REPORT OF THE MEETING OF THE OIE AD HOC GROUP TO REVIEW THE BOVINE SPONGIFORM ENCEPHALOPATHY CHAPTER IN THE OIE TERRESTRIAL ANIMAL HEALTH CODE

Paris, 22-24 September 2003

The OIE ad hoc Group to review the bovine spongiform encephalopathy (BSE) chapter in the OIE Terrestrial Animal Health Code (referred to in brief as “the ad hoc Group”) met at the OIE Headquarters from 22 to 24 September 2003.

The members of the ad hoc Group and other participants are listed in Appendix I. The Agenda adopted is given in Appendix II.

On behalf of Dr B. Vallat, Director General of the OIE, Dr A. Thiermann, President of the OIE Terrestrial Animal Health Standards Commission, welcomed the participants and thanked them for their willingness to work on some essential issues. He brought to the attention of participants the discussions on bovine spongiform encephalopathy (BSE) at the 2003 General Session, including the requests by Member Countries for a simplification of the BSE country categorisation system.

The ad hoc Group noted that the OIE needed to continue to work closely with other international organisations such as the World Health Organization (WHO) to address animal and human health matters in the BSE chapter. Dr Thiermann described the collaborative work the OIE was engaged in with Codex in the OIE’s new mandate on animal production food safety, to address gaps and avoid duplicating international standards in this area. He also explained that the OIE is working with the WHO on the human health issues. The ad hoc Group proposed to the Director General to maintain this cooperation in order to retain a well-balanced Terrestrial Animal Health Code (referred to in brief as the “Terrestrial Code”).

Some recent advances in the understanding of the infectivity of BSE were provided by Dr D. Matthews (see Appendix III) and they were used as a reference to revise the current Terrestrial Code.

The ad hoc Group reiterated its position regarding references to other transmissible spongiform encephalopathies (TSEs) in the BSE chapter. It believed that it was necessary to retain these references to other TSEs, which remained relevant to theories of the origin of the BSE and concerns that sheep may have become infected with BSE. It emphasised that other TSEs should only be considered in the context of the risk they posed to BSE in cattle.
The *ad hoc* Group discussed the issue of simplifying the BSE categorisation. First of all, the Group examined options for reduction of country status categories in the BSE chapter from five to three. Options for naming the categories were discussed, and included “negligible risk”, “controlled risk” (where a BSE risk had been identified or BSE cases had been detected and control measures were clearly in place) and “unclassified” (where control measures were not clearly in place, or where there were insufficient data to categorise the country). In the context of simplification of the *Terrestrial Code*, especially with respect to assisting countries in the current “provisionally free” category to enter a category of “negligible risk”, the *ad hoc* Group believed that it was appropriate to emphasise the use of surveillance as specified in Appendix 3.8.4. to supplement data provided by risk assessments. This would enable surveillance data to be taken into account by any group tasked with evaluating categorisation as “negligible risk”, in addition to data available from the risk assessment, together with dates of implementation of control measures. The *ad hoc* Group considered that additional targeted surveillance may allow a judgement on whether entry to a “negligible risk” category was possible in a period of time shorter than that specified in the *Terrestrial Code*. In addition, should some countries have insufficient data for an appropriate risk assessment, or should a country identify cases before there has been any implementation of statutory controls, the surveillance could again assist in either categorisation or defining a timetable for re-categorisation.

The *ad hoc* Group revised some articles in the *Terrestrial Code* including the Appendix on surveillance, on the basis of the latest scientific information and comments from Argentina, Australia, Canada and the United States of America (USA), which had been examined in the Terrestrial Animal Health Standards Commission (referred to in brief as the “Code Commission”) meeting in July 2003.

Amendments proposed by the *ad hoc* Group were as follows:

1) In Article 2.3.13.2, the terms “reviewed annually” were introduced as any risk assessment should take into account the current or revised conditions, and the latest scientific information. Regarding potential factors to be identified for risk assessment, reference to importation of embryos/oocytes was deleted because *in vivo* derived bovine embryos are regarded as a safe commodity and embryos from other species do not pose a direct risk of BSE in cattle.

2) Articles 2.3.13.3 and 2.3.13.5, regarding the treatment of affected cattle and their progeny, were revised to improve their consistency with other articles and to include more appropriate management procedures such as permanent identification and movement controls.

3) In Articles 2.3.13.5 and 2.3.13.6, regarding the calculation of the BSE incidence rate, an increased level of surveillance which complies with the combined requirements of Articles 3.8.4.2 and 3.8.4.3 was added to increase the reliability of the outcome. The cut-off limit was raised from one case per million to two cases per million taking into account the implementation of passive and active surveillance.

4) Article 2.3.13.8 was repositioned to follow Article 2.3.13.1 (to emphasise the need for risk-based decision-making) and modified to delete references to tallow and dicalcium phosphate, and to add a reference to restricted commodities. The *ad hoc* Group recommended that tallow and dicalcium phosphate be deleted from the list of safe commodities after considering recent scientific evidence from the Scientific Steering Committee of the European Union (EU) and comments from the USA and the EU.
5) In Article 2.3.13.19 the lists of specific risk materials (SRMs) relating to moderate risk and high risk countries were combined; references to dorsal root ganglia and trigeminal ganglia were deleted as they were considered to fall within the term ‘skull and vertebral column’; thymus and spleen were considered safe while tonsils and intestine from cattle of all ages were considered to be unsafe for trade.

6) Appendix 3.8.4.

   a) In “Introduction”, text was added to reinforce the importance of the risk assessment in determining country status and that surveillance should focus on the sub-population containing cattle displaying clinical signs consistent with BSE.

   b) The text was revised to give more guidance in understanding Table 1. The ad hoc Group stressed that the requirements under Article 3.8.4.2 should be met first and, in the case of a shortfall, those of Article 3.8.4.3 should be met.

   c) In considering the scale of surveillance required in accordance with Article 3.8.4.3, empirical evidence suggested that many more animals would need to be tested in order to detect BSE in this sub-population in comparison with the effectiveness of surveillance of clinically affected animals (Article 3.8.4.2). Nevertheless, this population may be easier to target, and would serve as an appropriate reinforcement of surveillance of clinical cases.

Joint meeting

On the third day of the meeting, participants attended a joint meeting with the OIE ad hoc Group for evaluation of country status for BSE in accordance with the Terrestrial Code. The joint meeting discussed ways of dealing with other TSEs in the risk assessment and with the requirement for a 7 year surveillance period for provisionally free status recognition.

The following issues were discussed:

. the requests of Member Countries for a simplified BSE categorisation system;

. clarification of the consideration of other TSEs in the risk assessment; and

. strengthening the Appendix on surveillance.

Both ad hoc Groups agreed that, regarding the evaluation of provisionally free countries, the required surveillance period of 7 years had a sound scientific basis and any shortening of that period needed to be balanced by appropriate surveillance for the period of implementation, to provide an equivalent level of assurance.

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.../Appendices
MEETING OF THE OIE AD HOC GROUP
TO REVIEW THE BOVINE SPONGIFORM ENCEPHALOPATHY CHAPTER IN THE
OIE TERRESTRIAL ANIMAL HEALTH CODE

Paris, 22-24 September 2003

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OIE ad hoc Group to review the BSE chapter in the OIE Terrestrial Animal Health Code/September 2003
MEETING OF THE OIE AD HOC GROUP
TO REVIEW THE BOVINE SPONGIFORM ENCEPHALOPATHY CHAPTER IN THE
OIE TERRESTRIAL ANIMAL HEALTH CODE

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Adopted Agenda

1. Update on significant scientific advances on BSE and its relationship with other TSE’s
2. Discussion on the 2003 Terrestrial Animal Health Code Chapter and Appendix on BSE
3. Any other issues
UPDATE ON SIGNIFICANT SCIENTIFIC ADVANCES ON BOVINE SPONGIFORM ENCEPHALOPATHY BY DR D. MATTHEWS

Dr D. Matthews provided an update on two key experiments that were of relevance to the chapter on bovine spongiform encephalopathy (BSE).

The attack rate studies at the Veterinary Laboratories Agency were intended to determine the minimum infectious dose (LD50) following oral challenge. The first study had exposed four month old calves to doses ranging from 300g to 1g of BSE infected bovine brain. As this study had not reached an end point, with 7/10 calves dying of BSE in the 10g and 1g challenge groups, a further study had exposed calves to doses as low as 0.001g by mouth. Although still in progress, it was clear that doses as low as 0.01g had successfully infected calves. The additional data suggested that the ID50 could still be around 0.35g. Cross contamination of feed with such small amounts of mammalian meat-and-bone meal (MBM) were clearly difficult to prevent or detect.

In the continuing pathogenesis studies, an additional 12 months of data since the last BSE ad hoc Group had strengthened the case for reconsideration of the list of tissues that should be defined as specific risk materials (SRMs). Central nervous system (CNS) tissues collected at 18, 22 and 26 months post oral exposure, and inoculated intracerebrally into calves, had not transmitted BSE to the challenged calves. CNS collected at 32 months post infection had killed the group of challenged calves with a mean incubation of 24 months. Although impossible to precisely define the time of entry of infectivity to the CNS on the basis of such limited data, the results do indicate that entry is later than seen in sheep or murine scrapie where it is traditionally considered to appear at approximately 50% of the incubation period.

No further cattle inoculated with tonsillar tissue had succumbed to BSE (1/5 collected at 10 months post-inoculation), and the remaining animals had now survived 12 months beyond the expected incubation period of 45 months. It remained possible that this result was due to residual oral inoculum lodged in the palatine tonsil used as inoculum. No infectivity had been detected in thymus collected during the pathogenesis study.

Nictitating membrane from naturally infected cattle, collected at the point of clinical disease, had also transmitted following intracerebral challenge of cattle, but once again the results were contradictory. The single calf to die had succumbed with an incubation of 31 months, but the remaining 4 cattle remained alive at 42 months post-inoculation.

There was still no evidence of infectivity in pooled muscle collected at 32 months post-inoculation (at a time when the CNS was both infectious and positive by immunohistochemistry). That assay had now been in progress 81 months. Similarly spleen was negative at 57, 62, 55, 54 months post challenge for tissues collected at 6, 10, 18, 26 months post-inoculation. This result reinforced earlier results where either pooled spleen or pooled peripheral lymph nodes from naturally infected cattle had failed to transmit to following intracerebral challenge of calves after a study lasting 110 months. Although the presence of infectivity could not be excluded, if present, it had to be at a titre of <10-1 i.c. LD50/g.
Appendix III (contd)

A summary of BSE in sheep pathogenesis studies indicated that in susceptible sheep, of genotype ARQ/ARQ, there was widespread distribution of infectivity within the gastrointestinal tract and lymphoid tissues, especially by the clinical phase of disease. In partially or fully resistant sheep (ARQ/ARR or ARR/ARR), there was no evidence of infectivity or immunostaining in the same range of tissues at 22 months post infection. Remaining animals were clinically healthy at 71 months post challenge.
CHAPTER 2.3.13.

BOVINE SPONGIFORM ENCEPHALOPATHY

Article 2.3.13.1.

The recommendations in this Chapter are intended to manage the human and animal health risks associated with the presence of the bovine spongiform encephalopathy (BSE) agent in cattle (*Bos taurus* and *B. indicus*) only.

Article 2.3.13.1(bis)

The following commodities may be safely traded:

1. without BSE related restrictions and regardless of the BSE status of the country:
   a. milk and milk products
   b. semen and *in vivo* derived cattle embryos collected and handled in accordance with the recommendations of the International Embryo Transfer Society
   c. hides and skins (excluding hides and skins from the head)
   d. gelatin and collagen prepared exclusively from hides and skins (excluding hides and skins from the head)

2. subject to the prescribed conditions relating to the BSE status of the cattle population of the exporting country or zone:
   a. cattle
   b. fresh meat and meat products
   c. gelatin and collagen prepared from bones
   d. tallow and tallow derivatives, and dicalcium phosphate

Article 2.3.13.2.

The BSE status of the cattle population of a country or zone can only be determined on the basis of the following criteria:

1) the outcome of a risk assessment reviewed annually identifying all potential factors for BSE occurrence and their historic perspective, in particular:
   a) the potential for introduction and recycling of the BSE agent through consumption by cattle of *meat-and-bone meal* or *greaves* of ruminant origin;
   b) importation of *meat-and-bone meal* or *greaves* potentially contaminated with a transmissible spongiform encephalopathy (TSE) or feedstuffs containing either;
   c) importation of animals or embryos/oocytes (other than cattle embryos described in Article 2.3.13.8.) potentially infected with a TSE;
Appendix IV (contd)

d) epidemiological situation concerning all animal TSE in the country or zone;

e) extent of knowledge of the population structure of cattle, sheep and goats in the country or zone;

f) the origin and use of ruminant carcasses (including fallen stock), by-products and slaughterhouse waste, the parameters of the rendering processes and the methods of animal feed manufacture;

2) on-going awareness programme for veterinarians, farmers, and workers involved in transportation, marketing and slaughter of cattle to encourage reporting of all cases of neurological disease in adult cattle;

3) compulsory notification and investigation of all cattle showing clinical signs compatible with BSE;

4) a BSE surveillance and monitoring system with emphasis on risks identified in point 1) above, taking into account the guidelines in Appendix 3.8.4.; records of the number and results of investigations should be maintained for at least 7 years;

5) examination in an approved laboratory of brain or other tissues collected within the framework of the aforementioned surveillance system.

Standards for diagnostic tests are described in the Terrestrial Manual.

Article 2.3.13.3.

BSE free country or zone

The cattle population of a country or zone may be considered free of BSE should the following conditions be met:

1) a risk assessment, as described in point 1) of Article 2.3.13.2., has been conducted and it has been demonstrated that appropriate measures have been taken for the relevant period of time to manage any risk identified;

2) either:

a) there has been no case of BSE; and either:

i) the criteria in points 2) to 5) of Article 2.3.13.2. have been complied with for at least 7 years; or

ii) the criteria in point 3) of Article 2.3.13.2. have been complied with for at least 7 years and it has been demonstrated that for at least 8 years no meat-and-bone meal or greaves have been fed to ruminants;

OR

b) all cases of BSE have been clearly demonstrated to originate directly from the importation of live cattle, and the affected cattle as well as, if these are females, all their progeny born within 2 years prior to and after clinical onset of the disease, if alive in the country or zone, are permanently identified, and their movements controlled, and when slaughtered or at death, are completely destroyed. Their last progeny born within 2 years prior to, or after, clinical onset of the disease, if alive in the country or zone, have been slaughtered and completely destroyed; and either:

i) the criteria in points 2) to 5) of Article 2.3.13.2. have been complied with for at least 7 years; or
ii) the criteria in point 3) of Article 2.3.13.2. have been complied with for at least 7 years and it has been demonstrated that for at least 8 years no \textit{meat-and-bone meal} or \textit{greaves} have been fed to ruminants;

OR

c) the last indigenous case of BSE was reported more than 7 years ago,

i) the criteria in points 2) to 5) of Article 2.3.13.2. have been complied with for at least 7 years; and

ii) the feeding of ruminants with \textit{meat-and-bone meal} and \textit{greaves} derived from ruminants has been banned and the ban has been effectively enforced for at least 8 years; and

iii) the affected cattle as well as:

- if these are females, all their progeny born within 2 years prior to and after clinical onset of the disease, if alive in the country or zone, are permanently identified, and their movements controlled, and when slaughtered or at death, are completely destroyed, and

- all cattle which, during their first year of life, were reared with the affected cattle during their first year of life, and which investigation showed consumed the same potentially contaminated feed during that period, or

- where the results of the investigation are inconclusive, all cattle born in the same herd as, and within 12 months of the birth of, the affected cattle if alive in the country or zone, are permanently identified, and their movements controlled, and when slaughtered or at death, are completely destroyed.

\textbf{Article 2.3.13.4.}

\textbf{BSE provisionally free country or zone}

The cattle population of a country or zone may be considered as provisionally free of BSE should the following conditions be met:

1) a risk assessment, as described in point 1) of Article 2.3.13.2., has been conducted and it has been demonstrated that appropriate measures have been taken for the relevant period of time to manage any risk identified;

2) either:

a) there has been no case of BSE; and either:

i) the criteria in points 2) to 5) of Article 2.3.13.2. are complied with, but have not been complied with for 7 years; or

ii) it has been demonstrated that for at least 8 years no \textit{meat-and-bone meal} or \textit{greaves} have been fed to ruminants, but the criteria in point 3) of Article 2.3.13.2. have not been complied with for 7 years;
OR

b) all cases of BSE have been clearly demonstrated to originate directly from the importation of live cattle, and the affected cattle as well as, if these are females, all their progeny born within 2 years prior to and after clinical onset of the disease, if alive in the country or zone, have been permanently identified, their movements controlled, and when slaughtered or at death, are completely destroyed, their last progeny born within 2 years prior to, or after, clinical onset of the disease, if alive in the country or zone, have been slaughtered and completely destroyed; and either:

i) the criteria in points 2) to 5) of Article 2.3.13.2. are complied with, but have not been complied with for 7 years; or

ii) it has been demonstrated that for at least 8 years no meat-and-bone meal or greaves have been fed to ruminants, but the criteria in point 3) of Article 2.3.13.2. have not been complied with for 7 years.

Article 2.3.13.5.

Country or zone with a minimal BSE risk

The cattle population of a country or zone may be considered as presenting a minimal BSE risk should the country or zone comply with the following requirements:

1) a risk assessment, as described in point 1) of Article 2.3.13.2., has been conducted and it has been demonstrated that appropriate measures have been taken for the relevant period of time to manage any risk identified;

2) EITHER:

a) the last indigenous case of BSE was reported more than 7 years ago, the criteria in points 2) to 5) of Article 2.3.13.2. are complied with and the ban on feeding ruminants with meat-and-bone meal and greaves derived from ruminants is effectively enforced, but:

i) the criteria in points 2) to 5) of Article 2.3.13.2. have not been complied with for 7 years; or

ii) the ban on feeding ruminants with meat-and-bone meal and greaves derived from ruminants has not been effectively enforced for 8 years;

OR

b) the last indigenous case of BSE has been reported less than 7 years ago, and the BSE incidence rate, measured using a level of surveillance which complies with the combined requirements of Articles 3.8.4.2. and 3.8.4.3., and calculated on the basis of indigenous cases, has been less than one per million during each of the last four consecutive 12-month periods within the cattle population over 24 months of age in the country or zone (Note: For countries with a population of less than one million adult cattle, the maximum allowed incidence should be expressed in cattle-years.), and:

i) the ban on feeding ruminants with meat-and-bone meal and greaves derived from ruminants has been effectively enforced for at least 8 years;

ii) the criteria in points 2) to 5) of Article 2.3.13.2. have been complied with for at least 7 years;
iii) the affected cattle as well as:

- if these are females, all their progeny born within 2 years prior to and after clinical onset of the disease, if alive in the country or zone, are permanently identified, and their movements controlled, and when slaughtered or at death, are completely destroyed, and

- all cattle which, during their first year of life, were reared with the affected cattle during their first year of life, and, which investigation showed consumed the same potentially contaminated feed during that period, or

- where the results of the investigation are inconclusive, all cattle born in the same herd as, and within 12 months of the birth of, the affected cattle if alive in the country or zone, are permanently identified, and their movements controlled, and when slaughtered or at death, are completely destroyed.

Article 2.3.13.6.

Country or zone with a moderate BSE risk

The cattle population of a country or zone may be considered as presenting a moderate BSE risk if:

1) a risk assessment, as described in point 1) of Article 2.3.13.2., has been conducted, and the other criteria listed in Article 2.3.13.2. are complied with;

2) the BSE incidence rate has been measured using a level of surveillance which complies with the requirements of Appendix 3.8.4. and is:

   a) if based only on surveillance in accordance with Article 3.8.4.2., greater than or equal to, one indigenous case per million and less than or equal to, one hundred indigenous cases per million within the cattle population over 24 months of age in the country or zone calculated over the past 12 months; or

   b) if based on surveillance in accordance with Articles 3.8.4.2., 3.8.4.3. and 3.8.4.4., greater than, or equal to, one case per million and less than, or equal to, two hundred indigenous cases per million within the cattle population over 24 months of age in the country or zone calculated over the past 12 months; or

   c) less than two indigenous cases per million for less than four consecutive 12-month periods (Note: For countries with a population of less than one million adult cattle, the maximum allowed incidence should be expressed in cattle-years);

3) the affected cattle as well as:

   a) if these are females, all their progeny born within 2 years prior to and after clinical onset of the disease, if alive in the country or zone, are permanently identified, and their movements controlled, and when slaughtered or at death, are completely destroyed, and

   b) all cattle which, during their first year of life, were reared with the affected cattle during their first year of life, and, which investigation showed consumed the same potentially contaminated feed during that period, or

   c) where the results of the investigation are inconclusive, all cattle born in the same herd as, and within 12 months of the birth of, the affected cattle, if alive in the country or zone, are permanently identified, and their movements controlled, and when slaughtered or at death, are completely destroyed.
Appendix IV (contd)

Countries and zones where the BSE incidence rate has been less than one indigenous case per million within the cattle population over 24 months of age during each of the last four consecutive 12-month periods, but where at least one of the other requirements to be considered as provisionally free from BSE or as presenting a minimal BSE risk is not complied with, shall be considered as countries or zones with a moderate BSE risk.

Article 2.3.13.7.

Country or zone with a high BSE risk

The cattle population of a country or zone may be considered as presenting a high BSE risk if it cannot demonstrate that it meets the requirements of another category.

Article 2.3.13.8.

Regardless of the BSE status of the exporting country, Veterinary Administrations should authorize without restriction the import or transit through their territory of the following commodities:

1) milk and milk products;
2) semen and in vivo derived cattle embryos collected and handled in accordance with the recommendations of the International Embryo Transfer Society;
3) protein-free tallow (maximum level of insoluble impurities of 0.15% in weight) and derivatives made from this tallow;
4) dicalcium phosphate (with no trace of protein or fat);
5) hides and skins;
6) gelatin and collagen prepared exclusively from hides and skins.

Article 2.3.13.9.

When importing from a BSE free country or zone, Veterinary Administrations should require:

for all commodities from cattle not listed in Article 2.3.13.8

the presentation of an international veterinary certificate attesting that the country or zone complies with the conditions in Article 2.3.13.3. to be considered as free of BSE.

Article 2.3.13.10.

When importing from a BSE provisionally free country or zone, Veterinary Administrations should require:

for cattle

the presentation of an international veterinary certificate attesting that:

1) the country or zone complies with the conditions in Article 2.3.13.4. to be considered as provisionally free of BSE;
2) cattle selected for export are identified by a permanent identification system enabling them to be traced back to the dam and herd of origin and are not the progeny of BSE suspect or confirmed females.
Article 2.3.13.11.
When importing from a country or zone with a minimal BSE risk, Veterinary Administrations should require:
for cattle
the presentation of an international veterinary certificate attesting that:
1) the country or zone complies with the conditions in Article 2.3.13.5. to be considered as presenting a minimal BSE risk;
2) the feeding of ruminants with meat-and-bone meal and greaves derived from ruminants has been banned and the ban has been effectively enforced;
3) cattle selected for export:
   a) are identified by a permanent identification system enabling them to be traced back to the dam and herd of origin and are not the progeny of BSE suspect or confirmed females exposed cattle as described in point 2) b) iii) of Article 2.3.13.5.;
   b) were born after the date from which the ban on the feeding of ruminants with meat-and-bone meal and greaves derived from ruminants has been effectively enforced.

Article 2.3.13.12.
When importing from a country or zone with a moderate BSE risk, Veterinary Administrations should require:
for cattle
the presentation of an international veterinary certificate attesting that:
1) the country or zone complies with the conditions in Article 2.3.13.6. to be considered as presenting a moderate BSE risk;
2) the feeding of ruminants with meat-and-bone meal and greaves derived from ruminants has been banned and the ban has been effectively enforced;
3) cattle selected for export:
   a) are identified by a permanent identification system enabling them to be traced back to the dam and herd of origin and are not the progeny of BSE suspect or confirmed females exposed cattle as described in point 3) of Article 2.3.13.6.;
   b) were born after the date from which the ban on the feeding of ruminants with meat-and-bone meal and greaves derived from ruminants has been effectively enforced.

Article 2.3.13.13.
When importing from a country or zone with a high BSE risk, Veterinary Administrations should require:
for cattle
the presentation of an international veterinary certificate attesting that:
1) the country or zone complies with the conditions in Article 2.3.13.7. to be considered as presenting a high BSE risk;
2) the feeding of ruminants with meat-and-bone meal and greaves derived from ruminants has been banned and the ban has been effectively enforced;

3) all affected cattle as well as:
   a) if these are females, all their progeny born within 2 years prior to and after clinical onset of the disease, if alive in the country or zone, are permanently identified, and their movements controlled, and when slaughtered or at death, are completely destroyed, and
   b) all cattle which, during their first year of life, were reared with the affected cattle during their first year of life, and, which investigation showed consumed the same potentially contaminated feed during that period, or
   c) where the results of the investigation are inconclusive, all cattle born in the same herd as, and within 12 months of the birth of, the affected cattle, if alive in the country or zone, are permanently identified, and their movements controlled, and when slaughtered or at death, are completely destroyed;

4) cattle selected for export:
   a) are identified by a permanent identification system enabling them to be traced back to the dam and herd of origin and are not the progeny of BSE suspect or confirmed females;
   b) were born at least 2 years after the date from which the ban on the feeding of ruminants with meat-and-bone meal and greaves derived from ruminants was effectively enforced.

Article 2.3.13.14.

When importing from a BSE provisionally free country or zone, Veterinary Administrations should require:

for fresh meat (bone-in or deboned) and meat products from cattle

the presentation of an international veterinary certificate attesting that:

1) the country or zone complies with the conditions in Article 2.3.13.4. to be considered as provisionally free of BSE;

2) ante-mortem inspection is carried out on all cattle from which the meat or meat products destined for export originate.

Article 2.3.13.15.

When importing from a country or zone with a minimal BSE risk, Veterinary Administrations should require:

for fresh meat (bone-in or deboned) and meat products from cattle

the presentation of an international veterinary certificate attesting that:

1) the country or zone complies with the conditions in Article 2.3.13.5. to be considered as presenting a minimal BSE risk;

2) ante-mortem inspection is carried out on all cattle from which the meat or meat products destined for export originate;
3) cattle from which the meat or meat products destined for export originate were not subjected to a stunning process, prior to slaughter, with a device injecting compressed air or gas into the cranial cavity or to a pithing process (laceration, after stunning, of central nervous tissue by means of an elongated rod-shaped instrument introduced into the cranial cavity);

4) the fresh meat and meat products destined for export do not contain brain, eyes, spinal cord or mechanically separated meat from skull and vertebral column from cattle over 30 months of age, all of which have been removed in a hygienic manner.

Article 2.3.13.16.

When importing from a country or zone with a moderate BSE risk, Veterinary Administrations should require:

for fresh meat (bone-in or deboned) and meat products from cattle

the presentation of an international veterinary certificate attesting that:

1) the country or zone complies with the conditions in Article 2.3.13.6. to be considered as presenting a moderate BSE risk;

2) the feeding of ruminants with meat-and-bone meal and greaves derived from ruminants has been banned and the ban has been effectively enforced;

3) ante-mortem inspection is carried out on all bovines;

4) cattle from which the meat or meat products destined for export originate were not subjected to a stunning process, prior to slaughter, with a device injecting compressed air or gas into the cranial cavity or to a pithing process;

5) the fresh meat and meat products destined for export do not contain brain, eyes, spinal cord, distal ileum the tissues listed in point 1) of Article 2.3.13.19. nor mechanically separated meat from skull and vertebral column from cattle over 6 months of age, all of which have been removed in a hygienic manner.

Article 2.3.13.17.

When importing from a country or zone with a high BSE risk, Veterinary Administrations should require:

for fresh meat and meat products from cattle

the presentation of an international veterinary certificate attesting that:

1) the country or zone complies with the conditions in Article 2.3.13.7. to be considered as presenting a high BSE risk;

2) the meat destined for export does not contain brain, eyes, spinal cord, distal ileum the tissues listed in point 1) of Article 2.3.13.19., all of which have been removed in a hygienic manner;

3) the meat destined for export, if obtained from animals over 9 months of age, has been deboned and does not contain nervous and lymphatic tissues exposed during a deboning process, all of which have been removed in a hygienic manner;

4) the meat products destined for export are derived from deboned meat and do not contain the tissues listed in point 1) of Article 2.3.13.19. nor nervous and lymphatic tissues exposed during a deboning process, nor mechanically separated meat from skull and vertebral column of bovine animals, all of which have been removed in a hygienic manner;
Appendix IV (contd)

5) a system is in operation enabling the fresh meat and meat products destined for export to be traced back to the establishments from which they are derived;
6) ante-mortem inspection is carried out on all bovines;
7) the cattle from which the meat or meat products destined for export originate:
   a) were identified by a permanent identification system enabling them to be traced back to the dam and herd of origin;
   b) are not the progeny of BSE suspect or confirmed females; and either:
      i) were born after the date from which the ban on the feeding of ruminants with meat-and-bone meal and greaves derived from ruminants has been effectively enforced; or
      ii) were born, raised and had remained in herds in which no case of BSE had been confirmed for at least 7 years;
   c) were not subjected to a stunning process, prior to slaughter, with a device injecting compressed air or gas into the cranial cavity or to a pithing process;
8) the feeding of ruminants with meat-and-bone meal and greaves derived from ruminants has been banned and the ban has been effectively enforced;
9) all affected cattle as well as:
   a) if these are females, all their progeny born within 2 years prior to and after clinical onset of the disease, if alive in the country or zone, are permanently identified, and their movements controlled, and when slaughtered or at death, are completely destroyed, and
   b) all cattle which, during their first year of life, were reared with the affected cattle during their first year of life, and, which investigation showed consumed the same potentially contaminated feed during that period, or
   c) where the results of the investigation are inconclusive, all cattle born in the same herd as, and within 12 months of the birth of, the affected cattle, if alive in the country or zone, are permanently identified, and their movements controlled, and when slaughtered or at death, are completely destroyed.

Article 2.3.13.18.

Ruminant-derived meat-and-bone meal or greaves, or any commodities containing such products, which originate from countries with a minimal, moderate or high BSE risk should not be traded between countries.

Article 2.3.13.19.

1) From cattle originating from a country or zone with a moderate or a high BSE risk, that were at the time of slaughter over 12 months of age, the following commodities, and any commodity contaminated by them, should not be traded for the preparation of food, feed, fertilisers, cosmetics, pharmaceuticals including biologicals, or medical devices: brains, eyes, spinal cord, tonsils, thymus, spleen, intestines, dorsal root ganglia, trigeminal ganglia, skull and vertebral column, and derived protein products derived from the preceding. Food, feed, fertilisers, cosmetics, pharmaceuticals or medical devices prepared using these commodities should also not be traded.
2) From cattle of all ages originating from a country or zone with a moderate or a high BSE risk, the following commodities, and any commodity contaminated by them, should not be traded for the preparation of food, feed, fertilisers, cosmetics, pharmaceuticals including biologicals, or medical devices: tonsils and intestine, and protein products derived from them.

From cattle originating from a country or zone with a moderate BSE risk, that were at the time of slaughter over 6 months of age, the following commodities, and any commodity contaminated by them, should not be traded for the preparation of food, feed, fertilisers, cosmetics, pharmaceuticals including biologicals, or medical devices: brains, eyes, spinal cord, distal ileum, skull, vertebral column and derived protein products. Food, feed, fertilisers, cosmetics, pharmaceuticals or medical devices prepared using these commodities should also not be traded.

3) From cattle, originating from a country or zone with a minimal BSE risk, that were at the time of slaughter over 30 months of age, the following commodities, and any commodity contaminated by them, should not be traded for the preparation of food, feed, fertilisers, cosmetics, pharmaceuticals including biologicals, or medical devices: brains, eyes and spinal cord, skull, vertebral column and derived protein products. Food, feed, fertilisers, cosmetics, pharmaceuticals or medical devices prepared using these commodities should also not be traded.

**Article 2.3.13.20.**

Veterinary Administrations of importing countries should require:

for gelatin and collagen prepared from bones and intended for food or feed, cosmetics, pharmaceuticals including biologicals, or medical devices

the presentation of an international veterinary certificate attesting that the bones came from:

1) a BSE free or provisionally free country or zone, or from a country or zone with a minimal BSE risk; or

2) a country or zone with a moderate BSE risk; and

a) skulls and vertebrae (excluding tail vertebrae) have been excluded;

b) the bones have been subjected to a process which includes all the following steps:

i) pressure washing (degreasing),

ii) acid demineralisation,

iii) prolonged alkaline treatment,

iv) filtration,

v) sterilisation at $\geq 138^\circ C$ for a minimum of 4 seconds,

or to an equivalent process in terms of infectivity reduction.

**Article 2.3.13.21.**

Veterinary Administrations of importing countries should require:

for tallow and dicalcium phosphate (other than protein-free tallow as defined in Article 2.3.13.8.) intended for food, feed, fertilisers, cosmetics, pharmaceuticals including biologicals, or medical devices
Appendix IV (contd)

the presentation of an international veterinary certificate attesting that it originates from:

1) a BSE free or provisionally free country or zone, or

2) a country or zone with a minimal BSE risk, and it originates from cattle which have been subjected to an ante-mortem inspection for BSE with favourable results and has not been prepared using the tissues listed in point 3 of Article 2.3.13.19., or

3) a country or zone with a moderate BSE risk, and it originates from cattle which have been subjected to an ante-mortem inspection for BSE with favourable results and has not been prepared using the tissues listed in point 2 of Article 2.3.13.19.

Article 2.3.13.22.

Veterinary Administrations of importing countries should require:

for tallow derivatives (other than those made from protein free tallow as defined in Article 2.3.13.8) intended for food, feed, fertilisers, cosmetics, pharmaceuticals including biologicals, or medical devices the presentation of an international veterinary certificate attesting that:

1) they originate from a BSE free or provisionally free country or zone, or from a country or zone with a minimal BSE risk;

OR

2) they have been produced by hydrolysis, saponification or transesterification using high temperature and pressure.

Article 2.3.13.23.

Careful selection of source materials is the best way to ensure maximum safety of ingredients or reagents of bovine origin used in the manufacture of medicinal products.

Countries wishing to import bovine materials for such purposes should therefore consider the following factors:

1) the BSE status of the country and herd(s) where the animals have been kept, as determined under the provisions of Articles 2.3.13.2. to 2.3.13.7.;

2) the age of the donor animals;

3) the tissues required and whether or not they will be pooled samples or derived from a single animal.

Additional factors may be considered in assessing the risk from BSE, including:

4) precautions to avoid contamination during collection of tissues;

5) the process to which the material will be subjected during manufacture;

6) the amount of material to be administered;

7) the route of administration.
**APPENDIX 3.8.4.**

**SURVEILLANCE AND MONITORING SYSTEMS FOR BOVINE SPONGIFORM ENCEPHALOPATHY**

**Article 3.8.4.1.**

**Introduction**

Surveillance for bovine spongiform encephalopathy (BSE) has at least two goals: to determine whether BSE is present in the country, and, if present, to monitor the extent and evolution of the epizootic, thus aiding control measures and monitoring their effectiveness.

The cattle population of a country or zone not free from BSE, will comprise the following sub-populations in order of decreasing size:

1. cattle not exposed to the infective agent;
2. cattle exposed but not infected;
3. infected cattle, which may lie within one of three stages in the progress of BSE:
   a) the majority will die or be killed before reaching a stage at which BSE is detectable by current methods;
   b) some will progress to a stage at which BSE is detectable by testing before clinical signs appear;
   c) the smallest number will show clinical signs of disease.

A surveillance programme on its own cannot guarantee BSE status and should be determined by, and commensurate with the outcome of the risk assessment referred to in Article 2.3.13.2. and should take into account the diagnostic limitations associated with the above sub-populations and the relative distributions of infected animals among them.

Surveillance programmes developed before the advent of rapid diagnostic tests focused on the sub-population containing cattle displaying clinical signs compatible with BSE as described in Article 3.8.4.2. While surveillance should focus on the sub-population containing cattle displaying clinical signs consistent with BSE as described in Article 3.8.4.2, the sub-population where it is difficult to access all cattle displaying such clinical signs, investigation of other sub-populations using the new diagnostic techniques may provide a more accurate picture of the BSE situation in the country or zone. A surveillance strategy programme may therefore need to combine several strategies. Recommended strategies for surveying the various sub-populations are described below.

Available data suggest the possibility that a gradient might be established to describe the relative value of surveillance applied to each sub-population. All countries should sample sub-populations identified in Articles 3.8.4.2. and 3.8.4.3. In countries where surveillance of cattle identified in Article 3.8.4.2. is unable to generate the numbers recommended in Table 1, surveillance should be enhanced by testing larger numbers of cattle identified in Article 3.8.4.3. Any shortfall in the first two sub-populations should be addressed by the surveillance, which can be complemented by sampling of normal cattle over 30 months of age at slaughter according to Article 3.8.4.4. Exclusive dependence on random sampling from normal cattle is not recommended, unless the number of samples examined annually is statistically sufficient to detect a disease prevalence of 1 in 1,000,000.
Surveillance for BSE requires laboratory examination of samples in accordance with the methods described in the Terrestrial Manual.

For surveillance purposes, testing a part of the population is consistent with Chapter 1.3.6. on surveillance and monitoring of animal health.

**Article 3.8.4.2.**

**Examination of cattle displaying clinical signs consistent with bovine spongiform encephalopathy**

Cattle affected by illnesses that are refractory to treatment, and displaying progressive behavioural changes such as excitability, persistent kicking when milked, changes in herd hierarchical status, hesitation at doors, gates and barriers, as well as those displaying progressive neurological signs without signs of infectious illness are candidates for examination. Since BSE causes no pathognomonic clinical signs, all countries with cattle populations will observe individual animals displaying compatible clinical signs consistent with BSE. It should be recognised that cases may display only some of these signs, which may also vary in severity, and such animals should still be investigated as potential BSE affected animals.

Table 1 indicates the minimum number of animals exhibiting one or more clinical signs of BSE that should be subjected to diagnostic tests according to the total cattle population over 30 months of age. The calculations assume a prevalence of one BSE clinically affected animal per one million adult cattle; a mortality rate not exceeding one percent per year in adult cattle; and a prevalence of central nervous system (CNS) signs not exceeding one percent within dying cattle.

As this sampling is not random, and as the mortality rate and prevalence of CNS signs within dying cattle may vary, the numbers indicated in this table are a subjective interpretation rather than a strict statistical deduction. This table should only be employed as a general guideline. Sampling in excess of the number indicated, ideally extending towards all cattle over 30 months of age showing clinical signs consistent with BSE, would give greater confidence in the outcome and is to be encouraged. In those cases, where there is a shortfall in the number of samples required under this article, the difference may be made up by any combination of samples defined under Articles 3.8.4.3 and 3.8.4.4.

**Table 1. Minimum number of annual investigations of cattle showing clinical signs consistent with BSE required for effective surveillance according to the total cattle population over 30 months of age**

<table>
<thead>
<tr>
<th>Total cattle population over 30 months of age</th>
<th>Minimum number of samples to examine</th>
</tr>
</thead>
<tbody>
<tr>
<td>500,000</td>
<td>50</td>
</tr>
<tr>
<td>700,000</td>
<td>69</td>
</tr>
<tr>
<td>1,000,000</td>
<td>99</td>
</tr>
<tr>
<td>2,500,000</td>
<td>195</td>
</tr>
<tr>
<td>5,000,000</td>
<td>300</td>
</tr>
<tr>
<td>7,000,000</td>
<td>336</td>
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<tr>
<td>30,000,000</td>
<td>425</td>
</tr>
<tr>
<td>40,000,000</td>
<td>433</td>
</tr>
</tbody>
</table>

* Need to develop numbers for populations lower than 500,000
Examination of targeted cattle displaying clinical signs not necessarily indicative of bovine spongiform encephalopathy

Cattle over 30 months of age that have died or have been killed for reasons other than routine slaughter should be examined. This population will include cattle which have died on farm or in transit, ‘fallen stock’, and stock sent for emergency slaughter.

Many of these cattle may have exhibited some of the clinical signs listed in Article 3.8.4.2, which were not recognised as being consistent with BSE. Experience in countries where BSE has been identified indicates that this population is the second most appropriate population to target in order to detect BSE. Empirical evidence indicates that surveillance conducted on one clinical suspect from Article 3.8.4.2, is equivalent to that conducted on 100 or more animals in this category in terms of its ability to detect BSE within an infected cattle population. This factor should be applied in calculating the minimum sample size in this category to substitute for any shortfall in the sample numbers specified in Article 3.8.4.2.

Examination of cattle subject to normal slaughter

In countries not free from BSE, sampling at routine slaughter is a means of monitoring the progress of the epizootic and the efficacy of control measures applied, because it offers continuous access to a cattle population of known class, age structure and geographical origin. Empirical evidence indicates that surveillance conducted on one clinical suspect from Article 3.8.4.2, is equivalent to that conducted on 5,000 to 10,000 animals in this category in terms of its ability to detect BSE within an infected cattle population. This factor should be applied in calculating the minimum sample size in this category to substitute for any shortfall in the sample numbers specified in Articles 3.8.4.2 and 3.8.4.3.

Within each of the above sub-populations, countries may wish to target cattle identifiable as imported from countries or zones not free from BSE, cattle which have consumed potentially contaminated feedstuffs from countries or zones not free from BSE, offspring of BSE affected cows and cattle which have consumed feedstuffs potentially contaminated with other TSE agents.