UNITED STATES DEPARTMENT OF AGRICULTURE

FOOD SAFETY AND INSPECTION SERVICE

+ + + + +

HARVARD BOVINE SPONGIFORM ENCEPHALOPATHY (BSE) RISK ASSESSMENT TECHNICAL MEETING

+ + + + +

July 25, 2006
1:00 p.m.

Jefferson Auditorium
1400 Independence Avenue, SW
Washington, D.C.

FACILITATOR: DAVID GOLDMAN, M.D., M.P.H.
Assistant Administrator
Office of Public Health Science
Food Safety and Inspection Service
U.S. Department of Agriculture

PARTICIPANTS:

DR. RICHARD RAYMOND
DR. BARBARA MASTERS
DR. JOSHUA T. COHEN
DR. UDAY DESSAI

I-N-D-E-X

P-R-O-C-E-E-D-I-N-G-S

(1:00 p.m.)

DR. GOLDMAN: -- Goldman. I'm the Assistant Administrator here at FSIS for the Office of Public Health Science. And I want to thank everyone here for your attendance, your attention, and your participation in today's meeting.

You should have received an agenda, as well as a short executive summary as you came in, and I'll mention the agenda in a little bit more detail after we have our official welcome.

I first want to introduce to you Dr. Richard Raymond who is our Undersecretary in the Department of Agriculture for Food Safety. He was appointed to this position in July 2005, and has just passed his first anniversary in this position. He is overall responsible for overseeing the policies and programs of the U.S. public Food Safety and Inspection Service, as well as Chairing the U.S. Codex Steering Committee and Chair of the National Advisory Committee on Microbiological Criteria for Foods. He has extensive experience in his past in developing and implementing public health

programs and policies designed to improve public health. Prior to joining USDA last year, he served as the Director of the Nebraska Department of Health and Human Services, Regulation Licensure Division and worked on various initiatives to include developing the local Health Department System in Nebraska as well as initiating several anti-bioterrorism initiatives. Please join me in welcoming Dr. Raymond.

(Applause.)

DR. RAYMOND: Thank you, David, and welcome to you all this afternoon, and most importantly, I thank you all for being here this afternoon for this important meeting.

I think it's reassuring to me at least to see the number of people who will come to listen to a very technical discussion of the Harvard Risk Assessment Study, a very important study, and I don't mean to belittle the importance of it, but to see the number of people here who want to learn more about it is encouraging to me. Education is probably the most powerful tool that we have in public health. And so the more people we have educated on what this Risk

Assessment means, and how to interpret it, and what it says about food safety, particularly related to BSE requirements. The more people we can educate, the more people that can communicate that to their constituents or to their readers of their media, to their watchers of their television, the more people we could educate through you, you can help us on this one. This is extremely important as we move down the path of our final rule on BSE from the food safety standpoint. There will be a comment period, obviously, a public comment period on that rule when it gets to that point, and the more people that understand it, the comments will be --

We are in the process, as you know, of getting that final rule through the Agency, through the Department steps. We've analyzed 22,000 comments that came on the interim final rule. We have analyzed the Harvard Risk Assessment, and we certainly have taken a long hard look at the enhanced surveillance that APHIS has done to determine the prevalence of BSE in the American cattle herd. And you heard a lot about that last week when that announcement was made to go to more

of a maintenance testing mode from the enhanced surveillance. That information, along with this information, we're going to discuss today, guarantees that we have the safest food supply in the world, particularly when it comes to prions and cow disease, and we will continue to say that because the more people understand the science behind it, the more they will trust us when we say that repeatedly.

So once again, I thank you for coming today to listen, and then eventually today, to share your concerns and have an open and frank discussion with our experts. I do not claim to be one of those. I will sit and listen and let these gentlemen be the experts. So once again, consider yourself welcomed. Now we'll get on with the better part of the meeting.

DR. GOLDMAN: Thank you, Dr. Raymond.

Next, I'd like to introduce to you the FSIS Administrator, Dr. Barbara Masters, who was made Administrator on August 1st, 2005. In this position, she's responsible for leading FSIS and its mission of protecting public health and food safety and food defense.

Dr. Masters began her FSIS career in 1989, as a veterinary medical officer near Hot Springs, Arkansas, and has held a variety of posts in the Agency both in the field and at headquarters. Since March 2004, Dr. Masters served as the Acting Administrator. During that time, she raised and signed a big training investment in the 10,000-employee workforce to a record $20,000,000, as well as enhanced communications with both internal and external audiences. Please welcome Dr. Masters.

(Applause.)

DR. MASTERS: Thank you, Dr. Goldman. Good afternoon. I'm certainly pleased to be here today to participate in this important meeting. I want to personally thank our Office of Public Health Science, our Office of Policy Programming Employee Development, and our Office of Public Affairs, Education and Outreach for all the work that they put in putting this meeting together. I always say these kind of meetings don't happen if it doesn't take a lot of employees working together to put these kind of meetings together.

I also want to thank our representatives from

our sister agencies, the Animal and Plant Health Inspection Service, and the Food and Drug Administration for joining us this afternoon, and I appreciate them being with us today.

And I also want to thank all of you for your participation.

We are holding this meeting as yet another step in our standard procedure of keeping the public involved in our rule making process on issues affecting public health. We believe that this should be a public process and have worked very hard to make all of our actions as open and transparent as possible. This meeting is also an important step in risk communication.

I think all of you are certainly aware that in 1998, and we were just all talking about how long it had been since 1998, that USDA entered into a cooperative agreement with Harvard and Tuskegee University Center for Computational Epidemiology to conduct an investigation of the BSE regs in the United States. That report was released in November of 2001, and resubmitted in October of 2003, following a peer review. Then in December of 2003, we had the discovery of the

cow infected with BSE in Washington State.

In addition to several new policies designed to reduce the risk from meat infected -- meat from infected animals that would enter the human food supply, the Secretary of Agriculture also convened a panel of international BSE experts to evaluate USDA's investigation of that BSE case, and subsequent risk management measures. These steps combined with the over 22,000 comments that Dr. Raymond mentioned on this subject were taken into account as USDA then again contracted with Harvard to revise the risk assessment model to reflect the new information and mitigations. These aspects include: development of a new baseline for the risk assessment model; analysis of the effects of the measures implemented by USDA and the Food and Drug Administration following discovery of BSE in December of 2003; and the review of recommendations made by the panel of international BSE experts.

Harvard submitted an updated risk assessment to USDA, and the final report and model were submitted last fall following a rigorous peer review. The peer review process involved attaining scientific experts

through a process independent of FSIS. I think it's important for you to know that FSIS did not select the reviewers or influence their comments. FSIS received their comments and addressed them in the revised model that's being presented today. All of these elements, the model, the risk assessment, and the peer review comments were posted on the Website earlier this month. So you all have had an opportunity to look at all these, and they're still available if you didn't look at them already. As Dr. Raymond indicated, all of this data along with the other 22,000 comments that we received and the results of the APHIS BSE surveillance data, of course, are being considered as we finish up work on our final FSIS BSE rule.

We certainly look forward to a constructive afternoon and again, appreciate your being here with us today. With that, I'm going to turn the program back over to Dr. Goldman, and he'll introduce you to the rest of the afternoon. Thank you very much.

DR. GOLDMAN: Thank you, Doctors Raymond and Masters, for your welcome and for your overview about why we're here today.

If you'll look at your agenda, you'll see that we have two technical presentations coming up right now, and they really are the focus of this meeting. Then we will have a Q&A period, which will be slightly different than our usual, and I want to tell you about that here in a minute.

So that in addition to having an opportunity to interact with the primary discussions that you'll hear from in just a minute, we also, as Dr. Masters mentioned, have representatives both from the FDA and APHIS here, who are here in the front row, as well as from the FSIS Risk Management Group, who will help us should there be questions that pertain to their interest in the results from Harvard.

And in the case of the FDA and Harvard model, some of the FDA proposed risk application strategies, which is the reason FDA was invited to participate. I'll introduce those representatives when we get to that portion of the agenda. But without any delay, I'm going to turn now to our technical discussion.

Dr. Joshua Cohen is a lecturer at the Tufts New England Medical Center Institute for Clinical

Research and Health Policy Studies in the Center for Evaluation of Value and Risk.

Dr. Cohen's research focuses on the application of decision analytic techniques to the public health risk management problems with a special emphasis on the proper characterization and analysis of uncertainty. His work covers a range of issues including: cell phone use while driving; alternative fuels for transit buses and school buses; trade offs between nutritional benefits of fish and resulting exposure to mercury; and the risk associated with BSE in the U.S.

Dr. Cohen currently serves on the National Academy of Sciences Committee charged with reviewing the EPA's risk assessment of dioxin, and on EPA's Clean Air Science Advisory Committee that is now reviewing that Agency's latest air quality criteria documented for lead.

He received both his Ph.D. in Decision Science and his B.A. in Applied Mathematics from Harvard University, and of course, he is here today to tell you about his work while he was with the Harvard Center for

Risk Analysis. Please welcome Dr. Cohen. (Applause.)

DR. COHEN: Thank you for that introduction, and thank you for having me today. I also want to thank USDA for involving me in this research over the years, and it has been a number of years now going back to 1999.

And the other thing I just want to warn you, there's a fair amount of material I'm going to present today. It does not cover all of the details about the assessment. Those are, as you've heard, available on the Web. There will be about I think 48 slides, and they're numbered in the lower right-hand corner, so you'll know just how much more of me you have to tolerate as the time goes on here.

So I guess without further delay, the work I'm going to describe today was carried out for USDA's Food Safety and Inspection Service, or FSIS. The work was done while I was at the Harvard School of Public Health Center for Risk Analysis. The main tool we used is the Harvard BSE Simulation Model.

The first risk assessment conducted using that model was delivered to USDA in November of 2001. A USDA

contractor then identified four outside scientists -- four scientists outside of the Department to review that model. The review and revisions to the Harvard's methodology were completed in October of 2003. The October 2003 model served as the starting point for the work done on the project I'm going to describe now.

As you know, the first U.S. case of BSE was discovered in Washington State in December of 2003. USDA's Food Safety and Inspection Service awarded a grant to Harvard shortly thereafter to update and refine the model to assess risk associated with the introduction of BSE into the U.S. and to assess the impact of various risk management strategies.

The work described here underwent formal peer review in the fall of 2005, according to OMB Information Quality Peer Review Guidelines. This talk provides an overview of this work. Details are available in the supporting technical reports. Those reports, as I just mentioned, the one with review comments and our response to those comments, are available on the USDA/FSIS Website.

The remainder of this talk has three parts.

First I will describe the model's basic structure i.e. the structure inherited from the October 2003 version of the model. Although I'll then spend a fair amount of time describing the revisions made to our work, or the FSIS project, so that it best represents the U.S. at the time the Washington State BSE case was discovered, accommodates evaluation of new risk management strategies and reflects recently available scientific information. It's important to keep in mind that as a result of these changes, estimates generated as part of this project cannot be precisely compared to the results from the October 2003 risk assessment.

The second part of the talk will describe the scenarios we evaluated. The base case scenario considers the introduction of 10 infected cattle into the U.S. I'll describe how we scaled up this introduction in order to improve the model's numerical stability and what sort of inferences can reliably be made using results generated from this scaled-up scenario. Measures taken, either taken or proposed to mitigate BSE risk fall into three categories, including: those adopted by USDA after December 2003; measures

considered by FDA; and proposals advanced by the International Review Subcommittee of the Secretary's Advisory Committee on Foreign Animal and Poultry Diseases. The sensitivity analyses were conducted to determine the extent to which our results depend on various assumptions.

The third part of this talk describes our results, including the key statistics we used to characterize the risk of BSE spreading and the extent to which humans become exposed to the BSE agent. Finally, I'll recap our major conclusions.

I turn now to the first part of the talk, the model's basic structure and the updates made from this project for FSIS. This slide illustrates the model's basic structure. Each simulation must include a means by which BSE is introduced into the U.S. The introduction can be via the import of infected cattle or contaminated feed, for example. The exact nature of the introduction is not the focus of the model nor is it critical to the model's predictions. The model's emphasis is on what happens after BSE is introduced into the U.S.

Once BSE is introduced into the model cattle population, the simulation characterizes both the dose response relationship and the degree of exposure among cattle. The dose response relationship quantifies the probability that an exposed animal will contract BSE as a function of the magnitude of the exposure in addition to the animal's characteristics, such as age. In particular, the model assumes that young cattle are more susceptible to contracting BSE than are older cattle. Exposure also depends on various cattle characteristics such as age. For example, the model assumes that young cattle receive more animal protein supplements than older cattle, and hence, are more likely to be exposed to contaminated feed.

If an animal becomes infected with BSE, the model characterizes the disease development, that is how the distribution of the BSE agent among various tissues changes over time, and how much of it is present in different tissues. In general terms, the agent is present in the gut in the period following infection. Later, it moves to the spinal cord, brain and other nervous system tissue. At the end of the incubation

period, which generally lasts for several years, the quantity of BSE agent present in the animal's body grows rapidly, mostly in the brain and spinal cord. It is at the end of the incubation period that clinical signs of disease become evident.

When the animal either dies or is slaughtered, the infectivity is distributed among tissues that may go to animal feed or to food potentially available for human consumption. Keep in mind that not all food potentially available for human consumption is actually consumed. Some of it is disposed of due to spoilage or just not consumed even if it is presented as part of a meal. In theory, all infectivity in beef derived from ruminant protein, exits the cattle agricultural system. Some infectivity is destroyed during rendering used in feed for animals other than cattle or exported from the U.S.

On the other hand, the model assumes that infectivity can be recycled for a variety of reasons, including contamination, mislabeling, misfeeding. The model also accounts for the use of blood meal in cattle feed. Note that the cycle illustrated in this figure

can continue over time. If a lot of BSE-contaminated feed gets back into other cattle, the prevalence of the disease can grow over time; otherwise, it can decrease. To determine what happens, we instruct the model to simulate a 20-year period following the introduction of BSE into the U.S.

It's important to understand that what happens following the introduction depends in part on the assumptions we make, but it also depends on chance. For example, the first time the simulation trial -- the first time we executed a simulation trial, all the infected cattle might be sent to rendering plants that use a technology that is very effective at destroying infectivity. For the second simulation trial, they may be sent to a plant that uses an ineffective technology. The 20-year histories generated in these two cases will differ.

To characterize the range of possibilities, we have run the model repeatedly. We initialize the model, execute the single simulation trial, and record results. Then we repeat the process. After generating many trials, we have a large collection of different possible

outcomes, each one generated based on what might randomly occur during any given simulation trial.

Finally, all these results can be collected and described in terms of a histogram that is representative of the probabilities of a probability distribution. For example, we can estimate distribution from the number of cattle that become infected with BSE over the 20-year period. That's just the basic model.

Now, I want to talk about the updates we made to the model for this project. The model used for the October 2003 risk assessment was updated for reasons that fall into three categories. First, we incorporated new information into the model to best characterize conditions in the U.S. just prior to the discovery of the BSE positive animal in Washington State. Second, we revised the model to accommodate the evaluation of new risk mitigation measures that were not evaluated as part of the October 2003 assessment. Finally, we wanted to take into account recently available scientific information about the possible presence of BSE in tonsils.

This slide lists the five sets of updates made

to the model as part of this project. Note that because of these revisions, the results from the project cannot be directly and precisely compared to the results from earlier risk assessments conducted using this model as I mentioned earlier.

The first update to the model involves antemortem inspection. The model allows for specification of allowable slaughter uses based on the findings of the antemortem inspection, and in particular, whether the animal can be slaughter for use in either human food or animal feed.

This slide illustrates how antemortem inspection worked in the October 2003 version of the BSE simulation model. In that version of the model, the determinations made at antemortem inspections depended upon two factors: first, whether antemortem inspection identifies clinical signs consistent with BSE; and second, whether the animal has clinical signs of a disease or condition other than BSE that would require condemnation of the animal. The antemortem detection of BSE signs depends, of course, on whether the animal has reached the clinical stage of the disease. The

probability that the animal will be rejected based on other factors is assumed to depend on age. The assumed rules for use of the animal in animal feed or human food also appear on this slide.

To the two factors that the October 2003 model accounted for as part of the antemortem inspection process, the revised model adds ambulatory status. That's the middle column in yellow. Note that in the base case, ambulatory status does not influence the disposition of material taken from the animal. This functionality is added for the purpose of evaluating alternative scenarios.

In any case, the probability that an animal infected with BSE will become non-ambulatory depends on the animal's BSE clinical status. In particular, BSE clinical animals are more likely to be non-ambulatory than animals that have not reached that stage of the disease. Ambulatory status in turn influences whether antemortem inspection will detect the presence of BSE clinical signs. It turns out that clinical signs of BSE are more likely to be detected in cattle that are ambulatory because of many typical signs of BSE such as

gait disturbances can only be observed in an animal that is able to rise from a recumbent position and walk. Ambulatory status also influences the probability that inspection will lead to the condemnation of the animal based on signs of a disease or condition unrelated to BSE.

Our specific assumptions are as follows: antemortem inspection identifies 95 percent of animals with BSE clinical signs that are ambulatory. If a BSE clinical animal is not ambulatory though, the antemortem inspection detection probability drops to 85 percent. Finally, we assume that the vast majority of cattle infected with BSE are ambulatory regardless of their clinical status although far more animals with clinical disease become non-ambulatory than non-clinical animals. Note that these estimates are very uncertain, but as I'll describe later, these assumptions have very little impact on the simulations' predictions.

The second update to the model is the addition of tonsils as a tissue group that can contain the BSE agent. The revised model assumes that at any point during the incubation period, 0.2 percent of the total

infectivity in the animal is in the tonsils.

The third update to the model has to do with specified risk material infection. In the October 2003 version of the model, specified risk materials can be extracted from the carcass and diverted from future use only among animals that are slaughtered. In the revised version of the model, diversion of specified risk materials can apply to both slaughtered animals and to animals that die either on the farm or on the way to slaughter. Keep in mind that in the base case, there is no diversion of specified risk materials. As a result, this update does not affect the base case, but instead, only affects one of the alternative scenarios.

The fourth update has to do with parameter values rather than the structure of the model. In particular, we revised assumptions having to do with feed ban compliance rates at rendering plants and feed production facilities to reflect more recently available data. For the purposes of describing what we did, it is useful to distinguish two types of feed ban violations. The first is called mislabeling. It refers to packaging of prohibited material in a manner so that it appears to

be legal to use as cattle feed. The second, called cross-contamination, occurs in plants that produce both material allowed in cattle feed, called non-prohibited, and material can not be so used, called prohibited. In plants that produce both prohibited and non-prohibited materials, cross-contamination can occur if cleanup is not complete before switching to production of non-prohibited material.

Based on data collected through September 2003, by U.S. FDA, we estimated mislabeling rates to be 2.3 percent at rendering facilities and 4 percent at feed production facilities. We estimated the cross-contamination rates to be 1.8 percent at rendering facilities and 1.9 percent at feed production facilities. As shown in this slide, these revised assumptions differ from the assumptions used in the October 2003 risk assessment. As I will describe later, however, these assumptions do not have a strong influence on the models' predictions.

It's also worth noting that the data we used to develop our base case assumptions for mislabeling and cross-contamination may overstate noncompliance rates,

and hence, have led us to overestimate rates for these events.

First, the rates reported represent the proportion of facilities with at least one violation, not the reporting of material mishandled. If the facilities in violation that were identified by FDA are correctly handling at least of the material they are processing, then the overall proportion of material that is being mishandled may be less than the proportion we are using.

Second, because of changes in reporting requirements, all the data we used are from September 2003 and earlier. With the discovery of the Washington State BSE case in December of 2003, it's possible that the degree of vigilance at rendering and feed production facilities has increased since that time.

The final update made to the model for this analysis has to do with the assumed contamination of bone-in-beef by the BSE agent. Both the October 2003 and the revised assessment assume that if the spinal cord is not removed prior to splitting, 30 percent of the infectivity in spinal cord can end up in bone-in-

beef cuts for animals 12 months of age and older. However, the October 2003 assessment assumed that slaughter facilities do not produce bone-in-beef cuts from animals older than 24 months. Hence, it restricted this route of contamination to animals age 12 to 23 months. The revised assessment extends the production of bone-in-beef cuts and hence, the potential for this contamination to animals 24 months of age and older.

Now that I've described the simulation model structure, any updates made for the purpose of the FSIS analysis, I want to talk about the scenarios we analyzed. I will first talk about the base case analysis, then about the what-if scenarios we analyzed, and finally, about the sensitivity analyses conducted to evaluate the robustness of our conclusions in the face of uncertainty associated with our assumptions.

The base case used in the October 2003 assessment considered what would happen following the introduction of ten BSE infected cattle into the U.S. We therefore started with that scenario as our base case for the current analysis. Because FSIS was interested in comparing the impact of alternative scenarios and

because the more recent contamination and mislabeling data collected by FDA suggested that if anything, feed ban controls are more effective than we had assumed in the October 2003 analysis, there was a need for greater precision. FSIS requested that we conduct 750,000 simulation trials for each scenario. We did that for the base case. Unfortunately, writing that scenario tied up a 2.8 gigahertz computer for 4 weeks raising questions about the usability of evaluating all 17 scenarios FSIS wanted us to look at. Post processing of the output from such a simulation posed further logistical problems. We needed a faster way to achieve this level of precision.

For the purpose of achieving the desired precision in less time, we ran fewer trials but introduced more infected cattle at the beginning of each trial. In particular, we ran 50,000 trials rather than 750,000. At the beginning of each trial though, we introduced 500 infected animals rather than 10. It turns out that we can figure out what would happen on average in the original base case with 10 infected animals introduced from the inflated base case where we

introduced 500 infected animals. That is because the mean of quantities, the mean, the arithmetic average of quantities like the number of animals that become infected after the simulation starts or potential human exposure turned out to be proportional to the number of infected animals introduced. So to figure out what the mean would be for the 10 infected animal base case, we take the results from the 500 infected animal base case and divide by 50. Note that the same relationship does not hold true for output percentiles. So there is something that we give up by using this strategy. This approach works because the introduction of each infected animal is an independent event. You can think of each such animal starting its own miniature outbreak. The U.S. agricultural system is so big that each animal outbreak does not interact with the others for all practical purposes. As a result, the total number of events scaled linearly with the number of infected animals introduced.

From base case, we were able to test the hypothesis that the average value of the output quantities would increase by a factor of 50 when we

scaled up the number of animals by a factor of 50. The results support this hypothesis as shown by the entries in the right column of this table. Keep in mind that the output of the simulation is rounded to two significant digits, and the rounding is likely to be responsible for much of the deviation from the ratio 50 that we would expect. In any case, the deviations from the factor of 50 are very small.

Importantly, the scaled up base case achieved the desired precision and saves a lot of run time. The precision of the results is approximately proportional to the total number of infected animals introduced over all simulation trials. Execution time depends largely on the number of trials run. Running the 10 infected animal base case 750,000 times results in the introduction of 7.5 million animals. That's 10 times 750,000. Running the 500-infected animal base case 50,000 times results in the introduction of 25 million infected animals. So the latter combination achieves even better precision. It's also a lot faster taking only 3 days to run rather than 4 weeks.

Note that although the mean scales with the

number of infected animals introduced, i.e., by a factor of 50, the percentiles do not. I'm wanting to spend time talking to you about this so that you understand why our scenarios introduced 500 animals into the U.S. It is not because believe that such an introduction is possible. Instead, it was done for the sake of computational convenience. It allows us to estimate the mean output values with a high degree of precision in a lot less time. That discussion was very a very technical one. I now want to get back to the substantive aspects of the analysis: the what-if scenarios involve measures that might be used to reduce the spread BSE among cattle, potential human exposure to the BSE agent or both. We considered scenarios reflecting changes that have already been made by FSIS, changes that were under consideration by FDA, and changes that were proposed by the International Review Subcommittee.

The USDA/FSIS scenario included measures aimed at directly reducing contamination of the human food supply by the BSE agent. These measures included: prohibiting the use of non-ambulatory cattle for human

food; prohibiting the use of SRMs for human food. That's specified risk materials. Note that most of the materials designated as SRMs by USDA/FSIS are only considered SRMs if: they are from cattle 30 months of age and older; the ban on the use of small intestines and tonsils applies to all cattle; finally, prohibiting the use of vertebral columns and skulls from cattle 30 months of age and older as source materials in advanced meat recovery; and banning the use of mechanically separated meat for human food. Mechanically separated meat from other species such as pork is still permitted.

What-if scenarios under consideration by FDA aim to reduce the spread of BSE among cattle. These measures included a prohibition on the use of ruminant blood in ruminant feed, and requiring that facilities processing both prohibited and non-prohibited materials, either meat and bone meal or feed maintain dedicated production lines. The idea here is that such a requirement would reduce the risk of cross-contamination.

Finally, we evaluated two scenarios proposed by the International Review Subcommittee. The first

scenario is a prohibition upon the use of SRMs for human food consumption or animal feed. In particular, this scenario banned use of brain, spinal cord and vertebral column from cattle 12 months of age or older and a ban on the use of intestines from all cattle. Importantly, this scenario assumed that specified risk materials from animals that died prior to slaughter would also be controlled. Finally, the scenario assumed perfect compliance with these rules. As a result, the results provided upper bound on the effectiveness of this strategy. More realistic estimates of the effectiveness can be developed by interpolation between the base case and this best case.

Dr. Dessai will provide more detail on removal compliance scenarios.

The second scenario was prohibition on use of any MBM in ruminant feed. The idea is that a ban on the use of animal protein in ruminant feed would in an ideal world eliminate any potential for cross-contamination or mislabeling. It would not, however, eliminate the possibility of misfeeding.

We constructed eight sensitivity analyses.

This slide summarizes the assumptions for the first three. To understand this slide, consider the first sensitivity analysis. Sensitivity analysis 1 looked at what happens if we assume higher cross-contamination and mislabeling rates in rendering and feed production plants. In particular, this scenario investigated the impact of changing the assumed value for four parameters.

The first parameter is the renderer contamination probability. This parameter represents the probability that a given packet of non-prohibited meat and bone meal produced in a mixed rendering plant will be contaminated with prohibited material processed at the same plant. The base case value for this parameter is 1.8 percent, and that appears in the second column from the right. The base case value for -- I'm sorry. While the corresponding sensitivity analysis for this parameter, the probability is 14 percent, and that appears just to the right of that in the column furthest to the right. The second parameter is the renderer mislabel probability. This parameter represents the probability that a packet of prohibited meat and bone

meal will be mislabeled as non-prohibited. The base case value for this probability is 2.3 percent, and the sensitivity analysis probability is 5 percent. The third and fourth parameters that are adjusted in this scenario are the contamination and mislabel probabilities for feed production plants. The feed producer base case value for the contamination probability is 1.9 percent while the sensitivity analysis value is 16 percent. The feed producer base case value for the mislabeling probability is 4 percent, and the sensitivity analysis value is 5 percent. The remaining sensitivity analyses are specified in an analogous manner.

Sensitivity analysis 2 evaluated the impact of assuming a higher misfeeding rate. Sensitivity analysis 3 evaluated the impact of assuming a less favorable mix of rendering technologies are used in U.S., i.e., that overall rendering is less effective at eliminating the BSE agent. Sensitivity analysis 4 considered the impact of assuming that a greater proportion of bone-in-beef cuts are potentially available for human consumption. Sensitivity analysis 5 evaluated the impact of assuming

that antemortem inspection is less effective than as assumed in the base case. Sensitivity analysis 6 evaluated the impact of assuming a longer incubation period. Finally, sensitivity analysis 7 and 8 looked at a wide range of assumptions for the assumed proportion of cattle that are non-ambulatory.

The next part of the presentation describes the results from the base case what-if scenarios and for the sensitivity analyses. Before doing so, though, I will talk about the type of simulation output we focused on. As I'll describe below in the next several slides, the BSE simulation generates estimates from many different quantities. We are interested in answering two questions. First, to what extent are humans potentially exposed to the BSE agent through consumption of beef and beef products? To get at this question, we looked at the total potential human exposure to BSE estimated by the simulation. It is important to keep in mind that the estimate is expressed in terms of cattle oral ID50s. A cattle oral ID50 is the amount of BSE that will infect the bovine with 50 percent probability when ingested. Available data suggests that there is a

species barrier that makes the BSE agent less potent in humans than in cattle, that is, the risk posed to humans is smaller.

Second, to what extent does BSE spread among cattle in the U.S.? There are two output quantities that help us answer this question. The first is simply the number of cattle that become infected after the initial introduction of BSE. The second is the disease reproductive constant designated R0. The R0 statistic requires a bit of explanation. It is defined to be average number of new BSE cases resulting from each incident BSE case. For example, if R0 is 2, then the number of BSE cases will grow over time following the introduction of an initial case. In particular, the introduction of one case will on average result in two additional cases which will in turn result in the introduction of four new cases, and these four cases will in turn result in the introduction of eight new cases and so on. The behavior of the disease depends critically on whether R0 exceeds 1. For example, in this figure, this figure illustrates the difference between a R0 of 1.2 and a R0 of 0.8. When R0 is 0.8,

the prevalence declines over time. When it is 1.2, it grows over time. The simulation estimates R0 as the ratio of the number of newly infected BSE cases over the course of the simulation to the number of BSE cases that dies during the course of the simulation. Because BSE is primarily spread among animals through feed, the opportunity for transmission from one animal to another occurs largely after the death of an infected animal. The number of BSE infected animals that die therefore serves as an estimate for the number of animals that have an opportunity to spread disease.

Before showing you examples illustrating the rest of the output generated by the simulation, I want to remind you that this simulation is probabilistic. That is, the specific events differ from trial to trial even if the assumptions remain fixed. We therefore run the simulation many times to characterize the range of possible outcomes, 50,000 in case of the inflated base case for 500 animals, infected animals introduced. It's possible to characterize the outcome distribution using a figure or by reporting the summary statistics such as the mean, median, quartiles, 5th and 95th percentiles.

A table like the one in this slide was generated for each simulations scenario. I'm showing you this one as an example for the purpose of outlining the type of information generated by the simulation. You do not need to focus on the specific values on the table, which I know are difficult to see. Details are available in the Risk Assessment's technical report, and in the October 2003 Risk Assessment. Note that for each quantity, this table reports the mean and several key percentiles. For the sake of completeness, I want to also point out that the model generates a set of standard figures for each scenario simulated. Those figures just help to describe how conditions evolve during the simulation period. For example, this figure illustrates how BSE prevalence changes over time as well as the extent to which those values differ from simulation trial to simulation trial. The horizontal axis represents time while the vertical axis, which is on the log scale represents the number of infected animals. In looking at this figure, please note that the specific values are not important. Instead, I want you to see how this figure illustrates the trend of BSE

prevalence over time. Because 0 cannot be displayed on the log scale, the vertical scale in that figure on the left, we created a second figure that illustrates the proportion of trials for which there was a non-zero prevalence during each of the simulation years. You can see that in the early years of the simulation, that the BSE prevalence is always non-zero. Then starting with the year 10, the probability that prevalence will exceed 0 drops below 100 percent, finishing at 13 percent in year 20. Note that this figure reflects an impossibly large assumed introduction of 500 animals into the U.S., 500 infected animals.

Now for the results. First, the base case. The first table on this slide shows the simulation's mean predictions for the number of new BSE cases and/or potential human exposure to the BSE agent following the import of 10 infected animals over the subsequent 20-year period. The second table shows the corresponding predictions for the base case following the import of 500 infected animals. As mentioned earlier, the means for these quantities scale linearly with the number of infected cattle introduced. So the values are about 50

times greater in the second table than they are in the first one.

The percentile estimates do not scale in this manner. The distributions in the first table are more skewed than they are in the second table. That is in a relative sense the value of the 10-animal base -- the values for the 10-animal base case are somewhat more uncertain than they are for the 500-animal base case.

Recall that R0 is the ratio of the number of new BSE cases to the number of BSE infected animals that died during the simulation. Because it is a ratio, we would not expect its value to scale with the number of animals introduced. In particular, both its numerator and denominator scale, so the overall ratio does not. Nonetheless, the R0 estimated for the 500-animal base case is noticeably larger than the R0 for the 10-animal base case. It appears that this difference arises because the distribution for R0 is highly skewed. The 500-animal base case effectively leads to more sampling of the far right tail of that distribution, and hence, a higher estimate for the mean. It's also important to note that for both of these base case scenarios, the

average value of R0 is well under 1. More importantly, the probability that R0 is anywhere near 1 appears to be very small.

Recall that the human exposure estimates are expressed in terms cattle oral ID50s. The cattle oral ID50 is the amount of BSE that will infect the bovine with 50 percent probability when ingested. For humans, available data suggests that the risk is much smaller. I've included this table to give you an idea of the level of precision achieved by the model. The first table details the precision of the mean and percentile estimates to the number of new cases of BSE. The second table contains the corresponding values estimated for potential human exposure to the BSE agent. In each of these tables, there are three rows. The middle row is the central estimate for that column of statistics, the mean or one of the percentiles. The top and the bottom rows are the end points of a 95 percent confidence interval. As you can see from these tables, the 95 percent confidence intervals are generally only a couple of percent of the central estimates.

This slide shows the impact of the what-if

scenarios on predicted number of BSE cases in the U.S.

Note that these values are all rounded to two significant figures. In any case, the results in this table indicate that all but one of those scenarios have very little impact on the predicted number of new BSE cases in the U.S. Only the ban on the use of specified risk materials, from the animals above the age of 12 months, has a substantial impact on the spread of BSE among cattle. This ban, which was proposed by the International Review Subcommittee applies to both animal feed and to food is no doubt the ban on the use of these materials in feed that is responsible for this result.

This slide assumes -- shows -- this slide shows the impact of the what-if scenarios among predicted potential human exposure to the BSE agent. The International Review Subcommittee's proposed ban on the use of SRMs from animals 12 months of age and older has a substantial impact. The USDA/FSIS ban on the use of SRMs from animals 30 months of age and older has almost as great an impact on the potential human exposure. Eliminating the use for human food of advanced meat recovery product derived from the

vertebral column or the skull of animals 30 months of age and older has a smaller but still very noticeable impact on predicting human -- potential human exposure reaching -- reducing mean potential exposure over the 20-year period from 3,800 cattle oral ID50s to 2,200 cattle oral ID50s. Recall again that the cattle oral ID50 refers to the quantity of the BSE agent that will result in infection in cattle with 50 percent, not in humans.

This slide shows the sensitivity analysis results from the number of new BSE cases in the U.S. These results indicate that most assumptions have very little impact on the model's predictions. The most important source of uncertainty in this analysis is the misfeeding rate. The pessimistic value for this assumption which exceeds the base case value by about an order of magnitude, increases the mean prediction for the number of new BSE cases from about 180 to 2,600 cases. Moreover, the R0 renderer reaches at least 1 in 5 percent of the simulation trials. Increasing the incubation period by a factor of 2, decreases the predicted number of new cases by a factor of about 4 to

43 cases. Assumptions pertaining to the type of rendering technology used and assumptions about cross-contamination and mislabeling in rendering and feed production plants have at most a modest impact on the model's predictions.

For human exposure, a somewhat larger number of parameters have a noticeable impact on the predicted potential exposure to the BSE agent. What is striking, however, is that none of the assumptions have a particularly large impact on predicted potential human exposure. The assumption having the largest impact, the assumed misfeeding rate, increases predicted potential human exposure by a bit more than a factor of 2. Other parameters have a smaller impact on predicted potential human exposure.

Here are the major conclusions. First, under base case scenario, which represents conditions in the U.S. just before the December 2003 discovery of the BSE case in Washington State, the model predicts that the introduction of BSE into the U.S. would result in minimal spread of the disease. In particular, the average number of new cases for each instant case of BSE

would be well under 1, that is the R0 is less than 1. As a result, disease prevalence would tend to decrease over time. Following the introduction of 10 infected animals into the U.S., the total potential of human exposure over the subsequent 20-year period would be less than 100 cattle oral ID50s. Now that's the 10 infected animal base case, not the 500-animal introduction base case. It's worth keeping in mind that this exposure is probably more than a factor of 10,000 less than total human exposure in the UK.

Second, when we look at the assessment of the risk mitigation measures, we see the following. Of the measures put into place by USDA/FSIS, a ban on the use of specified risk materials for human food has by far and away the largest impact on human exposure. Banning the use of advanced meat recovery product derived from vertebral columns and skulls of cattle 30 months of age and older has a smaller but still noticeable impact on human exposure. Neither of these measures has a very important impact on the spread of disease among cattle. Measures considered by FDA have very little impact on either human exposure or on the spread of BSE among

cattle. Among the proposals made by the International Review Subcommittee, the ban on all uses of SRMs from cattle 12 months of age and older has a substantial impact on both human exposure and the spread of disease among cattle. Taken together, these results indicate that banning the use of specified risk materials can have a substantial impact on key outcomes.

Finally, regarding the sensitivity analysis, it's clear that the most influential of the uncertain parameters is the assumed misfeeding rate. Using a pessimistic value for this parameter, i.e., assuming it is 15 percent rather than the base case value of 1.6 percent, results in 5 percent possibility that the R0 parameter could reach 1. Even under these circumstances though, total human exposure remains relatively limited. Importantly, the impact of other sources of uncertainty is much smaller. In the absence of adopting any additional risk control measures, the U.S. agricultural system is robust. That is, it limits the spread of BSE if imperfectly. Resulting potential human exposure to the BSE agent through the consumption of beef and beef products is limited, especially when compared to the

experience in the UK, which were several orders of magnitude higher.

Substantial reductions to this already relatively limited risk can be achieved through controls on the use of specified risk materials. The most important sources of potential human exposure are animals 30 months of age and older and for younger animals, infectivity in the distal ileum. Finally, the most important source of uncertainty is the assumed misfeeding rate. Thank you very much, and I'll take questions later in the program.

DR. GOLDMAN: Thank you, Dr. Cohen, for that very thorough presentation. We will hold any specific questions for Dr. Cohen for the Q&A, which will be coming up after the next presentation.

Once FSIS received this very thorough analysis from the Harvard Center for Risk Analysis, the Agency had an interest in running some additional scenarios that would explore several things: one, the effect of combining mitigations, which the Harvard analysis did not do; we also wanted to model the less than perfect compliance with SRM removal; and finally, wanted to

model SRM removal from younger cattle. To that end, we had Dr. Dessai and his BSE group within the Risk Assessment Division conduct that analysis, and he will present that, the findings of that analysis now.

So let me introduce Dr. Dessai. Dr. Uday Dessai is the Director for the Microbiology Division in the Office of Public Health Science at the Food Safety and Inspection Service. At the Microbiology Division, he is responsible for overseeing microbial food safety activities associated with meat, poultry and egg products and manages the staff responsible for the microbiological baselines, diverse microbiological issues of significance to this Agency as well as the National Advisory Committee on Microbiological Criteria for Foods.

Prior to joining the Microbiology Division, Dr. Dessai was the Chief of the Regulatory Analysis and Exposure Modeling Branch in the Risk Assessment Division at OPHS. At the Risk Assessment Division, Dr. Dessai led all of the FSIS risk assessment activities related to BSE, including managing the contract for the work that you just heard described.

Dr. Dessai has a diverse background with education training, and work experience in multiple disciplines, including agriculture, microbiology, biotechnology, food science and nutrition, risk assessment and public health.

Please welcome Dr. Dessai for the second technical presentation today.

(Applause.)

DR. DESSAI: Thanks, David, for that introduction and good afternoon everybody.

I have decided to have just about 15 slides for you this afternoon. In this presentation titled, "Technical Update to the Harvard BSE Risk Assessment, FSIS Scenario Analyses," I will provide you with the relevant background for considering additional work at FSIS, the scenarios modeled and the results of the scenarios.

The next slide will provide an overview of this presentation. The presentation is organized under three main topics: (1) modeling considerations in the Harvard BSE model; (2) known cases of BSE in the United States; and (3) FSIS scenarios. Under the topic

modeling considerations, I will reiterate some of the points already discussed by Dr. Cohen, and highlight additional points that are related to FSIS' work. Under the topic known cases of BSE in the United States, I will make a brief mention of the BSE positive animals and the context for Harvard BSE model. Under the next heading FSIS/USDA scenarios, you will be provided with the background from the additional work and why SRM removal compliance scenarios were modeled for FSIS. We will end this presentation with concluding remarks.

In the next slide, we will focus on the modeling considerations for the revised 2005 Harvard BSE Model. As discussed earlier, one of the ways the model can be initiated is through the introduction of certain number of infected cattle. The geographic source of infectivity as well as whether the source is indigenous or from another country does not influence the outcome of the model. As discussed by Dr. Cohen, the model can be initiated using any hypothetical number of BSE infected of animals. To simulate a scenario more realistically, a lower number of animals may be preferred. Generally an introduction of 10 BSE infected

animals provides results that are robust enough to be used for the comparisons of the base case and the alternative scenarios or say FSIS mitigations.

As mentioned previously, it is important to note that in the Harvard BSE model, the potential human exposure is expressed specifically as cattle oral ID50s that accumulate over a period of 20 years. Even though to increase the numerical stability of the model output, large number of iterations and animal combinations may be used as described earlier. With the current combinations of infected animal-iterations, results obtained are within about 3 percent range. To measure the effect of FSIS mitigations, alternative scenarios and the base case were run with the same combination of BSE infected animals and iterations. The two outputs are used to compute results as percent reduction or percent change in potential human exposure. The FSIS scenario tables shown later will reflect model output comparisons at the mean only.

To allow for comparisons of the effect of a mitigation with the base case, a perfect (100 percent) compliance was assumed. The compliance issue was

handled by running certain scenarios for changed level of compliance.

In the next slide, we briefly review the known cases of BSE in the United States. Thus far, we've had three positive cases of BSE in the U.S. The first case, a 6.5-year-old animal was confirmed positive in December 2003. This cow was imported from Canada to the United States. The second BSE positive was from Texas, a 12-year-old cow that was confirmed in 2005. The third BSE positive case was from Alabama, a 10-year-old cow that was confirmed positive in 2006.

In the next slide, we will review aspects of Harvard BSE model in the context of the BSE positive animals detected in the United States. The revised 2005 Harvard BSE model can be initiated using different hypothetical numbers of BSE infected cattle: for instance, 1, 10, 500 and so on, to measure the effect of mitigations of interest. We do not need to run the exact number of animals every single time we may get a BSE positive animal in the country. For instance, we have three cases now, and if we have an additional fourth case, we do not have to run the model again. The

revised 2005 Harvard BSE base case scenario predicted roughly about 3.5 new cases of BSE when 10 BSE infected cattle were introduced in the United States. The current number of BSE positive animals detected in the United States are within the prediction of the model if one were to assume that infectivity from external sources of 10 infected BSE animals was at some time introduced into the United States. However, a point to be noted is that the model does not account for existing infectivity for instance the current BSE infected animals at the base case. We specify the number of BSE infected animals to initiate the model, which is 10, 20 or 500, et cetera, and the base case would then run those number of infected animals without taking into account the 3 existing BSE infected animals in the country. The focus of FSIS was not the absolute values of the output, but the ability to measure the effectiveness of FSIS mitigations.

The next slide will review the background for modeling exercise scenarios. The revised 2005 Harvard BSE model showed that a ban on use of SRMs has the biggest impact on the spread of BSE among cattle and

potential to human exposure that was emphasized earlier by Dr. Cohen. The International Review Committee recommended removal of SRMs from cattle 12 months and older. The 2005 BSE scenarios that were modeled by Harvard considered SRM removal from cattle 30 months and over. FSIS needed to explore the maximum potential of infectivity that will be removed through SRM removal. As described earlier, to allow for a comparison of the effect of a mitigation with the base case, a perfect (100 percent) compliance was assumed for the scenarios done by FSIS, unless otherwise stated. While we know, the importance of SRM removal in the reduction of the potential human exposure to BSE, FSIS needed to explore the impact of less than perfect compliance in SRM removal.

FSIS scenarios to further explore the strengthening of SRM removal mitigations are outlined here. SRM removal from younger cattle scenario included two subsets: First, SRM removal from cattle which are 12 months and older, and SRM removal from cattle 24 months and older. Second, of course, the combinations of those with a ban on non-ambulatory cattle. The less than

perfect (100 percent) compliance value was run separately, and we ran 100 percent to up to 95 percent compliance to see how these scenarios influence the potential human exposure.

The table in the next slide summarizes the results for SRM removal from younger cattle. The first column shows different scenarios. We have the Harvard scenario on top, cattle 30 months and over. Then we have a set of scenarios, which are for 24- and 12 month-old cattle. Then we have the combinations of those scenarios, plus a ban on non-ambulatory cattle. The results in this table clearly indicate that removing SRMs from younger cattle solely or in combination with a ban on non-ambulatory cattle did not provide any additional gain in terms of the reduction in potential infectivity reaching humans.

The next table deals with compliance scenarios. Less than perfect compliance was modeled at 99, 98 and 95 percent to see its impact on potential human exposure. In this table, the first row shows percent SRM removal modeled by FSIS, and the second row shows corresponding percent reduction in human exposure

when compared to the base case. In the range of compliance model, the model output indicates that for every 1 percent drop in compliance in SRM removal from 100 percent, 98 percent and at 95 percent, there is a corresponding about 1 percent increase in potential human exposure to BSE. FSIS is fully cognizant of the importance of SRM removal as well as the extent of compliance in reducing the potential human exposure to BSE.

And now to conclude, removal of SRMs from cattle under the age of 30 months, did not provide additional benefit to further reduce potential human exposure to BSE. The model output shows that for every 1 percent drop in compliance for removal of SRMs, there was about 1 percent increase of potential human exposure to BSE. Additionally, it is important to note that although the hypothetical introduction of 500 infected cattle was for computational convergence and to reduce model run time, say from 30 days to about 3 days, the results which are expressed in percent change, for FSIS mitigation scenarios are equally relevant for any number of animals. Overall, we remain confident that FSIS

measures in conjunction with all other safeguards by our partner Agencies continue to provide the utmost protection to U.S. consumer and livestock. With that, I'd like to thank you for your time this afternoon, and would like to take this opportunity to thank one and all who have contributed to this work directly or indirectly.

DR. GOLDMAN: Thank you, Dr. Dessai, for that presentation. The meeting to this point has been technical presentations both of the output from the Harvard revision to the Risk Assessment, as well as the additional scenarios run by FSIS. So we want to take full advantage of the opportunity to -- for you all to ask our technical presenters any questions. But I mentioned earlier, we also have invited to this meeting today representatives from the FDA and APHIS. We have up front here, Doctors Morrie Potter and Burt Pritchett from the FDA and Dr. Lisa Ferguson from the Animal and Plant Health Inspection Service, as well as one of the FSIS -- Dr. Dan Englejohn here in the front row, so that if there are any questions that extend beyond those that might be answered by our technical presenters, they may

be able to assist us.

I do want to emphasize at this point that the focus is on the technical presentations that you heard, the model construction, the scenarios that were run, and the analyses that were conducted so we would like to focus your questions here on this aspect.

I would also ask that if you have a question or a comment, if you'd please come to one of the two microphones in this room in the two aisles, and please identify yourself by your name and affiliation so that we can get that recorded into our transcript, which we expect will be available in 2 to 3 weeks. It typically takes that long to have the transcript available, but we want to be able to acknowledge you in the transcript.

I'll also mention at this point that the PowerPoint presentations will go up onto the FSIS Website after this meeting.

So with that, I'll ask if there are any questions or comments from the audience?

DR. DETWEILER: My name is Linda Detweiler. I'm in affiliation with the University of Maryland part-time, and then I'm a consultant for a number of

companies.

I guess my primary question is in regards to non-ambulatory status using the base case, it didn't seem to make much of facts on the reduction of human exposure. However, in the sensitivity analysis, your comment back to reviewer 1 was that you can increase the human exposure by approximately 50 percent. So that -- in that regards, that's pretty significant or at least significant in a relevant term for human dose. So what data were used in order to come up with the assumptions and also the continued assumptions that you would have that level of antemortem performance between 85 and 95 percent?

DR. GOLDMAN: I'll ask our presenters to come to the podium and answer your questions.

DR. COHEN: Yeah, actually, we developed the assumption regarding the antemortem inspection performance based on I think what we got from USDA personnel. So but they would have to comment on that particular parameter.

DR. DESSAI: We'll get back with you on that question as to where the data came from because this

model's being -- was being updated, and we had several pieces of data to update the model, especially those parameters. So we'll get back to you where the data came from.

DR. DETWEILER: Can I get you some -- I'll get you some input if that's okay. All right. Because I do think that's really significant in regards to one of the protections for human health, and if you look at reviewer 1 provided data from United Kingdom as well as European median suggestion that 50 percent was optimistic, lower than European median. I think that's one set of data you could use.

You look at the North American situation, the first domestic case -- well, the first case we found in Washington State, actually was presented for slaughter, it passed. It was not picked up as BSE suspect. It went for human consumption. First case in Canada actually was not picked up as a BSE suspect. It took 4 months to have it tested. I think there is relevant -- according to CFIA, the remainder of their cases were non-ambulatory. They were not picked up as BSE suspects. They were only picked up because of the

3D/4D.

And I think significantly, and this is something maybe to look at, I think the U.S. rabies surveillance at slaughter is another good indicator of a level of maybe -- of antemortem performance. According to some data that I received each year about less than 10 animals are condemned by FSIS for neurological disease, right? Now APHIS has an on-going program of slaughter for scrapie, okay. Not all the sheep were tested, but a good portion of the adults are tested. In the last 3 years since April of 2001, they picked up 258 cases of scrapie that actually passed antemortem inspection.

Okay. So even if you gave optimistic and not over those 30 -- over those 3 years that were condemned were found to be scrapie positive, but even if you saw 30 as nonconvincing, that's still only about 11 percent detection rate using scrapie in very similar clinical science. I'll tell you from somebody that's worked with scrapie in the field over 20 some years, especially non-ambulatory it's very, very difficult. So I think that really needs to be looked at as far as an assumption.

Oh, one other important thing because of this whole -- I'm sorry, the reason I really brought it up, is because these non-ambulatory or end stage diseased animals that you look at and do research, which you did not have when you did this, but the Germans, the Japanese and British have now found that the disease when it finished -- when it replicates in the brain and the spinal cord, actually comes down through the parasympathetic nerve chains through the synapse into the synaptic nerves through the muscle masses. So those animals again, we're not testing every animal that's slaughtered, so if they're allowed into the human food chain, SRM protections are not going to take that peripheral distribution out.

DR. GOLDMAN: Thank you, Dr. Detweiler, for that comment. I'll take this opportunity to say that we are obviously recording your comments, and we will consider those comments as we make our final determinations in terms of the rule. Thank you for that comment.

Is there any other questions or comments?

MR. HANSEN: Hi. My name is Michael Hansen

from Consumer's Union, and one question that I have that I could follow up from what Dr. Detweiler talked about, it seems to me that the two key characteristics that -- or the sensitivity analysis that do for human impact about the antemortem sensitivity analysis is important, but also the misfeeding rate becomes important in determining how many cases we're going to have. And so, she talked about the problems with the assumption of the 95 and 85 percent for the worse case -- for the assumptions for your sensitivity analysis for antemortem inspection.

I'd like to bring up for the misfeeding rate or mislabeling rate, you have your worst case scenario as 14 percent, and the base case is 2.3 percent. But if you look, the General Accounting Office in 2000, pointed out in their report that -- in their report of September 2000, that out of all the facilities they looked at, 24 percent of all the facilities holding retracted material, that is, that were handling ruminant meat and bone meal, 24 percent of the 6,000 that they looked at, did not label. So there were no labels at all. So right there, that is a rate that's much higher than 14

percent. And I would also point out from your compliance rates, what's most important is the compliance in the field because all these products can still be put on the market. They just have a label that says, "Do not feed the cattle ruminants." If a farmer or a rancher thinks that these regulations are silly, there's nothing to stop them from buying feed from one source and feeding it to another. So I would ask for your -- have you try for your sensitivity analysis using higher figures rather than 14 percent. And also, since you made models for your worst-case scenarios, they should just be everything stays the same and only one parameter changes. I'd like to know what happens if you have the worse case scenario for the antemortem inspection, and rather than make it 85 or 95, say, you use the 11 percent that Dr. Detweiler says, and say you use for a mislabeling rate, 30, 40 or 50 percent just to get an outside view. I'd like to know when you look at multiple worst-case scenarios, what values you find. And I think that's an important simulation that needs to be done.

DR. COHEN: Thanks for your comment,

Mr. Hansen. I know you've been involved in this subject for a long time. In no particular order, first of all regarding the simultaneous testing of extreme pessimistic assumptions, I think if you go back and you look at the October 2003 Risk Assessment, you'll see that we do consider simultaneously pessimistic assumptions for misfeeding and mislabeling and so on. And one thing, if you pile on enough pessimistic assumptions simultaneously, you can drive R0 above 1, but I would stress that you have to pile on quite a few, including misfeeding rates that are very high. And it's important to distinguish between misfeeding and mislabeling, two things that you mentioned in your comments: that mislabeling rate is a rate at which material is not properly labeled, and misfeeding is the rate at which farmers improperly administer properly labeled prohibited feed to cattle. The data you had worked for mislabeling.

Now, what our sensitivity analyses show both in this assessment and in the earlier assessment is that mislabeling does not have a very big impact on either the spread of the disease or on subsequently human

exposure. I would also add that the data that we are using is newer. The data are newer than the GAO Report that you cited.

So while, of course, we scientists always like more data, and it would help to reduce uncertainty, the newer data running up through September 2003, indicate that in fact compliance rates have improved when it comes to mislabeling.

To say one more thing about misfeeding, that, of course, is an uncertain parameter because it's difficult to go out and measure an activity which by definition, is not legal. But the worst case value that is being used in this assessment, assumes that 1/7th of the prohibited material, 15 percent, is being administered to cattle. So, you know, whether it's plausible for that rate to be that high or not, you know, others will have to judge, but one has to realize that that is a pretty extreme assumption even on the face of it.

MS. SMITH DEWAAL: Dr. Goldman, Caroline Smith DeWaal with the Center for Science in the Public Interest.

My first question, can you just define, because I did not see it in the Harvard analysis, could you just define for the audience what specified risk material is?

DR. GOLDMAN: It was in one of the slides. I can pull it up or --

MS. SMITH DEWAAL: Just -- we don't need a complete list. I just want a sentence on what the materials are.

DR. GOLDMAN: It's -- and I would like other people who know that this stuff better than I do to chime in where necessary. But basically what we're talking about is central nervous system tissue: brain, spinal cord, distal ileum, tonsils, and there are a few other items. I mean there's an actual detailed list. But that's sort of -- it's where scientists believe the agent is in the highest concentrations.

MS. SMITH DEWAAL: I asked that question in part because FDA actually came out with a different list of specified risk material. WE call it SRM light because it doesn't actually include all the high risk material which that Agency's using for its most recent

regulatory actions.

I thought that this new risk assessment was a very significant piece of work in part because of the recognition that the removal of SRMs is vital to controlling BSE both in the cattle population and in the human population. I was struck with the fact that you did support the International Review Subcommittee recommendations that all SRMs from the animals 12 months or older should be removed in both human and animal feed. That was a good recommendation when it was made. It would certainly documented through this risk assessment as being the right approach.

What troubles me is the fact that USDA still is not using that kind of approach, and I think it's largely driven by the economics and the fact that we don't require cattle in this country to be identified. So while in our review of the number of the animals which have been found with BSE in this country, when you say the Alabama cow was 10 years old, is that USDA's guess? They don't really know how old the animal was because the animal's not required to be ID'd in any way in this country.

So I think that the recommendations you made are good, but I think it also challenges the Government to why they're not using the most protective approach of banning SRMs of animals 12 months or older from both human and animal feed. And I think we've got to push the Government to take the most protective approaches when it comes to SRM. They're not doing it right now. In fact, the Food and Drug Administration is coming up with definitions that exclude some of this high risk material from animals.

DR. COHEN: And if I could respond?

DR. GOLDMAN: Sure.

DR. COHEN: Let me just clarify the conclusions of our report. You're absolutely correct in pointing out that our analysis found that the SRM removal had the largest impact on exposure of humans to the BSE agent and to the spread of the disease. However, this is a risk assessment. It does not make recommendations as to whether because of that, the Government or anyone else should, in fact, implement that policy.

There are various things that we did not

consider. We certainly did not consider cost. We did not consider any countervailing risks that one might be able to imagine. For example, disposal or something like that. I mean I'm making this up on the spot, but an analysis that would decide whether that is a good idea is different from an analysis that decides what benefit it would have in terms of its impact on human exposure and animal health.

It also is important to keep in mind that 99 percent reduction of a tiny number may not warrant anything. Again, that's a risk management decision in terms of how big is this risk, and whether or not the 99 percent reduction warrants whatever it costs and tradeoffs that involves. That is not anything that is in my area of expertise, and it's not something that was in this risk assessment report.

DR. GOLDMAN: Thanks, Dr. Cohen. Thanks, Caroline, for your questions. Anyone else want to respond at all with a comment?

MR. CORBO: Tony Corbo, from the consumer organization, Food and Water Watch.

About a year ago, when I was working in the

public system, we released noncompliance reports on the specified risk removal regulation. I was -- since back -- you pointed out that compliance with the SRM removal is critical in this -- in the mitigation of BSE. Can you update us in terms of what the compliance rate is with SRM removal in FSIS regulated establishments?

DR. COHEN: I'm going to ask Dr. Englejohn to comment on your question.

DR. ENGLEJOHN: Thank you for your question, Tony, but I don't think that this would be the forum to give a response to that, but I would say generally that the Agency has, in fact, been tracking our compliance with regards to SRM removals over this past year, and our hope is to be able to release a report soon so it will have real numbers for the most current information.

UNIDENTIFIED SPEAKER: Don't sit down, Dan.

(Laughter.)

DR. GOLDMAN: Any other questions or comments?

MR. McELVAINE: I'm Mike McElvaine, USDA Office of Risk Assessment and Cost Benefit Analysis.

I know I'm not an expert on a lot of things here, but responding to a couple of comments and

questions here. You know, I wonder whether the Agency or one of the Agencies, FDA, USDA, is going to consider a cost benefit analysis, you know, as we look at the number of -- for the surveillance, you know, as we reduce from surveillance levels, down to the maintenance level surveillance. There was comments from several groups, and I said, "Well, you know we're not looking for ways to, you know, we should be spending the money," you know, and the question is well what did you find in 18 months? Are we considering the costs of removing the SRMs and all of that when we have proof or at least evidence from the European situation, UK situation, that the disease is dying out, is being managed apparently by what they've already done? My question is are we going to look at the money, the costs? You know, I hate to measure cost against lives, but I question the cost against something we cannot measure with a disease that appears to be going away. How's that for a general question?

DR. GOLDMAN: I appreciate that question, which I think clearly extends beyond the technical presentations we've heard, but I don't know if anyone

wants to respond to that? And that microphone isn't working --

UNIDENTIFIED SPEAKER: Okay.

DR. GOLDMAN: -- and if you would like to use mine.

UNIDENTIFIED SPEAKER: The response would be, as Dr. Goldman, and I think Dr. Masters mentioned at the beginning, which would be that the information we have today, comments that we receive are going to -- risk managers, particularly, the within the FSIS as we move forward with our rule making process. And as part of that rule making process, there is a cost benefit analysis that would be done that we'd look at what we believe to be more exact figures today than what we had when we issued our interim final rules. And as is the case with all Federal Agencies, I'm sure that FDA and APHIS would be doing the same, as they move forward with their rule making. So as part of our final process of moving forward with getting a final rule published, which we did put in our regulatory -- that we did expect to be moving forward with that this calendar year. That would be part of that process.

DR. DETWEILER: Linda Detweiler. This is more of a comment in response to Michael, and I would just caution everybody about having a party that the disease is going away. I think Europe has a lot of data to support there, you know, over time, a lot of tests to support that. But North America, we should take heed to the last Canadian case, the age, and how far -- the ban is. It has to have implications for the United States with the number of animals, and the amount of feed that we brought in. So I just caution, not to say that we have this large level of disease by any means, but before we start saying it's all gone, please take heed of that last case or even four cases, 32,000 tests in Canada in the last 6 months. Significant, folks.

DR. GOLDMAN: Thanks for that comment. Are there any other questions or comments from the audience?

(No response.)

DR. GOLDMAN: Okay. I think then if there aren't any other comments or questions, we will move to our conclusion here.

I first want to thank our principal discussers, Doctors Cohen and Dessai, for their

impeccable presentations, as well as all of you who have listened and asked questions during the meeting today. The Agency, FSIS, does take very seriously its obligation to involve stakeholders at various steps in its regulatory process, and your participation today has helped to ensure that we've met that obligation.

We have heard a very clear and detailed presentation from Dr. Cohen about how the Harvard Center Risk Analysis updated the original BSE model, how it evaluated various mitigation strategies, either those that were implemented or proposed by modeling their impact on the spread of BSE among cattle, as well as modeling the potential risk to human health from the BSE agent, and finally, how the analysis analyzed the relative impact of the assumptions in a model through its sensitivity analysis.

We heard the results of the modeling, which I think substantiates that measures put into place by FSIS in January 2004, are protecting the public from exposure to the BSE agent, and it quantifies the extent to which each of the mitigations adds to that protection. Specifically, the revised and updated models show that

removing non-ambulatory cattle from the food supply reduces human potential exposure by about 3 percent. Prohibiting use of SRMs from advanced meat recovery systems on animals 30 months and older reduces potential BSE exposure to humans by approximately 40 percent, and removing SRMs from animals 30 months and over almost completely eliminates potential human exposure to the BSE agent.

We heard from Dr. Dessai a discussion of the results obtained by FSIS in conducting additional modeling of combinations of mitigations, removal of SRMs from cattle younger than 30 months, as well as the impact of less than perfect compliance with the SRM -- with SRM removal. Importantly, this additional modeling confirmed that SRM removal is by far the most effective mitigation in preventing human exposure to BSE, that there does not appear to be any additional benefit from SRM removal from younger cattle, and that there is no synergism between mitigations that would greatly enhance the protection already provided by SRM removal. We heard clearly that compliance with SRM removal is an important factor in protecting the public, and we were

able to quantify its impact. Specifically, FSIS has also confirmed that removal of SRMs from cattle under the age of 30 months did not provide an additional benefit to reduce potential human exposure, and that for every 1 percent drop in compliance for removal of SRMs, there is roughly a 1 percent increased potential to human exposure.

Finally, and importantly, we heard and recorded and appreciate your questions and comments, which as I said will become part of the transcript of this meeting and will be available within the next couple of weeks.

Before we conclude I want to acknowledge several people and groups. First of all, I want to acknowledge Dr. Bill James, who's sitting in the second row here, who was involved in the original Harvard Risk Assessment, and as well, the current Harvard Risk revision since the late nineties, and without his leadership, we would not be to where we are today with that. So I want to thank him for that service. He's currently the Deputy Assistant Administrator in our Office of International Affairs. So thank you,

Dr. James.

I also want to thank and acknowledge the SIPO Staff, that is the Strategic Initiatives and Outreach Staff of the Office of Public Affairs Education and Outreach who again have put together this meeting and logistics for the meeting.

And finally, I want to echo Dr. Dessai's thanks to the BSE Team, as we call it in FSIS, members of the various divisions in OPHS, members of the Office of Policy who have collaborated on both the products and the meeting itself.

And finally, I want to also thank Dr. Cohen for coming down to represent the Harvard Center for Risk Analysis even though he has since moved on to Tufts University in Boston. We appreciate his effort in the analysis and his presentation today.

So with that, unless there are any final comments, we'll conclude this meeting and thank you for your attendance.

(Applause.)

(Whereupon, at 3:00 p.m., the meeting was concluded.)

C E R T I F I C A T E

This is to certify that the attached proceedings in the matter of:

HARVARD BOVINE SPONGIFORM ENCEPHALOPATHY (BSE)

RISK ASSESSMENT TECHNICAL MEETING

Washington, D.C.

July 25, 2006

were held as herein appears, and that this is the original transcription thereof for the files of the United States Department of Agriculture, Food Safety and Inspection Service.

_____

Saundra Howard, Reporter

FREE STATE REPORTING, INC.