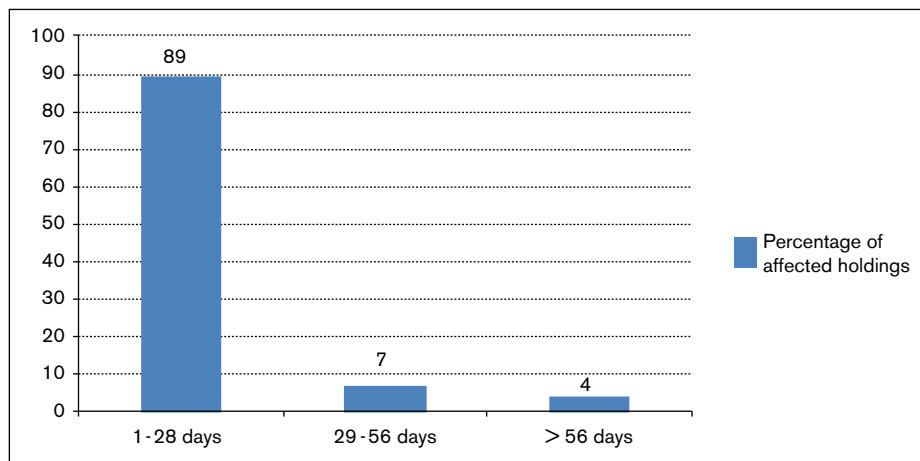


**Figure 12:** Ratio between vaccination and the occurrence of outbreaks of LSD



**Figure 13:** Theoretical time frame of exposure of animals to infection after vaccination





**Figure 14:** Percentage of outbreaks of LSD in the former Yugoslav Republic of Macedonia analysed through the theoretical timeframe of exposure shown in Figure 13

number of outbreaks began to decrease and reached the lowest when vaccination coverage reached 100 percent.

With LSD present and spreading rapidly in-country, the means of transmission had to be analysed. The veterinary service issued several measures to ban movements of cattle and events that could facilitate the spread of the disease. These restrictive measures, however, can easily lead to illegal movements of animals, which can be a possible pathway for transmission but cannot be the logical explanation for all outbreaks. With respect

“ The peak of vector activity in June was followed by the peak of the disease in June and July ”

to vector monitoring, the authors noticed that the peak of vector activity in June was followed by the peak of the disease in June and July. Whether *Culicoides* is relevant to the Macedonian situation is a matter for further research, which we hope will take place. The authors presented the results from the monitoring of *Culicoides* in 2016 in Figure 10, without any implications.

The main unresolved question for the veterinary service about LSD outbreaks in 2016 is the very high number of post-vaccination outbreaks. One possible explanation is that peaks of the outbreak and the vaccination programme were taking place at the same time, and that most of the animals were hence in the incubation period when vaccinated. In the absence of sufficient and reliable scientific data on the incubation period, however, it is safe to assume that the incubation period for the disease can be up to 28 days; the data also suggest that there

is a similar time for the onset of immunity. As described in the *EFSA Urgent Advice on Lumpy Skin Disease*, the antibodies appear ten days after inoculation and peak at 30 days post-inoculation: it is hence reasonable to conclude that at least 28 days must elapse for the onset of immunity. By merging these two periods we presented a timeframe reflecting the period in which, theoretically, the animals could be infected regardless of vaccination (Figure 13).

When the post-vaccination outbreaks in the former Yugoslav Republic of Macedonia are analysed in relation to the theoretical timeframe indicated in Figure 13, 89 percent of post-vaccination outbreaks were reported within the 28 days post-vaccination with a median of nine days, 7 percent were reported within 56 days of vaccination with a median of 40 days, and 4 percent were reported within beyond 56 days. The distribution of the outbreaks is presented in Figure 14.

Finally, from the experience gained we can conclude that:

- vaccination of animals is the most effective measure in controlling LSD;
- both vaccines used in the former Yugoslav Republic of Macedonia were shown to be effective;
- considering the lack of data on the epidemiology of LSD, with the exception of the positive experience in Israel, the Macedonian and regional veterinary services chose an appropriate policy for controlling LSD;
- apart from the policies applied, the regional approach was crucial for effective control of LSD;
- the LSD situation in the former Yugoslav Republic of Macedonia has helped to identify the gaps and weakness of the veterinary service by putting to the test the procedures in place and the capacity of the available resources;
- the threat of intrusion of vector-borne transboundary animal diseases such as LSD can be best prevented

by vaccination, whereas “wait and vaccinate” policies can lead to the repetition of the LSD situation in 2016;

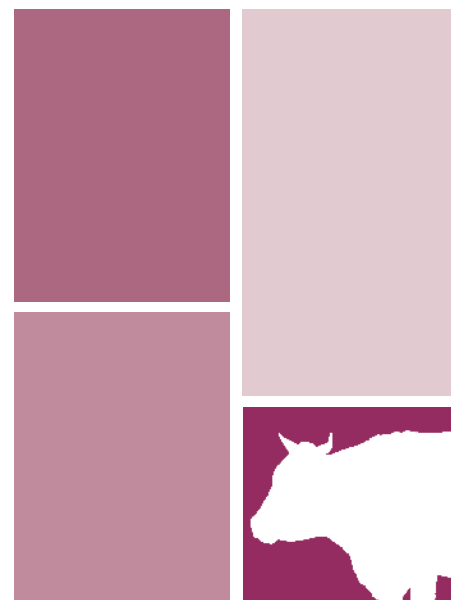
- control and eradication of LSD solely by regular control measures such as stamping out are not feasible; and
- with respect to vector-borne transboundary animal diseases, we have to consider new approaches in the light of new scientific findings with a view to greater preparedness to prevent and control the diseases.

## ACKNOWLEDGMENTS

The authors wish to thank: the European Commission for contributing vaccine and supporting the purchase of vaccine for prevention and control of LSD; GF-TADs for fostering the regional approach and keeping abreast of new developments in the region; FAO for its support during the crisis in 2016; the countries of the region for professional collaboration and successful prevention of further spread of the disease; the private veterinary practitioners; and the management and staff of the Food and Veterinary Agency for their dedicated engagement during 2016. <sup>360</sup>

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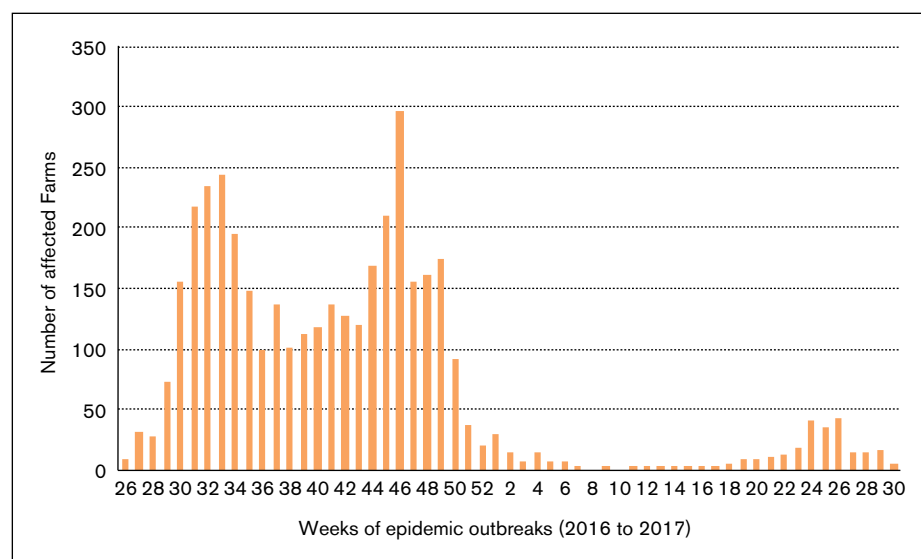
## SITUATION

## Lumpy Skin Disease epidemics in Albania

**Contributors:** Ledi Pite, Edi Fero, Admir Ago, Matilda Xhepa,<sup>1</sup> Jonida Boci, Ani Vodica,<sup>2</sup> Ermira Rizvanolli and Ali Lilo<sup>1</sup>

Albania has about 360 000 cattle farms, of which 80 percent are small-scale subsistence farms that have one or two animals. On 6 July 2016 clinical signs of Lumpy Skin Disease (LSD) were reported for the first time in the village of Vlashaj in Bulqizë district close to the border with the Former Yugoslavian Republic of Macedonia. The disease was clinically diagnosed on 28 June and reported to the veterinary service by 6 July. The epidemic spread quickly and was showing a declining trend by the end of 2016. LSD was reported in 3 568 outbreaks on farms and in 948 of 3 000 villages in 30 of Albania's 36 districts. Morbidity was estimated at 42 percent and mortality at 12 percent on the basis of the clinical cases reported. Subsistence farms were predominantly affected. The epidemic continued during 2017, though fewer outbreaks were recorded from the middle of February to the beginning of May – 318 outbreaks on farms and in 198 villages to date. Morbidity is estimated at 22 percent and overall mortality at 6 percent on the basis of the clinical cases reported.

Figure 1 shows the number of farms affected per week since the LSD outbreaks started in 2016. There was an initial peak followed by a decrease in the occurrence of LSD from the beginning of September to the end of October 2016, followed by a second peak. It is noteworthy that after a gap a small number of LSD cases occurred in April 2017. Figure 2 gives a map of the villages affected during 2016. The two periods during which villages were affected – from the end of June to September, and from the end of September to the beginning of January – are shown in different colours in Figure 2. The information in the map shows the propagation of the disease from the eastern to the western part of Albania. By the beginning of May 2017 the epidemic had emerged in the southern part of Albania, but it seemed to be decreasing; Figure 3 shows



**Figure 1:** Farms affected per week from week 26 of 2016 to week 30 of 2017

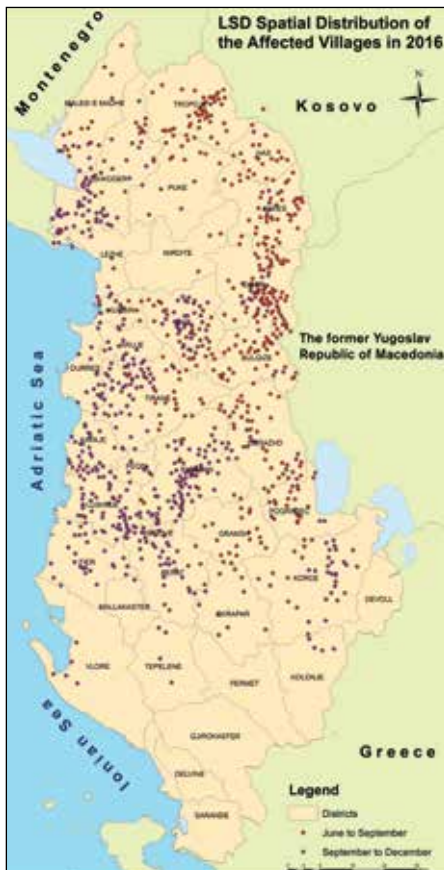


*The clinical examination and symptomatic treatment of LSD*

<sup>1</sup> Ministry of Agriculture, Rural Development and Water Administration, Albania

<sup>2</sup> Food Safety and Veterinary Institute, Albania





**Figure 2:** Spatial distribution of villages affected by LSD in 2016



**Figure 3:** Spatial distribution of villages affected by LSD from beginning of May to the beginning of August in 2017



**Figure 4:** Spatial distribution of LSD vaccination, by district in 2016

these cases from the beginning of May to the beginning of August 2017.

The data were collected by private veterinarians who reported clinical cases to state veterinarians, who in turn entered the data into the national Livestock and Veterinary Information System database, which is known as RUDA. The state veterinarians followed up the cases by collecting additional information and samples, which were sent to the Food Safety and Veterinary Institute of Albania.

Laboratory confirmation of the disease was initially carried out by the Bulgarian Food Safety Agency using the real-time polymerase chain reaction (rtPCR). The Albanian Food Safety and Veterinary Institute subsequently conducted rtPCR diagnosis of the collected samples: it tested 2 275 diagnostic samples and obtained 881 positive results with rtPCR.

A national emergency control plan was immediately prepared to manage human and financial resources of the veterinary service. A ban on animal movements from farms to abattoirs and livestock markets was initially enforced. Mass vaccination by private veterinary clinics was started on 26 July 2016: the first phase was conducted until September and the second from December 2016 to January 2017 according to the availability of vaccines. Emergency vaccination started on large farms first

to prevent immediate large-scale losses. Veterinarians faced considerable difficulty in reaching remote holdings during this period. Figure 4 shows the spatial distribution of vaccination in 2016, by district. In May 2017 mass vaccination by private veterinary clinics was started with a view to protecting cattle from the outbreaks; data recording is ongoing.

While the veterinary service was facing the LSD incursion, veterinary reform was taking place and veterinary activities such as vaccination data entry were delegated to private veterinary clinics. In view of the emergency situation, data on vaccination were initially entered and stored in the database created under the Protection Against Zoonotic Diseases, Albania (PAZA) project funded by the European Union. The PAZA project provided training in vaccination data entry, and from December state veterinary database operators entered the vaccination data into the improved module of the national Livestock and Veterinary Information System database. In spite of difficulties related to information management, the data on livestock identification and registration were entered into the system according to national regulations.

Monitoring of the vaccination campaign was conducted in collaboration with PAZA

and students of Faculty of Veterinary Medicine of the Agricultural University of Tirana. The awareness campaign on farm biosecurity and good veterinary practice was addressed by all levels of the veterinary service, also in collaboration with the PAZA project. The requirements for international reporting to the World Organization for Animal Health (OIE) and Animal Disease Notification System of the European Union were fulfilled.

Initially, 75 000 doses of live homologous LSD vaccine were donated from the Directorate-General for Health and Food Safety of the European Commission; subsequently 480 000 live homologous LSD vaccine doses were provided by the Government of Albania. As a form of compensation, the Government replaced dead animals on farms affected by LSD with improved-breed Jersey and Holstein heifers.

The Albanian veterinary service faced numerous technical and administrative challenges in relation to controlling LSD. Re-organization with a view to delivering a modern veterinary service has been initiated in Albania. The state veterinary service at the central level will play a crucial role in improving private veterinary services in terms of delivering veterinary activities and in involving farmers in disease surveillance and control. <sup>360</sup>



## SITUATION

# Lumpy Skin Disease in Kosovo, 2016

Contributors: Valdet Gjinojci<sup>1</sup> and Naomi Honhold<sup>2</sup>

The Kosovo veterinary authorities took preparatory actions for a possible incursion of lumpy skin disease (LSD) as soon as it was reported in eastern Greece in mid-2015. The timeline in Table 1 gives a summary of the actions.

## PUBLIC AWARENESS

A meeting for government and private field veterinarians was held in August 2015 when the infection had entered western Greece. A further meeting was held in April of 2016 when the disease was first reported in the

former Yugoslav Republic of Macedonia. At both meetings the disease and its control were described and discussed.

A disease manual for field veterinarians produced and circulated in April 2016 gave information about LSD with a view to raising awareness so that suspect cases would be reported. Several suspect cases were reported and investigated, but they proved negative.

A two-sided A5 flyer produced for farmers gave basic information about LSD, including assurances with regard to human health (Figures 2a and 2b). The flyer focused on

brief messages rather than a mass of detailed information because previous experience in Kosovo had shown that farmers usually did not read leaflets with a large amount of text. Design of the flyer commenced shortly before the first reported case, and flyers were distributed as soon as they had been produced. A post-outbreak survey showed that 87 percent of farmers had found the information in the flyer to have been useful or very useful. A copy of the English language version, which was translated from Albanian, is attached.

## COST-BENEFIT ANALYSIS

A cost-benefit analysis was undertaken to investigate the economic justifications for control by mass vaccination or culling. It was clear that culling would soon become prohibitively expensive because of the compensation involved, and that disposal of carcasses would also be difficult and expensive. Mass vaccination was found to have a positive benefit in terms of costs on the basis of moderate assumptions about levels of infection. The cost-benefit analysis is available from the KFVA.

## CONTROL POLICY

On the basis of epidemiological principles and the cost-benefit analysis, the advice on control given by the European Union "Technical Assistance for the Animal Health Department of the KFVA and the Food and Veterinary Laboratory" (KAHL) project, which worked with KFVA, was that culling of infected herds should be limited to the first one or two affected premises at most, because it was very unlikely that culling beyond that would prevent spread. Mass vaccination was recommended as the best available control policy. The preferred choice of vaccine would be a homologous LSD vaccine, though a 10x dose of a heterologous vaccine against sheep and goat pox (SGPX) could be used if no homologous vaccine were available. This policy was adopted.

**Table 1:** Timeline for Lumpy Skin Disease in Kosovo 2016

August 2015	Workshop on LSD held at the Kosovo Food and Veterinary Agency (KFVA) for government and private veterinarians, using experience from Israel and Turkey. Estimated that if the disease spread at the same pace as across Turkey, LSD could be expected to enter Kosovo in May 2016.
Aug 2015–May 2016	Suspect cases of LSD reported and investigated. All negative.
April 2016	LSD reported from the former Yugoslav Republic of Macedonia.
April 2016	Workshop on LSD held at the KFVA for government and private veterinarians. This described the disease and its control. It was estimated that LSD would enter Kosovo within the next two months.
April 2016	Disease manual on LSD produced and distributed to field veterinarians in Albanian and Serbian, which are official languages in Kosovo.
Mid-June 2016	Design of an information flyer for farmers on LSD in Albanian and Serbian.
16 June 2016	First reported case of LSD in Kosovo from border area close to Serbia. Emergency vaccine requested from the EU – 50 000 doses.
16 June–16 July 2016	Infection spreads to all areas of Kosovo within four weeks.
11 July–18 July 2016	Distribution of LSD information flyer to farmers.
11 July 2016	EU provides 25 000 doses of LSD vaccine. Vaccination applied in areas of Kosovo considered at higher risk of early spread and further introductions; these areas border the former Yugoslav Republic of Macedonia and Serbia.
August 2016	The Government approves the expenditure required to purchase and use 235 000 doses of LSD vaccine.
15 September 2016	Arrival of 235 000 doses of homologous LSD vaccine. See below under Vaccination.
16 September–11 November 2016	Mass vaccination of cattle in Kosovo.
November 2016	No further cases reported.

<sup>1</sup> Chief Executive Officer, Kosovo Food and Veterinary Agency (KFVA)

<sup>2</sup> Team Leader, European Union technical assistance for the Animal Health Department of the KFVA and the Food and Veterinary Laboratory project



## CULLING

The index case was a single isolated animal, which was culled. Subsequently, infected animals were not culled.

## VACCINATION

Vaccination against LSD in Kosovo in 2016 was carried out in two phases. The vaccine used in both phases was an homologous vaccine against LSD produced by Onderstepoort Biological Products (OBP Lumpy Skin Disease vaccine).

After the initial incursion in mid-June 2016, Kosovo requested an emergency supply of vaccine from the European Union (EU), as had other countries in the region. The EU donated 25 000 doses of vaccine, which arrived in Kosovo in early July 2016. These were mostly used in premises near the initial outbreak and premises near the borders with Serbia and the former Yugoslav Republic of Macedonia, which were both infected at that time. The premises were identified as being at high risk, and the vaccine was used there in an attempt to limit introduction and to slow the spread of infection. In these areas, 23 596 vaccinations were recorded using the EU donated vaccine; this suggests a wastage rate of 6 percent, which is common during vaccination campaigns.

In the event, slightly more than 25 000 vaccinations were recorded in Kosovo between 11 July to 15 September 2016 at 3 819 premises. It is likely that small amounts of vaccine were obtained privately, possibly via Albania.

The infection spread across Kosovo in a few weeks, and the territory became endemically infected. This is not surprising, given the rate of spread seen in other countries.

Subsequent efforts by the Chief Executive Officer of KFVA, with support from the KAHL project and in particular the cost-benefit analysis, succeeded in obtaining funding from the Government of Kosovo for the procurement and administration of a further 235 000 doses of LSD vaccine. This was to be used in a mass vaccination of all cattle across Kosovo. The vaccine was delivered on 15 September 2016 and deployed in the field from 16 September. From this batch, 213 938 animals were recorded as vaccinated at 41 345 premises. This indicates

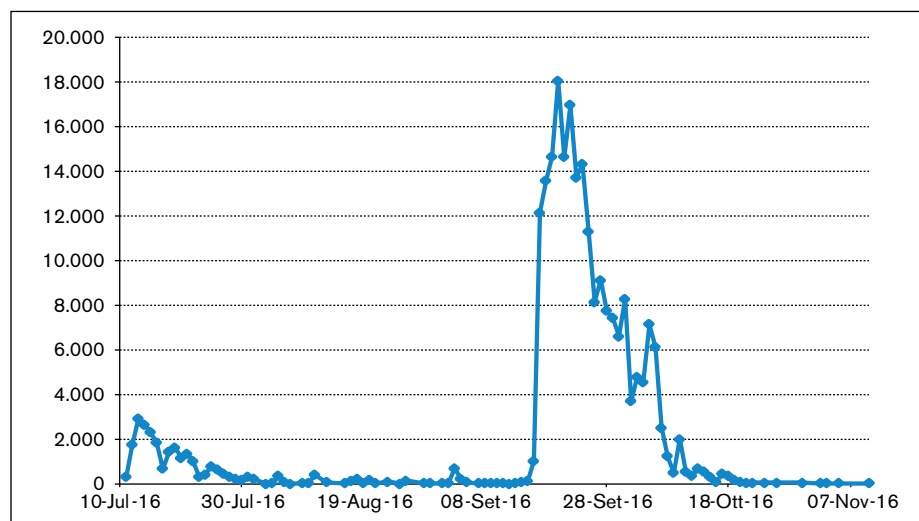


Figure 1: LSD vaccinations in Kosovo, by date

a wastage rate of 9 percent, which is acceptable in a vaccination campaign.

The numbers of premises and animals vaccinated in the two phases – 11 July to 15 September 2016, and 16 September to 10 November 2016 – and the overall figures are shown in Table 2.

Combining the two sets of vaccinations may seem a simple matter of addition, but data checks showed that although there were no records of animals being vaccinated twice, 976 of the premises with vaccinations before 16 September also had vaccinations on or after that date to complete a previous partial vaccination. This means that the total of vaccinated premises is slightly lower, though the total number of cattle vaccinated remains the same. The total number of recorded vaccinations is 239 643 at 44 188 premises in all municipalities of Kosovo.

Graph 1 shows the numbers of recorded vaccinations by date from 11 July to 10 November 2016, and the use of the initial donated doses and the second batch purchased by the Government.

Checks of the data in the national identification and registration system showed that the overall number of registered premises in Kosovo was 56 380, and that the registered cattle population was over 340 000. Both figures are considerably higher than the number of premises and cattle vaccinated. However, it is not surprising that the recorded registrations are higher than expected: it is

known that there is an issue of under-reporting of farms that become inactive or that pass from one generation to the next. There is also a known issue of failure to notify deaths of livestock. These are common issues with identification and registration systems. It follows that the overall herd coverage rate of 78.1 percent and the animal coverage rate of 70 percent will be underestimates. The individual animal rates in particular are likely to be underestimated: the 2014 agricultural census gave a cattle population of 262 000, albeit on more than 66 000 premises that were recorded as having cattle.

## COMPENSATION

In 2016, a Government commitment was made to compensate owners of cattle that died from LSD (i.e. that had not been culled). Eventually 1 500 cattle were said to have died of the disease, and their owners will be compensated at a rate of €1 000 per animal.

## OUTCOME

Reported clinical cases stopped shortly after mass vaccination had been completed.

## LESSONS LEARNED

The policy decision to undertake mass vaccination against LSD in cattle in Kosovo had a successful outcome. Vaccination will need to be repeated in future years, but there is debate as to whether this should be a government-funded activity, and if so how long it should last.

A set of economic criteria for evaluating the role of the Government in controlling livestock diseases has recently been established in Kosovo. They can be summarized as:

- Is there a human health risk?
- Is there a threat to national food security?
- Is there a nationally significant threat to trade in livestock or livestock products?
- Is there a nationally serious threat to livestock production that either farmers

Table 2: LSD Vaccination figures in Kosovo, 2016

Phase	Premises	Animals
Between 11 July and 15 September 2016 (EU donation)	3 819	25 705
From 16 September to 10 November 2016 (Kosovo purchase)	41 345	213 938
<b>Overall</b>	<b>44 188</b>	<b>239 643</b>

or the private veterinary system cannot control without government resources?

- Is there a significant threat to the livelihoods of particular groups of poor farmers?
- Does inaction or inappropriate action by some farmers create a serious problem for other farmers?
- Is there a regional control programme or an EU requirement for control?

Any disease must meet one or more of these criteria to justify involvement of the Government.

In 2016, LSD was an emergency situation: it was spreading rapidly in a naïve population, was a serious national-level threat to livestock production and farmers and private veterinarians could not control it without the use of government resources to produce an adequate response. So the situation in the first year clearly met one of the criteria for government involvement – but this will not be the case for subsequent years unless a coordinated and funded regional programme is established. Even in this situation there must be an exit strategy of disease eradication with prevention of re-incursion, or an acceptance that the disease will persist.

Kosovo is committed to participation in any regionally funded vaccination programme. In the absence of such a programme, it is recommended that, in future years, farmers seek and pay for vaccination from private veterinarians. The role of KFVA will be to licence

the vaccine and allow its import and sale to private veterinary practitioners. Even in a publicly funded vaccination campaign, the option of cost-sharing could be considered, with, for example, the Government providing the vaccine free of charge and the farmer paying private veterinary practitioners for the vaccination service.

The Government's promise of compensation for cattle that not been culled but had died from the disease had of course to be honoured. But this raises questions about the use of compensation. A basic principle of compensation is never to pay for an animal that is already dead, only for those that are culled as part of the official control programme. There are several reasons for this. It is often difficult to prove what an animal dies from and veterinarians can come under pressure from their clients to say that an animal died of a particular cause even when this is not certain or even when it is clearly not the case. Such situations were reported in Kosovo in 2016. Paying compensation for dead animals creates a moral hazard.

Perhaps more importantly, paying compensation for dead animals breaks the clear and important purpose of compensation – to encourage early reporting so as to accelerate the response and hence the effectiveness of control measures. If farmers know they will be compensated for dead animals, they have no incentive to report quickly. It is an important principle that compensation be used as a control tool with a view to accelerating the

reporting and control of outbreaks, thereby minimizing the overall size and cost of an outbreak.

The only situation in which compensation for a dead animal might be paid is anthrax, because the carcass is the major source of contamination. For all other severe livestock diseases, the dead animal is not spreading the disease significantly compared with a live animal. But even in the case of anthrax, other countries in the region have shown that post-mortem compensation creates a moral hazard.

## CONCLUSION

LSD spread rapidly across Kosovo after its initial introduction, and it was controlled by means of mass vaccination. The cost-benefit analysis indicated that this would result in the optimum economic outcome. Because only the Government could arrange vaccination at the necessary short notice, it was undertaken as a government-funded emergency campaign. Even so, there were some delays on obtaining the required funding.

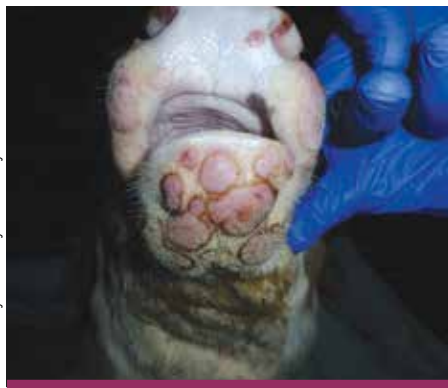
Public awareness in the form of previous training for private veterinary practitioners and literature aimed at farmers played an important role in early detection and public understanding of the disease.

Issues of compensation and who should pay for vaccination have been raised, and need to be discussed. Kosovo will nonetheless participate fully in any regional control programme in future years. <sup>360</sup>



Figure 2: Two-sided A5 flyer produced for farmers on basic information about LSD





## SITUATION

# Successful Control of Lumpy Skin Disease of Cattle in Montenegro during 2016

Contributors: Vesna Dakovic<sup>1</sup> and Drago Marojevic<sup>2</sup>

**L**umpy skin disease (LSD) of cattle was first reported in Montenegro in July 2016. The disease had previously progressed successively through the former Yugoslav Republic of Macedonia, Serbia, Albania and Kosovo. After a month and a half the disease was brought under control in Montenegro, and further spread to the north-west was halted.

After the LSD outbreak in the former Yugoslav Republic of Macedonia, the Montenegrin Administration for Food Safety, Veterinary and Phytosanitary Affairs concluded that there was a very high risk of an LSD outbreak in Montenegro. The measures for prevention and control recommended by the World Organisation for Animal Health (OIE) and the European Food Safety Authority (EFSA) were implemented, and there was intensive work to ensure the provision of vaccines to prevent the disease. At the same time the Government established the expert team for LSD in cattle, which comprised staff from the Veterinary Division of the Administration for Food Safety, Veterinary and Phytosanitary Affairs, specialized veterinary offices and veterinary inspectors. The expert team consulted the European Commission Directorate-General for Health and Food Safety (DG SANTE) and the Global Framework for the progressive control of Transboundary Animal Diseases (GF-TADs) Standing Group of Experts on Lumpy Skin Disease for South-Eastern Europe, and made the decision to start preventive vaccination before an outbreak could occur. Unfortunately the Municipality of Gusinje in the north-eastern region of Montenegro was struck by the disease in July 2016 before the vaccination programme could commence.

Montenegro is a small country in the Balkan Peninsula that has been an independent state since 21 May 2006. It is bordered by Albania in the south-east, Kosovo



**Figure 1:** Map of Montenegro

Source: <http://www.asybijela.com/sMontenegro.html>

in the east, Serbia in the north-east, Bosnia and Herzegovina in the north and north-west, Croatia in the north-west and the Adriatic Sea to the west and south-west. Italy is its nearest neighbour to the west.

Montenegro has an area of 13 812 km<sup>2</sup>, of which 38 percent is agricultural land; of this, 62 percent is pasture. The population is 620 029, of whom 40 percent live in rural areas and engage in agriculture. Agricultural holdings in Montenegro are fragmented: an average holding covers 4.6 ha, with an average of 3.3 breeding cattle. According to the database, which was updated after the recent cattle vaccination programme, the bovine population is 93 350. Because the country is characterized by high mountains

with wide plateaux, agriculture is dominated by traditional cattle breeding, which involves taking the cattle to mountain pastures – originally called *katuni* – from May to October. During the winter animals stay in low-lying areas and are kept indoors.

The LSD outbreak coincided with the summer season, with the cattle in high pastures. With confirmation of the first case in Gusinje, which is close to the border of Albania where the disease had already been confirmed, the first challenge was recognized. The border between Montenegro and Albania is characterized by mountains of 2 000 m or more, which means that infected insects must have flown at

those heights to transmit LSD from Albania to Montenegro. This seemed barely possible. The expert team accordingly decided to slaughter and dispose of all the animals in infected herds, according to European legislation, EFSA recommendations and the EU and OIE standards. These measures had been applied by all the countries affected by LSD prior to its appearance in Montenegro. In the initial outbreak, ten cases were detected in ten holdings.

The disease unexpectedly broke out in four more municipalities in the Bjelasica mountain area near the borders with Kosovo and Serbia: 80 percent of the 556 recorded cases of LSD occurred in these four municipalities (See Table 1).

**Table 1:** Distribution of recorded cases of LSD in Bjelasica mountain area, Montenegro in 2016

Municipality	No. of holdings	No. of diseased animals
Bijelo Polje	123	145
Berane	80	112
Mojkovac	60	105
Kolašin	61	86
<b>Total</b>	<b>324</b>	<b>448</b>

<sup>1</sup> Director of Administration for Food Safety, Veterinary and Phytosanitary affairs of Montenegro

<sup>2</sup> Director of Veterinary Medicine, University of Belgrade

The second unexpected outbreak occurred at this time that put additional pressure on the response by the Veterinary Administration. Most of the LSD outbreaks were in the north-eastern region of Montenegro, but an outbreak was detected in the remote village of Mala Crna Gora in the north-western region at an altitude of 2 000 m. Three LSD cases were detected on a single holding, but there were no subsequent cases.

In late August, when there was a high level of confidence that the disease had been brought under control in the central north-eastern part of the country, two hotspots emerged at the western border: this led to a suspicion that the disease was present in Bosnia and Herzegovina, but this was proved not to be the case.

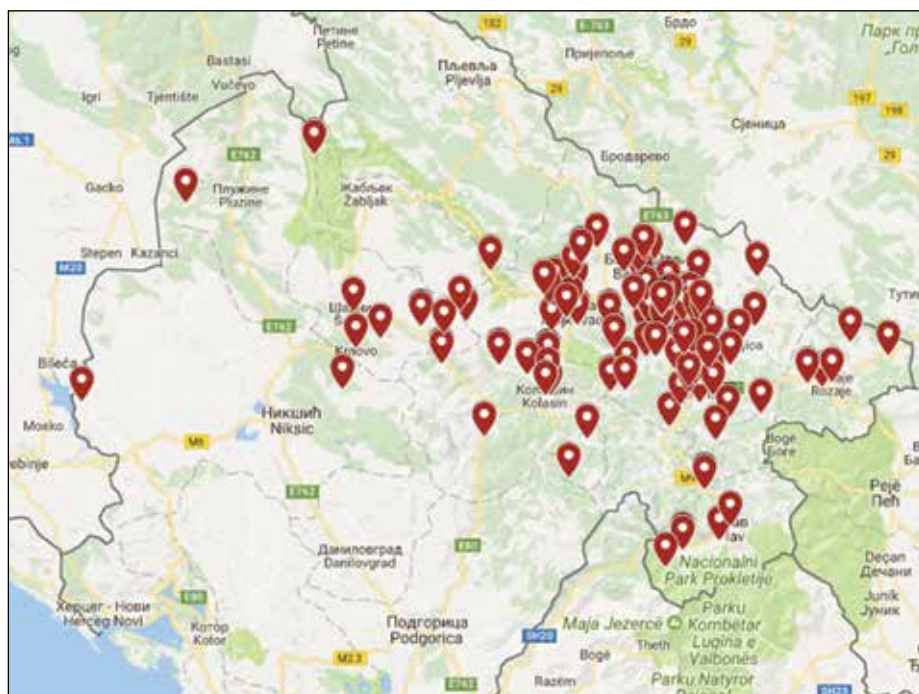
As a result of a parallel planning process before the outbreaks, the national cattle vaccination programme started ten days after the first detection of LSD in Montenegro, and was completed in 15 days. All Montenegrin veterinarians, including retired people, and the staff of the Veterinary Administration were engaged in a mass vaccination that covered virtually 100 percent of the cattle. At the same time animals for which laboratory testing confirmed the disease were culled, and the carcasses were safely disposed.

As of early September, the LSD outbreak had been controlled. After 10 September a single case was confirmed in a bovine animal that had not been vaccinated as a result of the owner's negligence. It is reasonable to claim that the disease was halted in Montenegro in 2016 – but vaccination must

become mandatory in the coming years. Now, 2017, is the time to make new decisions as to when to commence LSD vaccination in the coming years, the intervals between LSD vaccinations and how they can be aligned with vaccination against bluetongue, which was also confirmed in Montenegro in 2016. The Veterinary Administration must also identify and budget the funds required to implement the vaccination measures.

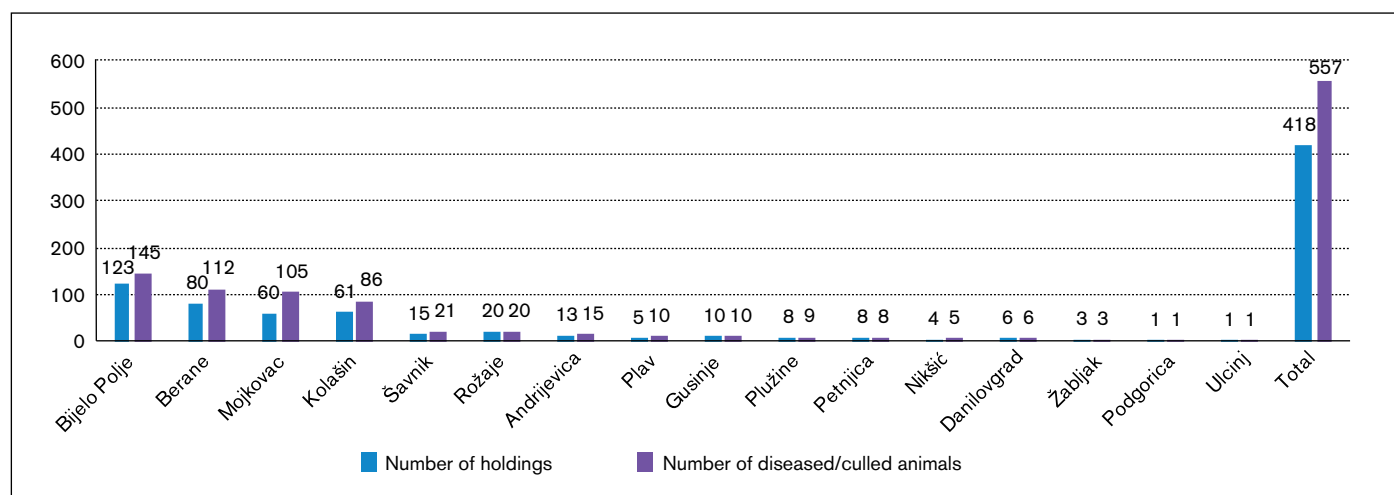
Control of LSD control entailed a 0.5 percent reduction in the livestock population. The cost of vaccines, the vaccination programme and implementation of controls and compensation paid for animals culled amounted to EUR 1.5 million; this was provided from national funds for crisis measures. The total budget for veterinary administration was EUR 1.1 million for animal health measures, and with the cumulative costs of culling animals affected by LSD in 2016 and compensation for animal deaths, the vaccination campaign and other crisis-driven measures constituted a significant financial burden on the national administration.

The involvement of all veterinary offices and services, the cooperation of local administrations and the Extension Service and the work of numerous institutions and individuals ensured that LSD was brought under control in Montenegro. This successful control effort also halted the movement of LSD further up the western side of the Balkan Peninsula. In the process, the Veterinary Administration faced many dilemmas, ambiguities and decision-making challenges, and some aspects of the epidemiology of the disease were not fully understood, particularly in relation to vector movements. Technical knowledge however – sometimes intuition – and the experience gained from regional colleagues, enables Montenegro to apply the appropriate measures and bring the disease under control. <sup>360</sup>



**Figure 2:** LSD outbreaks in Montenegro (July-August 2016)

Source: <http://www.asybijela.com/sMontenegro.html>



**Figure 3:** Number of animals infected with LSD in Montenegro





## SITUATION

## Enemy Approaching: the Austrian Veterinary Authority prepares for Lumpy Skin Disease

Contributor: Simon Stockreiter<sup>1</sup>

The Austrian livestock sector is comparatively small with 2 million cattle and 60 000 cattle farmers, most of whom farm extensively. A large number of cattle are free-range, especially in the Alps where most animals spend the summer months on the mountain pastures. The agricultural sector in Austria is nonetheless an important element in the economy: animals and animal products are traded internationally and are highly valued in and outside the country. Austria has been spared large outbreaks of highly contagious animal diseases for decades, but now an animal disease is approaching that has the potential to change this situation – Lumpy Skin Disease (LSD). This article provides an overview of the ways in which Austrian veterinary services, which are administered by the Ministry of Health and Women's Affairs, are dealing with the emerging danger. Their approach is to some extent empirical: it has not been tested in an outbreak but it is based on analysis of the threat, and the policies formulated reflect observations of what has and has not been successful in stopping the spread of disease in recently infected countries.

### BACKGROUND

LSD is a typical pox disease caused by the capripox virus. In cattle – and in wild buffaloes, giraffes and impalas – generalized skin lesions appear; clinical signs include fever, lachrymation and nasal discharge. Painful, firm, round swellings and nodules occur on the skin and subcutaneous tissue and sometimes even affect the underlying muscles. LSD is transmitted by direct contact and by blood-feeding vectors. The long incubation period of 28 days (OIE Code, 2017) is an important factor in the spread and control of the disease.

Before 2006, LSD was confined to Africa but it has spread since then on a large scale across the Middle East via Turkey and to Europe: the first cases were confirmed in Thrace and subsequently in Greece in 2015. Some European Union (EU) Member States have now been affected.

### STAYING INFORMED

In order to plan effective control measures the veterinary administration must have detailed knowledge of the current situation. As a member of the EU, Austria has the advantage of access to various information channels such as the Animal Disease Notification System database, which provides an up-to-date overview of the situation in countries affected by LSD.

Visual representations of the current situation and the progression of disease outbreaks are powerful tools that enable the veterinary authorities to keep non-technical audiences informed. Interested parties such as the media, politicians and stakeholders require information in a more concise form than that used by veterinary experts. The Austrian Agency for Health and Food Safety (AGES) accordingly monitors the current disease situation on the basis of Animal Disease Notification System data with a view to presenting the available information as accurately as possible (see Figure 1). Since the appearance of LSD in south-eastern Europe, these reports have been updated weekly and published on the homepage of the Federal Ministry of Health and Women's Affairs.

International information exchange is also important in keeping abreast of current developments of the disease situation and the control measures being applied. The EU Member States have access to information at the international level through the regular meetings of the Standing Veterinary Committee in Brussels and meetings of chief veterinary officers, from reference laboratories and national experts, and through the FAO/OIE Global Framework for the Progressive Control of Transboundary Animal Diseases, which has been a valuable source of information since LSD started to spread. Various scientific institutions such as the European Food Safety Authority and numerous research facilities are of course part of the information network and have provided useful risk assessments based on recent data.

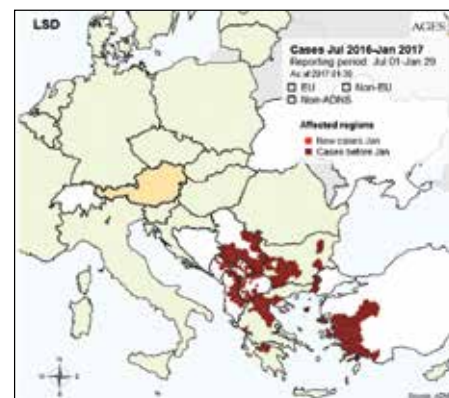


Figure 1: Screenshot from the weekly LSD situation report published by AGES

At the national level, veterinary authorities of the Austrian Federal Countries were fully briefed on the situation at an early stage. Official veterinarians, whose daily work enables them to create awareness of the disease among animal owners, are kept informed about the international epidemiological situation and the relevant regulatory frameworks through web-based seminars – also known as webinars – which they find extremely useful.

### FORMING INTERNATIONAL ALLIANCES

In view of the nature of LSD and analysis of its spread, it is obvious that small-scale national control measures are not effective. Austria has for some years cooperated with the veterinary administrations and central European chief veterinary officers in Bulgaria, Croatia, Slovenia, Slovakia, the Czech Republic, Hungary and Romania. At a meeting in June 2016 the numerous issues concerning LSD were analysed and the urgent need for common action was recognized. There is consensus that all measures applied and every Euro spent on controlling the disease in areas that are already affected will reduce the risk of progressive spread into central Europe. Providing additional financial resources for the control of the disease cannot therefore be regarded as merely altruistic.

<sup>1</sup> Department for Crisis Coordination, Communication and Law, Federal Ministry of Health and Women's Affairs

## SHARING RESPONSIBILITIES

In the spring of 2016 it was clear that attempts in Greece to confine LSD by using mass vaccination would not be successful, therefore the Austrian Ministry of Health sought contact with the Austrian stakeholders. As mentioned earlier, Austria has not experienced outbreaks of highly contagious animal diseases for a long time, hence there is little public awareness of the serious implications of such a situation. The consequences of an LSD outbreak and the control measures required would have far-reaching effects in a number of sectors, some of which are outside the remit of the veterinary administration.

With this in mind, the Federal Ministry of Health and Women's Affairs contacted the Austrian Chancellery and the ministries of finance, the economy, the environment and foreign affairs to explain the implications of an LSD outbreak in Austria on the basis of the situation reports referred to above. It was made clear that an outbreak of LSD in Austria had to be considered likely and that it would have serious economic effects.

Various stakeholders' organizations and individual stakeholders such as dairy and meat-processing companies, retailers and animal insemination centres were informed at a number of meetings of the serious situation in Europe and asked to provide analyses of the consequences for them of an outbreak of LSD and the consequent trade restrictions. It was made clear at the outset that although recent animal diseases in Austria had been handled by the veterinary administration and specific parts of the agricultural sector, an outbreak of LSD could not be the sole responsibility of the veterinary administration and that collaboration and solidarity among the various sectors would be required.

## PRACTICAL ARRANGEMENTS

Outbreak scenarios and a risk assessment for Austria were prepared by AGES on the basis of experiences in the countries already affected by LSD, and data were adapted to the situation in Austria in terms of animal densities and trade flows and the resulting risks. Consideration was also given to further courses of action to mitigate specific risks.

A programme for the early detection of LSD has now been developed. As soon as LSD approaches to within 100 km of the Austrian border a surveillance programme will be launched to identify any outbreaks in Austria during the incubation period. Monthly virological monitoring has been started for this purpose that uses the geographic reference units used for the Bluetongue monitoring programme: this will ensure detection of 5 percent prevalence of LSD with 95 percent probability. As soon as the disease approaches to within 50 km of the national border, the frequency of monitoring will increase to twice a month. Sampling kits

have been prepared by the National Reference Laboratory and sent to all veterinary authorities (see Figure 2) with a view to ensuring that the correct samples can be taken immediately and safely in the event of any clinical suspicion.

A procurement process for vaccines took place. The advisory board of the Federal Ministry of Health and Women's Affairs recommended that in the event of an outbreak of LSD in Austria the entire cattle population should be subject to protective vaccinations. Because vaccination must be conducted on the basis of the current risk assessment for three consecutive years, a call for tenders was launched for 6.9 million vaccine doses to ensure that the vaccine is available; 500 000 doses are to be stored in Austria so that vaccination can start immediately.

A draft vaccination programme states that vaccination is to be conducted with different priorities to make efficient use of the resources available. The plan is that when an outbreak is detected, vaccination starts immediately in the "infected zone" of 20 km around the outbreak and the vaccination area is subsequently extended until the entire cattle population in Austria is vaccinated. An unresolved problem is that the current EU regulation requires vaccination of newborn calves, which would not be feasible in the present circumstances in Austria; it is anticipated, however, that vaccinations of calves will be conducted together with the annual re-vaccinations of older animals, and a risk assessment of this procedure has already been agreed. The national database to be used for the documentation of vaccinations and disease control measures has been adapted for an LSD epidemic to give field veterinarians limited access to it, assuming the need to use additional contracted staff in fighting LSD. Such access has hitherto only been possible for official veterinarians.

Last but not least it will be necessary to adapt the contingency plans of central and local veterinary authorities to LSD. Many questions are still to be clarified: which biosecurity measures are necessary, for example, to what extent are samples to be taken, how are feedstuffs and daily quantities of milk to be disposed of, and how will sufficient staff be recruited? The answers to these questions are still being developed. Workflows and areas of responsibility at the level of the national crisis centre are still subject to revision, and work is ongoing to establish clear structures as early as possible in the planning phase to ensure that a stringent process is established.

It would be presumptuous to believe that preparedness for all eventualities is possible, given the catastrophe that an outbreak of LSD would be. It is clear that if there is an incursion of LSD many unpredicted eventualities could arise and that the reality may prove to be different from that envisaged in the planning phase: a large number of ad hoc solutions will accordingly be required. Issues classified as "unlikely" in the current environment could well turn out to be real in the event of an emergency, particularly with regard to providing additional financial and human resources.

In view of the approaching threat, the Austrian veterinary authorities are preparing as best they can for this largely unpredictable scenario. Many dispositions have already been made, and many more lie ahead. There is, however, always the hope that all these preparations will remain untested because LSD does not spread further towards our borders. <sup>360</sup>

## REFERENCE

OIE. 2017. *Infection with lumpy skin disease virus*. In OIE Terrestrial Animal Health Code (2017), Chapter 11.9. Article 11.9.1. OIE, Paris. Available at [http://www.oie.int/fileadmin/Home/eng/Health\\_standards/tahc/current/chapitre\\_lsd.pdf](http://www.oie.int/fileadmin/Home/eng/Health_standards/tahc/current/chapitre_lsd.pdf)



**Figure 2:** Specific sampling kit for official veterinarians provided by the Austrian National Reference Laboratory



## COORDINATION

## Ad-hoc expert meeting on Lumpy Skin Disease in the Balkans

Belgrade, 25 July 2016

**Contributors:** Daniel Beltrán-Alcrudo,<sup>1</sup> David Paton,<sup>2</sup> Eran Raizman<sup>3</sup> and Andriy Rozstalnyy<sup>1</sup>

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**L**umpy skin disease (LSD), a viral disease of cattle characterized by nodules on the skin, is spread mainly by mosquitoes, flies and other arthropods. LSD has hitherto been restricted to sub-Saharan Africa, but it is now spreading to other areas. It entered Europe for the first time in 2014: Cyprus and Greece were the first two countries in the European Union (EU) to report infection. LSD re-emerged in Greece in April 2016 and spread rapidly first to Bulgaria and then to the former Yugoslav Republic of Macedonia, Serbia, Kosovo<sup>4</sup> and Albania. In response, the FAO Regional Office for Europe and Central Asia started to investigate the best way to assist countries in the region controlling LSD infections and improve preparedness in at-risk countries.

In view of the threat, the Global Framework for the Progressive Control of Transboundary Animal Diseases (GF-TADs) for Europe launched its Standing Group of Experts on Lumpy Skin Disease in July 2016.<sup>5</sup> The chief veterinary officers of central and south-eastern European countries requested FAO to organize an ad-hoc group of LSD experts to review the current scientific evidence and investigate prevention and control measures. The meeting took place at the Hotel Crowne Plaza in Belgrade on 25 July 2016. The 18 participants included LSD virology and epidemiology experts from countries reporting infections and those at risk – Austria, Bulgaria, Hungary, Israel, the Russian Federation and Serbia – and from international research centres, FAO and the Joint FAO/IAEA Programme on Nuclear Techniques in Food and Agriculture.

The Serbian chief veterinary officer opened the meeting, stressing the need to update guidelines and recommendations to ensure

that they were fit-for-purpose, practicable, harmonized and regionally relevant; modified stamping out in vaccinated herds was mentioned in particular.

The representatives from Israel, the Russian Federation and Bulgaria shared their experience with the disease, updating the epidemiological situation and highlighting current strategies and challenges.

The delegates shared their experiences with culling of animals and described the strategies applied before and after vaccination. In Israel, for example, various culling approaches had been combined with vaccination: these ranged from complete stamping out in the first outbreak in 1989, to modified stamping out and vaccination in 2004, and to a concerted annual programme of vaccination of the entire cattle population in 2013, with culling limited to severe clinical cases. The latter approach was effective in controlling the disease, which has not been reported since. Bulgaria had to apply the EU directives, which require total stamping out in all situations. Serbia and the Russian Federation had applied modified stamping out in affected vaccinated areas, where animals

with clinical signs of LSD were culled and the remainder vaccinated, with complete stamping out in cases of LSD incursions into zones considered disease-free.

### DISCUSSION

The following items were discussed with a view to revision of existing measures: any changes would, of course, have to be technically sound, scientifically based, risk-assessed and feasible.

#### 1. Review and rank the ways in which the LSD virus could be transmitted between holdings

The main risks for transmission are associated with transfer of virus by vectors such as insects feeding on live infected animals, and possibly direct contact between infected and naive animals. Illegal movements of live animals were highlighted as a problem in Bulgaria. The risk of transmission from sub-clinically infected and recently vaccinated animals remains to be determined. Animals should develop protective immunity within 21 days of vaccination hence are unlikely to transmit infection. Commodities derived



Cattle grazing in Eastern Turkey

©Eran Raizman

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<sup>2</sup> The Pirbright Institute, UK

<sup>3</sup> FAO Animal Production and Health Division, Rome, Italy

<sup>4</sup> This designation is without prejudice to positions on status, and is in line with UNSCR 1244 and the ICJ Opinion on the Kosovo Declaration of Independence.

<sup>5</sup> See [http://web.oie.int/RR-Europe/eng/Regprog/en\\_GF-TADS%20-%20Standing%20Group%20LSD.htm](http://web.oie.int/RR-Europe/eng/Regprog/en_GF-TADS%20-%20Standing%20Group%20LSD.htm)

from healthy animals vaccinated at least 28 days previously hence constitute a very low – even negligible – risk in terms of spreading LSD. The possibility of virus transmission by non-biting arthropod vectors that feed on infected carcasses and mechanically transmit virus cannot be excluded, but no studies of the topic have been published. Other indirect routes of transmission involve much lower risk.

Meat is not a significant risk for transmission, and the risk associated with milk not destined for animal consumption can be mitigated by means of pasteurization and transport in closed containers. Raw hides are more likely to be contaminated with virus than meat or milk.

### Recommendations

More transmission studies are needed to enhance the understanding of risks. Priority actions to prevent transmission are culling and safe and humane destruction of infected animals, vaccination to reduce shedding and susceptibility, and movement controls to prevent long-distance spread through direct contact or insect transmission.

## 2. Review current measures and propose updated guidance, and actions to be taken after confirmation of LSD on a holding, including alternatives to on-site burial

The practicality of carcass disposal methods depends on factors such as the number of animals involved, the environment and the availability of resources and facilities. Some countries rely on routine veterinary services, and do not have specialist teams to assist with such operations. Alternatives to on-site burial include other on-site disposal methods and off-site disposal. On-site incineration by pyres or mobile incinerator units may be possible in some circumstances. Off-site alternatives include movement of suspected or apparently healthy in-contact live animals for slaughter at abattoirs with a view to providing heat-treated meat products: this was done in the Russian Federation when on-site disposal units were unavailable, but there is a risk of vector-borne spread from the live animals during transit and at the abattoir. Animals with severe clinical manifestations must be culled on-site and the carcasses transported to incinerating facilities. On-site killing followed by movement of carcasses for rendering, burial, or incineration may involve risk because non-biting arthropod vectors may feed on the carcasses prior to disposal. Vector control is difficult, and may lead to environmental damage for little benefit. Further assessments are needed of the survival of LSD virus in the environment, its infectious potential and the role of different vector species in transmission.

### Recommendations

There are various options, but movement of live animals with clinical disease is a high-risk strategy. Even after culling, measures such as spraying with disinfectant and insect repellents and covering should be taken to prevent vectors from accessing carcasses prior to disposal. Timely and thorough cleaning and disinfection of premises after stamping out is essential.

## 3. Review the Bulgarian proposals for modification of the measures to be taken after confirmation of LSD in animals recently vaccinated against LSD virus

The proposal is for modified stamping out – culling of clinical cases only – in herds vaccinated in the preceding 28 days. The review concluded that vaccination with the Neethling vaccine strain should provide immunity against infection within 21 days. Most of the outbreaks in vaccinated holdings in Bulgaria and Serbia occurred within 14 days of vaccination, although one case was reported in Serbia after 19 days. In the Russian Federation, a live attenuated sheep pox virus vaccine strain is used. Cattle vaccinated with the Neethling vaccine strain sometimes show clinical signs that resemble mild LSD – this is sometimes referred to as “Neethling disease” – whereas animals vaccinated with sheep pox vaccine do not. Differentiation in laboratories between vaccine and wild-type virus may be possible within one or two days if differential polymerase chain reaction (PCR) or sequencing are used: this may delay the slaughter of infected animals, especially if samples have to be referred to specialist laboratories in other countries.

Clinical cases constitute the highest risk for virus spread: they should hence be culled and destroyed as soon as possible. Subclinical cases are probably a lower risk for transmission, and in a vaccinated population the susceptibility of potential recipients will also be reduced. In Israel, various culling approaches have been combined with vaccination: these approaches were complete stamping out, modified stamping out and vaccination, and mass vaccination with culling limited to severe clinical cases. The latter approach was effective in controlling LSD, which has not recurred since.

In some recently affected countries – the Russian Federation and Serbia are examples – modified stamping out is used in vaccinated herds, and only clinical cases are culled. It is not yet possible to evaluate the effectiveness of these approaches. The experience of the Russian Federation in fighting LSD in 2015, when diseased and apparently healthy in-contact animals were totally stamped out, was that the approach was effective but very costly. Current EU legislation requires Member States to cull all animals in an infected herd, even if the herd has been vaccinated.

Culling of clinical cases in vaccinated herds could be supplemented by laboratory tests on the remaining animals, provided such capability is available. Serological tests could be used to check post-vaccination immunity, and virological testing could identify viraemic animals sub-clinically infected with wild-type LSD virus for culling; but false negative test results for viraemia are possible, and there will be a delay between sampling and test results during which further spread of the virus might occur. Culling of vaccinated animals is not generally acceptable and may reduce the



LSD skin lesions infested with flies





Typical clinical sign seen in LSD

uptake of vaccination and reporting of clinical cases: it may also have a negative impact on solidarity in terms of preventive vaccination to protect neighbouring countries.

The measures required for rapid eradication of infection may be different from those suitable for cost-efficient disease control and eventual eradication. Other vector-borne diseases such as bluetongue in Europe have been controlled by vaccination without culling, but strict movement controls were applied – a waiting period of 60 days post-vaccination before allowing movement, 28 days after serological testing or 14 days after testing through PCR.

#### Recommendations

Countries without laboratory capacity for differentiating vaccine and wild-type virus and undertaking serology require support for training and referral of samples for testing by reference laboratories. There is a rational case for using modified stamping out in vaccinated populations: the socio-economic issues and the cost-benefit ratio in various contexts should be analysed. A flexible approach to stamping out is probably warranted, but a minimum time after vaccination must be agreed.

#### 4. Review the Bulgarian proposals for modification to measures relating to: i) restocking of holdings depopulated after LSDV; and ii) movements of animals and animal products after vaccination

i) The restocking proposal is that animals vaccinated at least 28 days previously could be moved to premises where stamping out has been implemented, provided that at least 40 days have elapsed from cleaning and disinfection and that there have been no outbreaks within 20 km.

Although LSD virus can survive for prolonged periods in the environment,

the risk of infection from environmental contamination is low, especially among vaccinated animals; it is further reduced by thorough cleaning and disinfection of holding facilities. The possibility of long-term survival in vector populations cannot be excluded, however. Vaccinated animals, once immune, are much less susceptible to infection from residual infectivity at depopulated, cleaned and disinfected premises or from risks attributable to virus activity at neighbouring premises. General depopulation is not part of the strategy for reducing the spread of LSD. Where culling is implemented without vaccination or where vaccination is limited, it may be difficult to find vaccinated animals to repopulate premises after stamping out.

#### Recommendations

Restocking should be permitted after a minimum of 21 days, as specified in EU legislation, provided that the animals have been vaccinated at least 28 days previously and that premises have been thoroughly cleaned and disinfected; both conditions must be confirmed by veterinary certification.

ii) The proposal for movements of animals and animal products after vaccination is that animals may be moved from one vaccination zone to another 28 days or more after vaccination. This could include movement from a vaccination zone in one country to a zone of the same status in another.

Because animals may not be moved from protection or surveillance zones, the proposal applies only to animals outside such zones or animals in zones where the restrictions have been lifted. Vaccinated animals face little risk of being infected or spreading infection, and may hence be moved between vaccination zones of equivalent health status. In view of the potential for vector-borne spread of LSD, the risk of transiting animals through zones with higher health status is unacceptable, especially if other countries are involved.

#### Recommendations

Movements of vaccinated animals should be allowed between vaccinated zones of equivalent health status in the same country,



LSD affected calf

and in other countries provided that animals do not transit a region of higher health status and that animals to be moved are inspected and certified as healthy by veterinarians.

#### 5. Identification of likely scenarios for spread of infection in the Balkan and Central European region, and effects and duration of control options that could be assisted by modelling and other studies

With vaccination almost complete in all affected countries in the Balkans, the threat to western Europe is likely to arrive through Romania or Bosnia and Herzegovina and Croatia. There is little evidence that topography interferes with the spread of LSDV: but there is evidence that preventive vaccination is crucial to prevent the spread of the virus. Preventive vaccination in Bosnia and Herzegovina, Croatia and northern Serbia would create a buffer zone to protect Hungary and Romania and countries further west. The restricted zone in countries applying emergency vaccination should be large enough to prevent spread to other regions. Countries threatened by LSDV should urgently establish vaccination programmes.

#### Recommendations

Contingency preparations for preventive vaccination are essential. Countries affected by LSD for the first time must extend their vaccination zones beyond the initial foci of infection to prevent onward spread to other countries. Modelling studies may be helpful, but the needs are clear.

#### 6. Identify information to be collected and shared by countries affected by LSD, particularly to assist modelling of spread and the effects of control measures and reviews of the effectiveness of current vaccines

It is essential to collect full epidemiological information about outbreaks, risk factors, vaccination coverage and vaccine breakdowns to identify and quantify the risks of spread of infection. Countries should have a geo-referenced cattle identification database that covers vaccination and laboratory test results at the individual and herd levels. The European Commission for the Control of Foot-and-Mouth Disease (EuFMD) and regional veterinary services are collecting data on outbreaks, regional denominators and vaccination, which can be combined with geographical and climate information. Disease-control operations tend to take priority over investigations intended to enhance understanding of LSD infections: during culling, for example, it can be difficult



FAO/Kai Wiedenhofer

Farmer and veterinarian taking count of the cows to be vaccinated

or impractical to sample enough animals to establish matters such as attack rates and the extent of subclinical infection, or to evaluate diagnostic tests. Additional resources for this may be provided by research institutes and veterinary schools. Even where immediate testing of samples is impractical, samples and information should be collected for later evaluation.

The manufacturers of the Neethling strain vaccines are not licensed in Europe, and might not meet the good manufacturing practice (GMP) standards expected. In Israel the quality of each batch of vaccine purchased for LSD control is checked for potency and innocuity, but this is not the case in Europe. The LSD vaccine manufacturers recommend annual revaccination, partly for reasons of animal turnover, but the duration of immunity is poorly understood; a figure of two to three years appears in the literature. Correlates of protection have not been established, but it would be useful to obtain information about post-vaccination antibody dynamics. There is a need to collate data on levels of adverse reactions to vaccination and, especially, on cases presenting with clinical signs similar to LSD. In Bulgaria some potential vector species have been collected to test for carriage of LSD virus, but no systematic studies are in progress.

### Recommendations

FAO should coordinate the development of a checklist of minimum information to be collected during outbreaks with a view to harmonizing data collection for modelling of disease spread in different countries and the associated risks.

Veterinary services in countries with LSD and those at risk should collaborate with experts in epidemiology, modelling, diagnosis and vector biology. They should cooperate to address disease-related questions, some of which can only be answered during outbreaks, such as which vectors are carrying LSD virus, how far they can fly, the attack rate among animals in affected herds and the antibody dynamics of the immune response to vaccination. Small longitudinal studies to follow up outbreaks and vaccinations are also required. Study designs could be drawn up by experts in reference laboratories and funding sources should be investigated.

Israel has not used stamping out since the 2013 outbreaks, so there are live animals that could be studied for duration of immunity including their possible purchase and challenge under controlled conditions in biosecured facilities.

Countries using vaccination should monitor the coverage. Contingency preparations for vaccination should include quality checks on vaccines purchased for future use.

### GENERAL CONCLUSION

Further research is needed to fill the many knowledge gaps: the nature, onset and duration of vaccine-induced immunity needs to be investigated along with the presence, survival and significance for transmission of virus in animal products, the environment and different vectors. Research is also needed to develop and validate simple tests for differentiating wild-type and vaccine virus, and for high-throughput serological assays. <sup>360</sup>





## COORDINATION

# Lumpy Skin Disease: Country situation and capacity reports

Contributors: Andriy Rozstalnyy, Ryan Aguanno and Daniel Beltrán-Alcrudo<sup>1</sup>

## INTRODUCTION

Participants from veterinary services in the Balkan region – Albania, Bosnia and Herzegovina, Bulgaria, the former Yugoslav Republic of Macedonia, Kosovo and Serbia – and the Caucasus – Armenia, Azerbaijan and Georgia – and from Hungary, the Russian Federation and Ukraine attended the FAO regional workshop on lumpy skin disease (LSD) prevention and control strategies in Budapest on 7–9 March 2017. Representatives of dairy cattle associations and companies involved in genetics and pharmaceuticals also participated.

The countries were provided with a PowerPoint template describing the national farming sector, laboratory capacities, control measures against LSD and challenges encountered. This report summarizes the presentations to give a condensed overview of the range of strategies and capacities in the region. Presentations can be downloaded.<sup>2</sup> Information about Turkey was extracted from the article *Lumpy Skin Disease: Situation, Surveillance and Control Activities in Turkey* in this empres360.

## CATTLE POPULATION

Cattle populations in all the affected countries are usually housed in smallholdings. Population data were not always available, which presents a significant challenge for the implementation of disease prevention and control actions in terms of the time required to vaccinate, track and inspect all farms, and the number of stakeholders who must be reached by awareness campaigns. Because smallholders have greater reliance on individual animals, the consequences for their livelihoods are greater when disease is present: this gives rise to concern among veterinary services that disease may be

unreported. Seasonal migration, which presents a difficulty for the restriction of cattle movements, takes place in all three Caucasus countries but is mostly absent in the Balkans. This movement usually implies increased animal contact among herds and lower bio-security standards. Similarly Asian buffalo populations, which are also susceptible to LSD, are more significant in the Caucasus and Turkey, though always in small numbers.

## DIAGNOSTIC CAPACITIES

Diagnostic capacities in these regions vary, but basic facilities are available in all countries except Kosovo. In many of the countries, testing capacity may be overwhelmed if multiple outbreaks are detected simultaneously because currently reported maximum testing capabilities may be inadequate. Countries in the region have now vaccinated significant numbers of cattle, so

**Table 1:** Cattle and buffalo populations in the Balkan and Caucasus regions

Country/territory	Total cattle	Smallholdings as % of farms	Seasonal migration	Buffalo population
Albania	475 700	57	No	80
Armenia	674 400	-	Yes	No
Azerbaijan	2 452 000	75	Yes	115 000
Bosnia and Herzegovina	300 000	-	No	No
Bulgaria	778 900	59	Yes	-
Georgia	834 300	90	Yes	16 000
Hungary	932 300	-	No	Yes, limited
Kosovo	290 000	Most	-	-
The former Yugoslav Republic of Macedonia	228 800	83	No	55
Montenegro	98 266	-	Yes	7 540
Russian Federation	18 992 000	-	No	Yes, limited
Serbia	886 700	-	No	No
Ukraine	3 770 000	-	No	No
Turkey	14 223 100	-	N/A	121 800

**Table 2:** Diagnostic capacities in the Balkan and Caucasus regions

Country/territory	PCR gel-based	PCR real-time	Virus isolation	Serology	24/7 sample testing	Max capacity of sample testing/day <sup>1</sup>
Albania	Yes	Yes	No	No	No	70-80
Armenia	Yes	Yes	No	No	Yes	30+
Azerbaijan	No	Yes	No	Yes	Yes	-
Bosnia and Herzegovina	No	Yes	No	No	No	-
Bulgaria	Yes	Yes	No	No	Yes	44
Georgia	No	Yes	No	No	-	100
Hungary	Yes	Yes	Yes	Yes	Yes	400+
Kosovo	No	No	No	No	No	-
The former Yugoslav Republic of Macedonia	Yes	Yes	Yes	No	Yes	70
Montenegro	Yes	Yes	No	No	Yes	50
Russian Federation	Yes	Yes	Yes	Yes	Yes	200
Serbia	Yes	Yes	Yes	No	Yes	300
Ukraine	No	Yes	No	No	Yes	100

<sup>1</sup> FAO Regional Office for Europe and Central Asia, Budapest

<sup>2</sup> Regional workshop on lumpy skin disease (LSD) prevention and control strategies. Budapest, Hungary, 07 – 09 March 2017. Presentations available at [www.fao.org/europe/events/detail-events/en/c/470556/](http://www.fao.org/europe/events/detail-events/en/c/470556/)

<sup>1</sup> Highest daily capacity for any test type



A villager with their cattle in Eastern Europe

there is an urgent need for a widely available laboratory test to differentiate infected from vaccinated animals (DIVA) to assist epidemiological surveillance and trade in live animals.

### LSD VACCINATION CAMPAIGNS AND VACCINE USE

Because stamping out alone is very costly and not effective in halting the spread of LSD, the decision to vaccinate was made by all the countries with LSD infections. Vaccination coverage in targeted areas was successful in most cases. Harmonized vaccination strategies for the region should continue to be encouraged. Most countries rightly plan to begin their 2017 vaccination campaigns before the virus "season". Vaccination has

not been used up to now in Bosnia and Herzegovina or Ukraine.

By the time the meeting took place, many countries have begun the tender process for vaccines for 2017. This was advisable given that vaccine production companies need to produce large numbers of doses, which probably affect delivery dates. The meeting participants encouraged countries without the disease to stock enough vaccine doses to enable rapid reaction against a possible LSD incursion into their territories or along their borders. A range of heterologous and homologous vaccines are available in the market, but their efficacy is not well established. Vaccine challenge studies being finalized at the CODA-CERVA veterinary and the agrochemical research centre in Belgium will bring some light to this issue.

**Table 3:** LSD vaccination campaigns by country

Country/territory	Date of 1st LSD outbreak	2016 vaccine campaign start/end	2017 vaccine campaign start/end	Vaccination strategy	vaccination coverage % in vaccinated area
Albania	28 June 2016	26 June–25 December	January	Whole country	Unknown
Armenia	08 December 2015	July–September	Unknown	Buffer zone	37
Azerbaijan	07 July 2014	February–April	March–April	Whole country	82
Bulgaria	12 April 2016	28 April–15 July	January: 4-month olds; March: adults finish within 1 month	Whole country	100
Georgia	01 November 2016	Unknown	Unknown	Along borders with Armenia, Azerbaijan and Turkey, plus the west of country	100
Hungary	-	N/A	Only if disease within 100 km of border	50 km buffer on border	N/A
Kosovo	24 June 2016	11 September–12 October	May	Whole country	Unknown
The former Yugoslav Republic of Macedonia	18 April 2016	24 May–31 July	March	Whole country	96.7
Montenegro	21 July 2016	01–17 August	January: calves; May: adults finish within 1 month	Whole country	100
Russian Federation	07 July 2015	May–October	January	Buffer zone	90–100
Serbia	04 June 2016	24 June–01 September	January	Vaccination of calves	99.7
Turkey	06 August 2013	All year	Unknown	Ring	80–90

**Table 4:** Vaccines used, and related issues

Country	Vaccines used and manufacturer (dose)	Present stock	Adverse reactions detected	Started tender for vaccine for campaigns in 2017
Albania	LSD vaccine for cattle, and Lumpyvax	185 000 (Lumpyvax)	Lumpyvax: 159 cattle with LSD clinical signs after vaccination	Yes
Armenia	ARRIAH vaccine: x5 for 3–6 months; x10 for >6 months	Unknown	No	No
Azerbaijan	Unknown	Unknown	Unknown	Yes: September 2016
Bosnia and Herzegovina	N/A	N/A	N/A	
Bulgaria	LSD vaccine for cattle, and Lumpyvax	50 000 from EU bank in December 2016 for calves	Yes: lower milk output, large nodules, oedema at injection site	Starting now
Georgia	POXVAC: 10x	Unknown	Yes: abortions	Unknown
Hungary	Lumpyvax	210 000	N/A	No
Kosovo	LSD vaccine for cattle	1 000	Unknown	No
The former Yugoslav Republic of Macedonia	LSD vaccine for cattle, and Lumpyvax	67 500 (Lumpyvax)	Unknown	Yes
Montenegro	LSD vaccine for cattle	20 000	Unknown	Yes
Russian Federation	ARRIAH vaccine	Yes	No	Yes
Serbia	LSD vaccine for cattle	Unknown	Unknown	Yes – March 2017
Turkey	Penpox-M: 3x	Unknown	Yes	Unknown

Note: List of LSD vaccines and producers: i) LSD vaccine for cattle – Onderstepoort Biological Products, South Africa; ii) Lumpyvax – MSD Animal Health; iii) ARRIAH vaccine – sheep pox vaccine from the Federal Centre for Animal Health, Russian Federation; iv) POXVAC – sheep pox vaccine by Vetall, Turkey; and v) Penpox-M – sheep pox vaccine by Pendik Institute, Turkey





A farm with ISO14001 (environmental management systems) in Southern Europe

**Table 5:** Responses to LSD outbreaks, by country

Measure	Applied			Not applied
Contingency plan available	Al, Ar, BH, Bg, Ko, Mn, RF			Az, Ge
Cattle movement control	Al, Ar, Bg, Ko, Mn, RF, RM, Se, Tu			Az
Cleaning and disinfection	Al, Ar, Bg, Ko, Mn, RF, RM, Se, Tu			Az
Stamping-out policy	Total, all animals: Bg, Se	Partial, only animals with clinical signs: Ar, Ko, RM, Ru	Partial (only severe cases)	Az, Al, Ge
Disposal of carcasses	At site: Ar, Bg, Ko, Mn, RM, Se	Outside: Al, Ko, RM, Se	Into a plant: Ko	
	Burning: Ar	Burial: Al, Bg, Ko, RM, Se	Rendering:	
Vector control	Animals: Al, Ar, Bg, Mn, RM, Se	Facilities: Al, Ar, Bg, Mn, RM, Se	Environment: Al, Bg, Mn, RM, Se	
Clinical surveillance	Active, no. of samples: Bg, Se 540	Passive, no. of samples: Al 6 453, Ar, RM >2 000		
Serosurveillance	No. of samples: Al 3 500, Se 219			Az, Bg, Ko, RF

Abbreviations: Al = Albania; Ar = Armenia; Az = Azerbaijan; BH = Bosnia and Herzegovina; Bg = Bulgaria; Ge = Georgia; Ko = Kosovo; Mn = Montenegro; RF = Russian Federation; RM = The former Yugoslav Republic of Macedonia; Se = Serbia; Tu = Turkey

**Table 6:** Challenges identified in LSD management

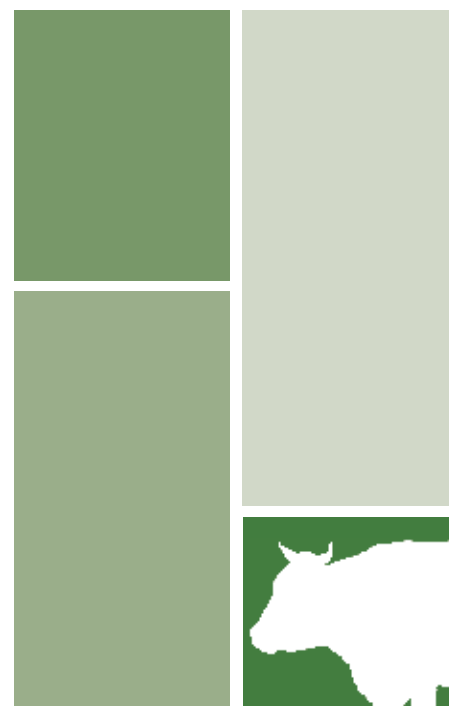
Policy	Farming system	Vaccine	Laboratory	Capacity
Enforcing animal movement controls	No animal identification	Ordering enough vaccine and payment	Lack of LSD laboratory supplies and knowledge	Training of stakeholders at all levels
Support for national governments and institutions	Illegal movement during restrictions	Availability of vaccine from the producer	Detection of virus in the field	Increased financial resources for an unknown time
Lack of compensation policies makes culling difficult	Traditional farming, numerous smallholders	Vaccination of newborns	Virus detection vs antibody detection	Destruction of animal carcasses and products
Possible export bans and a lack of agreement among neighbouring countries	Shared pastures and migratory farming	Determination of vaccination area in case of disease detection: border vs country		Few resources to examine wildlife and the environment
Trade and transit of live animals and products in country	Low level of disease awareness at time of outbreaks	Decision to start with preventative vaccination		Maintaining high-level awareness over many years
Harmonization of a regional approach outside the EU		Selection of appropriate vaccine		Lack of emergency funds and equipment

## OUTBREAK RESPONSE

In most of the countries affected, emergency responses were implemented with priority given to cattle movement controls and cleaning and disinfection of farms. As expected, stamping out strategies were more substantial in countries in the European Union. Clinical and sero-surveillance reporting is lacking in most countries.

## CHALLENGES FACED BY THE VETERINARY SERVICES

A variety of challenges were identified that ranged from policy-related issues at the national and regional levels to issues related to the capacities of laboratories and veterinary services. Most of the challenges were identified by several countries. <sup>360</sup>





## COORDINATION

# Lumpy Skin Disease in south-eastern Europe

## The response of the European Union

Contributors: Francisco Reviriego Gordejo and Dimitrios Dilaveris<sup>1</sup>

**L**umpy skin disease (LSD) is endemic in many African countries and was, until a few years ago, considered exotic to Europe. Since 2012, however, LSD has been spreading on an unusually large scale throughout the Middle East and into Turkey, where it arrived in 2013 and is now considered endemic all over the country.

In Cyprus, LSD was reported for the first time in November 2014 only in those areas of the Republic of Cyprus in which the Government of the Republic of Cyprus does not exercise effective control. The disease was brought under control by means of vaccination in the affected areas.

The disease was confirmed in the European part of Turkey (Turkish Thrace), in May 2015 and subsequently in the border areas of Evros prefecture in Greece in August 2015. The measures undertaken by the Greek authorities as described elsewhere in this issue – stamping out of outbreaks and a mass vaccination campaign – combined with winter conditions brought LSD to a controlled state and from December 2015 no new outbreaks were recorded until the disease returned to Greece in early April 2016 in an LSD restricted area of low vaccine coverage. Only a week later LSD was detected for the first time in Bulgaria, initially in an area at a considerable distance from the outbreaks in Greece. From April to July 2016, the disease entered or recurred in seven countries of south-eastern Europe successively – Greece, Bulgaria, the former Yugoslav Republic of Macedonia, Serbia, Kosovo,<sup>2</sup> Albania and Montenegro.

All affected countries resorted immediately to mass vaccination against LSD aiming at a swift, high vaccination coverage of at least 95 percent in a uniform manner – all cattle in all holdings – as this appeared to be the

most, and possibly the only, effective control measure against the disease.

European Union (EU) legislation, Directive 92/119/EEC in particular, imposes the total slaughter and destruction of all cattle present in the holdings affected by LSD as soon as infection is confirmed. This is followed by the establishment of a protection zone with a minimum 3 km radius and a surveillance zone with a minimum 10 km radius, with special restrictions for cattle and any products thereof that may spread the disease. According to the same Directive vaccination is possible, subject to conditions, while additional measures can be decided by the European Commission (EC).

### THE EUROPEAN UNION'S SWIFT RESPONSE TO THE 2015–2016 LSD EPIZOOTIC IN SOUTH-EASTERN EUROPE

The epidemiological situation of LSD in the Middle East had already alerted the EU. Early in 2013, when LSD was first reported in Turkey, the European Commission Directorate-General for Health and Food Safety (DG SANTE) requested the European Food Safety Authority (EFSA) to produce its first scientific opinion on LSD, with emphasis on the risk of introduction into the EU. By the time this scientific opinion<sup>3</sup> was published in January 2015 an expert mission had already been sent to Cyprus, in those areas of the Republic of Cyprus in which the Government of the Republic of Cyprus does not exercise effective control, to provide assistance related to an LSD outbreak.

The next landmark occurred in June 2015, when LSD was first reported in Turkish Thrace, very close to the Greek border. Following this significant event, Greece implemented enhanced disease surveillance along the Evros River. The storm broke a couple of months later in the second half of August 2015, when LSD

crossed the Greek border and began to spread rapidly through the Evros river delta, which appeared to be a very favourable ecosystem for LSD, propagating at an unprecedented speed. Within two weeks the EU veterinary services realized that the disease could not be contained solely by a stamping out policy in that part of the EU. As a result the European Commission rapidly granted a preliminary approval to the Greek authorities to begin emergency vaccination against LSD using a live homologous vaccine imported from South Africa under emergency legal provisions.<sup>4</sup>

The end of 2015 found Greece with a total of 117 outbreaks: the furthest was at 300 km from the original point of entry and the LSD restricted/vaccination area covered its north-eastern provinces. The disease stopped spreading in the areas of Greece that had completed LSD vaccinations. Experts from the European Commission<sup>5</sup> and its Community Veterinary Emergency Team (CVET)<sup>6</sup> identified vaccination as the highest priority for the control of LSD and vaccine supply as the biggest obstacle to implementation.

At that early stage the sustainability of the EU LSD control policy appeared questionable and delivering success seemed challenging. There was, therefore, very intense activity in preparation for a possible re-emergence of the disease in 2016. Indeed in the months after April 2016, the EU strategy for LSD control and eradication was subject to review under the leadership of DG SANTE, and readjustments focused in four main strategic objectives:

- support for the implementation of control measures – LSD vaccination campaigns;
- international coordination in the region;
- training, expert support and scientific advice; and
- review and refinement of LSD control measures in the EU.

<sup>1</sup> European Commission, Directorate-General for Health and Food Safety (DG SANTE)

<sup>2</sup> This designation is without prejudice to positions on status, and is in line with UNSCR 1244 and the ICJ Opinion on the Kosovo Declaration of Independence.

<sup>3</sup> See: <https://www.efsa.europa.eu/en/efsajournal/pub/3986>

<sup>4</sup> Art. 8 of Dir. 2001/82/EC on the Community code relating to veterinary medicinal products.

<sup>5</sup> See: [http://ec.europa.eu/food/audits-analysis/audit\\_reports/details.cfm?rep\\_id=3727](http://ec.europa.eu/food/audits-analysis/audit_reports/details.cfm?rep_id=3727)

<sup>6</sup> See: [http://ec.europa.eu/food/sites/food/files/animals/docs/reg-com\\_ahw\\_20151109\\_pres\\_lumpy\\_skin\\_disease\\_greece\\_cvet\\_en.pdf](http://ec.europa.eu/food/sites/food/files/animals/docs/reg-com_ahw_20151109_pres_lumpy_skin_disease_greece_cvet_en.pdf)



## SUPPORT FOR THE IMPLEMENTATION OF CONTROL MEASURES: LSD VACCINATION CAMPAIGNS

### EU LSD VACCINE BANK

A few days before the end of 2015, a DG SANTE public procurement procedure was launched for the purchase of an initial quantity of up to 400 000 doses of LSD vaccines to form the core of the EU LSD vaccine bank. The choice of type of LSD vaccine – live homologous vaccine, currently manufactured only outside the EU – was based on the scientific knowledge available and the 2015 EFSA scientific opinion.<sup>3</sup> By April 2016 the first contract had been signed, and vaccine doses were dispatched to several affected countries. Since then the EU LSD vaccine bank has had to be expanded: there were three such expansions in 2016, and procedures for a further expansion are already underway in 2017. By the end of 2016, 625 000 doses of LSD vaccines have been distributed in various EU and non-EU countries implementing LSD vaccination in south-eastern Europe completely free of charge with a view to supporting the early stages of their vaccination campaigns before national procurement of vaccines is possible (See Table 1).

### FINANCIAL SUPPORT FOR LSD VACCINATION

The LSD control measures implemented in the EU Member Countries such as stamping out and vaccination are subject to co-financing by the EU at a rate of at least 50 percent. Similarly, in view of the epidemiological situation, EU financial support became available under certain conditions for non-EU countries in the region that implemented LSD vaccination in 2016 in accordance with a regional strategy. This support covered the cost of LSD vaccines purchased with their own national funding.

The swift implementation of vaccination in the affected countries contained the progress of the disease, especially in Bulgaria and Serbia, which succeeded in keeping parts of their territories free from LSD. Preventive vaccination for LSD was also implemented, for the first time in history, in Croatia, yielding excellent results in terms of stopping the progress of the disease.

### INTERNATIONAL COORDINATION IN THE REGION

A Joint EFSA –DG SANTE Workshop – Strengthening regional cooperation in South East Europe and Middle East for prevention and control of Lumpy Skin Disease – involving EU and non-EU countries was held in Brussels on 11–12 May 2016. It was the first large-scale EU coordination initiative for the region, and it coincided with the rapid spread of LSD in Bulgaria, the former Yugoslav Republic of Macedonia and Greece in April

**Table 1:** EU LSD vaccine bank grants in 2016

Country	LSD vaccine grants (EU vaccine bank)
Bulgaria	200 000 doses
Greece	150 000 doses
The former Yugoslav Republic of Macedonia	50 000 doses
Serbia	50 000 doses
Kosovo <sup>2</sup>	25 000 doses
Albania	75 000 doses
Montenegro	25 000 doses
Croatia	50 000 doses
TOTAL	625 000 doses

2016. The workshop demonstrated the benefits of creating a working group for LSD that would bring together all the countries in the region to discuss the situation and design future coordinated policies.

In the light of this and in view of further LSD spread to Serbia and Kosovo,<sup>2</sup> delegates of the World Organization for Animal Health (OIE), FAO, the European Commission and all participating countries in the region met in Brussels on 4–5 July 2016 under the umbrella of the Global Framework for the Progressive Control of Transboundary Animal Diseases (GF-TADs) for Europe. A joint decision was reached to create the Standing Group of Experts on LSD for South-Eastern Europe (SGE LSD) – a major milestone in regional coordination against LSD.

Three more meetings of the GF-TADs and SGE LSD took place in Lisbon on 21 September 2016, Istanbul on 12–13 December 2016, and in Paris on 25 May 2017. The group introduced for the first time the concept of a coordinated LSD vaccination policy in south-eastern Europe, and is now providing the joint platform that enables all countries in the area to discuss LSD on a regular basis with LSD experts, OIE, FAO and the European Commission (DG SANTE).

A major step forward in coordinated international action in the region was the LSD Ministerial Conference in Sofia, organized by the Bulgarian authorities on 8–9 September 2016. This conference endorsed at high political level multilateral political support for the above concept and has since enabled the full engagement of an LSD regional control policy in South East Europe, which is regularly reviewed under GF-TADs.

The central technical concept of this regional policy has been LSD vaccination of practically all cattle using live homologous vaccines against LSD, in line with the latest EFSA opinion. The coordinated vaccination campaigns of the affected countries and the preventive vaccination in Croatia appear to have stopped further spread of LSD to the north or east at least for the time being (see Figure 1).

## TRAINING AND EXPERT SUPPORT AND ADVICE

### EFSA SCIENTIFIC ADVICE

At the request of the European Commission, EFSA has already produced two scientific opinions in relation to LSD:

- Scientific Opinion on Lumpy Skin Disease [EFSA Journal 2015; 13(1):3986],<sup>7</sup> published on 13 January 2015, provides an update on the characterization of the disease, assesses the risk of introduction of LSD into the EU and the speed of spread, the risk of becoming endemic and its potential impact.
- Urgent advice on Lumpy Skin Disease [EFSA Journal 2016; 14(8):4573],<sup>8</sup> published on 9 August 2016 concluded that total stamping out and partial stamping out result in a similar probability of eradicating LSD only when vaccination is evenly applied so that 95 percent of the farms are vaccinated, with 75 percent of vaccinated animals effectively protected.

EFSA is currently working to provide further scientific and technical support.

### COMMUNITY VETERINARY EMERGENCY TEAM

Expert missions by the Community Veterinary Emergency Team (CVET)<sup>9</sup> have been organized and financed by DG SANTE to provide technical and scientific support in relation to LSD at the request of the authorities in countries affected or at risk. Since late 2014 there have been seven missions of this kind: to Cyprus in December 2014 and January 2015, Greece in November 2015 and April 2016, Serbia in June 2016 and the former Yugoslav Republic of Macedonia and Romania in June 2016. The CVET mechanism has proved to be an effective tool that enables rapid deployment of expert missions wherever there is a need for on-the-spot assessment of the LSD situation and expert scientific advice, often under emergency conditions.

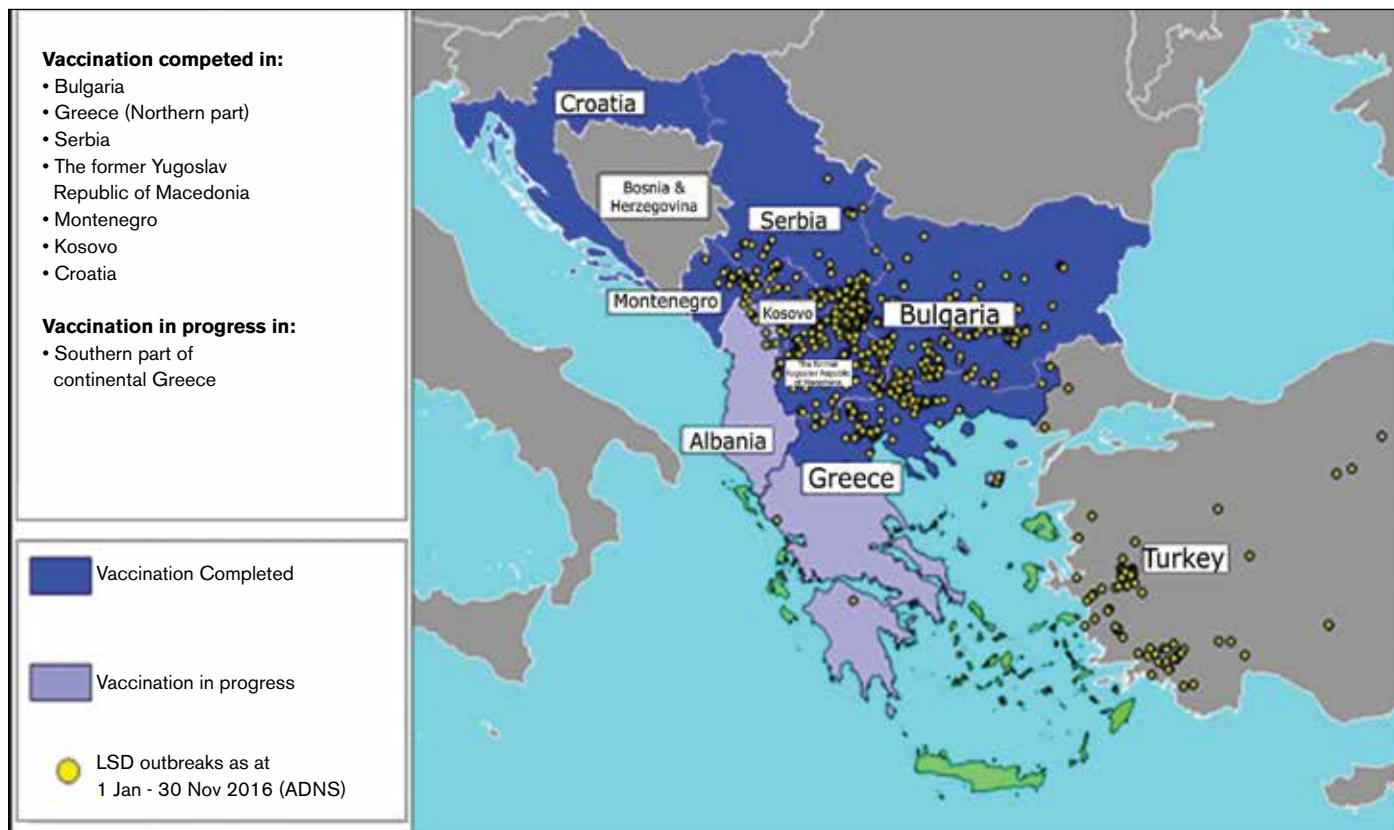
### LSD-RELATED TRAINING

The Better Training for Safer Food (BTSF) initiative of the European Commission provides training in the areas of food, animal feed, animal health and welfare and plant health. This has included events and seminars on LSD for EU Member Countries and non-EU countries in south-eastern Europe. In addition, the BTSF Sustained Technical Assistance Programme provided for LSD sustained technical assistance missions (STMs) of three to four days duration in the western Balkans and in Moldova.

<sup>7</sup> <https://www.efsa.europa.eu/en/efsajournal/pub/3986>

<sup>8</sup> <https://www.efsa.europa.eu/en/efsajournal/pub/4573>

<sup>9</sup> See: [http://ec.europa.eu/food/animals/animal-diseases/emergency-team\\_en](http://ec.europa.eu/food/animals/animal-diseases/emergency-team_en)



**Figure 1:** LSD vaccination in south-eastern Europe as at mid-November 2016

## APPOINTMENT OF AN EU REFERENCE LABORATORY FOR LSD

The EU Reference Laboratory for Diseases caused by Capripox viruses, including LSD (CODA-CERVA, Belgium) was officially appointed in January 2017. It provides the necessary coordination and technical support for LSD diagnostics and the overall control strategy of EU Member States and non-EU countries.

## REVIEW AND REFINEMENT OF LSD CONTROL MEASURES AT THE EU LEVEL

During the early stages of the LSD epidemic in Europe additional preventive measures – zoning, additional safeguards and vaccination – were implemented in the affected areas of Greece and Bulgaria through the adoption of country-specific Commission Implementing Decisions.

By November 2016, following the adoption of a coordinated regional strategy, all the above additional preventive measures were revised, consolidated and updated by Commission Implementing Decisions (EU) 2016/2008<sup>10</sup> and 2016/2009<sup>11</sup> in the light of the most recent scientific knowledge available and the consensus reached among the countries concerned, especially through the dialogue within the GF-TADs meetings.

The new rules promote:

- uniformity – a single set of control measures for LSD across the EU;

- proportionality – establishment of specific rules for “infected zones” and “free zones with vaccination”;
- sustainability – flexible trade rules that reduce the impact of LSD on trade without compromising safety;
- flexibility, such as the possibility of bilateral agreements; and
- lifting or refining of measures related to safe or low-risk products such as meat and milk.

As a result a new LSD zoning policy has been introduced in the EU that incorporates “free zones with vaccination” and “infected zones” (see Figure 2).

Under the new EU rules previous LSD-specific restrictions on meat are lifted and restrictions and risk-mitigation measures such as pasteurization for milk and dairy products apply only when those products are destined for animal feed. Safe movements of bovine animals and products such as skins and hides are enabled under certain conditions from one type of zone to another of the same or lower LSD status. This policy review confirmed the fact that the EU legal framework on animal diseases, despite the high requirements and standards it sets, it also provides the necessary flexibility for swift adjustment of the control measures and trade rules given the appropriate conditions and scientific basis, without compromising safety and legitimacy. The rapid implementation of preventive vaccination in Croatia and its swift adoption as

part of the EU and south-eastern Europe LSD control strategy was a major achievement in the framework of this response.

A timeline of the main interventions of DG SANTE with regard to LSD in south-eastern Europe between May 2015 and January 2017 are shown in Table 2.

## CONCLUSIONS – FUTURE STEPS

The challenge of the LSD epidemic in south-eastern Europe shows that a preventive policy based on the concept “prevention is better than cure” that stems from the EU animal health strategy is feasible and that it is best implemented as part of coordinated regional strategy. Given the fact that mass vaccination is the key measure in stopping spread of LSD, the European Commission will continue to support its coordinated implementation in EU Member Countries and in non-EU countries.

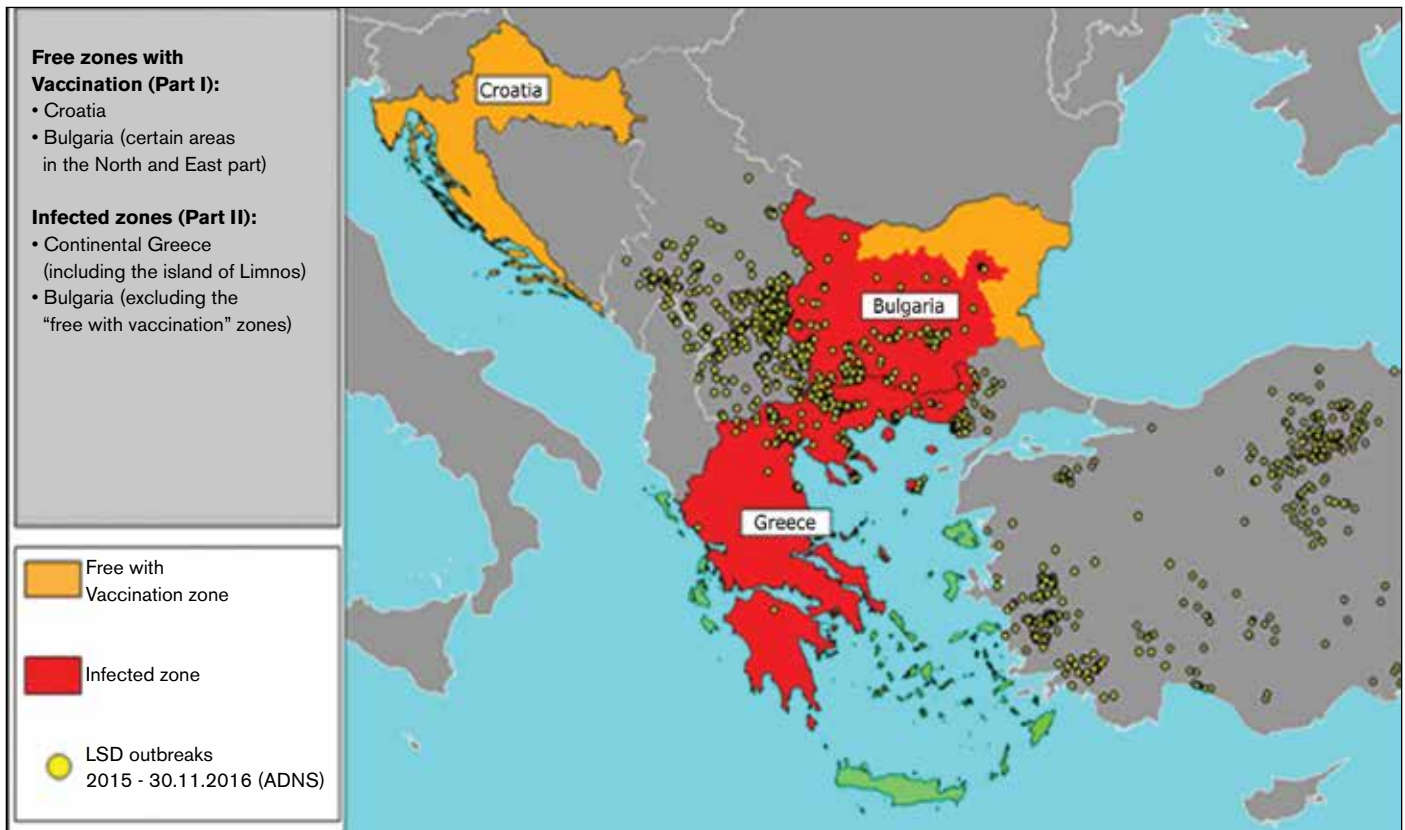
The European Commission will also foster regional coordination and cooperation among the countries of south-eastern Europe, particularly through regular GF-TADs activities with OIE and FAO.

## ACKNOWLEDGMENTS

The authors would like to thank GF-TADs, EFSA, the CVET experts, the BTSF team and all colleagues in the national veterinary authorities of the countries of south-eastern Europe who participated in the common efforts against LSD in south-eastern Europe in the past two years for their hard work and support throughout this period. <sup>360</sup>

<sup>10</sup> [http://eur-lex.europa.eu/eli/dec\\_impl/2016/2008/oj](http://eur-lex.europa.eu/eli/dec_impl/2016/2008/oj)

<sup>11</sup> [http://eur-lex.europa.eu/eli/dec\\_impl/2016/2009/oj](http://eur-lex.europa.eu/eli/dec_impl/2016/2009/oj)



**Figure 2:** LSD zoning in the EU, as at November 2016

**Table 2:** Timeline of DG SANTE 's major interventions for LSD between May 2015 and January 2017

	LSD epidemiological events	Month	Main DG SANTE actions
2015	<b>1<sup>st</sup> occurrence in European Turkey</b>	May	
	<b>1<sup>st</sup> occurrence in Greece</b>	Aug	Commission Implementing Decision (EU) <b>2015/1423</b> (Emergency safeguard measures and regionalization)
	<b>Greece starts vaccination</b>	Sep	Decision (EU) <b>2015/1500</b> (Refined LSD measures for Greece)
		Nov	<b>CVET</b> mission on LSD and Directorate F mission in Greece Decision (EU) <b>2015/2055</b> (LSD vaccination programme in Greece)
2016	<b>Recurrence in Greece</b> <b>1<sup>st</sup> occurrence in Bulgaria</b> <b>1<sup>st</sup> occurrence in the former Yugoslav Republic of Macedonia</b> <b>Bulgaria starts vaccination</b>	April	CVET mission on LSD in Greece Decision (EU) <b>2016/645</b> (LSD protective measures in Bulgaria) <b>Creation of the first EU LSD vaccine bank (400 000 doses)</b> <b>Vaccine grants to Bulgaria (150 000 doses) and Greece (50 000 doses)</b>
	<b>The former Yugoslav Republic of Macedonia starts vaccination</b>	May	Joint EFSA –DG SANTE workshop Strengthening regional cooperation in South East Europe and the Middle East for prevention and control of Lumpy Skin Disease <b>Vaccine grant to the former Yugoslav Republic of Macedonia (50 000 doses)</b>
	<b>1<sup>st</sup> occurrence in Serbia</b> <b>1<sup>st</sup> occurrence in Kosovo<sup>2</sup></b> <b>Serbia starts vaccination</b>	June	<b>CVET</b> missions on LSD in Serbia, the former Yugoslav Republic of Macedonia and Romania <b>1<sup>st</sup> expansion of the EU LSD vaccine bank (200 000 more doses)</b> <b>Vaccine grants to Serbia (50 000 doses), Kosovo<sup>2</sup> (25 000 doses), Greece (50 000 doses) and Albania (25 000 doses)</b>
	<b>1<sup>st</sup> occurrence in Albania</b> <b>1<sup>st</sup> occurrence in Montenegro</b> <b>Albania starts vaccination</b> <b>Kosovo<sup>2</sup> starts vaccination</b>	July	Publication of EFSA's "Urgent advice on lumpy skin disease" citing vaccination as the most effective tool against LSD Decision (EU) <b>2016/1183</b> (LSD vaccination programme in Bulgaria)  <b>GF-TADs 1<sup>st</sup> meeting</b> of the LSD expert group in Brussels
	<b>Montenegro starts vaccination</b> <b>Croatia starts preventive vaccination</b>	Aug	<b>Vaccine grant to Montenegro (25 000 doses)</b>
		Sept	Ministerial conference on LSD in Sofia New <b>EU Decisions on LSD</b> voted at the PAFF committee <b>GF-TADs 2<sup>nd</sup> meeting</b> of the LSD expert group in Lisbon <b>Vaccine grant to Croatia (50 000 doses)</b>
		Nov	<b>2<sup>nd</sup> expansion of the EU LSD vaccine bank (up to an additional 525 000 doses)</b> Adoption of Decisions (EU) <b>2016/2008</b> and <b>2016/2009</b> (Introduction of separate rules for zones "free with vaccination")
		Dec	<b>Vaccine grants to Albania (50 000 doses), Greece (50 000 doses) and Bulgaria (50 000 doses)</b> <b>GF-TADs 3<sup>rd</sup> meeting</b> of the LSD expert group in Istanbul, Turkey
		Jan	Adoption of <b>Commission Regulation (EU) 2017/140</b> . Designation of CODA-CERVA as the EU reference laboratory for LSD, sheep pox and goat pox
2017			





## COORDINATION

## Lumpy Skin Disease epidemics in Europe: Improving cooperation for controlling transboundary livestock diseases

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**T**his article describes the work of the European Food Safety Authority (EFSA) in providing a scientific basis for improving policies and facilitating cooperation among countries affected by and at risk of Lumpy Skin Disease (LSD).

### PHASE 1 – THE SPREAD OF LSD FROM AFRICA TO THE MIDDLE EAST: AN EMERGING RISK FOR EUROPE

A cattle disease caused by a capripox virus, LSD is characterized by fever and nodules on the skin, the mucus membranes and internal organs. It is mainly transmitted mechanically by blood-feeding arthropod vectors such as flies, mosquitoes and ticks. The disease can cause a reduction in milk production, abortions, sterility in bulls and damage to hides, which all lead to significant loss of income. Originally affecting cattle across Africa, LSD appeared in outbreaks in Israel, Jordan and Lebanon in 2012/13 and subsequently in Turkey, where it is now considered endemic. More recently the disease has spread from the Middle East to Europe.

### INITIAL EFSA SCIENTIFIC OPINION: REVIEW OF LSD, CONTROL MEASURES AND RELEASE AND IMPACT ASSESSMENT

In view of the spread of LSD throughout the Middle East, in 2014 the European Commission (EC) asked EFSA to issue a scientific opinion on LSD with a view to updating knowledge about the disease, assessing the risk of introduction and spread into the European Union (EU) and the possible effects, and judging the effectiveness of and hence justification for prevention and control measures (EFSA, 2015).

The assessment highlighted knowledge gaps such as the need for further research into the characteristics of LSD,

the susceptibility of hosts, transmission patterns and limited information about the susceptibility of wild hosts of LSD and their epidemiological role. There was evidence that only 50 percent of infected animals developed generalized skin lesions and that such animals could be viraemic and hence a possible source of the virus for vector transmission, even though transmission of the virus from sub-clinically infected animals has never been shown.

“ A mathematical model was developed to simulate the spread of LSD between farms and to assess the effectiveness of a policy ”

With regard to LSD transmission, some species of haematophagous arthropods are thought to be mechanical vectors of LSD virus (LSDV), but the role of individual species and the possible existence of biological vectors are unknown. Direct and/or indirect transmission, for example through fomites contaminated with secretions from infected animals, are not confirmed: they cannot be excluded, however, because the spread of LSDV is suspected in situations where the density of vectors is thought to be low. To date the main pathways for the spread of LSD between farms and regions involve the transport of infected animals and vectors. Movements of infected animals are the most efficient pathway for long-distance spread of LSD; movements of flying vectors are probably the main pathway over short distances.

Regarding the effectiveness of available control measures, the lack of vaccines that allow the differentiation of infected from vaccinated animals (DIVA) is a concern. The available vaccines are live attenuated capripox vaccines; those based on the homologous capripox LSDV

are effective in protecting animals, but there are possible purity and safety issues.

In the first EFSA opinion a mathematical model was developed to simulate the spread of LSD between farms and to assess the effectiveness of a policy of total culling at infected farms at different times from infection to reporting compared with culling only animals with general clinical signs. The model indicated that the latter policy would be adequate to contain 90 percent of epidemics around an initial infection site, but that the remaining 10 percent could spread up to 400 km from the initial site within six months. On the other hand the culling of whole herds at infected farms reduces the spread of LSDV substantially, and the sooner infected herds are detected and culled the greater the reduction of spread. In the scenarios produced with the model, an outbreak would be eliminated only if the policy of culling at infected farms were applied within 15 days after infection, which highlights the importance of early detection and prompt culling (see Figure 1).

### PHASE 2 – THE SPREAD OF LSD TO EUROPE

The first EFSA opinion was published in January 2015. Before that, LSD had been reported in December 2014 in the part of northern Cyprus not controlled by the Republic of Cyprus, and in the summer of 2015 LSD outbreaks were notified in eastern Greece that subsequently spread over the country. In the spring and summer of 2016 there were 1 000 outbreaks of LSD, first in Bulgaria and subsequently in the former Yugoslav Republic of Macedonia, Serbia, Kosovo,<sup>5</sup> Albania and Montenegro. On the eastern side of the Black Sea, LSD spread to Armenia, Azerbaijan, Kazakhstan, Georgia and the Russian Federation; there was also a northward spread from the Black Sea (see Figure 2).

### FOSTERING COOPERATION: THE EFSA/EC WORKSHOP ON LSD

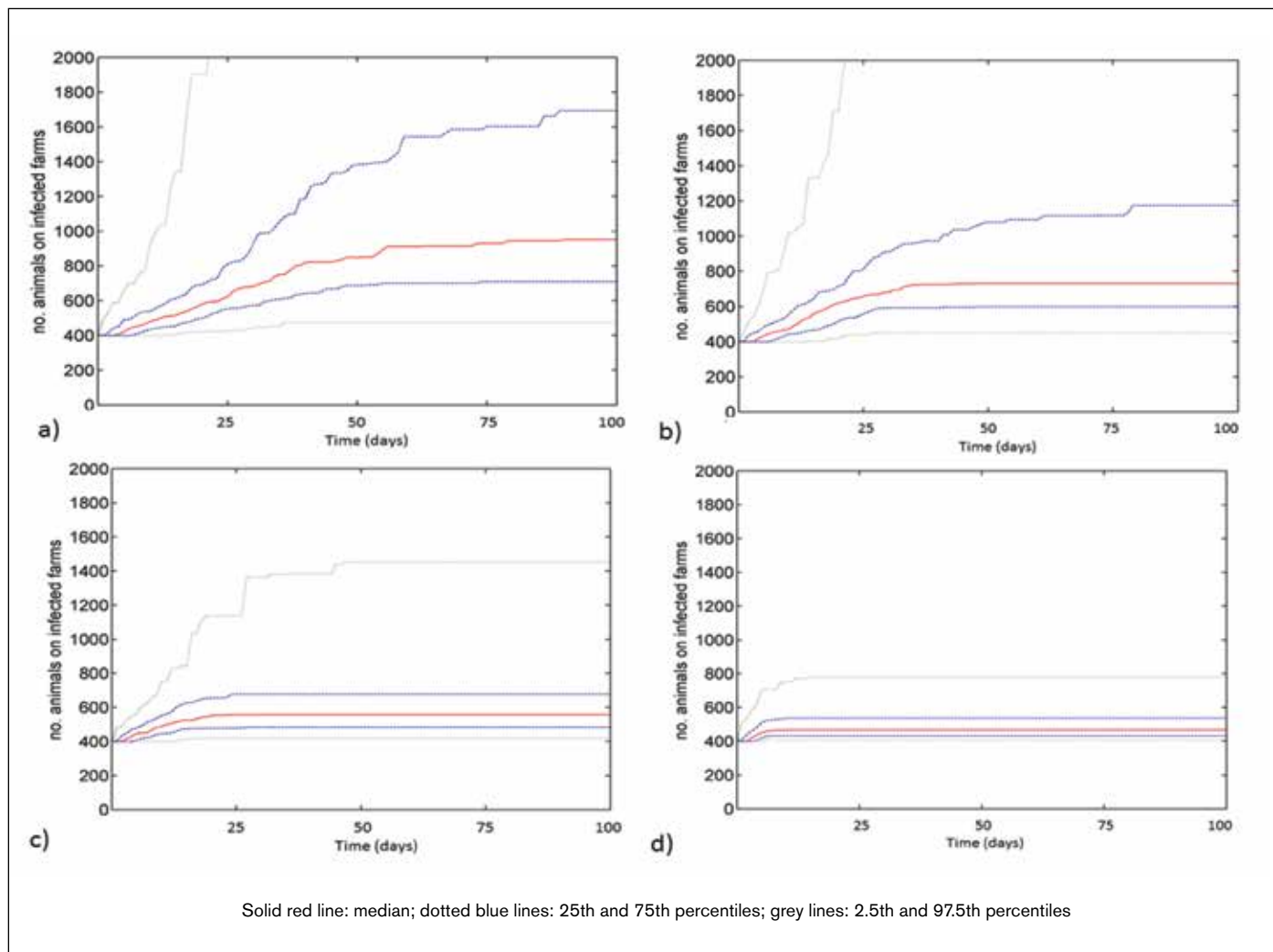
In view of the alarming situation, the Bulgarian Food Safety Agency notified EFSA at the end of 2015 of their concern about the spread of LSD from Turkey into the EU and of their

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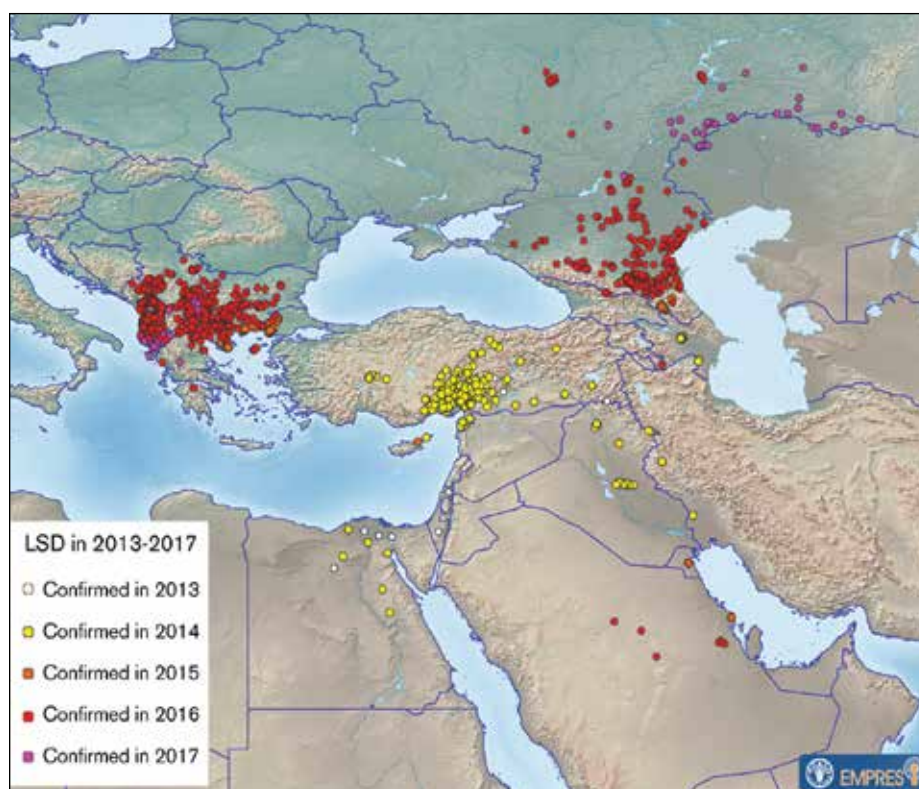


**Figure 1:** Estimates of the number of animals in infected farms in the scenario of LSD epidemics when: a) only generalized cases are culled, and when whole herds are culled – b) 28 days after infection, c) 15 days after infection and d) 7 days after infection

interest in a regional cooperation project to increase preparedness for LSD control. The EC Directorate-General for Health and Food Safety (DG SANTE) and EFSA accordingly organized a workshop on 11 and 12 May 2016 in Brussels with all interested parties with a view to: i) reviewing the latest available information on LSD; ii) increasing awareness of the epidemiological situation; and iii) establishing synergies at the regional level to improve LSD surveillance, prevention and control. The workshop was organized under the EC-funded EFSA Pre-Accession Programme (2015–2017), whose objectives are to promote understanding of the work of EFSA, share risk assessment expertise and create information-exchange mechanisms.

Chief veterinary officers and animal health directors from Albania, Bosnia and Herzegovina, Bulgaria, Cyprus, Greece, Israel, Jordan, Kosovo,<sup>5</sup> Lebanon, Montenegro,

<sup>5</sup> This designation is without prejudice to positions on status, and is in line with United Nations Security Council Resolution 1244 and the International Court of Justice opinion on the Kosovo Declaration of Independence.



**Figure 2:** LSD outbreaks notified in Europe and Middle East, 2013-2017 (EMPRES-i)



Serbia, Romania, the Russian Federation, the former Yugoslav Republic of Macedonia and Turkey – countries where LSD is or has been a concern – attended to update the delegates as to the current LSD situation in each country, control measures applied and laboratory and epidemiological capacities. Experts attended from DG SANTE, EFSA, FAO, the Secretariat of the Mediterranean Animal Health Network (*Reseau Méditerranéen de Santé Animale*; REMESA), the World Organisation for Animal Health (OIE) reference laboratory on capripox viruses at the Pirbright Institute (UK) and the Veterinary and Agrochemical Research Centre (CODA-CERVA, Belgium).

The various outputs of the workshop are described in its report (EFSA, 2016a). Leading scientists in LSD research gave an update on the epidemiology, diagnostics and control of LSD, with a focus on vaccines. Information was shared on LSD epidemiology, surveillance and control in the regions concerned, with country-specific needs for optimizing preparedness for LSD control, in which personnel capacities were a significant factor. The workshop also served to promote knowledge-sharing among the participants.

A further output was a list of agreed conclusions and recommendations on LSD prevention and control, which includes the following:

- The homologous live attenuated vaccine against LSD is currently the best choice. In case of shortage, heterologous vaccines – for example those based on a sheep pox strain – could also be considered even though they are less effective.

- Purity and potency checks of the available homologous vaccines should be carried out.
- An experimental model such as a challenge model is essential for testing the effectiveness of vaccines.
- No spread of vaccine virus from vaccinated to non-vaccinated animals has been demonstrated in the current experimental infection trials.
- Vaccines must be available and readily obtainable to ensure the effectiveness of disease control by emergency vaccination.

Research needs in relation to epidemiology, diagnostics and vaccines for LSD were also identified.

With regard to epidemiology, research should investigate: i) the sampling plan needed during current outbreaks to check herds of small and large ruminants; ii) the immune response to field virus and to the live attenuated vaccine strain, including the duration of protection, the presence and level of antibodies in blood, and the duration of protective immunity; iii) the use of current outbreaks to study the epidemiology of LSD; and iv) the establishment of coordinated entomological surveillance in the region.

Regarding diagnostics, the priorities were: i) development of DIVA standard tests to differentiate between vaccinated and infected animals; ii) molecular diagnostic tools for phylogenetic studies to track the origin of the LSDV strain; and iii) straightforward low-cost serological tests for surveillance and evaluation of the effectiveness of vaccination.

With regard to vaccines, the priorities were: i) the efficacy, safety, detection

and duration of immunity of currently available live vaccines against LSDV in cattle, to be evaluated through challenge experiments in controlled environments and experimental trials in the field to determine the effectiveness of vaccination; ii) the development of DIVA vaccines; and iii) the minimum required duration of vaccination campaigns.

It was recommended that control policies for LSD should be re-examined, taking into account the latest scientific knowledge and the epidemiological situation. In particular, there was a proposal to investigate the possibilities of protective vaccination before the onset of outbreaks and of control measures in vaccinated herds other than total stamping out when an outbreak occurs. The participants identified needs such as training in techniques for prevention and control of LSD: these included contingency planning, sound emergency practices and the organization of awareness-raising campaigns for LSD prevention and control. Other practical needs included access to LSD vaccines and vaccine banks, and laboratory equipment and training. Some of the organizations attending the workshop already offered training in relation to areas such as molecular methods, field vaccine efficacy studies and serological methods.

## CONTROL OF LUMPY SKIN DISEASE IN EUROPE

With the spread of LSD in the Balkans during the spring and summer 2016, the authorities in the countries affected have been implementing a policy of stamping out coupled with vaccination with live homologous vaccines because there is consensus that stamping out alone is inadequate for effective control of the disease. In response to the specific question raised by the Bulgarian authorities as to the implementation of stamping out in LSD-affected holdings, the EC asked EFSA to compare the implications of LSD spread when a partial stamping-out policy – culling of clinically affected animals only – is implemented and the implications of total stamping out of infected herds coupled with vaccination.

## URGENT EFSA ADVICE ON ASSESSMENT OF CONTROL MEASURES

To answer this question, EFSA developed a mathematical model for the transmission of LSDV between farms and different scenarios of stamping out – total, partial or none – combined with vaccination before or after

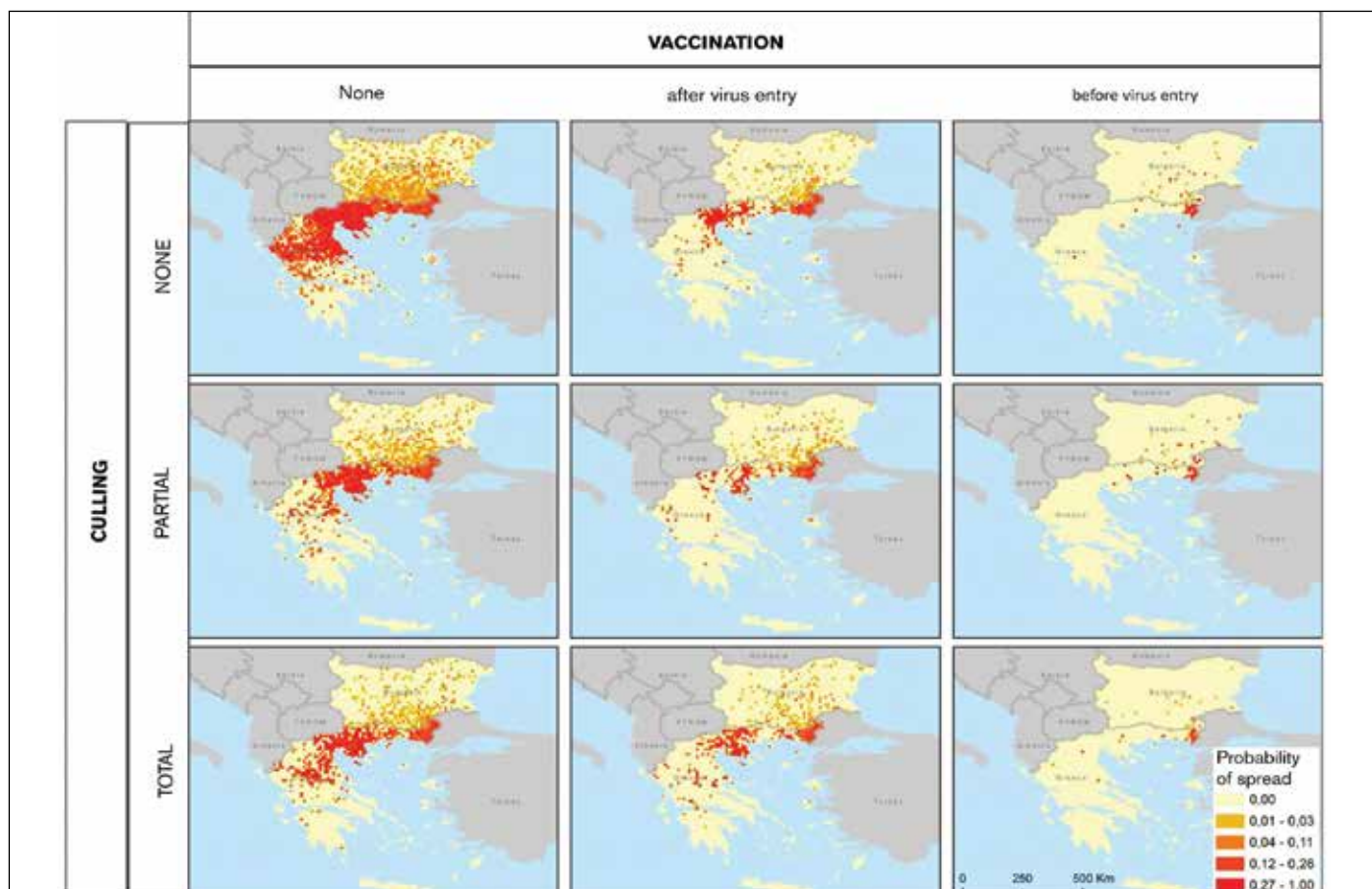


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Farmers preparing to leave with their tractor to cut feed for their livestock

<sup>6</sup> This value of vaccination effectiveness is confirmed by analysis of field data provided by the Greek authorities; it repeats previously published results.





**Figure 3:** Predicted effects of different combinations of vaccination and stamping-out strategies on the spread of LSDV in Bulgaria and Greece. The colour of the dots represent the percentage of simulations for which at least one farm in a  $0.1^\circ \times 0.1^\circ$  grid square becomes infected by the end of the year in which the incursion occurs. Vaccination effectiveness is set at 75 percent

virus entry, or no vaccination (see Figure 3). The model indicates that vaccination has a greater effect in reducing the spread of LSDV than any culling policy, even when vaccination effectiveness of only 40 percent is considered. If vaccination is evenly applied over 95 percent of affected farms and at least 75 percent of vaccinated animals are effectively protected,<sup>6</sup> total stamping out and partial stamping out have a similar probability of eradicating the infection.

When no vaccination is applied, or when the effectiveness of vaccination is low – 40 percent, for example – the probability of eradication is higher when total stamping out is implemented than when partial stamping out is used. In general, however, the model indicates that partial stamping out does limit increases in the number of farms affected. Vaccination is considered most effective in limiting the spread of LSDV if herds can be protected before the time of virus entry, but less effective when herds are protected after virus entry. No vaccination is the least effective option. Details of the assumptions in the model are provided in the full report (EFSA, 2016b).

### FINDING SYNERGIES IN DATA COLLECTION AND INFORMATION TO IMPROVE PREVENTION AND CONTROL: THE CURRENT WORK OF EFSA

Among the recommendations of the first meeting of the Standing Group of Experts on LSD for South-Eastern Europe<sup>7</sup> in Brussels in July 2016 was the proposal that: “The collection of surveillance data and scientific information that may be relevant (e.g. incidence, weather conditions) be coordinated for purposes of better risk assessment and management.”

In the light of this, the EC asked EFSA to carry out an updated epidemiological analysis based on the data collected by the Member States and neighbouring countries affected by or at risk of LSD. The analysis will focus on temporal and spatial patterns of LSD and will highlight the risk factors for LSD transmission. The data will be used to explore possible improvements of the mathematical models referred to earlier.

EFSA is implementing harmonized data collection from affected countries on the structure and distribution of cattle farms,

animal movements, LSD outbreaks, laboratory results and vaccination, using the EFSA Data Collection Framework.<sup>8</sup> The intermediate project report is expected by February 2017, and the final report by January 2018.

### DISCLAIMER

This paper is published under the sole responsibility of the authors, and may not be considered as an EFSA output. The positions and opinions presented are those of the authors alone, and are not intended to represent the views of EFSA. <sup>360</sup>

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<sup>7</sup> See: [http://web.oie.int/RR-Europe/eng/Regprog/en\\_GF\\_TADS%20-%20Standing%20Group%20LSD.htm](http://web.oie.int/RR-Europe/eng/Regprog/en_GF_TADS%20-%20Standing%20Group%20LSD.htm)

<sup>8</sup> See: <https://www.efsa.europa.eu/en/data/toolbox>

## COORDINATION

## Evaluation of vaccines against Lumpy Skin Disease using an optimized infection model: preliminary results

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**L**umpy skin disease (LSD) is a pox disease of cattle caused by the LSD virus (genus *Capripox*) and characterized by fever and nodules on the skin, mucosal membranes and internal organs. The disease can cause abortion, a reduction in milk production, sterility in bulls and damage to hides, which lead to significant loss of income. The disease, which originally affected cattle across Africa, spread to Israel, Egypt and Lebanon in 2012/13 and epizootics began in Turkey in 2013, Azerbaijan and Cyprus in 2014, in Armenia, Greece and the Russian Federation in 2015, and in Albania, Bulgaria, the former Yugoslav Republic of Macedonia, Georgia, Kosovo, Montenegro and Serbia in 2016. Mass vaccination appeared to be the only effective way to control this outbreak of vector-borne disease. But there is widespread hesitation with regard to using a live attenuated vaccine – currently the only type commercially available – because of the scarcity of independent verification of its efficacy and its safety in terms of side effects and contaminating agents, and because of international trade restrictions for live cattle and some cattle products.

Data on the efficacy and safety of vaccination are generally available from field experience only, which makes it difficult to choose the most suitable vaccine. The study at CODA-CERVA in collaboration with the Pirbright Institute aimed to: i) optimize a LSD virus (LSDV) infection model; and ii) evaluate and compare live and inactivated vaccines against LSD under standardized conditions using the optimized challenge model.

With regard to the first objective, the LSD Neethling virus strain and a field isolate from the 2012/13 LSD outbreak in Israel were compared by assessing the outcome of *in vivo* challenge. The range of compared variables included: i) clinical



*A veterinarian preparing for vaccination while a farmer tries to restrain the cow*

signs; ii) virological measures of the level, peak moment and duration of viraemia and virus secretion; and iii) humoral and cellular immunological parameters. Some variables, for example a fever spike at seven to eight days post-infection and seroconversion, were very similar; others such as clinical signs, viraemia and IFN $\gamma$  release were quite different for the two isolates used. Selection of the most suitable challenge virus for the vaccine evaluation experiments was conducted on the basis of the data gathered.

This optimized challenge model was used to compare several commercially available live attenuated vaccines based on LSD, or sheep pox or goat pox vaccine strains, and recently developed inactivated LSDV vaccines. Each trial used seven vaccinated animals and five unvaccinated control animals. The vaccinated and unvaccinated animals could be clearly

distinguished from the different virological, humoral and cellular immunological variables. In the vaccinated groups, different patterns of the variables were observed pre-challenge and post-challenge, which suggested differences in the safety and efficacy of the vaccines tested. Suitable, moderately suitable and unsuitable vaccines for field use in the current emergency were identified on the basis of these data.

### ACKNOWLEDGEMENTS

The studies that yielded these results were funded by: i) the Bill and Melinda Gates Foundation Grant Agreement, Investment ID OPP1126866; ii) the Belgian Federal Public Service of Health, Food Chain Safety and Environment, contract RT 15/3 LUMPY SKIN 1; iii) the European Commission and iv) CODA-CERVA in Ukkel, Belgium. <sup>360</sup>

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<sup>4</sup> This designation is without prejudice to positions on status, and is in line with UNSCR 1244 and with the ICI Opinion on the Kosovo Declaration of Independence.

## COORDINATION

# Surveillance and control of Lumpy Skin Disease: a challenge affecting three continents

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When it was first described in what is now Zambia in 1929, Lumpy Skin Disease (LSD) was considered to be an infection of cattle confined to sub-Saharan Africa. But in 1988 the virus was reported in Egypt (European Food Safety Authority [EFSA], 2015), and LSD subsequently appeared in countries in the Middle East and the Arabian Gulf.

In the last few years the geographic distribution of the virus has expanded rapidly, reaching Europe for the first time. It affected cattle in Greece in 2015 and Bulgaria in 2016 and cases were reported during the same period in Albania, the former Yugoslavian Republic of Macedonia, Montenegro, Serbia, the Russian Federation, the Islamic Republic of Iran, Kazakhstan and the Caucasus region.

Over the years, LSD has affected livestock production mainly in resource-poor countries. It is included in the World Organisation for Animal Health (OIE) list of notifiable terrestrial and aquatic animal diseases because of its serious economic impact on livestock production and trade. It has, however, received little attention from the veterinary science community, and research and development have been limited to the few countries where the disease was endemic (see Figure 1).

It is important to note that in sub-Saharan Africa, the LSD virus (LSDV) circulates with the other capripox viruses (CaPVs) of small ruminants – sheep pox virus (SPPV) and goat pox virus (GTPV). The geographical distribution of SPP and GTP virus is much wider than that of LSDV, and has been reported in several countries in Africa, Asia, the Russian Federation and south-eastern Europe (EFSA, 2014).

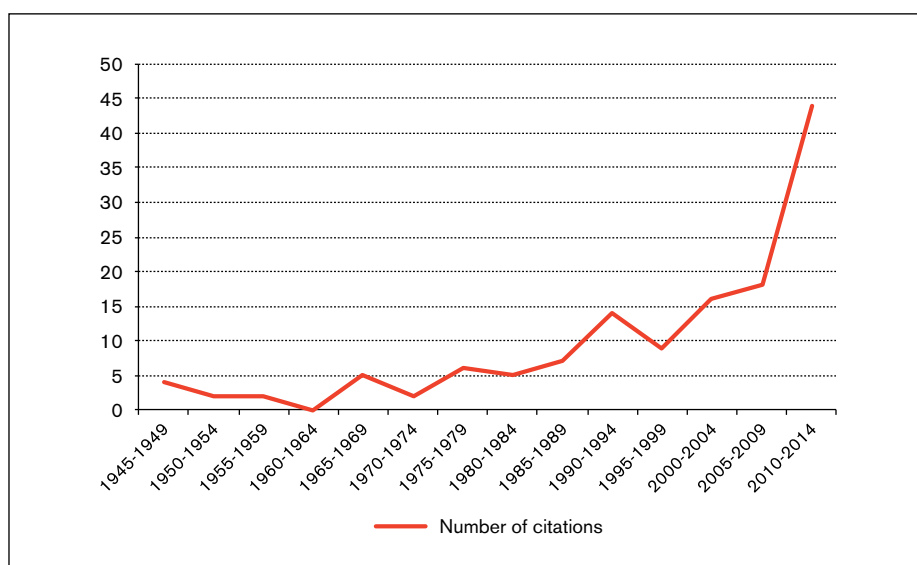
The Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture (AGE) and the FAO Animal Production and Health

Division (AGA) provide technical and laboratory-based assistance to help Member States to combat transboundary animal and zoonotic diseases (TADs), which include LSD. The support provided by FAO/IAEA consists of: i) research and development and collaborations with reference laboratories and research institutions; ii) transfers of technology and capacity building; iii) services such as support for sequencing; and iv) allocations of financial and human resources to countries where LSD is endemic or has recently appeared, particularly for laboratory investigations. This is consistent with the AGA/AGE mandate and with the work of the OIE collaborating centre for enzyme-linked immunosorbent assay and molecular techniques in animal disease diagnosis at the AGE Laboratory in Seibersdorf, Austria. This complements the support provided by AGA at the country and regional levels, for example in epidemiological surveillance and early-warning systems.

With regard to LSDV and GTPV infections, AGE and AGA are supporting Member States in rapid detection of disease, pathogen characterization, vaccines and vaccination and surveillance and epidemiology.

## FAO AND IAEA RESPONSE TO THE EMERGENCE OF LSD IN EUROPE AND CENTRAL ASIA

When LSD emerged in Greece in 2015 and spread to Bulgaria and other European countries in 2016, AGE and AGA mobilized resources for the countries requiring emergency assistance, with support from the IAEA Technical Cooperation Department. Missions were fielded in Bulgaria in April 2016 and Serbia in June 2016: these focused on laboratory capacity, harmonization of laboratory standard operating procedures (SOPs) and assessment of laboratory needs for emergency response. In the emergency response phase, AGE provided polymerase chain reaction (PCR) reagents and consumables such as PCR enzymes,



**Figure 1:** Number of PubMed citations

National Center for Biotechnology Information database, USA. The search on 30 October 2016 used "Lumpy Skin Disease" as key words; 174 citations were retrieved. A sharp increase in the number of scientific publications is observed from the 1990s, when LSD was reported outside sub-Saharan Africa. Between January 2015 and the time of writing – October 2016 – there were 40 citations in PubMed

<sup>1</sup> Animal Production and Health Section, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture (AGE), Vienna, Austria with its Animal Production and Health Laboratory, Seibersdorf, Austria



buffer solutions and DNA extraction materials to enable laboratories in recently affected and high-risk countries to conduct hundreds of diagnostic tests with LSD emergency toolkits. At the same time, AGE prepared and distributed PCR primers and PCR positive controls in the form of non-infectious DNA from cultured LSD, SPP and GTP viruses. Two training courses and a workshop were organized as part of the emergency response to familiarize veterinary laboratory staff with LSD and the most recent recommended diagnostic techniques (see below Diagnoses of CaPV infection in veterinary laboratories – AGE and AGA capacity building, and Table 1).

## RESEARCH AND DEVELOPMENT FOR LSD: RAPID AND COST-EFFECTIVE DETECTION

The control and eradication of TADs requires rapid detection and laboratory confirmation of infections. Although CaPVs can be isolated *in vitro*, the techniques can be time-consuming and may require special facilities in non-endemic countries: regulations may require work in biosafety level 3 laboratories, for example, and the assignment of specialists. PCR-based technology constitutes a sensitive and specific diagnostic tool: its application to rapid detection and typing of CaPVs has been explored by several research groups.

In the last five years, AGE and AGA experts have investigated the application of rapid and cost-effective immunological and molecular tools for the detection of LSDV, SPPV and GTPV that can be applied in laboratories with limited resources and on several PCR platforms. This led to the development and validation of gel-based PCR and real-time PCR protocols. The protocols developed in the AGE Laboratory (Seibersdorf) can be used for concurrent detection and genotyping of LSDV, unlike other molecular tests developed for the virus. The PCR-specific products and hence the genotype results can be visualized by gel electrophoresis (Lamien *et al.*, 2011a) or real-time PCR amplification followed by melting-curve analysis with no need for expensive labelled probes or genome sequencing (Lamien *et al.*, 2011b; Gelaye *et al.*, 2013).

It is known that most CaPV strains, especially those infecting small ruminants, are not strictly host-specific and can cross-infect sheep and goats. The clinical signs and lesions caused by CaPV infections of ruminants are similar and difficult to differentiate from those caused by other pathogens. The rapid genotyping methods therefore constitute a cost-effective laboratory tool for clinical differential diagnoses. A multi-pathogen detection platform based on a one-step multiplex reverse transcriptase real-time PCR (RT-qPCR) assay has recently been developed by AGE for simultaneous

detection of CaPV, *peste des petits ruminants virus*, *Pasteurella multocida* and *Mycoplasma capricolum* ssp. *capripneumonia* in pathological samples collected from small ruminants with respiratory signs (Settypalli *et al.*, 2016). An additional real-time PCR-based protocol is being validated at the AGE laboratory for simultaneous detection of eight different pox viruses affecting ruminants and camels.

## RESEARCH AND DEVELOPMENT: HIGH-THROUGHPUT PLATFORMS FOR SERO-SURVEILLANCE AND DISEASE MONITORING

Field-validated high-throughput laboratory tests enabling large-scale surveillance based on antibody detection are not currently available. In recently infected or at-risk countries the availability of simple and cost-effective serological assays would help to monitor vaccination coverage, map the circulation of the virus in new areas or populations and enhance understanding the epidemiology of CaPV infections with respect to sub-clinically affected animals and the role of wild ruminants or other animals as reservoirs. AGE and AGA are working with international laboratories and veterinary services in Member States with a view to developing and validating cost-effective and robust serological assays for CaPV antibody detection.

## DIAGNOSES OF CAPV INFECTION IN VETERINARY LABORATORIES: CAPACITY-BUILDING BY AGE AND AGA

Classical and novel testing procedures for LSD and other TADs must be transferred to the veterinary laboratories in countries infected or at risk. AGE is dedicated to this task, and has transferred SOPs adopted

by international reference laboratories and new technologies that it has developed and validated to veterinary laboratories in Africa, Asia and Europe. This has been done through missions to Member States and specialist training and workshops at AGE. Several fellowships supported by AGE have provided training in CaPV detection and genotyping techniques, which has improved disease detection and reporting: in 2016, for example, Burundi promptly reported the presence of LSDV on the basis of results obtained at a local laboratory. The training of a Burundian scientist and the supply of SOPs and reagents by AGE made this possible.

In view of the rapidity with which LSD spread in Central Asia, the Russian Federation and Europe in 2015/16, many laboratories in these regions were unprepared to address the situation: AGE and AGA therefore organized three training events on LSD and related CaPV infections (see Table 1). The first two were of one week's duration and held at the AGE laboratory in August 2016: they focused on increasing and updating laboratory capacities for rapid detection and typing of CaPV. The 37 participants from 22 Asian and European countries participated in practical laboratory training, seminars and lectures with a view to familiarizing technicians and managers with the diseases and their laboratory diagnosis. The third session, organized by AGE and AGA in November 2016, was a European regional workshop on epidemiology, diagnosis and control of TADs, with special emphasis on CaPV: experts from international reference laboratories and countries affected by LSD shared their data and experience and obtained up-to-date information on the epidemiology, control and diagnosis of CaPVs (see Table 1).

**Table 1:** Training courses on LSD and other CaPVs organized by the IAEA Technical Cooperation Department, AGE and AGA, 2012–2016

1. Garoua, Cameroon, 2012. Regional training course on major transboundary and zoonotic animal diseases: early detection, surveillance and epidemiology: focus on African swine fever, Capripox and Rabies. Partially supported by the FAO/OIE/World Health Organization IDENTIFY project.
2. Seibersdorf, Austria, 2012. Training on sequencing and molecular epidemiology of animal pathogens: focus on PPR, CBPP, CCPP, AI, ND, FMD and Capripox. Supported by the FAO/OIE/WHO IDENTIFY project.
3. Debre Zeit, Ethiopia, 2014. Training course on the diagnosis of transboundary animal diseases: pathogen typing using molecular techniques.
4. Seibersdorf, Austria, 2014. Training course on the diagnosis of transboundary animal diseases: practical approaches for introducing new assays for routine use in veterinary diagnostic laboratories.
5. Seibersdorf, Austria, 2015. Training course on transboundary animal disease diagnosis: sequencing and bioinformatic analysis of animal pathogen genomes.
6. Seibersdorf, Austria, 2016. Training course on nuclear and nuclear-related techniques for early and rapid detection and confirmation of pox virus infections in animals.
7. Seibersdorf, Austria, 2016. Workshop on advanced diagnosis and control of emerging transboundary animal diseases, with emphasis on Lumpy Skin Disease. Supported by the United States Department of Agriculture Animal and Plant Health Inspection Service.
8. Seibersdorf, Austria, 2016. Training course on transboundary animal disease diagnosis: respiratory diseases of small ruminants – PPR, CCPP, <i>Pasteurella</i> and Capripox.

## A HARMONIZED APPROACH TO LABORATORY DIAGNOSIS OF LSD AND CAPVS: THE AGE CONTRIBUTION

To improve the comparison of laboratory results, integrate monitoring and surveillance data and ensure reliable disease reporting, veterinary laboratories must adopt standard validated approaches for virus detection. AGE has accordingly distributed to Member States nine laboratory SOPs that originated from international reference laboratories or the AGE laboratory: these describe procedures for DNA extraction, PCR-based screening and confirmatory tests, purification of PCR products for sequencing and virus gene sequencing protocols. In the last quarter of 2016, AGE and AGA jointly organized an inter-laboratory trial for PCR-based detection of LSD and other CaPVs, using a panel of ten blind samples; 28 laboratories in 25 European and Asian countries were involved. This was supported by the IAEA Technical Cooperation Department and the Austrian Agency for Health and Food Safety.

## CONTROLLING LSDV: EVALUATION OF VACCINES AND DEVELOPMENT OF NEW VACCINE PROTOTYPES

In countries where LSD is endemic, vaccination is probably the most effective method of control. In countries where infections are recent, culling of infected and in-contact animals and movement restrictions have been effective when the infection was detected early and control measures were implemented immediately. In countries with limited resources, culling of infected and in-contact animals is often regarded as wasting a valuable source of food and may not be feasible. In some of these countries it may be impossible to implement movement restrictions for small and large ruminants (Tuppurainen *et al.*, 2014).

To date, only live attenuated vaccines are available for CaPV infections. In some instances these did not provide full protection and adverse reactions were reported, particularly in cattle vaccinated with LSD vaccines. Recent papers suggest that a new generation of safe and effective vaccines against LSDV, SPPV and GTPV is required: they should ideally be affordable and available for use in endemic and non-endemic countries without impeding international trade of live animals and their products (Tuppurainen *et al.*, 2014).

In the last decade AGE and AGA experts have been working with research institutions in various Member States to develop alternative approaches to LSD vaccines and to evaluate those that are currently available. The papers on CaPV vaccines

authored or co-authored by AGE are listed in Table 2. In view of the emergence of LSDV in previously disease-free areas and of the need for preventive vaccination in disease-free countries at high risk of infection, experts and international organizations are recommending the development of effective inactivated vaccines for LSD (EFSA, 2015); nuclear technologies such as gamma irradiation may be a reliable way to generate them. The humoral antibody response induced by existing vaccines does not correlate well with protection, because protection from LSD relies mainly on cell-mediated immunity. New tools are therefore needed for *in vitro* evaluation of the immune response to LSD vaccines and selection of appropriate vaccine strains. The AGE laboratory is researching and developing reliable and easily transferred *in vitro* systems for the evaluation of cell-mediated immunity in cattle, and work is in progress on several molecular Differentiating Infected from Vaccinated Animals (DIVA) approaches for SPPV and LSDV and on the molecular mechanisms governing CaPV attenuation. <sup>360</sup>

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**Lamien, C.E., Leleuta, M., Goger, W., Silber, R., Tuppurainen, E., Matijevic, M., Luckins, A.G. & Diallo, A.** 2011b. Real time PCR method for simultaneous detection, quantitation and differentiation of capripox viruses. *J. Virol. Methods* 171(1): 134–40.

**Settypalli, T.B., Lamien, C.E., Sperser J., Leleuta, M., Wade, A., Gelaye, E., Loitsch A., Minoungou, G., Thiaucourt, F. & Diallo, A.** 2016. One-step multiplex RT-qPCR assay for the detection of *peste des petits ruminants* virus, capripox virus, *pasteurella multocida* and *mycoplasma capricolum* subspecies (ssp.) *capripneumoniae*. *PLOS One* 11(4): e0153688. Available at: <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0153688>

**Tuppurainen, E.S., Pearson C.R., Bachanek-Bankowska, K., Knowles, N.J., Amareen, S., Frost, L., Henstock, M.R., Lamien, C.E., Diallo, A. & Mertens, P.P.** 2014. Characterization of sheep pox virus vaccine for cattle against lumpy skin disease virus. *Antiviral Res.* 109: 1–6.

**Table 2:** Publications authored or co-authored by AGE on CaPV vaccines and vaccination, 2000–2015

Title	Details
Capripox disease in Ethiopia. Genetic differences between field isolates and vaccine strain, and implications for vaccination failure	2015. <i>Antiviral Res.</i> 119: 28–35 DOI: 10.1016/j.antiviral.2015.04.008
Characterization of sheep pox virus vaccine for cattle against lumpy skin disease virus	2014. <i>Antiviral Res.</i> 109: 1–6 DOI: 10.1016/j.antiviral.2014.06.009
Protective efficacy of a single immunization with capripox virus-vectored recombinant <i>peste des petits ruminants</i> vaccines in the presence of pre-existing immunity	2014. <i>Vaccine.</i> 32(30): 3772–3779 DOI: 10.1016/j.vaccine.2014.05.025
Improved method for the generation and selection of homogeneous lumpy skin disease virus (SA-Neethling) recombinants	2007. <i>J. Virol. Methods.</i> 146(1–2): 52–60
Immune responses to recombinants of the South African vaccine strain of lumpy skin disease virus generated by using thymidine kinase gene insertion	2005. <i>Vaccine.</i> 23(23): 3061–3067
Control of <i>peste des petits ruminants</i> : classical and new generation vaccines	2003. <i>Dev. Biol. (Basel).</i> 114: 113–119
Development of a dual recombinant vaccine to protect small ruminants against <i>peste des petits ruminants</i> virus and capripox virus infections	2003. <i>J. Virol.</i> 77(2): 1571–1577
Comparative sequence analysis of the South African vaccine strain and two virulent field isolates of Lumpy Skin Disease virus	2003. <i>Arch Virol.</i> 148(7): 1335–1356
Importance of thymidine kinase activity for normal growth of Lumpy Skin Disease virus (SA-Neethling)	2002. <i>Arch Virol.</i> 147(3): 659–663
Goat immune response to capripox vaccine expressing the haemagglutinin protein of <i>peste des petits ruminants</i>	2002. <i>Ann. NY Acad. Sci.</i> 969: 88–91

## NEWS

## The FAO response to the threat of Lumpy Skin Disease in the Balkans and the Caucasus

Contributors: Daniel Beltrán-Alcrudo and Andriy Rozstalnyy<sup>1</sup>

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In 2013, lumpy skin disease (LSD) moved out of Africa and spread rapidly throughout the Middle East and into Turkey, where it is currently endemic. Since 2014, LSD has spread north-westwards into the Balkans – first into Greece, then Bulgaria, the former Yugoslav Republic of Macedonia, Serbia, Montenegro, Albania and Kosovo. There was a north-eastwards spread into the Caucasus – Azerbaijan, Armenia and Georgia – and into Kazakhstan and the southern part of the Russian Federation in 2014/16. When the vector season starts again in the spring of 2017 there is an increased risk that LSD will continue its spread to central Asia, western Europe and central-eastern Europe.

Because LSD is a new disease in the Balkans and the Caucasus, the veterinary services in countries that are affected or at risk have no previous experience of the disease and hence face serious challenges. There are also knowledge gaps related to epidemiology, vector ecology, immunity and vaccine effectiveness and the efficacy of the various control options. To address these challenges, FAO is assisting countries in the region with prevention and control of LSD.

The FAO approach to disease control is based on a close monitoring of the disease situation with EMPRES-i, which feeds into continuous risk assessment in and communication with countries that are affected or at risk. In the view of FAO, a harmonized regional approach involving prevention and control measures such as vaccination programmes and systematic sharing of data, lessons learned and best practices is the only effective way to target transboundary animal diseases such as LSD. It is crucial to involve stakeholders such as farmers, traders, processors and veterinarians: raising awareness and engaging with these groups will foster collaboration in

early detection and effective implementation of prevention and control measures. FAO believes that specific solutions must be found for each country, for example by piloting new approaches for risk mitigation and outbreak control as required.

### PAST ACTIVITIES WITH REGARD TO LSD

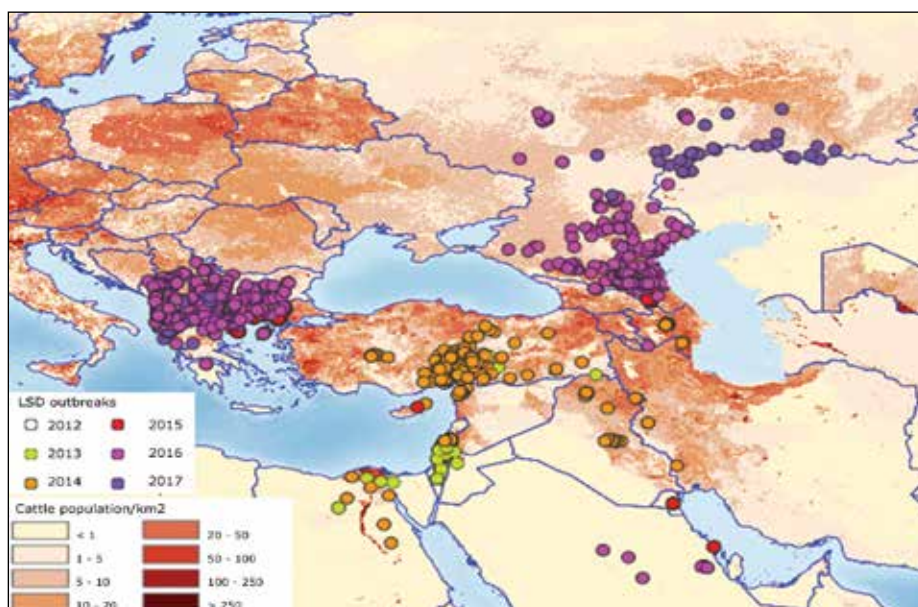
FAO has followed the spread of the disease and published two issues of EMPRES Watch – in November 2013 on LSD in the Middle East<sup>2</sup> and in September 2015 when LSD reached Europe<sup>3</sup> – with a view to assessing the risks inherent in the situation and providing a set of recommendations. Additional publications addressing the risk of LSD include the present EMPRES 360 Monograph on LSD, which analyses the situation by country, and the FAO's position on the sustainable prevention, control and elimination of LSD, particularly in Eastern Europe and the Balkans.

Regional meetings included the sub-regional workshop on LSD prevention and

control in Tbilisi on 11–12 November 2015 under the aegis of the Global Framework for the Progressive Control of Transboundary Animal Diseases (GF-TADs), which was attended by representatives of veterinary services in the European Union, Caucasus and Eastern Europe.

With the spread of LSD from the Middle East into the Balkans, an online meeting on LSD epidemiology and control strategies with a focus on effective vaccination was organized on 7 April 2015 through the European Commission for the Control of Foot-and-Mouth Disease (EuFMD), which also organized a two-day practical training on vector-transmissible animal diseases, with a focus on LSD, for Balkan countries on 31 May – 2 June 2016 in Stara Zagora, Bulgaria. The workshop provided background information on LSD, and gave participants hands-on experience of conducting vector surveillance, for example through trapping systems and identification.

At the request of chief veterinary officers from central and southern Europe, FAO



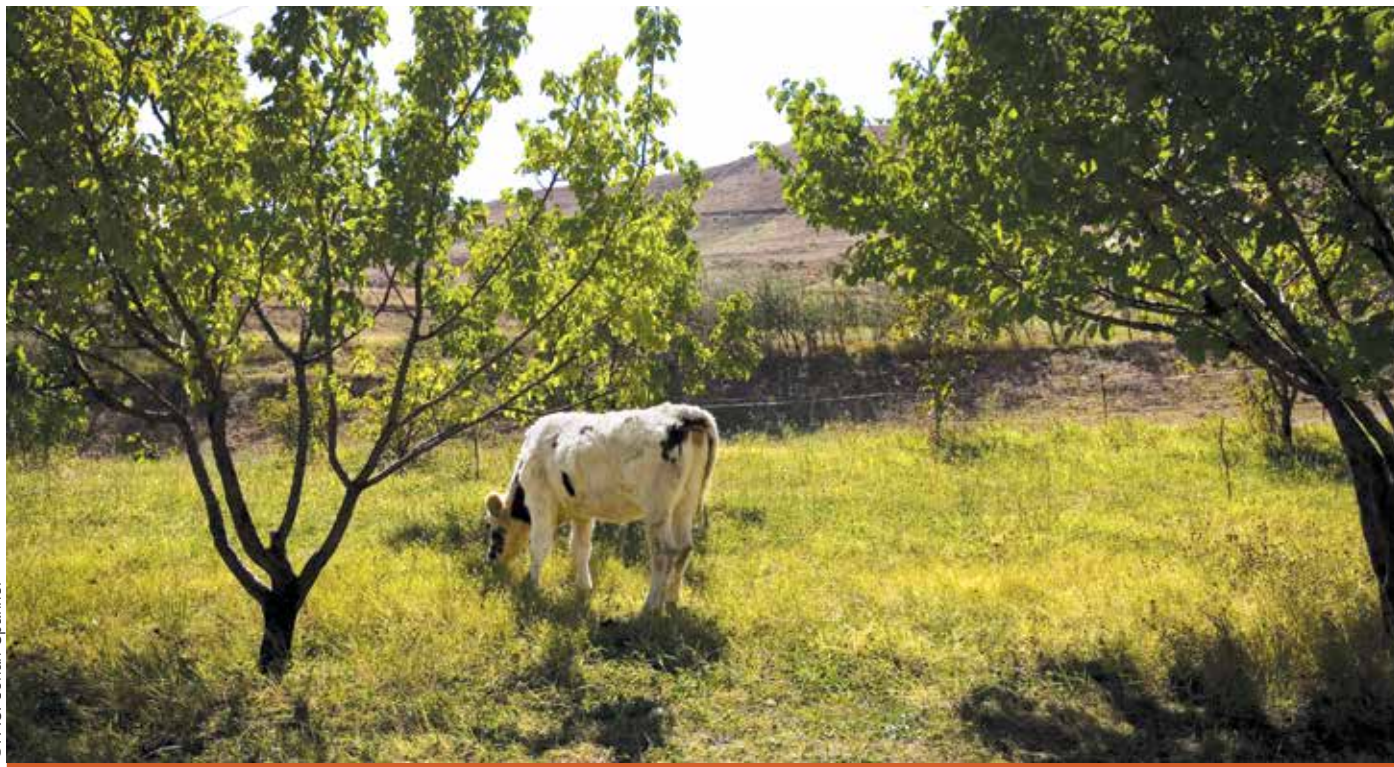
**Figure 1:** Annual Distribution of lumpy skin disease outbreaks by year in Eurasia overlaid by a cattle density map  
Source: EMPRES-i

<sup>1</sup> Food and Agriculture Organization of the United Nations (FAO)

<sup>2</sup> see [www.fao.org/docrep/019/aq706e/aq7063.pdf](http://www.fao.org/docrep/019/aq706e/aq7063.pdf)

<sup>3</sup> see: [www.fao.org/3/a-i5012.pdf](http://www.fao.org/3/a-i5012.pdf)





Farmers preparing to leave with their tractor to cut feed for their livestock

organized an ad-hoc meeting of LSD experts in Belgrade on 25 July 2016 to review current scientific evidence on prevention and control measures. The conclusions of the meeting, which took place can be downloaded.<sup>5</sup> FAO is also a member of the Standing Group of Experts on Lumpy Skin Disease in South-East Europe (SGE LSD),<sup>6</sup> which was launched on 4–5 July 2016 under GF-TADs to promote cooperation among countries affected by LSD.

### CURRENT ACTIVITIES WITH REGARD TO LSD

FAO is running three complementary projects on LSD assistance for the Balkans and the Caucasus. The initial workshop took place on 7–9 March 2017 in Budapest; the participating experts included representatives from the veterinary services of 12 countries and the beef and dairy cattle associations of three countries. The workshop enabled countries to share their experiences, improve their knowledge and discuss the most challenging issues through interactive thematic sessions moderated by experts that covered: i) contingency planning, risk management and communication; ii) awareness campaigns; iii) animal movement control; iv) insect control and environmental

effects; v) diagnostic tools and vaccination strategies; and vi) stamping out strategies.

A follow-up regional workshop was organized in Tirana on 10–11 May. The topics discussed during the workshop included cost-benefit analysis, vaccination strategies, contingency plans and risk communication. Representatives from cattle associations articulated their concerns and participated in discussions on how associations could coordinate with veterinary services and contribute to the prevention and control of LSD. The workshop also designed the framework and main activities for a future regional project on LSD prevention and control based on identified needs.

The project will include analytical work to assess the LSD situation and estimate the economic costs. Two major activities are: i) analysis of outbreak data in the Caucasus to assess the epidemiological situation, to understand patterns and risk factors and to identify possible pathways of disease spread by means of spatial analysis; and ii) an estimate of the direct and indirect financial losses resulting from LSD outbreaks, including a cost-benefit analysis of the main disease control options and, most importantly, the various vaccination and stamping-out approaches.

FAO released a *LSD field manual for veterinarians* for private and official field veterinarians, para-veterinary professionals and laboratory diagnosticians as a guide to the detection and diagnosis of LSD. The contents address basic epidemiology, clinical recognition, sampling and shipping of

specimens, and basic concepts for prevention and control. The manual has photographs and diagrams for practical application in the field. It is available in English, Albanian and Macedonian; it will soon be available in Russian, Serbian and Turkish.

FAO developed a contingency plan template for LSD to aid veterinary services in the development of their own national contingency plans specific to the country. This plan is a key instrument for preparedness and control of the disease.

In Georgia, FAO assisted the National Food Agency in developing a LSD contingency plan and in organizing two trainings; one for field veterinarians in February 2017 and one for laboratory diagnosticians on molecular diagnostics in March 2017. Awareness materials i.e. posters and leaflets were developed for field veterinarians and cattle farmers. In close collaboration with the veterinary authorities,

FAO is currently implementing a field training in the former Yugoslav Republic of Macedonia to improve field detection, prevention and control of LSD and bluetongue. The core trainers were trained in September. The training of trainer-approach will eventually reach approximately 250 veterinarians, both official and private, across all seven regions of the country. Each trainee will receive a copy of the LSD field manual in Macedonian.

All the above activities are in line with the recently published FAO position paper on the sustainable prevention, control and elimination of LSD in Eastern Europe and the Balkans. <sup>360</sup>

<sup>5</sup> [www.fao.org/fileadmin/user\\_upload/reu/europe/documents/Events2016/LSD/report\\_en.pdf](http://www.fao.org/fileadmin/user_upload/reu/europe/documents/Events2016/LSD/report_en.pdf)

<sup>6</sup> [http://web.oie.int/RR-Europe/eng/Regprog/en\\_GF\\_TADS%20-%20Standing%20Group%20LSD.htm](http://web.oie.int/RR-Europe/eng/Regprog/en_GF_TADS%20-%20Standing%20Group%20LSD.htm)

## TIMELINE 2012 – 2016

Year	Month of the start of the first outbreak	Locations
2006	January	LSD in Egypt
2006	July	LSD in Israel
2012	November	LSD in Lebanon
2012	July	LSD in Israel
2012	November	LSD in Lebanon
2013	February	LSD in West Bank
2013	April	LSD in Jordan
2013	August	LSD in Turkey and Iraq
2013	October	LSD in Egypt
2014	May	LSD in the Islamic Republic of Iran
2014	July	LSD in Azerbaijan
2014	November	LSD in Kuwait
2015	February	LSD in Saudi Arabia
2015	July	LSD in the Russian Federation
2015	August	LSD in Greece
2015	December	LSD in Armenia
2016	April	LSD in Bulgaria and the former Yugoslav Republic of Macedonia
2016	June	LSD in Serbia, Kosovo and Albania
2016	July	LSD in Kazakhstan and Montenegro
2016	November	LSD in Georgia

Source: WAHID



## NEWS

## Publications

AO published a field manual and a position paper on lumpy skin disease. The Animal Production and Health Manual 20 - **Lumpy Skin Disease (LSD) – A field manual for veterinarians** is available in English, Albanian, and Macedonian, and will soon be available in Russian, Serbian and Turkish. The manual aims to provide veterinary professionals and para-veterinary professionals with the information needed to promptly recognize, diagnose and respond to an outbreak of LSD. The manual will benefit livestock owners by improving LSD prevention and the biosecurity measures at livestock holdings. The Animal Production and Health Position Paper - **Sustainable prevention, control and elimination of lumpy skin disease - Eastern Europe and the Balkans**, discusses available options in further detail. Both publications are available online:

- **LSD field manual:** English, Albanian, Macedonian (Russian, Serbian, Turkish to follow) <http://www.fao.org/documents/card/en/c/1fcf63b0-80e9-4f8e-825f-10ea6e998479/>
- **LSD position paper:** English - <http://www.fao.org/3/a-i7827e.pdf>



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The Emergency Prevention System (EMPRES) is an FAO programme, founded in 1994, with the goal of enhancing world food security, fighting transboundary animal and plant pests and diseases and reducing the adverse impact of food safety threats. EMPRES-Animal Health is the component dealing with the prevention and control of transboundary animal diseases (TADs).

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