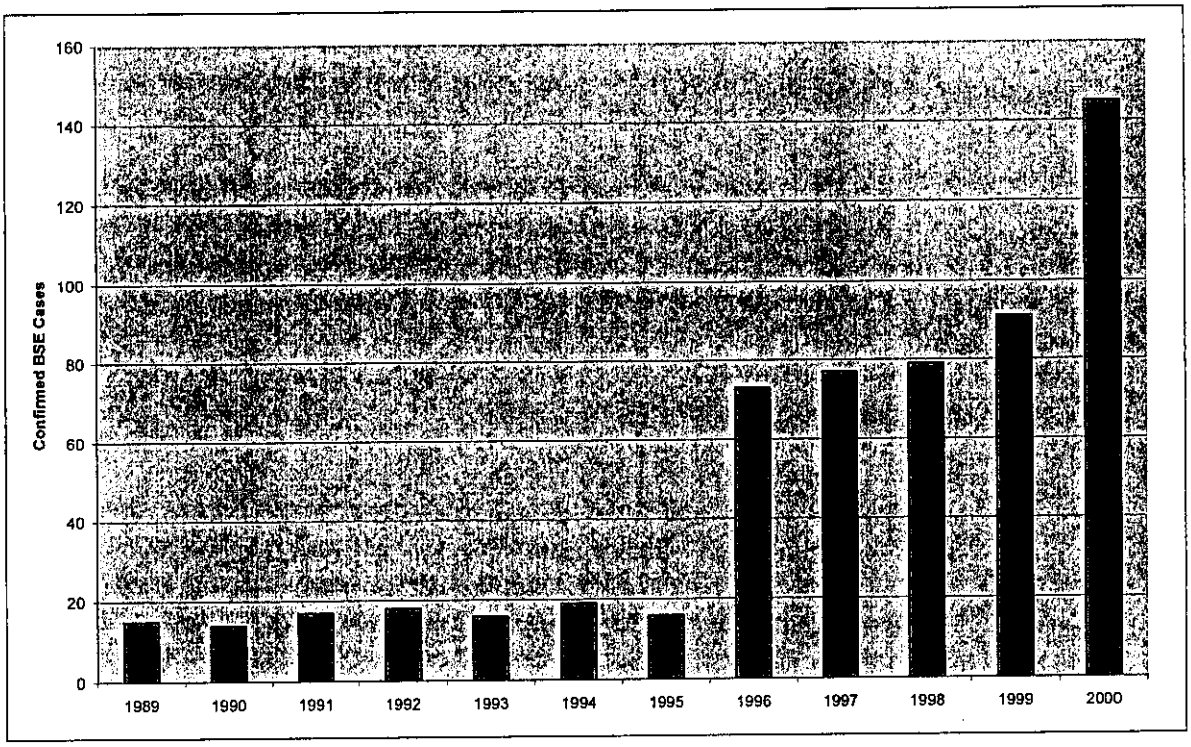
3. BSE IN IRELAND

3.1 Overview

The first case of Bovine Spongiform Encephalopathy (BSE) in the Republic of Ireland was recorded in 1989, 3 years after the disease was first identified in the United Kingdom. For the next seven years the number of cases remained at a fairly constant low level of between 14 and 19 per year. In 1996 the numbers started to increase reaching 145 in 2000 giving a cumulative total of 580 cases at 31st December 2000. The incidence of BSE is summarised in Figure 3.1. The increasing numbers of cases is clearly a cause for concern, but the numbers are still far less than in the United Kingdom which still had some 1270 cases last year (a reduction from 2274 in 1999) and a cumulative total of 177,611 to the end of 2000.

Figure 3.1: BSE Cases in Ireland



3.2 Infectivity in Animals Slaughtered

In order to assess the risk from DRG, it is necessary to have an estimate of the numbers of animals that are slaughtered for human consumption with a significant level of infectivity. In order to define when an animal would have "significant" infectivity it is necessary to understand how the BSE agent builds up over time following infection. MAFF in the UK have carried out a pathogenesis experiment to provide data on this.

The BSE Pathogenesis Experiment. Preliminary results of the BSE Pathogenesis Experiment have been given in the paper by Wells et al (1998). The purpose of the experiment is to determine the spatial and temporal development of infectivity and pathological change in cattle exposed to BSE. In the experiment a group of 40 calves were

selected from farms with no history of BSE and 30 were fed 100 grams of brain collected from BSE infected cattle at four months of age. Ten calves received no treatment and were kept as controls. At two months post infection 3 infected calves plus one control were killed and a range of tissues collected for analysis. This was then repeated at about four monthly intervals until clinical signs of the disease appeared. Tissues from the three infected animals were pooled, with a total of some 44 different tissues tested. Tissues were tested by preparing an homogenate of the tissue and injecting this directly into the brains of a group of 20 R111 laboratory mice. These mice are used because they have a known and repeatable response to BSE infectivity.

As far as this study is concerned the main results of this experiment are:

- Infectivity was detected in the brain and spinal cord of cattle killed at 32 months or more post infection. There had been no indication of infectivity in the central nervous system (CNS) at up to 26 months post infection (Note: there were no animals killed between 26 and 32 months).

- The first clinical signs were identified at 35 months post infection, 3 months after the first positive results.

- Infectivity has also been detected at 32 months post infection 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 specified bovine material (SBM) by virtue of being within the skull, but the latter would not.

- The results indicate similar levels of infectivity between the DRG and the brain and spinal cord.

In summary, the pathogenesis experiment has shown that there is significant infectivity present in the CNS at 3 months before clinical onset but not at 9 months. In previous risk assessments it has been assumed that there may be "significant" levels of infectivity up to one year before clinical onset, and it is proposed to use the same assumption here. It is also assumed that the infectivity in an animal within one year of onset is the same as that of a clinical case. In practice, the infectivity would be increasing over time so that this assumption is clearly cautious.

Model of the BSE Epidemic in Ireland. The Department of Agriculture Food and Rural Development (DAFRD) has commissioned a model of the BSE epidemic in Ireland from the Department of Statistics at University College Cork (UCC), National University of Ireland, Cork. The model uses data on the progression of the epidemic to predict the numbers of infected animals, and the numbers of infected animals slaughtered. Results for the year 2000 are given in Table 3.1.

The model has been set up to work on a calendar year basis so it cannot provide estimates of animals slaughtered within one year of clinical onset. Instead it estimates the numbers slaughtered in the same calendar year as clinical onset (BSE-0), in the year before onset (BSE-1) or two years before (BSE-2). Thus an animal slaughtered in December 2000 and predicted to have clinical onset of the disease in January 2001 would be classed as BSE-1. An animal classed as BSE-0 could be between 0 and 12 months of clinical onset, whilst an

animal classed as BSE-1 could be between 1 month and 24 months of clinical onset. For this assessment it is proposed to use BSE-1 as the basis for animals with significant infectivity. BSE-1 includes the numbers for BSE-0.

Table 3.1: Estimates of Infected Animals Slaughtered in 2000

Age Range	Total with infectivity	BSE-0	BSE-1	BSE-2
All ages	157	37	79	116
Less than 36 months	0	0	0	0
36 to 48 months	45	1	11	25
Older than 48 months	111	36	68	91

The total number of animals slaughtered used in this model is slightly different to the total numbers notified to the CMMS as shown in Table 2.1. The model uses numbers of cattle population data estimated from the Central Statistical Office livestock surveys which breaks the available population over different age groups at each calendar year from which the numbers slaughtered (and disposed of) can be calculated. The numbers slaughtered are thus estimated in a totally different way and the fact that the totals are similar (6% difference) is a good validation of the data.

On advice from the author of the model the 95% range for the results will be taken to x/2 to 2*x where the mean value is x. Where the result is 0 the 95% range can be assumed to be 0 to 3.

An important result from this model is that it is predicted that there would be no animals slaughtered in the calendar year before clinical onset at less than 36 months of age. The vast majority of animals slaughtered for domestic consumption, and certainly those normally used for prime beef cuts such as rib of beef and T-bone steaks, will be less than 36 months. The UCC model predictions suggest that there is no infectivity associated with animals slaughtered at less than 36 months. Whilst the expected value from the model is zero, the probabilistic assessment will include the possibility that up to 3 animals with significant infectivity could have been slaughtered at less than 36 months but at a low probability.

The model results also show that the numbers of animals slaughtered within one year of onset (BSE-1) will reduce from 79 in 2000 to 38 in 2001 and 20 in 2002. The associated risk levels would therefore also reduce. It will be important to monitor the actual situation to check that these results remain valid.

3.3 Source Term

The estimate of infected animals slaughtered can now be combined with the data on numbers slaughtered given in Section 2.1 to estimate the number of animals in the calendar year before clinical onset that would have been slaughtered for domestic consumption in 2000. This is summarised in Table 3.2. This shows that it is predicted that less than one bovine would have been slaughtered for domestic consumption in the calendar year before clinical onset of BSE in 2000.

Table 3.2: Estimate of Number of cattle slaughtered for domestic consumption in the calendar year before clinical onset of BSE in 2000

Age Range	Cattle slaughtered for domestic consumption	Percentage of all cattle slaughtered	Number of cattle slaughtered in the calendar year before clinical onset	
			All Cattle	Domestic consumption
Less than 36 months	195400	14.8%	0	0
36 to 48 months	7535	3.2%	11	0.35
Older than 48 months	2769	0.8%	68	0.57
Total	205704	10.9%	79	0.93

4. INFECTIVITY IN CNS TISSUE

A base assumption for the study is that the BSE infective agent can cause new variant Creutzfeldt Jakob disease (vCJD) in humans. This hypothesis has been strengthened by the results of research that has shown that the agents which cause BSE and vCJD are the same (Collinge et al, 1997; Bruce et al, 1997).

The infectivity (i.e. the potential to cause infection) of tissue from cattle with BSE is expressed in terms of its Infectious Dose 50 (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.

The infectivity of the BSE agent has been considered in detail by the Scientific Steering Committee (SSC) of the European Commission and their assessment presented in their opinion adopted at their meeting on the 13-14 April 2000 "Oral Exposure of Humans to the BSE Agent: Infective Dose and Species Barrier". This opinion is used as the basis for this risk assessment.

The estimates of infectivity levels in this section all relate to infectivity in central nervous system (CNS) tissues, i.e. the brain and spinal cord. DRG are part of the peripheral nervous system and the level of infectivity present may well be less than that in the CNS. The Pathogenesis experiment referred to previously did not provide data on infectivity levels. It is therefore assumed that the infectivity in DRG would be the same as that in the brain or spinal cord. Infectivity has not been identified in other peripheral nervous system tissues.

4.1 Infectious dose for cattle

The SSC concluded that the various approaches to assessing the infectivity from a clinically infected brain yielded a range of values from 10^1 to 10^3 cattle oral ID_{50}/g. They noted that the higher value may represent a worst case scenario if the oral route is more efficient than data suggests and a particularly high titre of infected brain is sampled. They conclude that such a high dose cannot be ruled out. The lower value is based in part on the results of the attack rate experiment carried out by the UK MAFF. It is noted that this experiment is incomplete and that it is not possible to obtain a final value for the infectious dose. The SSC gives some weight to the calculations of Diringer (1999) using the results of published and peer reviewed experiments. This results in an estimated infectious dose of 50 cattle oral ID_{50}/g.

From this data it is proposed to adopt a distribution of values ranging from 10 to 10^3 cattle oral ID_{50}/g with a best estimate value of 50 cattle oral ID_{50}/g.

4.2 Species barrier

The infectivity of BSE for humans is believed to be lower than in cattle due to the species barrier. The species barrier in this context is defined as the factor by which the effective infectivity in one species is reduced when given to a second species. Thus, if the cattle–human species barrier was 100, it would mean that 100 times more infective material would be required to infect a man than a bovine.

In their opinion, the SSC concluded that the size of the species barrier between BSE in ruminants and BSE in humans (vCJD) is not known. They considered that a worst case scenario considering no (=1) species barrier should be included, although available evidence indicates that values greater than one are likely to be more realistic. They recommended that, until more scientific data are available, for risk assessments of human exposure to potentially BSE infected products, a species barrier of about 1 should be considered as a worst case scenario and that the range from 10^4 to 10^1 be considered. This supports the assumptions made by DNV in previous risk assessments in which the species barrier was represented as a distribution using values of 10, 100, 1000 and 10,000 with equal probabilities, and a 1% probability of it being 1 (DNV, 1997 a & b). It is proposed to use the same distribution in this assessment.

4.3 Infectious Dose for Humans

The infectivity density of CNS tissue from an infected bovine to humans is obtained from the product of the infectious dose for cattle and the cattle human species barrier. Combining the distributions given above in the probabilistic assessment, results in an estimate of the median value of the infectivity density for humans of 0.26 human oral ID_{50} per gram, with a 95 percentile range of 0.002 to 44.

5. RISK ASSESSMENT

5.1 Overall Approach and Measures of Risk

The risk to the population of Ireland from any infectivity present in dorsal root ganglia has been evaluated by combining the data and assumptions presented in the previous sections in a simple "event tree".

The risk is presented in terms of the expected consumption of infectivity in terms of human oral ID_{50} units. A worst case assumption would be that exposure to one human oral ID_{50} unit would result in a 50% chance of infection and similarly exposure to 0.1 of an ID_{50} would result in a risk of infection of 5%. This is based on the underlying assumption that there is a linear dose response relationship and that there is no safe threshold. This is likely to be very pessimistic, especially for very low exposures.

Two measures are used. The first is the overall societal risk. This is determined from the total number of infectious units consumed by the entire population of Ireland within the year 2000. The second measure is the individual risk, which is represented as the expected consumption per year by any one individual of human oral ID_{50} units. A likely maximum value of individual risk has been assessed for the 2% of the population estimated to eat T-bone steak once a week. An average value of the individual risk has been estimated for the 67% of the population that eats beef weekly.

5.2 Event Tree

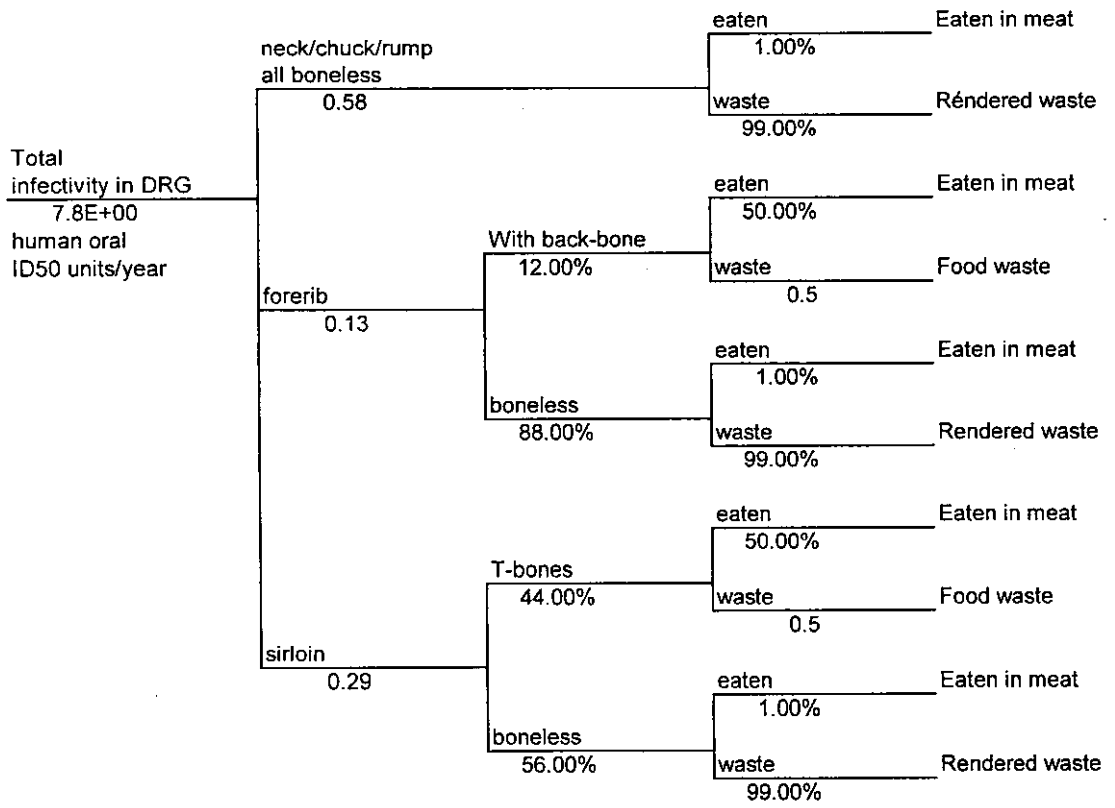
The event tree for assessing exposure to infectivity in DRG is shown as Figure 5.1. The starting point for the event tree is the total infectivity present in the DRG of all cattle slaughtered for domestic consumption in Ireland in 2000. This is estimated to have a median value of 8 human oral ID_{50} units, but with a 95 percentile range of .05 to 1400. This is calculated from the estimate of the number of animals with significant infectivity slaughtered for domestic consumption in 2000, as shown in Table 3.2, multiplied by amount of DRG present and the infectivity density in CNS tissue (section 4.3). The median value is shown on the event tree in Figure 5.1.

The first branch of the event tree reflects the cuts of meat along the vertebral column as discussed in Section 2.2. The probabilities simply reflect the fraction of DRG in that section of the carcase. Thus 4 out of 31 DRG (13%) are found in the fore rib section. The next branch considers the fraction of the fore rib or sirloin section that is sold as rib with vertebral column or T-bone steak respectively. The probabilities are based on the results of the survey of abattoirs reported in Section 2.3.

The final branch considers the fraction of the DRG that is eaten. For boneless cuts this is the fraction removed from the bone by the butcher, and for the bone-in cuts it is the fraction assumed to be consumed. Both these were discussed in Section 2.4.

FIGURE 5.1: EVENT TREE FOR DORSAL ROOT GANGLIA

Year : 2000
Case 1 On bone



	Probability	Group units/yr	Further reduction	Ultimate ingestion	
Eaten in meat	0.005806	4.5E-02	1	4.5E-02	7.2%
Réndered waste	0.574839	4.5E+00			
Eaten in meat	0.007742	6.0E-02	1	6.0E-02	9.7%
Food waste	0.007742	6.0E-02			
Eaten in meat	0.001135	8.9E-03	1	8.9E-03	1.4%
Rendered waste	0.112413	8.8E-01			
Eaten in meat	0.063871	5.0E-01	1	5.0E-01	79.7%
Food waste	0.063871	5.0E-01			
Eaten in meat	0.001626	1.3E-02	1	1.3E-02	2.0%
Rendered waste	0.160955	1.3E+00			
SUM	1	7.8	8.02E-02	6.25E-01	
Total from bone-in products				5.6E-01	89.3%
Fraction DRG in Bone-in cuts				14.32%	
Fraction of all DRG consumed				8.02%	

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On the right side of the event tree are 4 columns which summarise how the results are calculated. The first column gives the total probability for that pathway; it is the product of all the branch probabilities along that pathway. The second column gives the total number of infective units from that pathway and is the product of the probability in Column 1 with the total input infectivity. The third column is the infectivity ingested. These are the same values as in column 2 but only present if that infectivity is ingested by people. The final column gives the percentage of the total infectivity ingested for that pathway.

Note that the values given in Figure 5.1 are single point values and will be different to the results from the simulation as presented below. They are included to illustrate how the event tree is quantified.

5.3 Risk Evaluation

The event tree has been evaluated using a probabilistic risk assessment approach to reflect the uncertainties in the input parameters. Each variable has been defined as a distribution of values and the result calculated many times using a Monte Carlo simulation tool (Crystal Ball, Decisioneering Inc). The values used for the input data are presented in Appendix 1. The simulation has been carried out using Latin Hypercube sampling with 10,000 iterations.

5.4 Results

The results have been evaluated for two main cases, representing alternative assumptions for the amount of DRG that would be cut away from the bone with the meat when it is deboned. Both cases are assessed for meat being sold on the bone and for all meat being removed from the bone. In addition, for Case 1, two further cases are included to test the sensitivity to the range of values used for the DRG consumed from bone-in cuts. The results for the assessment are presented in Table 5.1, which gives the median values of the Societal Risk, the Maximum Individual Risk and the Average Individual Risk for each of the cases and Table 5.2, which in addition gives the 95 percentile ranges for the distribution of results.

5.4.1 Case 1

In Case 1 it is assumed that 1% of the DRG are cut away with the meat when bone is removed from the meat in the butcher shop, and so would be consumed with the meat. Case 1.1 is with meat sold on the bone and Case 1.2 with all meat sold off the bone. Where meat is sold on the bone, the amount of DRG consumed is assumed to be a range of values from 5 to 95% as explained in Section 2.4. The sensitivity to this range is tested with two additional cases, Case 1.3, where the amount of DRG consumed from bone in cuts is set at 5%, and Case 1.4 where it is set at 95%.

Table 5.1: Summary of Results

Case	DRG in meat from deboning	DRG consumed from bone-in cuts	Meat sold on the bone?	Societal Risk Total ID_{50} units in 2000	Average Individual Risk ID_{50} units per person/yr	Max Individual Risk ID_{50} units per person/yr	% due to bone-in
				Median	**Median**	**Median**	
1.1	1%	5-95%	Yes	0.6	2.10^{-7}	7.10^{-6}	89%
1.2	1%	n/a	No	0.08	3.10^{-8}	n/a	0%
1.3	1%	5%	Yes	0.1	5.10^{-8}	1.10^{-6}	46%
1.4	1%	95%	Yes	1	4.10^{-7}	1.10^{-5}	94%
2.1	0.1%	5-95%	Yes	0.5	2.10^{-7}	6.10^{-6}	99%
2.2	0.1%	n/a	No	0.008	3.10^{-9}	n/a	0%

For Case 1.1, the median value of the total infectivity ingested by the population of Ireland due to infectivity in dorsal root ganglia is estimated to be 0.6 human oral ID_{50} units, with a 95 percentile range from 0.003 to 110. This means that the model estimates that 0.6 human oral ID_{50} units of infectivity would have been consumed by the entire beef eating population of Ireland in 2000. This is about 7% of the total infectivity present in all DRG. About 90% of the infectivity consumed is estimated to be from bone-in cuts with these assumptions.

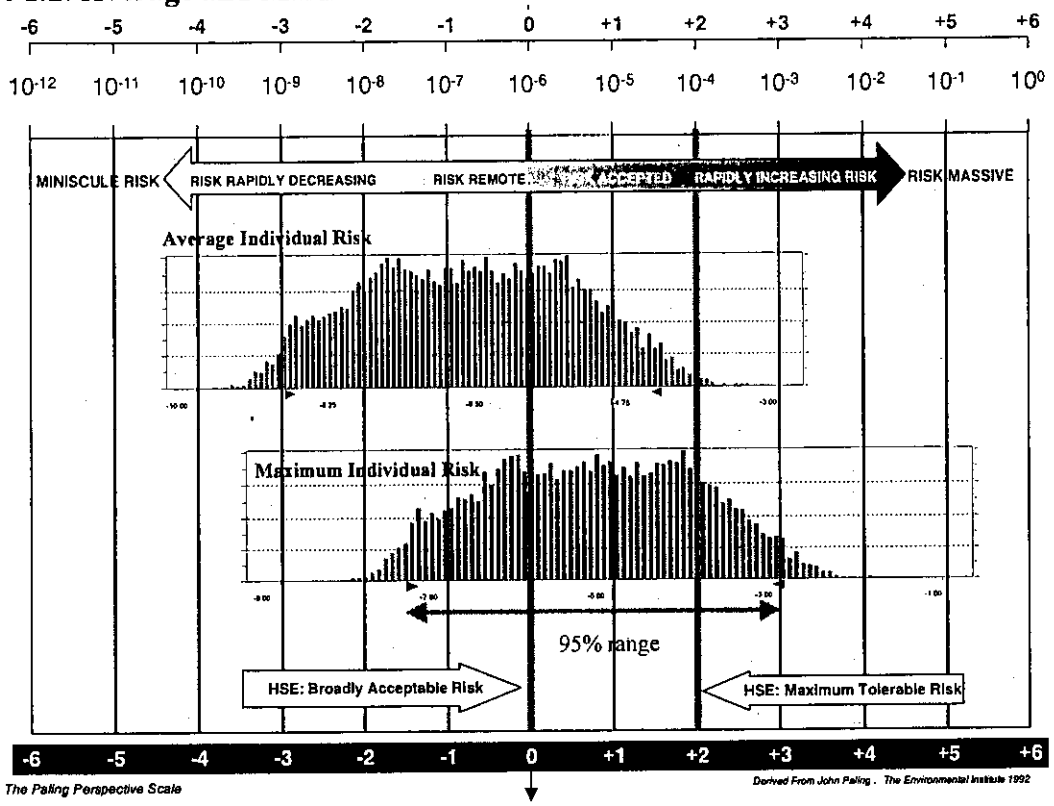
This risk is spread over a large number of people, and the average individual risk for those that eat beef regularly (67% of the population eat beef weekly according to the beef consumption survey; see section 2.3) is estimated to be 2×10^{-7} human oral ID_{50} units per person per year, with a 95 percentile range of 1×10^{-9} to 4×10^{-5}. The maximum individual risk for those eating T-bone steaks frequently (once a week) is estimated to be 7×10^{-6} human oral ID_{50} units per person per year, with a 95 percentile range of 4×10^{-8} to 1×10^{-3}.

The median value for the average individual risk is within the level of what would normally be considered acceptable. However, the range of values extend towards the top end of the range that may be considered tolerable. This is illustrated in Figure 5.2, which shows the distribution of values for the average individual risk on a logarithmic "Risk Perspective" scale.

Case 1.2 keeps the same assumptions as for Case 1.1, except that no meat is sold on the bone. The median value of the total infectivity ingested is now estimated to be 0.08 human oral ID_{50} units, and the median value of the average individual risk is reduced to 3×10^{-8} human oral ID_{50} units. The model predicts that banning the sale of beef on the bone reduces the societal and average individual risk by a little less than one order of magnitude.

Figure 5.2: Individual Risk of Ingestion of Infectivity (Human oral ID_{50} units /person/ year)

a) Case 1.1: Average and Maximum Individual Risk



b) Cases 1.2 & 2.2: All Meat Sold Off Bone

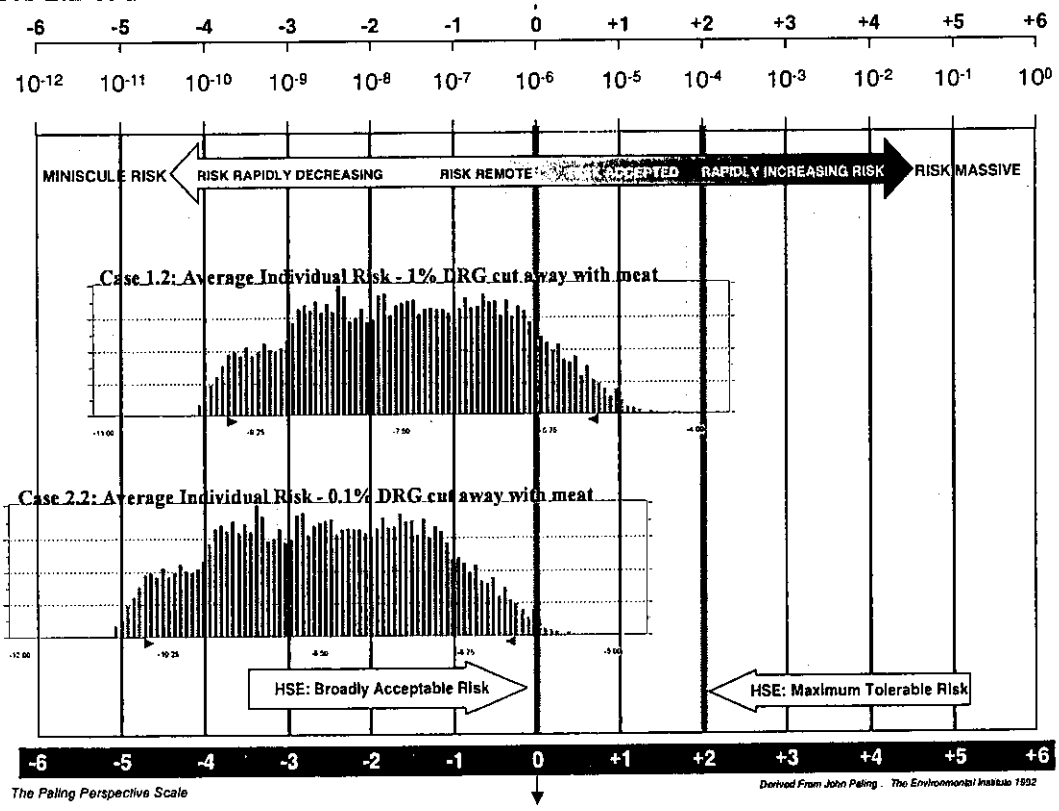


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Table 5.2: Risk Results with Ranges

Case	DRG in meat from deboning	DRG consumed from bone-in cuts	Meat sold on the bone?	Societal Risk Total ID_{50} units in 2000			Average Individual Risk ID_{50} units per person/yr			Maximum Individual Risk ID_{50} units per person/yr		
				Median	95% range		Median	95% range		Median	95% range	
1.1	1%	5-95%	Yes	0.6	3.10^{-3}	110	2.10^{-7}	1.10^{-9}	4.10^{-5}	7.10^{-6}	4.10^{-8}	1.10^{-3}
1.2	1%	n/a	No	.08	5.10^{-4}	14	3.10^{-8}	3.10^{-10}	5.10^{-6}	n/a		
2.1	0.1%	5-95%	Yes	0.5	3.10^{-3}	100	2.10^{-7}	1.10^{-9}	4.10^{-5}	6.10^{-6}	3.10^{-8}	1.10^{-3}
2.2	0.1%	n/a	No	.008	5.10^{-5}	1	3.10^{-9}	2.10^{-11}	5.10^{-7}	n/a		

The maximum individual risk is reduced by just over two orders of magnitude as there is no longer a relatively small group of more highly exposed individuals (those eating T-bones once a week).

In Section 3 it was reported that the UCC model of BSE epidemic in Ireland predicted that there were no animals slaughtered in the calendar year before clinical onset of BSE at less than 3 years of age. This would suggest that there is no risk associated with animals slaughtered when less than 3 years old, which represent 95% of the animals used for domestic consumption. However, in the probabilistic assessment it is assumed that there is a low probability of some animals being slaughtered in the calendar year before clinical onset. This results in 93% of the overall risk being due to animals slaughtered at more than 3 years old. Thus over 90% of the risk reduction could be achieved by banning the sale of beef on the bone only from cattle slaughtered at over 3 years of age, rather than from all cattle.

It is less likely that meat from the older animals would be used for cuts such as rib of beef and T-bone steaks, but there were no data to confirm this, and this has not been allowed for in the assessment. If this was confirmed it would reduce the risk levels.

Cases 1.3 and 1.4 have been included to examine the sensitivity to the assumption on the fraction of DRG present in bone-in cuts that would be consumed. For Case 1.1 this was taken as a normal distribution with a 95 percentile range from 5% to 95% as given in Section 2.4. In these cases single values at the extremes of this distribution are used for the fraction of DRG consumed, 5% for Case 1.3 and 95% for case 1.4. The results show that the Societal risk value is 0.1 for Case 1.3 and 1 for case 1.4 as compared with a value of 0.6 for Case 1.1. Thus this range of values for the fraction of DRG consumed from bone-in cuts results in a range of almost one order of magnitude. This compares with a 95 percentile range of about 4 orders of magnitude (3.10^{-3} to 110) for Case 1.1. Thus the uncertainty in the fraction of DRG consumed is relatively small compared to the uncertainties in the infectivity.

5.4.2 Case 2

In Section 2.4 it was reported that a brief study had indicated that 0.4% of the DRG would be removed from the bone with the meat during normal deboning procedures, but that a conservative value of 1% would be used in the study. That was the value used in Case 1. In Case 2 the sensitivity to this assumption is tested by assuming that only 0.1% of the DRG are removed with the meat.

In Tables 5.1 and 5.2 it can be seen that the results for Case 2.1, with the meat sold on the bone, are very similar to those of Case 1.1. Thus with meat sold on the bone the choice of value for the fraction of DRG removed with the meat makes little difference. This is because 90% or more of the risk arises from the bone-in cuts. However, a comparison of Case 2.2 with Case 1.2 shows that when beef is not sold on the bone this change in assumption reduces the risk by one order of magnitude. This also means that there is a bigger risk reduction from stopping the sale of beef on the bone. It is likely that the real position lies between Cases 1 & 2.

5.4.3 Exposure from an infected animal

In Section 3.3 it was reported that an average of 0.9 infected animals (all over 3 years of age) would have been slaughtered for domestic consumption in 2000. It is therefore likely that at least one infected animal would have entered the domestic food chain. An alternative approach to assessing the risk is to consider the exposure to infectivity to someone eating beef products from that animal.

The average weight of a DRG has been taken to be 0.5 grams. The model predicts that the median value of the infectivity present in any one DRG from an infected animal would be 0.1 human oral ID_{50} units, with a 95 percentile range from zero to 22. The detailed results show that 72% of all DRG would have less than 1 human oral ID_{50} units,. As only half of the T-bones cut from any one carcase would have DRGs present, there is therefore about a 14% risk of being exposed to more than 1 human oral ID_{50} unit of infectivity from eating one T-bone steak from an animal with significant levels of BSE infectivity.

The chance that any one animal has a significant level of infectivity is simply the expected number of infected animals (0.9) divided by the total number slaughtered for domestic consumption (205,700), giving a probability of 4×10^{-6}. The chance that any one T-bone steak contained more than one human oral ID_{50} unit of infectivity is estimated to be 7×10^{-7} (about one in a million). This is slightly greater than the median value of the average individual risk presented in Section 5.4.1. For someone who eats 50 T-bone steaks a year the risk would be about 3×10^{-5}; this latter is about 4 times greater than the maximum individual risk for Case 1.1.

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