MEETING OF THE OIE AD HOC GROUP ON SCHMALLENBERG VIRUS

Paris, 14 May 2012

1. Opening

A second meeting of the OIE ad hoc Group on Schmallenberg virus (the Group) was held at the OIE Headquarters, Paris, on 14 May 2012.

The Director General of the OIE, Dr Bernard Vallat, joined the meeting briefly, together with Dr Alejandro Thiermann, President of the OIE Terrestrial Animal Health Standards Commission, and Dr Karim Ben Jebara, Head of the OIE Animal Health Information Department. Dr Vallat thanked the Group for its input that had allowed providing scientific based information and recommendations to the OIE Delegates with the objective of ensuring safe international trade in animals and animal products. Recently the number of cases due to Schmallenberg virus had decreased, and the Delegate of an affected Member Country had sent a letter to the OIE, on behalf of other affected Member Countries, proposing to discontinue notification of Schmallenberg virus infections. According to the OIE procedures, endemic listed diseases should be reported on a 6-monthly basis; however, since Schmallenberg virus infection was considered an emerging disease but was not listed, the 6-monthly report would not be an option. The revised chapter on Criteria for listing diseases of the Terrestrial Animal Health Code was being presented for adoption at the forthcoming World Assembly in May 2012, after which the OIE would convene an ad hoc Group to revisit the list of terrestrial animal diseases and would propose a new list of diseases for approval by the Member Countries in May 2013. This Group could provide its opinion as to whether Schmallenberg virus infection should be a candidate for inclusion as an OIE listed disease, although probability of such inclusion might be low. Dr Vallat suggested that affected countries continue to notify outbreaks at least until end of May 2012; thereafter, notification could be discontinued after sending a final report, as the disease would be considered endemic, rather than emerging.

Dr Vallat also suggested that the Biological Standards Commission be requested to update the chapter on Bunyaviral Diseases (2.9.1) of the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals to include information on the diagnosis and surveillance of Schmallenberg virus infection.

On the request of an expert, Dr Vallat stated that if the Group proposed to rename the title on the OIE website from “recommendations” to “information”, this was probably acceptable for the Scientific Commission for Animal Diseases (the Scientific Commission).

2. Adoption of the agenda and appointment of chairperson and rapporteur

The Group was chaired by Professor Steven Edwards and Dr Brigitte Cay and Dr Stéphan Zientara acted as rapporteurs. The Group adopted the proposed agenda as the agenda for the meeting. The agenda and list of participants are attached as Appendices I and II. The Group noted the terms of reference provided to it (see Appendix III).

3. Feedback from the meeting of the Scientific Commission for Animal Diseases – February 2012

The Group noted that the Scientific Commission had reviewed and endorsed the report of the first meeting of the Group in February 2012.
It was noted that the tropism of Schmallenberg virus for embryos had not been demonstrated and hence, the Group decided to draw the attention of the Scientific Commission to this point, in relation to its opinion reflected in the Commission’s report (paragraph 1 of the point 5 of Appendix XI).

4. Evaluation of the epidemiological situation of Schmallenberg virus

The Group reviewed the epidemiological situation of Schmallenberg virus in the affected countries (The Netherlands, Belgium, Germany, France, the United Kingdom, Spain, Italy and Luxembourg).

Overall, the number of cases of malformed lambs, kids and calves had decreased. The number of cases peaked in February/March 2012, coinciding with the peak of lamb births. For calves, the highest number of cases extended until April 2012. The tail of the epidemic was expected to be reached in 2-3 weeks, meaning no or only very few new cases were expected by June 2012.

There was well-founded evidence that Culicoides played a major role in transmission of the virus.

Some particularities of specific countries were discussed:

- In Belgium, ten one-week-old asymptomatic calves were found PCR-positive (serology not available);
- In Germany, around 1500 cases of malformations were reported but very few new cases in lambs or kids were found in May 2012. Since a proportion of malformations in calves was PCR negative, the case definition in Germany was changed to include malformed seropositive pre-colostrum calves even if the PCR was negative;
- In France, there had been more than 1400 cases but now the number of cases had significantly decreased;
- In Spain, only one farm with seropositive animals was found. No animals had been imported in this farm and all surrounding farms had been found as sero-negative.

The Group considered the level of awareness by neighbouring countries in Europe and outside Europe should be further elevated in order to detect possible clinical signs resembling Schmallenberg virus infection.

5. Review of recent findings regarding Schmallenberg virus

The Group reviewed recent research findings from laboratories and available scientific knowledge on Schmallenberg virus, and reflected these in the updated OIE Technical Factsheet (see Section 7 below).

Particular observations were made as follows:

- The characteristics of the virus were typical of the Simbu sero-group but the virus was not a reassortant (contrary to Shamonda). The virus was considered as a previously unrecognised virus showing similarities with Douglas and Sithuperi viruses;
- Sero-prevalence and epidemiological studies in animals and humans had been carried out and the zoonotic potential of the virus was ruled out;
- Many experimental infection studies had taken place and others were in progress, advancing the knowledge on the pathogenesis, transmission and hosts as well as on the most suitable diagnostic samples material.
- There was tropism for the fetus but it was not known whether there was for the embryo. In cattle, the embryo was defined as an individual younger than 45 days post-fertilization;
- Culicoides were identified as probable vectors: virus had been detected by PCR in pooled heads from engorged females of four different species of Culicoides in Belgium. Schmallenberg virus genome was also detected in Culicoides pools in Denmark and Germany;
• An indirect ELISA for mass serological screening was now available;

• Reverse genetics was in progress;

• Additional diagnostic tests had been developed and full sequencing of selected virus strains in different locations had been performed. Methods for serology and molecular diagnostics should be harmonised to make results better comparable;

• Costs for developing vaccines, including licensing, would be expensive and EU co-financing was not considered justifiable. Some manufacturers were working on inactivated vaccines, but the registration procedure would take time (more than 250 days) and a Schmallenberg virus vaccine would therefore not be available until at least 2013.

There were still unanswered questions, such as whether the age of the dam at infection correlated with malformations; genetic variation (particularly the drift) that could explain the origin of the virus; differences in prevalence between countries (particularly north-south); further investigation on the vectors (other species involved, possibility of vertical transmission in the vectors).

6. Discussion on the risk of spread of the disease

The Group noted that there were still unknowns to foresee the risk of spread during the next vector season. The scientific-based estimations on the risk of transmission were updated according to the current knowledge.

7. Updating of OIE Technical Factsheet and of the recommendations endorsed by the Scientific Commission in February 2012

The Technical Factsheet was updated by the Group based on the latest scientific information. It was agreed that the key points from the recommendations should now be merged as additional information in an appendix, rather than a standalone recommendations document (Appendix IV of this report).

The Group reiterated that bluetongue had been referred to at its first meeting because of the common vectors involved. The shorter viraemic period in animals infected with Schmallenberg virus as compared to bluetongue made any other reference to bluetongue inappropriate. The Group also noted the negligible risk of transmission posed by animals seropositive to Schmallenberg virus.

8. Other matter

The Group did not have any other matter to discuss.

9. Adoption of report

The Group reviewed and amended the preliminary draft report provided by the rapporteurs.

…/Appendices
Appendix I

MEETING OF THE OIE AD HOC GROUP ON SCHMALLENBERG VIRUS
Paris, 14 May 2012

Agenda

1. Opening
2. Adoption of the agenda and appointment of chairperson and rapporteur
3. Feedback from the meeting of the Scientific Commission for Animal Diseases – February 2012
4. Evaluation of the epidemiological situation of Schmallenberg virus
5. Review of recent research findings regarding Schmallenberg virus and other genetically related vector-borne viruses
6. Discussion on the risk of spread of the disease
7. Updating of OIE Technical Factsheet and of the recommendations endorsed by the Scientific Commission in February 2012
8. Other matters
9. Adoption of report

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### List of participants

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MEETING OF THE OIE AD HOC GROUP ON SCHMALLENBERG VIRUS

Paris, 14 May 2012

Terms of Reference

1. Update on the current situation of Schmallenberg virus outbreaks.

2. Review recent research and scientific knowledge on Schmallenberg virus and other genetically related viruses.

3. Review and update the OIE Technical Factsheet, together with the recommendations endorsed by the OIE Scientific Commission on 16 February 2012, with the latest epidemiological and scientific knowledge available.
SCHMALLENBERG 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 \textbf{Bunyaviridae} family, within the \textit{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 \textit{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 herd level

- **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@fli.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.

**REFERENCES AND OTHER INFORMATION**

- ProMED-Mail from Published Date: 2011–11-19 Subject: PRO/AH/EDR> Undiagnosed illness, bovine - Germany, Netherlands (02): new virususp. Archive number: 20111119.3404: http://www.promedmail.org/direct.php?id=20111119.3404

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The OIE will update this Technical Factsheet when relevant
Additional Information

MEAT

Relevant knowledge: Only clinically healthy animals should be slaughtered. The viraemic period is very short. Transmission of the virus is most likely by vectors.

Risk of transmission to humans and animals: Negligible

MILK

Relevant knowledge: Milk should only be collected from clinically healthy animals. The viraemic period is very short. Transmission of the virus is most likely by vectors.

Risk of transmission to humans and animals: Negligible

SEMEN

Relevant knowledge: 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 (Experimental infection of bulls with Akabane virus, Parsonson IM, Della-Porta AJ, Snowdon WA, O'Halloran ML, Res Vet Sci. 1981 Sep; 31(2):157-60).

Risk of transmission to animals: Negligible for sero-positive bulls; negligible for sero-negative and PCR negative bulls.

EMBRYOS

Relevant knowledge: 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).

Recommendation: Safety measures applicable to Akabane virus should be followed.

Risk of transmission: 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

Relevant knowledge: The viraemic period is very short. Mild clinical signs might occur. Transmission is most likely by vectors.

Risk of transmission: Negligible for the following animals:
- PCR-negative after 7 days in a vector-free environment or,
- Sero-positive and PCR-negative.

LIVE PREGNANT ANIMALS

Relevant knowledge: The virus can persist in the fetus; this may result in the birth of virus positive calves, lambs and kids. The relevant stage of pregnancy for induction of viraemic newborns is not exactly known.

Risk of transmission:
- 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.