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OPINION AND REPORT

ASSESSMENT OF THE HUMAN BSE RISK POSED BY BOVINE VERTEBRAL COLUMN INCLUDING DORSAL ROOT GANGLIA.

ADOPTED BY THE SCIENTIFIC STEERING COMMITTEE AT ITS MEETING OF 16 MAY 2002

OPINION

In the light of (a) the results of the BSE monitoring carried out so far and in particular the age distribution of positive BSE cases and (b) the recent assessment of the possible risk posed by bovine dorsal root ganglia in Ireland, the Scientific Steering Committee (SSC) was asked:

(1) to assess a recent quantitative assessment of risk from possible BSE infectivity in dorsal root ganglia, produced for the Food Safety Authority in Ireland.

(2) to give a quantitative assessment of the BSE risk [for human consumers] posed by bovine vertebral column including dorsal root ganglia.

(3) to address the question of whether evidence can be found to justify an increase of the current age limit of 12 months for treating vertebral column as SRM in bovine animals? If yes, to which extent and under which conditions? If no, what would be the conditions for increasing the age limit?

On the basis of the attached report of the TSE/BSE *ad hoc* Group, the SSC answers the above three questions as follows:

1) Regarding parts (1) and (2) of the mandate on the quantitative assessment of risk from possible BSE infectivity in dorsal root ganglia

The SSC considers that the risk assessment produced for the Food Safety Authority in Ireland is scientifically sound but applies only to Ireland. The produced risk estimates cannot be generalised for other countries, because consumption patterns[1] and BSE incidence are different.

Preparing similar assessments for other countries, or for the EU's continental part as a whole, would require the collection of the appropriate information for these countries or for the EU, part of which is not likely to be readily available but would need to be collected by surveys.

An essential element in such risk assessment is the moment into the incubation period as from which the spinal cord and dorsal root ganglia can contain infectivity. Data from a single experiment, mostly referred to as the *cattle pathogenesis study*, has in the past been interpreted as showing that detectable infectivity in the spinal cord is only present in the last months of the incubation period, which would justify the consumption of meat-on-the bone or of vertebral column bones [for gelatine and fat production] up to an age of 12 months before the expected possible appearance of clinical signs. The SSC considers however that the BSE cattle pathogenesis study cannot be exploited to express the time of detectable infectivity in the Central Nervous System tissues as a fraction of the total incubation period and that the limited number of animals used in this study do not allow to conclude that infectivity is absent in the spinal cord until a few months before clinical signs are manifested.

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[1] Quantities consumed by individuals, parts of the carcass used for the production of meat-on-the-bone, frequency of consumption of meat-on-the-bone and other carcass parts to which dorsal root ganglia may be attached, age distribution of the animals slaughtered, ...

From experiments with other animal species and for which more data are available (e.g., mice, hamster, primates, sheep, ...) it may be concluded that the assumption made by the SSC on 12 January 2001 - i.e., that in general, as a reasonable worst case assumption, the dorsal root ganglia and the spinal cord are considered to pose a higher risk as from the second half of the incubation period - remains valid.

2) *Regarding part (3) of the mandate on evidence to justify an increased age limit above 12 months for treating vertebral column as SRM in bovine animals.*

   a. The SSC considers that neither the available results of the pathogenesis research nor the results of the 2001 rapid BSE testing programme reflecting the exposure situation until early 1998 permit to conclude on the question whether or not an increase of the age limit above 12 months for treating vertebral column as SRM in bovine animals born before the feedban is justified.

   b. For cattle born after the total feed-ban the SSC confirms its opinion of 12 January 2001 that such animals, *if the feedban is properly implemented,* should bear a low risk of being infected. A guidance on proper implementation of feedbans is provided in "*Effective feed ban: Guidance note for third countries, 18 July 2001*".[2]

   c. The SSC recommends that the various Member States assess the human exposure risk before and after the implementation over time of consecutive risk management measures as listed in the opinion of 12 January 2001, including the total feedban.

      Based on such assessments an evaluation for the whole EU will become possible and the SSC will be able to revisit and update its opinion on human BSE risk related to Specified Risk Materials, including dorsal root ganglia.

[2] web-site address: http://europa.eu.int/comm/food/fs/bse/index_en.html.

REPORT ON THE

ASSESSMENT OF THE HUMAN BSE RISK POSED BY BOVINE VERTEBRAL COLUMN INCLUDING DORSAL ROOT GANGLIA.

FINALISED BY THE TSE/BSE AD HOC GROUP MEETING AT ITS MEETING OF 2 MAY 2002

TABLE OF CONTENTS

I. BACKGROUND AND MANDATE

1. In its opinion of 9 December 1997 on Specified Risk Material (SRM), the SSC recommended that the vertebral column should be regarded an SRM because of the close association and possible contamination with the spinal cord and dorsal root ganglia.

In its opinion on Human Exposure of December 1999, the SSC stated that the brain, the spinal cord, the dorsal root ganglia respectively represent 64.1%, 25.6% and 3.8% of the total infective load in a BSE infected animal. It recognised in that opinion that based on quantitative data, the brain, spinal cord, dorsal root ganglia and trigeminal ganglia constitute the major hazards for direct human consumption.

From the SSC's opinion and report of 11 January 2002 on TSE Infectivity distribution in ruminant tissues *the following can be deduced:*

> Available data are incomplete and much of the information emanates from a single study of the distribution of infectivity after experimental oral exposure. Values of infectivity for the few tissues containing infectivity in experimentally exposed cattle, estimated from incubation period assay in mice, suggests that in most of the infected tissues infectivity is close to the limit of detection of the assay, even in central nervous system. Preliminary results of the re-evaluation of such tissues by bioassay in cattle compliment the mouse data, but such assays will not be completed for at least a further five years. In the experimental study of the pathogenesis of BSE in cattle after oral exposure to a relatively high dose of untreated BSE infective material, in which the lower limit of the incubation period range was 35 months, evidence of infectivity [by conventional mouse bioassay] in the CNS was detected at 32 months, but not at 26 months after dosing (Wells *et al.*, 1998). However, this study does not provide interpretable data on the relationship between the earliest detectable infectivity in CNS (or any other tissue) and incubation period, because the incubation period range of all animals in the study cannot be determined (because of the sequential kill design of the study). In naturally occurring BSE, the age (or stage of incubation) at which CNS material may contain infectivity is unknown and it is not possible from available results of experimental studies to predict when a case of BSE will show infectivity in the CNS. Dose response data of cattle infected orally with a dose of BSE infectivity closely similar to that administered to induce disease in the Pathogenesis Study (G. A. H. Wells, unpublished data) suggests a mean incubation of almost 45 months (range 33-55 months). From experimental studies of scrapie in rodents, after peripheral routes of exposure, and from data on naturally occurring sheep scrapie (Opinion on SRM of Small Ruminants Adopted 13-14 April 2000) infectivity in CNS occurs approximately 50% through the incubation period. It is not known if such a constant relationship might be applicable to BSE of cattle, but based therefore on available data, it seems not unreasonable to accept that infectivity may be first *detectable* in the CNS in natural BSE well in advance of clinical onset. This might be as little as 3 months before clinical signs, by conventional mouse bioassay, but theoretically at least, it could be 30 months, in an animal with an average estimated field case incubation of 60 months.

In its opinion of 12 January 2001 on the safety with regard to BSE of certain bovine tissues and certain animal derived products, the SSC considered that in general, as a reasonable worst case assumption, the dorsal root ganglia and the spinal cord are considered to pose a higher risk as from the second half of the

incubation period. The SSC concluded that meat on the vertebrae of animals above 12 months of age should not be consumed whenever it cannot be demonstrated that the animal is unlikely to be incubating BSE. The SSC also stated that the results of monitoring with rapid tests should add information in this respect.

Following the SSC opinion of 12 January 2001 (EC, 2001), bovine vertebral column was classified as SRM in animals over 12 months. Derogation was foreseen in certain countries and under certain conditions. Furthermore, a review of the age limit for removal of vertebral column was foreseen, in the light of the statistical probability of the occurrence of BSE in relevant age groups of the Community's bovine population. This review should be based on the results of BSE monitoring.

In the monitoring carried out between January and December 2001, some 8.5 million rapid BSE tests were carried out on bovine animals in the Community. Target groups for testing were healthy stock over 30 months (animals over 24 months in certain Member States) and risk animals and suspect cases.

2. In October 2001, Commission Services received the results of an *Assessment of risk from possible BSE infectivity in dorsal root ganglia* (DRG), carried out for the Food Safety Authority of Ireland (DNV, 2001). Although this risk assessment is applied to the specific conditions of Ireland, it provides also a methodological and scientific update of the DNV's risk assessment of 1997 (DNV, 1997) The latter risk assessment and its outcome has been widely quoted and exploited in the SSC's opinion of 14 April 2000 on *The UK decision to lift the ban on the consumption of meat on the bone* (E.C., 2000a) and in the SSC opinion of 15 September 2000 on *Export from the uk of bone-in veal* (E.C., 2000b).

3. In the light of (a) the results of the BSE monitoring carried out so far and in particular the age distribution of positive BSE cases and (b) the recent assessment of the possible risk posed by bovine dorsal root ganglia (DNV, 2001), the Scientific Steering Committee is asked:
   - to assess a recent quantitative assessment of risk from possible BSE infectivity in dorsal root ganglia, produced for the Food Safety Authority in Ireland. The assessment is attached.
   - to give a quantitative assessment of the BSE risk [for human consumers] posed by bovine vertebral column including dorsal root ganglia.
   - to address the question of whether evidence can be found to justify an increased age limit for treating vertebral column as SRM in bovine animals? If yes, to which extent and under which conditions? If no, what would be the conditions for increasing the age limit?

4. A report was prepared under the joint rapporteurship of Dr.G.Wells (bovine BSE pathogenesis aspects) and Dr.S.Bird (data analysis). The report was discussed, finalised and adopted by the TSE/BSE *ad hoc* Group at its meeting of 2.05.02.

II. QUANTITATIVE ASSESSMENT OF THE BSE RISK FOR CONSUMERS POSED BY BOVINE VERTEBRAL COLUMN INCLUDING DORSAL ROOT GANGLIA.

The only available scientific analyses on the quantification of the BSE risk for consumers resulting from exposure to the bovine vertebral column and dorsal root ganglia, are the quantitative assessments carried out by DNV for the UK (in 1997) and Ireland (2001). These reports estimate, for *consumers of these countries*, the risk of consuming infected dorsal root ganglia and the corresponding levels of infectivity expressed as human oral ID_{50}. The DNV (1997) report also estimates the risk resulting from a vertebral column contaminated with residual spinal cord material.

Depending upon the scenario and assumptions made[3], the results of these assessments are as follows:

UK, in 1997 (all consumed meat from animals below 30 months) (DNV, 1997):

- The median value of the total infectivity in DRG to which the whole UK population would have been exposed in 1997 (= the societal risk) ranges from 0.004 to 0.25 human oral ID_{50} units (with 0.05 human oral ID_{50} units for the most likely scenario). The corresponding 95% percentiles are $2x10^{-5}$ to 63 human oral ID_{50} units.
- The median value of the average individual risk ranges from $7x10^{-11}$ to $5x10^{-9}$ human oral ID_{50} units consumed in 1997 by each individual. The corresponding 95% percentiles are $4x10^{-13}$ to $1x10^{-6}$ human oral ID_{50} units.

Ireland, in 2000 (DNV, 2000): (before the obligation to remove the vertebral column from animals above 12 months and before the generalised rapid testing of animals, but taking into account that approx. 89% of the Irish meat production is exported):

- The median value of the total infectivity in DRG to which the whole Irish population would have been exposed in 2000 (= the societal risk) ranges from 0.008 to 0.6 human oral ID_{50} units. The corresponding 95% percentiles are $5x10^{-5}$ to 110 human oral ID_{50} units.
- The median value of the average individual risk ranges from $3x10^{-9}$ to $2x10^{-7}$ human oral ID_{50} units consumed in 2000 by each individual. The corresponding 95% percentiles are $2x10^{-11}$ to $4x10^{-5}$ human oral ID_{50} units.

The above risk estimates cannot be generalised for other countries, because consumption patterns[4] and BSE incidence are different. Preparing similar assessments for other countries, or for the EU's continental part as a whole, would require the preliminary collection of the corresponding information, part of

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3 The scenarios and assumptions cover, for example: the ratio boneless meat / meat-on-the bone; % of dorsal root ganglia removed with the bones, % of DRG eaten with the bone-in meat, etc.

4 Quantities consumed by individuals, parts of the carcass used for the production of meat-on-the-bone, frequency of consumption of meat-on-the-bone and other carcass parts to which dorsal root ganglia may be attached, age distribution of the animals slaughtered, ...

which is not likely to be readily available but would need to be collected by surveys.

It can, however, be reasonably assumed that the *current* risk (in 2002) in the EU Member States is unlikely to be significantly higher than risks in the UK in 1997 and in Ireland in 2000. At the time of these assessments, the BSE incidence in these 2 countries was higher than in any other EU country (with the exception of Portugal as compared to Ireland) and no improved surveillance using rapid BSE tests were in place.

Nevertheless, the estimated risks are not zero. However, as they result mainly [exclusively] from the infectivity present in animals in the last 12 months of incubation, it can be concluded that dorsal root ganglia and spinal cord residues on vertebral column bones do not pose a risk if they are sourced from animals that are sufficiently early into the incubation period for the risk that infectivity is present in those tissues being negligible.

III. INTERPRETATION OF THE BOVINE BSE PATHOGENESIS STUDIES WITH RESPECT TO THE TIME AFTER EXPOSURE AT WHICH INFECTIVITY CAN BE DETECTED IN THE CENTRAL NERVOUS SYSTEM AND SPINAL AND CRANIAL GANGLIA.

a. The SSC opinion of 11 January 2002 provides the state of knowledge in December 2001 on TSE Infectivity distribution in ruminant tissues (E.C., 2002.) It summarises the completed results of the bioassay of tissues from cattle experimentally infected with BSE agent and killed sequentially (VLA Pathogenesis study) by inoculation of mice. It also provides interim results of the bioassay of tissues from cattle in the Pathogenesis study by inoculation of cattle.

   The study design of the Pathogenesis study has been described previously (Wells *et al.* 1996, Wells et al., 1998). Briefly, forty Friesian/Holstein calves, born in 1991, were assembled from farms with no history of BSE. At four months of age, thirty were each dosed orally with 100g of pooled brain stems from seventy-five cases of BSE. Ten calves received no treatment and served as controls.

   Clinical monitoring of cattle was maintained throughout the study to detect the onset of clinical disease.

   Starting at six months of age, and then at four month intervals, until 22 months p.i., three challenged calves and one control calf were killed. Thereafter challenged and control cattle were killed at discretionary intervals, with the final kill at 40 months p.i.

   Tissues were sampled aseptically for infectivity assays in mice. After each sequential kill, inocula were prepared from 44 tissues, representing principally the lymphoreticular system (LRS), the peripheral nervous system (PNS) and the central nervous system (CNS), alimentary tract, striated muscles and major viscera. All inocula were prepared as ten per cent suspensions in saline, with the inclusion of antibiotics for certain tissues. Single tissue inoculum pools were made from the exposed cattle at each time point.

Inocula were similarly prepared from control animals, but from single tissues of each animal. Test and control inocula were injected by intracerebral (20µl) and intraperitoneal (100µl) routes into inbred mice for standard qualitative assay of infectivity.

Qualitative assays by the i.c. and i.p. inoculation of mice (RIII and/or C57BL) of a large range of tissues from the UK VLA Pathogenesis study of BSE have been completed (Wells *et al.*, 1996, 1998, 1999 and unpublished data). No titration of infectivity in positive tissues has been carried out but an approximation of infectivity titre has been obtained from mean incubation period and data on titrations of BSE affected brain in the same mouse strains. For all tissues in which infectivity has not been detected it can be stated that they contain less than $10^{1.4}$ mouse (i.c./i.p.) $\log_{10}$ LD_{50}/g.

A study (VLA/CSG SE1821) of infectivity of a pool of brains from BSE affected cattle by simultaneous titration in cattle and mice, was also conducted to provide a measure of the underestimation of the titre of infectivity in tissues across the species barrier in mice (described in detail in E.C 2002). This established that the underestimation is a factor of 500 fold (G.A.H.Wells and S.A.C.Hawkins, unpublished data). Expressed as relative titres, 10^0 mouse (i.c./i.p.) LD_{50}/g is equivalent to $10^{2.7}$ cattle (i.c.) LD_{50}/g, or the limit of detection of the mouse bioassay (at approximately $10^{1.4}$ mouse [i.c./i.p.] LD_{50}/g) is equivalent to $10^{4.1}$ cattle [i.c.] LD_{50}/g. From this study also an approximate dose-incubation curve for infectivity of brain from BSE affected cattle was constructed. Following these results additional assays of selected tissues from the original pathogenesis study were conducted by the intracerebral inoculation of cattle. As yet this assay study has confirmed infectivity only in certain tissues which were already found to be positive by the mouse bioassay.

Utilising available dose-incubation response data from titrations of BSE affected brain material in mice and in cattle (see Sections II.4 and II.5 and **Tables 4-6** of EC, 2002) Results, relevant to spinal cord, from the above experimental studies, together with available equivalent information for natural clinical cases of BSE (Foster and Fraser 1994) are summarised in **Table 1**. The Table provides an iterim classification of the levels of infectivity detected in a small number of animals and apparent differences between tissues from experimental studies and natural cases cannot be considered significant. They may relate to stage of clinical disease and other factors.

Table 1: Tentative summary of preliminary estimations* on classification of tissues of cattle according to infectivity after experimental oral or natural exposure to the agent of BSE.

Infectivity titres**:

A = high	$10^{3.0} - 10^{5.0}$ in mouse;	$10^{5.7} - 10^{7.7}$ in cattle ***
B = medium	$10^{1.5} - 10^{3.0}$ in mouse;	$10^{3.3} - 10^{5.6}$ in cattle ***
C = low	$\leq 10^{1.5}$ in mouse;	$\leq 10^{3.2}$ in cattle ***

	EXPERIMENTAL			NATURAL
			clinical	clinical
months after exposure	**6-26**	**32**	**36-40**	**-**
Brain	-	***B*** / C	C	***A***
Spinal cord	-	C	C	A
Dorsal root ganglia	-	C	C	C
Trigeminal ganglion	-	-	C	

*: Refer to the report for further detail

**: The classification used is preliminary and arbitrary because of a skewed range of infectivity in cattle with BSE compared to sheep with scrapie. It does not correspond to the Groups or Categories used in previous similar estimates of scrapie infectivity in sheep tissues. Ranges of values are given as: Log_{10} mouse intracerebral/intraperitoneal LD/50 per g tissue, or Log_{10} cattle intracerebral LD/50 per g tissue.

***: Categories in bold in the table are based on bioassays in cattle and the remainder on bioassays in mice.

-: Negative

b. In cattle after experimental oral exposure to the agent of BSE[5] detection of infectivity in brain and spinal cord (by mouse bioassay) was relatively late (80-90%) in relation to the minimum incubation period recorded in that specific experiment). This however, does not provide information on the first occurrence of infectivity in CNS tissues, relative to incubation in field cases of BSE. It must be borne in mind that in this study tissue bioassays in mice were carried out on the pooled single tissue from 2-3 cattle killed at each sequential time point. As cattle for each kill group were unselected, animals within a group would have different incubation periods, dependant on the range of incubations for the given exposure dose. Dose response data of cattle infected orally with a dose of BSE infectivity closely similar to that administered to induce disease in the Pathogenesis Study (G. A. H. Wells, unpublished data) suggests a mean incubation of almost 45 months (range 33-55 months). At the time of clinical onset of disease in the exposed cattle in the Pathogenesis Study only 8 animals remained in the study and their

[5] Wells, G.A.H., Hawkins, S.A.C., Green, R.B., Austin, A.R., Dexter, I., Spencer, Y.I., Chaplin, M.J., Stack, M.J. & Dawson, M., 1998. Preliminary observations on the pathogenesis of experimental bovine spongiform encephalopathy (BSE): an update. Veterinary Record 142, 103-106..

clinical statuses relative to the times after exposure at which they were killed was as follows (Wells *et al*, 1998):

Months after exposure:	Clinical status:
36	+/-, +/-, -
38	+, +/-, +/- *
40	+, +/-*

+ : Definite Clinical Signs of BSE

+/- : Probable/early Clinical Signs of BSE

-: No consistent clinical signs of BSE

* : Individual cattle in which no pathology (vacuolation or PrP) was detected in the CNS

It is clear from this that most of the animals killed after the earliest clinical onset, at 35 months after exposure, were at an equivocal or early clinical stage. Two animals, one at 38 months and another at 40 months, did not show CNS lesions and may not have contributed to the CNS infectivity detected for each of their respective groups. If this were so, then in these animals, we can assume for the purpose of the present argument, that infectivity had not reached the CNS. This assumption places the interpretation of observed clinical signs in these animals into question and leaves the possibilities that they either remained preclinical cases or had not been infected. If it is then assumed that the incubation periods of all of the animals in the Pathogenesis Study would fall somewhere in the range determined by the dose response data of cattle infected orally (33-55 months) then the possible range of the interval between onset of detectable CNS infectivity (by mouse bioassay) and incubation period can be suggested from the combined data from these studies. Since infectivity was not detected at 26 months after exposure, but was present at 32 months, the interval between earliest possible CNS infection and minimum incubation period might be 33-27=6 months, whereas the interval between the earliest possible CNS infection and maximum incubation period could be 55-27=28 months. In attempting to relate this to natural disease the differences in the mean incubation period for the experimental study (45 months) and that estimated from age specific incidence in the epidemic (60 months, UK data), must be considered and is addresses further at c) below.

In its opinion of 12 January 2001 (EC, 2001) the Scientific Steering Committee concluded that, as a reasonable worst case scenario, based on available experimental results, it could be assumed that infectivity in the CNS can become detectable as from approximately half the incubation period. The justification for this assumption were:

- Animal numbers per experimental group in the Pathogenesis Study were small and so the above percentage (i.e 80-90%, in relation to the minimum incubation period recorded in *that specific* experiment) could well be revised downwards by studies still in progress.

- The time at which, during incubation, infectivity can first be detected in the CNS of animals with TSEs varies with the specific natural disease and, in experimental models, with host and agent variables, particularly those of PrP genotype, agent strain and route of exposure. In certain mouse models of scrapie using non-neural peripheral inoculation routes (including intragastric) detection of infectivity in brain occurs at 40-50% of the incubation period. In 263K hamster scrapie in hamsters the equivalent value is 25%. In certain models this has been shown to be preceded by infectivity demonstrable in the spinal cord.

As BSE has been found in animals below 24 months, a logical conclusion was to lower the threshold age for considering the vertebral column and dorsal root ganglia as risk materials to, for example, to 12 months.

c. However, an alternative argument has sometimes been advanced that infectivity would reach the CNS in the greater proportion of BSE cases at a much later age, because with a mean estimated age of onset of clinical signs of 60 months in field cases and assuming calfhood exposure, half of the incubation period is at approximately 30 months of age.

The doses of infected brain used in the Pathogenesis Study (100g) was relatively high and it is known that the incubation period shortens with increasing dose (EC, 2002). As all animals received the same dose, (and in cattle no genetic factors have been shown to affect susceptibility to BSE) it might also be expected that the incubation period distribution in the animals in this experiment would fall within the range of the incubation periods determined from the dose-response data of cattle infected orally with a dose of BSE infectivity closely similar to that administered to induce disease in the Pathogenesis Study (G. A. H. Wells, unpublished data) As discussed above a preliminary estimate from that study suggests a mean incubation of almost 45 months (range 33-55 months). This mean is clearly less than that indicated from epidemiological observations, for the majority of cases, but the range is, nevertheless, within that estimated for incubation periods for field cases. Thus, following this argument if one allows for a safety margin of some months, for the presence of infectivity at as yet undetectable levels, and given that infectivity in dorsal root ganglia may well be secondary to established CNS infection, it may be concluded that residual risk of vertebral column after removal of the spinal cord would be negligible in the vast majority of infected cattle aged below 24 months.

The TSE/BSE *ad hoc* Group however considers that the BSE in cattle pathogenesis study (Wells, 1998) cannot be exploited to express the time of detectable infectivity in the Central Nervous System tissues as a fraction of the total incubation period and that the limited number of animals used in this study do not allow to conclude that infectivity is absent in the spinal cord until a few months before clinical signs are manifested.

From other experiments with other animal species and for which more data are available (e.g., mice, hamster, primates, sheep, ...) it may be concluded

that the assumption made by the SSC on 12 January 2001, i.e., that in general, as a reasonable worst case assumption, the dorsal root ganglia and the spinal cord are considered to pose a higher risk as from the second half of the incubation period, remains valid.

d. A possible increase of the current age limit of 12 months for treating vertebral column as SRM in bovine animals, depends upon the age below which the probability of infectivity being present [at levels that pose a risk for humans] in the spinal cord and dorsal root ganglia would be remote. This in turn requires a [cost/benefit?] decision of what can be considered as an "acceptable" BSE incidence in terms of human exposure risk.

   The human exposure risk on its turn depend upon the he cattle – human species barrier, which is not known: it could be non-existent (barrier = 1) or even very high (e.g., 10.000). According to the SSC (EC, 2000c), values greater then one are likely to be more realistic.

IV. ANALYSIS OF THE AGE DISTRIBUTION OF RAPID-TEST BSE-POSITIVES IN EUROPEAN UNION IN SECOND SEMESTER OF 2001.

According to the EC (2002) draft report on BSE testing in 2001 a total of 8.501.457 bovine animals were tested in 2001in the framework of the monitoring programme, 2150 of which turned out positive. 8.441.360 bovine animals were tested by active monitoring (rapid tests on risk animals and animals slaughtered for human consumption) while 3.634 bovine animals were tested in the passive surveillance (animals reported as BSE suspects by the farmer or the veterinary practitioner and subject to laboratory examination). In addition, 56.463 animals were tested in the framework of BSE eradication. 49 % of positive cases were detected by the Active Monitoring and 51 % were detected by Passive Surveillance. Positive cases were found in all Member States except Luxembourg and Sweden.

Tables 2 to **9** hereafter are extracted from that report and provide a summary of the information which is relevant in the context of the current opinion.

Annexes 1 - 6 provide the details of the Age Distribution of Positive Cases in 2001, for the following categories of animals: fallen stock, (Healthy slaughtered animals), Risk Animals, Suspects and risk animals.