Scientific studies on SBV

- Studies co-financed by the Commission at the rate of 50% of eligible costs for the period **1 April 2012 to 31 December 2013** for the following Member States:
  - Belgium, Germany, Spain, France, Italy, the Netherlands and UK
- The results of these studies are expected to be published in April 2014
  - Progress reports with preliminary results were provided in March 2013
  - Some of the results presented here are preliminary and have not yet been published in scientific journals
  - EFSA has not yet conducted any assessment of the available results
- The outcome of the studies must be made available to the Commission, all Member States and EFSA and presented at the Standing Committee on the Food Chain and Animal Health

Overview of ongoing studies

Pathology
- Pathogenicity at different gestation stages
- Pathogenicity in non pregnant animals
- Immunity
- Impact and risk factors

Epidemiology
- Horizontal transmission
- Vectors
- Semen and Embryo
- Other species

Diagnostic
- ELISA
- RT-PCR
Pathogenesis studies

Pathogenicity at different gestation stages

Experimental infections at d60, d90, d120, d150 (cattle) and d20, d40, d60 (small ruminants)

Incubation period and viraemic period have been reported in several papers (incl. Wernike et al., 2013).

Pathogenicity in non pregnant animals

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Pathogenesis studies

Immunity

It could be shown, that re-infected cattle (experimental infection) were fully protected from viremia and that neither oral exposure nor contact infection could induce SBV-infection (no viremia, no seroconversion) (Wernicke et al., 2013)
<table>
<thead>
<tr>
<th></th>
<th>SBV</th>
<th>Simbu Virus</th>
<th>Reference</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of viremia</strong></td>
<td>2-6dpi</td>
<td></td>
<td>Hoffmann et al., 2012</td>
<td>(3 animals)</td>
</tr>
<tr>
<td><strong>Incubation time</strong></td>
<td>2-5 dpi</td>
<td></td>
<td>Hoffmann et al., 2012</td>
<td>(3 animals)</td>
</tr>
<tr>
<td><strong>Virus distribution</strong></td>
<td>Neurons of the gray matter</td>
<td></td>
<td>Varela et al., 2013</td>
<td>Mouse model- SBV synthetic</td>
</tr>
<tr>
<td></td>
<td>cerebrum, spinal cord, umbilical cord, placental fluid</td>
<td></td>
<td>Bilk et al., 2012</td>
<td>Virus distribution in malformed newborns</td>
</tr>
<tr>
<td><strong>Gestation susceptible period</strong></td>
<td>Cattle 62 to 173 d Sheep 28 to 56 d</td>
<td></td>
<td>Worst case scenario EFSA 2012</td>
<td></td>
</tr>
<tr>
<td><strong>Virus shedding and possible persistence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration of immunity</strong></td>
<td>Long lasting</td>
<td></td>
<td>Taylor &amp; Mellor, 1994</td>
<td>Akabane virus</td>
</tr>
</tbody>
</table>
Belgium: almost every domestic ruminant has already been infected by the virus. All samples before August 2011 were found to be sero-negative.

Netherlands: Outcome 1 – impact of the SBV infection on health and productivity of dairy cattle – Final report May 2013

Outcome 2 – impact of the SBV infection on health and productivity of sheep, potential risk factors - Final report August 2013

ON GOING
## Seroprevalence

<table>
<thead>
<tr>
<th>Country</th>
<th>Time of study</th>
<th>species</th>
<th>Within herd</th>
<th>Between Herd</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>Nov 2011 - Apr 2012</td>
<td>1082 sheep, 83 herds</td>
<td>84.31% (84.19-84.43)</td>
<td>98.03% (97.86-98.18)</td>
<td>Meroc et al., 2013</td>
</tr>
<tr>
<td>Belgium</td>
<td>Nov 2011 - Apr 2012</td>
<td>142 goats, 8 herds</td>
<td>40.68% (23.57-60.4)</td>
<td></td>
<td>Meroc et al., 2013</td>
</tr>
<tr>
<td>Belgium</td>
<td>Jan - Mar 2012</td>
<td>11635 cattle, 422 herds</td>
<td>86.3% (84.75-87.71)</td>
<td>99.76% (98.34-99.97)</td>
<td>Meroc et al, 2013</td>
</tr>
<tr>
<td>Belgium</td>
<td>Oct - Dec 2011</td>
<td>red deer 313 and roe deer 211</td>
<td>43%</td>
<td></td>
<td>Linden et al., 2012</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>Nov 2011 - Jan 2012</td>
<td>1123 Cattle</td>
<td>70-100%</td>
<td>72.5% (69.7-75.1)</td>
<td>Elbers et al., 2012</td>
</tr>
<tr>
<td>Sweden</td>
<td>After vector season 2012</td>
<td>Bulk milk test Cattle</td>
<td>72%</td>
<td></td>
<td>Chenais et al., 2013</td>
</tr>
<tr>
<td>Austria</td>
<td>Update to Dec 2012</td>
<td>Cattle, Sheep, Goats</td>
<td>90.77% 63.14% 71.68 %</td>
<td></td>
<td>Schiefer et al., 2013</td>
</tr>
</tbody>
</table>
**Assessment of the impact**

### Within Herds

<table>
<thead>
<tr>
<th>Country</th>
<th>Study period</th>
<th>Species</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>Mar 2012-?</td>
<td>362 (SBV+) sheep flocks, 40635 sheep, 38 districts</td>
<td>85% Normal birth, 12%&gt;95% Normal, 10%&lt;50% Normal, 61% Abnormal birth, 38 districts</td>
</tr>
<tr>
<td>France</td>
<td>Feb-Sep 2012</td>
<td>510 (SBV+) cattle herds, 37504 cattle, 16017 cows gave birth to 16175 calves</td>
<td>2% abortions of which 61% normal and 39% deformed, 98% full term of which 96% normal and 4% deformed</td>
</tr>
</tbody>
</table>

* In their study, Dominguez and coll. do not confirm the link of causality between malformation and abnormalities and infection with SBV (Dominguez et al., 2012).
Assessment of the impact - Sheep

Within Herds

- Pregnant animals in the flock
  - Abortions 4%
    - Aborted lamb normal 58%
    - Aborted lamb abnormal 42%
  - End of term gestation 96%
    - Stillborn or dead within 12h 13%
      - Deformed, Alive 12h after birth 2%
      - Normal 85%
    - Abnormal appearance 63%
      - Normal appearance 37%

* In their study, Dominguez and coll. do not confirm the link of causality between malformation and abnormalities and infection with SBV (Dominguez et al., 2012).
Assessment of the impact - Cattle

**Within Herds**

- Pregnant animals in the flock
  - Abortions 2%
    - Aborted calf normal 61%
    - Aborted calf abnormal 39%
  - End of term gestation 98%
    - Stillborn or dead within 12h 5%
    - Deformed, Alive 12h after birth 2%
    - Normal 93%
  - Normal appearance 45%
  - Abnormal appearance 55%

* In their study, Dominguez and coll. do not confirm the link of causality between malformation and abnormalities and infection with SBV (Dominguez et al., 2012).
For all affected countries, the number of SBV confirmed herds is low compared with the total number of herds. The maximum proportion of confirmed sheep herds per region is 6.6% and 4% for cattle herds.

Other measures of impact are necessary:

- Within herd impact
- Reduced fertility
- Reduced milk production
- Dystocia rates and welfare ...
In experimental infection studies, antibody responses in non-inoculated control which were kept in contact with inoculated animals, were not observed, neither in cattle, nor in sheep or goat. There were no indications for direct horizontal transmission of SBV.
“...prevalence of SBV in midges was 5-10 times higher when compared to BTV detection in *Culicoides* in Europe during 2002-2008.

Vector biology was positively influenced by climatological circumstances in 2011 with a prolonged vector season (several weeks due to higher temperatures than normal) and a higher survival rate and increased vector abundance (rain in summer and higher temperatures than normal in autumn)(Elbers et al., 2012; Regge.et al., 2012). “

ON GOING
Epidemiology studies

Criteria for the recognition of a vector:
1) recovery of virus from wild-caught specimens free from visible blood,
2) demonstration of ability to become infected by feeding on a viraemic vertebrate host or on an artificial substitute,
3) demonstration of ability to transmit biologically by bite and
4) accumulation of field evidence confirming the significant association of the infected arthropods with the appropriate vertebrate population in which disease or infection is occurring.

Activity areas:
1. Mosquito colony trials and testing *Culicoides* for SBV infection
2. Screening of *Culicoides* and mosquito field populations for SBV infections
3. Artificial infection of *Culicoides* and mosquito field populations with SBV
4. Vertical transmission of SBV

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Preliminary results seem to indicate that mosquito are not able to support viral replication. Also, no evidence of vertical transmission was obtained so far.
Epidemiology studies

Semen and Embryo

SBV has been detected in semen (straws) by FLI, CVI and ANSES (ProMed 21 Dec 2013), 0-4% of semen batches were SBV positive by RT-PCR.

Excretion levels of SBV in bovine semen have been monitored in several SBV seropositive bulls.

Subcutaneous inoculation of 6 calves with SBV positive semen (different Ct values) was performed resulting in viraemia in 2 (of 6) calves. It still needs to be proven if the virus can be transmitted via insemination.

Experimental inoculation in two semen producing bulls performed at CVI, resulted in SBV positive semen in both animals at different times after inoculation.
Epidemiology studies

Experimental infection in pigs and poultry were performed.

According to these first preliminary results pigs do not seem to be a replication host for SBV.

Also chicken are not susceptible for Simbu, Sabo, Sathuperi and Schmallenberg virus.

SBV antibodies have been detected in various wildlife species and high seroprevalences have been observed in roe deer (46%, CVI; 40%, FLI), wild boar (17%, FLI), moufflon (72% FLI), red deer (52%, FLI), fallow deer (33%, FLI; 42%,CVI), Sika deer (15%, FLI)
## What we know / assumptions

<table>
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<th>SBV</th>
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</thead>
<tbody>
<tr>
<td><strong>Routes of transmission</strong></td>
<td>Transplacental transmission of SBV has been demonstrated</td>
<td>Vectors – Culicoides, Horizontal animal to animal transmission has not been reported for Simbu serogroup viruses</td>
<td>Garigliany et al. 2012a,b; van den Brom et al. 2012</td>
</tr>
<tr>
<td><strong>SBV vectors</strong></td>
<td><em>C. Obsoletus</em> sensu stricto, <em>C. scoticus</em>, <em>C. chiopterus</em> and <em>C. dewulfi</em></td>
<td></td>
<td>Elbers et al 2013 De Regge et al 2012 vector competence?</td>
</tr>
<tr>
<td><strong>Transmission rate vector to host</strong></td>
<td></td>
<td>0.78/ Beta(7.38,2.13)</td>
<td>Baylis et al. 2008 based on an analysis of data on the transmission of bluetongue virus to sheep by <em>C. sonorensis</em></td>
</tr>
<tr>
<td><strong>Transmission rate host to vector</strong></td>
<td>0.014/Beta(2.9,210.5)</td>
<td></td>
<td>Belgian data: two pools out of 23 tested (each of 10 midges) positive for SBV Elbers et al., 2012</td>
</tr>
<tr>
<td><strong>Extrinsic incubation period</strong></td>
<td></td>
<td>BTV 9 estimate</td>
<td>Carpenter et al. 2011</td>
</tr>
</tbody>
</table>
What we know / assumptions

<table>
<thead>
<tr>
<th>Transmission of SBV via semen and embryos</th>
<th>SBV</th>
<th>Simbu Virus</th>
<th>Reference</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Akabane virus could not be detected in semen.</td>
<td>Parsonson et al., 1981</td>
<td>viraemic bulls experimentally infected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Akabane virus could not be isolated from bovine embryos</td>
<td>Singh et al., 1982</td>
<td>Donor cows exposed to viral infection</td>
</tr>
<tr>
<td>Detection of SBV-genome in semen 6 calves were experimentally inoculated, no clinical symptoms, 2/6 PCR positive</td>
<td></td>
<td></td>
<td>Preliminary results EU research</td>
<td>Subcutaneous inoculation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Host range</th>
<th>SBV</th>
<th>cattle, sheep, goats, and bison</th>
<th>FLI, 2012</th>
<th></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Reservoirs</th>
<th>SBV</th>
<th>red deer, roe deer, moufflon and alpacas</th>
<th>Jack et al., 2012 Meroc et al., 2012</th>
<th></th>
</tr>
</thead>
</table>
All ELISAs and VNT assays in the participating laboratories (De, Fr, NL, Be, UK) showed a rather good performance. There were few inter-laboratory differences. Less differences between participating laboratories were observed for the VNT and in general the VNT was more sensitive than ELISA (scientific publication in preparation).
The EU has demonstrated its capacity for rapid response to SBV in terms of scientific investigation and research.

Preliminary results from studies co-financed by the EC and Member States confirm assumptions used in the EFSA assessments.

Further information will be made available towards the end of 2013.