EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Scientific Steering Committee

OPINION OF THE SCIENTIFIC STEERING COMMITTEE ON SPECIFIED RISK MATERIALS OF SMALL RUMINANTS.

(FOLLOW-UP TO THE SSC OPINION OF 24-25 SEPTEMBER 1998 ON *THE RISK OF INFECTION OF SHEEP AND GOATS WITH BSE AGENT*)

ADOPTED

AT ITS MEETING OF 13-14 APRIL 2000

OPINION

On 24-25 September 1998 the Scientific Steering Committee (SSC) adopted its opinion on *The risk of infection of sheep and goats with BSE agent*. The SSC was invited to address, at its meeting of 13-14 April 2000, the following questions:

1. Did, since September 1998, any new evidence or data become available that justify a review of the risk evaluation presented in the above SSC opinion? Or conversely, does the absence of such evidence and considering the normal life span of small ruminants imply a review? Are there any new concepts or insights, possibly such as age limitation at slaughter demanding a review of the recommendations in that opinion?
2. Do existing risk management measures such as OTMS, DBES, slaughter controls, SRM and feed bans, etc. have the effect of reducing the risk of exposure of small ruminants to possibly BSE-contaminated meat-and-bone meal? Would such a conclusion justify a review of the relevant opinion?
3. Should, in the light of the answer given to question 1 and 2, the conclusions of the opinion of 24-25 September 1998 with respect to the sheep tissues to be removed from the food and feed chains and listed in the SSC opinion of December 1997, be revised? In particular; can the vertebral column of sheep and goats be considered safe for use in food, feed or fertilisers?

A Working Group was established to prepare the scientific bases to reply the above questions. It's report is attached to the present opinion.

On questions 1 and 2, the Scientific Steering Committee considers that the conclusions and recommendations in the opinion on "*The risk of infection of sheep and goats with BSE agent*" of 24-25 September 1998, are still valid, especially for what concerns the risk of feed exposure. It considers, however, that since 1998 the feed-borne risk has further decreased significantly following the implementation of MBM bans (provided they were fully effective) and the additional introduction of SRM bans in a number of EU Member States. However, should BSE have been introduced into small ruminant flocks and should it behave like scrapie, then the propagation risk has meanwhile remained unaltered.

Regarding Question 3, the SSC adopts at present, in the light of the analysis provided in the attached report, in view of the existing risk factors and in the absence of evidence that BSE is present in any national small ruminant flock, a prudent approach and states:

- The list of tissues and materials that possibly pose the highest risk includes: skull (head excluding skin and tongue) and spinal cord of all small ruminants above 12 months and the spleen of small ruminants of all ages.
- BSE in sheep has not been found under field conditions. However, because a large number of people might be exposed to a single infection source if it occurs, certain unprocessed meat products, such as mechanically recovered meat (MRM) derived from the vertebral column of small ruminants over 12 months of age would constitute a significant potential risk.
- Assessing the potential infectivity of the intestine and lymph nodes of sheep (experimentally) infected with BSE is underway and results are urgently needed to improve the risk assessment.
- However, if as a BSE case in sheep or goats occurs under natural conditions in a region or country, this will create a completely new situation. Wherever this risk occurs in an animal or flock, no tissues that are likely to contain BSE infectivity should enter any food or feed chain. The SSC recommends that risk scenarios be developed to be applied if BSE is discovered in sheep under field conditions.

For the concern about the safety of blood and appropriate slaughter methods, the SSC refers to its opinion on the *Safety of ruminant blood* adopted at its meeting of 13-14 April 2000.

The SSC finally suggests that the ongoing work on strain-typing of TSEs in sheep, on the development of BSE/scrapie differential diagnostic tests should continue and be further strengthened. It should also be initiated in other countries with scrapie where exposure to the BSE-agent may have occurred. The SSC also recommends that the coincidence of a number of TSE singleton cases in sheep in Switzerland, which was considered to be scrapie free before 1982, should be further examined, especially by strain typing in mice of the isolates.

SPECIFIED RISK MATERIALS OF SMALL RUMINANTS.

(FOLLOW-UP TO THE SSC OPINION OF 24-25 SEPTEMBER 1998 ON *THE RISK OF INFECTION OF SHEEP AND GOATS WITH BSE AGENT*)

REPORT FROM THE WORKING GROUP[1]

I. QUESTIONS AND MANDATE

On 24-25 September 1998 the Scientific Steering Committee (SSC) adopted its opinion on "*The risk of infection of sheep and goats with Bovine Spongiform Encephalopathy agent*". An extract from the executive summary is given in the background section hereafter.

The SSC was invited to address, at its meeting of 13-14 April 2000, the following questions:

1. Did, since September 1998, any new evidence or data become available that justify a review of the risk evaluation presented in the above SSC opinion. Or conversely, does the absence of such evidence and considering the normal life span of small ruminants imply a review. Are there any new concepts or insights, possibly such as age limitation at slaughter demanding a review of the recommendations in that opinion.
2. Do existing risk management measures such as OTMS, DBES, slaughter controls, SRM and feed bans, etc. have for effect that the risk of exposure of small ruminants to possibly BSE-contaminated meat-and-bone meal has been reduced. Would such a conclusion justify a review of the concerned opinion.
3. Should, in the light of the answer given to question 1 and 2, the conclusions of the opinion of 24-25 September 1998 with respect to the sheep tissues to be removed from the food and feed chains and listed in the SSC opinion of December 1997, be revised? More in particular; can the vertebral column of sheep and goats be considered safe for use in food, feed or fertilisers.

II. BACKGROUND

The currently available SSC opinions related to the risk of BSE being present in small ruminants and to tissues that possibly cause a risk if consumed by humans, can be summarised as follows:

1. Extract from the executive summary of the (SSC) opinion adopted on 24-25 September 1998 on *The risk of infection of sheep and goats with Bovine Spongiform Encephalopathy agent*.

   (…) In the light of the incomplete information available, the SSC concludes that it can not be excluded that BSE, once introduced, may be maintained and spread in the sheep and goat population by means of horizontal and vertical transmission.

[1] With minor editorial changes and additional explanations by the Scientific Steering Committee.

Because it has clearly been demonstrated that BSE can be orally transmitted to certain genotypes of small ruminants, and because it is likely that BSE-contaminated MBM has been fed to some sheep and goats, the Scientific Steering Committee has to assume that BSE could have been introduced into the sheep and goat population. Therefore it can not be excluded that the risk could persist, even after an effective implementation of a ruminant feed ban.

On the basis of data on feeding practices, sheep and goats in many countries have probably been exposed to the BSE agent through MBM. It is noted that the feeding practices, e.g., the age and extent of MBM feeding of sheep and goats, are different from cattle. These will also vary depending on whether the animals are to be used for meat, wool or dairy purposes.

The Scientific Steering Committee considers that if BSE in sheep and goats exists, the most likely way of introduction has been through infected MBM. It is possible that the BSE-agent has been maintained, propagated and/or recycled by horizontal and vertical transmission in sheep and goats if the agent behaves like scrapie in these species. Maternal transmission is unproven in goats. Other means of transmission are theoretically possible but regarded as extremely unlikely provided current measures are in place and effectively enforced

In the context of the geographical risk of BSE in small ruminants, special attention needs to be paid to the genotypes in the sheep population and the possibility of horizontal and maternal transmission of BSE in sheep and goats. No information is currently available but it is noted that study of maternal transmission of experimental BSE in sheep is in progress.

Given the existing uncertainties the SSC concluded that whilst BSE has not been identified in sheep and goats under field conditions, the previous or current geographical risks of BSE existence in sheep and goats can not be excluded. The risk of humans being exposed to the BSE agent originates from animals in the pre-clinical and clinical stage of the disease. It can be reduced by effective measures reducing the exposure risk, in particular safe sourcing, exclusion of the potentially most highly infected tissues (age-specific specified risk materials) from processing, reducing the age at slaughter for human consumption and application of validated processing methods with a proven potential to reduce/eliminate any residual BSE-infectivity.

These measures have been previously described by the SSC which considers [in September 1998, Secr.*] that there is no scientific reason for a change in that advice.*

The list of SRM should be regularly re-evaluated taking account of the results of ongoing epidemiological surveys on BSE in small ruminants and of new scientific data on BSE infectivity distributions in tissues of small ruminants, infectivity and transmission in small ruminants and whether in particular the lymphoreticular tissue should be considered more infective in sheep than they are in cattle.

In order to update this opinion, the SSC urges that EU Member States and other countries should urgently make available toe the European Commission relevant data and information which may be at their disposal.

2. In its opinion of 9 December 1997 *Listing of Specified Risk Materials: a scheme for assessing relative risks to man*, the SSC was of the opinion that in an animal (bovine, ovine or caprine) infected with BSE, a differentiation of the different tissues/organs with regard to their relative infectivity is possible. The different levels of infectivity reflect a graded phenomenon and it is unwise to assume that the BSE agent is either present or absent in any particular tissue of an infected animal.

   The SSC adopted the following table[2] categorising the potential infectivity of different organs in BSE-infected animals. For practical reasons relating to slaughterhouse contamination, some tissues are categorised at a higher level than warranted by their intrinsic infectivity.

Category	Organs
1. High infectivity	a) Bovine brain, eyes, bovine spinal cord and bovine dorsal root ganglia, *dura mater*, pituitary, skull and bovine vertebral column, lungs b) Ovine/caprine brain, eyes and spinal cord, dorsal root ganglia and vertebral columns; ovine and caprine spleens**,** lungs
2. Medium infectivity	a) Total intestine from duodenum to rectum, tonsils b) Bovine spleen, placenta, uterus, fetal tissue, adrenal, cerebrospinal fluid, lymph nodes
3. Low infectivity	Liver, pancreas, thymus, bone marrow, other bones nasal mucosa, peripheral nerves
4. No detected infectivity	Skeletal muscle, heart, kidney, colostrum, milk, discrete adipose tissues, salivary gland, saliva, thyroid, mammary gland, ovary, testis, seminal testis, cartilaginous tissue, connective tissue, skin, hair, blood clot, serum, urine, bile, faeces

In the same opinion of December 1997, the SSC suggests the following list of specified risk materials to be excluded from human and animal consumption except when derived from a BSE free country with a negligible risk. (see next page)[2]

[2] At its meeting of 13-14 April 2000, the SSC considered that the opinion of December 1997 on Specified Risk Materials (SRM), should be updated in the light of its SRM-related opinions adopted since then.

Tissue	Species	Age limit (months)	Basis
Brain	Bovine	>12	Infectivity
	Ovine*,	>12	"
	Caprine*	>12	"
Eyes	Bovine	>12	Infectivity
	Ovine*	>12	"
	Caprine*	>12	"
Dura mater	Bovine	>12	Contamination[1]
	Ovine*	>12	"
	Caprine*	>12	"
Pituitary	Bovine	>12	Contamination[1]
	Ovine*	>12	"
	Caprine*	>12	"
Skull	Bovine	>12	Contamination
	Ovine*	>12	"
	Caprine*	>12	"
Spinal cord	Bovine	>12	Infectivity
	Ovine	>12	Theoretical back infection[3]
	Caprine	>12	" " "
Dorsal root ganglia	Bovine	>12	Infectivity
	Ovine	>12	Theoretical back infection[3]
	Caprine	>12	" " "
Vertebral column	Bovine	>12	Contamination and low infectivity
	Ovine	>12	Contamination if back infected [3]
	Caprine	>12	Contamination if back infected
Spleen	Ovine	All	Infectivity[2]
	Caprine	"	"
Intestine	Bovine	All	Infectivity / Contamination[3]
	Ovine	"	" "
	Caprine	"	" "
Tonsils	Bovine	>12	Infectivity[4]
	Ovine	>12	"
	Caprine	>12	"
Lung	Bovine	>12	Contamination from brain via blood when animals are killed by pithing or stunning.
	Ovine,	>12	
	Caprine	>12	

* Practicalities may well dictate the removal of the heads of sheep and goats at all ages.

Footnotes to the above list:

1. Known CJD-transmission with human tissue
2. BSE infectivity found in spleen of BSE challenged sheep; assumption that goats would have displayed the same response if tested.
3. Ileal infectivity in calves; colonic infectivity in sheep scrapie and potential for contamination of adjacent colon as small intestine removed in slaughter houses.
4. PrP^{Sc} shown in man with nvCJD; also infectivity in scrapie sheep (see Table 2).

[3] This terminology was used in 1997 to highlight the unproven possibility that BSE from cattle had infected sheep.

The SSC further noted that in countries specified as at high risk of BSE it may be considered appropriate to reduce further the age limit for these tissues from 12 to 6 months. The risks from bovine tissues need to be considered separately from those of ovine and caprine origin. In high risk countries, all tissues from cattle over 30 month age may be considered as at greater risk and therefore be considered as SRM. Long bones from cattle below 30 months showing no clinical signs of BSE may be considered at present acceptable for human consumption.

III. RISK ASSESSMENT

III.1 On the risk that BSE has been introduced and propagated, and the effect of risk management measures

a. The most likely way of introduction of BSE into the sheep and goat population is through infected MBM. The efficiency of the implementation of feed bans is the key factor for the speed of decrease of the risk that BSE enters, is maintained, propagated or recycled in the sheep and goat flocks. It is essential to consider that, if the BSE agent behaves like scrapie in these species - and there are indications that such is the case (Foster et al, 1996) BSE in small ruminants should be considered as a flock disease and its propagation/maintenance could/would be similar to scrapie**.**

   A crucial point in the evolution of the risk in time is the date from which the MBM ban can be considered as being fully or optimally effective. The effectiveness of the MBM ban is related to controls on exclusion of SRM from food and feed chains, the application of rendering parameters ("133°C/20’/3 bars") and, measures to avoid cross contamination.

   The number of Born After the Ban (BAB) cases in cattle is considered to be an indicator of the effectiveness of the MBM ban. A decline in incidence of cattle with BSE in the UK was not detected until the modal age of onset of clinical signs (4-5 years) was complete in 1992, four years after the ban was put in place (Wilesmith and Ryan, 1992). In the case of BSE the majority of exposures were in dairy calves. For the small ruminant population although the decrease in risk of exposure from infected feed would be immediate following an effective MBM ban, the evidence to support that it was effective might not become evident quicker than it did for cattle even though the incubation period for BSE in sheep after oral challenge is shorter than that in cattle (Foster et al , 1996) and it may not become evident at all. This is because, in comparison to the timing of exposure of calves, the exposure of small ruminants through MBM, is likely in most cases to have been at a later stage in their life, leaving less time to develop clinical disease. Dependent on various sheep management procedures, however, also very young lambs may have been fed concentrates (containing MBM), resulting in clinical disease at a younger age. If lambs for slaughter were exposed it would be unlikely that any decline would be observed as they would be killed before the onset of clinical signs.

   Two other points are relevant. First, the study of experimental BSE in sheep used brain material whereas in the natural situation the source would be MBM (*i.e.* cooked infected material). There is evidence from historical data (Dickinson, 1968) that heat treating inoculum is associated with a

lengthening in incubation period. Second, if no sheep or goats actually developed disease from feed exposure prior to the ban no decline would be expected or detectable after the ban, even if the ban was totally effective.

Once BSE was introduced, the disease could theoretically be spread horizontally or perinatally/maternally and could be perpetuated, independently from the exposure to MBM. However, this could[4] would only lead rather slowly to a significant increase of TSE clinical cases over a long period, unless particular susceptible genotypes are prevailing in exposed flocks. Occurrence of scattered epidemics of BSE in sheep cannot be entirely ruled out. At this moment, however, where in most countries effective feed bans have not been implemented before 1996, an increase in observed cases through horizontal or peri-natal infections, if occurring is highly unlikely to be detectable even in high quality surveillance networks. Despite greater awareness of the possibility of BSE in sheep, resulting in more efficacious surveillance systems, no significant increase of TSE cases in sheep or goats following the occurrence of the BSE epidemic in cattle has been noticed in the United Kingdom (L.Hoinville, WHO Consultation, 1-3.12.99).

The risk of new exposures to BSE through MBM has been reduced considerably in the EU after the implementation of an MBM ban in July 1994, especially in the Member States that apply, in addition, an SRM ban. The most likely explanations for the presence of BSE in sheep and goats, if it were to exist now, are as follows. In younger sheep, born after the MBM ban was completely effective, this could have occurred by propogation by maternal, including peri-natal transmission, or horizontal transmission. In sheep born before the MBM ban was completely effective, an additional source could have been infected feed. There is no new evidence to support these assumptions. Neither are data available on the rate of the transmission, if occurring at all, but horizontal transmission is considered to be more important than maternal/peri-natal transmission which is also insufficient in the case of scrapie to sustain or perpetuate an epidemic.

b. Some new data on BSE in sheep are extensively discussed in the report on "The criteria for diagnosis of clinical and pre-clinical TSE disease in sheep and for differential biochemical diagnosis of TSE agent strains", especially the publication by Baron *et al* (1999) "Similar signature of the prion protein in natural sheep scrapie and bovine spongiform encephalopathy-linked diseases". It was concluded that this study did not demonstrate BSE in 21 French sheep isolates as glycoform analysis on its own is not sufficient for strain typing in sheep. In a new paper on these 21 isolates (Baron *et al*, 2000, under publication) it was suggested that on the basis of the glycoform pattern, all the French isolates studied so far would belong to the group of scrapie cases with type A electrophoretic pattern. Therefore it was not necessary to revise the report on "The risk of infection of sheep and goats with BSE agent". Moreover, in the frame of the UK research

[4] It is not known for certain that that there would be an increase in clinical cases over time: this depends also on the relative efficiency of feed-borne and other routes of transmission. Also, an increase in incidence of clinical cases following the introduction of BSE to sheep is not inevitable although it is not known how likely it is.

projects SE1423 “Transmission studies for the detection of BSE in sheep”, SE1919 “Studies to identify possible homologies between TSEs” and SE1938 “Strain typing of isolates of natural scrapie: correlation with host PrP genotype and clinical and pathological phenotype” to date 32 cases have been inoculated for more than 320 days in RIII mice, and none of the interim results are indicative of the BSE agent. The coincidence of a number of TSE singleton cases in sheep in Switzerland, which was prior to the BSE epidemic considered to be scrapie free should be further examined, especially by strain typing in mice of the isolates.

c. In conclusion the working group considers that no evidence has become available that indicates that BSE is present in small ruminant flocks and that the opinion on “*The risk of infection of sheep and goats with BSE agent*” of 24-25 September 1998, is still valid, especially for what concerns the risk of feed exposure. It considers, however, that since 1998 the feed born risk has further decreased significantly following the implementation of MBM bans (provided they were fully effective) and the additional introduction of SRM bans in a number of EU Member States. However, should BSE have been introduced into small ruminant flocks and should it behave like scrapie, then the propagation risk has meanwhile remained unaltered. The outcome of the in-progress studies investigating the possible transmission of BSE in sheep from dam to offspring (including if infectivity is present in the placenta) will critically inform on the likelihood of maternal transmission, but not necessarily on horizontal transmission between related or unrelated sheep. These data are urgently needed in order to refine the opinion on the propagation of BSE in sheep.

2. On the risk of sheep tissues, more particular on the vertebral column

The paper of Wells *et al* (1999) reports the finding of infectivity in bone marrow of cattle experimentally infected by the oral route with BSE at 38 months after the exposure during the clinical phase of disease. However, (titres were not measured) bone marrow pooled from three cattle in only one group of cattle was found positive. Amongst the possible explanations of this single observation, cross contamination during sampling has been mentioned and cannot be ruled out totally. In Suffolk sheep, but not in goats with natural clinical scrapie, similar low grade infectivity has been found in one of nine bone marrow samples from the sternal ends of the ribs (Hadlow *et al* 1980, 1982). From early results of the transmission of BSE to sheep studies (UK project SE1423) some ARQ/ARQ infected sheep have widespread PrP^{Sc} demonstrable in the lymphoreticular system tissues from 16 months after exposure, but there are, as yet, no corresponding bioassay results for infectivity. This does not exclude finding infectivity or PrP^{Sc} at other (including younger) ages. Taking into account that infectivity in the vertebral column would mainly originate from the spinal cord and dorsal root ganglia, it should be noted that PrP^{Sc} was only detected, in the case of natural scrapie, in the spinal cord at more than 50% of the incubation period, an incubation period that in most genotypes will be more than 2 years. This neural pathway is likely to be similar for scrapie and BSE strains of the agent. Therefore the vertebral column from sheep and goats under the age of 12 months can

presently be considered to pose a negligible risk in most circumstances. (But see also further).

3. On sheep tissues to be possibly removed from the food and feed chains.

The Working Group considers that ideally 3 separate SRM lists should be drawn-up:

- For cattle
- For sheep and goats when there is no evidence for BSE occurring (as now).
- For sheep and goats assuming that BSE has been confirmed

These lists should be regularly up-dated in the light of new information that is being obtained from experiments in progress. As mentioned in the SSC opinion listing Specified risk materials (December 1997) and in the opinion on the Safety of gelatine (March 1998), one could consider modulating these lists according to the geographical risk and/or according to the risk reduction level aimed for.

At present, there is no evidence of BSE occurring in sheep or goats. In the light of the preceding paragraphs (1) and (2), the working group considers with respect to the SSC opinion of 24-25 September 1998 on "*A listing of specified risk materials: a scheme for assessing relative risks to man*":

- The list of tissues and materials that possibly pose the highest risk includes: skull (including the brain, pituitary gland, dura mater, eyes and tonsils) and spinal cord of all small ruminants above 12 months and spleen of small ruminants of all ages.
- BSE in sheep has not been found under field conditions. However, because a large number of people might be exposed to a single infection source if it were to occur, certain unprocessed meat products, such as MRM and offals derived from especially the vertebral column and head of animals over 12 months of age constitute a significant potential risk.
- No scientific conclusion can be drawn whether the intestine or parts of the intestine should be considered as a risk tissue. No experiments/tests have indeed been carried out on the intestine of BSE infected sheep. However, there are some indications that BSE in sheep behaves like scrapie in regard to pathogenesis. Parts of the intestine that contain Peyer's patches, but not all parts of the intestine, are infective in scrapie-infected sheep over eight months old (first detected at ten months but not at eight, Hadlow et al 1982). A similar distribution occurs in other animal TSEs that have been tested. Furthermore, if spleen was infective, then also is the intestine and lymph nodes. The potential infectivity of the intestine and lymph nodes of sheep (experimentally) infected with BSE is underway and results are urgently needed to improve the risk assessment.
- Other tissues might be determined to be risk tissues in the light of research[5].

If the above list was to be adopted the risk to humans would be significantly reduced if BSE were to occur in the future.

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[5] For example also on lymph nodes published definitive evidence is lacking.

However, if BSE in sheep or goats was to occur under natural conditions in a region or country, wherever this risk occurs in an animal or flock no tissues that are likely to contain BSE infectivity should enter any food or feed chain. The assessment of the risk for humans will need to be amended and strengthened and should include elements such as (non exhaustive list):

- amending the list of tissues (at appropriate ages) to be removed from the food and feed chains, taking into account the results of the ongoing studies, in particular involvement of the LRS system in the case of BSE in sheep and the results of titrations to define the infectivity levels of various tissues at different stages of the infection. In that respect, the results on placenta will be of particular interest. If infectivity and PrP^{Sc} is found, placenta material could be used for testing "in vivo" and the implication would be that peri-natal/maternal and horizontal infection is likely to occur.

  Note on the issue of age: Hadlow et al (1982) did not find infectivity in the CNS of Suffolk sheep until 25 months of age. According to Van Keulen (1999), PrP^{Sc} was found[6] under natural conditions in the vertebral column (T8-T10, plus obex) of one out of two VRQ/VRQ sheep[7] with scrapie, at 10 months of age[8] (or at 36-47% of the incubation period of 21-28 months). In the experiment sheep were examined at. 5,10,14,17 and 21 months. The next batch showed positivity at 14 months, which equals 50 to 66.6% of the incubation period. The genotype used for the Van Keulen study is considered rare in the general sheep population (see Van Keulen, 1998). According to Van Keulen (personal communication, 2000) a nation wide survey showed that this genotype occurs in less than 0.5% (0.41%) of the tested animals. All other genotypes in the Netherlands show longer incubation periods and then also proportionally later times of detecting positivity in the various organs. Admittedly, in some instances shorter incubation periods have been reported. Given an average incubation period of 3 to 5 years (for most cases), the logic cut-off point of 12 months would remain valid if one aims to cover most of the risk, not the very last bit.
- localisation of where the risk is most a significant (e.g flocks at risk, other flock members, in contact sheep, flocks moving sheep into the flock or receiving sheep from the flock in the preceding X years);
- the age of an animal;
- presence or absence of certain risk management measures at the flock level (compulsory slaughter, destruction by incineration of the whole flock) and at the country level.
- breed, PrP genotype, type of flock, geographical location etc.

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[6] On the presence of PrP^{Sc} versus infectivity: see the Pre-Opinion of the SSC of 2-3 March on *Oral exposure of humans to the BSE agent:infective dose and species barrier*.

[7] These have the shortest incubation period with the Dutch scrapie strains encountered by the authors.

[8] PrP^{Sc} was detected in the intermediolateral column (IMLC) of the thoracic segments (T8-T10) after 10 months, which may indicate centripetal spread to spinal cord here, then in several spinal ganglia at 21 months of age (centrifugal). The possible retrograde spread through sympathetic and parasympathetic efferent fibers would imply infectivity in those fibres - running in the same foramina intervertebrales as the afferent fibres and also the dorsal root ganglia. When removing the spinal cord, the nerves in these foramina will remain, i.e. be within the vertebral column.

The Working Group also considers that, should a case of BSE in sheep be found, its origin, location and epidemiology should be carefully studied. The risk may be different depending upon whether the case was, for example, related to an infected vaccine or an isolated one or occurring in an area with a dense sheep population.. In the latter case the disease might have been widely disseminated by maternal/horizontal transmission before it was detected. The responses may also be different if an outbreak was related to a confirmed feed source for example.

IV. SUMMARY OF CONCLUSIONS AND RECOMMENDATIONS

Regarding Questions 1 and 2, the working group concludes that the conclusions and recommendations in the opinion on "*The risk of infection of sheep and goats with BSE agent*" of 24-25 September 1998, are still valid, especially for what concerns the risk of feed exposure. It considers, however, that since 1998 the feed-borne risk has further decreased significantly following the implementation of MBM bans (provided they were fully effective) and the additional introduction of SRM bans in a number of EU Member States. However, should BSE have been introduced into small ruminant flocks and should it behave like scrapie, then the propagation risk has meanwhile remained unaltered.

Regarding Question 3 the working group therefore considers, at present, in the absence of evidence that BSE is present in any national small ruminant flock:

- The list of tissues and materials that possibly pose the highest risk includes: skull (including the brain, pituitary gland, dura mater, eyes and tonsils) and spinal cord of all small ruminants above 12 months and spleen of small ruminants of all ages.
- BSE in sheep has not been found under field conditions. However, because a large number of people might be exposed to a single infection source if it were to occur, certain unprocessed meat products, such as MRM derived from the vertebral column (and head) of animals over 12 months of age constitute a significant potential risk.
- The potential infectivity of the intestine and lymph nodes of sheep (experimentally) infected with BSE is underway and results are urgently needed to improve the risk assessment.

The Working Group suggests however that risk management scenarios are developed, both at flock and at region/country level, in case of few ($1/10^6$), medium ($1\text{-}10/10^6$) or large numbers ($>100/10^6$) of BSE in sheep should be discovered under field conditions Lists of SRMs to be removed could be modulated according to the different scenarios. They should be elaborated on the most recently available scientific evidence.

The Working Group finally suggests that the ongoing work on strain-typing of TSEs in sheep, on the development of BSE/scrapie differential diagnostic tests should continue and further be strengthened where it is already ongoing (e.g., UK, France) or initiated in other countries with scrapie but where exposure to the BSE-agent may have occurred. It also recommends that the coincidence of a number of TSE singleton cases in sheep in Switzerland, which was considered to be scrapie free before 1981 should be further

examined, especially by strain typing in mice of the isolates. (According to Fankhauser *et al* (1982), the very first case of scrapie ever reported in Switzerland occurred in a goat in 1981. No further cases of scrapie were observed until after the advent of BSE in Switzerland (first case of BSE end of 1990) (M.Vandevelde, personal communication, 2000))

V. ACKNOWLEDGEMENTS:

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VI. MATERIAL USED FOR THE RISK ASSESSMENT.

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