3. ASSESSING HUMAN EXPOSURE RISK

3.1. Definition

Ideally, Human Exposure Risk (HER) would be expressed as the expected number of people that could be exposed to BSE infectivity from one infected bovine entering the human food chain and processed as an animal declared fit for human consumption.

However, the infectious dose to humans is currently not known. Therefore the Cattle Oral Infectious Dose (CoID), as defined by the SSC in its opinion of 26 March 98, will be used as an indicator of infectivity. The HER will then be defined in terms of the number of consumers exposed to the BSE agent. The extent of exposure will be expressed in $CoID_{50}$.

3.2. General Approach to Assessing the Human Exposure Risk

The Human Exposure Risk (HER) in any country, and at any point in time, will depend on four main factors:

- ⇒ the likelihood that an animal infected with BSE enters the human food chain;
- ⇒ the amount and distribution of infectivity in that animal;
- ⇒ the ways in which the various tissues that could contain infectivity are used in the food chain; and
- ⇒ the marketing of infected foods produced in other countries.

The first of these, the likelihood that an animal infected with BSE enters the human food chain, is the Processing Risk, and will not be considered further here.

The approach taken in this opinion is to consider the exposure in the human population if that one infected animal is slaughtered and processed "normally" for human consumption.

The second factor, the amount of infectivity in that animal to humans will depend on many things, including the length of time after the animal was infected and the overall infectivity of BSE infected tissue to humans. There is much uncertainty and variability in these factors, but, in general, they will be common to all countries. They are discussed below, but do not play a major part in differentiating the HER of different countries.

It is the third of these main factors, the ways in which the various tissues that could contain infectivity are used (hereafter called "routes"), that may differ between different countries, and so could cause variations in the HER, even if the Processing Risk is the same. Any method to assess the HER must therefore concentrate on this factor.

3.3. Steps in Assessing the Human Exposure Risk

3.3.1. Hazard identification

The hazard being considered in this report is the BSE agent. The SSC assumes that consumption of the BSE agent in food can result in variant CJD.

3.3.2. Exposure

Exposure of humans to the BSE-agent depends on the source and the route by which it reaches the consumer.

As the dose response relationship for humans is not known, it is proposed to present the level of exposure in terms of consumption of defined amounts of the BSE agent, measured in Cattle Oral Infective Doses (CoID). However, the SSC wishes to emphasise that the $CoID_{50}$ is used in this opinion only as an indicator and should not be confused with the Human Oral Infective Dose ($HoID_{50}$), which is not known.

3.4. Exposure Assessment

3.4.1. Sources of Infectivity

Different species, as shown by experimental and natural infection, are able to carry the BSE agent. However, this opinion is confined to bovines as the source of the agent. The terms of reference are related to "normal consumption pattern". Therefore the committee did not examine the case of special at-risk groups in the population, for example those exposed to SRMs through the alleged consumption of pet foods. Moreover, because of the lack of data, it was not possible to examine the case of particularly sensitive groups of the population such as children.

The distribution of infectivity in a typical bovine BSE case was considered by the SSC in their opinion on SRM of 9 December 1997 and on the BSE-risk of 19 February 1998. The latter showed that the total infectivity in one animal with clinical BSE is about 8,000 $CoID_{50}$, and that the majority of this infectivity (about 95%) was from the brain, the spinal cord, and the trigeminal and dorsal root ganglia (TRG & DRG). The distal ileum also carries a measurable infectivity and for spleen and eyes a low level of infectivity is assumed based on scrapie experiments. Together these tissues carry about 99% of the infectivity in a clinical BSE case (see table 1).

In making this estimate of the distribution of infectivity, it was assumed that 0.1g of infected brain tissue or spinal cord would make up one cattle oral ID50 (CoID50). This assumption is based on the interim results of the pathogenesis experiment being carried out by the UK MAFF. The infectivity in TRG & DRG is assumed to be the same, while the relative infectivity of other tissues (Ileum, spleen and eyes) is estimated to be lower. This information is based on limited data from mouse bioassay results, for both BSE and scrapie.

With regard to infectivity in other tissues the SSC refers to its opinion of 29 October 1999. There it was noted that "muscle tissue has never been found infective, even from BSE cattle in the later stages of infection, in spite of the fact that peripheral nerves, lymphatic tissue and blood are associated with muscle." It was further shown that currently available experimental data are "strongly suggestive of no infectivity associated with the lymph nodes and spleen in orally infected cattle."

It is known that infectivity builds up in an infected animal over time, so that the infective load in any particular animal will depend on the length of time since that animal was infected with BSE, and what proportion of the incubation period that represents. However, little is known about the dynamics of this. Also, there is no way of knowing when any particular animal would have been infected and age is therefore only an approximation, assuming as a conservative assumption that the animal was infected shortly after birth. The initial dose consumed and the route of transmission will also influence the infective load.

Tissue	Infectivity density ($CoID_{50}/g$)	Weight (kg) per 537 kg Animal	ID_{50} per BSE Case	% of total infective load per animal	Cumulative load
Brain	10	0.5	5,000	64.1%	64.1%
Spinal cord	10	0.2	2,000	25.6%	89.7%
Trigeminal ganglia	10	0.02	200	2.6%	92.3%
Dorsal root ganglia	10	0.03	300	3.8%	96.1%
Ileum	3.20E-01	0.8	260	3.3%	99.4%
Spleen*	3.20E-02	0.8	26	0.3%	99.7%
Eyes	3.20E-02	0.1	3	0.04%	99.74%

Table 1: Total Infectivity in a BSE Case (*Some data suggests that the extrapolation from scrapie to BSE is not valid and then that spleen is unlikely to be infective.)

In addition to the total infective load, the distribution of the BSE-infectivity in the animal's body also changes over time. The MAFF pathogenesis experiment (Wells *et al*, 1998) has shown that at early stages of the incubation, the intestines are infective while at later stages of the incubation, the CNS carries significantly higher infective loads. Little is known about the way by which the infectivity moves through the body. No infectivity was found in the other tissues that were tested for BSE; i.e., the level of infectivity was below the detection level for the mouse bioassay.

On the basis of the available knowledge, it is possible to define three categories of cattle which have different potential levels of infectivity, mainly as a function of their age at slaughter. Depending on the category, the infectivity which could enter the food chain will differ, both in quantity and with regard to the specified risk tissues:

⇒ Veal Calves (less than 1 year). The level of infectivity in the CNS tissues of these animals can be considered to be negligible. However, there may be infectivity in the intestines, in particular the Ileum.

⇒ Prime Beef (older than 1 year, but less than 30 months). These animals could, if infected at birth, show some level of infectivity, though it would be very unlikely to be the same as in a fully developed case of BSE. The CNS is not necessarily highly infective, even if the animal was infected at birth.

⇒ Mature Cattle (older than 30 months). If infected early in their live, these animals may show infectivity levels close to those of clinical BSE-cases, even if no clinical symptoms are apparent. It is clearly evident from the Swiss surveillance of fallen stock and the UK surveillance of cattle over 30 months i.e. those excluded from the food chain under the Over Thirty Months Scheme (OTMS), that apparently healthy but nonetheless infected animals do enter the human food chain in countries where BSE is prevalent in the cattle population. In this category of bovines, the level of infectivity will be high and the CNS is certain to be highly infective.

3.5. Routes of Exposure

It is recognised that there are a number of possible routes by which humans could be exposed to the BSE-agent. This is illustrated in Figure 1. This report refers only to exposure via direct consumption of SRM or of meat products containing them.

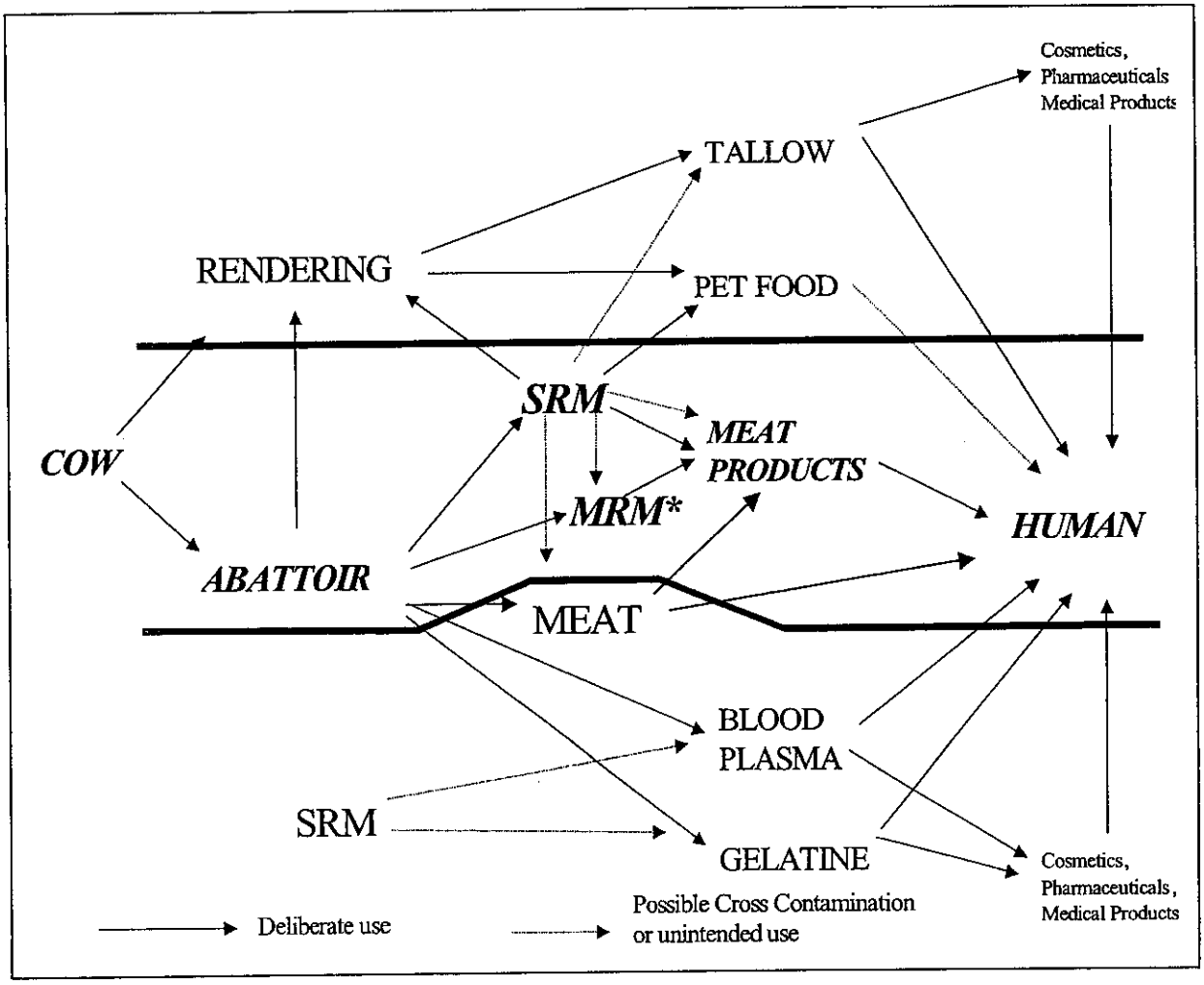
As mentioned above, the large majority of the infectivity in a (clinical) BSE-case will be in the Specified Risk Materials (SRM). In order to assess the routes by which the BSE-agent could reach the consumer, it is therefore necessary to consider all possible ways that SRM could be consumed.

For the purpose of this report, three main routes by which SRM could reach the consumer are distinguished.

3.5.1. Direct consumption

SRMs are consumed as such by the consumer. It is known that brain and spinal cord (amourette in French) are consumed in this way, as well as ileum and all the small intestine (andouillette in French) from young veal (<6months). Even spleen and eyes might occasionally be eaten. Trigeminal ganglia and dorsal root ganglia are not consumed as such, although there will be some direct consumption of DRG (and possibly spinal cord) from cuts of meats served on the bone and including part of the vertebral column (e.g. T-bone steak, rib of beef).

Figure 1. Potential Routes of Exposure to Infective Cattle Tissues
(This opinion deals only with the routes between the two Lines and the factors printed in ***bold italics***; * MRM = Mechanically Recovered Meat, see opinion of the SCVPH, 2/1998)



3.5.2. Indirect consumption.

SRM is transformed and integrated into food products in such a way that it is not detectable by the consumer. The inclusion of SRM into food products may happen voluntarily or by contamination.

3.5.2.1. Voluntary inclusion of SRM.

The use of brain or spinal cord in "paté" or sausages is an example of the voluntary use of SRM. Other SRM may also be included into food products as direct ingredients. Data are available from a recent study in Germany, where there is no ban on the use of SRM in human food, and (bovine) brain tissue was included in sausages. Lücker *et al* (1999_a-1999_d), detected CNS in 14.5% of the 69 samples of a specific sausage (Kochmettwürste) which were analysed using immuno-assays specific to bovine CNS.

3.5.2.2. Contamination of edible products with SRM.

Contamination is always possible if the inclusion of SRM is technically possible and does not create quality problems. Also MRM could be contaminated, particularly if it is produced, inter alia, from vertebral column that could include both DRG and spinal cord. It should be noted that, from a technical point of view, MRM could be included in many "meat" products. Tallow and gelatin would normally not contain any SRM but certain contamination of the raw material with brain or spinal cord could occur.

3.5.3. Estimation of the Exposure Level and of the number of persons exposed.

In order to estimate the expected number of people that would be exposed to an infected dose, several critical factors have to be considered. Some of them are related to the Sources, others to the Routes.

3.5.4 Critical factors determining the HER

3.5.4.1 Critical factors as regards to Sources

⇒ Processing risk. The probability that an infective bovine is slaughtered for food is the most relevant parameter for the Human exposure risk. Its assessment is not the subject of this report.

⇒ Age of the infected animal that is slaughtered and "normally" processed. It influences the infective load and its distribution between the tissues of the animal as indicated by the categories given in Section 3.4.1.

⇒ Infected animals per batch. As long as the BSE-cases remain geographically scattered, the number of exposed consumers would be proportional to the number of processed BSE-infected animals and the average exposure dose would remain rather constant.

If the BSE-density is so high that more than one infective animal could enter a single batch of production, the number of consumers exposed would remain stable while the dose per exposed individual would increase proportional to the number of infected animals entering the batch.

3.5.4.2. Critical factors as regards to Routes

⇒ Processing conditions. In principle, processing conditions could influence the level of infectivity in the product. It is known, for example, that certain production processes for gelatine and tallow reduces the infective load at least a 1,000-fold. (See SSC opinions on these products). However, normal cooking and industrial food processing of the products addressed in this opinion are unlikely to affect the level of infectivity.

⇒ Batch size. The batch size of food products into which SRM is integrated directly (meat products, paté, sausages) or indirectly (via MRM) will significantly influence the number of persons exposed. Larger batches may expose a higher number of people to a smaller dose, and vice-versa.

⇒ Serving size. Together with the batch size, the serving size influences the dose of exposure and the number of persons exposed.

⇒ Contamination. The potential for contamination with SRM (e.g. of MRM) will increase the likelihood of exposure to infectivity. The dose of exposure due to contamination is likely to be low, although the number of persons exposed could be high depending on batch and serving size as above.

⇒ Use of SRM. Deliberate use of SRM will increase the infectious load and hence the exposure dose.

Note: The route into which a given SRM will be channelled, largely depends on two factors:

⇒ Price. The relative price for brain, spinal cord and other SRM for direct consumption (direct eating), integration into higher value added products (paté or sausages), MRM (for low value added food products or pet-feed) or rendering will determine the use made of these tissues. Generally there will be a tendency to choose the most profitable option. For example, the price of the brain or spinal cord for human consumption is between 3,000 and 5,000 FF/ton (460 to 760 €/tonne). The value for the same tissues included in MRM for pet food can be 5 times lower (1,000 to 1,700 FF/ton or 150 to 250 €/tonne).

⇒ Outlet. The size of the different market outlet for the different tissues will also influence the use of the SRM. This size depends, inter alia, on traditions and eating habits but it will also be influenced by legislation.

3.6 Quantitative exposure assessment

The SSC attempted to estimate human exposure risk from all food-borne exposures, including via gelatine and tallow. However, the issue is far more complex than for geographic BSE risk and there is very limited quantitative data available for most of the critically important variables.

The SSC requested detailed information on the use made of different bovine tissues from the Member States. Only three responded but in rather global and qualitative terms only. That information has been taken into account in establishing the scenarios described below.

In the longer term, it should be possible to construct stochastic models to estimate human exposure to not only the BSE agent but other food borne hazards such as dioxin or ochratoxin. Therefore for the purpose of the present opinion, the SSC has focussed on what is possible, i.e. scenarios, with no data on the probability of their occurrence.

4. EXPOSURE SCENARIOS

The following scenarios are intended to illustrate realistic values for the human exposure risk resulting from one infected bovine entering the human food chain and processed as an animal declared fit for human consumption.

4.1. Scenario 1 - Maximal distribution, only indirect consumption

Note: This scenario is based on data generated from a household survey in 1993, food composition databases and interviews with food industry and govern,ent departments. While the assumptions are felt to be realistic for this historic situation, it is not assuming that they describe a currently existing situation. However, it is the opinion of the SSC that the scenario illustrates a realistic upper end of the number of people that could be exposed to the BSE-infectivity. For details of calculation see Annex 1.

4.1.1. Assumptions

The entire infective material of a BSE-case is included in mechanically recovered meat (MRM). It is important to understand that a smaller amount of infectivity entering the MRM would contaminate the same amount of product – only the average infective load would be lower.

MRM is produced in batches of 5 to 7 tonnes. This information was obtained from industry and refers to current production of MRM for pet-food. It is confirmed by quality control prescriptions of the industry, which require destruction of at least 5 tonnes of MRM (=one batch) if a quality problem is recognised (bacterial contamination etc.).

About 7kg of MRM is obtained from one animal. Thus one batch contains material from up to 1,000 animals. If one of these animals is infective, the entire batch is contaminated, and it is assumed that any infectivity would be distributed evenly throughout the batch.

The average MRM content of food products varies between 100% ("meat" filling of cheap stuffed pasta could technically have been made from MRM only) and 5 to 10% (minced meat preparations, for example, could contain that fraction of MRM without technological problems).

Minced meat is normally sold in packages of 600g to households with 2.7 persons on average.

Cheap meat stuffed pasta contains about 13% of filling and is sold in 1,000g packs per household averaging 2.7 persons.

4.1.2. Conclusions

Given the large batch size and the small proportion of MRM in meat-products, one animal could contaminate 5 tonnes (pasta filling) to 116 tonnes (minced meat) of food products.

A large number of servings could thus be contaminated, albeit with a low average dose per serving.

Calculations based on the assumptions made, indicate that one 5-tonne-batch of MRM could expose about 200,000 (via "pasta") to 400,000 persons (via minced meat preparations) to the BSE infectivity (see annex 1).

The same calculation showed that the average infective load would be between 0.023 and 0.043 CoID50 per consumer if the entire infective load of the animal ends up in MRM. Excluding CNS-SRM (Brain, spinal-cord, trigeminal and dorsal route ganglia[10]) from the production of MRM would reduce the dose of exposure by about 95%.

4.2. Scenario 2 - Mean distribution, only indirect consumption

The following scenario is based on assumptions only. It serves as an illustration of a medium level of dispersion of the BSE infectivity.

4.2.1. Assumptions

The entire brain and spinal cord (700g) are mixed into paté or sausages up to a fraction of 5%.

The average serving of "paté" or sausage is 50g to 100g and could hence contain 2.5g – 5g brain or spinal cord.

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[10] Because of the risk of contamination with CNS, the vertebral column and head-bones should not be used for MRM production.

Each serving is eaten by a different person.

The remaining 12 % of the infectivity are rendered or directly fed to animals.

4.2.2. Conclusions

If "paté" or sausages are prepared in batches of 14kg, i.e. where the 700g of brain and spinal cord are just 5%, 280 servings of "paté" or 140 servings of sausages could be contaminated by one single infectious animal.

The average infective load would be between 25 and 50 $CoID_{50}$ per consumer.

If the batches are larger and the fraction of brain and spinal cord included is lower, the number of contaminated servings would increase and the infective load per consumer would decrease accordingly.

4.3. Scenario 3 – Concentration, only direct consumption

This scenario is based on realistic historical data. The assumption, that the entire infectivity outside the brain is not entering the food chain is, however, rather optimistic.

4.3.1. Assumptions

No MRM produced from bovine material.

Brain directly eaten at average servings of 100g.

The remaining infective tissue is rendered or directly fed to animals.

4.3.2. Conclusions

5 persons would eat the brain of the assumed infected animal. They would be exposed to 1,000 $CoID_{50}$, each.

The estimated exposures from these and similar scenarios are plotted in Figure 2, as number of exposed consumers against exposure dose, measured in $CoID_{50}$. No attempt has been made to consider the relative likelihood of these outcomes.

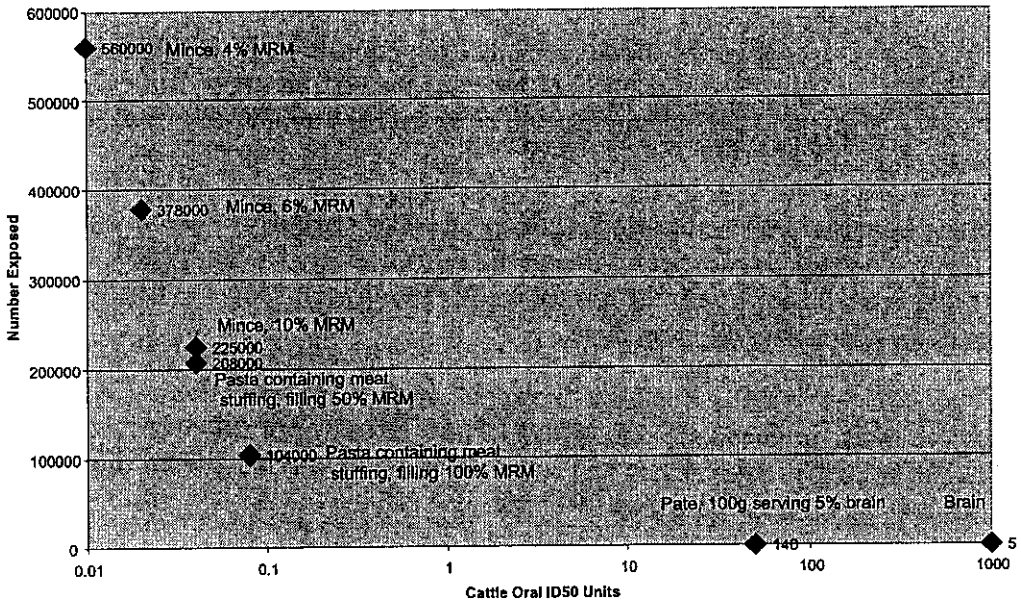

Figure 2: Summary of Exposure Estimates from Scenarios

- Mince, 4%, 6% MRM = Minced meat, containing 4%, 6% MRM, servings of 100g
- Meat stuffed pasta, filling 50%, 100% MRM = Meat stuffed pasta, filling consists of 50%, 100% MRM, serving = 370g containing 13% filling
- "Paté", 100g serving, 5% brain = "Paté" prepared with 5% brain and served at 100g portions.
- Brain = Brain, directly consumed in servings of 100g