3.1.3.1 Rendering Inactivation

Rendering may reduce the amount of BSE infectivity in material by subjecting it to heat and pressure. Different rendering systems (*e.g.*, continuous, batch, and vacuum) inactivate BSE or scrapie infectivity to different degrees (Taylor et al., 1995, Taylor et al., 1997, Schreuder et al., 1998). Table 3-3 quantifies the base case assumptions for the reduction in infectivity achieved by each technology and the proportion of animals rendered using each technology. The sensitivity analysis varies these proportions and the degree of inactivation achieved. Table <renderFactor> in file renderer (see Appendix 1) provides further documentation of these assumptions.

Table 3-3
Infectivity inactivation achieved and proportion of cattle processed by different types of rendering systems

Technology	Infectivity Inactivation Achieved (log base 10)	Proportion of cattle rendered
Batch	3.1 logs	5%
Continuous/fat added	2 logs	45%
Continuous/ no fat added	1 log	45%
Vacuum	0 logs	5%

3.1.3.2 Meat and Bone Meal Production

U.S. regulations recognize three types of rendering facilities, designated here as nonprohibited, prohibited, and mixed. A nonprohibited plant processes only porcine, equine or poultry (nonruminant species) and produces animal-based protein products that can be used legally in cattle feed. A prohibited rendering plant may process ruminant or mink raw materials, among others, and produces prohibited MBM that may not be used in cattle feed. Mixed plants produce both nonprohibited and prohibited MBM. These plants must use separate production lines or a common line with specified cleanout procedures. The base case assumes that 94.9999% of cattle remains are sent to prohibited rendering plants, 5% are sent to mixed plants, and 0.0001% are sent (incorrectly) to non-prohibited plants.

The base case assumes that cattle infectivity can reach bovines in several ways. Material from a prohibited rendering plant could be mislabeled and used in the formulation of cattle feed. Mislabeling could also occur in a mixed plant. A mixed plant could contaminate non-prohibited MBM by using incorrect source material or by failing to completely flush and clean shared processing machinery. A nonprohibited plant might contaminate their MBM by using prohibited

source material although this is unlikely. Even if non-prohibited MBM is contaminated, the potential for bovine exposure is reduced by the fact that much of this MBM goes to uses other than cattle feed.

Table 3-4 describes the disposition of MBM infectivity based on the flow shown on Figure 3-7. Further documentation of these assumptions appears in the discussions accompanying the <probMisLabel>, <probContamination>, and <fracContaminate> tables in the renderer file, and the discussion accompanying the <probDestination> table in the MBMTransporter file (see Appendix 1).

Table 3-4
The Flow of Infectivity Through the Rendering Process

Figure 3-7 Flow Reference Number	Label[a]	Description
1	To P MBM	Infectivity sent to rendering for prohibited MBM
2	SRM Elimination	Infectivity eliminated from potential use in animal feed or human food if specified risk material ban in place
3	Render Elimination	Infectivity removed through inactivation by rendering
4	Contam. NP MBM	Infectivity from P MBM that contaminates NP MBM in mixed rendering facilities
5	Mislabel P MBM	Infectivity in P MBM mislabeled as NP MBM
6	Out after Render	Infectivity in rendered material not used for livestock feed

Notes:

a. Entries in the "Label" column refer to the descriptors used in the output tables in the results Section (see Appendix 3A).

3.1.3.3 Feed Production

FDA feed ban regulations restrict use of prohibited MBM to feed manufacturers that produce only prohibited feed, or to manufactures that produce both prohibited and non-prohibited feed (mixed producers), so long as they adhere to procedures that minimize the risk of contamination. The base case assumes that at mixed facilities, prohibited feed could contaminate

non-prohibited feed. In addition, the base case assumes that prohibited feed can be mislabeled in facilities producing both prohibited and non-prohibited feed. The documentation in Appendix 1 (see parameter group feedProducer) details these assumptions in further detail.

When recycled animal tissue (i.e., blood meal or MBM) is used as a supplement to animal feed, the material can be divided among feed portions consumed by many cattle. The base case assumes that infectivity in the blood meal from a single animal is divided among 89 cattle (see the documentation in Appendix 1 for the numCowsReceiving parameter in the proteinInfector parameter group). How widely infectivity in recycled protein is distributed is more complicated. If the infectivity does not contaminate non-prohibited MBM or non-prohibited feed, then it remains contained in a single "packet" that can be divided among 89 cattle. However, if contamination occurs during the rendering process, then a portion of the infectivity is transferred to the affected non-prohibited MBM packet. That non-prohibited packet has the potential to exposure an additional 89 cattle. Finally, if contamination occurs during feed production, it is assumed that a portion of the infectivity is transferred to the affected non-prohibited feed packet. That non-prohibited feed packet likewise has the potential to expose an additional 89 cattle. Table 3-5 describes the flow of cattle infectivity through the feed production process.

Table 3-5
The Flow of Cattle Infectivity through the Feed Production and Use Processes

Figure 3-7 Flow Reference Number	Label[a]	Description
7	To P Feed	Infectivity in P MBM that goes to production of P livestock feed
8	To NP Feed	Infectivity in NP MBM reaching NP Feed
9	Contam NP Feed	Infectivity from P Feed that contaminate NP Feed in mixed feed mills
10	Mislabel NP Feed	Infectivity in P Feed mislabeled as NP Feed
11	To Blood	Infectivity reaching cattle feed through use of blood meal
12	Out After Feed Prod	Infectivity in livestock feed not used for cattle

Notes:

a. Entries in the "Label" column refer to the descriptors used in the output tables in the results Section (see Appendix 3A).

3.1.3.4 On Farm Feeding

The practice of administrating correctly labeled (*i.e.*, with the label "DO NOT FEED TO RUMINANTS") prohibited feed to cattle on the farm is referred to as "mis-feeding." The base case assumes that correctly labeled prohibited feed will be administered to cattle with a probability of 1.6%. Documentation accompanying the feeder file (see Appendix 1) explains our derivation of this estimate. Table 3-6. describes the flow of cattle infectivity on the farm.

Table 3-6
The Flow of Cattle Infectivity on the Farm

Figure 3-7 Flow Reference Number	Label[a]	Description
13	Misfed	Quantify of infectivity in materials fed to cattle in non-bovine livestock feed
14	To Cattle	Total infectivity reaching cattle through feed

Notes:

a. Entries in the "Label" column refer to the descriptors used in the output tables in the results Section (see Appendix 3A).

3.1.4 Potential Human Exposure

The base case assumes that humans can be exposed to BSE infectivity either by directly consuming infected cattle organs, such as brain, spinal cord, eyes, and distal ileum, or by consuming contaminated products, including meat or processed meat containing spinal cord or DRG, or organs containing CNS emboli, such as liver, heart, or kidneys. Table 3-7 details the assumed availability of these tissues.

Table 3-7
Potential Human Exposure

Organs/tissues	Description/Assumptions
Brain	Brain is considered to be a variety meat and reaches the consumers labeled as such. The base case assumes that 1% of all cattle brains are potentially available for direct human consumption.
Spinal cord	Beef spinal cord is considered to be a variety meat and reaches consumers label as such. The base case assumes that 1% of the spinal cord is potentially available for human consumption.
Blood	The base case assumes that 5% of the cattle blood is potentially available for human consumption in meat food products, including sausages, blood pudding, *etc.*, and that the infectivity in blood is limited to the potential contribution from brain and spinal cord emboli. Sensitivity analysis investigates the possibility that BSE disease itself also contributes to the infectivity in blood at a concentration that can be as high as the level of detection.

Table 3-7
Potential Human Exposure

Organs/tissues	Description/Assumptions
Distal Ileum	Distal ileum is considered to be a variety meat and reaches the consumers labeled as beef intestines. The base case assumes that 1% of the distal ileums are potentially available for human consumption. In the U.S., distal ileum does not reach consumers as natural sausage casings.
Contaminated Organ Meat	Brain and spinal cord are responsible for infectivity in organ meat when air-injected pneumatic stunning is used (not reflected in the base case). Liver, heart, and kidney are sold as variety meat. The base case assumes that 60% of the liver, 50% of the heart, and 25% of the kidneys are potentially available for human consumption.
Eyes	Bovine eyes are considered a variety meat and reach consumers labeled as beef eyes. The base case assumes that 1% of eyes are recovered and potentially available for human consumption.
Contaminated muscle meat	The base case assumes that spinal cord can contaminate edible meat during the splitting process. It is further assumed that other processes, such steaming or washing do not reduce this contamination.
AMR	Total infectivity in AMR product is the sum of the contributions from spinal cord and DRG contamination. The amount of spinal cord contaminating AMR product depends on whether the spinal cord is removed, as required by FSIS regulation for plants using AMR, and on whether the carcass is mis-split.
Beef on bone	Total infectivity in beef on bone is the sum of the contributions from spinal cord contained in these cuts of meat and DRG attached to these bones. Spinal cord has the potential to reach consumers if it is not removed from the spinal column and if it remains attached to the backbone as bone-in steak. The base case assumes that about 30% of the backbones from steers and heifers are sold bone-in and that because these cuts do not undergo AMR processing, they retain the spinal cord. Although regulations do not require removal of the spinal cord from the backbones that do not undergo AMR (FSIS Directive 7160.2, 1997), many slaughterhouses remove it anyway (Robert Brewer, personal communication). Note that even if the spinal cord or DRG on beef on bone reaches consumers, this material is not likely to be eaten.
Trigeminal Ganglia	The base case assumes that the trigeminal ganglia (TG) does not contaminate cheek meat because it is located at the base of the cranium. Sensitivity analysis investigates the impact of assuming that TG contaminates cheek meat 1% of the time and that when such contamination occurs, it amounts to 1/1000 of the infectivity in TG.

3.2 Impact of Alternative Assumptions on Cattle Infected and Human BSE Exposure

We evaluated the relative importance of 15 sources of uncertainty by determining how each individually influences model predictions for two cumulative outcomes over a 20-year period – the total number of cattle that become infected after the introduction of 10 infected animals at the beginning of the period, and the amount of BSE infectivity (quantified in terms of the number of cattle oral ID_{50}s) in food produced for human consumption over that period. In particular, we ran the base case simulation 1,000 times and recorded the arithmetic mean values for each of these two outcomes.

We then altered each of 15 sets of assumptions, one at a time, setting all of the other assumptions to their base case values. Each assumption was alternatively set equal to each of its bounding values. The "best case" value refers generally to that bounding value for an assumption expected to result in the smallest predicted risk of BSE spreading, whereas the "worst case" value refers generally to that bounding value for an assumption expected to result in the largest predicted risk of BSE spreading. For each alternative value, we again ran the simulation 1,000 times and recorded the mean values of the two outcomes described above.

Alternative assumptions evaluated fall into the following categories:

- Section 3.2.1 – Maternal BSE transmission rate;
- Section 3.2.2 – Slaughter process assumptions, including the quantity of infectivity in an animal with clinical BSE, the probability that AM inspection will detect an animal with clinical signs of BSE, the type of stunners used, the probability that the spinal cord is removed;
- Section 3.2.3 – Rendering and feed production process assumptions, including the extent to which rendering reduces infectivity, the probability that prohibited MBM will contaminate non-prohibited MBM, the magnitude of the contamination when this it occurs, the probability that mislabeling prohibited MBM will be mislabeled as non-prohibited, the probability that prohibited feed will contaminate non-prohibited feed, the magnitude of the contamination when it occurs, the probability that prohibited feed will be mislabeled as non-prohibited, and the probability that correctly labeled prohibited feed will be incorrectly administered to bovines on the farm.
- Section 3.2.4 – Food inspection, including in particular, the fraction of tissue in each tissue group recovered for human consumption;

- Section 3.2.5 – Farm practices, including the fraction of all animals that die on the farm that are sent to rendering.
- Section 3.2.6 – The possibility that BSE-infected cattle carry infectivity in blood
- Section 3.2.7 – The possibility that humans are exposed to BSE infectivity in trigeminal ganglia

The parameter values used for each analysis are detailed in Appendix 2.

3.2.1 Maternal BSE transmission Assumptions

We evaluated the assumption that the probability that a mother in the last one-sixth of its BSE incubation period will transmit disease to a calf it gives birth to with 10% probability (base case). The best case value for this assumption was assumed to be 0% (*i.e.*, mother-to-calf transmission does not occur), and the worst case value for this assumption was assumed to be 13%.

3.2.2 Slaughter Process Assumptions

For assumptions related to the slaughter process that have been evaluated as part of the uncertainty analysis, Table 3-8 details base case, best case, and worst case values.

Table 3-8
Base Case, Best Case, and Worst Case Values for Slaughter Process Assumptions

Assumption	Base Case	Best Case	Worst Case
Cattle oral ID_{50}s in carcass of a full-blown BSE case	10,000	5,000	20,000
Antemortem inspection clinical BSE detection rates	90%	99%	50%
Proportion of cattle stunned using an air-injection pneumatic stunner	0%	0%	15%
Probability that the spinal cord is removed			
Plants using AMR	98%	99.9%	80%
Plants not using AMR	50%	99%	10%

3.2.3 Render and Feed Production Process Assumptions

For assumptions related to the rendering process, the feed production process, and to on-farm feed practices that have been evaluated as part of the uncertainty analysis, Table 3-9 details base case, best case, and worst case values.

Table 3-9
Base Case, Best Case, and Worst Case Values for Render Process, Feed Production Process, and On-Farm Feed Practice Assumptions

Assumption	Base Case	Best Case	Worst Case
Proportion of animals rendered using various technologies			
Batch (3.1 logs reduction)	5%	5%	5%
Continuous/fat added (2.0 log reductions)	45%	85%	20%
Continuous/no fat added (1.0 log reduction)	45%	5%	70%
Vacuum (no reduction)	5%	5%	5%
Rendering – Contamination of non prohibited MBM by prohibited MBM in mixed facilities			
Probability for a particular prohibited packet	14%	5%	25%
Magnitude of contamination[a]	0.1%	0.01%	1.0%
Rendering – Probability that prohibited MBM will be mislabeled as non-prohibited MBM when produced by either a mixed or prohibited rendering plant	5%	2%	10%
Feed Production – Contamination of non prohibited MBM by prohibited MBM in mixed facilities			
Probability for a particular prohibited packet	16%	5%	16%
Magnitude of contamination[a]	0.1%	0.01%	1.0%
Feed Production – Probability that prohibited feed will be mislabeled as non-prohibited feed when produced by either a mixed feed production plant	5%	2%	33%
Probability that correctly labeled prohibited feed will be incorrectly administered to cattle	1.6%	0.1%	15%

Notes:

a. Refers to the proportion of the prohibited packet that ends up in the non-prohibited packet when contamination occurs.

3.2.4 Proportion of Tissues Recovered for Human Consumption

Table 3-10 details the base case, best case, and worst case assumptions regarding the proportion of tissue recovered for human consumption. Note that none of these sets of assumptions include a specified risk material (SRM) ban.

Table 3-10
Base Case, Best Case, and Worst Case Values for the Proportion of Tissues Recovered from Cattle for Human Consumption

Tissue	Base Case	Best Case	Worst Case
AMR Meat	0.98	0.98	0.98
Blood	0.05	0.025	0.3
Bone (in-bone cuts of meat)	0.98	0.98	0.98
Brain	0.01	0.001	0.02
Dorsal root ganglia	0	0	0
Eyes	0.001	0	0.002
Ileum	0.01	0.001	0.02
Heart	0.5	0.3	0.6
Kidney	0.25	0.15	0.35
Liver	0.6	0.4	0.7
Lung	0	0	0
Muscle	0.98	0.98	0.98
Spinal Cord	0.01	0.001	0.02
Trigeminal ganglia	0	0	0

3.2.5 Proportion of Animals That Die on Farm that Are Rendered

The base case assumes that 85% of the animals that die on the farm (*i.e.*, before they are sent to slaughter) are rendered. The best case assumes that this proportion is 60%, while the worst case assumes that it is 99%.

3.2.6 The Possibility That BSE-Infected Cattle Carry Infectivity in Their Blood

The base case assumes that cattle infected with BSE do not carry infectivity in their blood (although emboli formation may result in blood contamination). We consider the possibility that 0.016% of the infectivity in an animal with BSE is carried in the blood, a value that is consistent with the assumption that its concentration is at the level of detection in an animal with a full-blown case of BSE (SSC, 2000a).

3.2.7 The Possibility that Humans are Exposed to BSE Infectivity in Trigeminal Ganglia

The base case assumes that the trigeminal ganglia harbor no infectivity prior to the passage of 50% of the period between infection and the manifestation of clinical signs, but that after that time, they harbor 2.6% of the total infectivity. It assumes further that no trigeminal ganglia tissue is recovered for human consumption. The uncertainty analysis evaluates the impact of assuming that 0.1% of the infectivity in the trigeminal ganglia (as much as 0.0026% of the total infectivity) is recovered for human consumption with 1% probability, and that with 99% probability, none of this infectivity is recovered for human consumption.

3.3 The Base Case: Impact of Alternative Sources of Infectivity

This section describes how we used the model to evaluate the impact of different sources of infectivity on the model's predictions. For each of the scenarios considered, we adopted the base case assumptions. Infectivity sources evaluated include: spontaneous development of disease (Section 3.3.1), importation of infected cattle (Section 3.3.2), scrapie in sheep (Section 3.3.3), chronic wasting disease (CWD) in deer/elk-derived protein supplements (Section 3.3.4), CWD from direct contact with infected mule deer, white tail deer and/or elk (Section 3.3.5), transmissible mink encephalopathy in mink (Section 3.3.6), a TSE in pigs (Section 3.3.7), and a TSE in chickens (Section 3.3.8).

3.3.1 Spontaneous BSE

Because there are no measurements of an incidence rate for spontaneous BSE in cattle, we use the observed age-specific sporadic rate for CJD in humans as a proxy, adjusting the ages to reflect the difference between the natural lifespan for bovines (approximately 20 years) (Nowak et al., 1983) and the much longer natural lifespan for humans (approximately 75 years). For example, the CJD incidence rate for 75-year old humans is assumed to represent the BSE incidence rate for 20-year old bovines. Making this adjustment and taking into account the incubation period for BSE yields the age-specific rates that appear in Table 3-11.

Developing age-specific rates is necessary because the often-quoted incidence rate for sporadic CJD in humans of one per million per year hides substantial variation across age groups. The disease is virtually never seen before age 30 and has a peak incidence between ages 60 and

65 (Collinge and Palmer, 1997). If this pattern (Figure 3-8) is applicable to sporadic BSE, then estimated rates in cattle must reflect the age structure of the disease.

Finally, recall that the human CJD rates used to estimate the incidence rate for BSE represent the rate at which clinical cases appear in the population. Therefore, the rates in Figure 3-8 cannot be used to estimate the rate at which new pre-clinical cases might develop. Instead, the case age-specific clinical incidence rates must be advanced by the duration of the period between infection and the manifestation of clinical signs. The median incubation period for BSE is approximately four years (Section 3.1.1.5). Table 3-11 lists the sporadic BSE rates inferred from the human sporadic CJD rates. Note that the fourth column from the left (the spontaneous BSE new infection rate) is similar to the third column from the left (the spontaneous CJD new clinical case rate) but is offset by three rows, representing four years.