REPORT OF THE OIE AD HOC GROUP ON PORCINE REPRODUCTIVE AND RESPIRATORY SYNDROME

Paris, 9–11 July 2013

A meeting of the OIE ad hoc Group on Porcine Reproductive and Respiratory Syndrome (hereafter the Group) was held at the OIE Headquarters in Paris from 9 to 11 July 2013.

1. Opening

Dr Gideon Brückner, Acting Head of the Scientific and Technical Department and President of the Scientific Commission of Animal Diseases, welcomed the Group members on behalf of Dr Bernard Vallat, the Director General of the OIE. He explained to the participants the process of chapter development for the OIE Terrestrial Animal Health Code (Terrestrial Code), since the main task of the Group would be to draft a new chapter for Porcine Reproductive and Respiratory Syndrome (PRRS).

Dr Alex Thiermann, President of the Terrestrial Animal Health Standards Commission, suggested the Group to use the chapter on Aujeszky’s disease and the recently adopted chapter on classical swine fever (CSF) of the Terrestrial Code as templates, but to create and adapt the text to the particularities of PRRS.

2. Adoption of the agenda, appointment of a chairman and rapporteur

Dr Trevor Drew was appointed as chairman and the OIE Secretariat helped with the rapporteur functions.

The agenda and list of participants are attached as Appendices I and II, respectively.

3. Overall considerations

Dr Drew had served as Chairman of the last meeting of an ad hoc Group on PRRS that took place in 2008. Dr Drew explained that the Group then felt that a Terrestrial Code chapter could not be developed because of a number of reasons that could be responded now. At that time, PRRS had emerged in the Asian continent and the global status of the disease was still uncertain. Since 2008, diagnostic tests have improved and the emergence of virulent isolates has been observed for both type-1 and type-2 PRRS virus (PRRSv) strains. Laboratories would have to face continuous challenges because of the emergence of new isolates in endemic situations. Finally, three countries, namely Chile, South Africa and Sweden, had achieved PRRS eradication and could serve as examples to provide general recommendations, even if a unique approach could not be provided.

The Group followed the Terrestrial Code chapters on Aujeszky’s disease and CSF as recommended, but realised that the chapter on Aujeszky’s disease might need revision of the wording and structure to align it with recently updated chapters.

Similarly, the Group noted that the chapter on PRRS in the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (Terrestrial Manual) also needed a revision to take into account the different types of vaccines available and the latest molecular tests.
4. Development of the draft Terrestrial Code Chapter on PRRS

Article on General provisions

The definition of ‘infection’ and hosts for the purposes of the Terrestrial Code were drafted by the Group taking the chapter on CSF as a model taking into account the differences of PRRS as follow;

- PRRSv isolation is complex and not commonly available, but laboratories should be encouraged to improve their capabilities in this respect.

- Vaccination is widely used to control and eliminate PRRS in many countries. The most effective vaccines use modified live virus but there is a risk that PRRS vaccine strains may be transmitted to unvaccinated pigs. The Group argued that a country using modified live vaccines could not be considered free from PRRS. Inactivated vaccines were available but, although safer, the effectiveness of those currently licensed was limited. The Group agreed to recommend an update to the Terrestrial Manual chapter on PRRS, particularly on the vaccine section, to take account of the different types of vaccines.

- Although both wild and domestic pigs (Sus scrofa) are susceptible, the role played by wild pigs in the epidemiology of PRRS is not recognised to be of significance.

- Incubation period: the Group agreed that the time from infection to clinical signs would be between 2-14 days, with an average of one week. For the purposes of the Terrestrial Code, this time period was agreed to be set at 14 days.

- Infective period: Variable figures in the literature led the Group to consider the extension of the infective period to range between an average of 3 to 40 days, although in some instances it could last for several months, as in the case of semen from infected boars.

Article on safe commodities

The Group listed those commodities considered safe for trade and identified the need to define casings, skins and trophies in the glossary of the Terrestrial Code including the standard processes to which they are subjected.

Articles on status

The Group decided to continue following the chapter on CSF which appeared more updated than Aujeszky’s disease chapter for the development of the article on free status, taking into account the obvious differences especially in relation to official status. For example, the notion of compartment had not been developed when the chapter on Aujeszky’s disease was last reviewed. The management options at the compartment level were taken into account for PRRS in the same article as for country and zone.

The Group drafted the criteria for freedom taking into account the risk posed by circulating vaccine virus that would prevent a country with vaccinated animals from claiming freedom.

Regarding point 4 of Article X.X.3., the Group was keen to highlight the risk posed by circulating vaccine virus and that in the absence of challenge, vaccinated animals would generally no longer have antibodies after 6 months.

To recover the free status after an outbreak, negative test results one month after the last positive was eliminated was considered sufficient for the Group, rather than the three months recommended for CSF, since there were fewer chances of virus persistence in the environment or in pig populations without detection. Emergency vaccination with subsequent removal of vaccinated animals was considered as an option in a modified stamping-out policy.

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Articles on importation of live pigs

- Even if clinical signs of PRRS were not specific and variable, pigs should be clinically healthy in order to be imported; the Group agreed to retain the standard sentence used for other chapters in the Terrestrial Code.

- Breeding boars were considered to pose a higher risk than other pigs, given the high risk posed by PRRSv transmission due to the duration of excretion of virus in semen. The Group therefore felt that boars had to be kept in a free country, zone or compartment for 6 months rather than 3 months.

- A differentiation was made between pigs for breeding/rearing and pigs for slaughter.

- Recommendations for import of wild and feral pigs, whether from infected or free areas, were drafted.

- For both breeding pigs and wild and feral pigs, testing before shipment was included.

Articles on importation of semen

- Recommendations were drafted to specify the testing regime of donor animals from PRRS infected countries or zones before entering the pre-entry isolation facility, in the pre-entry isolation facility, and in the artificial insemination centre.

- Monthly serological testing was recommended in the artificial insemination centre in PRRS infected countries or zones because of the difficulties recognised in maintaining artificial insemination centres continuously free from PRRS using less frequent testing.

- The Group noted that the links in Article 4.6.4. to disease specific chapters needed revision and that circular references should be eliminated. If the new provisions drafted for PRRS were adopted, the correct reference to the PRRS article should also be inserted.

- Testing for viral nucleic acid in every batch of semen was introduced to facilitate trade of semen of sero-negative boars where other conditions could not be met. Sero-positive boars can pose a risk since they may intermittently excrete virus in semen for prolonged periods². The Group recommended that the Terrestrial Manual was updated to include these tests.

Articles on importation of embryos

The Group drafted the recommendations regardless of the PRRS status of the country of origin. Trade of pig embryos was considered very uncommon. Transmission of PRRS to the foetus happened if the sow was infected during gestation rather than through embryo transfer anyway.

Articles on importation of fresh meat

It is generally considered that traded fresh meat handled under standard commercial conditions represent a negligible risk of containing sufficient level of infectious virus to establish an infection in a susceptible pig on the assumption that pigs are generally not exposed to unprocessed meat. Such handling would involve exsanguination, chilling and maturation. Virus becomes rapidly inactivated at pH<6 which is reached during the maturation process (pork meat drops to pH 5.5-5.6 within 24 hours, during the maturation process). Recent information regarding some newly emerging highly pathogenic strains has found its distribution to be in alveolar epithelial and vascular endothelial cells³ and meat may pose a risk if the necessary pH to inactivate the virus is not reached. The Group concluded that fresh meat following such handling presents a negligible risk of infection with PRRSv.

Decades of international trade involving millions of tonnes of pork from endemic countries does not seem to have resulted in the introduction of virus or exotic genotypes into new areas. Experimental evidence of oral transmission shows variable results, depending mainly on the degree of maturation and the quantity of infected pork meat fed to susceptible pigs (Appendix III).

Taking the above into account and the approach followed in the recently adopted chapter on PPR, the Group drafted recommendations for the import of meat, regardless of the PRRS status of the country of origin.

Apart from anecdotal illegal movements of wild pig meat had happened in the past, the Group argued that wild boar meat was not very frequently imported. For this reason, risk by wild pig meat import was considered very low and provisions were drafted without testing requirements.

**Articles on importation of other products**

The Group considered the rest of products to be highly processed material that would pose a negligible risk since they would be submitted to heat treatments (>37°C) that would inactivate PRRSV.

The Group concluded that the risk posed by certain offal due to lack of equivalent maturation may be higher than that posed by meat, and developed recommendations to mitigate this risk.

Finally, no specific recommendations were drafted for import of swill given PRRSV easy inactivation in the environment.

**5. PRRS specific surveillance guidelines**

The Group listed a number of characteristics unique to PRRS that required drafting specific surveillance Articles and would be finished in a next meeting.

**6. Other issues**

No other issues.

**7. Finalization and adoption of the draft report**

The Group reviewed and amended the draft report provided by the rapporteur. The Group agreed that the report would be subject to a period of circulation within the Group for comments. The report was finalised by correspondence.

…/Appendices
MEETING OF THE
OIE AD HOC GROUP ON PORCINE REPRODUCTIVE AND RESPIRATORY SYNDROME

Paris, 9 – 11 July 2013

Agenda

1. Opening
2. Adoption of agenda, appointment of chairman and rapporteur
3. Overall considerations
4. Development of the draft Terrestrial Code Chapter on PRRS
5. PRRS specific surveillance guidelines
6. Other issues
# MEETING OF THE OIE AD HOC GROUP ON PORCINE REPRODUCTIVE AND RESPIRATORY SYNDROME

**Paris, 9-11 July 2013**

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## List of participants

### MEMBERS

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prof. Zygmunt Pejsak</td>
<td>(OIE Reference Laboratory for PRRS)</td>
<td>Poland</td>
</tr>
<tr>
<td>(National Veterinary Research</td>
<td>Institute Partyzantow Str. 57 24-100 Pulawy</td>
<td></td>
</tr>
<tr>
<td>Tel: +48-81 889 30 30</td>
<td>Fax: +48-81 886 25 95</td>
<td></td>
</tr>
<tr>
<td><a href="mailto:zpejsak@pivet.pulawy.pl">zpejsak@pivet.pulawy.pl</a></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dr Trevor Drew</td>
<td>(OIE Reference Laboratory for CSF)</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>Head of Statutory and Exotic</td>
<td>Programme Veterinary Laboratories Agency</td>
<td></td>
</tr>
<tr>
<td>Virus Programme</td>
<td>Weybridge Woodham Lane, New Haw, Addlestone</td>
<td></td>
</tr>
<tr>
<td>Tel: 44 (0)1932 357 637</td>
<td>Fax: 44 (0)1932 357 239</td>
<td></td>
</tr>
<tr>
<td><a href="mailto:trevor.drew@ahvla.gsi.gov.uk">trevor.drew@ahvla.gsi.gov.uk</a></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dr Torben Grubbe</td>
<td>Danish Veterinary and Food Administration</td>
<td>Denmark</td>
</tr>
<tr>
<td>Station Parken 31-33</td>
<td>2600 Gidostrup</td>
<td></td>
</tr>
<tr>
<td>Tel: +45 72 27 65 39</td>
<td>Email: <a href="mailto:tgr@fvst.dk">tgr@fvst.dk</a></td>
<td></td>
</tr>
<tr>
<td>Hernán Rojas Olavarría</td>
<td>CERES Consulting</td>
<td>Chile</td>
</tr>
<tr>
<td>Apoquindo 3401 oficina 21</td>
<td>Providencia Santiago</td>
<td></td>
</tr>
<tr>
<td>CHILE</td>
<td>Tel: +56-9-82996315</td>
<td></td>
</tr>
<tr>
<td><a href="mailto:liolemus@gmail.com">liolemus@gmail.com</a></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dr Howard Pharo</td>
<td>Manager Import &amp; Export Analysis</td>
<td>New Zealand</td>
</tr>
<tr>
<td>Ministry for Primary Industries</td>
<td>Pastoral House 25 The Terrace PO Box 2526, Wellington</td>
<td></td>
</tr>
<tr>
<td>Tel: (64) 4 894 05 05</td>
<td>Fax: (64) 4 894 07 31</td>
<td></td>
</tr>
<tr>
<td><a href="mailto:Howard.Pharo@mpi.govt.nz">Howard.Pharo@mpi.govt.nz</a></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dr Tung Nguyen</td>
<td>Vice Director, National Centre for Veterinary</td>
<td>Vietnam</td>
</tr>
<tr>
<td>Diagnostics</td>
<td>No. 11 - 78th lane - GIAI PHONG st.</td>
<td></td>
</tr>
<tr>
<td>Phuong Mai - Dong Da - Hanoi</td>
<td>Cell: +84 98 252 0606 / 91 2525 012</td>
<td></td>
</tr>
<tr>
<td><a href="mailto:nguyentungncvd@hotmail.com">nguyentungncvd@hotmail.com</a></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dr Gary Bührmann</td>
<td>Chief State Veterinarian Boland</td>
<td>South Africa</td>
</tr>
<tr>
<td>Directorate Veterinary Services</td>
<td>Private Bag X1, Elsenburg 7607.</td>
<td></td>
</tr>
<tr>
<td>South Africa</td>
<td>Tel: 021 808 5026</td>
<td></td>
</tr>
<tr>
<td>Fax: 021 808 5125</td>
<td><a href="mailto:GaryB@elsenburg.com">GaryB@elsenburg.com</a></td>
<td></td>
</tr>
<tr>
<td>Dr Scott Allen Dee</td>
<td>(invited but could not attend)</td>
<td>USA</td>
</tr>
<tr>
<td>Department of Veterinary</td>
<td>Medicine College of Veterinary Medicine</td>
<td></td>
</tr>
<tr>
<td>Population</td>
<td>University of Minnesota</td>
<td></td>
</tr>
<tr>
<td>Medicine</td>
<td>385e Animal Science/Veterinary Medicine Building</td>
<td></td>
</tr>
<tr>
<td>St. Paul, MN 55108</td>
<td>Tel: 612-625-4786</td>
<td></td>
</tr>
<tr>
<td>Fax: 612-625-1210</td>
<td><a href="mailto:sdee@mpivet.com">sdee@mpivet.com</a></td>
<td></td>
</tr>
</tbody>
</table>

### SCIENTIFIC AND CODE COMMISSION REPRESENTATIVES

<table>
<thead>
<tr>
<th>Dr Gideon Brückner (President Scientific Commission)</th>
<th>30 Schoongezicht 1 Schultz Street Somerset West 7130 SOUTH AFRICA Tel: (27) 218 516 444 Mobile: (27) 83 310 2587 <a href="mailto:gbrueckner2@gmail.com">gbrueckner2@gmail.com</a></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Alex Thiermann (President Code Commission)</td>
<td>12 rue de Prony 75017 Paris FRANCE <a href="mailto:a.thiermann@oie.int">a.thiermann@oie.int</a></td>
</tr>
<tr>
<td>Dr Gideon Brückner</td>
<td>Acting Head Scientific and Technical Department <a href="mailto:g.brueckner@oie.int">g.brueckner@oie.int</a></td>
</tr>
</tbody>
</table>

### OIE HEADQUARTERS

<table>
<thead>
<tr>
<th>Dr Bernard Vallat (Director-General)</th>
<th>Dr Marta Martínez Avilés (Veterinary epidemiologist)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 rue de Prony 75017 Paris FRANCE <a href="mailto:b.vallat@oie.int">b.vallat@oie.int</a></td>
<td><a href="mailto:m.martinez@oie.int">m.martinez@oie.int</a></td>
</tr>
<tr>
<td>Dr Gideon Brückner (Acting Head)</td>
<td>Dr Kio Kio Hong (Chargé de mission)</td>
</tr>
<tr>
<td>Scientific and Technical Department</td>
<td>Scientific and Technical Department</td>
</tr>
<tr>
<td><a href="mailto:g.brueckner@oie.int">g.brueckner@oie.int</a></td>
<td><a href="mailto:k.hong@oie.int">k.hong@oie.int</a></td>
</tr>
</tbody>
</table>
The effect of the nature of PRRS virus on the likelihood of transmission in meat

PRRSv has a delicate lipid envelope which is inactivated by lipid solvents and heat (Fauquet et al., 2005). It persists for 1-6 days at 20-21°C, 3-24 hrs at 37°C and 6-20 minutes at 56°C. Although the virus is very stable when stored at temperatures of -70°C to -20°C, it is considerably less stable when stored at normal refrigeration temperatures; at 4°C about 90% of infectivity is lost within a week. PRRSv is stable at pH 6.5 to 7.5, but infectivity is rapidly lost at pH below 6 and above 7.5 (Zimmerman et al., 2006).

The main target cells for PRRSv are macrophages, particularly those in lungs and lymph nodes. While alveolar macrophages are the most favoured cell for replication, only about 2% of these cells become infected, even at the peak of virus replication in the lungs (EFSA, 2005).

Transmission has been demonstrated by multiple routes of exposure – intranasal, intramuscular, oral, intrauterine and vaginal. Pigs are extremely sensitive to parenteral exposure, and considerably less so by other routes (Zimmerman et al., 2006).

Presence of PRRS virus in meat

Virus isolation has limited sensitivity to detect low titres of virus - the limit to detection in meat was reported by Bloemraad et al. (1994) to be about $10^{3.8}$ TCID$_{50}$ per g while later (Van der Linden et al., 2003) considered it to be somewhat lower at $10^{1.8}$ TCID$_{50}$ per g. RT-PCR is considerably more sensitive, and its use has led to higher estimates of infectivity in meat (Magar & Larochelle, 2004; Van der Linden et al., 2003). However, since RT-PCR detects viral RNA rather than infectious virus, its use alone appears to result in overestimation of the likelihood of infectivity being present in meat (Baker et al, 2007; Hermann et al, 2007; Jakobs et al., 2010). While feeding trials appear at first sight to be the most objective test of infectivity in meat, they must be carefully designed to avoid horizontal transmission between recipient pigs (Magar & Larochelle, 2004; Van der Linden et al., 2003). Moreover, the high cost of feeding trials mitigates against their wider use in more fully exploring the issue of infectious dose of PRRSv.

As discussed by Farez & Morley (1997), several studies carried out in the 1990s reported the isolation of PRRSv from meat and associated regional lymph nodes of small numbers of pigs. Bloemraad et al. (1994) took meat samples from four artificially infected pigs, two of which were slaughtered at 5 days post inoculation (PI), and two at 10 days PI. Virus was present in leg muscle of one pig at 5 days PI – the titre at zero hrs post-mortem was $10^{2.7}$ TCID$_{50}$ and by 24 hours post-mortem (stored at 4°C) the titre was $10^{1.9}$ TCID$_{50}$. In another pig slaughtered at 10 days PI the virus was found in diaphragm muscle 24 hours post mortem at titre of $10^{0.8}$ TCID$_{50}$ – this titre was considered to be the limit of detection by tissue culture. However, by 48 hr post mortem, no virus was detectable in any of the muscle specimens from any of the four pigs held at 4°C. Mengeling et al. (1995) isolated PRRSv from meat of only one of six experimentally infected pigs, while Magar et al. (1995) were able to isolate virus from muscle and lymph nodes of two pigs at 7 days PI but not at 14 days PI.

Several studies on meat at the point of slaughter were also carried out in the 1990s. Larochelle & Magar (1997) collected meat samples from packages of frozen meat ready for export from four Canadian processing plants in an area where PRRS was endemic. No virus could be isolated from 2,190 individual carcass samples pooled in groups of five prior to testing. Frey et al. (1995) sampled fresh pork derived from commercially slaughtered pigs in the USA. Virus was isolated from six sample pools out of a total of 1,049 sample pools taken from 178 lots of fresh pork (40,000 lb per lot). Most positives were obtained only after multiple cell culture passages, and virus titres were so low that confirmation by re-isolation was not always successful and had to be done by RT-PCR. In Taiwan 85% pigs tested at three abattoirs were seropositive for PRRSv, but none of 472 carcass samples of market pigs at slaughter were positive by RT-PCR (Wang, 1999).
These studies collectively demonstrated that the likelihood of isolating virus from meat of pigs at slaughter was low and as a result it was generally considered in the 1990s that meat was unlikely to be a vehicle for transmission of PRRS.

**Trials feeding meat to pigs**

Feeding trials have demonstrated that it is possible to transmit PRRS virus to susceptible recipients through the consumption of infected meat. However, these studies have had a number of shortcomings and, most significantly, none of these studies have attempted to transmit PRRS using meat that has been subject to normal commercial slaughter & meat handling practices.

Van der Linden *et al.* (2003) took meat samples at slaughter from 24 pigs that had been artificially infected with PRRSv 11 days earlier. At this point 12 of the 24 samples were positive for PRRS by virus isolation. After freezing for 10 days at -23°C, samples were tested by virus isolation and RT-PCR. Although only two out of the 24 samples were positive by virus isolation at this point, all but one sample was RT-PCR positive. After 14 days storage at -23°C, two 500g samples of raw muscle meat from each donor pig were thawed, cut into pieces about 7cm³ and fed over 2 days (250g per day) to two recipient pigs. Thus, each of the 48 recipient pigs consumed 500g of raw meat over 2 days. Recipient pigs had been deprived of food for 2 days, and uptake by these animals was classified as good or moderate, and recipient pigs were observed to chew the meat samples. Three days after feeding, 50% of the recipient pigs (24 of 48) were viraemic. Although by 6 days after feeding all 48 recipient pigs were viraemic, the authors were unable to determine whether they had become infected by eating meat or by horizontal transmission from the other recipient pigs. Nevertheless, four of the recipient pigs that became viraemic by day 3 had been fed meat from which virus could not be detected either before or after freezing, suggesting that there was sufficient infectivity in 500g of raw muscle meat to infect recipient pigs even when the titre was below the detection limit of virus isolation. Although the question of infectious dose was not examined in detail, Van der Linden *et al.* (2003) also demonstrated oral transmission of PRRS by feeding 500g meat samples spiked with PRRSv at a titre of $10^{8.8-3.3}$ TCID₅₀ per g.

Magar and Larochelle (2004) found that 19 of 1027 meat samples (1.85%) randomly collected at two Canadian slaughterhouses were positive to PRRSv by RT-PCR, even though only one sample was positive by virus isolation. When meat from 11 of the RT-PCR positive carcasses was fed to pairs of recipient pigs, in quantities from 1.05 kg to 1.8 kg over 2 days, seven of the 11 pairs (63%) became infected. From this study it may be concluded that approximately 1.2% of pigs at slaughter can be expected to have infectious virus in meat, at least under North American conditions, despite the titre of virus being below the threshold of detection by virus isolation.

Both of the above feeding trials exhibited design deficiencies. The large amounts of meat fed to each of the recipient pigs (500g over 2 days in the case of van der Linden *et al.* (2003), and a variable amount from 1.05 to 1.8 kg over 2 days in the case of Magar & Larochelle (2004) leave ample room for speculation as to how this result should be interpreted regarding the level of risk posed by scraps of meat that may be incorporated into pig swill. Both of these studies reported that pigs were reluctant to eat the pork pieces, even though in the case of the Van der Linden *et al.* (2003) study the meat had been cut into pieces just under 2 cm cubes. Apparently in view of its low palatability, the recipient pigs in both trials were starved for 24 hours prior to the feeding event in order to encourage consumption.

However, Molina *et al.* (2009) further investigated the transmissibility of PRRS by ingestion of meat from infected animals, and reported that while 13 of 89 muscle samples (14.6%) were positive for PRRS by RT-PCR at various intervals post infection, in none of these 13 cases did the feeding of 100-200g of meat to individually housed recipient pigs result in infection.

None of the feeding trials described to date have used meat samples that have been subject to normal commercial processing and handling conditions. Post-slaughter bleeding, maturation, refrigeration, and other delays can be expected to have a profound effect on the titre of PRRSv in pig meat before it reaches the point of retail.
References


