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Assessment of Risk from Possible BSE Infectivity in Dorsal Root Ganglia

For the

Ministry of Agriculture, Fisheries and Food

and the

Spongiform Encephalopathy Advisory Committee

Approved by:.....
Philip J Comer
Director of Environmental Services

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Management Summary

Results from the BSE Pathogenesis Experiment being carried out by the Central Veterinary Laboratory have indicated the presence of infectivity in some tissues closely related to the spinal cord, but which would not formally be defined as SBM in the United Kingdom. These tissues are the dorsal root ganglia, which would probably remain attached to the vertebral column after the spinal cord is removed, and may on occasion be included in meat for human consumption. SEAC have requested that a formal risk assessment be carried out to determine the level of risk to people due to the possibility that there could be infectivity in these tissues from cattle under the age of 30 months.

The results of the pathogenesis experiment indicate that significant levels of infectivity are present in CNS tissues, including the dorsal root ganglia, in the three months prior to clinical onset of the disease. At nine months prior to clinical onset no infectivity has been detected.

Estimates have been made of the number of cattle that could have infectivity in CNS tissues at the time of slaughter for human consumption, of the likelihood that the dorsal root ganglia would not be discarded with the bone during boning-out, and that dorsal root ganglia contained in meat sold as bone-in would be consumed. The data have been combined in a simple event tree, and the risk evaluated using Monte Carlo simulation.

Two measures of risk have been determined, both of which are based on the consumption of human oral ID_{50} units. The first measure is the total consumption per year of human oral ID_{50} units for all people in the United Kingdom. This is a measure of societal or group risk. The second measure is the individual risk, which is represented by the expected consumption per year by any one individual of human oral ID_{50} units.

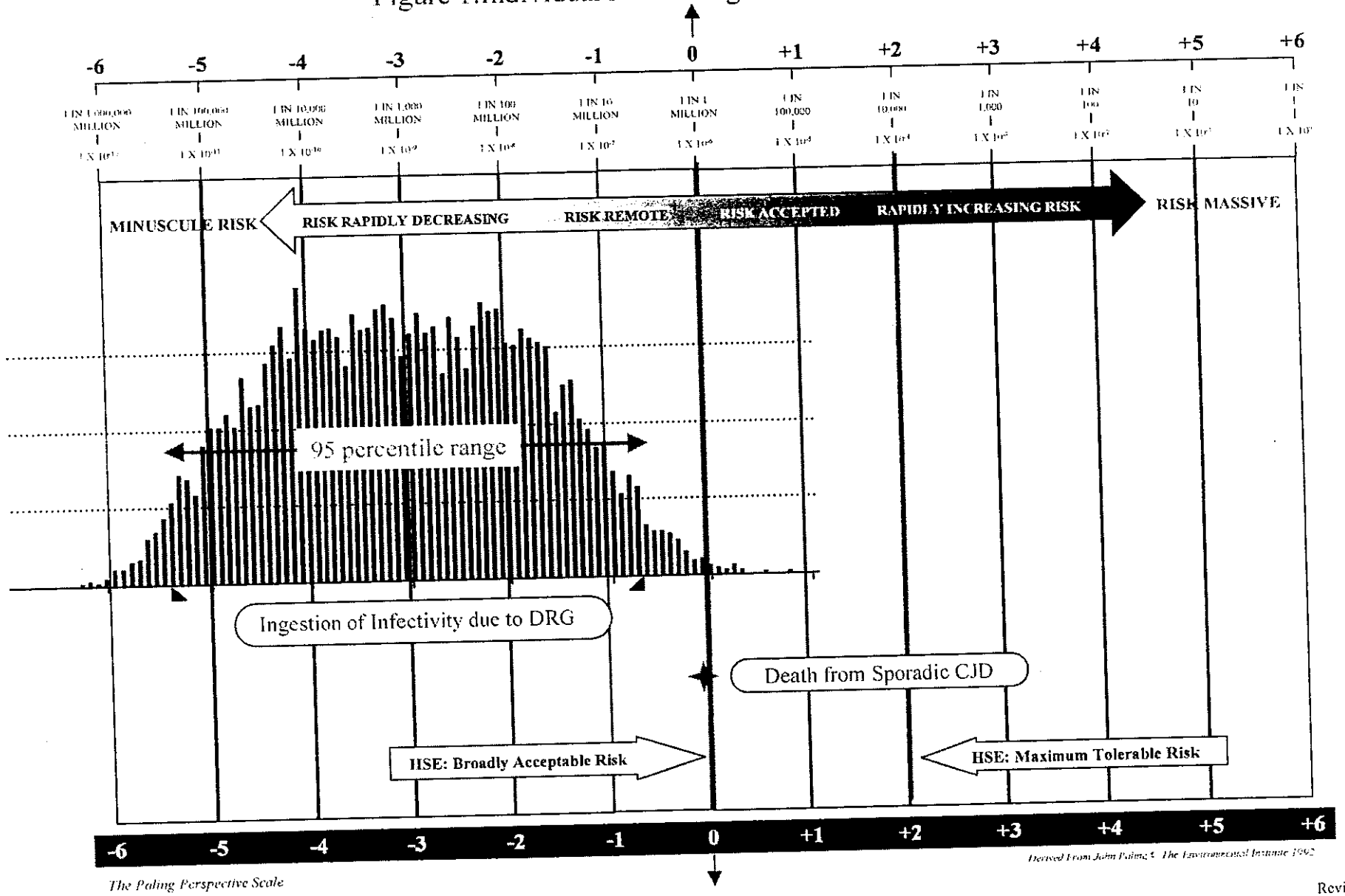
Total Ingestion of infectivity
The median value of the total ingestion of infectivity due to infectivity in dorsal root ganglia of cattle with infectivity in the CNS at less than 30 months of age, has been estimated to be 0.05 ID_{50} units over the whole UK population in 1997. The 95% range is from zero to 11 ID_{50} units, and the probability of the total ingestion being less than 1 is 80%.

With the continuing fall in numbers of confirmed BSE cases, the value for 1998 would be less, about 75% of the value in 1997.

The results also show that 24% of this total ingestion of infectivity is due to bone in meat (range 10% - 45%). The remainder is due to the proportion of DRG left in the meat in boning out operations.

Individual risk
The median value of the individual risk of ingestion has been estimated to be 9×10^{-10} ID_{50} units per person per year. The 95% range is from 5×10^{-12} to 2×10^{-7} ID_{50} units per person per year, which is some four orders of magnitude. The results are illustrated on a risk perspective scale on Figure 1.

Figure 1:Individual Risk of Ingestion of Infectivity



The Paling Perspective Scale

Derived from John Paling's The Environmental Institute 1992

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1. INTRODUCTION

1.1 Background

Results from the BSE Pathogenesis Experiment being carried out by the Central Veterinary Laboratory have indicated the presence of infectivity in some tissues closely related to the spinal cord, but which would not formally be defined as SBM in the United Kingdom. These tissues are the dorsal root ganglia, which would probably remain attached to the vertebral column after the spinal cord is removed, and may therefore be included in meat for human consumption. SEAC have requested that a formal risk assessment be carried out to determine the level of risk to people due to the possibility that there could be infectivity in these tissues from cattle under the age of 30 months.

Det Norske Veritas have carried out a series of studies for the Environment Agency to assess the risk from BSE infectivity through environmental pathways. As a result of this experience, DNV were requested by the Ministry of Agriculture, Fisheries and Food to undertake this study. This study has used a similar approach to the previous risk assessments carried out, and draws on the information and knowledge obtained.

1.2 Objective

The Objective of this study to quantify the risks to people from the consumption of beef products due the possible contamination with infectivity contained in the dorsal root ganglia of cattle with BSE infectivity when they are slaughtered.

2. METHOD

In order to assess the risk from infectivity in the Dorsal Root Ganglia (DRG) it is necessary:

1. To assess the expected number of cattle that may have significant levels of infectivity when they are slaughtered at less than 30 months of age.

2. To assess the level of infectivity in the DRG.

3. To assess the likelihood that DRG would be included in edible meat, rather than being discarded with the bone.

4. To assess the likelihood that the DRG contained in a piece of meat sold as bone-in (e.g. rib of beef, T-bone steak) would be consumed.

2.1 The Pathogenesis Experiment

It is not the place of this report to present the results of the Pathogenesis Experiment. However, results that are of relevance to this study are summarised below.

1. Infectivity has now been detected in the brain and spinal cord of cattle killed at 32 months or more post infection. There has, so far, been no indication of infectivity in the CNS at 26 months post infection.

2. The positive result at 32 months post infection is approximately three months before the first clinical signs were seen.

3. Infectivity has also been detected in nervous tissue that is closely associated with the brain (the trigeminal ganglion) and the spinal cord (mid-cervical and mid-thoracic dorsal root ganglion). The former would be included in the definition of SBM by virtue of being within the skull. The latter is not defined as SBM, and would probably remain attached to the vertebral column after the spinal cord is removed.

4. The results indicate similar levels of infectivity between the DRG and the brain and spinal cord (at least at the present time there are no data on which to differentiate them).

5. The experiment is not complete, and the above could be modified in the light of new results.

The following conclusions are drawn for inclusion in this study:

1. Significant levels of infectivity are present in CNS tissues, including the DRG, in the three months prior to clinical onset of the disease. At nine months prior to clinical onset no infectivity has been detected. To add a margin of safety it will be assumed that infectivity may be present up to 9 months prior to clinical onset.

2. Infectivity in the DRG is assumed to be at the same level as other CNS tissues.

2.2 Numbers of Infected Cattle Slaughtered

Since April 1996, cattle over 30 months have been slaughtered separately and kept out of the human food chain; this is the over 30-month scheme (OTMS). Since nearly all cases of BSE have occurred in cattle over 30 months of age, the OTMS cattle will include most of those that are at an advanced stage of incubation at the time of slaughter.

If significant infectivity is only present in the CNS up to 9 months before clinical onset, it follows that an animal with infectivity at less than 30 months of age will develop clinical symptoms within 38 months of age if it is not slaughtered before then. Data showing age at onset for the BSE epidemic for the period 1986 to 1997 is summarised in Table 2.1.

Table 2.1: Confirmed BSE cases by Age at Onset and Year (UK)

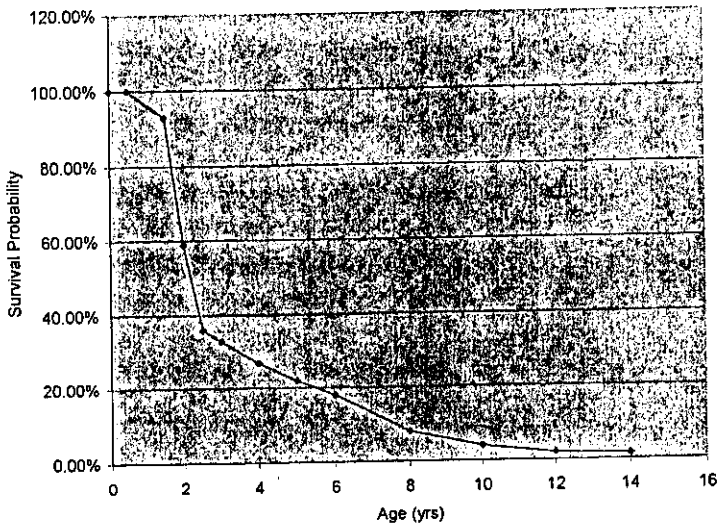
Age at onset (months)	Year of Onset												Total
	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997*	
Under 31	1	1	6	18	20	14	13	4	2	1	2	0	82
Under 34	2	3	14	35	42	37	22	10	7	2	4	0	178
Under 38	3	12	48	111	274	154	75	35	26	20	11	4	773
Under 41	3	24	87	207	591	616	208	115	76	73	43	21	2064
Under 45	4	54	232	467	1267	2133	674	465	256	236	144	65	5997
All ages	12	460	3143	7775	14612	25856	37151	33771	22910	13812	7375	2564	169441

* To 31 October 1997

Table 2.1 shows that there have been 773 cases of BSE (0.46% of all cases) with an age at onset of less than 38 months over the entire epidemic, most of which occurred from 1988 to 1992. The table also shows that the number of cases under 38 months has declined more rapidly than the total number of cases. Over the period 1994 to 1996 the number of cases under 38 months declined from 26 to 11. Up to the 31st October 1997 there have been 4 cases under 38 months in age in 1997. At this rate, it would be expected that there would be a total of 5 cases under 38 months in 1997, and this is assumed to reduce to 3 in 1998.

Estimates of survival probability by age have been made by Donnelly et al (1997), based on cattle census data and on National Milk Records. Their results are reproduced as Figure 2.1.

Figure 2.1: Survival Probability by Age



These data shows that the survival probability at age 24 months is 59%, whereas at age 30 months it is 36%. Thus, 39% of the cattle alive at 24 months have been slaughtered by the age of 30 months. At 38 months of age the survival probability is 32%, and thus a further 11% would be killed between 30 months and 38 months of age. However, these data are based on the period before the OTMS came into effect. It is likely that cattle that were slaughtered between 30 months and 38 months of age, would now be slaughtered before 30 months. ***For the purpose of this study it will be assumed that 46% of the cattle alive at 24 months have been slaughtered by the age of 30 months.***

It is assumed that cattle slaughtered between 24 and 30 months of age have the same risk of infection as those that survive to 38 months. The number of animals slaughtered between 24 and 30 months which have a significant level of infectivity may then be estimated as follows:

Number of cattle alive at 24 months	=	N
Number slaughtered by 30 months	=	0.46 x N
Number alive at 38 months	=	(1 – 0.46) x N
Cases of BSE with ages less than 38 months	=	I
Rate of BSE cases (< 38 months) per animal	=	I / (1 – 0.46)N
Number with infectivity at < 30 months	=	I x 0.46N / (1 – 0.46)N
	=	0.85 x I

Thus the expected number of animals with significant infectivity at 30 months is 0.85 times the number of BSE cases at age 30 to 38 months.

Conclusion: The estimates for the number of infected cattle slaughtered for food following the introduction of the OTMS are therefore 4 in 1997 and 3 in 1998. The data suggest that there is a negligible risk of infectivity in animals slaughtered at 24 months of age or less.

2.3 Infectivity in CNS Tissues

The infectivity (i.e. the potential to cause infection) of tissue from cattle with BSE is expressed in terms of its ID_{50} value. This is the dose (i.e. the quantity which each person would need to consume) to cause infection of 50% of the exposed population. This term acknowledges that some people may become infected from much smaller doses, while others may be uninfected after consuming much larger doses.

2.3.1 Infectious Dose for Cattle

An experiment is in progress at the MAFF Central Veterinary Laboratory to identify the effect on cattle of oral doses of BSE infected cattle brain. Based on the information from these experiments in April 1997, SEAC advised that "The best estimate to date from an experiment still in progress is that the oral ID_{50} of clinically affected BSE brain for cattle is about 1 gram." As noted, the experiment is still in progress, and if further cattle were to become affected then the estimate of the oral ID_{50} might change. Following further discussions of this with SEAC it was decided to take a precautionary view and assume that the mean value of the oral ID_{50} for cattle is 0.1 gram (i.e. 10 oral ID_{50} units per gram).

For sensitivity tests, a maximum value 1g is assumed. A minimum value is not evident from this data, but a 90%ile of 0.01g is assumed.

2.3.2 Infectious Dose for Humans

The infectivity of BSE for humans is expected to be lower than in cattle due to the species barrier. In the absence of experimental data on the cattle-human species barrier, SEAC have suggested a probabilistic uncertainty analysis using values of 10, 100, 1000 and greater than 1000 with equal probabilities, and less than 1% probability of it being 1. For the event trees in this study, a best-estimate value is required, and a value of 10 is used, being the most pessimistic of the relatively likely values suggested by SEAC.

The best estimate of the oral infectivity of whole-brains from BSE cases for humans is 1 human oral ID_{50}/gram. The confidence range would be 0.0001 to 10.

It is assumed that infectivity in the dorsal root ganglia is the same as that in the brain and spinal cord. It has been estimated that the weight of dorsal root ganglia in a typical carcase is 30 g. There are a total of about 60 DRG in a carcase.

2.4 Fate of Dorsal Root Ganglia

Following slaughter, the carcase is sawn in two and the spinal cord removed as SBM. The dorsal root ganglia would not be removed with the spinal cord but remain attached to the vertebral column. The subsequent fate of the DRG will depend on how the carcase is dressed.

Investigation of carcases by MAFF veterinarians, and by experienced butchers from the Meat and Livestock Commission (MLC), has demonstrated that the DRG are very closely attached to the vertebral column and would be very unlikely to be removed in normal boning out operations. This is especially true with the pressures on a commercial operation. The vertebral column may not be used for MRM, and since August 1997 must be treated as SBM.

In the UK most beef reaches the consumer without bone. Where meat is purchased with the bone in, the DRG could still be present in cuts such as a Rib of Beef, and a T-bone steak. If a Rib joint is being carved in a restaurant (e.g. a carvery), it is most unlikely that it would be carved so as to remove the DRG from the bone. However, the bone may subsequently be used to make stock. In a domestic environment the joint may be carved closer to the bone; even so, it is considered unlikely that the DRG would be removed. With a T-bone steak, it is again considered relatively unlikely that the DRG would be consumed unless the bone was thoroughly cleaned.

To assess the fate of the DRG it is first necessary to consider the types of cut of meat along the length of the vertebral column. There are five main sections, the neck, chuck, fore rib, sirloin and rump (MLC, 1980). Neck and rump cuts are always sold boneless, and the same is true for chuck most of the time.

The Sirloin cut includes the 6 lumbar vertebrae and 3 thoracic vertebrae; i.e. 9 out of the total 30 (30%) of the vertebrae and therefore DRGs. It is used to produce both fillet steak and sirloin steak, both boneless, and also T-bone steaks. Some may also be used for a bone-in sirloin roast, but this is not common.

The Fore Rib normally includes 4 ribs and thoracic vertebrae, and therefore 13% of the DRGs. The Fore Rib is used for both rib roasts on the bone, but is also prepared as boneless rolled or as steaks. When fore rib is sold bone-in, it is common for the bone of the vertebral column to be removed, and to leave only the rib bone (Stone et al, 1990). This would remove the DRG. It has been estimated that 90% of catering outlets would remove the vertebral column from rib roasts, and about 70% of retail butchers and multiples (MLC, 1997).

It has been estimated that overall some 5% of meat is sold bone-in in the UK. This will include a number of cuts including leg/shin, top ribs, brisket etc. The only bone-in cuts of possible concern due to DRG are those which could include the vertebral column, i.e. T-bone steaks and rib roasts.

Data from the Meat and Livestock Commission (MLC) indicate about 6 million T-bone steaks are sold annually, which would be equivalent to about 300,000 carcases. Some 2.25 million prime beef carcases are slaughtered in the UK. Thus T-bones will be produced from about 13% of the cattle slaughtered.

Some 12,000 tonnes of retail fore ribs are sold at about 7kg each, which would be produced from about 860,000 carcases. Also, 13,000 tonnes of catering fore ribs are sold at about 8kg each, which would be produced from about 810,000 carcases. About 30% of fore ribs are produced from imported meat. Thus 27% of the UK production goes to retail fore ribs and 25% to catering fore ribs, leaving 48% for boneless cuts.

The following assumptions have been made to assess the potential exposure to DRG. It is stressed that these are estimates based on judgement.

1. When meat is removed from the bone it is assumed that 99% of the DRG will remain attached to the vertebral column. It is assumed that this is the same for commercial boning plants as for retail butchers. This is thought to be conservative, and in commercial plants it is likely that 100% would remain attached to the vertebral column.

2. For meat sold as bone-in whether domestic or catering, it is assumed that the DRG will be consumed 5% of the time.

3. RISK ASSESSMENT

The risk that the there could be some BSE infectivity in non SBM tissue present in cattle slaughtered for human consumption has been assessed by combining the data and assumptions presented in the previous section in a simple "event tree". Two measures of risk have been determined, both of which are based on the consumption of human oral ID_{50} units. The first measure is the total consumption per year of human oral ID_{50} units for all people in the United Kingdom. This is a measure of societal or group risk. The second measure is the individual risk, which is represented by the expected consumption per year by any one individual of human oral ID_{50} units.

For small doses, the quantity ingested provides an extremely pessimistic estimate of the risk, because of the probable existence of a safe threshold which is at present unquantified.

3.1 Event Tree

The event tree for assessing the exposure to infectivity in DRG is shown as Figure 3.1. The infectivity in the material is given on the left side of the event tree. This is simply the mass of material per animal times the infectivity density times the number of infected animals slaughtered in that year.

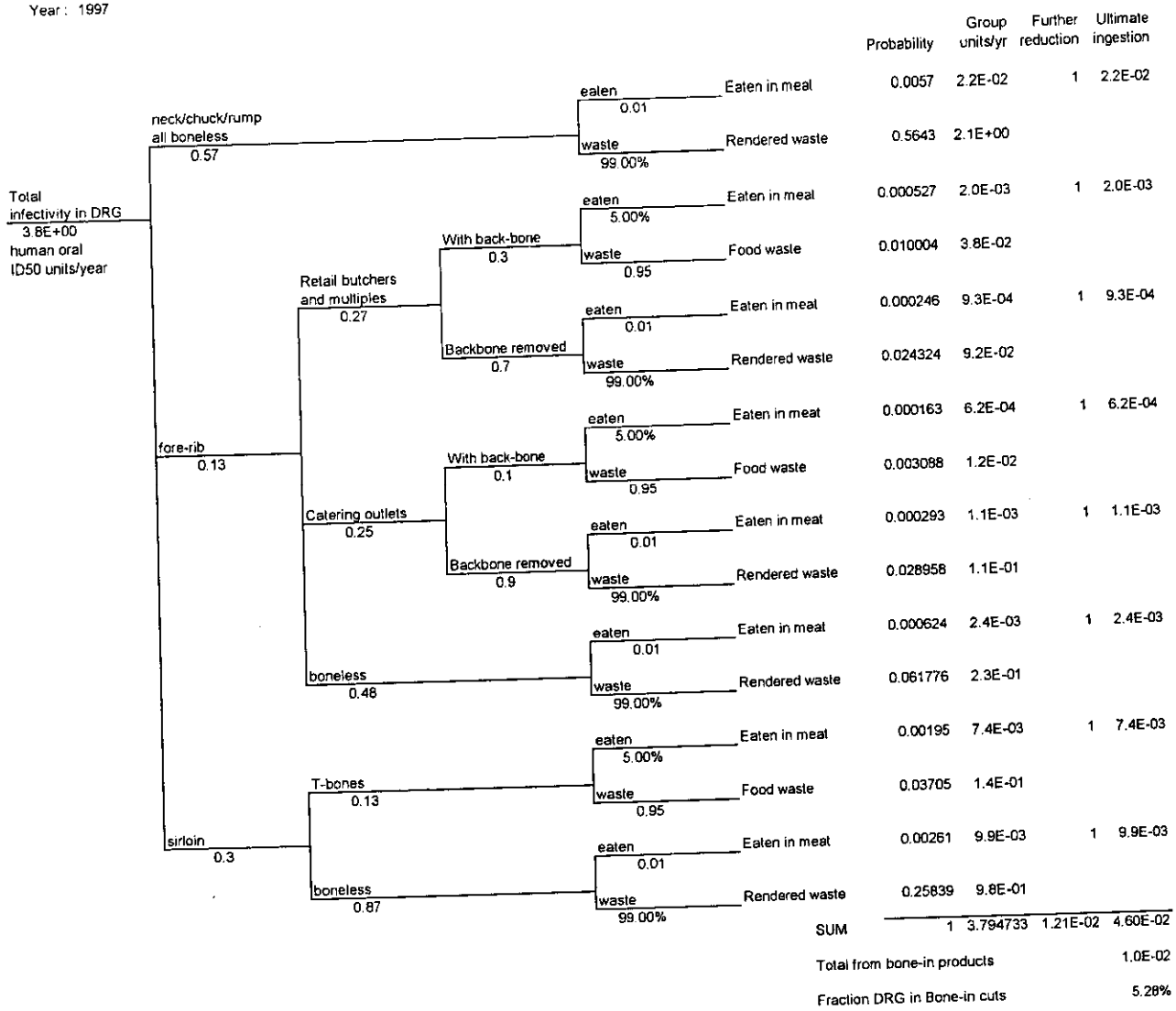
On the right side of the event tree there are four columns. The first of these gives the total probability for that pathway. This is simply the product of all the branch probabilities along the pathway. The second column gives the resulting total infectivity units for that pathway. This is the product of the probability in column 1 with the total input infectivity. The third and fourth columns only have values when that pathway can result in that infectivity being ingested. Column 3 is only used if there is further reduction of the infectivity, for example if the infectivity is input to another event tree. Column 4 gives the ultimate ingestion.

3.2 Risk Evaluation

The risk results have been evaluated using Monte Carlo simulation in order to take account of the uncertainty in the input parameters. Each variable has been defined as a distribution of values rather than as a single point value, and the result calculated many times using a simulation program.

FIGURE 3.1 : EVENT TREE FOR DORSAL ROOT GANGLIA

Year : 1997



	Probability	Group units/yr	Further reduction	Ultimate ingestion
Eaten in meat	0.0057	2.2E-02	1	2.2E-02
Rendered waste	0.5643	2.1E+00		
Eaten in meat	0.000527	2.0E-03	1	2.0E-03
Food waste	0.010004	3.8E-02		
Eaten in meat	0.000246	9.3E-04	1	9.3E-04
Rendered waste	0.024324	9.2E-02		
Eaten in meat	0.000163	6.2E-04	1	6.2E-04
Food waste	0.003088	1.2E-02		
Eaten in meat	0.000293	1.1E-03	1	1.1E-03
Rendered waste	0.028958	1.1E-01		
Eaten in meat	0.000624	2.4E-03	1	2.4E-03
Rendered waste	0.061776	2.3E-01		
Eaten in meat	0.00195	7.4E-03	1	7.4E-03
Food waste	0.03705	1.4E-01		
Eaten in meat	0.00261	9.9E-03	1	9.9E-03
Rendered waste	0.25839	9.8E-01		
SUM	1	3.794733	1.21E-02	4.60E-02
Total from bone-in products				1.0E-02
Fraction DRG in Bone-in cuts				5.28%

3.3 Input Data

The definitions of the input assumptions are summarised below.

Cattle Man Species Barrier
Probability distribution; Discrete values:

1	1%
10	24.75%
100	24.75%
1000	24.75%
10,000	24.75%

Infectivity of BSE infected brain
Log Normal Distribution; geometric mean 10, 95% ile 100, range 1 to 1000

Number of Clinical cases < 38 months old
Poisson Distribution; Rate = 4.

Weight of dorsal root ganglia in a carcase
Normal distribution; Mean = 30g, Standard Deviation = 3g.

Fraction DRGs in Fore Ribs
Normal distribution; Mean = 13%, Standard Deviation = 1.3 %.

Fraction DRGs in Sirloin
Normal distribution; Mean = 30%, Standard Deviation = 3.0 %.

Fraction Sirloin sold as T-bone
Normal distribution; Mean = 13%, Standard Deviation = 1.3 %.

Fraction Fore Rib sold by retail butchers/multiples
Normal distribution; Mean = 27%, Standard Deviation = 2.7 %.

Fraction Fore Rib sold by retail catering
Normal distribution; Mean = 25%, Standard Deviation = 2.5 %.

Fraction backbone removed by retail butchers
Normal distribution; Mean = 70%, Standard Deviation = 7.0 %.

Fraction backbone removed by catering butchers
Normal distribution; Mean = 90%, Standard Deviation = 9.0 %.

Probability Infectivity does not remain in bone
Log normal distribution; Mean = 1%, Standard Deviation = 0.5 %.

Likelihood of Infectivity being consumed from bone-in meat
Log normal distribution; Mean = 5%, Standard Deviation = 1%.

Proportion of UK population eating beef
Normal distribution; Mean = 88%, Standard Deviation = 9%.

3.4 Results

3.4.1 Total Ingestion of infectivity

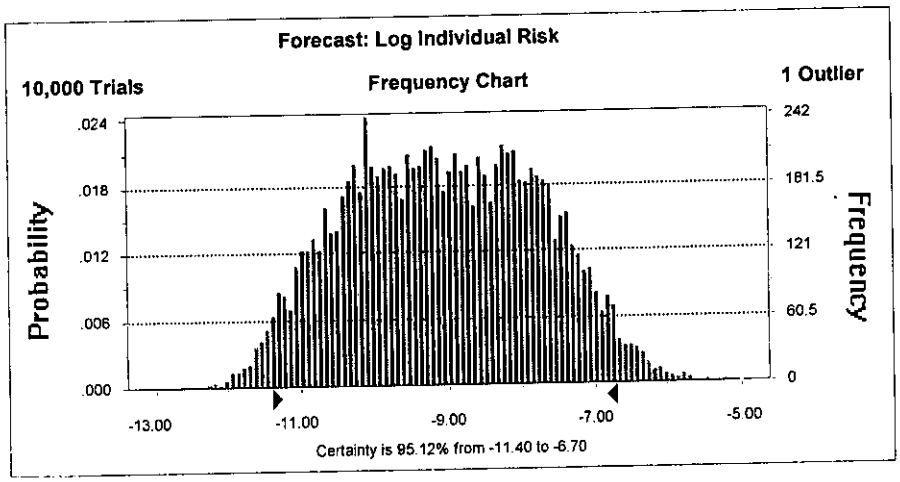
The median value of the total ingestion of infectivity due to infectivity in dorsal root ganglia of cattle with infectivity in the CNS at less than 30 months of age, has been estimated to be 0.05 ID_{50} units over the whole UK population in 1997. The 95% range is from zero to 11 ID_{50} units, and the probability of the total ingestion being less than 1 is 80%.

The results also show that 24% of this total ingestion of infectivity is due to bone in meat (range 10% - 45%). The remainder is due to the proportion of DRG left in the meat in boning out operations.

3.4.2 Individual Risk

The median value of the individual risk of ingestion has been estimated to be 9×10^{-10} ID_{50} units per person per year. The 95% range is from 5×10^{-12} to 2×10^{-7} ID_{50} units per person per year, which is some four orders of magnitude. The frequency distribution of the log of the individual risk is shown in Figure 3.2.

Figure 3.2: Frequency Distribution of the Log of Individual Risk

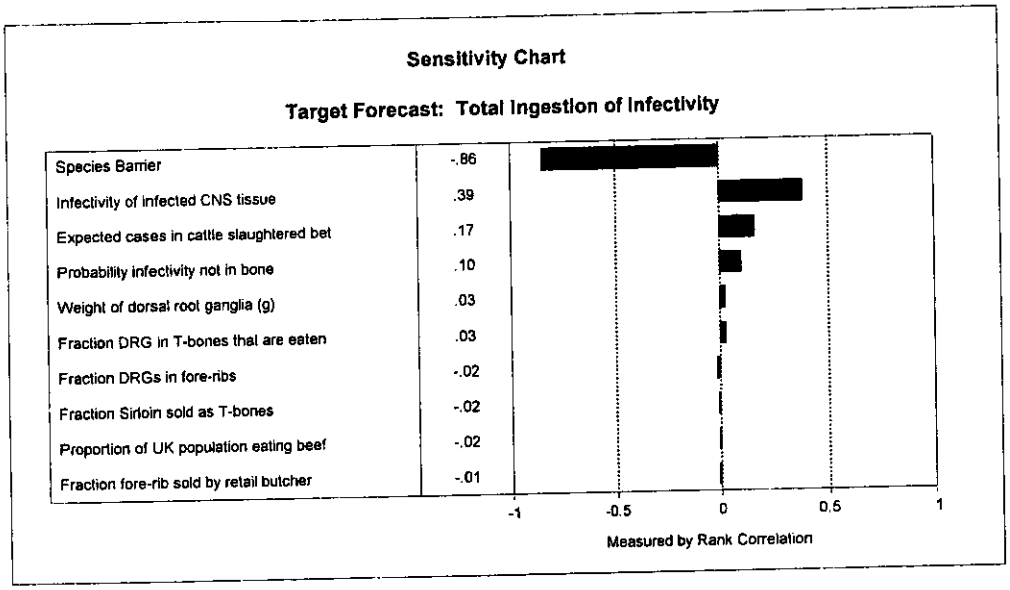


The individual risk has been estimated by dividing the total infectivity ingested by an estimate of the number of people in the UK that eat beef. This could be refined by obtaining data on the numbers of people that eat certain cuts of meat (Rib roasts, T-bone steaks, etc). However it is not expected that this would make a substantial difference to the results.

3.4.3 Sensitivity

The sensitivity of the individual risk result to the individual input assumptions is shown in Figure 3.3. This shows the contribution to the overall variance from each of the input parameters. This shows that the sensitivity is dominated by the variation in the Species Barrier, which has been defined with a uniform distribution over four orders of magnitude. The next most important parameters are the estimated infectivity in infected tissue, the number of animals with infectivity slaughtered and the proportion of infectivity that is removed from the bone into the edible portion in a boning out operation.

Figure 3.3: Sensitivity of Individual Risk to Input Uncertainties



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