Opinion of the Scientific Panel on Animal Health and Welfare on a request from the Commission related on the

"Definition of a BoHV-1-free animal and a BoHV-1-free holding, and the procedures to verify and maintain this status."

EFSA-Q-2005-018

Adopted by the AHAW Panel on 15 December 2005

SUMMARY OF THE OPINION

The Animal Health and Welfare panel of EFSA was invited by the European Commission to issue a scientific opinion on the definition of a BoHV-1 free animal and herd and to describe the requirements needed to reach herd freedom, the role of vaccination and the risks of release of the virus into free holdings, following the adoption of Commission Decision 2004/558/EC, which provides additional measures to ensure that the objectives of Article 9 of Council Directive 64/432/EEC are being met, with limited implications for trade.

A working group was set up by the AHAW scientific panel to develop a report defining the hazard - BoHV-1, describing the experiences of member states that eradicated the virus, the role, if any, of vaccination, methods of diagnosing infected animals, programmes used to monitor BoHV-1 freedom in member states/zones, risk pathways for possible routes of infection and methods to characterise the risk posed by cattle from zones of differing BoHV-1 status. This risk assessment was limited to a release assessment. The group recognised that all control strategies should be based on strict biosecurity measures. The scientific report formed the basis for the discussion that established the conclusions and recommendations that are expressed in this opinion.

While most BoHV-1 infections are subclinical, severe cases of IBR are associated with significant welfare problems. Virus is mainly spread between animals in close contact with little evidence of aerosol spread over distances greater than a few meters, or by fomites. Semen and embryos may carry the virus and are recognised to pose a risk.

Initial programmes to eliminate BoHV-1 in Europe were based on strict biosecurity measures and culling of test-positive animals. More recently plans have also incorporated an initial phase of control using vaccines that allow differentiation of the animal's response to vaccine virus from its response to field virus (DIVA vaccines). This phase aims at reducing the number of newly infected animals, facilitating culling in the final phase of eradication.

Controls intended to obtain or maintain regional BoHV-1 free status with vaccination limit movement of cattle from herds of lesser status that are not officially recognised by EU regulations into those regions. The value of private or voluntary schemes in assuring freedom of cattle from BoHV-1 infections may vary with the controls employed.

The following answers to the questions posed in the mandate were derived from the risk assessments carried out by the group. An animal free from BoHV-1 infection was defined as follows.

The BoHV-1 free status of an animal may be ascertained more accurately if it has not been vaccinated. Non-vaccinated animals can be tested by the more sensitive gB-blocking ELISAs.

Taking into account the specificity and sensitivity of diagnostic tests, the epidemiological characteristics of BoHV-1 infection and the efficiency of surveillance programmes an animal can be considered to be free from BoHV-1 infection if it is not showing clinical signs of IBR/IPV/IPB and it meets one of the following criteria:

a) It has been subjected to a specific protocol** that provides a sufficient probability (99.98 %*) that the animal is not infected, or

b) It originates from a BoHV-1 free herd in a BoHV-1 free zone where the applied surveillance programme provides a sufficient probability (99.8%*) that herds are not infected.

The requirements for a bovine herd to be qualified as free from BoHV-1 infection are conditional on:

a) All infected animals have been removed and

b) It follows biosecurity measures that prevent introduction of BoHV-1 by any means and either:

c) It must participate in a specific protocol** providing a sufficient probability that infection is not present, or

d) It is in a free zone, where the applied surveillance programme provides a sufficient probability (99.8%*) that herds are not infected.

* *Based on the calculations for a free zone (see the scientific report)*

** *A protocol includes reference to repeat testing, vaccination, status of herd/region, quarantine, etc and also the time period of "freedom" from BoHV-1*

The testing requirements and equivalent strategies to be used for qualifying herds/region and animals as free from BoHV-1 infection are described in the Scientific report.

TABLE OF CONTENTS

1. TERMS OF REFERENCE

1.1. Background

Articles 9 and 10 of Council Directive 64/432/EEC[1], which was updated by Directive 97/12/EC, provide for the possibility to grant additional guarantees in support of an approved eradication programme or free status attained in relation to diseases listed in Annex E (II) to that Directive. So far such additional guarantees are only laid down for Aujeszky's disease and Infectious Bovine Rhinotracheitis (IBR). IBR is one of the clinical expressions of an infection with the Bovine Herpes Virus-1 (BoHV-1).

The guarantees are to be granted when a Member State has introduced for all or part of its territory a compulsory national control programme complying with certain criteria and where it can demonstrate a steady progress towards control and eradication of disease concerned.

While there are 5 Member States or regions thereof recognised as free from IBR in accordance with Article 10, Germany is currently the only Member State with an approved programme (Decision 2004/558/EC[2]). The eradication measures for BoHV-1 in that Member State follow the recommendations of the Terrestrial Animal Health Code of the OIE and are complemented by the use of marker vaccines as recommended by the report of the Scientific Committee on Animal Health and Animal Welfare (SCAHAW) of 25/10/2000[3].

Certain Member States introduced voluntary or sector-supported programmes for the eradication of IBR which are based on different criteria, notably in relation to the use of marker vaccines and discriminatory tests. Although individual holdings in such Member States may have a IBR-status similar to holdings under an approved programme, the non-compulsory nature of the control measures and the lack of guarantees provided by the competent authorities, for example the notifiability of the disease, complicate the recognition of these voluntary programmes as being equivalent.

Following the adoption of Decision 2004/215/EC[4], which applied to Germany the additional guarantees for IBR, as they were granted since the adoption of Decision 95/109/EC[5], problems were encountered in relation to intra-Community trade in bovine animals originating in Members States of different status with regard to IBR due to the prevention of cattle of lower IBR status entering Germany.

Consequently, the Commission adopted Decision 2004/558/EC, which provides derogations and additional measures to ensure that the objectives of Article 9 of Directive 64/432/EEC are being met with limited implications for trade.

1.2. Mandate

In view of the above, the Commission asks the European Food Safety Authority:

1. To issue a scientific opinion on:

- a definition for an animal free from BoHV-1-infection.
- the requirements for a bovine herd to be qualified as free from BoHV-1-infection;

2. To describe in detail:

- the testing requirements and, if appropriate, the equivalent alternative strategies to be used for qualifying the herds as free from BoHV-1-infection;

---

1 OJ 121, 29.7.64, p. 1977/64. Directive as last amended by Regulation (EC) No 21/2004 (OJ L 5, 9.1.2004, p. 8.)
2 OJ L 249, 23.7.2004, p.20.
3 http://europa.eu.int/comm/food/fs/sc/scah/out49_en.pdf
4 OJ L 67, 5.3.2004, p. 24. Decision repealed by Decision 2004/558/EEC
5 OJ L 79, 7.4.1995, p.32. Decision repealed by Decision 2000/502/EC (OJ L 200, 8.8.2000, p. 62.)

- the role of vaccination, notably by the use of marker vaccines, in an eradication programme for BoHV-1-infection;
- the risks of introduction of the BoHV-1 into a free holding.

1.3. Scope of the Report

The recognition of an official regional or national programme to control and eradicate Infectious Bovine Rhinotracheitis (IBR) and consequent granting of Article 9 or 10 of Directive 64/432/EEC status by the European Commission has caused concerns associated with the trade of cattle into such regions or member states due to the potential spread of the causative virus. This report attempts to define the risks that infected animals may pose if moved into IBR free, or aspiring to be free, herds and also to describe the conditions that are likely to give rise to the highest probability of freedom from IBR.

The working group agreed that the scope of the report should consider infections with BoHV-I virus not just the clinical entity of Infectious Bovine Rhinotracheitis. Socio-economic factors associated with infections by the virus are not considered. As there is no evidence that BoHV-I virus poses a risk to human health, food safety related aspects of infections were not considered.

Based on what is requested in the mandate the risk assessment in this report is limited to a qualitative release assessment. The release assessment includes all events related to a potential release of BoHV-1 as a consequence of animal trade between Member States. The release assessment was considered to end when the animals reach the destination farm (See Fig 1, pg. 13).

When considering control programmes, unless otherwise stated the term “vaccinated animals” refers to animals vaccinated with a “marker” vaccine.

All off-farm movements of animals were considered to be official i.e. legal - the consequences of illegal acts are not considered.

The properties of the virus are considered initially. The history of the control of IBR in Europe, methods to diagnose infected animals and surveillance strategies are considered subsequently. Pathways associated with release of the virus are assessed. And finally freedom from IBR was considered in terms of “probability of freedom” rather than in terms of absolute freedom.

2. RISK ASSESSMENT

2.1. Data Collection

2.1.1. Hazard Characterisation

CONCLUSIONS

- Infections of the majority of *Bovidae* with BoHV-1 are mild to inapparent. Although seroconversion is a reliable marker of infection, the latent nature of the infection and the associated spontaneous virus reactivation means that an infected animal must be considered infective for the rest of its life.
- The majority of transmission is by contact or short range aerosol spread and most of the other forms of transmission may be controlled by adherence to established biosecurity measures.
- Although BoHV-1 will infect most *Bovidae, Suidae* and *Camelidae*, only members of the Bovinae are considered of significance in the epidemiology of IBR/IPV/ IBP.
- Vaccination will significantly reduce transmission risks in an infected herd and, although it will not prevent infection, marker vaccines are available to discriminate between vaccinated and field virus infected animals.

RECOMMENDATIONS

- Freedom from BoHV-1 infection can only be established and maintained by the culling (test and removal) of field virus-infected Bovinae and by the adherence to biosecurity measures applied to breeding, trade and husbandry activity.
- Although the available evidence shows that BoHV-1 aerosol transmission is limited to a few meters, due to evidence that BoHV-1 may be excreted in faeces, it is recommended that slurry from acutely infected animals should not be spread on pasture contiguous with that grazed by susceptible cattle.
- Steps should be taken to ensure that the core skills for the early recognition of IBR are acquired by stock-keepers and veterinarians.
- When cattle originate from a herd that has not a BoHV-1 control programme they should not be unloaded from vehicles at staging points.
- DIVA vaccination strategies should be part of an eradication concept in farms/zones with a high BoHV-1 prevalence.

2.1.2. Control / Eradication

CONCLUSIONS

DIVA-vaccines have been demonstrated to be efficacious and safe for use in control and eradication programmes of BoHV-1, and can thus contribute to regions/countries becoming free of BoHV-1. Much of the same data as above can be found in a report from the SCAHAW from 2000; "Bovine Herpesvirus 1 (BHV1) marker vaccines and the accompanying diagnostic tests", and can be found on internet address: http://europa.eu.int/comm/food/fs/sc/scah/out49_en.pdf

Considering the many similarities between Suid herpesvirus - 1 (SuHV-1) and BoHV-1, and the previous experience with SHV-1 vaccination programmes, it is likely that a consistent zone-wide vaccination programme will result in a strong decline in the number of cattle and herds infected with BoHV-1 in that zone.

RECOMMENDATIONS

- All control strategies should be based on strict biosecurity measures
- Cattle vaccinated with conventional vaccines should be considered as infected animals.
- Countries or regions that are free of BoHV-1 infection should not vaccinate.
- If the prevalence of the virus in a herd or zone is low, test and removal procedures should be used to eliminate the virus from that herd or zone.
- If the prevalence is moderate to high in a zone or farm that aims to become free of BoHV-1, the first steps of eradication should be based on the use of DIVA vaccination to decrease the prevalence of infected animals possibly followed by test-and-removal procedures
- The likelihood of a region becoming free of BoHV-1 is higher when DIVA vaccination is applied to a zone instead of a single farm.
- When BoHV-1 eradication is attempted vaccinated animals should not be allowed to trade freely without further controls.

2.1.3. Diagnosis

CONCLUSIONS

– The BoHV-1 free status of an animal may be ascertained more accurately if it has not been vaccinated. Non-vaccinated animals can be tested by the more sensitive gB-blocking ELISAs. Moreover, VNT or the new indirect ELISAs can be used as a confirmatory test. Additionally, indirect ELISAs allow the sensitive and specific detection of BoHV-1 antibodies in bulk milk samples from non vaccinated herds.

– The BoHV-1 free status of a single animal vaccinated with a gE-deleted BoHV-1 marker vaccine can only be determined using gE-antibody blocking-ELISAs. Due to the sensitivity values of the available gE-antibody tests false negative results do occur more often than with conventional test systems.

– Some fresh sera (not frozen and not heat-inactivated) may give a weak false positive response in both gB- and gE-blocking ELISAs

– Only a limited number of reference serum samples is available to be used for validation and harmonization of test systems for the detection of BoHV-1 antibodies.

– PCR is increasingly used in routine diagnosis. However these tests are not yet officially (i.e. OIE) validated for trading purposes. Therefore the level of harmonization of the results is not known at the moment.

RECOMMENDATIONS

– Each animal selected to ascertain the BoHV-1 free status without further epidemiological information should be unvaccinated and should originate from a certified BoHV-1 free farm. Serology can then be performed by the most sensitive tests including confirmatory tests (gB-blocking ELISAs, indirect ELISAs, and 24 h VNT).

– Member States should ensure that the diagnostic sensitivity should not be reduced by the level of pooling of samples. Standard sera should act as controls.

– To ascertain the BoHV-1 free status of a marker-vaccinated animal, requirements in addition to a negative serological test result are required (more epidemiological data of the herd, obligatory vaccination of the complete herd, usage of gE ELISAs as a “herd

test"). Due to the fact that gE-seroconversion is often late, quarantine intervals of more than 28 days (a minimum of 35 days is recommended) should be considered.

- Only limited amounts of EU1, EU2 and EU3 standard sera are still available. There is need to prepare a new extended panel of critical lyophilized serum (and milk) samples taken from infected as well as from vaccinated or vaccinated and subsequently infected animals. This panel of primary standards (gold standards) should be used and possibly distributed by the responsible laboratories at a national level. The primary standards should be used to validate newly developed tests and to harmonise tests between responsible laboratories at a national level.
- Inter-laboratory proficiency comparisons in the EU should be held on a regular basis to get insight into performance of diagnostic laboratories.
- Each Member State should nominate a reference Laboratory for IBR in order to harmonise the control procedures.
- In addition, an Evaluation Panel should be prepared to be used by the reference laboratories to verify the performance characteristics of test kits batches (indirect-, gB-blocking-, gE-blocking ELISAs) used for routine laboratory diagnosis (see Report of the Second FAO/IAEA/OIE Consultants Meeting on "OIE Guidelines for Validation and Certification of Diagnostic Assays for Infectious Animal Diseases").
- The PCR is increasingly used in routine diagnosis. In order that this method is generally accepted, an inter-laboratory comparative test should be organized. Appropriate measures should be taken according to the results;
- Laboratories carrying out diagnostics for BoHV-1 should ensure that the standard serum EU2 or a secondary (national) reference standard ("working standard") from it is identified as being positive.

RECOMMENDATIONS FOR FUTURE RESEARCH

- Serology on blood samples from DIVA vaccinated animals can only be performed by the relatively less sensitive gE-blocking ELISAs. A confirmatory test for the presence of gE-specific antibodies using different protocols does not exist. The development of an independent and sensitive confirmatory test would be an important advance.
- A sensitive and specific milk test for the detection of gE-antibodies is not available. Therefore, the development of a reliable milk assay for the detection of BoHV-1-gE-antibodies is necessary.

2.1.4. Monitoring or Surveillance

CONCLUSIONS

- Member States or zones which were recognised by the European Commission under Article 9 and 10 of Directive 64/432/EC have been already implementing IBR monitoring or surveillance programmes for many years. Geographical situation, breeding methods, prevalence at start of the programme, testing methods, test intervals, place of sampling (at farm or at slaughter), number and age of tested animals per herd varies significantly between the different countries and zones.
- The requirements for maintaining the BoHV-1 free status and for restoring the free status after an outbreak vary significantly between the different Member States.

RECOMMENDATIONS

- Minimum requirements should be laid down, not only for article 9 status (Decision 2004/558/EC) but also for achieving and for maintaining article 10 status of Directive 64/432/EC.

2.2. Risk Pathways

CONCLUSIONS OF THE RISK ASSESSMENT

The outcomes of any risk assessment are affected by the assumptions that are made during the assessment. For this assessment, the consequences of illegal acts were disregarded, and it was also assumed, that biosecurity measures to prevent introduction or spread of BoHV-1 at any level were correctly implemented and complied with. To our knowledge, there were no data available concerning the incidence of illegal acts and about the incorrect implementation and compliance with biosecurity measures. Therefore, it was not possible to include these situations in the risk assessment. It is recognised that the probabilities as presented in Tables 7 to 11 (see scientific report) may not reflect the actual situation and may underestimate the probability of release of BoHV-1 into a free herd if the assumptions for the risk assessment are not met.

Based on the assumptions described above and in the tables, the likelihood of release of BoHV-1 into a free herd via the introduction of a new animal is considered **medium** if the animal originates from a herd located in a country or zone without disease control programme, and either without vaccination or with vaccination without marker vaccine (Table 7). The likelihood that BoHV-1 positive animals are not detected during the quarantine period is considered negligible, but a new infection during the quarantine period, at collection centres, or during transport cannot be excluded. This infection may then lead to a release of BoHV-1 in the herd of destination.

The likelihood of release of BoHV-1 into a free herd via the introduction of a new animal is considered **very low using a gB ELISA** and **low using a gE ELISA** if the animal originates from a herd participating in a voluntary BoHV-1 control programme (Table 8). The reasoning behind this is that the voluntary nature of the disease control programme makes it more difficult to control the virus within the zone, and therefore re-introduction of the virus into the herd of origin is more likely to occur. If gE DIVA vaccines are used, the less sensitive gE blocking ELISAs need to be used for surveillance purposes, which increases the likelihood of false-negative test results.

There are a few important assumptions for this conclusion. Biosecurity measures on-farm, during the quarantine period, at the collection centres, and during transport need to be properly implemented and complied with. If new animals are introduced during the quarantine period, if animals infected with BoHV-1 are collected at the same place as free animals, and if trucks are not properly cleaned between transports, the likelihood of infection during these periods is increasing and consequently, the likelihood of release will increase as well.

The likelihood of release of BoHV-1 into a free herd via the introduction of a new animal is **negligible** if the animal originates from a herd in a country or zone with Art 9 or 10 status of Council Directive 64/432/EC (Table 9, 10 and 11). The reasoning behind this is that mandatory surveillance programs are in place, which document the herd status on a regular basis under current risk management measures. Cattle coming from a herd in an Art 9 country or zone are additionally placed in quarantine and are tested. The sequence of these measures leads to a negligible likelihood of BoHV-1 release.

There are a few important assumptions for this conclusion. Firstly, the quality of the surveillance programs needs to be sufficient to detect infected herds. Secondly,

biosecurity measures during isolation, at collection centres and during transport need to be properly implemented. Else, cattle free of BoHV-1 may become infected during these periods and lead to a BoHV-1 release.

In all scenarios, the implementation of biosecurity measures was considered very important. Biosecurity measures are generally recognised, but are often not implemented correctly. Therefore, control of the correct implementation of these measures seems to be a critical point to reduce the likelihood of the release of BoHV-1 into a free herd. Additional regulations may be needed if cattle from countries or regions that do not have an Art 9 or Art 10 status are introduced into free herds to lower to likelihood of BoHV-1 release.

2.3. Risk Characterisation

CONCLUSION AND RECOMMENDATION

There is not a single definition of a BoHV-1 free animal, because the probability that an animal is truly free from BoHV-1 depends on the *a-priori* probability of infection and the quality of the testing protocol applied. The best way to proceed would be 1) define an acceptable probability that an animal is falsely declared BoHV-1-free; 2) establish the a-priori probability of infection in the zone or group of herds participating in a certification scheme; 3) combine 2) with the quality parameters of the testing protocol (if any) to obtain 1).

It is doubtful whether an acceptable probability of 1 in a million is realistic, even for animals in a zone that has been free for BoHV-1 for a long time. An acceptable probability of 1 in 100,000 cannot be achieved for animals in infected regions and requires testing of animals in zones that became recently free from BoHV-1. Without testing, the probability of freedom from BoHV-1 of an animal in the latter zones is comparable with that of an animal from an infected region that went through quarantine. The Risk Manager needs to decide the level of Probability that is acceptable.

3. Proposed definition of BoHV-1 free herd and BoHV-1 free animal

Taking into account the sensitivity and specificity of diagnostic tests, the epidemiological characteristics of the BoHV-1 infection and the efficiency of surveillance programmes:

An animal can be considered to be free from BoHV-1 infection if it is not showing clinical signs of IBR/IPV/IPB, and if it meets one of the following criteria:

a) It has been subjected to a specific protocol** that provides a sufficient probability (99.98 % *) that the animal is not infected, or

b) It originates from a BoHV-1 free herd in a BoHV-1 free zone where the applied surveillance programme provides a sufficient probability (99.8 %*) that herds are not infected.

A bovine herd can be classified as free from BoHV-1 infection if:

a) All infected animals have been removed and

b) It follows biosecurity measures that prevent introduction of BoHV-1 by any means and either:

c) It must be subjected to a specific protocol** providing a sufficient probability that infection is not present, or

d) It is in a free zone, where the applied surveillance programme provides a sufficient probability (99.8 %*) that herds are not infected.

** Based on the calculations for a free zone (see scientific report)*

*** A testing protocol includes reference to repeat testing, quarantine, etc and also the time period of "freedom" from BoHV-1*

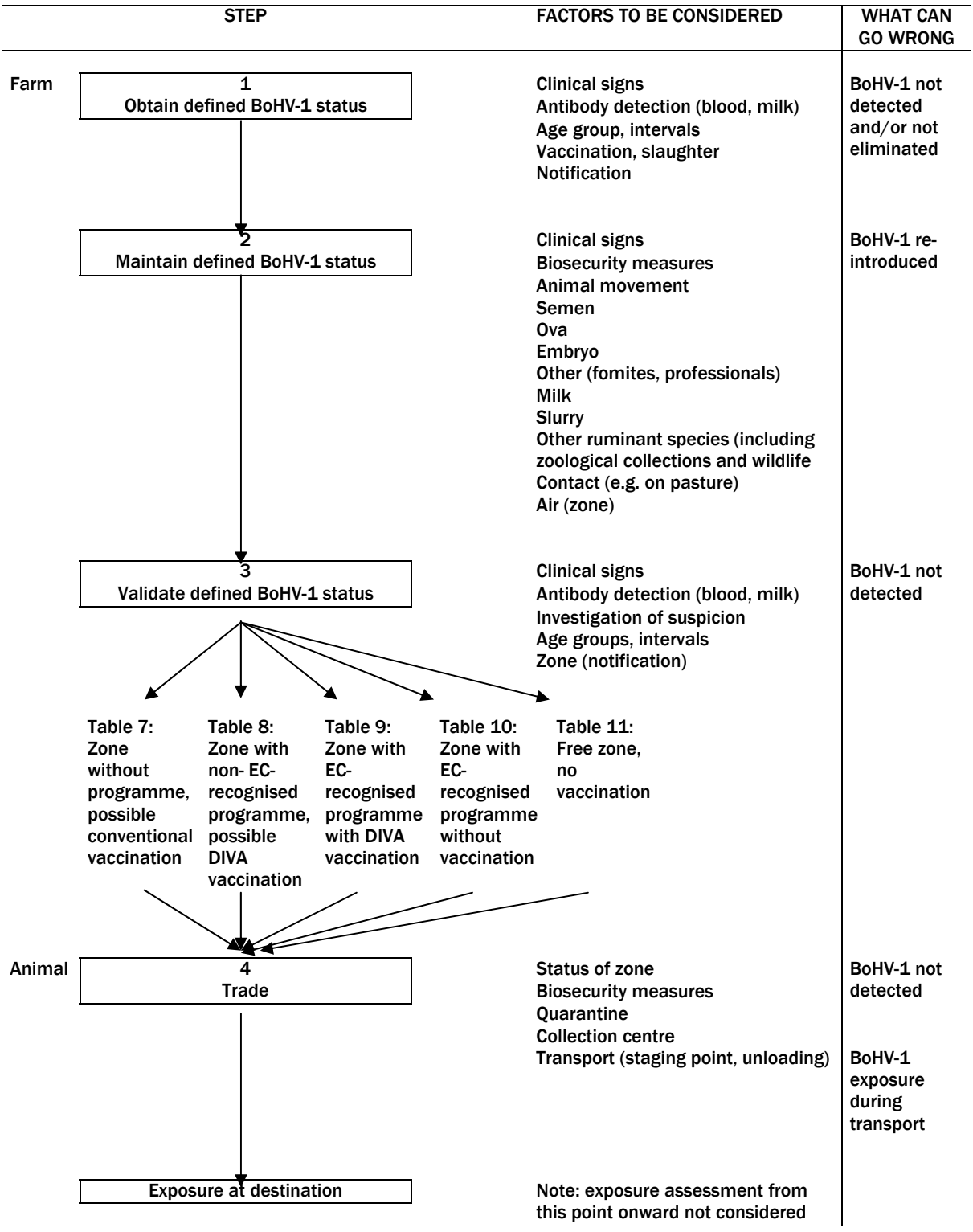

Figure 1: Risk pathway for BoHV-1 release related to intra-community movement with cattle between member states

4. DOCUMENTATION PROVIDED TO EFSA

Letter sent on the 31/01/2005 with ref. SANCO/E2/AEF/rd (04) D/522492 rev.2, from Mr. Bernard Van Goethem, from the Directorate E – Food Safety: plant health and welfare, international questions, Health and Consumer Directorate-General.

5. REFERENCES

All references are available in the scientific report.

6. AHAW Scientific Panel Members

Bo Algers
Department of Animal Environment and Health,
Swedish University of Agricultural Sciences,
Skara,
Sweden

Harry J. Blokhuis
Animal Sciences Group,
Wageningen University and Research Centre,
Lelystad,
The Netherlands

Donald Maurice Broom
Department of Veterinary Medicine,
University of Cambridge,
Cambridge,
United Kingdom

Ilaria Capua
Istituto Zooprofilattico Sperimentale delle Venezie,
Legnaro, Padova,
Italy

Stefano Cinotti
Facolta di Medicina Veterinaria Alma Materstudiorum,
Università di Bologna,
Bologna,
Italy

Michael Gunn
Central Veterinary Laboratory
Young's Cross
Backweston
CoKildare
Ireland

Jörg Hartung
Institute for Animal Hygiene, Animal Welfare and Behaviour of Farm Animals,
University of Veterinary Medicine Hanover,
Hanover,
Germany

Per Have
Danish Institute for Food and Veterinary Research,
Copenhagen,
Denmark

Xavier Manteca Vilanova
School of Veterinary Science,
Universitat Autònoma de Barcelona,
Barcelona,
Spain

David B. Morton
Biomedical Services Unit,
University of Birmingham,

Birmingham,
United Kingdom

Michel Pépin
Laboratoire d'Etudes et de Recherches sur les Petits Ruminants et les Abeilles, Agence Française de Securité Sanitaire des Aliments (AFSSA),
Sophia Antipolis,
France

Dirk Udo Pfeiffer
Royal Veterinary College,
University of London,
London,
United Kingdom

Ronald John Roberts
University of Stirling,
Stirling,
United Kingdom

José Manuel Sánchez Vizcaino
Facultad de Veterinaria,
Universidad Complutense de Madrid,
Madrid,
Spain

Alejandro Schudel
Office International des Epizooties,
Paris,
France

James Michael Sharp
Department of Pathology,
Veterinary Laboratories Agency,
Penicuik,
United Kingdom

Georgios Theodoropoulos
Department of Anatomy and Physiology of Farm Animals,
Faculty of Animal Science,
Agricultural University of Athens,
Athens,
Greece

Philippe Vannier
Poultry and Swine Research Laboratory,
Agence Française de Securité Sanitaire des Aliments (AFSSA),
Ploufragan,
France

Marina Verga
Facoltà di Medicina Veterinaria,
Università di Milano,
Milano,
Italy

Martin Wierup
Department of Biomedical Sciences and Veterinary Public Health,
Swedish University of Agricultural Sciences,

Uppsala,
Sweden

Marion Wooldridge
Centre for Epidemiology and Risk Analysis,
Veterinary Laboratories Agency,
Weybridge,
United Kingdom

7. ACKNOWLEDGEMENTS

The working group drafted the scientific risk assessment, which was then reviewed and revised by Panel. The working group was chaired by Dr. Michael Gunn on behalf of the AHAW Panel. The members of the working group were:

- Dr. Michael Gunn (Chairman), Dr. Ernst Stifter , Dr. J.A. Kramps, Dr. Malcom Banks, Dr. Martin Beer, Dr. Peter Wagner, Dr. Katherine Stärk, Dr. Manon Schuppers, Dr. Pierre Kerkhofs, Prof. F.Schelcher, Prof. J.A. Stegeman and Prof. Dr. J.T. van Oirschot