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Abstract: Schmallenberg virus (SBV) was first recognized in the late summer of 2011 when Germany and the Netherlands detected transient illness in adult cattle. Spread of SBV occurred within a few months. The discovery of SBV was unexpected and its spread was rapid and continues with over 3,000 reported infected premises in 9 affected countries.

Morbidity and mortality caused by SBV infection is relatively low and the Health Protection Agency in the United Kingdom has labeled SBV as a low-impact disease relative to all animal agriculture; however, to individual animal owners, the impact may be significant. SBV is not an OIE listed disease and the EU has not imposed movement, quarantine, or stamping-out requirements. There is no current vaccine or treatment for SBV. SBV is estimated to be non-zoonotic and there are no reported human cases.

The spread pattern of SBV is similar to bluetongue virus 8 (BTV8), suggesting that transmission occurred primarily through vectors, likely of *Culicoides* species. If SBV were introduced into the United States, spread would be rapid and difficult to control because cattle, sheep, and goats have no immunologic resistance.

A review of pathways by which SBV might be introduced into the United States indicates that existing regulations, control pathways, and recently enacted controls are sufficient to mitigate and greatly minimize the likelihood of introduction of SBV to the United States from live animals and animal products. Based on these factors, the likelihood of introduction of SBV to the United States via all pathways, including live animals, animal products, trade, or passenger traffic, is currently considered very low.

Keywords: ruminants, Schmallenberg virus, orthobunyavirus, deformities, midges, *Culicoides*

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ACRONYMS

Acronyms	Meaning
AHS	arthrogryposis hydranencephaly syndrome
APHIS	Animal and Plant Health Inspection Service
AQIM	Agriculture Quarantine Inspection Monitoring
BSE	bovine spongiform encephalopathy
BTV8	bluetongue virus 8
BVD	bovine viral diarrhea
CBP	Customs and Border Protection
CDC	Centers for Disease Control and Prevention
CFIA	Canadian Food Inspection Agency
EFSA	European Food Safety Authority
EHD	epizootic hemorrhagic disease
ELISA	enzyme-linked immunosorbent assay
EU	European Union
FLI	Friedrich-Loeffler-Institut (Germany)
FSIS	Food Safety and Inspection Service
GTA	Global Trade Atlas
OIE	World Organization for Animal Health
PCR	polymerase chain reaction
PPQ	Plant Protection and Quarantine
RNA	ribonucleic acid
rRT-PCR	real-time reverse transcription polymerase chain reaction
RT-qPCR	reverse transcription-quantitative polymerase chain reaction
SBV	Schmallenberg virus
USD	United States dollars
USDA	United States Department of Agriculture
VS	Veterinary Services

1. EXECUTIVE SUMMARY

The qualitative likelihood of importing the Schmallenberg virus (SBV) via all pathways including live animals, animal products, trade, or passenger traffic is very low. A review of possible pathways by which SBV might be introduced into the United States indicates that existing regulations, control pathways, and recently enacted controls—such as prohibition of germplasm import from the European Union (EU)—are sufficient to mitigate and greatly minimize the likelihood of the introduction of SBV into the United States.



The discovery of SBV in Europe was unexpected; its spread was rapid and continues with 4,712 reported infected premises as of June 8, 2012 in the 9 countries that are known to be affected. Clinical signs of the new disease were first recognized in the summer of 2011 when Germany and the Netherlands detected transient illness in adult cattle. By the end of 2011, stillbirths and deformities were recognized in lambs and kids. SBV was identified as a new virus in the orthobunyavirus group by the Fritz-Loeffler-Institut in November 2011.

Spread of the disease from Germany and the Netherlands to France, Luxembourg, Belgium, Italy, Spain, and the United Kingdom occurred within a few months. The pattern of spread was similar to bluetongue virus 8 (BTV8), suggesting that transmission occurred primarily through vectors, likely of the *Culicoides* species. The discovery of SBV in two species of European midges from Belgium supports transmission primarily via *Culicoides* vectors. Neither the exact *Culicoides* vector, nor clinical disease attributed to SBV, appears to be present in the United States although over 110 species of potentially competent *Culicoides* are present. Based on current literature, the possibility of dispersion of the European vectors over water by natural events, such as wind, are small. Assuming that cattle, sheep, and goats in the United States are immunologically naïve – and that North American *Culicoides* species are potential vectors – it can be estimated that if SBV were introduced into the United States spread would be rapid and exceptionally difficult to control.

Morbidity and mortality caused by SBV infection as estimated from World Organization for Animal Health (OIE) Weekly Disease Reports appear relatively low. The Health Protection Agency in the United Kingdom has labeled SBV as a low-impact disease relative to all animal agriculture. However, to individual animal owners, the impact may be significant. SBV is not an OIE listed disease and the European Commission (EC) has not imposed movement, quarantine or stamping-out requirements, as would be required if the disease were listed. There is no current vaccine or treatment for SBV; the only recommended control measure is to reduce exposure to vectors. SBV is thought to be non-zoonotic; there are no reported human cases despite presumed close contact of farmers in Europe with infected or diseased animals. SBV is not known to be carried by pet dogs and cats; thus, the risk of introducing SBV into the United States via humans or pet dogs and cats is estimated to be very low.

2. BACKGROUND

In Germany and the Netherlands, beginning in about August 2011, adult cattle were detected with clinical signs that included mild to moderate fever, reduced milk yield, loss of appetite, loss of body condition, and diarrhea. Tests conducted by the Friedrich-Loeffler-Institut (FLI) in Germany initially ruled out common pathogens [3]. Metagenomic analyses on blood samples from affected cattle indicated the presence of a novel orthobunyavirus previously undetected in Europe and provisionally named Schmallenberg virus (SBV) after the small town in Germany where the first positive samples from cows showing clinical signs of the previously unrecognized disease were detected using stored serum. This new virus appears to be an orthobunyavirus related to Shamonda viruses of the Simbu serogroup. The Simbu serogroup includes Akabane, Aino, and Shamonda viruses, which are known pathogens of ruminants and which are predominantly spread through biting midges of the *Culicoides* species [2]. In December 2011, abortions and stillbirths, accompanied by fetal abnormalities in sheep and goats, were also attributed to the newly identified SBV [3]. SBV is not known to exist in the United States, and could present both an animal health and economic threat to United States cattle, sheep, and goat industries and perhaps to ruminant wildlife. SBV does not appear to affect humans [4].

3. METHODOLOGY

3.1. Risk assessment methods

This assessment is qualitative and categorizes likelihoods using the terms and definitions defined in Table 1. This assessment evaluates the best information available prior to publication recognizing that as an emerging disease available peer-reviewed literature is limited.

Table 1. Likelihood Assessment Terms and Definitions [5]

Term	Definition
Negligible	So rare it does not merit consideration
Very Low	Very rare but cannot be excluded
Low	Rare but does occur
Medium	Occurs regularly
High	Occurs very often
Very High	Events occur almost certainly

3.2. Data collection and limitations

SBV has only recently appeared and the etiology of the resulting syndrome is not yet fully characterized. There are few published journal articles and much information remains hypothesized or incompletely documented. Information used in constructing this pathways assessment comes from information published by reputable institutes on the Internet. The availability of more detailed information in the future could alter the likelihood estimates of risk presented in this preliminary pathways assessment.

4. HAZARD IDENTIFICATION AND CHARACTERISTICS

4.1. Identification

SBV is known to occur in Europe in cattle, sheep, goats [6] and one American bison (*Bison bison*) located in Germany [7] and more recently, deer and roe deer[8]. There is no information concerning the susceptibility of non-domestic ruminants to SBV, but other viruses of the Simbu serogroup are known to affect exotic and domesticated ruminants. Antibodies to Akabane virus (closely related to SBV), have been found in horses, donkeys, buffalo, deer, camels and pigs. Mermet, Peaton, and Oropouche viruses of the Simbu serogroup have been detected in birds and mice, and hamsters can be experimentally infected [6].

The phylogenetic tree (Figure 1) shows that the S segment sequence is distinct but clusters closely with Shamonda Viruses within the Simbu serogroup, which suggests that the novel virus is a shamanda-like virus with the genus *Orthobunyavirus*.

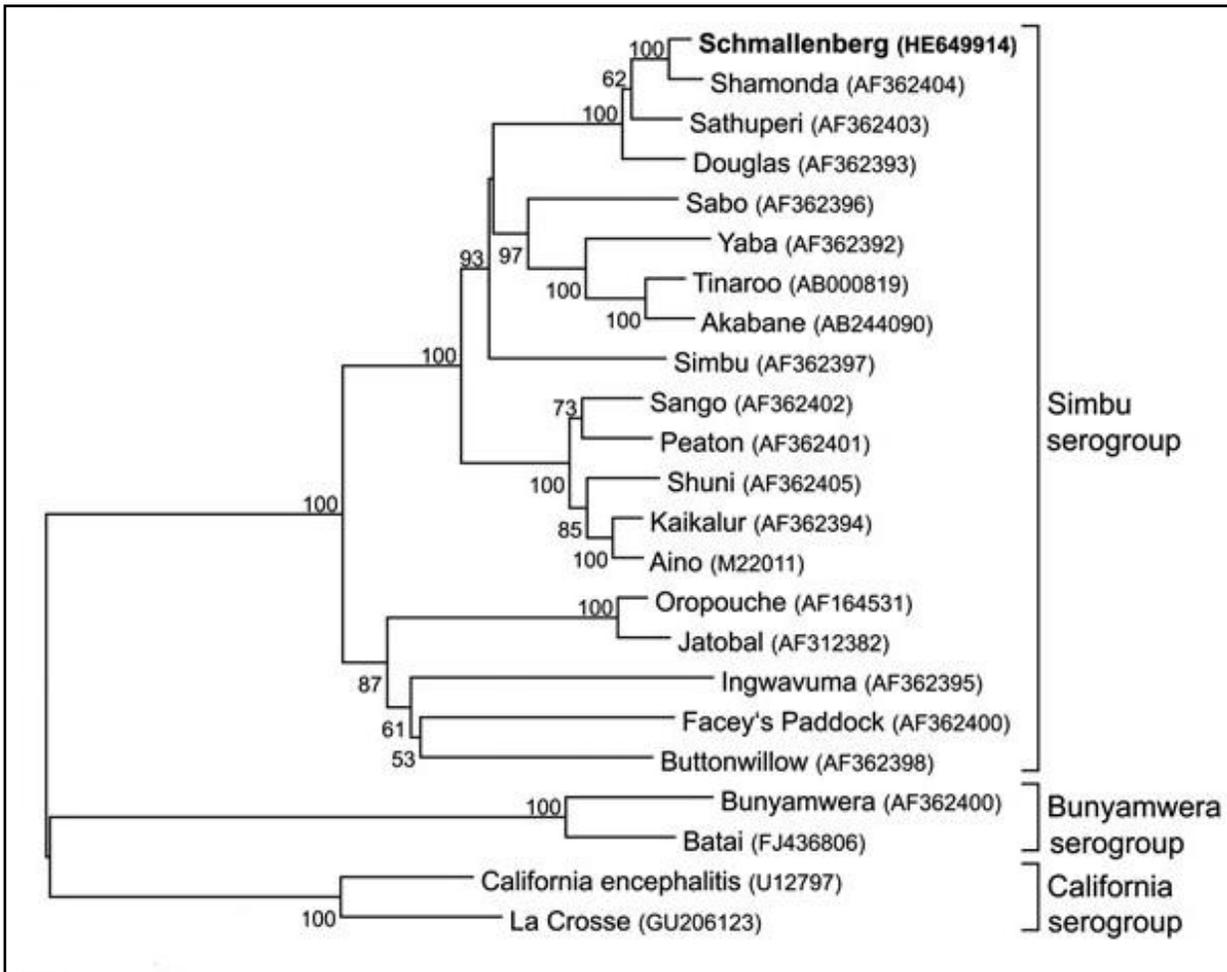


Figure 1. The phylogenetic relationship of SBV to orthobunyaviruses of the Simbu, Bunyamwera, and California serogroups[2].

4.2. Characteristics

In adult cattle SBV infection may be clinically inapparent; but, when recognized, the acute phase is characterized by fever ($>40\text{ }^{\circ}\text{C}/104\text{ }^{\circ}\text{F}$), impaired general condition, anorexia, reduced milk yield (by up to 50%) and diarrhea. Individual animals recover within a few days and herds within 2 to 3 weeks. Clinical signs have not been reported in adult sheep, goats, or the single bison. Fetal malformations associated with late-term stillbirths and abortions of lambs and kids have been attributed to SBV infection of immunologically naïve dams during early gestation. Malformations in stillborn lambs and kids (such as arthrogryposis, hydrocephaly, brachygnathia inferior, ankylosis, torticollis, or scoliosis) are not pathognomonic for SBV[9]. Malformed live newborns often display hydranencephaly, hypoplasia of the central nervous system, porencephaly, and subcutaneous edema[10].



Human disease attributed to SBV infection has not been reported in the affected countries[11]. The closest orthobunyaviruses related to SBV do not cause disease in humans; however, more distantly related orthobunyaviruses, such as Oropouche and Iquitos viruses, are zoonotic and therefore the ability of SBV to cause human disease cannot be entirely excluded. A risk assessment prepared by the Netherlands' National Institute of Public Health and the Environment in December 2011 concluded that the virus is unlikely to cause disease in humans[4].

4.3. Case definitions

In the United States, case definitions for SBV have been published in a USDA APHIS document entitled "Schmallenberg Virus Disease Information, Case Definition and Guidance"[12]. These definitions are modified from those used in Europe, which vary slightly by Member State and are published by the European Food Safety Authority [13]. The OIE has not published SBV case definitions.

In the United States, official case definitions vary by age and disease status:

In fetuses and neonates

- **Suspect case:** Susceptible species with clinical signs consistent with SBV infection.
- **Confirmed case:** Confirmation of viral infection in a suspect case by a real-time reverse transcription polymerase chain reaction (rRT-PCR), virus isolation, or other method of SBV antigen detection.

In adult animals with past exposure to SBV

- **Suspect case:** Ruminants or other susceptible species with pregnancies terminating in abortions, stillbirths, and congenital malformations in offspring characteristic of arthrogryposis hydranencephaly syndrome (AHS).

- **Confirmed case:** Confirmation of SBV antibodies by enzyme-linked immunosorbent assay (ELISA) or other method of detection in herds with confirmed cases of SBV by antigen detection.

In adult animals acutely infected

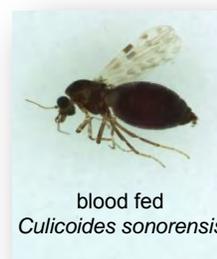
- **Suspect case:** Susceptible species (especially cattle) exhibiting clinical signs consistent with SBV infection.
- **Confirmed case:** Confirmation of viral infection in a suspect case by rRT-PCR, virus isolation, or other method of SBV antigen detection.

For flocks or herds:

- Any flock/herd with one or more animals confirmed with SBV infection per case definitions above.

4.4. Transmission

Information is currently being collected for transmission and epidemiologic studies in Europe [13]. Direct animal-to-animal transmission has not been demonstrated and is not suspected [6]. The presence of SBV in two species of midges has been documented [14], and vertical transmission across the placenta is reported in OIE documents to occur but without reference to species [6]. Recently published information specifically suggests that SBV crosses the placenta in cattle [15].



4.4.1. Vectors

The spread of SBV was originally noted to follow the geographical pattern of BTV8 as it spread throughout the EU [16]. BTV8 is known to be transmitted by biting midges of various species [17]. Similarly, other orthobunyaviruses, such as Akabane virus, are also spread by *Culicoides* species, so it was suspected that SBV was vector-borne. Midges trapped in Belgium during September and October 2011 have recently been analyzed. SBV was detected in the heads of midges identified as *C. obsoletus* and *C. dewulfi*. Detection in the heads of the midges suggests that they are amplification vectors and that the insects have not just tested positive subsequent to a blood meal on viremic animals [14].

4.4.2. Vertical transmission

Vertical transmission with the pathogen crossing the placenta from the dam to the fetus is reported by the OIE without reference to species [6], however, a recent study suggests placental transfer specifically in cattle [15].

4.5. Diagnosis

4.5.1. Differential diagnosis

In adult cattle, acute infection is characterized by fever ($>40\text{ }^{\circ}\text{C}/104\text{ }^{\circ}\text{F}$), impaired general condition, anorexia, reduced milk yield (by up to 50%), diarrhea and recovery within a few days for individuals and two to three weeks for herds[6]. The clinical signs of SBV infection are not pathognomonic, but are shared among many diseases, including bluetongue, epizootic hemorrhagic disease (EHD), foot-and-mouth disease, bovine viral diarrhea (BVD), border disease (and diseases caused by other pestiviruses), infection with bovine herpesvirus 1, and other herpesviruses, Rift Valley fever, bovine ephemeral fever, and the effects of toxic substances[6].

Malformations in newborn or stillborn lambs and kids are also not pathognomonic for SBV. Malformations include arthrogryposis, hydrocephaly, brachygnathia inferior, ankylosis, torticollis, and scoliosis. Similar sets of signs can be caused by toxic substances, genetic factors, bluetongue virus, pestiviruses, and other viruses of the Simbu serogroup, such as Akabane virus[6]. The lack of specificity of observed clinical signs in infected adults, stillborn fetuses, and malformed neonates means that a definitive diagnosis of SBV can only be made based on clinical signs in conjunction with appropriate laboratory tests[12].

4.5.2. Laboratory diagnosis

Confirmed laboratory tests for SBV originally consisted of rRT-PCR and cell culture for isolation of the virus from tissue brain samples including cerebrum and cerebellum[18]. Serologic tests by immunofluorescence and serum neutralization[6] are used for detection of SBV in serum samples from live animals. In a recent development, the Animal Health Laboratory located in Maisons-Alfort, France released an indirect ELISA test, which is based on recombinant SBV nucleoprotein antigen. Independent studies calculate the new test's specificity to be 99.75 percent, and 98.9 percent correlation with other serological techniques[19].

4.6. Geographical distribution of affected premises

SBV infections have been reported in Germany, Netherlands, Belgium, United Kingdom, France, Italy, Luxembourg, Spain, and Denmark[20]. As of June 8, 2012, the total number of infected premises is 4,712 (Figure 2)[1].

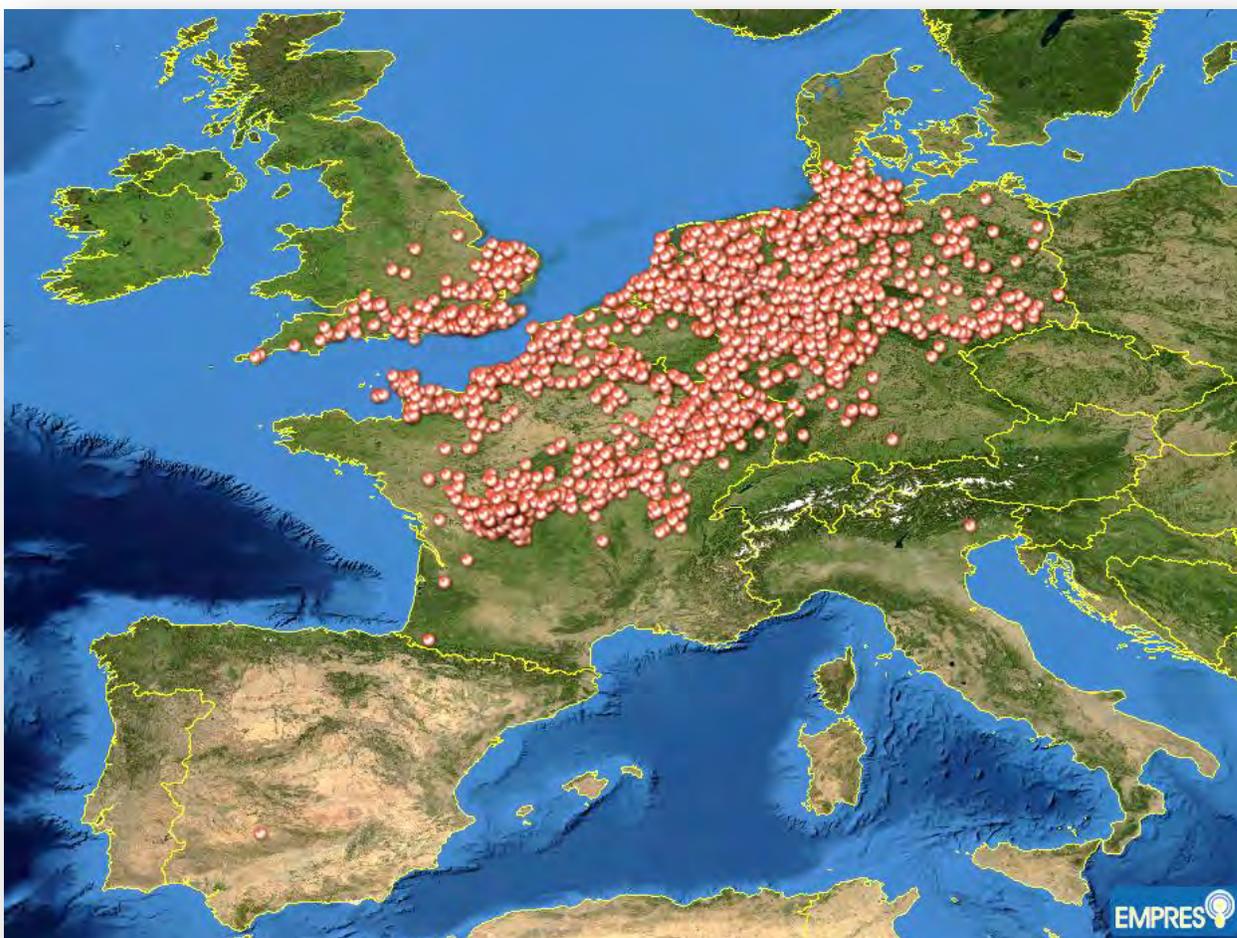


Figure 2. Location of SBV-infected premises

June 8, 2012 Map used with acknowledgment: GvdH/Flutrackers.com[1]

4.7. Control

There is no specific treatment or vaccine for SBV infection. A vaccine is reported to be in development [21]. Protection of susceptible animals from biting midges is the best possible mitigation for reducing exposure or infection[6].

4.8. OIE status

SBV is not a notifiable disease according to OIE[22]. However, it is notifiable as an emerging disease with significant morbidity or mortality or zoonotic potential, as described in Article 1.1.3.1.e of the OIE Terrestrial Animal Health Code[23]. The OIE has not recommended movement, containment, or control restrictions based on the presence of SBV[10]. See Appendix A for the OIE Technical Factsheet (dated May 2012).

5. PATHWAYS ASSESSMENT

The following narrative describes the potential pathways by which SBV could be released from a country currently affected, introduced into the United States, and expose susceptible animals.

5.1. Live domestic animals

5.1.1. Release pathway

The European countries currently affected with SBV are also those considered by APHIS to be affected with bovine spongiform encephalopathy (BSE). Due to existing restrictions for live ruminants originating from countries APHIS considers affected with BSE, live animals of the affected species and their derivative products are “not permitted to be imported into the United States” by title 9, *Code of Federal Regulations*, parts 93 and 94[24]. The countries affected by these restrictions are those currently within the EU, or those that follow EU legislation and allow unrestricted movement of live animals within the EU. These countries include: Austria, Belgium, Bulgaria, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, and United Kingdom (including its Crown Dependencies). However, although other restrictions and certifications may apply, APHIS does not prohibit the importation of germplasm (semen and embryos) from ruminant species with respect to BSE.

Inspection of trade data in the Global Trade Atlas further indicates that no live ruminants are imported into the United States from the EU[25]. This effectively demonstrates lack of introduction of any live ruminants from the affected countries and from EU countries in which SBV may exist but is not yet reported.

APHIS recently published a proposed rule that, if implemented, would facilitate the importation of live ruminant species from some European countries that might qualify in the future as negligible or controlled risk for BSE. This rule is not factored into this pathways analysis.

5.1.2. Exposure pathway

In the nine European countries that have reported the presence of SBV, affected animals are reported to be domestic cattle, goats, sheep[6], one American bison (*Bison bison*) located on a farm in Germany [7] and more recently, deer and roe deer[8].

Domestic ruminants in the United States are of similar species and bear genetic similarity to European domestic ruminants; thus, similar species in the United States are likely to be infected with SBV, should it be introduced.

If live SBV-infected domestic ruminants were imported and released into the United States, the possibility of direct transmission from animal-to-animal cannot be ruled out, but it is considered very unlikely and needs further investigation according to the OIE[6]. If SBV were able to be transmitted by competent domestic midge species, and if they fed on imported viremic animals,

sustainable transmission might occur because of the presence of midge species known to transmit bluetongue virus[17].

The qualitative likelihood of the entry or release of SBV into the United States via legal importation of foreign-origin live domestic animals with subsequent exposure of U.S. domestic animals is characterized as very low.

5.2. Live exotic ruminants and other species pathways

5.2.1. Release pathway

No open-source reports of SBV occurring in non-domestic ruminants, or any other species, have been discovered as of April 30, 2012. Importation of wildlife is highly restricted by the title 50, *Code of Federal Regulations*, part 14[26] and requires permits from one or all of the following: U.S. Fish and Wildlife Services[27], the Centers for Disease Control and Prevention, and USDA:APHIS:Veterinary Services[27].

5.2.2. Exposure pathways

The OIE provides no information on the susceptibility of exotic ruminants such as camelids and llamas, or other non-domestic ruminants, to SBV[6]. Related viruses of the Simbu serogroup are known to affect non-domestic ruminants, and antibodies to Akabane virus have been found in horses, donkeys, buffalo, deer, camels, and pigs. Some Simbu serogroup viruses (Mermet, Peaton and Oropouche viruses) have been detected in birds, and mice and hamsters can be infected experimentally[6].

The likelihood of the entry (or release) of SBV into the United States via importation of foreign non-domestic ruminants or foreign exotic animals with subsequent exposure of domestic exotic or domestic ruminant animals is characterized as very low.

5.3. Semen release pathway

According to the OIE, the viremic period in SBV-infected animals appears very short, and the OIE recommends that semen should only be collected from clinically healthy animals[6]. In one study of eight bulls experimentally infected with Akabane virus, virus was not detected in semen during the viremic period[28]. For other vector-borne diseases, such as bluetongue virus, transmission via semen collected from viremic animals is possible. The OIE recommends that mitigations for bluetongue virus, when applied to SBV, should provide sufficient assurance of safety for semen regarding SBV, because the infective period of SBV is shorter than that of bluetongue virus[10].

5.4. Embryos release pathway

The OIE states that the viremic period for SBV in adult animals is very short and that embryos should be collected from clinically healthy animals. SBV affects embryos and fetuses in a manner similar to that of Akabane virus, so safety measures applicable to Akabane virus should be implemented. Risk from seronegative donor animals is negligible. Animals should be seronegative for 21 days after the collection[10].

5.5. Exposure pathway for semen and embryos

Because the risk pathways for semen and embryos may be similar to those of Akabane virus and bluetongue virus, shipments of bovine germplasm collected in EU countries after June 1, 2011, are no longer eligible for importation into the United States. Consignments of bovine germplasm from the EU must additionally include a statement on the official export health certificate that they were collected prior to June 1, 2011 or that they were collected in vector-proof facilities from animals that have tested negative to approved tests. Sheep and goat semen protocols are being negotiated with the EU and are being revised to include restrictions for SBV. Other APHIS import requirements continue with no change. Cervid and camelid germplasm shipments are not affected by these additional restrictions for SBV[29].

5.6. Live animal pathway summary

Importation of known affected species of live domestic ruminants (except for cervids and camelids) from the nine EU countries in which SBV has been reported is currently prohibited because of previous import restrictions designed to prevent BSE from entering the United States. Exotic ruminants have not been reported as susceptible to SBV, but many such species are currently prohibited under APHIS restrictions for BSE; thus, it currently appears unlikely that SBV could be introduced to the United States via infected live exotic ruminants from any source. The likelihood of importing live infected domestic ruminants from Europe is characterized as low. Given the current restrictions on the import of bovine germplasm, the likelihood of importing SBV to the United States via importation of ruminant semen or embryos is characterized as very low.

6. ANIMAL PRODUCT PATHWAYS

6.1. Food pathways

6.1.1. Release pathways for food

Food imports of greater than 50 pounds are regulated and permits are issued by USDA Food Safety and Inspection Service (FSIS) as required by title 9, *Code of Federal Regulations*, part 327[30, 31]. Smaller amounts are inspected by Plant Protection and Quarantine (PPQ) Port Veterinary Medical Officers and/or Customs and Border Protection officers at the port of entry and are confiscated and safely destroyed when not in compliance with published regulations and issued permits[32].

6.1.2. Exposure pathways for food

Regardless of the amount of food imported, abundant and specific regulations concerning the types and amounts of food that are or are not permissible apply[33]. In all cases, untreated ruminant meat and products that convey significant risk of either human or animal disease are highly regulated. Items which might pose a risk of human or animal disease are confiscated, denatured, and destroyed at specific facilities designed to mitigate any risk[32]. Further, the OIE states that the risk of SBV transmission through meat or milk is negligible[10].

The likelihood of introducing SBV via imported food is characterized as very low.

6.2. Animal products release pathways summary

All animal products, including food, biologics, and other products are required by various regulatory agencies to be treated to mitigate the possible entry of human and animal pathogens. These treatments are designed to inactivate the worst-case (hardest-to-kill) pathogens and are likely to be highly effective in mitigating any risk of importing SBV in food or animal products. Confiscated illegal or non-conforming products are destroyed in strict chain-of-custody procedures and in special containment vessels to greatly minimize any threat of pathogen release[34]. Restrictions have not been placed by APHIS on any ruminant products or byproducts except germplasm[29]. Resistance of SBV to physical and chemical treatments was extrapolated from the California serogroup of orthobunyavirus and published by the OIE[6]. SBV infectivity is estimated to be lost or significantly reduced by exposure to 50 to 60 °C for at least 30 minutes. SBV is also estimated to be susceptible to common disinfectants, such as 1% sodium hypochlorite, 2% glutaraldehyde, 70% ethanol, and formaldehyde. Outside the host, the virus does not survive for long periods (n.b., long period not defined by OIE)[6].

The likelihood of introducing SBV into the United States via any type of animal product (except frozen skins and hides from Mexico, as discussed below) is characterized as very low.

7. OTHER ANIMAL PRODUCTS PATHWAYS (TRADE WITH EUROPE, MEXICO, AND CANADA)

7.1. United States imports of animal products from Europe

According to the Global Trade Atlas, during the period from June 1, 2011 to January 31, 2012, approximately \$6.5 billion United States dollars' (USD) worth of ruminant-derived animal products were imported from the EU to the United States[25]. Examples of these products include meat, fats, blood, hides and skins, and animal hair. If unregulated, these items could pose some risk of importing SBV; however, these items are highly regulated and importation requires treatments sufficient to prevent the entry of BSE, which are likely sufficient to also prevent entry of SBV into the United States[35].

7.2. Canada's ruminant and animal products imported from the EU

From June 1, 2011 to January 31, 2012, Canada imported \$672.5 million USD worth of ruminant-derived animal products from the EU[25]. The Canadian Food Inspection Agency regulates and issues permits for importation of live ruminants and animal products that originate in areas with controlled BSE risk in accordance with OIE standards[36]. Canada has further imposed a specific SBV import testing requirement for the animals from which semen is permitted to be imported into Canada including cattle, bison, water buffalo, sheep and goats and for cattle and bison from which embryos are derived [37]. These regulations reflect international standards and are sufficient to substantially mitigate the import of SBV-infected material into Canada where it could possibly be exported into the United States.

7.3. Import data for live ruminants and animal products imported from Canada into the United States

From June 2, 2011 to January 31, 2012, United States imported about \$397 million USD worth of ruminant-derived animal products from Canada[25], some of which may have originated in the EU. Live bovine animals from Canada are permitted entry to the United States, and non-pregnant sheep and goats under the age of 12 months may enter as feeders for slaughter, or for immediate slaughter[38]. It may not be possible in all cases to determine the actual origin of these animals and materials; however, imports from Canada are regulated by the title 9, *Code of Federal Regulations*, parts 93.417 through 93.421, and 93.435 and 93.436 [39], which account for differences in United States and Canadian ruminant import regulations[29]. Factors such as the estimated short viremic period for SBV (2-3 days)[10] coupled with USDA import requirements are likely to substantially mitigate the risk of introducing SBV into the United States via animals or animal products previously imported from the EU then re-exported to the United States[40].

7.4. Mexico's imports of ruminants and animal products from the EU

From June 1, 2011, to December 31, 2011, Mexico imported about \$322 million USD worth of animal products, and about \$6.7 million USD worth of animals from the EU[25]. Mexico's import trade data is not available for evaluation because Mexico no longer publishes the breakdown of imports and exports into subcategories[25]; thus, the risk of importing SBV into Mexico via live ruminants or animal products cannot be estimated

7.5. United States imports of animals and animal products from Mexico

Trade with Mexico includes live ruminant animals and ruminant derived products, of which some may have originated in the EU. Imports of live animals from Mexico are regulated by title 9, *Code of Federal Regulations*, part 93.424 through 93.429[41]. Fresh ruminant hides or skins are also allowed and are required to be treated with acaricide or to have been frozen for 24 hours[42]. Freezing is not a treatment listed in the OIE Technical Fact Sheet on SBV as effective against near-relatives of SBV (extrapolated from the California group of orthobunyaviruses)[6]. It is stated by the OIE[6] that live SBV is not likely to survive in the environment for "long periods," but the period is not explicitly stated by OIE. Because the value of animals and animal products imported from the EU to Mexico is no longer available, it is not possible to estimate the risk of introducing SBV into the United States via Mexican exports previously imported from the EU.

7.6. Summary of imported animal products pathways

Import of animal products from the EU, Canada, and Mexico is controlled by permits from the USDA:APHIS:Veterinary Services[38], as well as USDA's FSIS[30]. Before entering the United States, specified treatments are required and are designed to exclude significant pathogenic agents. USDA's PPQ service further inspects and fumigates vehicles and containers arriving at U.S. ports according to procedures specified in their Agricultural Quarantine and Inspection Monitoring Handbook[43]. The qualitative import risk of importing SBV from Canada or Mexico

via any type of animal or animal product, except frozen skins and hides from Mexico, can be characterized as very low. The origin of skins and hides from Mexico cannot be known with certainty, and they are not treated by a method known or suggested sufficient to inactivate SBV; thus, the risk of introducing SBV into the United States via frozen imported skins and hides from Mexico cannot be estimated.

8. ZOOONOTIC POTENTIAL AND PASSENGER TRAFFIC

8.1. Zoonotic potential

SBV has not been implicated in human disease[4] [11]. Shamonda, Aino, and Akabane viruses, which are most closely related to the SBV, are pathogenic only in livestock. Viruses within other serogroups of the genus Orthobunyavirus are zoonotic, including California encephalitis virus, La Crosse encephalitis virus, Tahyna virus, Bataivirus, Inkoovirus, and snowshoe hare virus. Oropouche virus, similar to SBV, is a member of the Simbu serogroup and can cause febrile disease in humans accompanied by headache, dizziness, photophobia, skin rash, myalgia, arthralgia, and malaise. Iquitos virus causes illness in humans that includes fever, general malaise, headache, retro-orbital pain, myalgia, arthralgia and chills[4]. There have been no reports of unusual human illness from the regions where SBV has been identified [4]. The veterinary health service of the Netherlands indicates that farmers from affected farms have been specifically asked for symptoms of illness, and none have been reported. Based on these findings, zoonotic transmission of SBV cannot be excluded but is considered unlikely.

8.2. EU-Mexico-Canada passenger traffic

During 2011 (latest available report), which includes the time from June 2011 to December 2011 that SBV was being actively spread, 11,986,795 passengers arrived in the United States from Western Europe[44]. Available information that humans[4] are not susceptible to SBV and dogs and cats have not been reported susceptible to SBV infection. Thus neither human passengers, nor accompanying dogs and cats, whose travel originated in the EU are likely to have exposure of SBV.

In the same period, 21,028,177 visitors arrived from Canada and 13,414,020 from Mexico[44]. In total, about 46.5 million visitors, with unknown travel and SBV exposure, arrived in the United States. SBV is not known to be zoonotic or carried by pet dogs and cats; thus, the risk of introducing SBV into the United States via humans or pet dogs and cats is estimated to be very low.

9. EUROPEAN VECTORS OF SBV

9.1. Identity of potential European vectors

SBV is related to a group of orthobunyaviruses found mainly in Asia, Africa, and Australia. The genetic sequence most closely resembles that of Shamonda, Akabane, and Aino viruses. Shamonda, Aino, and Akabane viruses are primarily transmitted by *Culicoides* spp.[45]. In

Australia, Akabane virus is transmitted by the same *Culicoides* species that transmits bluetongue virus, *C. brevitarsis*[46]. In Southern Europe, bluetongue virus is transmitted by *C. imicola* and *C. dewulfi*. *C. obsoletus*, *C. scoticus*, and *C. chiopterus* are involved in the transmission of bluetongue in Northern Europe, including the Netherlands[47]. Recently, the SBV has been detected using RT-qPCR in Belgium in the heads of two *Culicoides* species: *C. obsoletus* and *C. dewulfi*. These two species are common vectors of bluetongue in Belgium[14].

9.2. Worldwide distribution of *Culicoides* species and BTv8 as a model of transmission

There are more than 1,400 species of *Culicoides* distributed around the world. These biting midges feed primarily on mammals, but also on birds, amphibians, and reptiles. They transmit more than 35 types of arboviruses to domestic animals, including African horse sickness, bovine ephemeral fever, Akabane virus, and bluetongue virus. Bluetongue virus is present in many countries of the world, including North America, parts of South and Central America, Southeast Asia, Europe, the Middle East, Africa, and Australia. There are about 30 *Culicoides* species implicated in the transmission of bluetongue virus. *C. insignis* is a vector of the bluetongue virus in South America, *C. brevitarsis* in Australia, *C. fulvus* in Asia, and *C. imicola* is the main vector of bluetongue virus and African horse sickness in Southern Europe [48] [47] [49] [50].

9.3. Discussion of *Culicoides* in the United States

The major vectors of bluetongue virus in the United States are the biting midges *C. sonorensis*, *C. occidentalis*, and *C. insignis* [17]. Bluetongue virus occurs primarily in the southern United States where *Culicoides* species are widespread. The majority of recent studies indicate that *C. sonorensis* is the primary vector of bluetongue virus in the United States[51] [52]. The peak season for bluetongue infection is midsummer to early fall. There are 24 bluetongue serotypes with 5 (serotypes 2, 10, 11, 13, and 17) currently present in the United States. In the absence of competent vector populations, animal-to-animal transmission of bluetongue is not sustainable[51] [53] [48].



9.4. Natural dispersion and vector mitigation factors

In a 2011 analysis of *Culicoides* dispersal[54] that might have influenced the spread of bluetongue virus in 2006, 54 percent of outbreaks occurred through (presumably midge) movement of infections over distances of no more than 5 km; 92 percent of outbreaks occurred over distances of no more than 31 km; and only 2 percent over distances greater than 31 km. This suggests that high-frequency, long-distance, single-jump infections are unlikely. Apparent long-distance infections more likely resulted from sequential short-range infections, much like a stepping-stone effect. Downwind movement is responsible for only 39 percent of all infections, and highlights the contribution to disease spread of upwind midge movement, which accounted for 38 percent of all infections. Initially, low midge flight speed is reduced nearly to zero with

upwind movement because modeled wind speeds were usually greater than midge flight speed. The shortest distance between Europe and the United States is 6,420 km over water. It appears unlikely that infected midges could either fly or be blown to the United States. Moreover, the importation of *Culicoides* species via cargo containing plant material, or as hitchhikers on live animals are small due to specific life cycle requirements of midges such as a certain amount of water and organic material required for larval survivability.

9.5. Likelihood of introduction of potential European vectors of SBV into the United States

The likelihood that European *Culicoides* vectors could fly or be wind driven to North America and cause introduction of European *Culicoides* vectors of SBV into the United States is very low because of the great uninterrupted distance over water and demonstrated predominance of “short-jump” infections of less than 5km attributed to the limited flight range of *Culicoides* vectors.

10. DIRECT SBV IMPORTATION (LIVE VIRUS AND REAGENTS), PERMITS, AND CONTAINMENT

After the discovery of SBV, the FLI received numerous requests for samples of the virus. FLI stated that it will not file patents, or other related applications, which would delay or impair disclosure of information; and that it will freely distribute samples of the virus, the protocol for genome detection, and sequence information on the viral genome to serious researchers. FLI considers requests for reagents to be used for non-commercial (research) and commercial purposes that respect their material transfer agreement[55]. SBV is not currently listed on the United States National Select Agent Registry (although the closely related Akabane virus is currently listed as a Select Agent)[56]. For importation to the United States, if a material is suspected or known to contain etiologic agents or has not been tested for etiologic agents, a CDC Etiologic Agent Import Permit may be required[57]. Further, USDA:APHIS:VS regulates the import of all animal-origin materials that could represent a disease risk to U.S. livestock, and the import and transport of infectious organisms and vectors of disease agents. This includes not only animal products and byproducts, but biological materials that contain, or have been in contact with, certain organisms and animal materials (including cell cultures)[38]. The Food and Drug Administration also regulates imported vaccines, blood, and biologics that, although primarily for human use, may contain ingredients of animal origin[58]. Tightly regulated import of agents, serums, drugs, and biologics greatly diminishes the likelihood of importing SBV via one of these products. The likelihood of importing SBV via legally imported live viruses, or legal serums and biologics, can logically be characterized as very low.

11. SUMMARY

The discovery of SBV in Europe was unexpected and its spread was rapid, and continues with over 4,000 reported infected premises in the 9 affected countries. Clinical signs of the new disease were first recognized in Germany and the Netherlands as transient illness in adult cattle; but secondarily, stillbirths and deformities similar to those caused by Akabane virus were

recognized in lambs and kids. SBV was tentatively identified as a new virus in the orthobunyavirus group by the FLI in November 2011. Spread of the disease from Germany and the Netherlands to France, Luxembourg, Belgium, Italy, Spain, the United Kingdom and Denmark occurred within a few months. The pattern of spread was similar to BTV8, indicating that spread occurred primarily through vectors, likely of *Culicoides* species. The discovery of SBV in two species of European midges from Belgium appears to support transmission primarily via *Culicoides* vectors. Neither the currently identified *Culicoides* vectors, nor clinical disease attributed to SBV, appear to be present in the United States.

Based on current literature, the possibility of dispersion of the European vectors over water by natural events such as wind is small. Assuming that cattle, sheep, and goats in the United States are immunologically naïve, and that some North American *Culicoides* species are competent vectors (i.e. *Culicoides sonorensis*), if SBV were introduced to the United States, spread would be rapid and exceptionally difficult to control. Morbidity and mortality caused by SBV infection, as estimated from OIE Weekly Disease Reports[59], appear relatively low and the Health Protection Agency in the United Kingdom has labeled SBV as a low-impact disease[60] relative to all animal agriculture; however, to individual animal owners, the impact may be significant. SBV is not an OIE listed disease and the EC has not imposed movement, quarantine, or stamping-out requirements as would be required if the disease were listed. There is no current vaccine or treatment for SBV, and the only recommended control measure is to reduce exposure to vectors. A review of possible pathways that SBV might be introduced—coupled with a study of currently applicable live-animal and animal-product import regulations—indicates that existing regulations, control pathways, and recently enacted controls (such as prohibition of germplasm import from the EU) are likely sufficient to mitigate the introduction of SBV into the United States from live animals or animal products. SBV is believed to be non-zoonotic and there are no reported human cases. The overall likelihood of importing SBV via all pathways discussed, based on the best information available, is very low.



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APPENDIX A. OIE TECHNICAL FACTSHEET FOR SBVURL: http://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/A_Schmallenberg_virus.pdf**OIE TECHNICAL FACTSHEET****SCHMALLEMBERG VIRUS**[Aetiology](#) | [Epidemiology](#) | [Diagnosis](#) | [Prevention and Control](#) | [References](#)

Schmallenberg virus was discovered in November 2011 and epidemiological, immunological and virological investigations are on-going in several European countries. The information presented in this technical factsheet reflects the epidemiological observations and research done to date (May 2012), together with data extrapolated from genetically similar viruses of the same genus and serogroup.

AETIOLOGY**Classification of the causative agent**

The "Schmallenberg virus" is an enveloped, negative-sense, segmented, single-stranded RNA virus. It belongs to the *Bunyaviridae* family, within the *Orthobunyavirus* genus. The Schmallenberg virus is a member of the Simbu serogroup viruses, which includes Shamonda, Akabane, and Aino viruses.

Field and laboratory studies indicate a causal relationship between Schmallenberg virus infection and the reported clinical signs.

Resistance to physical and chemical action

From extrapolation from the California serogroup of Orthobunyaviruses:

- Temperature:** Infectivity lost (or significantly reduced) at 50–60°C for at least 30 minutes.
- Chemicals/Disinfectants:** Susceptible to common disinfectants (1 % sodium hypochlorite, 2% glutaraldehyde, 70 % ethanol, formaldehyde)
- Survival:** Does not survive outside the host or vector for long periods.

EPIDEMIOLOGY

According to the epidemiological investigations, reinforced by what is already known about the genetically related Simbu serogroup viruses, Schmallenberg virus affects ruminants. Serological studies indicate that it is not zoonotic. Transmission in animals is by insect vectors and then vertically *in utero*.

Hosts

- Confirmed by PCR or virus isolation:
 - Cattle, sheep, goats
 - Bison
- Confirmed by serology only:
 - Red deer
 - Roe deer
 - Alpaca
 - Mouflons
- *Humans:* Epidemiological and virological studies of human populations considered to be at risk did not demonstrate evidence of zoonotic potential.

Transmission

- Epidemiological investigations indicate insect vector transmission.
- Vectors: Schmallenberg virus genome was detected in several *Culicoides* species. Further information is required to determine whether mosquitoes play a role.
- Vertical transmission across the placenta is proven.
- Direct transmission from animal to animal is very unlikely.
- Further research is still needed to confirm these transmission routes and to determine the competent insect species.

Viraemia and incubation period

Experimental infection in cattle and sheep showed no clinical signs or mild symptoms at 3 to 5 days post-inoculation with an incubation period of between 1 and 4 days and viraemia lasting for 1 to 5 days.

Sources of virus

Material found to be positive in virus isolation (up to May 2012):

- Blood from affected adults and brain from infected fetus.

Material found PCR positive (up to May 2012):

- Organs and blood of infected fetus, placenta, amniotic fluid, meconium.

Occurrence

Only some Orthobunyaviruses had been reported in Europe but viruses from the Simbu serogroup had never been isolated in Europe before 2011.

Schmallenberg virus was first detected in November 2011 in Germany from samples collected in summer/autumn 2011 from diseased (fever, reduced milk yield) dairy cattle. Similar clinical signs (including diarrhoea) were detected in dairy cows in the Netherlands where the presence of Schmallenberg virus was also confirmed in December 2011.

Since early December 2011, congenital malformations were reported in newborn lambs in the Netherlands, and Schmallenberg virus was detected in and isolated from the brain tissue. Up to May 2012, The Netherlands, Belgium, Germany, United Kingdom, France, Luxembourg, Spain and Italy have reported stillbirth and congenital malformations with PCR positive results.

For detailed information on the occurrence of this disease worldwide, see the *OIE World Animal Health Information Database* (WAHID) interface [<http://www.oie.int/wahis/public.php?page=home>].

DIAGNOSIS**Clinical diagnosis**

Manifestation of clinical signs varies by species: bovine adults have shown a mild form of acute disease during the vector season, congenital malformations have affected more species of ruminants (to date: cattle, sheep, goat and bison). Some dairy sheep and cow farms have also reported diarrhoea.

- Adults (cattle)
 - Probably often inapparent, but some acute disease during the vector-active season
 - Fever (>40°C)
 - Impaired general condition
 - Anorexia
 - Reduced milk yield
 - Diarrhoea
 - Recovery within a few days for the individuals, 2–3 weeks at the herd scale
- Malformed animals and stillbirths (calves, lambs, kids)
 - Arthrogryposis/ Hydranencephaly
 - Brachygnathia inferior
 - Ankylosis
 - Torticollis
 - Scoliosis

The exact rate of malformation is not known and varies depending on the stage of gestation at the time of infection.

Lesions

In malformed newborn:

- Hydranencephaly
- Hypoplasia of the central nervous system
- Porencephaly
- Subcutaneous oedema (calves)

The symptoms can be summarised as arthrogryposis and hydranencephaly syndrome (AG/HE)

Differential diagnosis

For the acute infection of the adults:

The symptoms are not specific. All possible causes of high fever, diarrhoea and milk reduction should be taken into account.

For the malformation of calves, lambs and kids:

- Other Orthobunyaviruses
- Bluetongue
- Pestiviruses
- Genetic factors
- Toxic substances

Laboratory diagnosis**Samples**

Samples should be transported cooled or frozen

From live animals for the detection of acute infection:

- EDTA blood
- Serum
 - At least 2 ml, transported cooled

From stillborns and malformed calves, lambs and kids:

- Virus detection:
 - Tissue samples of brain (cerebrum and brainstem)
 - Amniotic fluid
 - From live newborn:
 - Amniotic fluid and placenta
 - (Meconium)
- Antibody detection:
 - Pericardial fluid
 - Blood (preferably pre-colostral)
- Histopathology
 - Fixed central nervous system, including spinal cord

Procedures

Identification of the agent

- Real-time RT-PCR (Bilk et al., 2012); commercial PCR kits are available
- Cell culture isolation of the virus: insect cells (KC), hamster cells (BHK), monkey kidney cells (VERO)

Serological tests on serum samples

- ELISA: commercial kit available
- Indirect Immunofluorescence
- Neutralization test

For further information, reference material and advice, refer to Dr Martin Beer (Martin.Beer@fti.bund.de), Institute of Diagnostic Virology, Friedrich-Loeffler-Institut, Federal Research Institute for Animal Health, Greifswald-Insel Riems, Germany.

PREVENTION AND CONTROL

There is currently no specific treatment or vaccine for Schmallenberg virus.

Sanitary prophylaxis

Control of potential vectors during the vector-active season may decrease the transmission of virus. Reschedule of breeding outside the vector season should decrease the number of fetal malformations.

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The OIE will update this Technical Factsheet when relevant

OIE TECHNICAL FACTSHEET

Additional Information

MEAT

<i>Relevant knowledge:</i>	Only clinically healthy animals should be slaughtered. The viraemic period is very short. Transmission of the virus is most likely by vectors.
<i>Risk of transmission to humans and animals:</i>	Negligible

MILK

<i>Relevant knowledge:</i>	Milk should only be collected from clinically healthy animals. The viraemic period is very short. Transmission of the virus is most likely by vectors.
<i>Risk of transmission to humans and animals:</i>	Negligible

SEMEN

<i>Relevant knowledge:</i>	The viraemic period is very short. Semen should be collected from clinically healthy animals. From 8 bulls experimentally infected with Akabane virus, virus was not found in semen even during the viraemic period (<i>Experimental infection of bulls with Akabane virus</i> , Parsonson IM, Della-Porta AJ, Snowdon WA, O'Halloran ML, Res Vet Sci. 1981 Sep; 31(2):157-60.).
<i>Risk of transmission to animals:</i>	Negligible for sero-positive bulls; negligible for sero-negative and PCR negative bulls.

EMBRYOS

<i>Relevant knowledge:</i>	The viraemic period is very short. Embryos should be collected from clinically healthy animals. Akabane virus is classified under the category 4 (diseases or pathogenic agents for which studies have been done or are in progress that indicate that either no conclusions are yet possible with regard to the level of transmission risk; or the risk of transmission via embryo transfer might not be negligible even if the embryos are properly handled between collection and transfer).
<i>Recommendation:</i>	Safety measures applicable to Akabane virus should be followed.
<i>Risk of transmission:</i>	According to the current knowledge, the risk from sero-negative donor animals is negligible. Sero-positive and PCR-negative donor animals at the day of insemination should be also considered with negligible risk.

LIVE NON-PREGNANT ANIMALS

<i>Relevant knowledge:</i>	The viraemic period is very short. Mild clinical signs might occur. Transmission is most likely by vectors.
<i>Risk of transmission:</i>	Negligible for the following animals: <ul style="list-style-type: none"> - PCR-negative after 7 days in a vector-free environment or, - Sero-positive and PCR-negative.

LIVE PREGNANT ANIMALS

<i>Relevant knowledge:</i>	The virus can persist in the fetus; this may result in the birth of virus positive calves, lambs and kids. The relevant pregnancy time to induce viraemic newborns is not exactly known.
<i>Risk of transmission:</i>	<ul style="list-style-type: none"> - Negligible for the offspring of sero-negative animals tested twice in a vector-free environment (within 28 days), - Negligible for the offspring of animals sero-positive before insemination, - Undetermined for the offspring of all animals not covered by the previous bullets.

