October 31, 2002

Review of the Evaluation of the Potential for Bovine Spongiform Encephalopathy in the United States

Conducted by the Harvard Center for Risk Analysis, Harvard School of Public Health and Center for Computational Epidemiology, College of Veterinary Medicine, Tuskegee University

Final Report

Prepared for

U.S. Department of Agriculture
Food Safety and Inspection Service
Office of Public Health and Science

Prepared by

RTI
Health, Social, and Economics Research
Research Triangle Park, NC 27709

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1 Introduction

At the request of the U.S. Department of Agriculture, RTI asked three experts to review the Bovine Spongiform Encephalopathy (BSE) risk assessment conducted by the Harvard Center for Risk Analysis, Harvard School of Public Health, and the Center for Computational Epidemiology, College of Veterinary Medicine, Tuskegee University (H-T BSE study).

1.1 REVIEWERS

RTI recruited two European reviewers who are experts on different aspects of BSE, one U.S. reviewer who is an expert in U.S. beef cattle production and processing systems, and a team of two U.S. reviewers who are experts in risk assessment methods and modeling. We contracted with the experts to perform the reviews, sent them the H-T BSE study and model, and provided the experts with guidelines for conducting the reviews.

The reviewers' training and experience represent several areas of expertise relevant to the BSE risk assessment model. Their full biographies and resumes are included in Appendix A of this document. Below, we present brief biographical sketches of the reviewers' relevant experience:

- Dr. H. Christopher Frey is an associate professor at North Carolina State University, Raleigh. He specializes in uncertainty and variability analysis, exposure and risk assessment, process modeling, air pollution characterization, and other related fields. He is developing methods for sensitivity analysis of food safety risk models. He has been involved in numerous risk assessment modeling exercises.

Dr. Frey's contributions have been recognized by national awards, including a Faculty Early Career Development grant from the National Science Foundation in 1997, and the 1999 Chaucey Staff Award from the Society for Risk Analysis.

- John C. Galland has a Ph.D. in ecology from the University of California-Davis and is a full professor in the Departments of Clinical Sciences and Diagnostic Medicine/Pathobiology, College of Veterinary Medicine at Kansas State University. He is co-coordinator of Public Health and Epidemiology courses in the professional curriculum. He has worked with a number of animal diseases, modeled distribution and movement of large animal groups, and has done extensive research on *E. coli.* At Kansas State, Dr. Galland created a microbiology laboratory to conduct research under the Good Laboratory Practices (GLP) Act to undertake government and industry contract work. From 1994 to 2000 he was Corporate President of Animal Health Systems, Inc., a software development company specializing in custom large database applications, voice recognition, and electronic identification systems.

- Dr. Zheng Junyu is a post-doctoral associate who works with Dr. H.C. Frey. His research involves uncertainty and variability analysis and air pollution. Dr. Junyu is also experienced in risk assessments and developing computer models using C++. Dr. H.C. Frey and Dr. Junyu were the reviewers for the modeling aspects of the BSE risk assessment (henceforth, they are referred to as the "NCSU Team").

- Dr. Bram E. C. Schreuder is a senior scientist at the DLO-Institute for Animal Science and Health (ID-Lelystad), Department of Statutory Tasks, in the Netherlands. He is a trained veterinarian, specializing in small ruminant diseases, and is specifically involved in BSE and scrapie research. In 1990, he became project coordinator of the multidisciplinary BSE/scrapie research project of the ID-DLO. He received his Ph.D. in 1998; his thesis studied the epidemiological aspects of scrapie and BSE, including a risk assessment study.

- Dr. John William Wilesmith is a visiting professor in the Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, University of London; and Veterinary Head, Epidemiology Team, State Veterinary Services, Department for Environment, Food and Rural Affairs. Since 1987, his research efforts have concentrated on BSE in cattle and other TSEs in animals and man and foodborne zoonotic infections. This work has

involved developing effective collaborations with colleagues involved in the medical epidemiological aspects of the diseases, and until 2000 he was the Veterinary Laboratories Agency's TSE R&D and Surveillance Programme Manager.

This report is a compilation of the reviewers' comments. The opinions expressed in this report do not necessarily represent RTI's views on the H-T BSE study report.

1.2 EVALUATION CRITERIA

RTI asked the reviewers to respond to the following set of evaluation criteria to facilitate the organization and presentation of their comments:

1. Identification of data and critical evaluation of evidence.
   a. Have all key studies and data been identified?
   b. Have the data been correctly interpreted and emphasized?
   c. Please address the validity and appropriateness of all input data used in the model.

2. Overarching logical structure of the risk assessment.

3. Biological plausibility of the assumptions.

4. Are the mechanics of the model consistent with known biology?

5. Appropriateness of modeling techniques (model mathematics and equations).

6. Have the risks been appropriately characterized?

7. Does the risk assessment identify and characterize the following:
   a. Key sources of variability and uncertainty
   b. Critical assumptions
   c. Important data gaps

8. Usefulness of the results for risk management.

9. User friendliness of the model: Is the model documentation adequate to allow individuals to conduct "what if" calculations?

In Section 2, we first present the reviewers' general comments on the study. Then, in Sections 3 through 12, we present the reviewers' more specific comments, which are grouped according to the evaluation criteria described above to facilitate the understanding of the comments:

- Section 3: the identification of data and critical evaluation of evidence (i.e., identification of all key studies and data, correct interpretation of the data and emphasis, and validity and appropriateness of the data);
- Section 4: the logical structure of the risk assessment;
- Section 5: biological plausibility of the assumptions;
- Section 6: consistency of model mechanics with known biology;
- Section 7: appropriateness of modeling techniques;
- Section 8: appropriate characterization of the risks;
- Section 9: identification and characterization of key sources of variability and uncertainty, critical assumptions, and important data gaps;
- Section 10: usefulness of the risk assessment;
- Section 11: user friendliness of the model; and
- Section 12: editorial comments.

In these sections, reviewers' names are provided at the end of their comments.

For some of the criteria, the reviewers provided detailed comments and, in some cases, alternative ways or solutions to address the issue. Sometimes, reviewers provided their comments as questions or expressed doubts about particular issues. For most of the comments, we include information such as page number, paragraph number, and section to facilitate locating the relevant section in the H-T BSE study report. However, a few general issues appear throughout this report and, in these cases, we do not provide the exact section of the H-T BSE study.

Many reviewers' comments do not fit exclusively under one specific evaluation criterion; a number of comments may be relevant to several criteria. Therefore, to maintain the report's structure and continuity, we repeat a few of these comments under the appropriate evaluation categories. Wherever applicable, we provide references for related comments.

Although this report is largely self-standing, it does not always include adequate background information from the H-T BSE study. Therefore, it should be read in conjunction with the H-T BSE study text.

2 General Comments

This section provides the reviewers' general comments on the following topics:

- strengths of the model,
- weaknesses of the model,
- clarity of the model structure,
- complexity and level of detail,
- omission of exposure routes,
- presentation of model outputs,
- basic aspects of BSE, and
- treatment of literature and expert knowledge.

2.1 OVERALL STRENGTHS OF THE MODEL

1) The authors have done a commendable job in constructing a simulation model for assessing the risk of introduction and spread of BSE in the U.S. They have considered the size and population dynamics of the United States cattle population, sources of infection, and practices that logically may increase risk of contamination or spread at slaughter, rendering, and feed establishments. A major strength of the model is that it is heuristic. That is, it specifies at least some initial factors that logically should affect risk and places them in a structure that allows their importance to be assessed. Formally defining parameter values and specifying the assumptions of the model also allow for discussion. Development of the model has highlighted knowledge gaps. Another strength of the model is that it predicts that BSE risk in the U.S. is low, which to date is confirmed by observation. In validating the model, the authors found that it also was able to

predict other observations. The authors do a good job in depicting the results of the simulations as histograms of the probability that the result exceeds zero.

2) In general, the study gives a thorough overview of the many possible infection routes of both cattle and humans for BSE. The various risks are all analyzed separately at first, and then later combined in a simulation model that calculates the overall BE risk. The authors have made a commendable effort to gather the available information on the topic, and put all that together into one major risk assessment study for BSE, focusing on the USA, but apparently also suitable for other countries, as shown in the "model validation" to the Swiss data. Resulting is a very good overview of the US methods to handle BSE to prevent recycling of infectivity to cattle, and to safeguard human food against infections. From our (European) point of view it is clear that the US has been very lucky to have a very low import risk, otherwise, they would have had the same BSE problem as most EU countries are presently facing.

2.2 OVERALL WEAKNESSES OF THE MODEL

1) To the extent that the model identifies factors that might affect risk, the model has utility in a heuristic sense. However, the lack of data to support the assumptions, but more importantly, the lack of data on other factors that could have a greater effect on risk, limits the predictive value of the model. After all, the outbreak in Great Britain was because of an unforeseen event—a change in the rendering process that resulted in a prolonged period of exposure to many animals. Because of the long incubation period of the disease, the impact of this change was not detected for years following the change in rendering practices. The model should explore the effects of such events.

The authors state that the U.S. Department of Agriculture asked them to evaluate, should BSE arise in this country, the robustness of U.S. measures to prevent the spread of BSE among animals and between animals and humans (page i). Therefore, the deliverable to USDA requires that the contractor begin with the given that an introduction has occurred. People (animal), place, and time factors, such as the source of infection, the level of infectivity introduced, the location or locations of introduction, temporal aspects of the

introduction, and factors of the feed distribution system that would spread contamination after an introduction, should be considered.

A model is relevant if it leads or might lead to a different conclusion or reaffirms a previous conclusion. This model tells us no more than our current experience tells us. The nature of the disease and the means of infection tell us that the risk is low, so why is a model needed? No BSE has been detected in the U.S. currently, nor is it likely to occur given existing practices, so it is not surprising that results of the simulations reveal that the risk is low, especially when the assumptions are based on events that occur with low frequency and low volumes of "infectivity."

2.3 CLARITY OF MODEL STRUCTURE

1) The authors have failed to present the structure of the model in sufficient detail for a thorough critical review. Each parameter of the model has been defined and the values assigned to each justified according to what little data exist and logic, but the mathematical relationships among the parameters that led to the results are not described well in the report. The authors should describe how the model parameters relate to each other and the evidence that the parameters relate to each other that way in reality.

It was difficult to understand the structure of the model from the information provided in the report. Perhaps, if the reader examined the computer code and had sufficient time, he could understand the model's structure; however, a better approach would be to make the structure of the model clear in the documentation.

2) The authors chose a simulation model, which results in a black box model that cannot be checked for programming errors. The huge number of parameters included to make the analysis really thorough and detailed also leads to a method that is difficult to assess afterward. The modeling should be more transparent because users may inadvertently make changes that can result from the inability to see every detail of the programming. The input variables are carefully stated separately and can therefore be checked.

2.4 COMPLEXITY AND THE LEVEL OF DETAILS

1) The model probably is too complex for the data that are available and for the purposes intended. Would a more parsimonious model be as predictive? Given that most of the parameters are close to zero, the model will be extremely sensitive to parameter values and the structure of the model. For instance, the number of cattle infected in the base case following import of 10 infected animals is seven in a population of more than 130 million animals. How sensitive is this value to the assumptions of the model and structure of the model? The level of detail among the components of the model is highly variable and the authors do not discuss how this affects the model results. For instance, what effect would reducing the number of age categories have on the results? Or what effect would varying the accuracy (decimal places) of blood meal consumption have on the results?

The authors include an age-specific death rate for the cattle population component of the model. This level of detail probably is irrelevant. The authors themselves state that the U.S. cattle population data are not broken down in sufficient detail and are inconsistent among those who report such statistics, and that "…the rate at which BSE spreads does not in general depend on this statistic [the U.S. cattle population]" (Page 48, Section 3.1.1.1, Para. 2). Except, perhaps, in the most rudimental way, why incorporate a population dynamics component into the model?

The authors state (Page 50, Section 3.1.1.4, first line) that there is no direct evidence of BSE transmission from cow to calf, so should it be included?

Sensitivity analysis can be useful in addressing some of the above questions. Although the authors report the results of sensitivity analyses, the parameters are considered one at a time so the effect of interactions (synergistic effects) among the parameters cannot be assessed. Evaluating the presumed extreme values (best and worst cases) does not allow exploration of the entire range of possibilities (a response surface analysis). Allowing a greater range of variability would provide a better understanding of the behavior of the model and its stability. The authors did not rank the factors by their effect on the results. They did not report if the sensitivity analyses

revealed any factors that would drive the system or that would cause the model to "blow up."

The authors state that they take into account age, type, and gender (e.g., Page 48, Para. 3, first line), but in evaluating susceptibility and natural death only age is considered. Also, the probability of birth is constant (one birth per year = 0.0833 monthly probability) unaffected by age, type, or gender (Appendix 1, Page 9). Thus, it appears that age, type, and gender really only affect initial population size in the model. The authors claim several times (e.g., Page 49, second line) that population size "…has a very limited impact on the simulation results…," so why include it in the model, especially with the amount of detail they have incorporated to calculate estimations?

2.5 OMISSION OF EXPOSURE ROUTES

The authors have insufficiently specified or omitted parameters that may be more likely to affect BSE infection.

1) Spatial considerations are not considered in the model. The model does not consider the distribution system for feed. If contamination occurred in a specific area, how widespread would it become?

2) Perhaps because the model was constructed before the events of September 11, 2001, the model does not include the possibility of an intentional introduction of BSE into the U.S. The model includes scenarios that are highly unlikely to occur, and if they did occur, they would be mitigated by existing production and processing practices. The model ignores the more likely scenario of an unexpected introduction, such as bioterrorism or a breakdown or alteration of practices that destroy prions or the spread of prions. The change in rendering practices that was largely responsible for the Great Britain outbreak was an unexpected scenario. If the authors began with the assumption that the "experimental unit" is the prion ("infectivity") and not an infected animal, then scenarios that test the effectiveness of practices that destroy prions and spread of prions could be evaluated.

3) It is generally accepted that the highest risk for BSE is from (1) import of live cattle or MBM from a country with BSE, (2) an

internal processing system that is incapable of reducing infectivity below a certain threshold level (mainly the rendering system), or (3) exposure of ruminants to the end products of (2), be it purposely or accidental, by cross contamination.

Although it is commendable that all possible routes and potential risks are addressed, the emphasis could have been placed more on the above limited number of priority routes, instead of dwelling into sometimes highly theoretical routes. In other words, some of the reported unlikely infection routes are easily dismissed by the model with a simple statement, whereas others are investigated to a surprisingly deep level.

The study concerned lists as three main routes, also the scrapie transmission and the spontaneous BSE case, at the same level of ranking as the above listed priority routes.

Just one example of this inconsistency with what we consider major risks: It has not been addressed what happens in Mexico in terms of MBM exposure, whereas it is stated that from 750,000 up to 2.5 millions of animals are imported annually (p. 22) from Mexico (and Canada). More or less only a conclusion is presented "that it is extremely unlikely that these animals pose a risk of introducing BSE in the USA". Maybe they don't pose any risk, but what if they had been fed contaminated starter ratios as calves in Mexico? Even if they would not live until patent clinical stages, they could introduce infectivity into the system, which is, as we concluded in the SSC, in the case of the US, not very stable.

4) A recent study has shown that prions can be found in the muscle of BSE-infected mice. Such a finding in cattle would dramatically alter the structure of the model and the risk estimates.

5) One is naturally concerned that the risk assessment ignores the importation of BSE through contaminated feedstuffs, other than MBM as a specific commodity. There is, perhaps arguably, disproportionality in the whole exercise. On the one hand it considers the risk of emboli, a relatively low phenomenon, but there happens to be some limited research on this aspect. On the other hand, the risk of importation from contaminated fish meal which is known to be both adulterated with MBM illegally and have MBM added legitimately to produce fish meal with a known protein content (because fish meal has a variable protein content depending

on its source) is ignored. The same is true for the contamination of other feed ingredients. This may have been considered and dismissed, but it deserves some consideration and comment.

2.6 PRESENTATION OF MODEL OUTPUTS

1) The practical use of the simulation as provided has not been made easy. This is disconcerting, because a great deal of effort has clearly gone into this project.

2) The reader must drill down through several layers to the output desired. The tabular output (Appendix 3A) makes it difficult to compare, for instance, the variation in the output and the mode of infection with alternative assumptions. With a different tabular format, as shown in Table 2-1, not only can the variation within a particular mode of infection (e.g., maternal) be seen, but also "interactions" between, say, maternal and protein might be seen.

Table 2-1. Mode of Infection

Assumption	Case	Maternal	Spontaneous	Protein	Blood	Exogenous
Import 10	Base	0	0	2.9	0.003	0
Maternal	Best	0	0	4.1	0.011	0
	Worst	.78	0	3.2	0.007	0
Total ID50s	Best	.57	0	2.6	0.004	0
	Worst	.67	0	4.5	0.012	0

2.7 BASIC ASPECTS OF BSE

1) The feeling one obtains from reading this report is that the primary objective was to construct a relatively complex quantitative simulation model. This approach ignores some basic aspects of BSE. The overriding one is that if a cattle population becomes infected and MBM is fed to cattle, then no rendering system is capable of effectively inactivating the BSE agent. Transmission to and amplification by cattle is therefore possible. There is a lack of discussion on and assessment of the probability of the introduction of the BSE agent into the U.S. cattle population from imported animals, animal products, and animal feedstuffs. This is somewhat

fundamental and would have provided additional basis for the risk assessment.

2.8 TREATMENT OF LITERATURE AND EXPERT KNOWLEDGE

1) The review and synthesis of the published literature and expert knowledge is somewhat patchy. One is left with the notion that there has been insufficient consultation with researchers in the field, which could have provided an ongoing peer review. One is concerned that this could be used to generate criticisms that are somewhat inevitable in such a politically laden subject. It would be preferable to see the review and synthesis of the knowledge available mapped on to the basic components of the risk assessment. This is done to some extent but mainly on the detail rather than the broader risks.

2) Many assumptions in the report were based on expert judgments. However, the basis for using these judgments in the BSE risk assessment should be explained as fully as possible.

3 Identification of Data and Critical Evaluation of Evidence

One of the initial steps in a risk assessment is to identify the available data and critically evaluate the available evidence for suitability in the analysis. The reviewers evaluated the BSE risk assessment data and evidence in response to three questions:

- Have all key studies and data been identified?
- Have the data been correctly interpreted and emphasized?
- Are all input data used in the model valid and appropriate?

We provide their comments on these three questions in this section and number them to differentiate the comments.

3.1 HAVE ALL KEY STUDIES AND DATA BEEN IDENTIFIED?

1) Judging from the impressive list of references at the end of the main text, the authors did not miss many key studies. However, a few references in the text of the Appendices (e.g., the ones mentioned on Pages 4 and 5 of Appendix 2) are not explicitly listed. These Appendices did not contain a list of references, nor were the individual references included in the overall list starting at Page 101.

All known key data seem to have been identified, but some simple tables showing the input data would have been useful: for example, the numbers of imported risk animals, by country and birth cohort (the latter could not be retrieved from the report, although they were listed in SSC [2000d]), and tonnage and origin of imported MBM, by country and year. In many cases, data on the above examples are in the text, but tables could have been helpful.

2) Since completion of the Harvard/Tuskegee report, a new study could have a profound effect on the risk assessment of BSE. The study, "Prions in Skeletal Muscle," was published in the proceedings of the National Academy of Science (NAS, 2002). The study's authors (Bosque et al.) report that mouse skeletal muscle can propagate prions. The concern is that meat could be a source of infection, "…even if it is largely free of neural and lymphatic tissue…." Although, the accumulation of prions in muscle has been demonstrated only in mice, to meet the requirements of the statement of work (to assess the robustness of production and processing practices to prevent spread), the possibility of prions in meat should be addressed. For instance, how effective would testing biopsied tissue in asymptomatic animals be in detecting infected animals? How effective would practices such as steam pasteurization and irradiation, designed to reduce bacteria, be in deactivating prions?

3) It is perhaps unusual to comment on the Executive Summary, but in the second sentence on Page iv, third paragraph, it would have been helpful to include the time when the prohibition of the rendering of animals that die on the farm was introduced. The actual timing of the introduction of this intervention remains mysterious throughout the text.

4) With respect to Section 2.1.3, third paragraph, one reviewer said the following:

- One of the original publications on the epidemiology of BSE (Wilesmith et al., 1988) is not quoted here or elsewhere in this report. This paper describes the first evidence of age-dependent susceptibility.
- In the third paragraph, fifth line, on Page 12, it is uncertain whether the studies attributed to a personal communication from Dr. Linda Detwiler are the studies in progress in Great Britain. If so, a little detail on their design would have been

appropriate, together with a discussion of the possible effects of the results on this risk assessment.

5) With respect to Section 2.2, one reviewer said the following:

- In the fifth sentence of the first paragraph, additional references would have been appropriate that would have confirmed the quoted author's initial assessment, for example, papers by Ferguson and Donnelly (2000).
- The first sentence of the second paragraph would have benefited from the appropriate references, such as Wilesmith and Ryan (1992, 1993); Hoinville (1994); Stevenson, Wilesmith et al. (2000), and the Ferguson and Donnelly (2000) papers. A number of these are not quoted at all. The quantitative estimates of the reduction in risk provided by the analyses that are reported in these papers seem appropriate to any risk assessment. In the third sentence onwards, the paragraph is also somewhat deficient in quoting primary references. For example, the paper by Wilesmith, Ryan, and Atkinson (1991) appears to be the primary paper on changes in rendering practices. There are other important observations on changes in rendering practices such as the work of Taylor (1995) and observations by Paul Brown (Brown, 1998) in the *Lancet*.

6) With reference to Section 2.3.7.1, BSE in pigs, as a clinical disease or subclinical infection, has presented a concern worldwide. They were clearly of potential importance in Great Britain because of the inclusion rate of MBM. In simple terms, pigs could represent an effective "sump" for the BSE agent, in which the BSE agent is effectively removed from the feed system, or at the other extreme they could represent a means of amplification. The evidence from Great Britain could have perhaps been used to strengthen this section, specifically the last part of the second paragraph on page 29 and the third paragraph on this page. Evidence indicates that subclinical infection is not a problem in pigs, and this is not presented. In addition, evidence suggests that clinical disease in pigs has not occurred in the pig population in Great Britain. This has probably gotten lost in various reports.

7) One reviewer notes that Section 2.4.3 does not refer to papers on the risks of the introduction of infection via infected animals exported from the UK to other EU member states (Schreuder et al., 1997) nor on the introduction of infection into Switzerland via MBM (see, for example, papers by Hörnlimann).

8) With respect to Section 3.1.1.5, one reviewer mentioned the following:

- ➤ In the first paragraph, more discussion of the incubation period distribution would be useful because the model outputs do not provide very precise estimates of the incidence of the clinical incidence. The confidence bounds are very large.
- ➤ One major concern is that the risk assessment ignores the importation of BSE through contaminated feedstuffs, other than MBM as a specific commodity. This, perhaps arguably, underlines disproportionality in the risk assessment. On the one hand it considers the risk of emboli, a relatively low phenomenon, but there happens to be some limited research on this aspect. On the other hand, the risk of importation from contaminated fish meal, which is known to be both adulterated with MBM illegally and have MBM added legitimately to produce fish meal with a known protein content (because fish meal has a variable protein content depending on its source), is ignored. The same is true for the contamination of other feed ingredients. This may have been considered and dismissed, but it deserves some consideration and comment. Also, see the general comment on basic aspects of BSE.

3.2 HAVE THE DATA BEEN CORRECTLY INTERPRETED AND EMPHASIZED?

1) The H-T BSE study authors have done their best to incorporate the existing data in their estimates of the parameters selected for inclusion in the model. Not much hard data exist that could be used directly for setting parameter values. Therefore, the authors used indirect data to justify logical arguments for setting a parameter to a particular range of values. The authors may have included some factors in their model simply because some indirect data could be found.

The reviewers had concerns that the importance of some parameters has been overestimated and others underestimated.

2) A rather optimistic choice was made in case of doubt or insufficient hard evidence or data. These concerns relate to overall model weaknesses in the general comments section. In the summary section, on Pages 98 and 99, several of the main issues that involve assumptions that cannot be verified with confidence are discussed, and several of them could serve as perfect examples of what has been argued here, that optimistic choices for favorable

outcome or reassuring nuances are presented (e.g., the implementation rates, the "remote chance that an infected animal had been imported from the UK").

Reviewers commented on the import of MBM.

3) The UK export statistics mention a shipment of 20 tons to the U.S. in 1989. Such a quantity was enough to spark the Swiss epidemic. This part of import risk was considered negligible probably because the U.S. authorities could not corroborate this figure. The statement (Page 22, second paragraph, last sentence) that overseas shipping of MBM was economically noncompetitive seems questionable because at least for the period when MBM was almost available for free in the UK, it did get all the way to South-East Asia in large quantities. Figures from Southern State Cooperative of recent years are moot in this respect.

A reviewer also commented on the import of live cattle from the UK.

4) Because the USDA reported that about half of the animals imported in the risk period did not really enter the food chain, these were considered to carry no risk (Section 3.4.3). The report does not provide details or evidence to support this statement. Other arguments regarding the potential risk of import of live cattle from the UK, such as animals not being from a BSE-infected farm, and BSE not being a recognized disease (Page iii, last paragraph), are questionable. Admittedly, not many were imported at the peak of the risk period.

5) With respect to rendering (Table 3-3, Page 61), two log reduction for atmospheric continuous rendering with added fat is optimistic. Also there is a doubt about the statement on Page 25 (Appendix 1, second paragraph, last sentence) that addition of fat increases the inactivation.

6) In Section 3.1.2.3 on stunning, it is assumed for the base case that air-injected stunning is not used in the U.S., based on conversations with involved persons (Page 55, first paragraph, seventh line). However, it seems that the model is based on unlikely events such as air-injected stunning. Therefore, the model may be limited and may become obsolete. In Section 3.1.2.4 (Page 56, second paragraph, last sentence), the assumption that stunners

not using air injection never cause contamination of the blood (during exsanguination) with brain material needs to be modified.

7) The remark in Section 4.5 in the last line on Page 99 does not sound very scientific: "exposure could not have been substantial because we did not see many cases," having in mind the German experience. About the level of achieved surveillance, more will follow.

8) In Section 2.3.9.1 on plate waste, it is said to mainly contain vegetable material (third paragraph, second sentence), and vegetable protein must be added to give it the correct nutritional value. The major question is why one would not add mammalian protein here instead of vegetable?

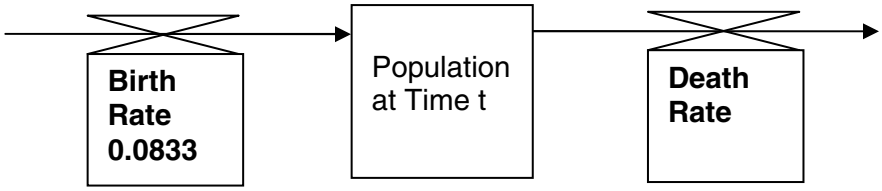
9) A reviewer commented on ProbPassAM (Section 2.1.1, Appendix 1, Page 9). If it is their intent, the authors should specify that ProbPassAM is the probability that a BSE-infected animal, not just an animal, passes AM inspection. The authors state that the probability of an animal passing AM inspection is age dependent. They provide the references that were used to derive these estimates. Because BSE evolves slowly, their argument that BSE in older animals is more likely to be detected makes sense, but the age-dependent variation is for animals without clinical signs. Thus, the probabilities really represent the age-dependant chance occurrence that an infected animal passes. Variations in probabilities for the three age categories are minute (to third decimal, Appendix 1, Section 3.1.1, Page 38). The authors do not specify variation in ProbPassAM in animals with clinical signs by the actual clinical signs, where variation in the probability among animals is likely to be higher than variation among age categories. Therefore, it appears that in one instance the parameter is overestimated and in the other underestimated.

What is important from an inspection point of view is to pay greater attention to early signs of disease. The probabilities also do not reflect improvements in detection over the 20-year time span. If the 0.10 probability chosen by the authors is an average probability of passing infected animals with early signs and animals with late signs, perhaps it is appropriate. If it represents the probability of passing an infected animal in the later stages of disease, then the

estimate is probably high, because the neurological signs would be obvious to an inspector.

10) Reviewers commented on the cattle population parameters (Appendix 3A). The output tables list epidemic statistics such as the numbers of cattle infected and the numbers infected exhibiting clinical signs. It appears that cattle population parameters were included in the model to simulate epidemic statistics, which is also suggested in Figure 3-1 of the H-T BSE study report. Cattle population parameters specified in the H-T BSE study report are ProbBirth, ProbDeath, and InitSize. From an epidemiological point of view, these variables can be used to estimate the size of the "national herd," which can define cattle at risk, and transmission of prions, for instance between cow and calf, which can define spread. However, the authors do not define clearly how the population parameters affect the output. That is, the mathematical relationships, if there are any, among the population parameters. Figure 3-1 in the H-T BSE report is not sufficient in describing the relationships. The authors do not report the density-dependent process used. They might consider using Forrester (rate/state) diagrams to depict the relationships in an easy to understand figure. For instance, a simple way to convey to the reader the factors that affect the size of the cattle population might be as shown in Figure 3-1.

Figure 3-1. Forrester (rate/state) Diagram to Depict Relationships between Population Parameters



A rate that increases the population and a rate that decreases the population determine the size of the herd at a point in time. Then the authors can elaborate. For instance, the rate of increase is affected by the current age-specific size of the population at time t-1 and the birth rate. The rate at which the population decreases is affected by the death/slaughter rate. The number culled for slaughter (and other factors) affects the death rate.

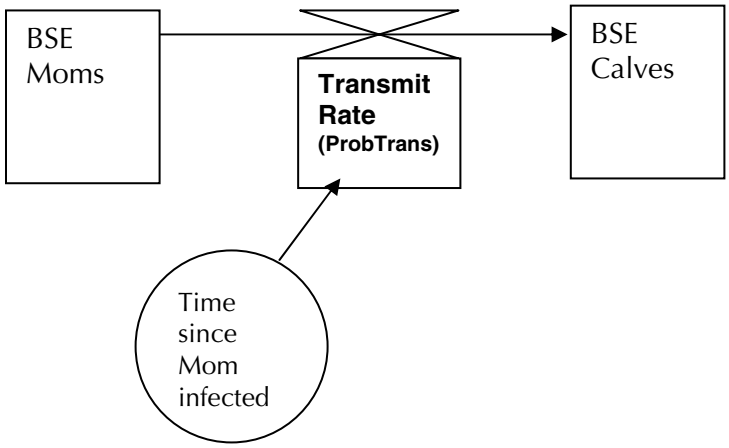
In Table 3.4.1, the "natural" death rate is age-specific (Appendix 1, Page 45). It should be reported that the unit for age is months, and that the values tabulated are for beef cattle. Overall, the units of measurement should be included in all tables. Throughout the report, the stage of production is not considered. For instance, the death rate is different for stocker cattle on pasture than for feedlot cattle and varies seasonally and geographically and certainly by producer. When should details such as these be included in the model and when should they be excluded? More rationale should be given for the variables selected and for those omitted.

Population parameters were important in the Great Britain outbreak because destroying infected animals served to reduce the incidence rate and disease spread. It is unclear how the population parameters are used in this model.

11) About maternal transmission, one reviewer noted the following. The parameters "beginCalving" and "endCalving," the beginning and ending age when cows give birth, are defined in Appendix 1, Pages 10 and 11. They are included presumably to estimate maternal transmission of prions to offspring or perhaps to determine the period at which transmission could occur. However, the actual relationship among the variables is not described. Therefore, one would have to examine the computer code to understand the relationships. Again, the authors might consider depicting the relationship as shown in Figure 3-2.

"ProbTrans" is a probability that a new born calf becomes infected if the mother is infected and the mother has lived through at least a fixed fraction of her incubation period and its value is 0.1 (Appendix 1, Section 2.2.2, Page 10). The fixed fraction is specified by <maternalContagiousPoint> parameter and its value is 0.833 (Appendix 1, Section 3.1.7.3, Page 76). Therefore, it appears that probTrans is a conditional probability that can take on one of the two values, which might be depicted by a Warnier-Orr diagram that the authors could use as a means of making the relationship easier for the reader to understand:

Figure 3-2. Forrester Diagram to Depict Relationships for "Begincalving" and "Endcalving"



[Fraction of incubation period > 0.833] {ProbTrans = 10%
[Fraction of incubation period < 0.833] {ProbTrans = 0%

If the condition within the square brackets [ ] is true, then the assignment to the right of the curly brace { is made. Also, the authors need to specify if the fraction is >0.833 or ≥0.833.

12) Apparently, the incubation period for BSE is assigned a value between 0 and >130 months according to the probability distribution "ClinicalDate" (Appendix 1, Pages 73-76). It is assumed that although the table indicates >130 months, the highest value actually used was 130.

13) A few assumptions are based on data extrapolated from dairy cattle and beef cattle or other animals. Do the results sum over all "types" of cattle?

14) The number of cattle among which blood meal from a single slaughtered animal is divided is estimated as described in Section 2.3.1 (Appendix 1, Page 11). Apparently, the blood collected from individual animals at slaughter establishments is pooled. The authors calculate the expected amount of blood meal consumed by a dairy cow to determine the number of animals (88) fed by a single 4,000 lb batch of blood meal. It is not clear how this number is used along with estimates of blood meal consumption (Table 3.3.3, Appendix 1, Page 39) by each bovine type, gender, and age combination to estimate the number of cattle infected by blood. Also, the value for the number of animals fed by a single batch of

blood meal is reported as 88 in Appendix 1, on Pages 11 and 23, but 89 in Appendix I, Page 66. Which of these two numbers is correct? Because the units in the output tables (Appendix 3A) are not given, it can only be a guess that the value for blood (in mode of infection) represents cattle numbers infected by blood.

15) One reviewer commented on the lack of emphasis on exposure routes. It is generally accepted that the highest risk for BSE is from

- ➤ import of live cattle or MBM from a country with BSE;
- ➤ an internal processing system that is incapable of reducing infectivity below a certain threshold level (mainly the rendering system); and
- ➤ exposure of ruminants to the end products of the second way (be it purposely or accidental, by cross-contamination).

Although it is commendable that all possible routes and potential risks are addressed, the emphasis could have been placed more on the above limited number of priority routes, instead of dwelling on sometimes highly theoretical routes. In other words, some of the reported unlikely infection routes are easily dismissed by the model with a simple statement, whereas others are investigated to a surprisingly deep level. This comment is also related to the general comment on complexity and level of detail.

The study apparently treats the scrapie transmission (Section 2.3.3, Page 23) and the spontaneous BSE case (Section 2.3.1, Page 21) at the same level as the above listed priority routes. Below we provide an example of this inconsistency with what is considered major risks.

It is stated that from 750,000 up to 2.5 million animals are imported annually from Mexico and Canada (Section 2.3.2.3, Page 22). However, the H-T BSE study report does not address what happens in Mexico in terms of MBM exposure. In general, the report says it was extremely unlikely that those animals posed a risk of introducing BSE in the U.S. Perhaps the imported animals do not pose any risk, but what if they had been fed contaminated starter ratios as calves in Mexico? Even if such animals would not live until patent clinical stages, they can introduce infectivity into the system. The Scientific Study Committee (SCC) concluded that this was an area for consideration (or concern) in the case of the U.S.

16) The third paragraph on Page iii discusses the risk presented by the 334 animals brought into the U.S. from the UK between 1980 and 1989. The text states: "These animals were imported as breeding stock, not as beef or dairy breeding animals. This fact is likely to have reduced their potential for exposure to BSE before their export from the UK" (fifth line). There is a misunderstanding here as discussed below.

The cattle exported from the UK have carried a greater risk of being infected by BSE than the other members of their natal cohorts that were not exported. An assessment based solely on the incidence in the home-based remnant of the cohort can therefore be misleading. The reason for this elevated risk is because the exported animals are more likely to have received commercial concentrate feed, especially beef breeds that had a much lower exposure to feedstuffs containing MBM. One reason for this was to ensure that they were in the best physical condition. Examples of this apparent differential risk for exported animals are the animals of the Saler breed, which was exported to Canada, and animals exported to Denmark and Germany. More generally, at the beginning of the clinical epidemic, pedigree dairy herds were disproportionally represented. Their exposure to MBM was relatively greater than for other commercial herds, because of showing animals and general traditions of managing such herds. Unfortunately a proportion of the early affected pedigree herds was the source of Friesian heifers for export to Portugal to restock after the Contagious Bovine Pleuropneumonia (CBPP) outbreak there.

17) The second paragraph in Section 2.1.1 on Page 6 describes transmission of TSE disease in the case of sheep-borne scrapie. It is stated that TSE transmission has been inked to the use of vaccines. There is not much evidence that a relatively crudely prepared louping ill vaccine has been associated with transmission. The evidence from the Italian outbreak is far from conclusive.

18) It would have been more correct if "at least experimentally" was inserted after "transmitted" in the second sentence of the second paragraph of Section 2.1.2.

19) With reference to Anderson et al. (1996), it is stated in Section 2.1.3, third paragraph, that the susceptibility of animals peaks at 1.31 years of age and then decreases based on back

calculation of the BSE model. There not only is a slight misunderstanding of the Anderson paper, but also an error in this paper that unfortunately has never been amended.

The peak susceptibility quoted is not derived by a back calculation. However, it is derived from a research institute's cattle herd that had a very unusual feeding profile and this is the "error." In Great Britain, exposure to feedstuffs containing MBM is relatively rare between 6 months of age and approximately 2 years when heifers start to calve. This error is perpetuated in the Woolhouse and Anderson (1997) paper, which is not a separate investigation (i.e., both papers are part of the same investigation). Moreover, it has not been possible to determine the profile of age-dependent susceptibility and whether it does occur. This would require a laboratory-based study because the natural feeding pattern throughout the first 2 years of the life of cattle in Great Britain precludes the necessary epidemiological analysis of this putative age-dependent susceptibility.

The synthesis of the current evidence on this aspect is important to the risk assessment. If there is an age-dependent susceptibility it is not absolute. That is, all ages are susceptible. The age at which cattle are exposed orally and parentally to the BSE agent in experimental challenges in Great Britain has been 4 months. This is the age at which calves would have achieved their maximum intake of commercial concentrate feedstuffs under Great Britain conditions. The results from the British attack rate study, involving oral exposure to varying amounts of brain tissue from terminal cases of BSE, has resulted in an incubation period/age at clinical onset distribution similar to that observed in naturally occurring cases. The epidemiological evidence from the epidemic in Great Britain is that age at exposure does not influence the incubation period.

In the ninth line of the third paragraph, it is hypothesized that age-related susceptibility is associated with permeability of the intestine to large protein. A reference to the hypothesis is required because the change in permeability of the bovine intestine with age does not explain the apparent age-dependent susceptibility. The quoted changes occur too early after birth.

In the second paragraph on Page 12, findings from the attack rate experiments are discussed for the dose of BSE agent. The

researchers should have made themselves aware of the attack rate study conducted in Great Britain. The lowest dose in the original study (a follow-up study using lower doses is in progress) was 1g. The results of this study should have been included here. There appears to be some confusion here and therefore a concern that the researchers may not have made the best use of the research results available, which is a "trap" generally advised against in terms of interpretation and use of the results of the bovine pathogenesis study. Essentially, the researchers have assumed that all of the animals in the pathogenesis study, exposed to 100g brain orally, had an incubation period of 36 months. This is not true and probably arises from a lack of synthesis of the results from these two studies; the attack rate study, although initiated at the same time as the pathogenesis study, was the scoping study for the latter. The problem is that in the attack rate study the 10 animals were exposed to 100g brain orally. However, the same exposure dose used in the pathogenesis study had incubation periods that ranged from 33 to 61 months. It is not correct to assume that all of the pathogenesis study animals had the same relatively short incubation period. Therefore, the proportional calculation described in Section 2.10.1, Appendix 1 will produce conservative estimates of infectivity and underestimate this value.

20) Section 2.2.1 describes scrapie in sheep as one of the possible causes of the BSE epidemic in the UK. The section is a little muddled in that it starts discussing transmission of sheep scrapie between sheep and then goes on to the sheep scrapie origin. The latter is a little simplistic and half-hearted. Again, this section is a little short on primary references and reviews of considerations of the origin, for example Kimberlin (1997). The comment on the feeding of concentrates to calves not taking place other than in Great Britain except Australia (Page 14, last sentence) is not true. The EU-sponsored Great Britain exercise clearly indicated that the feeding of concentrates containing MBM to calves was not restricted to Great Britain/UK. Thus, there is a misquotation regarding the feeding of concentrates to calves, which needs to be corrected to make accurate international comparisons. Finally, the last sentence of Section 2.2.1 could be misinterpreted by the uninformed to mean that cattle are not susceptible to oral exposure to sheep scrapie. This is not true.

21) Section 2.2.2 discusses sporadic BSE as one of the possible causes for the UK epidemic. The first sentence of this section is rather vague and conflicting. Is this referring to relativity to all other countries or just to the U.S.? The evidence suggests that this is only true for the U.S. Occurrence of sporadic BSE according to age of cattle is discussed in the second paragraph. The age distributions of the UK animals are specifically mentioned. However, other European countries certainly have dairy cow populations with similar age distributions, which needs to be considered here.

22) As discussed in Section 2.2.3, toxic agents and other hypotheses as a possible cause of the BSE epidemic in the UK are discussed here. The other hypotheses may not deserve any great attention in such a risk assessment. They could have been dismissed either by reference to reviews by others such as the Spongiform Encephalopathy Advisory Committee (SEAC) in Great Britain or by the EU's SSC. As it stands, it is misleading. For example, the "Organophosphate Pesticides hypothesis" has not been a singular hypothesis. It has changed significantly throughout the epidemic by its protagonist. Also, in the last sentence in the first paragraph of Section 2.2.3.2, it is stated that resulting conditions from copper deficiency had signs and pathological changes similar to those of BSE, which is not true. Section 2.2.3.5 discusses pituitary hormones, but the fact that transmission via hormones derived from bovine pituitaries was considered in the original epidemiological study has been ignored.

23) As discussed in Section 2.3.7.1, there is a theoretical risk that cattle could be exposed to a TSE from porcine-derived protein. One of the two potential sources of this exposure can be a natural TSE that infects pigs. Section 2.3.7.1 discusses infectivity in pigs due to TSE infection. BSE in pigs, as a clinical disease or subclinical infection, has been a concern worldwide. They were clearly of potential importance in Great Britain because of the inclusion rate of MBM. In simple terms pigs could represent an effective "sump" for the BSE agent, in which the BSE agent is effectively removed from the feed system, or at the other extreme they could represent a means of amplification.

The evidence from Great Britain could have perhaps been used to strengthen this section. This is so specifically for the last part of the second paragraph and the third paragraph on Page 29. Some

evidence indicates that subclinical infection is not a problem in pigs, and this is not presented. Also, some evidence shows that clinical disease in pigs has not occurred in the pig population in Great Britain. This has probably got lost in various reports. However, if one assumes that the incubation period in pigs is the same as that for BSE in cattle and the surveillance for neurological disease in pigs in Great Britain is equally effective for such disease in cattle, then the number of expected cases in the pig population in Great Britain can be tens of thousands. On the first assumption there is no evidence to dismiss it. On the second assumption, evidence indicates that the surveillance of disease, including neurological disease, in pigs is more effective than in cattle in Great Britain.

BSE in pigs was detected by a neuropathologist whose specialism was neurological disease in pigs. Also, during the BSE epidemic outbreaks of neurological disease in pigs in Great Britain were detected, brought to the attention of MAFF scientists, and investigated. The main point is that the third paragraph on Page 29 has a touch of innumeracy. The percentage of pigs slaughtered at less than 6 months of age is not an important statistic compared to the number of pigs that reach a potentially susceptible age (~5 years), and this is what the analysis of the pig population referred to above was concerned with. There is really no evidence that pigs are important in the epidemiology of BSE, but quoting percentages rather than absolute numbers is not helpful in such an important risk assessment.

24) Actions taken in the UK to check BSE are described in Section 2.4.2, Page 37. The fifth sentence (line 7) indicates that the ban on specific bovine offal (SBO) as ingredients in feed stuff helps to identify tissues with the highest infectivity. It should be indicated that these high risk tissues were identified as a result of research on sheep scrapie. This sentence also could be more fully referenced. The last sentence of the paragraph is more accurate if it is moved to be the penultimate sentence. Because by 1997 the additional ban on the use of mammalian-derived protein in 1996 could not possibly have had any effect on the clinical incidence.

To make the second paragraph more realistic, it may be noted that the SBO ban, with respect to the human food supply, was introduced in 1989 because of the knowledge that when the

"scrapie agent" successfully crosses to another species, it can have altered transmission characteristics with respect to other species. Also, the tissues listed as the SBOs, such as brain and spinal cord from cattle older than 6 months, are incomplete.

The chronology of events that is suggested in the third paragraph is not correct. The national surveillance for Creutzfeldt-Jakob Disease (CJD) was formally instigated in May 1990, which is clear from the CJD Surveillance Unit's website. In Table 2-2, the chronology of BSE-regulated actions in the UK contains errors. For example, there was no "selective culling" in 1990, and spinal cord in animals older than 6 months was included in the original SBO ban. There are perhaps some other important exclusions even though this is a summary table. For a detailed chronology, refer to the six monthly progress report on the BSE epidemic published by the Ministry of Agriculture, Fisheries, and Food (MAFF) (now the Department for Environment, Food, and Rural Affairs or DEFRA), which is available on their web site.

The two measures to prevent the BSE epidemic described in the last two paragraphs of this section are confused as different bans. The reality was that in March 1996, the SEAC's recommendation was for the deboning of carcasses of animals older than 30 months of age together with the removal of all obvious lymphatic and nervous tissues. This was not possible because of an insufficient number of deboning plants. The political decision was therefore made, at the Prime Ministerial level, to remove all animals over 30 months old from the human chain. The ban on bone-in-beef was introduced as a precautionary measure as a result of the later results from the BSE pathogenesis study (in cattle) conducted in Great Britain that suggested that infectivity may be present in dorsal root ganglia.

25) In Section 2.4.5, BSE surveillance in the U.S. was evaluated. The section reads as if there is a little complacency about the surveillance for BSE, and CJD/vCJD in the U.S. A more critical evaluation appears to be appropriate. There have clearly been a number of problems with surveillance for clinical BSE. The first is the general level of surveillance in the U.S. and other countries. The second is the fact that at low incidence BSE is clearly a difficult disease to identify because of its more behavioral, rather than neurological, clinical presentation in at least the early clinical phase and the rather variable clinical signs. Thirdly, a concentration on

suspect rabies cases has not proved to be very effective within continental Europe; this is mainly because rabies is endemic in the less cattle-dense areas and such surveillance (on its own) can therefore exclude a significant proportion of the cattle population. Fourthly, "downer" cows are probably not the best targets for BSE surveillance.

The time frame of the BSE risk assessment work is not clear. The executive summary indicates a starting year of 1998 and the scientific references section contains some papers published in May 2001. An improved awareness of the extent and magnitude of the incidence of BSE in EU member states in continental Europe emerged towards the end of 2000. Any comment on the omission of what has been learned or stressed from this additional surveillance in Europe, arising from the use of the more rapid and economical tests described in Section 2.4.1, may be misplaced. However, two related aspects emerge. The first is that testing animals at slaughter improves quite dramatically our knowledge on the incidence of BSE in countries with a low incidence of clinical BSE and therefore a relatively poor awareness of the intricacies of the clinical picture. Secondly, targeting surveillance to the more general category of fallen stock/casualty slaughter animals, rather than just "downer" cows is a much more effective method.

A comparison of surveillance for CJD/vCJD in the U.S. with that in the UK and the more widely based EU funded surveillance project would have been helpful because there do seem to be some differences. A lack of change in the observed incidence of CJD in the U.S. could be interpreted as providing evidence of no increased intensity in surveillance. This comment is made in light of the findings from those countries that have participated in the international project on CJD surveillance.

3.3 ARE ALL INPUT DATA USED IN THE MODEL VALID AND APPROPRIATE?

Several comments in the previous section are also appropriate here.

1) In spite of the somewhat critical examples, the overall level of accuracy of data and their appropriateness are good. The H-T BSE study authors did indeed have access to good expert opinions/panels. However, a general observation is that, in

instances where subjective interpretations had to be given, an optimistic choice was regularly made, as suggested earlier in this report.

2) It is important to validate the data (content validity) and the operations (construct validity). The authors define parameters (constructs) operationally based on data. Most, if not all, data on which the parameter estimates are derived are valid, and the logic in which the data are used to estimate parameters is basically sound. The validity of the model (predictive validity) cannot be evaluated effectively because the means by which the parameters affect the output is not described in the report. It would be more informative to describe how the parameters relate to each other and the evidence that the parameters relate to each other that way in reality.

3) Since there exist important data gaps in model inputs of the risk assessment model, assumptions were made. Upon review, it was found that most of these assumptions are based on the assumed or judged trustworthiness of references and expert judgments. For example, most of the references come from published government reports and journal papers. Therefore, these assumptions may be reasonable but it is important to explain as fully as possible the basis for their use in the BSE risk assessment. In some cases, it might be better to assume a continuous probability for a model input instead of using some assumed discrete value because uncertainty in the model inputs can be any values. For example, for the input parameter "number of importation of infected cattle into U.S.," the model simulated the introduction number of 1, 5, 20, 50, 200 and 500; however, a log-uniform distribution with a lower bound of 1 and an upper bound of 500 would more realistically represent the possible number of importation of infected cattle into the United States in the real world.

4) Although it is appropriate to include parameters about the population dynamics of cattle, the sources of infection, and the practices at the farm, processing establishment, and renderer, one should be concerned about the lack of data about each and the omission of parameters that may more likely affect BSE infection. Some data included are relevant, yet not complete; other data are more complete, yet irrelevant. The level of detail is highly variable. The authors do not discuss how varying the level of detail affects the

model results. For instance, what effect would reducing the number of age categories have on the results? Or what effect would varying the accuracy (decimal places) of blood meal consumption have on the results?

5) Section 2.1 outlines the characteristics of TSE. A general suggestion for this section is that the authors could have included the occurrence of TSE in other Felidae and ungulates in zoological collections. The first paragraph on Page 4 discusses kuru, a fatal disease that affected the Fore population of Papua, New Guinea. It is also stated that the neurological signs of kuru are similar to those of scrapie, which is not true. Kuru is typified by the occurrence of myoclonus that is not a feature of scrapie; it is a clinical sign observed in cattle with BSE.

6) A small point regarding the Japanese study cited in Section 2.1.3, second paragraph under sheep: the international research population working on sheep scrapie doubts the veracity of the Japanese reference to a scrapie case with arginine homozygosity.

7) Section 2.4 describes the measures taken to protect against BSE. The third sentence states that infected tissues are not allowed in human or animal food supply, which is not entirely true, especially when a temporal aspect is considered.

8) Section 3.1.1.5, Page 51, discusses the BSE incubation period and time until death caused by BSE. In the second paragraph, a uniform distribution of the time from the manifestation of clinical signs and death/euthanasia between 2 and 6 months is assumed. This assumption needs more discussion because it is clearly at variance with the distribution observed in British cattle (e.g., Figure 3 in Wilesmith et al. [1988] [a paper not listed in the references]). It is not clear to what extent the simulation is sensitive to the assumed distribution.

9) Section 3.1.2.1 discusses the level of infectivity and distribution of infectivity throughout the carcass. Table 3.10.1 (organDistribution) on Pages 63 and 64 of Appendix 1 does not match what is quoted from the British pathogenesis study in this section. Infectivity was found in the small intestine from 6 to 18 months post infection. Also, Table 3-1 (Page 53) lists that the distal ileum has 100 percent infectivity. Table 3.10.1 has a zero for the proportion of an animal total infectivity in the ileum for animals 0 to

18 months of age. This should be one. It is impossible to determine if this is an error carried forward into the computations or merely a typographical error.

10) Section 3.3.2 evaluates the effect of importation of infected cattle as a source of infectivity on model prediction. There can be no disagreement with conducting simulations assuming a range (1 to 500) of infected cattle to determine the robustness of the U.S. cattle population. However, the assumption that they were infected at 12 months is dubious (second paragraph). The modal age at infection for British cattle, the most likely source of infection, is 4 months of age. Again, one is not certain of the sensitivity of this assumption to the simulation.

11) In Section 4.4.3, the likelihood that BSE infectivity could have been introduced into the U.S. by cattle imported from the UK is addressed. In the fifth paragraph (line 8), the authors state that "USDA's estimate of the number of clinical cases that surveillance would have detected in the year 2000 with 95 percent probability" are plotted in Figure 4-7. The basis of this statement would have been of benefit. Is this based on the use of the screening tests of slaughtered cattle, or merely on clinical surveillance, or on this plus surveillance of fallen stock and casualty slaughtered animals or on combinations of these methods of surveillance?

12) It is cited that for each animal in the UK that developed clinical signs, another four animals went undetected (Appendix 2, Page 3, second paragraph). Use of such multiplicative factor is a little simplistic. The ratio of infected animals to those that develop clinical signs will not be constant through any epidemic. Also, some amendment would be appropriate in the second paragraph to account for the fact that animals exported from the UK carried a greater risk of infection than those retained in the UK.

13) In the H-T BSE study, the sequence of control measures in Switzerland that bring about the growth and decline of the BSE epidemic is clearly stated. For the U.S., the model mainly states the present state of affairs, with a feed ban and regulations about prohibited rendering and feed. However, the model ignores the practices in the past. Before 1997 there apparently was no feed ban. A proper assessment of the rendering and feeding risks at that

time is missing. Although it is probably included in the model, these details were not apparent in the report.

14) There is a minor comment regarding birth rate assumptions on Page 49. The model assumes a (constant?) birth rate from 24 months onward. This is obviously somewhat besides the actual truth, because it would lead to an average age at first calve of 30 months, whereas this is probably closer to 24 months. The strong peak in calving around the ages of 24 and 36 months, which is neglected in this model, may explain the difficulties in getting the age distribution and population size to fit with the data on culling.

4 Overarching Logical Structure of the Risk Assessment

The reviewers agree with the risk assessment process. However, they had general and specific comments on the overall structure of the risk assessment, risk factors and their values, epidemics, and presentation issues. We number them to differentiate the comments.

1) In general, a typical risk assessment includes four important components: hazard identification, exposure assessment, dose-response assessment, and risk characterization (NRC, 1994). The BSE risk assessment model includes these four components. Therefore, the risk assessment methodology is appropriate.

2) In general, the methodology was found to be sound and efficient, although the large uncertainty in many of the needed parameter values makes the choice for a simulation model rather suboptimal, because many different simulation results make it hard to actually interpret these results.

3) The report shows a tendency to underestimate the risks of BSE transmission in the U.S., reasons for which are discussed earlier in this report. This tendency is mainly based on the bottom-up methodology of listing all the possible (imaginable) risks and subsequently quantifying those. In comparison, the EU-SSC Geographical BSE Risk studies take the top-down approach of following all the risk material to see where it goes. "If it cannot be accounted for properly, it must pose a risk." Thus, the two methods look at the problem from totally opposite sides, with the EU generally overestimating the risk and this study generally underestimating the risk. Another point where the report tends to

underestimate the BSE risk is in quantifying the parameters, as discussed in Section 4.2.

4) The H-T BSE study authors want to determine the effect on animal health and potential human exposure after introducing BSE-infected animals into the U.S. cattle population and looking at other sources of introduction (spontaneous, feed, animal-to-animal). They have developed a simulation model with a set of initial underlying assumptions that they call the "base case" scenario. They claim that the base case scenario, the logical structure of which is depicted in Figure 3-1 of the H-T BSE study, represents the present state of the cattle population including government regulations and prevailing agricultural practices. Also, see the general comment on the clarity of the model's structure.

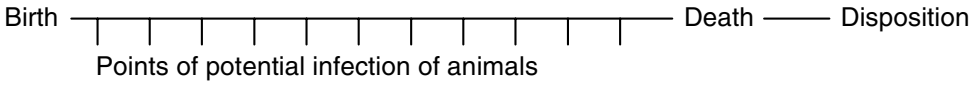
The authors constructed a stochastic model consisting of four components (Figure 3.1 and Appendix 1). The four components are cattle population dynamics, the slaughter process, rendering and feed production practices, and infectivity in material for human consumption. The authors might consider illustrating each component as shown in Figure 4-1 to understand them better. Rate/state diagrams, such as the one in Figure 4-2 might also be used.

The authors depict in Figure 3-1 that the sources of infectivity drive the system by infecting the cattle population. Epidemiologists and ecologists have constructed many stochastic models of epidemics, which the authors could have used to build on for a more complete description of the dynamics common to epidemics, and then the authors could have customized the model to include the particular factors associated with BSE. However, the need to construct a complex population model does not seem to be important because this disease basically is noncontiguous.

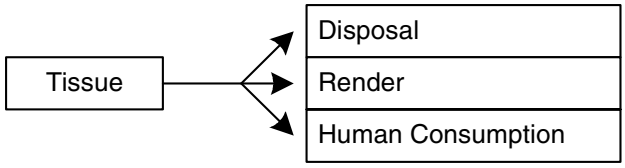
5) Although Figure 3-1 describes the basic process, the processes involved from the birth of an animal to its death and ultimately the fate of it remain unanswered. The conclusion is that the basic structure is rather constrained and ignores important information.

Figure 4-1. Four Components of Simulation Model

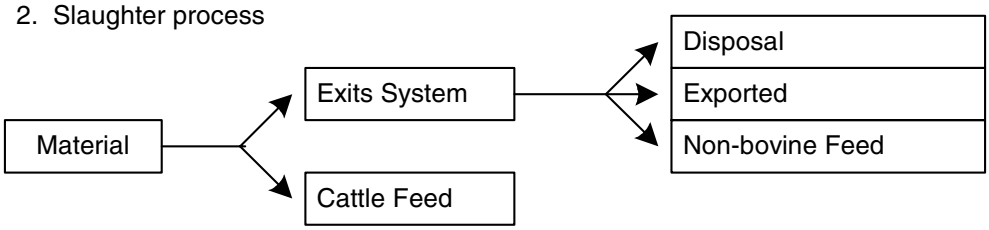
1. Lifestyle of cattle in United States



Where death is slaughter, BSE death, or other death and disposition is slaughter, disposal, or rendering.



2. Slaughter process



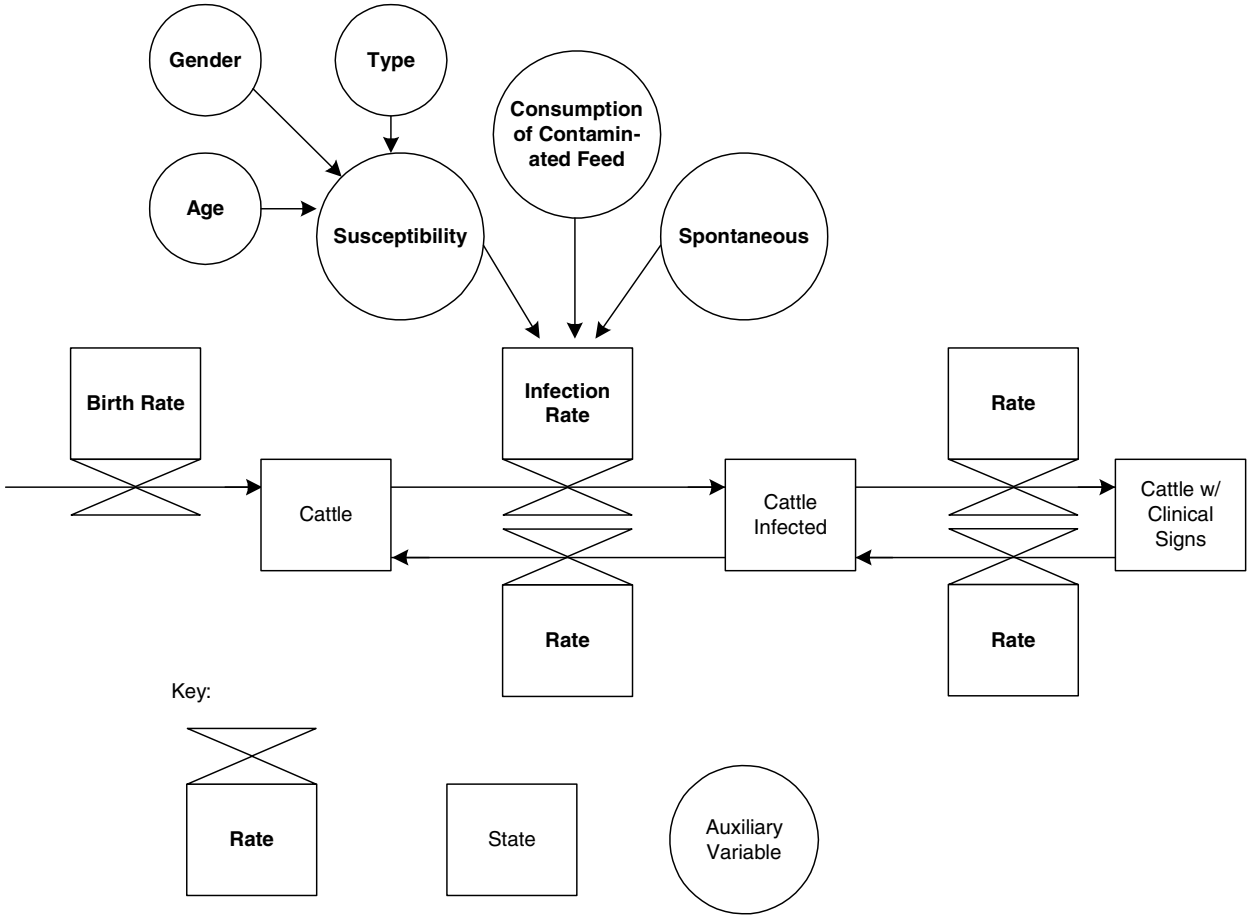
3. Disposition of material sent to rendering

4. Infectivity of material presented for human consumption

6) Some probabilities are specified in a tricky way. For instance, probFeedOK is the probability that prohibited feed is not fed to cattle (Appendix 1, Page 13). Why not just estimate the probability that a mistake is made?

The H-T BSE study authors have identified practices such as inspection, stunning, splitting, advanced meat processing, and segregation of rendering products, which *a priori* could lead to prion ("infectivity") spread. The model, while appearing to be comprehensive, is limited because it is based primarily on events that are unlikely to occur (e.g., pneumonic stunners now are rarely used). It appears that some factors were chosen if any data existed, rather than by identifying critical control points of production and processing practices that might lead to contamination. Although the H-T BSE study authors consulted with experts, the model derivation was their nonexperimental knowledge of the meat and rendering industries, which this reviewer believes also limits its scope. Do we have the means to track feed ingredients through the system? How widely are the ingredients distributed? What effect does cattle

Figure 4-2. Rate/State Diagram for the Modeling Process



movement, which is extensive, have on spreading the disease? What economics are involved? Could a more general model be constructed that could be modified easily by the user to estimate the risk that other diseases might establish in the U.S.?

7) An initial phase of the risk assessment, in addition to the necessary review of published literature and available expert information, could have been an international (relative) risk assessment. This may have only been possible during the latter stages of the course of the risk assessment project. However, given the revelations in continental Europe, and other countries of the world following active and targeted surveillance, a more appropriate and defensible risk analysis may have emerged. Several examples to strengthen this claim have been provided in this report. This is simply, and obviously, because when a risk has materialized, it is somewhat easier to conduct a risk assessment. There has been

some validation using the Swiss data and information, but, as previously noted, it can be misleading, or as the authors admit, could be for reasons of chance.

8) The BSE model has not formally been validated. It used a Switzerland case to test the plausibility of the model prediction. It is difficult to conduct a formal validation for the BSE model because there are no known controlled experiments in which the introduction and consequences of BSE to a country have been monitored and measured. Nonetheless, it must be acknowledged that the validity of the model is not fully established. Also, it is not apparent what efforts are made to verify the model.

5 Biological Plausibility of the Assumptions

The reviewers commented on whether the assumptions are in line with the biology. We number their comments to differentiate them.

1) There has to be some doubt about the apparent use of a constant ratio of subclinically infected animals and clinically affected animals. It should be noted at this point that the H-T BSE study report is difficult to assimilate, because in some sections, notably the Background and Executive Summary, risks are rather summarily dismissed, but in the actual model they are apparently addressed in a more cautious way. The following draws attention to a number of the key assumptions.

2) For the development of infectivity within an infected animal (Figure 3-6), the decrease of infectivity in the animal after 20 months (Section 3.1.2.1, Page 53, tenth line) is an assumption not based on reality but on detection in an experimental model. The abnormal prion protein (PrPSc) does not leave the body; it most likely continues to spread through the body to (temporary) undetectable levels. The model would benefit from such an assumption. This may have a major impact on the results, because one is then forced to state that "undetectable levels" of infection in animal products are probably nonzero.

The subsequent exponential increase in the last stage seems to be a good choice, but a motivation for the chosen growth rate (not in the report?) would be welcomed. The way to handle the curve for shorter or longer incubation periods is reasonable as discussed in

Section 3.1.2.1, although one can discuss that it is more likely that this growth rate is always equal in all animals, but the moment that the exponential phase starts has large variation. However, the latter point has probably minimal impact on the results.

3) With respect to incubation period (ip), the model that has employed the ip used has some problems in terms of the predicted incidence because it lacks precision.

4) The absence of considering an exogenous source via imported feedstuffs in general rather than via meat and bone meal is an omission, as discussed in comment 8 in Section 4.1. Some investigation is required to examine the plausibility of the dismissal of this source. A relative risk approach, as part of the whole process, may have precluded this omission because trading between EU member states, which have not employed the full set of risk-reducing measures, has resulted in infection "moving around" clandestinely. It may be that the U.S. has effectively been protected by statutory means or simply by traditional international trading patterns. However, the current risk assessment is a little open to criticism from "the outside world," which may not be fair to the research teams.

6 Are the Mechanics of the Model Consistent With Known Biology?

The reviewers agree that in general the modeling appears to be consistent with the biology. However, the reviewers have a few reservations, primarily because the model structure was not clear enough to properly analyze. Gaining an understanding of the model mechanics would have required inordinate time resources. Although the model could not be analyzed, the reviewers agree that it is critical for the model to be analyzed in detail. Consequently, the model review was performed by the NCSU team. However, they found that the model documentation in the report as well as in the code of the model was insufficient to evaluate accuracy and plausibility of the model mechanics.

7 Appropriateness of Modeling Techniques (Model Mathematics and Equations)

The reviewers' main concern is the lack of adequate information about the model structure, equations, techniques, and other components. We number their comments to differentiate them.

1) It may be the case that the BSE model appropriately simulates the possible sources and pathways of the animal or human exposed to the infected BSE products when BSE is introduced into the U.S, and the possible measures to decrease the exposure and spread of BSE during the slaughter process and rendering and field production process. However, there is no documentation of the analytical approach used in the model; therefore, an assessment of the appropriateness of the simulation model is extremely difficult. The development of the BSE model appears to follow the general model development approach, including model conceptualization and model design, employed by the Michigan Department of Environmental Quality (Michigan DEQ, 2002). However, details regarding the analytical approach are lacking.

We did not find mathematical equations to describe the BSE simulation model in the report or any other documents available. Though there are some limited descriptions about the simulation model in the report, these are not specific or clear enough. For example: (1) What are the mathematical equations in the simulation model? (2) What are the exposure assessment models? (3) Do they correctly represent the simulation process? (4) What are

the dose-response equations? (5) How are the risks calculated based upon exposure assessment and dose-response relationship?

Therefore, these reviewers strongly recommend that the model developers provide the detailed information on the BSE model in the report, including all mathematical equations used to represent the lifecycle of cattle, exposure pathways, slaughter processes, rendering and feed production process, exposure assessment, dose-response relationship, the process by which humans consume or are exposed to the infected materials or products, and risk characterization.

2) For the sensitivity analysis, the authors chose a specific selection out of a huge number of parameters. An explanation of why other parameters were not assessed should be included. There were a few parameters that were not tested but may give interesting results. A Spanish hypercube method may also be worth doing.

3) It is very unclear up to what level stochasticity is incorporated into the model; this should be explained in the report. Given the methods, it seems likely that major parts of the model use a deterministic calculation and only "critical parts" are worked out fully stochastically. An explanation of that system and why it was chosen would be helpful. More detail about the precise calculation method would be worthwhile, especially for stochastic components.

4) Why was the stopping criterion of 1,000 runs used for the simulation runs? Did the model always converge at 1,000 runs?

8 Appropriate Characterization of the Risks

The reviewers believe that qualitatively the risks have been appropriately characterized; however, because modeling comprises most of this risk assessment, the quantitative aspect is of interest. The reviewers' general impression is that the results of the modeling exercise may underestimate potential problems. The reviewers list a few issues that may lead to miscalculation or misspecification of the risk. We number their comments to differentiate them.

1) In terms of procedures or approaches used in the BSE risk assessment, the BSE model correctly and appropriately followed the general risk assessment procedures (NRC, 1994). However, as mentioned in previous sections of this review, because there is no detail on the analytical exposure assessment models, dose-response function, and risk characterization models, it cannot be determined if these models are correctly implemented and how risk is characterized based upon exposure and dose-response assessment.

2) The underestimation of the risk can be seen most clearly from the "validation" with the Swiss data: at first it looks as if the model really fits very well to this data set. However, a more thorough assessment shows that the model underestimates the problem enormously, because the recent active surveillance for BSE in the EU has shown that only about 10 percent of the test-detectable BSE cases were actually reported and found in the normal passive surveillance with obligatory reporting (also reported by Doherr). This would suggest that the true number of cases in the Swiss epidemic will have been much higher than the actual detected number to which this model was compared. Unpublished

modeling results of Cohen et al. can show more accurate numbers on the BSE cases. The model validation would have been more valuable if the model could have shown an epidemic pattern over time, which allows for a far more comparable result than the total number of cases over time. The model may/does give these results, but it cannot be seen or understood from the report.

3) The reviewers are concerned about how the H-T BSE study authors addressed the minutiae. The prime example is the treatment of emboli following stunning. This possible means of contaminating carcasses has been an issue for Great Britain where, obviously, the incidence of BSE has been considerably greater than elsewhere. One has the impression that this source of carcass contamination is included because there are a few papers on this. The outcome is apparently that the relative risk for the human population is considered in the analysis/simulation, but the readers wonder if a few minor aspects have been disproportionately emphasized. Also, see the general comment on the level of detail. In such a large and politically important disease problem, there is bound to be a body of unpublished research results and synthesis, which can be included in the study to make it more comprehensive and up to date.

4) In a similar vein, one is concerned with the somewhat theoretical approach used for what could be summarized as the nonadherence of the Food and Drug Administration (FDA's) MBM ban. This seems to be based rather simply on the views of industry-based advisors of where things go wrong rather than an analysis of how accidental or illegal contamination and therefore exposure could occur. The basic and difficult problem of the relatively small amount (<1g) of infected material required to infect cattle seems to have been ignored and perhaps not appreciated (see comment 12, Section 4.2). A fuller, more field-based analysis, together with an examination of the problems encountered in Great Britain, would be helpful. This would have overcome the problem that it was apparently not possible to monitor the effectiveness of the FDA's ban. Logically, there was no way of "policing" this ban, because no means of surveillance to detect illegal ingredients was available. Moreover, the legislation banning MBM was selective and left a number of potential loopholes, which meant that a means of

surveillance to detect nonadherence to the statutory ban was important.

5) In discussing slaughter rate on Page 49, it should be noted that dairy cows are culled primarily for reproductive and production reasons.

6) In discussing BSE dose-response on Page 50, the authors write about a hypothetical alternative sigmoid dose-response (end of first paragraph). However, how and whether it was used is not mentioned. Also, it is stated that there is no direct evidence of BSE transmission from cow to calf in discussing maternal transmission. But why it was used anyway is not justified. Also, the authors state that the base case assumes calves are born to infected cows during the last one-sixth of the incubation period, but they state earlier that the incubation period was between months and years. So, specifically, what cut-off point was used?

9 Identification and Characterization of Variability, Uncertainty, Critical Assumptions, and Data Gaps

Although generally several comments can be relevant to this topic, we provide only specific comments on variability, uncertainty, critical assumptions, and data gaps that mainly influence the risk. We number their comments to differentiate the them.

9.1 KEY SOURCES OF VARIABILITY AND UNCERTAINTY

1) In Section 3.2 of the H-T BSE study report, the authors list 15 sources of uncertainty that they evaluated individually for influences on the model predictions for two outcomes:

- 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 ID50s) in food produced for human consumption over that period.

In addition to varying the parameters to reflect a best case and worse case, the authors considered the impact of different sources of infection on the model's predictions, described in Section 3, Pages 71-79 and compared the model's predictions with alternative

scenarios. The parameters evaluated in the sensitivity (uncertainty) analysis are listed in detail in the synopsis.

2) The method used for evaluating the contributions of uncertainty in inputs to uncertainty in model predications has key shortcomings. The chosen method in the BSE risk assessment model is to evaluate the influence of one individual uncertainty source while setting all of the other assumptions or uncertainty sources to their base-case values. For example, when considering the impact of the uncertainty in maternal BSE transmission rate on the model prediction, the other 14 uncertainty sources are set to their base-case point estimates. This kind of analysis should be referred to as "sensitivity analysis," not as "uncertainty analysis" as described in the report. Although uncertainty analysis and sensitivity analysis are closely related, they are two different disciplines. Uncertainty analysis assesses the uncertainty in model outputs that derives from uncertainty in all inputs when simulated simultaneously. Sensitivity Analysis assesses the contributions of the inputs to the total uncertainty in analysis outcomes (Cullen and Frey, 1999). Therefore, the results from the BSE model "uncertainty analysis" do not represent the full range of uncertainty in the risk of animal or human exposed to BSE associated with simultaneous contributions from all uncertainty inputs. Instead, what is reported is an individual contribution of one uncertainty input to the partial uncertainty in the model output, the risk such as associated with animal or human exposure to BSE.

3) Variability refers to the heterogeneity of values with respect to time, space, or a population. For example, in exposure assessment, variable quantities include the rate at which individuals consume specific dietary items and the body weights of the individuals (Cullen and Frey, 1999). Variability can be represented by *a frequency distribution* showing the variation in a characteristic of interest over time, space. Uncertainty arises due to lack of knowledge regarding the true value of a quantity. For example, there may be uncertainty regarding the proportion of animals that die on the farm that are rendered. Uncertainty can be quantified *as a probability distribution* representing the likelihood that the unknown quantity falls within a given range of values (Frey, 1997).

Although the BSE model evaluates the impact of how comparison of various uncertainty sources influences the model predication, there

is no distinction between variability and uncertainty in the model inputs or outputs. In typical practice, in an exposure or risk assessment model, the model inputs can be divided into those that are variable, those that are uncertain, and those with some aspects of each (Bogen and Spear, 1987; IAEA, 1989; Morgan and Henrion, 1990; Finkel, 1990; Frey, 1992). For example, in the BSE model, maternal BSE transmission rate is variable across different mothers, but it is also uncertain because there is no knowledge regarding its true value. It is not possible to determine whether there are variables that are misspecified as uncertain that instead should have been arranged distribution for variability because there is not enough description of the characteristics of most of the input variables. Therefore, based upon the information presented in the model documentation, it is not possible to determine which inputs should be arranged distributions for variability and/or uncertainty.

Variability and uncertainty have different ramifications for decision-makers (Cullen and Frey, 1999). Uncertainty forces decision-makers to judge how probable it is that risks will be overestimated or underestimated for every member of the exposed population, whereas variability forces them to cope with the certainty that different individuals will be subjected to risks both above and below any reference point one chooses (NRC, 1994). Therefore, it is recommended that both sources of variability and uncertainty be identified and distinguished and that variability and uncertainty analysis be done in the BSE risk assessment model.

4) In Section 2, at the beginning of Page 26, the authors state the uncertainty in ascertaining the potential risk posed by oral exposure to Chronic Wasting Disease (CWD):

> Ascertaining the potential risk posed by oral exposure to CWD is further complicated by the following sources of uncertainty. First, there are no accurate statistics documenting the number or type of deer and elk killed by hunters. Second, the type of deer and elk that can be hunted in different geographic areas varies. Third, the disposition of deer and elk remains after slaughter is uncertain. Finally, the prevalence of the disease in all but the highest risk areas is unknown.

The authors have found no data for key sources of uncertainty.

5) On Page 55 at the end of the first paragraph, the authors state, "Our base case assumes that clinical BSE cases would be detected at AM inspection 90 percent of the time. Because this value is highly uncertain, our uncertainty analysis evaluates the impact of using a wide range of values on the results of our simulation (see Section 3.2.2)." However, it was found that only two values were evaluated.

6) Table 2.18-1 (Appendix 1, Page 31) specifies joint probability as a percentage but Table 2.2.2.3 (Appendix 2, Page 8) specifies it as a probability. (Also, the reviewers wonder if the decimal point is in the correct place.) Consistency among the units or measures of the probability would be nice.

7) The authors have done a sensitivity analysis where they altered the parameter values one at a time to determine the effect on the model's predictions, varied values defining the source of infectivity to determine the effect on the model's predictions, and compared the model's prediction for other scenarios. These are all important means to determine the model's behavior and reliability. The sources of variability are largely only considered individually, so synergistic effects cannot be assessed. The authors have been careful to select "reasonable" values for the best and worst cases, but allowing a greater range of variability would provide a better understanding of the behavior of the model and its stability.

8) Key sources of variability that have been omitted are accidents that can sometimes happen and the intentional introduction of prions to feed or water; and a long-term change in practices by producers, processing establishments, and/or renderers that might result in prolonged exposure. Because of these omissions, one may wonder whether a more parsimonious model might be as predictive.

9) In the case of variability and uncertainty, the risk of infection through imported animals is addressed in a defensible manner, even though the probability of this incursion is not estimated. However, the age at infection ignores the information and the uncertainty of the incubation period and is not addressed. The summary of these aspects, perhaps somewhat harshly, is that the synthesis and critical review of the literature needs more attention.

10) Little information regarding the distributions of BSE model inputs and simulation techniques was provided for the so-called "uncertainty analysis." Therefore, key questions that should be addressed include the following: (1) How was the value of an input altered? (2) What sampling techniques were used? It is necessary to clearly list the distribution assumptions and parameters (if used) and to clearly describe related simulation techniques when doing uncertainty analysis. The description in the report regarding the "uncertainty analysis" of the BSE model is not clear enough for users or reviewers to understand how the "uncertainty analysis" (if any) is done.

9.2 CRITICAL ASSUMPTIONS

1) Surveillance efficiency, recognition rate of "clinical cases," and level of inactivation by local rendering are overestimated. Also, with respect to recognition rate (where only the very typical cases will be recognized), it is assumed that 90 percent (in the case of worst case, 50 percent) of the BSE clinical cases will be detected in the ante-mortem inspection, which is way off from the general feeling in the EU on this topic.

2) In discussing fracContaminate on Page 16, Appendix 1, the authors state that flushing and cleaning leave only 0.1 percent of the prohibited material behind. This cross-contamination as compared to European demonstrated rates is grossly underestimated, unless flushing and cleaning are done in a very different (and probably uneconomical) way.

3) The readability of the report could be improved by tabulating all assumptions, as was done for the slaughter process assumptions (Table 3-8, Page 68) and the render and feed production assumptions (Table 3-9, Page 69). On Page 67 (second paragraph, first line), the authors refer to 15 sets of assumptions, but present only seven bullets (does a bullet represent a set?). If each item within a bullet is summed, 17 assumptions can be identified. Also, the authors set parameters to three values: base case, best case, and worst case. But the justification for the specific values assigned is weak, because little data are available. Without hard data, the detailed list of assumptions for this process has heuristic

value but does not particularly strengthen the predictive value of the model.

4) The authors assume that "conditions affecting the spread of BSE in the U.S. would remain unchanged for the 20 years following its introduction" (Executive summary, Page i, third paragraph, sixth line). This is a huge assumption and probably unrealistic. As with most agents of disease, especially newly discovered agents (emerging diseases), prevalence increases over time largely because of more and improved testing over time. This has not been incorporated into the model. Often, agents, once thought rare, are found to be ubiquitous (e.g., E. coli O157:H7). The public health goal then is to prevent the agents from spreading or accumulating in critical locations, including animals, during critical periods of time.

9.3 IMPORTANT DATA GAPS

1) The authors state, "There exist considerable data gaps for many important model assumptions" (Page 87). The authors have done a commendable job of incorporating the available data, but this also has limited the scope of the model and/or has resulted in giving certain factors more weight (a larger contribution to the results) than perhaps is warranted.

2) On Pages 22 and 23 the introduction risks are discussed. The import of risk material from the UK is assessed properly, but the import of risk material from third countries seems largely ignored. The EU concluded long ago that lots of risk material from the UK was transported via third countries. Switzerland, for example, mainly got infected via France not directly from the UK. Thus, the introduction risk is probably underestimated, although it is plausible that this risk still remains very low.

3) An analysis of all imported MBM and feed in the 1980s would be welcomed. Confirming evidence that imported MBM was only used in pet food would also be useful.

4) "Tallow" at least deserves some more comments (Page 34), given the fact that traces of protein are certainly in there and that international flow of these products is even more difficult to quantify.

10 Usefulness of the Results for Risk Management

Reviewers had concerns regarding omission of certain factors and overemphasis of a few. For example, the model considers the rare scenario of pneumatic stunning but ignores the more plausible bioterrorism scenario. We number the reviewers' comments to differentiate them.

1) Because there have been extensive evaluations of the BSE sources leading to the possible BSE infectivity, different scenarios, and various risk management strategies, the results from the BSE risk assessment model can be useful to some extent for risk managers to evaluate options and select strategies to manage the risk of animals or humans exposed to the infected BSE products or materials if results from the BSE model are correct. For example, the BSE risk assessment model was used to evaluate the effect of the implementation of specified risk material bans on potential human exposure of BSE. The results from these analyses indicate that there is a dramatic effect if the bans were used, which provided implication for risk managers in determining whether the bans should be implemented. From the base-case analysis, it was found that the greatest potential source of infectivity in the feed system is animals that die on the farm and are rendered. These results will be helpful for risk managers in selecting the appropriate management strategies in order to reduce the potential risk of animal or human exposed to BSE. For example, in this case, information from the risk analysis results will help risk managers determine whether it is necessary to prohibit the rendering of animals that die on the farm.

However, because the BSE model could not distinguish between variability and uncertainty, and because not enough documentation is given to show if the BSE model is correctly implemented, the accuracy of risk analysis results from the BSE model needs further evaluation; therefore, the implications for risk management are limited. For example, key questions that should be addressed in the documentation include: (1) How do we know that the results are correct? (2) What is the variability across different individuals or different scenarios? (3) What is the uncertainty in model outputs that derives from uncertainty in all inputs?

2) The strength of the H-T BSE study is in offering a tool to characterize measures that can potentially contribute to reduce spread of BSE infectivity. Also, it helps in identifying pathways or practices that could contribute most to the spread of a potentially introduced infectivity. As such, the model and its application are very useful.

3) A model is relevant if it leads or might lead to a different conclusion or reaffirms a previous conclusion. The model tells us no more than our current experience tells us. No BSE has been detected in the U.S. currently, nor is it likely to occur given existing practices, so it is not surprising that results of the simulations reveal that the risk is low, especially when the assumptions are based on mistakes in rendering and other practices.

4) The risk management aspects have been adopted from measures instituted in other countries, notably driven by those in the UK and more latterly in the European Union member states. The various effects of the risk management procedures have been assessed in quantitative terms where possible and those with the most uncertainty identified, notably the misfeeding rate. The risk management practice of preventing the importation of feedstuffs potentially contaminated with meat and bone meal has not been addressed. Similarly, there is no assessment of the true adherence of the "FDA feed ban" or suggestions as to how this could be assessed in light of the analytical treatment of the potential leakage of infected material in the risk assessment model. This said, consideration has been given to assessing the relative effects of the risk management practices included in the model.

5) The model presents the regulations and "prevailing" production and processing practices only in general terms. No regulations appear in the model in detail, and the consequences of changes in regulation only could affect, for instance, the crude probability that a BSE-infected animal of a given age passed inspection. Likewise, no regulation factors for rendered material are included in the model, only probabilities that rendering mistakes are made. Emphasis has been placed on practices that increase risk but not on factors that may reduce risk. The model would have greater value if the authors had included factors that would allow questions that ask, "what if regulations are changed?" How would such changes in regulation reduce the likelihood of prion accumulation and spread? What are the links between regulation and risk? What effect would testing cows before parturition have on the variable ProbTrans?

6) As with most agents of disease, especially newly discovered agents (emerging diseases), prevalence increases over time largely because of more and improved testing over time. Regulations and practices also can change. This has not been incorporated into the model.

Further, the activities of many researchers are focused on developing diagnostic tests to detect the agents, products of the agents, or factors associated with the agents. The model does not include the probability that such diagnostic tests will become available during the period simulated.

7) Although the risk of BSE in the U.S. currently appears to be low, but one of the goals of model building can be to think outside the box—to test plausible, even if unlikely, assumptions.

11 User Friendliness of the Model

The model is helpful to the user if the model and its documentation are adequate to allow individuals to conduct "what if" calculations. Here, we present reviewers' comments about proper interpretation of the model's capability and how to make the model more useful. We number the reviewers' comments to differentiate them.

1) Based on the information in the file "Data File Documentation" and the reviewers' understanding of the source code, the BSE simulator is a DOS-based application and was developed under the Microsoft Visual C++ integrated development environment. Since it is a DOS-based application, command line prompts must be provided to users to run the simulator. These reviewers noticed that some prompt messages and error-handling measures are provided for users to complete the "what-if" inputs and calculations by command line prompts. The information might be enough if users strictly follow the input requirements and do not make any mistakes in preparing the inputs.

2) A good risk analysis includes risk communication, which needs improving in this manuscript. For a user to conduct "what if" experiments, the user would require access to the program and a user interface to modify the parameters. The user also would need some flexibility in modifying the inputs and outputs, which would require the user to be able to modify the code or add parameters through a user interface.

3) Many values of factors are binomial (step functions). The model does not allow the user to evaluate how the results are altered when the factors are allowed to vary on a continuous scale.

4) The authors need to qualify many of their statements so that the reader is not misled into thinking that the simulation results are fact. Following are several examples from the second and third paragraphs in the executive summary.

- The authors claim (Paragraph 2), "Our model allows us to predict, for example, the number of newly infected animals that should result from introduction of BSE, the time course of the disease, following its introduction, and the potential for human exposure to infectious tissue." The predictive value and accuracy of the model is only as good as the assumptions on which it is based.
- The authors state (Paragraph 3), "our analysis finds that the U.S. is highly resistant to any introduction of BSE or a similar disease." However, a qualifying statement at the end of the sentence is needed, such as: "…by the means and levels assumed." Also, it is dangerous to extrapolate to a similar disease.
- The authors state (Paragraph 3) that BSE is extremely unlikely to become established in the U.S. However, the disease does not have to become established to have a devastating effect on consumer confidence, world trade, and the economy.
- The authors claim (Paragraph 3), "… there appears to be no potential for an epidemic of BSE resulting from scrape, chronic wasting disease, or other cross-species transmission…" Such categorical denials cannot be proved based on assumptions. Therefore, the word *no* should be replaced with the word *little*.
- The authors state (Paragraph 3), "… on average only three new cases of BSE would occur." Authors need to include over what period of time.

5) In general, a distributed software tool should have clear documents such as a "Readme" file and a user manual to guide users to install the software onto users' local machines, and to help users to use the tool. These documents should clearly state the operating or support environment required for user machines to run the software tool, and the documents should be provided in the CD where users can easily access or find them. Such documents and files were not provided in the CD. These reviewers recommend that the authors of the software reorganize the installation CD and prepare a "Readme" file and user manual. The "Readme" file and user manual should include (1) more detailed introductions on the installation of the BSE simulator and requirements for the software and hardware environment to run the model; (2) a guide on how to

use the BSE simulator; and (3) the error-handling information in case errors occur when running the BSE simulator.

6) Attempts at using what was provided on the CD were disappointing. What is definitely required is a CD formatted such that it self loads and takes the user to the manual for use. Alternatively the CD could be provided with a hard copy guide/manual. Instead what is provided is a CD with a series of files and folders, which takes an inordinate amount of time to comprehend.

7) The model is, perhaps inevitably, complex in terms of the number of variables and "parameters." The authors state (last paragraph on Page 100): the model can also be used to evaluate hypotheses about sources and factors influencing the BSE spread. This is impossible to assess with any certainty. Only the original developers of the model could easily add sources.

The model may not be entirely relevant for risk assessments in other countries because of the U.S.-specific aspects, notably the way "misfeeding" is addressed in terms of noncompliance with the "FDA feed ban."

With this type of simulation, a new user may have to conduct a relatively large number of runs to determine the effects of the interactions within the model when changes to input values are made. It does seem that the authors have adopted this multirun approach themselves. This is not an adverse criticism necessarily because this type of approach can obviously be helpful. However, if additions to the model were made, then a fairly substantial block of work would be necessary to examine the consequences.

8) For input requirements to run the simulator, many requirements are specified in the file "Data File Documentation," such as, "All user-defined parameters are stored in a series of ASCII text files. Although neither the name or number of files used to specify the parameters matter, all text files containing a parameter definition must be listed in a single text file, and the file containing this list must be located in the directory from which the simulation is executed, and it must be provided to the simulator as its sole argument from the DOS command line . . . all top level elements must appear exactly once in the set of parameter files provided by the user. . . ." These instructions include many "must" statements,

which implies that the input format requirements are rather strict and any mistakes that users make in preparing the input parameter files will lead to failure in running the simulator. In addition, the instructions mentioned a few times that "the user must create a text file listing all the parameter files" in the document; however, how many is meant by "all"? This information is not shown in the report nor in any other documents.

Based on the experience of the reviewers' running the simulator, it is very tedious and frustrating to prepare such input files and it will take users much time to correctly prepare the input files in order to run the simulator. Therefore, these reviewers infer that the BSE simulator is not user-friendly, especially with regard to user data input. Although it is a DOS-based application, there are better approaches to allow users to easily run the simulator. For example, pure command line prompts guiding users to input parameters are better than organizing a series of text files with strict format requirements.

Based on the reviewers' experience in using and developing Visual C++ programs, a main advantage of Visual C++ is that it provides a very strong graphical user interface and programming features and an easy way for software developers to create a graphical user interface software tool. In general, a software tool with a graphical user interface is more friendly.

Much of source code in the BSE simulator is used for data inputs and error handling of input parameters or files. Based on the reviewers' experience, the time spent in writing those codes is enough to develop a very good graphical user interface to help users input parameters of the model and to present the outputs from the model. Therefore, it is suggested that the BSE simulator have a graphical user interface to allow users to more easily input the parameters.

9) A problem with the H-T BSE study is that, although each parameter is defined and values specified, the formulae that incorporate the parameters are not specified. Perhaps if one examined the computer code, this information could be learned, but this information in the written document can be easily communicated to the reader.

10) An executable program called Madcow.exe and its C++ source code were provided on the CD. Although it was not in these reviewers' scope to check the correctness of the source code and to verify the BSE simulator, a review of the source code was attempted. Since there are no documents that describe the structure design of the simulator and the logical relationship between the different C++ class files, and because there are not enough comments in the source code, it is impossible for a reviewer to understand the design and internal structure of the BSE simulator.

The development of a software tool often involves the following procedures: requirements analysis, structure design, coding, and verification (testing) (Darnell and Margolis, 1996). A conceptual structure design and a comprehensive verification are necessary for any software implementation of simulation models. The former will help a software tester and users to understand a software tool and the models inherent in the software tool. The latter will ensure that the models inherent in the tool and algorithms used in the models are correctly implemented. However, in the documents available, no such documents were found. Thus, the following questions could not be answered: (1) What is the structure design of the BSE simulator? (2) Has the BSE simulator been verified? If it has, a verification report should be provided so that the users can have evidence that the results from the BSE simulator are correct. If the software has not been verified, how do developers know the algorithms in the simulator are correctly implemented? Therefore, these reviewers recommend that a comprehensive verification process be done. The verification process should include algorithms, data, coding, input/output, and other necessary verification procedures. A verification report should be provided for reviewers to evaluate the correctness of implementation of the BSE simulator. Inclusion of a conceptual structure design report is recommended so that the software testers or reviewer can understand the basic structure of the simulator and logical relationships between different components.

12 Editorial Comments

To improve the quality of the draft, the reviewers provided their editorial comments and comments on writing style and other aspects of the report. The list below is not exhaustive, but it can be used as a guideline.

1) In Section 2.1, "Creutzfeldt" is mistyped, as is "Scheinker," the latter occurs later also.
2) The word "the" is used unnecessarily throughout the report.
3) The word "similarly" is used often as a nonsequencer.
4) Replace "all of the" with "all."
5) Change "might also be" to "also might be"; "has also been" to "also has been"; "is also" to "also is."
6) The authors sometimes speak of disease when they mean the disease agent.
7) The authors sometimes are confused about the "species barrier": species barriers do not compromise (Page 8).
8) Eliminate unnecessary words: replace "by the fact that" with "because" (e.g., Page 13, 34, 48 [twice], 62); "There has been no" (page 24).
9) Word order: change "be readily deactivated" to "be deactivated readily" (Page 35)
10) Avoid "etc." (e.g., Page 65) and "among others" (page 61)—instead, specify list.
11) The word "packet" is jargon—needs to be defined or an alternate word used (Page 63).
12) Table 3-6 (Page 65) Mistake in description of misfed. In Table 3-7, description of spinal cord, "label" should be "labeled." In Table 3-7, description of blood, sensitivity analysis does not investigate, people investigate. In Table 3-7, why is air-injected pneumatic stunning not reflected in the base case, other than it is not used widely since recent government recommendations have been issued?

Why is it assumed that "steaming or washing" does not reduce contamination? Most processing establishments, after removal of the spinal cord, steam vacuum the channel and surrounding tissue. Do the authors have evidence that this is ineffectual?

13) Section 3.2.7, first sentence, Page 71: Replace "… prior to the passage of 50 percent of the period" with "until"; replace "…but that after that time…" with "when." Paragraph is confusing and should be rewritten.

14) The authors imply that there is substantial variation across age groups, but they do not provide the evidence (e.g., Page 71, last sentence). However, it is observed that people as young as 19 years of age have died of CJD. To use crude estimates of age-specific rates in humans as an estimate for cattle, even with "adjustments" is too much extrapolation. These are guesses and again point for the need for data. On Page 72, authors state, "… cattle muse reflect the age structure of the disease" — needs qualification statement.

15) On Page 73 (Note b, Table 3.1.1), why did the authors assume that a spontaneous CJD case observed in a young child was erroneous?

16) On page 73 (last line), the authors state they have simulated the introduction of 1, 5, 20, 50, 200, and 500 12-month old female dairy cows. Why were these numbers selected? Why were only dairy cows considered?

17) Why was the value 600 ID_{50} selected (Page 75, first line). Choice of word "ensure," second line Page 75, is confusing.

18) Spelling error (Page 103, fourth reference, Collinge et al. (1997) "Prion" misspelled.

19) Page 4, Appendix 1: under comment of <probTrans>, "he" should be "the."

20) Page 45, Appendix 1: What are the appropriate significant numbers? Is it relevant to carry out the decimal to six places?

21) Appendix 3A (Table of contents): Same labels for tables should be used as in table of contents

22) Appendix 3A. Abbreviations in table should be defined as well as units of measurement.

23) Spelling error (Appendix 3A, TOC, Section 2.5): "Dieing" should be "dying."

24) Appendix 3A: In the tables, why are only the "Disposition of ID50s" numbered and not other outputs?

25) In Appendix 3A Table: Unsure of what variables in the list of variables in tables correspond to figures labeled

ID50s to cattle and ID50s to humans. Also, is "number of cattle infected" the same as "total infected" or "total infected w/o imports"?

26) Why does it appear that so many values exceed the 95th percentile in the box and whisker graphs in Appendix 3B?

27) "Non-ambulatory" is the preferred term for "Downer." Though both terms could be used interchangeably, using non-ambulatory is recommended.

28) Please give page numbers when referencing the appendices.

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A Reviewers' Professional Experience

Dr. H.Christopher Frey

Dr. H. Christopher Frey is an Associate Professor of Civil Engineering at North Carolina State University, Raleigh. His research includes quantification of variability and uncertainty in air pollutant emission factors and emission inventories, measurement and modeling of highway vehicle emissions, modeling and assessment of advanced air pollution control and prevention systems, and risk assessment methods. Sponsors of Dr. Frey's research program include the U.S. Department of Energy, U.S. Environmental Protection Agency (EPA), U.S. Department of Agriculture, and the National Science Foundation. Dr. Frey's contributions have been recognized by national awards, such as the 1999 Chauncey Starr award from the Society for Risk Analysis, a Faculty Early Career Development (CAREER) Grant by the National Science Foundation in 1997, and a 1992 AAAS/EPA Environmental Science and Engineering Fellowship. Dr. Frey has participated on several national panels, including an EPA Science Advisory Board subcommittee on Residual Risk and several EPA workshops pertaining to the development and application of probabilistic methods in environmental science and engineering. In April 1998, Dr. Frey chaired an EPA workshop on methods for the development and use of probability distributions to represent environmental data. On numerous occasions, Dr. Frey has been a peer reviewer for major EPA documents, including technical reports, regulatory support documents, and Reports to Congress. Dr. Frey has approximately 120 publications, including journal articles, conference papers, and technical reports. He also has coauthored a book on "Probabilistic Techniques in Exposure Assessment."

Dr. John C. Galland

John C. Galland has a Ph.D. in ecology from the University of California-Davis and is a full professor in the Departments of Clinical Sciences and Diagnostic Medicine/Pathobiology, College of Veterinary Medicine at Kansas State University, Manhattan, KS. He was elected to the Faculty Senate and established research linkages between Argentina, Jordan, and the University. He is co-coordinator of Public Health and Epidemiology courses in the professional curriculum. Dr. Galland acquired more than $1.75 million in research funds and played a major role in creating the first entrepreneurial center on campus. He created a microbiology laboratory to conduct research under the Good Laboratory Practices (GLP) Act to undertake government and industry contract work. From 1994 to 2000 he was Corporate President of Animal Health Systems, Inc., a software development company specializing in custom large database applications, voice recognition, and electronic identification systems, in Manhattan, KS. Through the university entrepreneurial center, he successfully launched a new software product into the marketplace. The database application included over 1 million lines of custom C++ software. He represented the corporation's research and development in outside discussions and technical forums. He has published numerous articles in journals such as the *Journal of Veterinary Diagnostic Investigation*, *American Journal of Veterinary Research*, and *Veterinary Microbiology*.

Dr. Zheng Junyu

Dr. Zheng Junyu is a post-doctoral associate who works with Dr. H.C. Frey. His research involves uncertainty and variability analysis, and air pollution. Dr. Junyu is also experienced in risk assessments and developing computer models using C++. Dr. H.C. Frey and Dr. Junyu were the reviewers for the modeling aspects of the BSE risk assessment.

Dr. B.E.C. Schreuder

Bram E.C. Schreuder is a senior scientist at the DLO-Institute for Animal Science and Health (ID-Lelystad), department of Statutory Tasks. He is a trained veterinarian, specialising in small ruminant diseases, and more recently specifically involved in BSE and scrapie research. He became in 1990 project co-ordinator of the multi-disciplinary BSE/scrapie research project of the ID-DLO, and did his

PhD in 1998 on epidemiological aspects of scrapie and BSE, including a risk assessment study. During this period, the ID-Lelystad became the national reference laboratory for the diagnosis of both BSE and scrapie. The BSE/scrapie project group studied among others the association between PrP genotype and scrapie susceptibility, improved the histopathological diagnosis of TSE's by fine-tuning immuno-histochemical methods, and was successful in developing a preclinical method for the diagnosis of prion diseases (patent application filed). These results are presently applied in a nation-wide scrapie control programme. Bram Schreuder was also involved in analysing various risk factors for the introduction and propagation of BSE in e.g. the Netherlands, in which he, among others, evaluated the import risk factors, the efficacy of hyperbaric rendering procedures in inactivating BSE and scrapie agents, using mouse-bio-assays. Throughout the project, cooperation between the various involved sections of the ID-DLO (ESM, Patholology, Molecular Recognition and Biology) and with other institutes was considered of major importance. The BSE/scrapie project group participates in three ongoing projects and an equal number of newly formulated EC-proposals.

Dr. John William Wilesmith

John William Wilesmith has postgraduate diploma in biometry from North East London Polytechnic and has completed a postgraduate course in medical statistics and epidemiology at the London School of Hygiene and Tropical Medicine, University of London; he completed his bachelor of veterinary science degree course at the University of Bristol and is completing his Doctor of Science at Massey University. He is a Visiting Professor in the Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, University of London and Veterinary Head, Epidemiology Team, State Veterinary Services, Department for Environment, Food and Rural Affairs. He is a member of the Royal College of Veterinary Surgeons, British Veterinary Association, Society for Veterinary Epidemiology and Preventive Medicine, International Society of Veterinary Epidemiology and Economics, Association of Veterinary Teachers and Research Workers, The Veterinary Research Club, and the Faculty of Public Health Medicine of the Royal College of Physicians of the United Kingdom. His epidemiological research interests have centered on investigating nationally important diseases and those of economic

or zoonotic importance together with the development of animal disease surveillance. The development of the use of geographical information systems (GIS), risk analysis, and novel analytical techniques has been of particular interest in this research. Specific research topics have included tuberculosis in cattle and badgers; Johne's disease in cattle; bovine mastitis; listeriosis in sheep and cattle; and foodborne zoonotic infections of farm animal species, notably salmonellosis in all species, campylobacteriosis of poultry, and VTEC 0157 infection of cattle. Since 1987, research efforts have concentrated on BSE in cattle and other TSEs in animals and man and foodborne zoonotic infections. This work has involved developing effective collaborations with colleagues involved in the medical epidemiological aspects of the diseases, and until 2000 he was the VLA's TSE R&D and Surveillance Programme Manager. More recently, with the advent of the foot and mouth disease (FMD) epidemic, interests have necessarily been more or less restricted to epidemiological studies on this epidemic, together with continuing research and surveillance on BSE and other TSEs. Dr. Wilesmith has received the following awards: Bledisloe Veterinary Award, awarded by the Royal Agricultural Society of England for effective contributions to animal health (1993); Dalrymple-Champneys award for contributions to veterinary research (1994); Membership of the Faculty of Public Health Medicine of the Royal College of Physicians of the United Kingdom (1997), and the Chiron Award of the British Veterinary Association (2000). Dr. Wilesmith has published extensively.

H. CHRISTOPHER FREY

EDUCATION

Ph.D.	Engineering and Public Policy	Carnegie Mellon University	1991
M.E.	Mechanical Engineering	Carnegie Mellon University	1987
B.S.	Mechanical Engineering	University of Virginia	1985

PROFESSIONAL EXPERIENCE

1999 - date Associate Professor, Civil Engineering, *North Carolina State University*
1994 - 1999 Assistant Professor, Civil Engineering, *North Carolina State University*
1991 - 1993 Research Associate, Center for Energy and Environmental Studies and Department of Engineering and Public Policy, *Carnegie Mellon University*
1993 Adjunct Assistant Professor, *University of Pittsburgh*
1988 - 1991 Graduate Research Assistant, *Carnegie Mellon University*
1987 - 1988 Environmental Engineer, *Radian Corporation*
1985 - 1987 Graduate Research Assistant, *Carnegie Mellon University*
1981 - 1986 Summer jobs at *General Electric*, *Voice of America*, *U.S. Naval Research Laboratory*, and *U.S. Army Fuels, Materials, and Lubricants Lab*.

HONORS AND AWARDS

1999 Chauncey Starr Award, Society for Risk Analysis
1992 AAAS/EPA Environmental Science and Engineering Fellowship
1992 AAAS Robert C. Bernard Environmental Science and Engineering Scholarship'
National Science Foundation CAREER award (1997-2001)
Member of *Tau Beta Pi*, *Sigma Xi*, *Pi Tau Sigma*, and *Omicron Delta Kappa*.

SELECTED PEER REVIEWED JOURNAL PAPERS (SELECTED 18 OF 21)

1. Frey, H.C., and S. Bammi, "Quantification of Variability and Uncertainty in Lawn and Garden Equipment NO_x and Total Hydrocarbon Emission Factors," *Journal of the Air & Waste Management Association*, in press for April 2002 issue.
2. Frey, H.C., and J. Zheng, "Quantification of Variability and Uncertainty in Utility NO_x Emission Inventories," *J. of Air & Waste Manage. Assoc.*, in press for June 2002 issue.
3. Frey, H.C., and S. Bammi, "Quantification of Variability and Uncertainty in Construction, Farm, and Industrial Equipment NO_x and Total Hydrocarbon Emission Factors," *ASCE Journal of Environmental Engineering*, revised and resubmitted.
4. Frey, H.C., and E.S. Rubin, "Probabilistic Evaluation of Advanced SO_2/NO_X Control Technology," *Journal of the Air and Waste Management Association*, 41(12):1585-1593 (December 1991).
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6. Frey, H.C., E.S. Rubin, and U.M. Diwekar, "Modeling Uncertainties in Advanced Technologies: Application to a Coal Gasification System with Hot Gas Cleanup," *Energy* 19(4):449-463 (1994).
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15. Frey, H.C., and S.R. Patil, "Identification and Review of Sensitivity Analysis Methods," *Risk Analysis*, 22(3) in press for June 2002 issue
16. Frey, H.C., and J. Zheng, "Quantification of Variability and Uncertainty in Utility NO_x Emission Inventories," *J. of Air & Waste Manage. Assoc.*, in press.
17. Frey, H.C., and S. Bammi, "Probabilistic Nonroad Mobile Source Emission Factors," *ASCE Journal of Environmental Engineering*, accepted May 2002
18. Frey, H.C., and J. Zheng, "Probabilistic Analysis of Driving Cycle-Based Highway Vehicle Emission Factors," *Environmental Science and Technology,* revised and resubmitted June 2002.

BOOKS (1)

1. Cullen, A.C., and H.C. Frey. *The Use of Probabilistic Techniques in Exposure Assessment: A Handbook for Dealing with Variability and Uncertainty in Models and Inputs*. Plenum: New York. 1999. 335 pages.

CONFERENCE PROCEEDINGS (SELECTED 7 OF 73)

1. Frey, H.C., M.D. Kini, S.R. Ranjithan, and S.Y. Fu, "Uncertainty, Bias, and Variability in Emission Factors for Light Duty Gasoline Vehicles," Paper No. 96-108B.03*, Proceedings of the 89th Annual Meeting* (held June 23-28 in Nashville, TN), Air and Waste Management Association, Pittsburgh, Pennsylvania, June 1996.
2. Frey, H.C., and D.A. Eichenberger, "Quantification of Uncertainty in Remote Sensing-Based School Bus CO and Hydrocarbon Emission Factors," Paper No. 97-RP143.07, *Proceedings of the 90th Annual Meeting* (held June 18-13 in Toronto, Canada), Air and Waste Management Assoc., Pittsburgh, PA, June 1997 (CD-ROM).

3. Zheng, J., A. Unal, and H.C. Frey, "Variability and Uncertainty Analysis of CO Exposure to Vehicle Passengers During Cold-Start, Proc. of 93rd Annual Meeting of the Air & Waste Management Association, Salt Lake City, Utah, June 18-22, 2000.
4. Zheng, J., and H.C. Frey, "Quantitative Analysis of Variability and Uncertainty in Emission Estimation: An Illustration of Methods Using Mixture Distributions," *Proc., Annual Meeting of the Air & Waste Manage. Assoc.*, Pittsburgh, PA, June 2001.
5. Bammi, S., and H.C. Frey, " Quantification Of Variability and Uncertainty In Lawn And Garden Equipment NO_x and Total Hydrocarbon Emission Factors," *Proceedings, Annual Meeting of the Air & Waste Management Assoc.*, Pittsburgh, PA, June 2001.
6. Li, S., and H.C. Frey, "Methods and Example for Development of a Probabilistic Per-Capita Emission Factor for VOC Emissions from Consumer/Commercial Product Use", *Proceedings, Annual Meeting of the Air & Waste Management Association*, Pittsburgh, PA, June 2002.
7. Abdel-Aziz, A., and H.C. Frey, "Quantification of Variability and Uncertainty in Hourly NOx Emissions from Coal-Fired Power Plants," *Proceedings, Annual Meeting of the Air & Waste Management Association*, Pittsburgh, PA, June 2002

TECHNICAL REPORTS (SELECTED 3 OF 46)

1. Frey, H.C., and D.A. Eichenberger, *Remote Sensing of Mobile Source Air Pollutant Emissions: Variability and Uncertainty in On-Road Emissions Estimates of Carbon Monoxide and Hydrocarbons for School and Transit Buses*, FHWY/NC/97-005, Prepared by North Carolina State University for NC Department of Transportation, Raleigh, June 1997.
2. Kini, M.D., and H.C. Frey, *Probabilistic Evaluation of Mobile Source Air Pollution: Volume 1, Probabilistic Modeling of Exhaust Emissions from Light Duty Gasoline Vehicles*, Prepared by NC State Univ. for Ctr. for Transportation and the Environment, Raleigh, December 1997.
3. Frey, H.C., J. Zheng, Y. Zhao, S. Li, and Y. Zhu, Technical Documentation of the AuvTool Software for Analysis of Variability and Uncertainty, Prepared by North Carolina State University for the Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC. February 2002.

SPONSORED RESEARCH PROJECTS (SELECTED 7 OF 23 SINCE 1992)

1. Probabilistic Evaluation of Technological, Environmental, and Economic Factors in Mobile Source Air Pollution, Center for Transportation and the Environment, North Carolina State University, 1994-1996, $150,000, Principal Investigator (with S. Ranjithan and E.D. Brill, Jr).
2. Quantitative Analysis of Variability and Uncertainty in Acid Rain Assessments, US DOE, 1995-1997, Principal Investigator
3. Analysis of Variability and Uncertainty in Emission Estimation, US EPA/OAQPS, 1998-2001, Principal Investigator on two projects with same title.
4. Development and Demonstration of a Methodology for Characterizing and Managing Uncertainties in Emission Inventories, U.S. EPA, 1998-2003, Principal Investigator (with MCNC as a subcontractor).
5. Probabilistic Modeling of Variability and Uncertainty in Urban Air Toxics Emissions, US EPA, 1998-2003, Principal Investigator
6. Development of a Module for Statistical Analysis of Variability and Uncertainty, EPA/ORD, 2002, Principal Investigator
7. Recommend Strategy for On-Board Emissions Data Analysis and Collection for New Generation Model, EPA/OTAQ, 2002, Principal Investigator

JOHN C. GALLAND, Ph.D.

ACCOMPLISHMENTS

2001-Present ***Full Professor*** Departments of Clinical Sciences and Diagnostic Medicine/Pathobiology
College of Veterinary Medicine
Kansas State University, Manhattan, KS

Elected Faculty Senate • Established research linkages between Argentina, Jordan, and the University • Co-coordinator of Public Health and Epidemiology courses in the professional curriculum

1994 – 2001 ***Associate Professor*** Food Animal Health and Management Center
College of Veterinary Medicine
Kansas State University, Manhattan, KS

Acquired more than $1.75 million in research funds • Major role in creating first entrepreneurial center on campus • Created microbiology laboratory to conduct research under Good Laboratory Practices (GLP) Act to undertake government and industry contract work • Experimental design advisor, Institutional Animal Care and Use Committee.

1994 – 2000 ***Corporate President*** Animal Health Systems, Inc., Manhattan, KS

Through university entrepreneurial center, founding President of software development company specializing in custom large database applications, voice recognition, and electronic identification systems • Successfully launched new software product into the marketplace • Database application included over 1 million lines of custom C++ software • Represent corporation's research and development in outside discussions and technical forums.

1990 – 1994 ***Assistant Professor*** Department of Clinical Sciences
College of Veterinary Medicine
Kansas State University, Manhattan, KS

Created first local area network on campus • Networked entire college • Created 36 station interactive multi-media computer center • Led department retreat on curriculum revision • Founding president of American Society of Veterinary Epidemiology and Economics • President USDA committee on Epidemiology and Economics of Animal Disease • College curriculum committee • Blue Ribbon Task Force on *E. coli* O157:H7 National Cattlemen's Association • Chairperson, Computing and Information Technology Advisory Committee: Computing and Network Services Subcommittee.

1987 – 1990 ***Principal Co-Investigator*** Bovine Somatotropin Target Animal Safety Study
Veterinary Medical Teaching and Research Center
University of California-Davis, Tulare, CA

Conferenced with United States Food and Drug Administration to build consensus on experimental design of a $3 million project • Solely responsible for automation of data collection, data management of over 284 measurements, and statistical analysis • Constructed data capture and analysis system • Supervised staff of nine computer services personnel • Responsible for quality control of all data capture and analysis's according to guidelines of Good Laboratory Practices Act.

FOOD ANIMAL HEALTH & MANAGEMENT CENTER • COLLEGE OF VETERINARY MEDICINE •
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MANHATTAN, KS 66506 • Office: (785) 532-4262 • FAX: (785) 532-4288 • galland@vet.ksu.edu
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1985 – 1990 ***Director*** Computer Services
Veterinary Medical Teaching and Research Center
University of California-Davis, Tulare, CA

Created networked computer laboratory • Responsible for development of analytical and statistical methods of data analysis • Responsible for development, design, coding, debugging, documentation, maintenance, and running of programs for faculty and graduate research • Statistical consultant • SAS programming • Budget writing and management.

1975 – 1979 ***Research Associate and Lecturer*** Wildlife-Fisheries Biology
University of California-Davis, Davis, CA

Taught upper division wildlife-fisheries course in behavioral ecology • Developed computer models to simulate distribution, movement and size of animal groups.

1972 –1975 ***Chairman*** Science Department
Evergreen High School
Jefferson County Public Schools, Lakewood, CO

Developed and coordinated large high school science program • Developed and taught award-winning course for upper level students to learn how knowledge is acquired through scientific research • Trained students in research skills such as experimental design and statistics • Acquired grants for students to conduct their own research which I supervised •Students presented their completed papers to local Academy of Science • Abstracts were published and distributed to potential sponsors for following year • Developed and taught course for students not motivated in science • Students and community members tackled problems that involved scientific thinking • Created and developed biology laboratories • Established science resource center • Developed multimedia center • Designed and constructed solar greenhouse and animal enclosure

1971 – 1972 ***Biology Teacher*** Golden High School
Jefferson County Public Schools, Lakewood, CO

Taught laboratory-oriented BSCS biology program • Recognized for my "Great Men in Science Lectures" in which I played the role of Mendel, Leeuwenhoek, Galvin, "Mr. Wizard", and others. Established and coached men and women's swimming teams

EDUCATION

1989	***Ph.D.***	Ecology	University of California-Davis	Davis, CA
1985	***M.S.***	Ecology	University of California-Davis	Davis, CA
1971	***B.A.***	Education	Adams State College	Alamosa, CO

SELECTED REFEREED PUBLICATIONS

Galland-JC, Hyatt-DR, Crupper-SS, and Acheson-DW. Prevalence, Antibiotic Susceptibility, and Diversity of *Escherichia coli* O157:H7 Isolates from a Longitudinal Study of Beef Cattle Feedlots. App. Environ. Micro., April, 2001. 67(4):1619-1627.

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Nietfeld-JC, Kelly-B, Dritz-SS, Feder-I, **Galland-JC**. Comparison of conventional and delayed secondary enrichment for isolation of *Salmonella* spp. from swine samples. J-Vet-Diagn-Invest. 1998 Jul, 10(3): 285-7.

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Brown-MH, **Galland-JC**, Davidson-HJ, Brightman-AH. The Phenol Red Thread tear test in dogs. Vet-comp-ophtalmol. Santa Barbara, CA: Veterinary Practice Pub. Co., c1994-. 1996. v. 6 (4) p. 274-277.

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Galland-JC. Interactive Multimedia and Case-based Learning in Veterinary Medicine—The Quantum Leap Approach, Journal Veterinary Medical Education, Volume 22(1), pp. 12-16.

Lean-IJ, Bruss-ML, Troutt-HF, **Galland-JC**, Farver-TB, Rostami-J, Holmberg-CA, Weaver-LD. Bovine ketosis and somatotrophin: risk factors for ketosis and effects of ketosis on health and production. Res-Vet-Sci. 1994 Sep, 57(2): 200-9

Galland-JC, Michaels-WE. Toward a Comprehensive Multimedia Instructional Delivery System for Veterinary Medicine, Journal Veterinary Medical Education, Volume 22(1).

Harms-CA, Hoskinson-JJ, Bruyette-DS, Carpenter-JW, **Galland-J**, Veatch-JK, Wilson-SC, Baier-JG. Development of an experimental model of hypothyroidism in cockatiels (Nymphicus hollandicus). Am-J-Vet-Res. 1994 Mar, 55(3): 399-404.

Gaines-JD, **Galland-J**, Schaefer-D, Nusbaum-R, Peschel-D. The economic effect of estrus synchronization in beef heifers on average weaning weight of calves. Theriogenology. Stoneham, Mass: Butterworth-Heinemann. Mar 1993. v. 39 (3) p. 669-675.

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Lean-IJ, Baldwin-RL, Troutt-HF, Bruss-ML, **Galland-JC**, Farver-TB, Rostami-J, Weaver-LD, Holmberg-CA. Impact of bovine somatotropin administration beginning at day 70 of lactation on serum metabolites, milk constituents, and production in cows previously exposed to exogenous somatotropin. Am-J-Vet-Res. 1992 May, 53(5): 731-41.

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Lean-IJ, Troutt-HF, Weaver-LD, Goodger-WJ, Bruss-ML, **Galland-JC**. Bovine somatotropin: management and industry implications. Compend-Contin-Educ-Pract-Vet. Trenton, N.J: Veterinary Learning Systems Company. Aug 1990. v. 12 (8) p. 1150-1153, 1156-1158.

Deluyker-HA, Weaver-LD, **Galland-JC**, Dukas-PA. Use of automated milk yield recording in production medicine. II. Compend-Contin-Educ-Pract-Vet. Lawrenceville, N.J: Veterinary Learning Systems Company. Oct 1989. v. 11 (10) p. 1307-1311.

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Goodger-WJ, **Galland-JC**, Christiansen-VE. Survey of milking management practices on large dairies and their relationship to udder health and production variables. J-Dairy-Sci. Champaign, Ill: American Dairy Science Association. Sept 1988. v. 71 (9) p. 2535-2342.

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Weaver-LD, **Galland-J**, Sosnik-U, Cowen-P. Factors affecting embryo transfer success in recipient heifers under field conditions. J-Dairy-Sci. 1986 Oct, 69(10): 2711-7.

Weaver-LD, **Galland-J**, Martin-PA, Versteeg-J. Treatment of Streptococcus agalactiae mastitis in dairy cows: comparative efficacies of two antibiotic preparations and factors associated with successful treatment. J-Am-Vet-Med-Assoc. 1986 Sep 15, 189(6): 666-9.

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Feder-IJ, Nietfeld-JC, **Galland-JC**, Yeary-T, Sargant-J, and R.D. Oberst. Comparison of *Salmonella choleraesuis* detection in porcine fecal specimens using PCR-hybridization or conventional culture techniques. Submitted, J. Clin. Microbiol., 2000.

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Claussen-KM, Hyatt-DR, Dritz-SS, **Galland-JC**, Nietfeld-JC, and Sargeant-JM. Effects of Subtherapeutic Antibiotics on Shedding of a Mixture of Tetracycline Susceptible and Resistant *Salmonella* spp. Experimentally Inoculated into Pigs. American Association of Swine Practitioners Meeting. Des Moines, IA March 8-11, 1998

Claussen-KM, Hyatt-DR, Dritz-SS, **Galland, JC**, Nietfeld-JC, and Sargeant-JM. Effects of Subtherapeutic Antibiotics on Shedding of a Mixture of Tetracycline Susceptible and Resistant *Salmonella* spp. Experimentally Inoculated into Pigs. 1998 Annual Phi Zeta Research Day Report. March, 1998. Kansas State University.

Claussen-KM, Hyatt-DR, Dritz-SS, **Galland-JC**, Nietfeld-JC, and Sargeant-JM. Effects of Tetracycline on Shedding of Susceptible and Resistant *Salmonella* spp. Experimentally Inoculated into Pigs. 1997 Swine Day Report. November 1997. Kansas State University Swine Industry Day.

Hyatt-DR, **Galland-JC**, Dritz-SS, Nietfeld-JC, Irwin-CK, Davison-C. Effects of Antibiotics on Shedding of *Salmonella typhimurium* In Experimentally Inoculated Pigs. 1996 Swine Day Report. Nov. 21, 1996. Kansas State University Swine Industry Day.

ABSTRACTS

Feder-IE, **Galland-JC**, Sargeant-J, Yeary-T, and Nietfeld-J. Comparison of PCR-Hybridization and Conventional Culture for the Detection of *Salmonella* in Porcine Environmental and Porcine Fecal Specimens. 19th Food Microbiology Symposium and Rapid Methods Workshop: Current Concepts in Foodborne Pathogens and Rapid and Automated Methods in Food Microbiology. University of Wisconsin, River Falls, WI, 1999.

D.R. Hyatt, **J.C. Galland**, S. Crupper, L. Hawkins, N. V. Anderson, G. L. Stokka. Prevalence of *Salmonella spp.*, *E. coli* O157:H7 and *Campylobacter* on Four Beef Cattle Feedyards Sampled over Thirteen Months. 98th General Meeting of the American Society for Microbiology. Atlanta, GA. May 16-21, 1998.

D.R. Hyatt, **J.C. Galland**, J.R. Gillespie, R.D. Oberst and J.M. Sargeant. Usefulness of a Commercially Available Enzyme Immuno-Assay for Shiga-like Toxins I and II in the Detection of *E. coli* O157:H7 in Cattle Feces. Joint Annual Meeting of the American Society for Microbiology, Missouri and Missouri Valley Branch and the Midwest Microbiology Educators Conference. Kansas City, MO. March 27-28, 1998.

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D.R. Hyatt, **J.C. Galland**, M. Selee, C. Davison, L. Helmle, C. Irwin, J. Harris, D.Woods, M. Hornback, D. Stuever, A. Carman, R. Lohman, L. Hawkins, N. Anderson, G. Stokka. Prevalence of *Salmonella* spp., *Campylobacter* and *E. coli* O157:H7 on Four Beef Feedyards Sampled over Time. Seventy-Eighth Annual Conference of Research Workers in Animal Disease. Chicago, IL. Nov. 10, 1997.

D.R. Hyatt, **J.C. Galland**, M. Selee, C. Davison, L. Helmle, C. Irwin, L. Hawkins, N. Anderson, G. Stokka. Antibiotic Susceptibility and Plasmid Profiles of *E. coli* O157:H7 Isolates from Beef Feedyard Cattle. Seventy-Eighth Annual Conference of Research Workers in Animal Disease. Chicago, IL. Nov. 10, 1997.

D.R. Hyatt, **J.C. Galland**, M. Selee, C. Davison, L. Helmle, C. Irwin, L. Hawkins, N. Anderson, G. Stokka. Clonal Diversity of *E. coli* O157:H7 Isolates from Beef Feedyard Cattle. Seventy-Eighth Annual Conference of Research Workers in Animal Disease. Chicago, IL. Nov. 10, 1997.

D.R. Hyatt, **J.C. Galland**, J.R. Gillespie and J.M. Sargeant. Usefulness of a Commercially Available Enzyme Immuno-Assay for Shiga-like Toxins I and II in the Detection of *E. coli* O157:H7 in Cattle Feces. Seventy-Eighth Annual Conference of Research Workers in Animal Disease. Chicago, IL. Nov. 10, 1997.

J.M. Sargeant, J.R. Gillespie, D.R. Hyatt, **J.C. Galland**, R.D. Oberst, R.K. Phebus, L.K. Bohra, M.P. Hays. The Frequency of *E. coli* O157:H7 in Beef Cows and Calves in Kansas: Preliminary Results. Seventy-Eighth Annual Conference of Research Workers in Animal Disease. Chicago, IL. Nov. 10, 1997.

J.C. Galland, D.R. Hyatt, S. Crupper, M. Selee, C.G. Davison, L. Helmle, C.K. Irwin, L. Hawkins, N.V. Anderson, G.L. Stokka. Prevalence, antibiotic susceptibility, and clonal diversity of *E. coli* O157:H7 at four beef feedyards sampled over time. Protecting the Public against Food Borne Pathogens: *E. coli*. (Poster) Georgetown University, Washington, DC September 25-26, 1997.

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Brightman-AH, **Galland-JC**, and Gerds-S. Diabetes mellitus and Keratoconjunctivitis in the dog. Twenty-Sixth Annual Meeting American College of Veterinary Ophthalmologists, Newport, RI, September 27-30, 1995.

Oberst-RD, Mosier-DA, **Galland-JC**. Amplification of Cryptosporidium DNA for assessing agricultural wastes. submitted to Working Group on Water Quality, U.S. Department of Agriculture for the Clean Water-Clean Environment-21st Century Conference. Kansas City, MO, March 5-8, 1995.

Stone-G, Oberst-RD, Hays-M, McVey-S, **Galland-JC**, Curtis R, Kelly S, Chengappa MM. Detection of *Salmonella typhimurium* from rectal swabs of experimentally infected beagles using a cultivation-PCR-hybridization procedure. submitted to 75th Annual Conference of Research Workers in Animal Diseases., Chicago, IL, Nov 14-15, 1994.

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Offenbach-LA and **Galland-JC**. Conference for Research Workers in Animal Disease, Chicago, Illinois, November 7-9, 1993. "A Decision Analysis of synchronization and insemination methods in beef heifers.

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Goodger-WJ, Farver-T, Johnson-P, DeSnayer-G, **Galland-JC**. 1992. The Identification of Management Factors Associated with Changes in Bulk Tank Somatic Cell Counts (BTSCC). Proceedings of the XVII World Buiatrics Congress and the XXV American Association of Bovine Practitioners.

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Goodger-WJ, Farver-T, Jasper,-D, **Galland-JC**, Blackman-K, Nugent-MK. 1989. Determining the Effect of Intramammary Devices on the Control of Environmental Mastitis. Proceedings of the 10th Annual Western Food Animal Research Conference, Fort Collins, Colorado.

Lean-IJ, Troutt-HF, Goodger-WJ, Holmberg-CA, Weaver-LD, **Galland-JC**. 1989. Bovine Somatotropin: A Review and Implications for the Dairy and Veterinary Industries of Somatotropin Use. In Recent Advances in Pastoral Technology. Proceedings of Post Graduate Foundation in Veterinary Science of Sydney University.

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Troutt-HF, **Galland-JC**, Lean-IJ, Goodger,-WJ, Holmberg-CA. 1988. Average Nutrient Values -Dry Matter Basis - Common Feed Stuffs, Tulare, California. In Proceedings California Veterinary Association, Anaheim, CA.

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Lean-I, Baldwin-RL, Troutt-HF, Bruss-ML, **Galland-JC**, Farver-T, Rostami-J, Weaver-L, Holmberg-C. Impact of Somatotropin (rBST) Treatment at Day 70 of Lactation on Cows Previously Exposed to BST. University of California, Davis, Tulare, California, 1988.

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RESEARCH GRANTS '

Funded

1999 **Galland, JC** and DR Hyatt. Veterinarian HACCP Training Program for Reducing On-Farm Foodborne Pathogens. USDA-CREES $53,000.

1999 J.R. Gillespie, **J.C. Galland**, D.R. Hyatt, R.D. Oberst, J.M. Sargeant. Ecology of *E. coli* O157:H7 in Beef Cow-Calf Operations from Ranch through Feedlot. United States Department of Agriculture, Cooperative State Research, Education and Extension Service. 1999. $198,347. 96-34359-2593

1998 J.R. Gillespie, **J.C. Galland**, D.R. Hyatt, R.D. Oberst, R.K. Phebus, J.M. Sargeant, K.D. Crabtree. Ecology of *E. coli* O157:H7 in Beef Cow-Calf Operations from Ranch through Feedlot. United States Department of Agriculture, Cooperative State Research, Education and Extension Service. 1998. $198,172. 96-34359-2593

1997 B.I. Osburn, **J.C. Galland**, J.M. Sargeant, D. Lein, C. Gay, D.R. Hyatt. An Electronic Identification System as a Key Component in HACCP Plans to Reduce Foodborne Pathogens in Non-Fed Beef. FAPMC Investigators in the Food Animal Production Medicine Consortium and Associated Institutions. United States Department of Agriculture, Food Safety and Inspection Service. 1997. $299,144. FSIS-12-W-97

1997 Dritz, SS, **JC Galland**, DR Hyatt, CK Irwin, JC Nietfeld, CG Davison. Effects of subtherapeutic antibiotics on shedding of a mixture of susceptible and resistant *Salmonella typhimurium* experimentally inoculated into pigs. AVMA Foundation $14,935.

1996 Troutt, HF, **JC Galland**, BI Osburn, JR Gillespie, E Mather, K Braun, J Schmitz. Prevalence of *Salmonella* spp in Cull Dairy Cows. USDA FSIS $235,000

1996 **Galland, JC**, SS Dritz, DR Hyatt, CK Irwin, JC Nietfeld, CG Davison. Antibiotic Induction of L-Form Bacteria. National Pork Producers Council, $3,631.

1996 Spire, MF, J Drouillard and **JC Galland**. Early Detection of Problem Implants using Infrared Thermography. Fort Dodge Animal Health, $11,890.

1995 Gillespie, JR, **JC Galland**, RD Oberst, NV Anderson, RK Phebus. Ecology of *E. coli* O157:H7 in Beef Cow-Calf Operations from Ranch through Feedlot. SRGP, $199,229/year for 5 years.

1995 **Galland, JC**, NV Anderson, GR Stokka. Emergence and Spread of Antibiotic-Resistant Human Pathogens in Cattle Feedyards, National Research Initiative Competitive Grant, $240,000.

1995 Anderson, NV, **JC Galland**, and MM Chengappa. Incidence of Responders to *Salmonella* ELISA among Feedyard Steers Compared to Positive Culture for *Salmonella* at Slaughter. Food Safety Forum, $9,999.

1995 **Galland, JC** and LL Hawkins. A Comparison of Production Performance Measures Among Steers Segregated in the Feedyard on Arrival from Pasture into Three Categories of Body Weight. National Farms, $5,000.

1995 **Galland, JC**. Epidemiological Study of Kansas Water Wells, KDHE, $6,000.

1995 RD Oberst, DA Mosier, **JC Galland**, D Upton. Evaluating Disease Potential of *Cryptosporidium* in Ecosystems Impacted by Livestock. Animal Health 1433, $43,500

1993 RD Oberst, DA Mosier, **JC Galland**, G Marchin, JK Koelliker. Amplification of *Cryptosporidium* DNA for assessing agricultural waste: Effect of soil and water quality. USDA/CSRS, Special Research Grants-Water Quality, $105,261.

1993 On Farm Food Safety and Environmental Monitor, Agricultural Experiment Station, $48,000.

1993 Galland, JC. A Center for Developing Interactive Multimedia for Veterinary Medicine. IBM, Gifts in Kind, $110,000.

1992 **Galland, JC** and GA Milliken. Epidemiological Study of Lead and Cadmium Exposure in Kansas, KDHE, $112,809.

1991 JA Pickrell, FW Oehme, C Layton, **JC Galland**, M Vanier, BW Fenwick, RD Oberst, WC Cash, D Troyer, S McVey, L Enochs, V Clegg, W Pallett. Enhancing Large Group Problem Based Learning in Veterinary Medical Education. Fund for the Improvement of Post-Secondary Education, U.S. Department of Education, $224,111.

1991 JA Pickrell, FW Oehme, C Layton, **JC Galland**, M Spire, M Vanier, BW Fenwick, RD Oberst, WC Cash, D Troyer, S McVey, W Moore, B Brandt, J Hancock, L Corah, G Brester, A Heber, JP Murphy, L Enochs, V Clegg, W Pallett, L Johnson.Case-based videotapes to enhance agricultural and veterinary medical education. USDA, Higher Education Challenge Grants Program, $79,993.

1991 **Galland, JC**. Support for Creativity in Instruction-Statistics, Film at 11, Associate Dean's Funds, $2,500.

1991 Injuries to Greyhounds in Races, Kansas Racing Comm., $39,877.

1991 **Galland, JC**. Integrating Voice Technology in Veterinary Record Keeping Systems, $4,000, Dean's Fund.

1991 A New Model of Veterinary Service for Farm Flock Sheep Producers, AVMA Foundation, $18,739.

1991 Decision Support Software to Aid Cow/Calf Managers and Researchers, $3,990, BGR Awards.

1991 Survey of Cow/Calf Management Practices, Faculty Development Awards, $3,990.

1991 A Survey of the Incidence of Osteochondrosis in Yearling Feral Horses.

Not Funded

1999 **J.C. Galland**, D.R. Hyatt. Mutators and Emergence of Antibiotic Resistant Pathogens. National Institutes of Health, Dept. Of Health & Human Services. $2, 655,238.

1999 **J.C. Galland**, D. R. Hyatt. Tracing Spread of Enteric Bacteria in Beef Production Using Fluorescent Dye.United States Department of Agriculture, Cooperative State Research, Education and Extension Service. $944,391.

1998 **J.C. Galland**, D.R. Hyatt. Microbial Consequences of Agricultural Antibiotic Use. Food and Drug Administration. $589,142

1998 **J.C. Galland**, J.M. Sargeant, D.R. Hyatt**,** G.A. Milliken, M. Boland, E. Barrett, and L. Spire. Food Safety and Public Health. Special Group Incentive Research Program. $50,000.

1997 **J.C. Galland**, D.R. Hyatt. Emergence and Spread of Antibiotic Resistant Enteric Bacteria in Beef Cattle Feedyards. USDA-NRICGP. 1997. $394,854

1997 Sargeant, JM and **JC Galland**. Distribution and Antibiotic Susceptibility of Mastitis Pathogens in Kansas Dairy Herds. Animal Disease 1433, $47,433.

1997 **Galland, JC**. Veterinarian Certified HACCP Program for Reducing ON-Farm Foodborne Pathogens. USDA FSIS, $196,764.

1997 HF Troutt, **JC Galland**, BI Osburn. Reduction of Salmonella and E. Coli on Non-fed Beef Carcasses including Recumbent Non-fed Beef Cattle: A HACCP Approach Model at Selected Slaughter Plants Across the United States. USDA FSIS, $919,502.

1996 Spire, MF, J. Drouillard and **JC Galland**. Infrared Thermographic Determination of the Dermatological Effects on the Skin of Cattle of Topically Applied High and Low Dose Fenthion, Cyfluthrin, and Dowanol, the Carrier. Bayer Animal Health, $8,831.

1996 Spire, MF, J Drouillard and **JC Galland**. Injection Site Reactions Associated with the Subcutaneous Administration of Parasiticides: Doramectin and Ivermectin, Pfizer Animal Health, $10,201.

1996 **Galland, JC**, JJ Iandolo, RD Oberst, RK Phebus. RiboPrinter Microbial Characterization System for Determining Microbial Genetic Diversity in Natural Habitats. NSF BIO/IID,MBE, $122,500.

1996 **Galland, JC**, D.R. Hyatt, Dritz, S.S., C.K. Irwin, J.C. Neitfeld, and C.G. Davison. Effects of subtherapeutic antibiotics on shedding of a mixture of susceptible and resistant *Salmonella typhimurium* experimentally inoculated into pigs. National Pork Producers Council, $43,778.

1996 **Galland, JC**, D.R. Hyatt, SS Dritz, J.C. Neitfeld. Antibiotic Induction of L-Form Bacteria, USRG, $3,631.

1996 **J.C. Galland**, D.R. Hyatt. Change in susceptibility pattern of *Salmonella typhimurium* in pigs given subtherapeutic antibiotics. Pfizer 1996 Competitive Research Grant Program. $9995.

1996 **J.C. Galland**, D.R. Hyatt. Change in susceptibility pattern of *Salmonella typhimurium* in pigs given subtherapeutic antibiotics. Dean's Fund - KSU, CVM. $9995.

1996 Spire, MF, M Dikeman, J. Unruh, H Walker, R Jones, **JC Galland**. Etiology of Bruising in Beef Cows. USDA CSREES NRICGP, $270,390.

1995 Gillespie, JR, **JC Galland**, RD Oberst, NV Anderson, RK Phebus. Epidemiology and Ecology of *E. coli* O157:H7 in Beef Cattle from Ranch through Feedlot. National Livestock and Meat Board Nutrition/Product Technology Research Program, $296,000.

1995 **Galland, JC** and NV Anderson. Evaluation of a HACPP Program for Reducing On-Farm Foodborne Pathogens. Animal Health 1433, $48,000.

1995 Spire, MF, **JC Galland** and C Dewey. Investigation of Morbidity/Mortality Rates of Mature Beef Cows Fed in Feedlot Environments, American Veterinary Medical Foundation and USDA 1433 Grant. $14,942

1995 Spire, MF, M Dikeman, J. Unruh, H Walker, R Jones, **JC Galland**. Determination of Critical Control Points in the Management of Cull Cows to Increase Market Value, Assure Food Safety, and Optimize Meat Quality and Composition. Phase I: Acquisition of Equipment and Expertise to Study Carcass Bruising. KSU Special Group Incentive Grant, $118,112.

1995 Spire, MF, M Dikeman, J. Unruh, H Walker, R Jones, **JC Galland**. Determination of Critical Control Points in the Management of Cull Cows to Increase Market Value, Assure Food Safety, and Optimize Meat Quality and Composition. Phase II: Etiology and Pathophysiology of Bruising in Cows. National Cattlemen's Association, $153,567.

1995 Spire, MF, M Dikeman, J. Unruh, H Walker, R Jones, **JC Galland**. Etiology of Bruising in Beef Cows. National Cattlemen's Association, $270,390.

1993 & A Comparison of Long Term Effects of Pediatric Gonadectomy in Puppies to a Control Group of Traditionally Neutered Littermates, AVMA.

1993 **Galland, JC**. A Proposal to Develop Multimedia/Mediated Instruction Facilities, Computer and Information Technology Advisory Committee, $64,350.

1992 **Galland, JC**. On-Farm Food Safety and Environmental Monitor, Dean's Research Grants, $5,000.

1992 **Galland, JC**. Integrated Problem Solving, Convince, $25,000.

1992 **Galland, JC**. Statistics in Veterinary Medicine, Dept. of Education - FIPSE, $256,380.

1992 **Galland, JC**. Learning Communities in Food Animal, Dept. of Education - FIPSE, $459,776.

1991 **Galland, JC**. Integrated Problem Solving in Veterinary Medicine - The Quantum Leap Approach, CONVINCE, $131,571.

1991 Gabbert, N and **JC Galland**. Comparison of Rate and Nature of Injuries to Greyhounds in 6, 8 and 9 Dog Races, Kansas Racing Commission, $53,513.74.

1991 **Galland, JC** and R Elmore. Co-Occurrence of Disease and Toxins in Livestock, Wildlife, Pets, and Humans on Farms, 1433 Proposal to Kansas Agriculture Experiment Station.

1991 **Galland, JC**. Inter-Institutional Learning Communities in Food Animal Veterinary Curriculum, USDA Higher Education Challenge Grant, $195,034.

1990 **Galland, JC**. Center for Food Animal, USDA Challenge, $49,987.

1990 **Galland, JC**. Toward the Establishment of a Center of Excellence for Training Veterinary Students in Food Animal Population Medicine, USDA Challenge Grant, $150,759.

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ELECTIONS AND APPOINTMENTS '

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- USDA Food Safety Panel, Washington DC, July 16–20, 2000
- President, American Society for Veterinary Epidemiology and Economics (1993-1997).
- Chairperson, Computing and Information Technology Advisory Committee: Computing and Network Services Subcommittee (1992-1993)
- Secretary, NCR-168: Epidemiology and Economics of Animal Disease Losses and Economics (1990-1991)
- President, NCR-168: Epidemiology and Economics of Animal Disease Losses and Economics (1991-1992)

INVITED SEMINARS '

2000 **J.C. Galland**, H.F. Troutt, R.L. Brewer, B.I. Osburn, C. Rossiter, D. R. Hyatt. Present concepts on beef contaminating pathogens. XXI World Buiatrics Congress, December 4-8, 2000, Punta del Este, Uruguay.

1999 **J.C. Galland**, G.A. Milliken, D.R. Hyatt, M.A. Hornback, K. Cudjoe. Power of Mixed Models in Structured Designs: Laboratory Instrument Evaluation. Eleventh Annual Kansas State University Conference on Applied Statistics in Agriculture. Kansas State University, Manhattan, KS. April 25-27, 1999.

1993 Blue Ribbon Task Force on *E. coli* O157:H7, Atlanta, Georgia, November 29-30, 1993.

1993 NCR-176 Meeting, Madison, Wisconsin, November 17-19, 1993.

1993 *E. coli* Regional Conference, Seattle, Washington, November 1-4, 1993.

1993 Logistic Regression Workshop, Washington, DC, October 20-22, 1993.

1993 SafeGuard: A Quality Assurance Program, XXVI American Association of Bovine Practitioners Conference, Albuquerque, New Mexico, September, 1993.

1993 Voice Control: Integrated Voice Technology with Veterinary Record Keeping: Process Records while Palpating Beef Cattle, XXVI American Association of Bovine Practitioners Conference, Albuquerque, New Mexico, September 17, 1993.

1993 National Cattlemen's Association Midyear Conference, August 2-8, 1993.

1993 Food Safety Strategy Meeting, Kansas City, Missouri, April 30-May 2, 1993.

1993 Water and the Future of Kansas Seminar, Manhattan, Kansas, March 3-4, 1993.

1993 Food Borne Diseases Workshop, Davis, California, January 7-11, 1993.

1993 Desktop Hardware and Software for Developing Interactive Multi-Media Instruction in Veterinary Medicine. Multimedia Mediated Instruction Fair, KSU, January 1993.

1992 Presentation at Academy of Veterinary Consultants in Denver, Colorado, December 3-5, 1992

1992 Computers in Distance Education. Faculty Development Workshop on Mediated Instructional Design, October, 1992.

1992 Safeguard - Quality Assurance Program. Implementation of a Cow/Calf IRM Computer Program in Veterinary Practice. September, 1992.

1992 Texas Longhorn Breeders Association of America, May, 1992.

1992 Record Keeping. Second Annual Canine Kennel Management, March, 1992

1991 "The Power of Computer Based Record Keeping for Registered Cattle Breeders". Texas Longhorn Breeders Association of America, October, 1991.

PANEL REVIEWER

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- USDA

AD HOC REVIEWER

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- Toxicology
- FDA, ARS, USDA, NRICGP

UNIVERSITY TEACHING

Postdoctoral Students

- Doreene R. Hyatt, 3 years, Head, Bacteriology Section College of Veterinary Medicine, Colorado State College
- Scott Crupper, 1 year, Assistant Professor, Emporia State College
- Ingrid Feder, 1 year, Research Scientist, USDA-ARS

Graduate Students

Major Professor:

- Christa Irwin M.S. Clinical Sciences
- Matt VanBalle Ph.D. Pathobiology

Ph.D. Committees:

- Brian Fergen Statistics
- Ting Jian Gong Computer Science
- YiWei Chiao Computer Science

Undergraduate student mentor:

- 1996-1999 Michael Hornback Microbiology
- 1998-1999 Tim Brown Microbiology
- 1998-1999 Melissa Murphy Microbiology
- 1998-1999 Matthew Devlin Biology
- 1996-1998 Dusty Woods Animal Science
- 1996-1998 David Stuever Microbiology
- 1997-1998 Jennifer Walker Animal Science
- 1997-1998 Leah Ferguson Animal Science
- 1997-1998 Mary Schrandt Animal Science
- 1997-1998 Elizabeth Koerner Microbiology

• 1997-1998	Leila Nyberg	Microbiology
• 1996-1997	Aaron Carman	Microbiology
• 1996-1997	Jim Harris	Microbiology
• 1996-1997	Rebecca Lohman	Microbiology
• 1996	Erika Barrett	Animal Science
• 1996	Emily Johnson	Animal Science
• 1997-1998	Christy Davison	Veterinary Technician
• 1997	Matthew Selee	Animal Research Technician
• 1997	Lori Helmle	Animal Research Technician
• 1997	Cara Fehl	Animal Research Technician
• 1997	Jason Galland	Data Entry
• 1997	Stephen Hogge	Assistant '

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Courses

- Statistics in Epidemiology (CS900)
- Production Medicine (CS875)
- Understanding Antibacterial Action and Resistance

Lectures

- Production Medicine Elective (CS849)
- The Interinstitutional Species-Specific Food Animal Production Medicine Program: Cow-Calf Rotation
- Continuing Education: Clinical Trial Design, Execution, and Interpretation
- Continuing Education: Clinical Epidemiology: Modern Tools for Solving Disease Problems
- Food Animal Learning Community
- Dairy Nutrition Mini-Elective
- Cow Herd Management Schedule, EpiInfo, CattleGuard
- Preharvest Food Safety (*Salmonella, E. coli, Cryptosporidium, Helicobacter*)
- Population Management Disease
- Toxicology: Essentials of Epidemiology

COMMITTEES

National

- American Society for Veterinary Epidemiology and Economics (ASVEE), Founding President (1993-1997)
- North Central Region-168: Epidemiology and Economics of Animal Disease Losses and Prevention, Secretary, 1990-1991
- North Central Region-168: Epidemiology and Economics of Animal Disease Losses and Prevention, President, 1991-1993

- The Interinstitutional Species-Specific Food Animal Production Medicine Program: ' Quantitative Applications Advisory Committee, Chairman, 1990-1994 '
- The Interinstitutional Species-Specific Food Animal Production Medicine Program, Co-Principal Investigator, 1994-Present
- Blue Ribbon Task Force on *E. coli* O157:H7, 1996

University

- Faculty Senate, 2000-Present
- Institutional Animal Use and Care Committee, 1998-Present
- Communicable Disease Committee, 2000
- Experimental Design Advisory Member, Institutional Animal Use and Care Committee,1998-2000
- Computing and Information Technology Advisory Committee, 1991-1993
- Computing and Information Technology Advisory Committee: Computing and Network Services Subcommittee, Chairman, 1992-1993
- Computing and Information Technology Advisory Committee: Executive Committee, 1992-1993
- Kansas Agricultural Experiment Station Strategic Planning Task Force, 1992-1995

College

- Curriculum Committee, 1991-1993
- Biomedical Research Building Planning Committee - Food Safety Subcommittee, 1998

Department

- Drug Therapy in Core Curriculum Committee, 1992-1993
- Curriculum Committee, 1991-1993
- New Supplies and Pharmaceuticals and Major Equipment Committee, 1990-1991, 1991-1992
- Hospital Management and Medical Records Advisory Committee, 1990-1991, 1991-1992
- Research (Scholarship), Library, and Animal Welfare Committee, 1992-1993

MEMBERSHIPS

- American Society for Microbiologists, 1999-Present
- American Association of Bovine Practitioners 1993-Present
- International Society for Ecosystem Health, 1999-Present
- American Society for Veterinary Epidemiology and Economics, 1993-1997

SPECIAL INTERESTS

Sailing, Flying, Competitive Swimming, Underwater Diving, Snow Skiing, Jazz Drumming

Junyu (Allen) Zheng

102, Hollingsworth Ct., Apt. H, Cary, NC 27513
Email: zhengjunyu@hotmail.com or jzheng3@eos.ncsu.edu
919-467-8197 (Home)
919-412 -0976 (Cell)

EDUCATION

Ph.D. in **Environmental Engineering**, North Carolina State University — Aug. '98 – May. '02
GPA : 3.6/ 4.0

MS In **Environmental Engineering**, Tsinghua University, Beijing, China — Sep. '93 – Jun. '96
GPA : 3.7/ 4.0

BS in **Water Supply and Drainage Engineering** — Aug. '87 – Jun. '91
Wuhan Urban Construction Institute ,Wuhan, China — First Class with Honors

AREAS OF INTEREST

- Probabilistic ecological or human health risk assessment, variability and uncertainty analysis
- Pollutant fate and transport modeling (water, air, and soil), scientific computing
- Software development in environmental system and database management

COMPUTER SKILL

Operating Systems: DOS, Windows 9x/2XP/NT, Unix, and Macintosh
Languages and protocol: Visual C++, C/C++, Fortran 90, Java, Visual Basic, Active X, SQL, Access, ODBC,DAO, HTML/XML, ASP and TCP/IP
Application software: Microsoft office, Analytic, SAS, Crystal Ball, ArcView GIS

STATISTICAL AND MATHMATICAL SKILLS

Bootstrap simulation, Two-staged Monte Carlo simulation, parameter estimation based on single or mixture distributions, measurement error analysis, multivariate regression analysis, time series analysis, nonlinear optimization

EDUCATION

Ph.D. in **Environmental Engineering**, North Carolina State University — Aug. '98 – May. '02
GPA : 3.6/ 4.0

MS In **Environmental Engineering**, Tsinghua University, Beijing, China — Sep. '93 – Jun. '96
GPA : 3.7/ 4.0

BS in **Water Supply and Drainage Engineering** — Aug. '87 – Jun. '91
Wuhan Urban Construction Institute ,Wuhan, China — First Class with Honors

WORK EXPERIENCE

Research Associate, Department of Civil Engineering, North Carolina State University — May.'02 – present

Research Project:

- Uncertainty analysis of SHEDS/Pesticide model (working with NCEA/ORD/EPA, RTP, NC)

Consulting Project:

Research Assistant, Computational Lab for Energy, Air and Risk, North Carolina State University — Aug. '98 – May. '02

Research projects:

- Study on quantification of variability and uncertainty: general methodology and software implementation (Ph.D. Dissertation)
  — The accompanying software AuvTool (Analysis of Uncertainty and Variability Tool), developed using Visual C, will become a module of the EPA/SHEDS (Stochastic Human Exposure and Dose Simulation) model for quantifying variability and uncertainty. The tool can also be generally

applicable any quantitative analysis fields where variability and uncertainty analysis is needed. The project is partly sponsored by the ORD office, EPA, Research Triangle Park, NC

- Development of probabilistic emission inventories and its software implementation with GUI using Visual C++, Visual Fortran 6.0, Microsoft Access and Graphic Control
- Probabilistic Exposure Assessment of PCBs in the community surrounding New Bedford Harbor

Consulting project:

- Probabilistic Exposure Assessment of PCBs in the community surrounding New Bedford Harbor
- Probabilistic Health Risk Assessment of *Salmonella* Enteritidis in Egg Products

Software Developer, Beijing Kelier Information System Inc. Beijing, China

- Responsible for the software development and its local network installation of Automatic Telephone Check Query System Aug. '96 – Dec. '97

Research Assistant, Environmental System Lab, Tsinghua University, China Sep. '93 – Jun. '96

Research projects:

- A study on application of Monte Carlo simulation to municipal wastewater marine disposal engineering (Master's Thesis)
- A feasibility study on Baoan (Shenzhen) municipal wastewater discharged into Zhujiang estuary

Water Supply Process Manager, Power Plant, Beijing Yanshan Petrol & Chemical Corp., Beijing, China July. '91 – Aug. '93

AWARDED PROPOSALS

1. Development of a Module for Statistical Analysis of Variability and Uncertainty, sponsored by Office of Research and Development, EPA, RTP, NC.
2. Uncertainty Analysis of the SHEDS/PESTICIDES Model, sponsored by Office of Research and Development, EPA, RTP, NC.

PUBLICATIONS

Journals:

Frey, H.C., J. Zheng " Quantification of Variability and Uncertainty in Air Pollutant Emission Inventories: Method and Example Case Study for Utility NOx Emissions , " (Accepted for publication, *J. of the Air and Waste Management Association)*

Frey, H.C., J. Zheng, "Probabilistic Analysis of Driving Cycle-Based Highway Vehicle Emission Factors," (Accepted for publication, 2002, *Environmental Science and Technology*)

Zheng, J. H.C., Frey, "Quantification of Variability and Uncertainty Using Mixture Distributions: Evaluation of Sample Size, Mixing Weight and Separation between Components," *Risk Analysis* (Submitted)

Zheng, J. H.C., Frey, "Quantitative Analysis of Variability and Uncertainty with Measurement Error: Methodology and Case Study" *Risk Analysis* (Submitted)

Peer-Reviewed Conference Paper:

Zheng, J., H.C. Frey, "Development of a Software Module for Statistical Analysis of Variability and Uncertainty," 2002 Annual Conference of A&WMA, Baltimore, MA, June 22-25, 2002

Frey, H.C., J., Zheng, , "Quantification of Variability and Uncertainty in Emission Inventories: A Prototype Software Tool with Application to Utility NO_x Emissions," 2001 Annual Conference of A&WMA, Orlando, Florida, June 24~28,2001

Zheng, J., H.C. Frey, "Quantification of Variability and Uncertainty in Emission Estimation Using Mixture Distribution," 2000 Annual Meeting Society for Risk Analysis Crystal City, VA, December 5, 2000

Zheng, J., A. Unal, H.C. Frey, "Variability and Uncertainty Analysis of CO Exposure to Vehicle Passengers During Cold-Start," 2000 Annual Conference of A&WMA, Salt Lake City, Utah, June 18~22,2000

Frey, H.C., R.Bharvirkar, J. Zheng, "Quantification of Variability and Uncertainty in Emission Factor," 1999 Conference of A&WMA, St. Louis, Missouri, June 15 ~ 19,1999

He,Q., J. Zheng, L. Ding, "Study on Environmental Monitoring System of Wastewater Ocean Disposal Engineering," The third conference on environmental issue across two sides of Taiwan Strait, Aug. 29 ~ 31, 1995, Beijing

Technical Reports:

Zheng, J., H.C. Frey, *AuvTool User's Guide*, Prepared by North Carolina State University for the U.S. Environmental Protection Agency, Research Triangle Park, NC. January, 2002

Frey, H.C. and J. Zheng, *Technical Documentation for Analysis of Variability and Uncertainty for the AuvTool*, Prepared by North Carolina State University for the U.S. Environmental Protection Agency, Research Triangle Park, NC. January, 2002

Frey, H.C., J. Zheng, *Methods and Example Case Study for Analysis of Variability and Uncertainty in Emission Estimation (AUVEE)*, Prepared by North Carolina State University for Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC, Feb. 2001.

Frey, H.C., Zheng, J., *User's Guide for Analysis of Variability and Uncertainty in Emission Estimation*, Prepared by North Carolina State University for Office of Air Quality Planning and Standards, U.S Environmental Protection Agency, Research Triangle Park, NC, September, 2000.

Frey, H.C., R. Bharvirkar, J. Zheng, *Quantitative Analysis of Variability and Uncertainty in Emissions Estimation, Final Report,* Prepared by North Carolina State University for Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency, Research Triangle Park, NC, July 1999.

PROFESSIONAL ACTIVITY

Co-Organizer, Workshop on Bootstrap Simulation and Two-Dimensional Monte Carlo Simulation: Dealing with Variability and Uncertainty, Mixture Distributions, Measurement Error, and Censored Data, Society for Risk Analysis, New Orleans, LA, December 8, 2002 with H. Christopher Frey (North Carolina State University).

Member of Society for Risk Analysis

Member of Air and Waste Management Association.

CURRICULUM VITAE

Name:	**Bram E.C. Schreuder**
Proposed position:	**Veterinary investigations specialist/ epidemiologist**
Years with firm:	**20**
Date, place of birth:	**April 17th, 1946; Leeuwarden**
Nationality:	**Dutch**
Civil status:	**married, 2 children (1977 and 1980)**

Present address:	**c/o DLO-Institute for Animal Science and Health** **P.O.Box 65 8200 AB Lelystad,** **The Netherlands** **phone: +31.320.238238 / 238385 (direct)** **fax: +31.320.238050** **E-mail: b.e.c.schreuder@id.dlo.nl**

Key qualifications

General disease investigation in large and small ruminants; registered specialist in small ruminant diseases; diagnostic investigations; research in tickborne diseases; design and organization of epidemiological surveys, disease-eradication and -control schemes.

Education:

State University Utrecht (1971)
(Subject faculty) Degree in Veterinary medicine
(Principal subjects) Veterinary medicine
(Minor subjects) Tropical animal health & husbandry
Postgraduate training in pathology (1980), diseases of small ruminants (1982), immunology (1985), project formulation (1990), molecular biology (1991), veterinary epidemiology (1992), animal health economics (1995);
PhD on epidemiological aspects of BSE and scrapie (Utrecht, 1998)

Experience Record:

LONG TERM ASSIGNMENTS

COUNTRY	EOD	NTE	ORGANIZATION/PROJECT	POST-TITLE
Netherlands	7107	7111	Various Private Practices	Locum
Afghanistan	7112	7312	FAO Demonstration in Animal Health	Associate Expert Epizootiology
Tanzania	7403	7602	FAO Research Tickborne Diseases	Epizootiologist Tickborne Diseases
Nigeria	7610	7812	DITH/MARA Veterinary Investigation Laboratory	Officer-in-charge
Netherlands	7911	0000	DLO-Central Veterinary Institute	Co-worker Dept. of Herd Health, Pathology and Epidemiology
	9101	0000	DLO-Inst. of Animal Science and Health (ID-DLO)	Teamleader scrapie/BSE project; co-ordinator Veterinary Development cooperation

SHORT TERM ASSIGNMENTS

COUNTRY	EOD	NTE	ORGANIZATION/PROJECT	POST-TITLE
Benin	8304	8310	FAO Laboratoire de Diagnostique Vétérinaire	Consultant diagnostique vétérinaire
Indonesia	8405	8407	DGIS/Euroconsult	Consultant in veterinary laboratory technique
Turkey	8506 8606	8508 8609	FAO / World Bank; Erzurum integrated rural development project	Consultant in veterinary investigations and laboratory techniques
Pakistan	8701	8702	Min. of Foreign Affairs - Emergency assistance	Project Identification Mission, Livestock Programs
Turkey	8703	8705	FAO / World Bank; ERDP	Consultant in veterinary epidemiology
Niger	8711	8711	USAID/TUFTS University; Projet d'élevage integré	Teaching diseases of small ruminants
Pakistan	8809	8810	Min. of Foreign Affairs; Vet. Training & Support Centre for Afghanistan	Training & Demonstration in Animal Health; project implementation
East Africa	8906	8907	FAO/DGIS East Coast Fever Vaccine production, Quality control and immunization	Formulation mission for ECF vaccine production and immunization in SADCC countries
Malawi	9003	9003	DGIS/FAO; ECF vaccine production and immunization	Tripartite evaluation mission; Malawi
Afghanistan	9105	9105	UNDP/Dutch Committee for Afghanistan (DCA)	Rehabilitation of veterinary services in Afghanistan; project formulation mission
Turkey	9110 9202	9110 9202	FAO research in sheep abortion in Central Anatolia	Epidemiological and laboratory diagnosis of small ruminant diseases
Afghanistan	9203 9301 9404	9204 9302 9404	DGIS / DCA-VTSC; rehabilitation of veterinary services in Afghanistan	Assessment of impact of veterinary programme; design and follow-up of impact-study
Tanzania	9408	9408	ID-DLO	project identification

Turkey and Afghanistan still ongoing

LANGUAGES	READ	WRITE	SPEAK
Dutch	Excellent	Excellent	Excellent (mothertongue)
English	Excellent	Excellent	Excellent
French	Good	Good	Good
German	Good	Fair	Fair
Farsi	n.a.	n.a	Fair
Kiswahili	Slight	Slight	Slight

Selected Relevant Publications:

Identification of allelic variants of the sheep PrP gene and their association with natural scrapie. P.B.G.M. Belt, I.H. Muileman, B.E.C. Schreuder, J. Bos-de Ruijter, A.L.J. Gielkens and M.A. Smits. J. of Gen. Virol. 1995; 76: 509-517.

Immunohistochemical detection and localization of prion protein in lymphoid tissue of sheep with natural scrapie. L.J.M. van Keulen, B.E.C. Schreuder, R.H. Meloen, G. Mooij-Harkes, M.E.W. Vromans, J.P.M. Langeveld. J. Clin. Microbiol. 1996; 34 (5): 1228-1231.

Preclinical test for prion diseases. B.E.C. Schreuder, L.J.M. van Keulen, M.E.W. Vromans, J.P.M. Langeveld, and M.A. Smits. Nature 1996; 381: 563.

BSE: a European problem. B.E.C. Schreuder and O.C. Straub. Vet Record 1996; 138: 575 (Letter Ed.)

PrP genotype contributes to determining survival times of sheep with natural scrapie. Alex Bossers / Bram E. C. Schreuder, Ida H. Muileman, Peter B. G. M. Belt and Mari A. Smits. Journal of Gen. Virol. 1995; 77:2669-2673 (short commun.).

Risk of BSE from the import of cattle from the United Kingdom into countries of the European Union. B.E.C.Schreuder, J.W. Wilesmith, J.B.M. Ryan and O.C. Straub. Vet Record 1997; 141: 187- 190.

Prion protein and scrapie susceptibility. M.A. Smits, A. Bossers and B.E.C. Schreuder. Vet Quarterly 1997; 19: 101-105.

Control of scrapie eventually possible? B.E.C. Schreuder, L.J.M. van Keulen, M.A. Smits, J.P.M. Langeveld, and J.A. Stegeman. Vet. Quarterly 1997; 19: 105-113.

Studies on the efficacy of hyperbaric rendering procedures in inactivating BSE and scrapie agents. B.E.C.Schreuder, R. E. Geertsma, L.J.M. van Keulen, J.A.A.M. van Asten, P. Enthoven, R.C. Oberthür, A.A. de Koeijer, and A.D.M.E. Osterhaus. Vet Record 1998; 142: 474-480.

Tonsillar biopsy as a tool for a pre-clinical diagnosis of scrapie. B.E.C. Schreuder, L.J.M. van Keulen, M.E.W. Vromans, J.P.M. Langeveld, and M. Smits. Vet Record 1998; 142: 564-568.

CURRICULUM VITAE - J. W WILESMITH

Name:	John William Wilesmith
Title:	Professor
Address:	Epidemiology Department, Veterinary Laboratories Agency (Weybridge), New Haw, Addlestone, Surrey, KT15 3NB, England
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Date of birth:	11 February 1948
Nationality:	British

GRADUATE AND POSTGRADUATE EDUCATION

1982-83	Postgraduate Diploma in Biometry, North East London Polytechnic.
1976-77	Postgraduate Course in Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine, University of London.
1966-71	Batchelor of Veterinary Science degree course, University of Bristol.
2001	Doctor of Science, Massey University (submitted)

POSTGRADUATE EMPLOYMENT AND EXPERIENCE

1971-76	Veterinary surgeon in mixed (mainly cattle, sheep and companion animals) veterinary practice, Llandeilo, Dyfed
1976-82	Veterinary Research Officer, Epidemiology Department, Central Veterinary Laboratory, New Haw, Addlestone, Surrey.
1978 (Mar-Oct):	Research Fellowship - Veterinary Epidemiologist, Bundesforschungsanstalt für Viruskrankheiten der Tiere, Paul-Ehrlich Strasse 28, Postfach 1149, 74-Tübingen, Germany.
1982-86	Senior Veterinary Research Officer, Epidemiology Department, Central Veterinary Laboratory, New Haw, Weybridge, Surrey.
1986-present	Grade 5, Head of Epidemiology Department, Central Veterinary Laboratory, New Haw, Addlestone, Surrey.

2000-present	Visiting Professor, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, University of London.
2001 (Feb-present)	Veterinary Head, Epidemiology Team, State Veterinary Services, Department for Environment, Food and Rural Affairs, 1a Page Street, London (for duration of FMD epidemic)

HONORARY ADVISORY POSITIONS

1978-present	Editor of English abstracts in *Tierärtzliche Umschau,* Terra-Verlag, Konstanz
1985-90	Member of Editorial Board of Veterinary Preventive Medicine.
1990-present	Member of Editorial Board of The Journal of Dairy Research.
1988	Scientific advisor to the Southwood Committee on Bovine Spongiform Encephalopathy.
1991	Member of advisory committee for the funding of research on the epidemiology of diseases of wildlife by the National Environmental Research Council.
1991	Advisor on Epidemiological Research projects funded by the Horserace Levy Betting Board of Great Britain
1988-1997	Expert advisor on animal diseases to DG VI, European Commission and member of the BSE Epidemiology Sub Group of the Scientific Veterinary Committee
1988-present	Expert advisor on TSEs and TB to the *WHO*.
1990-1997	Advisor to the Spongiform Encephalopathy Advisory Committee and member of the Epidemiology Sub Group of SEAC
1995-1997	Member of the Medical Research Council CJD Surveillance Committee
1995-present	Member of the MAFF/ Department of Health's Epidemiology of Foodborne Infections Group
1996-present	Founder member of the Academic Board of the VLA
1996-present	Consultant on veterinary epidemiology and the TSEs to FAO, Rome
1997-present	Expert advisor to DG XXIV, European Commission, member of Scientific Steering Group sub group on modelling of BSE and risk assessment of BSE in other member states. Consultant to the TSE/BSE *Ad Hoc* Group of the EU's Scientific Steering Committee.

1997-present	Adviser to, and VLA Observer, on the Spongiform Encephalopathy Advisory Committee (SEAC)and member of CJD Epidemiology sub group of the SEAC.
1998-present	Member of the Scientific Sub-Committee of The Home of Rest for Horses on research funding.
2000-present	Member of the Scientific Advisory Committee of the Animal Health Trust, Newmarket
2000-present	Scientific Adviser to The Horse Race Betting Levy Board on research funding
2001	Expert scientific adviser to the Research Assessment Exercise of Universities and Higher Education Institutes in GB

MEMBERSHIP OF PROFESSIONAL SOCIETIES

Royal College of Veterinary Surgeons

British Veterinary Association

Society for Veterinary Epidemiology and Preventive Medicine

International Society of Veterinary Epidemiology and Economics

Asociation of Veterinary Teachers and Research Workers

The Veterinary Research Club

The Faculty of Public Health Medicine of the Royal College of Physicians of the United Kingdom

CURRENT PhD STUDENT SUPERVISION

Mark Stevenson and Helen Benard, Massey University, Palmerston North

EXTERNAL PhD EXAMINER FOR:

University of Reading, England
Massey University, New Zealand
University of Bristol, England

PART-TIME TEACHING COMMITMENTS ON VETERINARY EPIDEMIOLOGY

Co-organiser of MSc in Veterinary Epidemiology, LSH&TM, RVC and VLA

MSc Veterinary Microbiology, Royal Veterinary College, London

MSc Laboratory Animal Science, Royal Veterinary College, London

MSc Animal Health, Royal Veterinary College, London

Modular Courses in Veterinary Epidemiology and Economics, University of Reading

MSc Veterinary Pathology, Royal Veterinary College, London

MSc Veterinary Epidemiology and Animal Health, Massey University, New Zealand

AWARDS

1993	Bledisloe Veterinary Award - awarded by the Royal Agricultural Society of England - for effective contributions to animal health.
1994	Dalrymple-Champneys award - for contributions to veterinary research
1997	Membership of the Faculty of Public Health Medicine of the Royal College of Physicians of the United Kingdom
2000	The Chiron Award of the British Veterinary Association (Citation: "Who by his outstanding dedication has served the veterinary profession and the nation through his contribution to understanding the origins of BSE and the creation of measures to control its distribution.")

SUMMARY OF RESEARCH INTERESTS AND ACTIVITIES

Epidemiological research interests have centred on the investigation of nationally important diseases and those of economic or zoonotic importance together with the development of animal disease surveillance. The development of the use of geographical information systems (GIS), risk analysis and novel analytical techniques has been of particular interest in this research.

Specific research topics have included:

- Tuberculosis in cattle and badgers
- Johne's disease in cattle
- Bovine mastitis
- Listeriosis in sheep and cattle
- Foodborne zoonotic infections of farm animal species, notably salmonellosis in all species, campylobacteriosis of poultry and VTEC 0157 infection of cattle.

Latterly, since 1987, research efforts have concentrated on BSE in cattle and other TSEs in animals and man and foodborne zoonotic infections. This has involved the development of effective collaborations with colleagues involved in the medical epidemiological aspects of the diseases, and until 2000 a was the VLA's TSE R&D and Surveillance Programme Manager.

More recently, since February 2001 with the advent of the FMD epidemic, interests have necessarily been more or less restricted to epidemiological studies on this epidemic, together with continuing research and surveillance on BSE and other TSEs.

SCIENTIFIC PUBLICATIONS

ANDERSON RM, DONNELLY CA, FERGUSON NW, WOOLHOUSE MEJ, WATT CJ, UDY HJ, MaWHINNEY S, DUNSTAN SP, SOUTHWOOD TRE, WILESMITH JW, RYAN JBM, HOINVILLE LJ, HILLERTON JE,

AUSTIN AR, WELLS GAH (1996) Transmission dynamics and epidemiology of BSE in British Cattle. *Nature* 382, 779-788.

BELL JC, WILESMITH JW (1981) Bovine mastitis caused by Bacillus cereus. Veterinary Record 108, 404.

BRADLEY R, ANDERSON PH, WILESMITH JW (1981) Changing patterns of nutritional myodegeneration (white muscle disease) in cattle in Great Britain. In: Metabolic Disorders in Farm Animals. Proceedings of the Fourth International Conference on Production Disease in Farm Animals (Greseche D, Dirksen G, Stangassinger M, eds).

BRADLEY R, ANDERSON PH, WILESMITH JW (1983) Changing patterns of nutritional myodegeneration (white muscle disease) in cattle in Great Britain. Bovine Practitioner 18, 30-32.

BRADLEY R, ANDERSON PH, WILESMITH JW (1987) Changing patterns of nutritional myodegeneration (white muscle disease) in cattle and sheep in the period 1975 - 1985 in Great Britain. Bovine Practitioner 22, 38-45.

BRADLEY R, WILESMITH JW (1991) Epidemiologie des Encephalopathies Spongiforms en Grande Bretagne. Epidemiologie et Sante Animale 19, 27-48.

BRADLEY R, WILESMITH JW (1993) The epidemiology and control of bovine spongiform encephalopathy (BSE). British Medical Bulletin 49, 932-959.

BRUGÈRE H, BANISSI-SABOURDY C, BRUGÈRE-PICOUX J, WILESMITH JW, BRADLEY R (1994) Electrochemical analysis of urine from sheep with scrapie and cows with BSE. Proceedings of a Consultation on BSE with the Scientific Veterinary Committee of the Commission of the European Communitiies, 14-15 September 1993, Brussels pp 359-367.

CAROLAN DJP, WELLS GAH, WILESMITH JW (1990) Bovine spongiform encephalopathy in Oman. Veterinary Record 126, 92.

CHEESEMAN CL, MALLINSON PJ, RYAN JBM, WILESMITH JW (1993) Recolonisation by badgers in Gloucestershire. In: Proceedings of a conference on the badger, March 1991. Irish Academy of Science, Dublin. pp78-93.

CHEESEMAN CL, LITTLE TWA, MALLINSON PJ, PAGE PJC, WILESMITH JW, PRITCHARD DG (1985) Population ecology and prevalence of tuberculosis in badgers in an area of Staffordshire. Mammal Review 15, 125-135.

CHEESEMAN CL, LITTLE TWA, MALLINSON PJ, REES WA, WILESMITH JW (1985) The progression of bovine tuberculosis infection in a population of *Meles meles* in south-west England. Acta Zoologica Fennica 173, 197-199.

CHEESEMAN CL, WILESMITH JW, RYAN JBM, MALLINSON PJ (1987) Badger population dynamics in a high density area. Symposium of the Zoological Society of London. 58, 279-294.

CHEESEMAN CL, WILESMITH JW, STUART FA, MALLINSON PJ (1988) Dynamics of tuberculosis in a naturally infected badger population. Mammal Review 18, 61-72.

CHEESEMAN CL, WILESMITH JW, STUART FA (1989) Tuberculosis : the disease and its epidemiology in the badger, a review. Epidemiology and Infection 103, 113-125.

CLIFTON-HADLEY RS, WILESMITH JW (1991) Tuberculosis in deer: a review. Veterinary Record 129, 5-12.

CLIFTON-HADLEY RS, WILESMITH JW, STUART FA (1993) *Mycobacterium bovis* in the European badger (*Meles meles*): epidemiological findings in tuberculous badgers from a naturally infected population. Epidemiology and Infection 111, 9-19.

CLIFTON-HADLEY RS, WILESMITH JW, RICHARDS MS, UPTON P, JOHNSTON S, (1995) The occurrence of *Mycobacterium bovis* infection in cattle in and around an area subject to extensive badger (*Meles meles*) control Epidemiology and Infection 114, 179-193.

CLIFTON-HADLEY, R.S., SAUTER, C., LUGTON, I., JACKSON, R., WILESMITH J.W. and DURR, P. (2001) *Mycobacterium bovis* infections. In: Infectious Diseases of Wild Mammals. Ed. E. Williams. Third edition. Iowa State Press

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Some properties of bovine leukaemia virus, its use seroepidemiological studies, and eradication of the disease from infected herds. In: Viruses in Naturally Occurring Cancers. Cold Spring Harbor Conference on Cell Proliferation. 7, 911-925.

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NATHANSON N, McGANN, KA, WILESMITH JW, (1995) The evolution of virus diseases: Their emergence, epidemicity and control. In: Molecular Basis of Virus Evolution. Eds. A.J. Gibbs, C.H. Calisher, F. Garcia-Arenal. Cambridge University Press, Cambridge, pp 31-46.

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STEVENSON, M.A., WILESMITH, J.W., RYAN, J.B.M., MORRIS, R.S., LOCKHART, J.W., LIN, D and JACKSON, R.. (2000) Temporal aspects of the bovine spongiform encephalopathy epidemic in Great Britain: individual animal-associated risk factors for the disease. *Veterinary Record* 147, 349-354

STEVENSON, M.A., WILESMITH, J.W., RYAN, J.B.M., MORRIS, R.S., LAWSON,A.B. PFEIFFER, D.U. and LIN,D. (2000) A descriptive spatial analysis of the bovine spongiform encephalopathy epidemic in Great Britain. *Veterinary Record* 147, 379-384

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B Model Outputs

One reviewer provided a summary of model outputs and uncertainty (sensitivity) analysis presented in the H-T BSE study report. This summary can help the reader get an indication of the reviewer's understanding of the H-T BSE study report.

B.1 MODEL OUTPUT–TABLES

The model results are based on assumptions about the model parameters (49 parameters as defined in Appendix 1, Pages 4-8). Supporting documentation about the parameters is presented in Appendix 1, Pages 9-38 and the parameter values that were used are tabulated in Appendix 1, Pages 38-82). The assumptions and parameter values for other simulations are presented in Appendix 2.

The authors present the results of the simulation runs in tables (Appendix 3A). There were 49 output tables, each representing 1,000 simulations. From these tables and figures the actual output of the model can be discovered. The output of simulation runs is divided into three groups:

- output when the assumptions are altered,
- output when the sources of infectivity are altered, and
- output when alternate scenarios are considered.

Output within each of these three categories is further divided as shown in Table B-1, and within each of these divisions, output is divided sometimes into best case and worst case (B/W). Each output table provides results (columns of table), such as mean, 5^{th}, 25^{th}, 50^{th}, 75^{th}, and 95^{th} percentiles, for 39 variables (rows of table)

Table B-1. Model Outputs[a]

Epidemic Statistics	Disposition of ID50s	Potential Human Exposure
• Total Infected*	• To Prohibited MBM*	• Brain*
• Total Infected w/o Imports	• Eliminated by SRM ban*	• Spinal Cord*
• Total Clinical*	• Eliminated by Rendering*	• Blood*
• Probability N Infected > 0	• To NP MBM-Contamination*	• Distal Ileum*
	• To NP MBM-Mislabeling*	• Contaminated Organ Meat*
Mode of Infection	• Out After Rendering*	• Eyes*
• Maternal	• To Prohibited Feed*	• Contaminated Muscle Meat*
• Spontaneous	• To NP Feed—Misdirected*	• AMR*
• Protein	• To NP Feed—Contamination*	• Beef on Bone*
• Blood	• To NP Feed—Mislabeling*	• Trigeminal
• Exogenous	• To Blood*	• Ganglia*
	• Out After Feed Production*	•
Mode of Death	• Misfed to Cattle*	**ID50 Sources**
• Slaughter	• Total to Cattle*	• From Slaughter
• Die on Farm—Render	• Total Potential to Humans*	• From Death on Farm
• Die on Farm—No Render		

[a]The asterisk indicates that results for this variable are also presented in a figure.

divided into six categories as listed in Table A-1 and defined in Appendix 3C, pages 3-5.

B.2 MODEL OUTPUT–FIGURES

The figures in Appendix 3B (584 figures) are the following:

- ➤ vertical bar graphs of the probability that the value for a variable exceeds zero, where the variables are cattle infected, cattle clinical, ID 50s to cattle, and ID50s to humans (each defined in Appendix 3C, Pages 5-6);
- ➤ horizontal bar graphs of the probability that the value for a variable exceeds zero, where the 15 disposition of ID50s variables are presented on one graph and the 11 ID50s to humans by tissue variables on another (each defined in Appendix 3C, Page 6); and
- ➤ box and whisker diagrams showing the five percentiles for the data depicted in each bar graph.

Thus, there are 12 output graphs for each simulation of 1,000 iterations.

B.3 SENSITIVITY (UNCERTAINTY) ANALYSIS

The following sources of uncertainty were evaluated individually for their influence on two outcomes: 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 ID50s) in food produced for human consumption over that period.

1. Base Case

- ➤ Base case—importation of 10 infected animals

Uncertainty (Sensitivity) Analysis When the Following Assumptions are Altered (Each bullet is an assumption under a numbered category):

2. Maternal Transmission

- ➤ Maternal transmission probability
  (Best case = 0; worst case = 0.13)

3. Slaughter Process

- ➤ Total cattle oral ID50s in clinical BSE case
  (Best case = Total infectivity halved; Worst case = doubled)
- ➤ Ante mortem inspection detection probability
  (Best case = ProbPassAM with BSE signs = 0.01; Worst = 0.50)
- ➤ Performance characteristics of the stunner (i.e., proportion of cattle stunned using air-injected pneumatic stunners)
  (Best and base case = 0; Worst case = 15 percent)
- ➤ Performance characteristics of the splitter process
  (Best case = Mis-split/AMD/spinal cord removal joint probabilities = doubled; worst case = halved?)

4. Rendering and Feed Process

- ➤ BSE transmissibility probability reduction achieved by rendering (B/W)
  (difficult to make comparison between Table 3.16.1, Appendix 1, Pages 72-73 and Table 2.2.3.1, Appendix 2, Page 9)
- ➤ Probability that Pr. MBM batch contaminants NP MBM (B/W)
- ➤ Fraction of Pr. MBM batch involved during contamination (B/W)
- ➤ Probability that Pr. MBM is mislabeled as NP MBM (B/W)
- ➤ Probability Pr. feed batch contaminates NP feed (B/W)

- ➤ Fraction of Pr. feed batch involved during contamination (B/W)
- ➤ Probability that Pr. feed batch is mislabeled as NP feed (B/W)
- ➤ Probability that Pr. feed intentionally fed to cattle (B/W)

5. Human Food

- ➤ Proportion of each tissue group available for human consumption (B/W)

6. Fraction of Animals Dying on Farm that are Rendered

- ➤ Proportion of animals dead on farm sent to rendering (B/W)

7. BSE Infectivity in Blood

- ➤ Infectivity in blood

8. BSE Infectivity in Trigeminal Ganglia

- ➤ Infectivity in trigeminal ganglia

Impact of Alternative Sources of Infectivity: Output when the following sources of infection are altered. Each bullet is a source under a numbered category. Asterisk indicates no output tables found.

9. Spontaneous BSE

- ➤ U.S.—impact of spontaneous with feed ban

10. Importation of BSE-Infected cattle

- ➤ Import 1 infected animal
- ➤ Import 5 infected animals
- ➤ Import 10 infected animals (base case)
- ➤ Import 20 infected animals
- ➤ Import 50 infected animals
- ➤ Import 200 infected animals
- ➤ Import 500 infected animals

11. Domestic Scrapie

- ➤ U.S.—impact of scrapie with feed ban
- ➤ Chronic wasting disease*
- ➤ TSE in domestic mink, pigs, and chickens*
- ➤ Recycled food wastes*

Alternative Scenarios to Test Model's Plausibility: Output when the following scenarios of infection are altered (each bullet is an assumption under a numbered category):

12. Clinical Cases in Switzerland between 1985 and 2001

- ➤ Switzerland: 1986 – 2000

13. Spontaneous BSE in U.S. before 1997 feed fan

- ➤ U.S.—impact of spontaneous with no feed ban

14. Impact of Importing Cattle from the UK during the 1980s

- ➤ U.S.: 1980 – 2010 with 0.1 ID50s reaching cattle in 1980
- ➤ U.S.: 1980 – 2010 with 1.0 ID50s reaching cattle in 1980
- ➤ U.S.: 1980 – 2010 with 5.0 ID50s reaching cattle in 1980
- ➤ U.S.: 1980 – 2010 with 10.0 ID50s reaching cattle in 1980
- ➤ U.S.: 1980 – 2010 with 50.0 ID50s reaching cattle in 1980

15. Implication of Various (2) Risk Management Strategies in the U.S.

- ➤ U.S.—SRM ban
- ➤ U.S.—No rendering of animals that die on farm
  1. Render reduction factors
  2. Rendering contamination
  3. Renderer mislabeling probability (2; 10 percent)
  4. Feed production contamination (*why were 0.05 and 0.25 selected?*)
  5. Feed production mislabeling probability
  6. Misfeeding probability
  7. Food Inspection
  8. Human food
  9. Fraction of animals that die on farm and are rendered