is finally prohibited.

A reminder that meat and bone meal was distributed out of the United Kingdom for this entire time period, but it was not supposed to be used to feed ruminant populations and that was understood by the British while they were exporting it.

This is a perfectly legal activity on the part of the UK to continue selling this meat and bone meal. Unfortunately it would seem likely that people did not pay attention to their warning not to use it in ruminant animals.

So this is an incidence curve. You just saw the data that tell you the number of cases but these are incidence curves for the United Kingdom and Ireland. On the left-hand side you can see what kinds of rates we're talking about, heading up towards 6,000 and 7,000 animals per million having the actual disease itself.

In fact, to show you this graph in any sensible way, I had to remove the data from Guernsey which was something like 20,000 per million but it obscures the trends in the graph. The point of showing you this is that if you institute all of the kinds of measures that the United Kingdom did institute, you can control the epidemic even though it

was extremely large within this country at one point.

This graph here now shows you the data for the United Kingdom. Those are the top lines. Here I have a pointer, although I neglected to get an instruction book on how to use the pointers. Give me a second. Okay. So these ones here are the data for the United Kingdom. This down here are the incident rate data for essentially the rest of the world. All of these other countries that are listed along here like Germany, Belgium, Denmark, France, etc., are all inside this little tiny line down here at the bottom. The purpose of this slide is to remind you of the difference in scale of the epidemic between the United Kingdom and virtually everywhere else at this point.

However, when you look at BSE reports as shown on this graph here, you have to be very careful. There are two indicators on this. Here is the pink line showing you the United Kingdom data. Here in yellow showing you the numbers of cases actually reported for Europe. Here we are talking about accumulating to 500 or 600 cases, whereas with the UK data we're talking about numbers of cases totally 40,000 per annum. Still the point is here is the UK data declining because they implemented all our measures and did a good job of it apparently. Here is

the data from the rest of Europe. The numbers are going up.

So, in fact, I was kind of astonished when I was doing this data for another presentation a few months ago to find something astonishing. The yellow bars here are the numbers of case reports from the United Kingdom and the green bars are the number of case reports from the rest of Europe. This is 1997 through he year 2001.

Look at this. In the year 2001 more cases have been reported. Actual cases. This isn't rates. More cases have actually been reported from the European continent than have been reported from the United Kingdom. That is the first time that's happened.

But I want to make sure that you'll understand that this epidemic has moved beyond the boundaries of the United Kingdom. Here are the incidence rates for some of the countries of the European Community. One of the principal countries of concern is Portugal, but we also have Irish data, Swiss data here, and that's Belgium. The rest of the other countries have so few cases they can't be sensibly graphed.

So in this particular curve here -- excuse

me. Hang on. Sorry. I may have said two incidence for this graph but I want to draw your attention that these are the numbers of cases that are reported in this particular graph here showing an upward number of cases in this pattern. This graph here shows you the incidence inside the countries and it's kind of important to keep track of this. This here is Portugal right here. This is Switzerland. The rest of the countries have very low incidence rates down here.

So, unfortunately though, it's not all good news, although I'm not exactly sure if I was giving you encouraging information on those previous slides. In any case, here is a list of countries that have had their first cases of BSE reported since about 2001. This is soon going to turn into a two-slide presentation for me. I've been able to keep it on one slide until just now.

Some of these countries went from reporting no cases to quite a few cases in a very short period of time, specifically Germany, Italy, and Spain. Other countries have reported only single cases like Slovakia, Slovenia.

It is significant that these guys are outside of the European Community, therefore, are not

necessarily paying attention to all of the European Community laws, although many of these countries are wanting to become associated with the European Community and may, indeed, be trying to implement this type of regulation. Then, of course, Japan with its first case outside of the European continent in indigenous herds.

Now, this graph was worked on by Anderson, et al. Some of you may be familiar with it. When I was showing you those numbers of cases of BSE in the United Kingdom, that is illustrated here by these yellow bars.

What Anderson, el al. did was they then modeled how many cases of BSE, how many animals had to be infected with BSE, that's the green bars, in order to end up with the number of cases of BSE actually seen clinically. This is the relationship that you see.

The point of this is here is 1985 when the very first animal was seen in the United Kingdom. Look at all the animals that would have been infected well ahead of the first case being seen in 1985. You think again about those countries I told you have had their first case.

I'm not telling you that they look like

this. I'm not saying that at all, but I'm alerting you that having a single case of BSE is without question concealing something. We just don't know what.

So in order to analyze some of this information a bit further in terms of which countries are actually at risk from bovine spongiform encephalopathy, I have been very generously supplied by some data from the United Kingdom.

This is Customs and Excise data from the United Kingdom. I wanted to use this data on behalf of the WHO to try and identify those countries in the world that were at the highest risk of having BSE cases so that we could go and do something about it. Unfortunately there are some very severe limitations with this data and I need to emphasize this to you before I start showing you the results of the data.

First off, this is only Customs and Excise data from the United Kingdom. I don't have information from the rest of continental Europe so you're not seeing any of the materials exported from France, from Spain, from Portugal, from Germany. None of the other countries.

Secondly, we've already discovered from some countries that did analysis based on the UK

Customs and Excise data that it isn't necessarily true that what the UK says it exported got imported. You don't always get a direct tally between the exportation and the importation information.

It's really, really important that each national authority verifies what it is that they actually imported. That is one of the major reasons why I have not provided the maps to the committee with all due respect because the data is certainly not true but it is indicative.

Another thing that is missing from this data that was already mentioned this morning, and I was very pleased to hear it mentioned, is the idea that the United Kingdom could have exported material onto continental Europe. That material was then repackaged and re-exported.

There is no obligation whatsoever in any trade law requiring the original; that is, the United Kingdom, to be placed on the labeling of this material so it goes out of the country, it's labeled Country X from the European Community, and there's no recognition, no ability for a country to know that they have imported tissues that originated from cattle in the United Kingdom itself.

Obviously illegal and what I like to call

uncontrolled movements are not reported in here. I invite you to think about many countries in many regions of the world where there is no way anybody is keeping track at borders of how these materials are actually being moved around.

Finally, this kind of data doesn't tell you anything about how these materials were actually used. Indeed, somebody may have imported an entire whole brain from an animal that actually was clinically ill with BSE, although heaven forbid that actually happened.

But if they didn't feed it to a cow, they didn't provide to anybody a risk that BSE is introduced into the Bovine population. In fact, if human beings ate that, they actually reduced the risk of BSE being disseminated through the population of animals in the country.

As macabre as it is to say, some countries in South America that imported fair amounts of these kinds of offals and used them themselves as human food actually protected their trade status because they ate it themselves instead of giving it to their cows. Anyway, that's unfortunate but true.

So now you will start to see a series of maps that look like this mapographical information.

There's a legend at the bottom here and the colors tell you something. The colors starting from the very pale color. I'm sorry but I see it doesn't project very nicely the difference between no data and less than five. It progresses through the pale greens, pale blues, down to black. This particular graph here is showing you exports of meat and bone meal from the United Kingdom to the rest of the world for the period 1988 to 1993. We analyze the data half a dozen different ways but we thought that this period here was probably the worse period to be exporting -- to be receiving meat and bone meal from the United Kingdom. I don't have it marked on this graph but I believe this is the same data as was used by the geographic BSE risk assessment. Is there anybody in this room who is sitting on the GBR scientific steering committee or the GBR ad hoc group who can confirm? No? Okay.

DR. FERGUSON: Maura, I didn't actually sit on the GBR but I went over and talked about our status and they were using both UK and their data. They also used Customs and Excise. They also used Eurostat data in some instances.

DR. RICKETTS: I don't use Eurostat data and I can explain to people why later if they want.

So here we are then and you can see that principally the distribution was into Europe but there was some distribution into parts of North Africa and India. This is black over here in Southeast Asia. Very, very little into South America. Very little into North America. Then South Africa and a couple of countries here in Africa.

DR. DeARMOND: Is Japan in it also?

DR. RICKETTS: Yes. Oops. My geography is so bad here and the map is so awful. Is that Japan? No? Is that Japan, do you think, or is that part of Russia still? That's Japan, isn't it? As I recall from the data, I actually do have the raw numbers here, too. We can look it up. Japan imported quite a bit of stuff.

Not just meat and bone meal is a problem in terms of risk to indigenous cattle herds. Obviously the importation of live bovines is also a problem. People could have imported cows because they were slaughtering them.

They could have been slaughtering them at two years of age, time when there is probably no risk but they could have been importing them for breeding purposes. They could have been importing them for fattening and keeping them for longer. We don't

really know.

In any case, if they were slaughtering them they could have rendered and recycled the materials. It's very hard to tell what the risk level is of any one of these cows that was exported. You can see that you get a different part of the world involved in the importation of these live bovine animals.

When you look at the data marked graphically for bovine offals, which I didn't include in this point because bovine offals are the materials that are the highest risk materials, it is notable that when the UK stopped using the old offals because of the SBO ban, that's when you saw this peak in exportation.

This graph here has a yellow line that is a grand total, a green line that's into the European Community, and a red line that's the rest of the world. I just want you to notice, though, that rather little in proportion went to the rest of the world.

However, if European countries were doing something with these offals, you know, making some product out of it and re-exporting, I don't have that data available to me. I can't trace that infectivity. So here is what the Bovine offals exportation looks

like on the map.

Then, as I was saying earlier, WHO was trying to do some analysis of the export data from the UK but we ran into these roadblocks almost immediately that we didn't have access to the kind of information that is required to truly analyze it in depth.

But the scientific steering committee and the geographic-based BSE risk assessment ad hoc group of the European Community did have access to more information than we have. The EC has reviewed, I think, perhaps 46 countries now in total for their risk.

And, of course, countries are submitting data to the European Community to have their risk assessed because they want to trade with the European Community and that's a very powerful tool for getting a lot of information exchanged. WHO has no such tool to use.

The BSE risk assessment process that they are involved in describes the risk of introducing BSE into a country and recycling it and makes actual estimates into three or four categories of the risk level. It does ask considerable information about internal risks.

If you map the GBR category in the four

categories from no risk to the chances that BSE are present in the country but you just can't exclude that kind of a risk, which is where the United States is right now, up to countries that haven't reported cases of BSE but you can't disregard the fact that they probably do have BSE up to the highest category which, at this point in time, just includes the UK and Portugal, I think.

One of the things that is really brilliant about the GBR categorization is that its category 3 countries are falling over one by one like dominos into category 4 so they had a number of countries, Spain, Italy, Germany, Slovakia listed as category 3 countries. Sure enough, within a year or two they all had cases of BSE.

My understanding is that Japan had an assessment done and that this assessment had results that were not in congruence with the Japanese government's desired result and they had these results withdrawn so this was not published information. Some countries certainly would have been reviewed, asked for withdrawal, and then you don't know what happened.

So back to WHO for a little bit. We had a consultation in 1999 where the consultants felt that the irradiation of BSE must remain the principal

public health objective of national and international animal health authorities.

In part as a result of that, and in part as a result of the analysis that we were doing on this data about exportation. The World Health Organization held a meeting in partnership with the Food and Agriculture Organization and the Office International des Epizooties that's in Paris. FAO is in Rome. WHO and FAO are UN agencies.

We called this meeting BSE Public Health, Animal Health, and Trade. What we are curious about was what's going on out there? What is the risk of BSE at international level? Why is there such a level of panic in the public when we're all going around saying there's a problem? Nobody is listening and cases appear and now there's a panic.

We thought have we missed something? We thought we should do a general review of the whole problem. Indeed, the tripartite consultation, which consisted of over 300 people, did conclude that, in fact, there is a global dimension to the BSE risk.

That, in fact, it's impossible to deny that BSE contaminated meat and bone meal has been distributed beyond the boundaries of European Kingdom -- United Kingdom, excuse me, and the European

Community even.

Anyway, this is actually a problem of an international scope. We identified these questions that have to be part of a risk analysis. First off, that a country needs to identify whether or not they have imported any of these potentially infected material.

They can't forget about illegal importati›n. They have to think about other countries importing and having repackaged these materials. They have to ask themselves strong questions about how these materials were actually used wanting to answer to find out whether or not cattle had access to this material cross-contamination being one of the biggest concerns.

Lastly, is there a rendering industry in the country or region. Is it possible that a country that does not have rendering actually might be exporting materials that are then being used for rendering. For instance, there is a very active industry in exporting bones in Africa.

I'm going to provide you a smattering of some of the recommendations from this consultation rather than everything. If you go to the website, I'm pretty sure that slide is shown to you. There's a

copy of the entire document available on the WHO website and it will be available in hardcopy and Spanish, French, and English any day now is my understanding. OIE is doing the actual printing.

In terms of public health, some of the issues that this committee has raised were also raised by the consultation. Consultation wanted to know why there wasn't a good pathway analysis describing where it is that human beings could be exposed to BSE. How come you can't just find it somewhere as a tool to assist developing countries. I think there are very few countries in the world that have done any kind of pathway analysis.

The other thing is they wanted to see a standardized international approach to figuring out whether or not food was safe to export. I don't know if this is possible. This would be something that would fall into the lap of the Food and Agriculture Organization. They would use the Codex Alimentarius. My understanding is that getting some into Codex can take years and requires the agreement of a large number of the member countries and can be quite complicated. This isn't a change that is going to occur overnight. We are hoping that food is going to become safe because of a recommendation from this

consultation. It is certainly going to take a long time before it happens, I think.

I did want you to see some of the exportation of food that we had data on from the Customs and Excise. Here, for instance, is bovine carcass meat exportations '78 to '98. Some countries received quite large amounts of bovine carcass meat.

In terms of the OIE, there are a number of products that are listed that are safe to be traded regardless of the situation even from a BSE infected country. Milk, for instance, is safe for trade and milk products. Meat is not listed as one of those safe-to-trade items.

The WHO has stated from several consultations that we don't think that meat carries infectivity that can cause illness in a human being. We think meat is safe to eat but only if the meat has actually been slaughtered and handled in a way that ensures there was no contamination of the meat. That would include everything from pithing through to how the saw was handled.

Anyway, this is interesting to look at. You can see that the materials are widespread but I'm not sure that this is actually describing to you much about where there are risks in human populations

because of the probable low actual risk of consumption of meat.

However, Bovine offal in meat preparations certainly would have contained infectivity. These are the countries that received some of these materials according to the Customs and Excise data.

The consultation itself reviewed the data from the UK, reviewed Eurostat data that was provided by the Scientific Steering Committee from the EC. Also a slightly different Eurostat data pack that comes from the food and agriculture organization. They identified these three problem areas for BSE.

First off, Southeast Asia. However, Southeast Asia may not have much of a risk for recycling of BSE because they have really huge populations of pigs and not large populations of sheep -- cattle, I mean. Therefore, maybe this isn't a problem. Maybe having this material eaten up by pigs is the best thing that ever happened.

The central and Eastern European countries are another matter. They've imported clearly contaminated materials and they do have cattle populations and they do have rendering industries.

Then the Mediterranean and North African region but, again, here they have large populations of

sheep and goats so if the sheep and goats are slaughtered very young, are not actually recycled very effectively, then it could be that a lot of the risk that was imported has actually just sort of washed away over time.

Who knows? We don't know. Nobody knows what's going on inside those sheep populations in North Africa. Nobody is doing surveillance in them. Nobody is testing these animals. Well, there are a few isolated pockets of people who are testing them but these are actually, in fact, at best described as questions.

We do not know what is actually going on inside these regions but think that there are regions that received important enough amounts of infectivity that they should receive the benefit of a proper risk analysis.

In terms of issues regarding how do you go about controlling BSE, the consultation at no point came up with any new recommendations or no new ideas. Nobody had new plans. Everybody said the kinds of things that are already being done by the United Kingdom, for example, are just fine. They just have to be done properly so no new kinds of special activities were recommended.

It is important, I thought, for the committee to recognize that risk management strategies that are used to control BSE should be commensurate with the actual size of the risk and, therefore, while the United Kingdom has a large epidemic so does Portugal and, therefore, they must do things as enormous as cut off the entire head, remove the whole spinal column. In countries with lower amounts of risk, you don't have to do the same amount of things in order to manage that risk.

The only way to determine the risk level of a country is by undertaking a risk assessment. No matter what happens, you have to audit compliance with all of the risk management strategies or it is irrelevant. Having a country send you regulations that describe what they say they are doing without providing any evidence that it is actually being complied with is insufficient.

In the case of, for instance, the United Kingdom reference was made this morning to these documents that are produced on a very regular basis in which you can read all of the investigations that were done. Paragraphs of information, tables, graphs, charts.

You can actually see all of the

investigations and they have a "name and blame policy" so if somebody is deficit, they actually put their names down. It's quite serious business.

I thought it was really important to remind everybody in this room something that you may well be aware of. It's important to know that the risk of human exposure could actually be higher in countries that don't have any surveillance system or who haven't evaluated the quality of the implementation of their management plan. It could be much higher in those countries than in countries where we know they have BSE and where we know they are doing something.

You have to be very careful to recognize that some countries are not undertaking the activities necessary to control their BSE epidemics and there are some countries where we may not be aware of the BSE cases simply because they are not looking for them in an appropriate way.

I think it really is very significant that in the European Community when they shifted from passive to active surveillance, that's when a whole bunch of countries showed up with cases of BSE. That's really important.

So is BSE present in other countries? We

don't know and we don't know because not enough in my opinion is being done to assist many of these countries in undertaking the work that is required for them to find out whether or not they are at risk.

Now, it is being evaluated. As I mentioned already, the GBR assessments are being done in countries but these are countries that are requesting assessments and that is because they want to establish a trade relationship with the European community.

If you're talking about countries that were net importers of material but who aren't attempting to establish a trade relationship with the European Community, they aren't going to request one of these GBR assessments to be done. They don't need to.

Now, the OIE is another matter. The OIE has a committee called the Foot and Mouth Disease Commission and the FMD Commission has officially been told by the executive committee of the OIE that countries really ought to be getting these evaluations done for their risk of having BSE in the country or not and they are voluntary.

There will be a certain amount of pressure put on people to get these done. I actually spent

three days in Paris with the OIE just last week while a group of people tried to figure out what would be the information that would be necessary to be received by the OIE in order to determine whether or not a country was living up to code so it could be considered having a BSE free status.

It's not going to be very easy. There were some questions among the committees about whether there were any countries in the world today who actually lived up to the full standard of the code and could be declared BSE free according to the code.

Certainly they said it would have to be reviewed on an annual basis, but they expected to receive 40 applications in the first year after making the announcement about what the methodology would be so there certainly is some interest. I think that is basically everything of importance from that slide.

So that is the end of my formal presentation actually. I would just leave this up for a few seconds. It has my e-mail address and also the publication's address for WHO where you can get a copy of this meeting report that I mentioned earlier. Thank you very much for your attention.

CHAIRMAN BOLTON: Thank you, Maura.

Now we'll open this up for questions for

Dr. Ricketts. I'll put my glasses on so I can see.

DR. BELAY: In considering the different rates of BSE in the different European countries, did you take into account the kind of surveillance they have in the different European countries? Obviously the surveillance is different from one European country to the other.

DR. RICKETTS: That is an extremely good point. When you see, for instance, that in switzerland the number of cases has risen or even the quite sharp jump in cases in France, there's no doubt whatsoever that the shift from passive to active surveillance accounts for those cases.

When the GBR first published about the value of active surveillance, they actually said expect a doubling in cases when you go from passive to active surveillance. At this meeting last week they said expect tripling to quadrupling of the numbers of reports of BSE activity.

In terms of those maps and things I showed you, no. It's just a very dumb kind of approach to the maps. Nothing sophisticated, just the numbers.

CHAIRMAN BOLTON: Steve.

DR. DeARMOND: You mentioned a time period for the exports of offal and meat and bone meal and

brain tissue. Did it extend beyond the -- your cutoff date was 1993? The period of time that you were showing us. I don't remember when it was. How far beyond -- how far into the '90s were these exports still proceeding from the United Kingdom?

DR. RICKETTS: Dr. Soul, would you like to address that question? You're going to be the expert on the exports from the United Kingdom. It's describing, please, the length of time in which specified bovine offals could have continued being exported from the United Kingdom.

The issue is that if you look at the straightforward United Kingdom export data, you see that the exportations began as soon as the SBO ban went into place in '88 and continued right through until the actual complete closure in 1996.

The content of those SBOs would have changed quite a lot over that time period because regulations were put in place regarding what was being taken out of the animals, whether it was being incinerated or was allowed to be used, etc., etc. Can you provide a time frame for all of that? I certainly wouldn't be able to. It's too much more detail than I can manage.

DR. SOUL: I think I mentioned that in my

talk actually. Can I do it outside the meeting, provide anybody with that data?

DR. RICKETTS: Okay. You have to know the regulations quite well to know what the content was of the SBO so I just basically took a simpleminded look at the regulations, or if I had the information available to me, I did exactly what the Scientific Steering Committee did.

DR. DeARMOND: For a lot of these countries that received large amounts, India, Japan, and Southeast Asia, they must have received mass quantities, tons of it. Have they continued to use this to feed animals even until very recently? Is that true?

DR. RICKETTS: I don't actually know for each individual country of the world whether or not they put in place a proper ruminant-to-ruminant feed ban and whether or not they are monitoring it. I was just speaking with Dr. Belay over the lunch break and he informed me that in Japan they continue to feed meat and bone meal to their animals.

Did I understand you correctly, Ermias?

DR. BELAY: I did not say meat and bone meal. I was talking about the SRM ban --

DR. RICKETTS: SRM. Oh, excuse me.

DR. BELAY: -- for protecting exposure to humans. Even then they recommend -- at least I was told that they recommend an SRM ban but did not make it a requirement in Japan. This is purely for human exposure.

DR. RICKETTS: You know what? A short answer to your question, I don't know what they do in a country-by-country basis. As I emphasized at the beginning, that's why it's important that the national authorities are consulted about what it is they actually do with this material and how they handle their animals.

We make no attempt in the WHO to keep track on a country-by-country basis what the regulation is and whether or not it's implemented. Any country that applies for an OIE status or goes through the GBR process, certainly that information would be requested from them. I don't have it.

CHAIRMAN BOLTON: Lisa.

DR. FERGUSON: I can try and address perhaps a bit of that. First of all, I think the export of meat and bone meal from the UK, actually that is where most ruminant product from the UK was absolutely stopped in '96 but that doesn't address what might have gone on either with stuff that's being

recycled through the community or elsewhere through other infected countries from Europe. There was a lot of that type of product that got shipped around the world that I don't think anybody will ever know.

As far as feed bans, feed bans were in place in Europe. Eastern Europe, they might have been in place on paper but I don't know how enforced they were. Beyond that, I mean, outside of North America, Australia and New Zealand, I don't think you'll find a feed ban anywhere else.

I know Japan had "a voluntary" feed ban in place but I don't think it really was -- nothing was happening. People didn't realize what was going on. Throughout the rest of Southeast Asia there is no regs in place for a feed ban per se. Now, as Maura mentioned, with a high pig population, that's where a lot of that stuff was going into, pigs and poultry, which helped.

CHAIRMAN BOLTON: Yes.

DR. GAMBETTI: Maura, is WHO or the European Community providing recommendations as for the criteria principle that should be used to establish a surveillance, let's say? The country wants to stop this, what kind of advice do you give them?

DR. RICKETTS: WHO does not provide direct advice on this because we are supposed to focus on human health so the OIE exist to give the information about the animal health so that's the OIE's job.

The OIE has an animal health code in which they include information about surveillance. The surveillance chapter for BSE is currently under revision. It's being worked on. I think that it will be in pretty good shape by the next executive committee meeting which is in May because I think it's my intention -- it is their intention to submit a revised chapter to their executive board in May of the next board meeting.

It will have a description of what a surveillance system can consist of. But, you know, I'm not a veterinarian either, and I'm not sure. I would really appreciate the opinion of one of the veterinarians when they use the code if it actually provides you with good enough information to run a surveillance system.

Regardless of whether you like or dislike what's in the OIE code, the information available from the European Community is right there for you on the web. There certainly are a large number of experts in the European Community countries who I know from

experience happily give out advice. In a moment's notice they describe what you need to do.

I think that some of the issues that have come out have been the issue of active versus passive surveillance where it is clear that active surveillance is required if there is any risk at all. Then the populations of animals that need to be studied as was mentioned this morning by Dr. Soul.

If you focus your attention on animals under 24 months, you're going to find nothing because you're just never going to get positive tests in that population anyway. There are certain populations of animals that have to be examined like the emergency slaughters, the downer cows, etc., the list that Dr. Soul provided for you.

DR. GAMBETTI: Recommendations are made concerning the number of animals to be examined in addition to the age range? For example, 100 percent, 20 percent, or not?

DR. RICKETTS: The OIE currently has a table of a minimum number of animals that has to be examined but it obviously is not a table that you would use if you were trying to say that you have no risk of BSE in your country as the numbers are too small to be statistically significant.

It's, I guess, a sort of starting point. You would be better off to address the question to somebody in the OIE about why they have even included a table with a minimum number. You don't go to the ad hoc?

DR. FERGUSON: I've not been a member of the ad hoc group. I know the BSE chapter in the code has changed drastically over the years and it's much better than it used to be. I can't remember how long ago. It's been probably at least six or seven years ago now when they put in that appendix specifically for the surveillance of BSE with a table and with recommendations.

It was meant to try and help out the international problem or conundrum of, "Okay, are you not finding BSE because you're not looking for it or are you not finding it because you truly don't have it?" The attempt was there to at least get countries started thinking down that road. I know that here in the U.S. we have attempted to use it if for nothing else a baseline and as kind of a goal to shoot for.

CHAIRMAN BOLTON: Are there other questions or comments? Okay, very good.

Thank you very much, Maura, for an excellent presentation.

DR. RICKETTS: Thank you.

CHAIRMAN BOLTON: Now we are going to open us this to the public and invite the public to make statements and/or comments. I'll leave this open briefly and see if there are any. If not, then we will move on to committee discussions. Is there anyone in the audience that would like to make a comment or ask a question of the committee or any of our speakers who are still present? I see none.

Okay. Therefore, we will then move on to committee discussion. That is discussion of the topic of the questions. I think I'll ask -- is David here? Dr. Asher? Bill? Okay. Dr. Freas will then present the questions.

EXECUTIVE SECRETARY FREAS: The first question reads, "Do members of the committee agree that the combination of measures implemented in the UK by the end of 1996 to protect the human food chain from BSE contamination are sufficient to obviate the need for donor deferrals based on subsequent travel or residence in the UK?"

CHAIRMAN BOLTON: Okay. Let's open this up for discussion. We have a number of these control measures and I'll just try to review them again. I've been jotting them down in my notes here. We have the

OTM, over-30-month rule. It's a slaughter rule so that animals over the age of 30 months cannot be incorporated into the food chain.

We have the SRM, specific risk material, ban. We have the surveillance issues active and/or passive surveillance. The discussion in there was compensation and things like that. We have the MRM as well. Would anyone like to start this out? Comments, questions, discussion?

Yes, Dr. Simon.

DR. SIMON: I'll just open as the industry representative because I know the question was raised during the prior discussion as the presentations were made about impact on supply. We don't have any data presented. I conferred briefly with Dr. Bianco and apparently there have been some estimates that if we extended the UK deferral to 2,000, there might be 1 to 1.5 percent loss of donors.

I know that the committee over the years has always been balancing this supply issue against the safety issue and how far to go and how much blood we would lose. I guess the comment that I think is most pertinent at this point is that the blood supply in the United States is very precarious. There is already interference with patient care on a frequent

basis because of inadequate supply.

I think you should assume anything that would be done that would further restrict supply has the potential to further impair patient care in one or a number of instances. It's hard to get accurate data because I think once the public is informed, these people often stop coming in.

CHAIRMAN BOLTON: Dr. Epstein.

MR. EPSTEIN: Yes. Toby, I just want to clarify FDA would agree that the anticipated donor loss from deferrals for a three-month exposure to the UK from 1980 through the year 2000 would be about 1.5 percent. However, that's only an additive 0.3 percent compared to a deferral for 1980 through '96 as FDA has just recommended in the final guidance.

The difference in the two recommendations is only an additive loss of 0.3 percent, not an additive loss of 1.5. 1.5 is the total loss. With the current policy we give you 1.2 percent of that loss.

Celso, if you have different figures, you can certainly dispute them but these are the estimates that came out of the April '99 survey.

DR. NELSON: Jay, is that with a six-month deferral for the UK versus three or is that --

MR. EPSTEIN: No, this is for the three month.

DR. NELSON: That's for the three month.

MR. EPSTEIN: This is for the three month.

DR. NELSON: And five years for the rest of Europe.

MR. EPSTEIN: Yes. There's the additive donor loss of changing the UK deferral from a three-month exposure history 1980 through '96 to three-month exposure history 1980 through 2000 is an additive loss of 0.3 percent.

CHAIRMAN BOLTON: Yes, Lisa.

DR. FERGUSON: Just a quick question. I heard Dr. Epstein mention 2000. Is that what we're looking at as a cut-off date or is the question perhaps a bit broader than that?

CHAIRMAN BOLTON: Well, yeah. The question actually doesn't mention 2000 or 2001. I think it's really post-1996 and so the issue, I suppose, would be to change that wording from 1996 to the present which would be sort of a moving target going forward.

Yes, Jay.

MR. EPSTEIN: I just want to be clear that FDA has not posed to the committee changing the cutoff

to any date after 1996. I think if the committee wants to open that Pandora's box, then you can discuss 1997, 1998, 1999. It then becomes, I think, less clear.

If the committee advises us that the set of measures implemented through the end of '96 were insufficient, then I guess we have to go down that road and ask were they ever sufficient or what additional measures are needed. FDA has not led with that question. It arose, you know, in the committee discussion. I think it is certainly a legitimate question.

I would ask Dr. Lurie, though, whether the sole basis for asking about deferral limited by the year 2000 was the paragraph that you cited in the risk report. Is there any other basis to pick that date as opposed to any other date?

DR. LURIE: Of 2000?

MR. EPSTEIN: Yeah.

DR. LURIE: No, really not. I'll make two points on that. 2000 is one of the more recently completed years. I'm not proposing 2000 particularly. We do have some evidence from the FSA, data that by 2000 compliance with various elements of the ban seemed to be quite high compliance.

My concern remains that at least on the basis of data presented to the committee today, we really know next to nothing about what happened prior to the year 2000. We have some evidence for at least some parts of the food ban that compliance was quite poor going back to 1996, for example.

Let me make one other point, though, which is I think the notion of having bans that extend through "the present" is something that we should always be leery of doing. What I mean by that is that -- I'll just take an example.

Jay, you and I just discussed this.

The ban on donations of blood by men who have had sex with men was implemented in the mid-'80s or so, at that point said 1997 through the present. In my view, at least, we haven't really gone back and revisited that and the present has now moved from 1984 to 2000.

I think those open-ended ideas are inherently dangerous sometimes as in when we don't know what compliance is at present in Europe, I think it needs to remain open-ended. If there is anyway to close that period, I think that it is really advisable to do that.

CHAIRMAN BOLTON: Additional questions?

Dean.

DR. CLIVER: I have nothing profound except as the token food safety person on the TSEAC, I feel obliged to at least remark that last year during one of our sessions I said I thought it would be a mistake to set at naught the efforts that had been put in place in the UK.

Clearly it's not about motivation of the UK. They aren't doing these things to make themselves look good to us. Having said that, if we say that they have accomplished nothing since 1996 and we're going to keep our same -- extend our deferral policy up to today, I'm not comfortable with that. I think it's going to set a very bad example for not only the UK but all the other BSE countries. I think what they are doing deserves recognition by this group.

I think from my own point of view I'm probably past the at risk age for the disease itself but if I were traveling with my children, I would certainly feel as comfortable about them eating beef or beef containing products in the UK as I do here in the United States. I would not say the same for the rest of Europe.

CHAIRMAN BOLTON: Yes. I would like to put this question actually in maybe a broader context,

and that is that, again, as I think I've said before, as we move forward and more countries demonstrate to be at risk with BSE, known cases of BSE. As we look at donors who have spent considerable time in each of those countries, would be feel that these kinds of regulatory measures would put those travelers and/or endemic population in a lower category of risk? And would we then use that to mitigate any sort of donor deferral policy.

Clearly this is going to happen as we move forward. If we don't, I think, begin to make these considerations, we are going to end up with a shrinking population of potential donors within this country and around the world.

It is at least my sense in part that the FDA is asking us to consider these general kinds of measures that were put in place in the UK and to ask are they sufficient to aviate the need for donor deferrals. Not just in the frame of reference of the UK but in the frame of reference of any country that has BSE. I would like again to open it up and get any comments from that perspective.

Dean.

DR. CLIVER: Well, clearly that was the intent of the two contingency questions. First we

consider what has been done in the UK and then, if that is enough, how might they be emulated and if that is not enough, what else ought they be doing? I think what has come up again and again is the credibility of enforcement and audit.

No matter how stringent measures you may declare, if you aren't enforcing them and they aren't being consistently validated and verified, in all probability paper regulations have never saved a life. Here I think we are asking are the measures appropriate, are they effective, and are they indeed being followed and carried out.

Then whether the vote is yes or no, we have contingency questions two and three to decide. Arguably it would have been well to have programmed those in such a way that we would answer both two and three regardless of the outcome of the vote on question one.

All the same, I think that's where we are. First we pass our own internal judgement on the adequacy of the UK measures as conceived and as executed and then deal with the rest of the world.

CHAIRMAN BOLTON: Kenrad.

DR. NELSON: I was quite reassured by the data from the '96 cohort that there were only seven

cases and possibly some of them were maternal transmission rather than feed. I didn't get a real sense of how large that cohort was and how it might have been affected by the under-30-month rule.

That is some pretty critical data in addition to the inspections looking at how many cases there are who have experienced this new control measure. I would have expected far higher than seven cases by now. I don't get a sense of how many more there would be because it's hard to know what the denominator is. That, I think, was pretty reassuring data. I wonder if anybody could comment on that.

DR. NELSON: I guess that was a question that sort of came up during the discussion of Dr. Soul's presentation and it never really got answered.

Dr. Soul, can you tell us how many animals were examined?

Is Dr. Soul here still? Yes. How large was the cohort that would have been over 30 months? Let's say if you applied a previous time during the epidemic, how many cases might you have expected in that cohort by now?

DR. SOUL: That's difficult but so far as part of the active surveillance program we have examined just over 7,000 of that cohort.

CHAIRMAN BOLTON: Seven thousand of the post '96 animals?

DR. SOUL: 1996 to 1997 cohort, yes.

CHAIRMAN BOLTON: So that's seven out of 7,000 roughly.

DR. SOUL: Well, four, I think, have been found as part of the active surveillance. Three were found as part of the passive surveillance. Sorry, I can't give you the figures for the --

DR. NELSON: And what was the age of the ones that were found? Were they all under 30 months or could they have been dairy cattle or something?

DR. SOUL: No, they are all over 30 months. They are all in the 1996/97 cohort.

DR. NELSON: Oh, okay.

DR. SOUL: While I've got the floor, could I just mention the question that was asked earlier. I think it was about then when was the SBO banning posed which was September 1990. SBO was banned at that point from incorporation into any meat or bone meal so it could not have been exported from the country after September 1990.

CHAIRMAN BOLTON: Dean.

DR. CLIVER: I think we're drifting here as far as what we are supposed to be considering.

Granted we want all the reassurance we can get that the BSE outbreak is under control, but when we refer back to 1996 as a point of departure for blood donor deferrals, this is about what people were eating in 1996, not what animals were born in 1996.

Those animals that were of edible age in 1996 were not the ones that were born that year. If we want to evaluate risk today, the 1996/97 are gone under the over-30-month rule. The question is what were people eating in the UK in 1996/97?

CHAIRMAN BOLTON: Well, I get the sense that Dr. Nelson was asking that because of wanting to determine the effectiveness of the ban as opposed to the direct human risk. In other words, in terms of the global protection of the various control measures. That is my assumption.

DR. CLIVER: I think that's fine but if we're going to talk about a cut off for deferrals, why '96 either is or is not appropriate, give them the question that we're supposed to decide here. As of 1996 people who were in the UK eating beef were not eating beef that was born in 1996/97.

We have to rachet backward two and a half years or less to see what the animals were eating that were fed to the people of that time. I said what I

said. I have no particular reservations about that. I'm simply saying that as we go off into the effectiveness of the meat and bone meal ban, we ought to be looking at 1996. We should be looking at people eating 1998/99 from animals that were born in 96/97 cohort.

CHAIRMAN BOLTON: But the question before the committee is not whether the date should be moved. The question before the committee is whether the measures, the combination of measures that were implemented by 1996 are sufficient to aviate the need for donor deferrals. We are really talking about the combination of measures. Are these control measures that were put in place sufficient to prevent really contamination or infection of humans through the food chain.

Peter.

DR. LURIE: Yes. I had a thought about Dr. Nelson's question. If I understand correctly, there are four BARB -- is that the preferred phrase? -- animals that were born -- that were detected our of 7,000 which is .06 percent. Right?

If you look at the data provided by Dr. Ricketts, at the peak of the BSE epidemic, if I'm reading these numbers correctly, the annual incidence

of BSE was about .8 percent. I have here about 8,000 per million which is .8 percent at the peak in Britain. Then the BARB rate is .06 percent. If I understand that correctly, it's only 10-fold lower.

DR. NELSON: No, I don't think that's a proper interpretation if I understand it because given the fact that symptomatic animals would be -- they were almost all dairy cattle. They were older and, therefore, a far higher proportion would have been infected. In this cohort they were all over 30 months so they were all in the higher risk group.

I suspect the figures are at least 10-fold higher than .8 percent. I've seen some estimates that the actual numbers of animals that might have been incubating infected prior that might have been slaughtered and consumed was far higher than the reports in Dr. Ricketts data.

DR. LURIE: That's a fair point for sure. I must say .06 percent as a prevalence rate, the prevalence was low, always under a couple percent. Now it's .06 percent. That's not as encouraging as I would hope.

DR. NELSON: That's with wide confidence limits and with the possibility of -- I don't know if there was a possibility of any of these being not feed

infected but maternal transmission. The data aren't large enough yet to be sure but they are encouraging.

CHAIRMAN BOLTON: Other questions? Lisa.

DR. FERGUSON: We spent a lot of time discussing sort of the incidence in cattle and how that curve has dropped off. I think if you just look at overall and you look at that, it shows that the measures that MAF or DEFRA -- sorry, old term -- are effectively working and are decreasing the epidemic.

I think for purposes of this question, I would say we perhaps should not focus our attention there as much as let's focus on what are they doing to prevent risky tissues from getting to people.

I mean, obviously decreasing the incidence in the cattle population is part of that, but I would say there are a couple of other things that are perhaps the more significant part to get to this question, and that would be SRM removals and the over-30-month scheme.

CHAIRMAN BOLTON: And let's not forget mechanically recovered meat.

Well, I'm sensing that there's not much enthusiasm for further discussion but I'm going to try one more time.

DR. GAMBETTI: I'm not sure I really

understand completely the question but from what I understand we are here using two different criteria. One for the UK and one for the continental Europe. In one case it's 1996 when the other is present.

If we look at -- I'm not sure I understand but my feeling is that if you look at the data it's actually not that different in terms of prevalence of BSE in the two countries if you consider those seven cases in the UK born after the ban and the Continental European case.

If you look under with that criterion, it looks to me that the UK and in terms of result of animal infected after the ban, the numbers are similar or comparable if I understand them correctly.

CHAIRMAN BOLTON: Well, I think there are still more cases of BSE in the UK than in any other individual country.

DR. GAMBETTI: (Off microphone.)

CHAIRMAN BOLTON: I'm not sure it's valid to consider only those but, again, I don't want to get into that. The point really is the issue that differentiates 1996 for the UK and the present for all other countries or these control measures that are put into place to prevent that contamination from entering the human food chain. The question then is are they

sufficient.

DR. GAMBETTI: And why not sufficient in Continental Europe then?

CHAIRMAN BOLTON: Because those are not at least officially in place. Those kind of control measures, and Maura can correct me if I'm wrong, they are certainly not comprehensive measures in any one country in place as they are in the UK. But, I think, again that is the issue I believe that the FDA would like us to address is as these things happen. For example, Switzerland, Germany, France. If they were to put these comprehensive measures in place, how would we feel about that affecting the donor deferral issue? I'll put it even one step further. Should we be so unfortunate as to have cases of BSE in this country? How would you feel as individuals putting these kinds of measures in place about protecting our food supply and would that then allow us to continue to be blood donors within our own system? Eventually we may face that issue as well.

Dean.

DR. CLIVER: From what I've just heard I was going to second what Lisa said, that it's not just about quelling the BSE outbreak, but at some point if you know the BSE is around, what are you doing to keep

the SRMs or whatever from being fed to people.

If we do pass this and go on to contingency question 2, I think, which he just said is the answer, the over-30-month rule and the SRM things are the key to human safety. Granted, it's a lot safer to live some place where you don't have BSE at all but with that said, what they are doing right, as far as human food chain on line 4 there, is SRM and OTM.

CHAIRMAN BOLTON: Steve.

DR. DeARMOND: I would like to just sort of reflect what Dean is saying. It seems to me, at least today, anyone who has eaten meat in Great Britain, or visited Great Britain regardless of whether they ate meat or not, is probably safe and not going to be a threat to the blood supply. My only question is when did that happen. In 1996 did everything go smoothly then? Did it take a year or two years for all the contaminated meat to really be lifted out? The '96 date is the only problem I have. I would think they have done everything. They've got a decreasing BSE and they've eliminated the real contamination that would, in fact, create variant CJD in humans. My question is the exact date.

CHAIRMAN BOLTON: Well, we are not

actually at this time being asked to evaluate whether we should change the date. We will postpone that and if they ask us that question, or if we want to volunteer that they should reconsider it, we could do that at a later meeting. But at this point, Colonel Fitzpatrick and then Dr. Asher. Dr. Scott first and then Dr. Asher.

DR. SCOTT: Dr. Asher put me up to it. I just wanted to respond I hope in a relevant fashion to what Dr. Gambetti was saying, to remind the committee that we still have a five-year residence in UK donor deferral after 1996. We're not saying that -- just to point out that we're not declaring residence in UK a non-deferral criteria.

CHAIRMAN BOLTON: I think I understood that. Three months from 1980 to 1996 and five years beyond that cumulative. This is the problem with this particular deferral issue is that it gets so complicated that nobody can figure it out.

Colonel Fitzpatrick, did you have a comment or question?

COLONEL FITZPATRICK: The wording of the question bothers me a little bit but --

CHAIRMAN BOLTON: That's par for the course.

COLONEL FITZPATRICK: Yeah. But I just wanted to kind of refocus. We're talking as we have always about this subject in sort of a void of knowledge. We're talking about applying the precautionary principle to a hypothetical risk. There is no known case of transmission. We've seen evidence that there may not be transmission by blood but we don't know that for sure yet.

We are using BSE as an indicator of a potential threat for variant CJD in the human population still not knowing specifically the transmission route of that agent to the human population.

In looking at the caseload of variant CJD in the UK, from what is being presented we aren't seeing a mirror image as one might expect epidemiologically of what you saw with BSE in the human population.

Once again, we don't know where we are on that curve with humans. We don't know if it's transmitted. Is it sufficient measures to guard the donor population or the patient population from a risk we don't know about? I don't know. Is it adequate based on the knowledge we currently have?

Judging from the clinical outcome of the

measures that the UK has put in effect, which is a sharp decline in BSE in their native population of cattle, measures to protect the human food chain from the presumed agent transmission based on the knowledge at hand, I would have to say this is as adequate as we know at the moment.

It's easy to get caught up in compliance issues and is it 100 percent but if they've only had one carcass with spinal cord in it since they started really enforcing compliance, I mean, I think Jay and USDA will say that is phenomenal and that goes beyond anything that we would even expect here. To me that is a great indicator as to the job they are doing.

CHAIRMAN BOLTON: I would agree.

Ermias.

DR. BELAY: I think there was significant development in the UK in 1996 according to my understanding and that was for the first time they introduced the OTM ban, the over-30-month scheme in 1996. That is an age group where a vast majority of BSE cases have been reported. If they could successfully remove the over-30-month animals from the human food chain, I think they may have successfully gotten rid of a majority of the infectivity that may have gone to the human food chain.

Now, the question obviously was whether or not enforcement of the OTM ban in 1996 was adequate. For that I do not have the answer. Probably Dr. Soul could address this. The way I would like to phrase the question is in practical terms how do they enforce this OTM rule? In other words, is there an inspector on the side looking at the animals to determine what the age of the animal is and rejecting them from getting into the slaughter houses?

I've also heard about passports, each animal having a passport. Do they check the passport to see how old the animal is and reject it? If you could give us an idea of how this practically was done, it could give us an idea of how the enforcement may have been carried out.

CHAIRMAN BOLTON: I'm going to ask that we not consider that at the moment because I think it's really off the question, number one. That is more like question two. What I would like to do is hold off on the specifics of exactly how those measures are implemented or overseen.

Peter, if you have a comment that's not directly --

DR. LURIE: Let me make sure I understand the question. The question then is the emphasis is no

longer for now on 1996. The emphasis is on the measures.

CHAIRMAN BOLTON: Exactly.

DR. LURIE: Do you like those measures. Do we think this combination of measures, those particular ones that supposedly were in effect in 1996, do we think they would be protected?

CHAIRMAN BOLTON: Right. And I think that we've had enough discussion to take a vote on this at this point. Then we can move on to discuss particular measures that are the most important or what have you. I think if there are no objections -- Dr. Scott has another comment.

DR. SCOTT: I apologize. One should look before one leaps. What we prefer to have is for the European donor deferral for five years or more in Europe but only including UK 1980 through 1996.

CHAIRMAN BOLTON: Okay. That's what I thought it was.

Now, if there are no objections, I will call for a vote on the question. I will reread the question. The question, at least as I have it written here is, No. 1. "Do members of the committee agree that the combination of measures implemented in the UK by the end of 1996 to protect the human food chain

from BSE contamination are sufficient to obviate the need for donor deferrals based on subsequent travel or residence in the UK?" We will have a voice vote.

EXECUTIVE SECRETARY FREAS: We'll go around the table starting with Dr. McCullough.

Dr. McCullough.

DR. McCULLOUGH: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Chamberland.

DR. CHAMBERLAND: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Lurie.

DR. LURIE: Yes.

EXECUTIVE SECRETARY FREAS: Colonel Fitzpatrick.

COLONEL FITZPATRICK: Yes.

EXECUTIVE SECRETARY FREAS: Dr. DeArmond.

DR. DeARMOND: Yes.

EXECUTIVE SECRETARY FREAS: Dr. McGee.

DR. McGEE: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Piccardo.

DR. PICCARDO: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Kagan.

DR. KAGAN: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Belay.

DR. BELAY: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Boyle.

DR. BOYLE: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Williams.

DR. WILLIAMS: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Harvath.

DR. HARVATH: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Gambetti.

DR. GAMBETTI: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Nelson.

DR. NELSON: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Bolton.

CHAIRMAN BOLTON: Yes.

EXECUTIVE SECRETARY FREAS: Ms. Walker.

MS. WALKER: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Hollinger.

DR. HOLLINGER: I think I'll say no just to see what it sounds like, but yes.

EXECUTIVE SECRETARY FREAS: Dr. Johnson.

DR. JOHNSON: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Priola.

DR. PRIOLA: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Mitchell.

DR. MITCHELL: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Ferguson.

DR. FERGUSON: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Stroncek.

DR. STRONCEK: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Tuazon. Excuse me. She's not here.

Mr. Rice.

MR. RICE: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Cliver.

DR. CLIVER: Yes.

EXECUTIVE SECRETARY FREAS: Dr. Linden.

DR. LINDEN: Yes.

EXECUTIVE SECRETARY FREAS: We would like to hear comments from our industry representatives at this time.

Dr. Simon.

DR. SIMON: Yes. I agree with the yes votes.

EXECUTIVE SECRETARY FREAS: Okay.

CHAIRMAN BOLTON: Clearly we discussed this far too long. It's an unanimous vote.

EXECUTIVE SECRETARY FREAS: It should be 26 yes votes unofficially.

CHAIRMAN BOLTON: Very good.

EXECUTIVE SECRETARY FREAS: No no votes.

CHAIRMAN BOLTON: That moves us on to question two which addresses some of the issues that

we have already been discussing. That is, "If the answer to question one is yes, which measures should the FDA consider to be of greatest importance when it considers future revisions and recommendations for determining the suitability of donors who spend time in other BSE countries?"

We could open that up again. I think that Lisa has already talked about the over-30-month rule and the mechanically recovered meat ban issue, and the specified risk materials. Are there other discussions? I don't know if we need to rank these in terms of importance. I don't know that the FDA is looking for that sort of an issue but to just lay out which ones we consider are essential or in that top tier of importance.

Steve.

DR. DeARMOND: It seems to me you need the combination. You wouldn't fool around with just doing one.

CHAIRMAN BOLTON: Dr. McCullough.

DR. McCULLOUGH: I possibly should know this and don't pursue it if the chair doesn't think it's a wise use of time. The OTM issue is obviously very attractive as a strategy to many people. In an over simple way, it does accept the fact that infected

cattle will be in the system. It's just that they have a very low level of infectivity at the time. My only question is there a real simple quick answer to how low is low in this case in these animals?

CHAIRMAN BOLTON: No. There isn't a simple answer. There are various strategies. The 30-month-rule really comes about as sort of half of the average incubation time of 60 months or five years. Some studies suggest that infectivity is not really significant until half of the incubation period.

Studies in animal models that have looked at these things a little more carefully are not quite so rosy with respect to that picture. I suspect that animals that are slaughtered at 30 months and under may very well have infectivity in the brain. Clearly they have it. They may have significant amounts but it is certainly much lower than it would be post-30 months.

Peter.

DR. LURIE: I agree with those measures, of course, but compliance is everything. As Dr. Cliver said, a paper rule never saved anybody's life if it's not complied with. I'll just give as an example something from the BBC news from this past Monday. I'll just read the first two or three

paragraphs.

"Meat from an offspring of a BSE infected cow has reached the human food chain the Food Standards Agency has revealed. The agency's advice to consumers that the risk to health from the incident is low. The 29-month-old animal was slaughtered in abattoir in Wales in November, put into the food chain, and none of the meat is now left." Compliance is everything.

CHAIRMAN BOLTON: Blaine and then Lisa.

DR. HOLLINGER: I think it was asked whether we ought to put this in some sort of importance. Maybe somebody can correct us but from what I gather from reading the information initially, this is from this 2000 thing here, it seemed to suggest that the Europeans were not doing the over-30-month rule. I don't know if that is correct. Somebody could correct me if I'm wrong. It seemed to me they were not following it which I think is a very important rule to put in play. So if we want to make that emphasis here, I would certainly emphasize it. That, along with the others, are very important. Could somebody correct me on that? That's what it said initially and I don't know if they put it into play since then.

DR. FERGUSON: Yes. I mean, in general terms throughout the rest of Europe the over-30-month scheme is not in place. I think there might be a few countries -- correct me if I'm wrong -- that have done that to a certain extent. I think Portugal did it for a while.

Throughout Europe that is not in place now. Most animals over 30 months are part of the active surveillance and are being tested but they are allowed to go into the food chain. Let me also just make the point that throughout the rest of Europe SRM bans were not really in effect until October of last year.

CHAIRMAN BOLTON: Just a moment, Dean.

I'm not sure I recall the figures exactly but in reading through this material, I think that you can see a reason why the over-30-month ban is not that attractive because the cost, I think, was in the two billion pound range, something on that order. It's clearly expensive. It's not something that somebody is going to undertake lightly. I do think it's a very effective way to control the spread.

First Dean, then Dick.

DR. CLIVER: Well, I was in Japan when they enacted their first big steps in October. There

is a huge difference between the over-30-month ban in the UK where no animal that's over 30 months old can become human food.

On the Continent the most advanced countries, as far as response is concerned, have an over-30-month rule that each carcass stays out on the rail while they do a rapid test on the brain and they are individually released for human consumption if they pass the rapid test.

If they fail the rapid test, a second rapid test is done on that carcass. If that one is failed, then it goes for immunohistopathology. If that is failed, then it is recorded as a passive surveillance case, if you will, and it doesn't go to human consumption.

In Japan they decided to do one better than that. At least as of October, all bovine animals slaughtered for human food, even suckling calves, if you will, that were going for veal are being tested.

I had a one-on-one with a member of parliament where I told them I thought that was very nice cosmetically but it was a waste of resources because if you require testing of animals that can't possibly give you a positive result, you are diverting resources from other potential areas or activities

that would enhance consumer safety.

With that said, the over-30-month has it occurs in Continental Europe is about testing every animal and the assumption that the test if valid and that the rapid test will pick up positives. The assumption is that if the rapid test is positive, it still has to be verified, whereas a negative is taken at face value.

That's a very different thing than saying we're not going to eat any animals over 30 months. I'm not advocating one over the other. I'm just saying that this is a very different consensual approach to control.

CHAIRMAN BOLTON: Dick.

DR. JOHNSON: It seems to me what measure should we consider. We shouldn't necessarily get down to specifics but there are two general categories of measures. The first one is their surveillance and their credibility because that's really been the problem with Germany and Italy until recently. If they say, "We're BSE free," and you know by the importation of cattle they're not, you need to say, "No, we're not going to accept that." Whether they are telling the truth.

The second is what regulations they put in

touch. In terms of what kind of feed they're using, how they are processing their meat, what the rendering is doing. Those have to be taken up individually. I don't think we should say that they have to put in place everything the British have done in order to be taken off the list.

I guess what they are asking us to do really, though, is to tell them which are of the greatest importance. I agree with Peter as well that monitoring an enforcement of any regulations are critical. Surveillance and reporting is critical.

Those are sort of similar types. Then you have the physical restrictions like ban of mechanically recovered meat or over-30-month ban of specified risk materials, those kinds of things that are there to physically prevent contamination of the food supply.

Are there other suggestions for which items are most important?

Ermias.

DR. BELAY: I think this idea goes with surveillance. Dr. Peter Soul also alluded to it; that is, the compensation issue. There is no adequate compensation and the cases could potentially go underground. They may not be deported. Having an

appropriate conversation system I think would be one measure that should be considered.

CHAIRMAN BOLTON: Dr. Cliver concurs with that, I think.

DR. CLIVER: Very important.

CHAIRMAN BOLTON: This is not a question that we can vote on unless we want to try to. I don't get the sense that we want to haggle out trying to argue about which one is No. 1, 2, and 3. I think that the FDA has probably heard our opinion.

I suppose we could vote on an issue something like do we agree that the measures put into place by the UK should be taken as a model for this and from that they may want to construct some paradigm of trying to allow countries to select one from column A and one from column B, two from something. I'm not sure how they would deal with that.

I don't sense that this is an issue that we are really going to be able to go around the table and meaningfully vote yes or no on. Any comments with respect to that? I see Jay is up already wanting to comment.

MR. EPSTEIN: Yes. I don't think that we need votes. It was the discussion that we were seeking and I think we've heard what we needed to

hear.

CHAIRMAN BOLTON: Okay. I would like to actually go on and look at question 3 because that question asks are there other things that we didn't hear the UK doing with respect to this. Are there suggestions for things that you didn't hear?

I mean, one of the things that sort of came out is that more stress on surveillance monitoring and enforcement, although that is part of the UK program. That would be spelled out. Are there any other suggestions for things that you did not hear that you would like to hear? None. Okay.

That will conclude that portion of the meeting. Now we will go on to the committee update and we'll have a presentation on the Harvard BSE Risk Assessment. How are we doing on time here? Oh, we're not bad. Summary and update. I'm not sure if Dr. Gray or Dr. Cohen will present that.

Is this Dr. Gray or Dr. Cohen?

DR. GRAY: Dr. Gray.

CHAIRMAN BOLTON: Dr. Gray, welcome. Thank you for coming.

DR. GRAY: Well, good afternoon, everyone. I first want to thank the committee for giving me the opportunity to talk to you. I realize you've been

through a very long and difficult day. You've done a lot of thinking. You've done all your work but I can't say that I'm your reward because --

CHAIRMAN BOLTON: For this committee, this is actually a short day.

DR. GRAY: Oh, yes. I've been to some of the previous meetings. I realize that. But what I would like to do is to just spend a little bit of time giving you an overview of the work that we did that was sponsored by the Department of Agriculture to look at the potential for BSE in the United States. If you want more detail, there are 500 pages of scintillating reading that is available to be downloaded from the USDA's website.

The other thing I would like to do before I start is looking around this room both on the committee and in the audience there's lots of folks here who did an awful lot to help us with this. I want to thank those of you who helped us directly and a lot of others who have done some of the work that was very important to us in getting our analysis done.

I'll go fairly quickly. This is sort of an overview. What I want to do then is leave a little time for discussion if you would be interested in that.

What the Department of Agriculture asked us to do -- I'm already realizing I'm going to have a lot of trouble with these slides but I think you have copies of them in your hands that will help. They asked us to look at ways in which BSE could get to the United States and, if it did, how it could spread.

That was really the question. Are the measures that are in place and the things that we're doing suff.cient to prevent the spread of the disease if it were to get here. We also were very interested, of course, because of the importance of dynamics and time in this, to be able to look at this over time.

Now, very briefly, this was done in a collaboration between folks at the Center for Risk Analyst at the Harvard School of Public Health. When we got involved in this we didn't know very much about BSE. We had an awful lot to learn. We were chosen for the project.

We worked with USDA because we have a background in working a lot of scientific technically difficult, complicated scientific issues with a lot of uncertainty. We teamed up with a group at Tuskegee University with a long history in working in animal health sorts of analyses. It was this team that did the project.

The first thing that we had to do is to try and understand the science. As I said, we came to this without a great deal of knowledge. That is where a lot of you in the room really helped us. We also had to learn the U.S. Agricultural system. We went to slaughter houses. We went to rendering facilities. We went to feed mills. We went to cattle markets. We got out there to understand the way the system works. We work with folks in the industry and consumer organizations in the government to help us get the data, get the information that we would need.

We ended up realizing what we needed to do to be able to make predictions, to look at what might happen in the United States, to build a quantitative model. I'm going to describe that in a little bit of detail. This was something that allowed us to look at a variety of hypothetical situations to understand the way in which the U.S. system would function if it were challenged by BSE.

As all of you know, there are a great number of uncertainties in the science of BSE. We went with the fundamental assumption that I think most of us in the room have, is that what we've learned from the UK is that no matter the origin of the disease, whether it comes from scrapie, from

spontaneous BSE, or from some other mechanism, it is spread through the use of rendered animal protein as a protein supplement in the feed of other animals.

This cycle is what allows the disease to spread from one sick animal to others. The disease is not easily spread. There may be some maternal transmission and we account for that, but the primary root of transmission from a sick animal to other animals is through the use of rendered protein.

This is sort of an overview of our model. Sort of boxes to show you how we move things around.

Maura, I didn't get the directions, either. I'm having more trouble than you did.

Just very briefly as an overview, we monitor the cattle population of the United States, somewhere on the order of 100 million animals. We follow in our model and I'll show you briefly in the results some of the many things that we are able to track.

For example, one of the important things we follow in the animal population is how many animals would be infected with the disease and how many of them would advance to a clinical state that could be detected especially with some sort of surveillance system that we have today.

These animals live out their lives and they die. They may be slaughtered. When they're slaughtered some of their tissues are taken for potential human consumption and we look to see ways in which BSE infectivity could potentially be available for human exposure.

Other parts when the animals have been used for human food go into the rendering system where they can be used for rendering and feed production. That material can potentially get back to the cattle population. In addition, animals that die but do not go through slaughter, that die on the farm, for example, can go directly to rendering.

We also have potential ways in which BSE infectivity could enter the United States. We look at a variety of them in our report. We look at scrapie and spontaneous BSE. We also look at the importation of infectivity. It could be bone meal. It could be sick animals. We use sick animals in our analysis but, in many ways, they are just a surrogate for another way to put BSE into the U.S. to see what happens.

Now, one of the important things about this model that has to be discussed is the fact that there are not data, of course, that we can use to

build what many statisticians or someone would think about as a predictive model that says, "We've seen so many cases, let's see what's going to happen in the future."

Again, we're working from a situation where, as far as we know, the disease is not present in the United States. We know enough about the science of BSE, about the U.S. agricultural system that we can build a model that describes how animals are grown, used, and disposed of in this country.

Our model is probabalistic and this reflects the fact that the entire system is probabalistic. Any particular animal that is chosen at any particular time to go to slaughter has nothing to do with its BSE status if the disease were here so we have to look at the fact that there are probability distributions for many, many of the parameters in our model.

One of the important things that we do here as sort of our bookkeeping device to follow the infectivity, to follow the disease around is to characterize infectivity as cattle oral ID_{50}. These cattle oral ID_{50}s, that I'll show you in just a minute, are in different parts of the animal at different parts of different times of incubation of

the disease and at different levels.

We follow those so that the age of an animal and how long it's been since it's been infected is very, very important in understanding then how many of these ID_{50}s can potentially go back to cattle or could go into the human food supply.

The final thing is that what we did in making our model is we tried to kind of average the entire situation across the United States. We recognize that there are a lot of differences in production methods, in animal husbandry practices across the U.S. They differ from California to Florida to Wisconsin, for example, if you look at dairy farming.

We tried to get insofar as we could data that averaged across the United States. Our model could be used with the appropriate data to do a particular state if you wanted, but we were trying to get a view of the entire country.

You can look at your handout for what is actually up here. This is the data that we relied upon to look at where infectivity was in an animal that was sick and how high it was when it was there.

This is based upon the pathogenesis studies that were done in the UK in which animals who

were exposed to BSE slaughtered a different times and about 45 of their tissues tested for infectivity. This helps us understand how the infectivity moves around in the animals and how it grows over time.

This is something that has been touched upon several times. These again are data from the pathogenesis experiment showing the growth of infectivity in an animal over time. These are based upon the studies in which specific tissues were taken from animals at different time points and assayed in a mouse bioassay for their ability to cause BSE.

There is a low amount of potential infectivity early in the disease that is found entirely in the distal ileum. As an animal approaches the state of having symptoms, actually getting to the point of exhibiting clinical signs of BSE, the amount of infectivity grows very, very rapidly and we assume it is then level as long as that animal goes on to live.

Those are a couple of the key assumptions that helped us to understand how much infectivity might be in an animal depending on how long it had been since it had been infected, and where that infectivity was, which particular tissues were the ones that we had to watch out for.

This isn't that important. We'll go by this.

I'm going to tell you quickly about three sort of sets of analyses that we did in our report. What we called our base case, the very first thing we tried to do was to characterize the United States agriculture system as it is today. The practices that exist, the number of animals that there are, the way in which they are used, the way in which they are disposed.

We also assumed insofar as we know BSE is not present in the United States so it wouldn't have been a very interesting analysis if there weren't some way to introduce the disease. What we did is assume that 10 imported BSE infected animals, specifically we made them dairy cows, just ten dairy cows incubating BSE were introduced into the United States system.

We then followed that for 20 years to see how that infectivity would move around, how many new cases of BSE could occur, how many of those cattle oral ID_{50}s, the accounting unit that describes the particular infectious tissues, how much of that could potentially be available for human exposure.

We also looked at some potential risk management options and several of them have been

discussed in some detail today. One of the things that we noticed, and I'll show you the results in just a moment, is that when you have the disease present, it looks like animals that do not go to slaughter but, in fact, died on a farm and died of BSE will introduce a great deal of infectivity into the system if, in fact, they are rendered.

We looked at as one risk management option, this is just one that was of interest to us based on other results, a ban on rendering cattle that die on the farm taking them out of the system. We also looked at a UK style specified risk material ban that removes, as you know, certain high-risk tissues from both the human and the animal food supply.

Again, we tested this with the introduction of 10 infected animals and the difference then between our base case and these cases gave us some idea of the effectiveness of these particular measures.

Finally, we looked at a few other things. We looked at the potential for imports to the United States of animals. We heard about those from Dr. Ricketts. Animals who were imported into the United States between 1980 and 1989 some fraction of the animals that came in their ultimate disposition either

isn't known or we know that, in fact, they went into the system. We tried to say something about the likelihood that those animals might have introduced BSE.

We tried working with folks in Switzerland to replicate or to use our model and data about the animal husbandry practices, the size of the herd, the demographics of the herd in Switzerland to see if we could reasonably predict the small outbreak of BSE that occurred there. They have very good data. They had worked very hard on trying to understand how infectivity got into their system.

We wanted to see if our model did even reasonably well in predicting that because there is no real way to validate our model. There is not a controlled experiment in which BSE has been introduced into a country and followed. Here we have something kind of close. It's more a test of plausibility rather than an exact validation.

Then we also looked at the potential for spontaneous disease. What if BSE is a spontaneous disease that follows the age structure of sporadic CJD in humans in its occurrence in the animal herd and what would that mean in the United States. We also looked at scrapie.

Very briefly, if we look at the results of our base case, this is the introduction of 10 sick animals 20 years out, what we find is that there are relatively few new cases of BSE in the United States. Remember this is a probabalistic model.

The average number over 1,000 iterations of each run -- excuse me, a 1,000 runs of each scenario was that there were about three new cases of BSE in the United States. The 95th percentile was about 11 over that 20-year period so these are new cases that arose from those animals that came in.

Most of these, getting back to the discussion that you've already been having, came from problems with compliance with the FDA feed ban. Our model assumes that the feed ban is not implemented perfectly, that there are opportunities for contamination, for mislabeling, for misfeeding, for some things to go wrong.

These data came as well as they could from work that has been done by FDA looking at compliance that came from estimates that we made about the amount of animal proteins that are used in livestock rations and things like that.

What we saw was that there were relatively few cases, again a mean of about three new cases in

addition to the 10 that we had introduced. Interestingly, and I mentioned this earlier, 40 percent of the animals are predicted to die on the farm. That is, we have both a variable incubation period in our model and then a varying period of life once an animal reaches the critical period where it becomes systematic, somewhere between two and six months. If that animal has not been chosen and doesn't go to slaughter after six months, we assume it dies on the farm. If that thing goes into rendering, that is a full-blown case with a maximum amount of infectivity that is going into the system. We found that that 40 percent of animals introduced 96 percent of the infectivity to the system. Most of that, of course, would go into a prohibited protein and prohibited feed channel but it's there in case of the opportunity for contamination or people not doing things properly to pass infectivity into cattle.

The other thing that we found is that even with the leaks in the feed bin the disease cannot be sustained in the United States. There is just not enough transmission from a sick animal to new animals to keep the disease going.

If you think about epidemic models, of course, if you think about R0 you need each case to

give rise to more than one case in order to support a disease in the population. In our model with our assumptions that does not happen in the United States.

As I said, 10 cases gives rise to three more on average. That just means that over that 20-year period with the introduction of 10 animals, the disease has disappeared from the United States in virtually all cases.

Now, what I would like to do, and this is going to be the hard part, is to show you some of the results from our model that allow us to make those kinds of conclusions.

I'm very sorry to those of you in the back who don't have this in the same detail. I'm glad the folks here have these in full pages. This is a table that describes the -- that captures the entire 20-year period. This is adding up everything over 20 years.

For example, up here we have the very top line is total infected. This is the total number of animals that had BSE. You can see the mean is 13 and that is those 10 animals that we introduced plus three more.

You can also see that most of the time, in fact, there are very few new cases of BSE and it's only very occasionally that some combination of events

happens, again usually having to do with things getting through the feed ban that allows infectivity to get from a sick animal to another animal.

Here the other thing that we tracked, the total number of infected without imports is at 2.9 that I told you. The number clinical tells us how many of these animals actually reached a point where they would have had clinical disease and had been able to be detected. One of the things you can see here is it's very, very small.

One of the things it tells us is if this were to happen in the United States, we probably wouldn't even see it. So if 10 animals came in we wouldn't see it. We would have a few new cases but, in addition, this last line, probability and infected is greater than zero, that means at the end of our -- with our thousand iterations or thousand runs of this scenario, how many times at the end of that 20 years was BSE still present in the United States. How often was the -- what was the probability the number of animals infected was greater than zero and you can see it's zero.

The thing we can say is they could be introduced. They could give rise to a few more cases. It's a situation that we virtually certainly would

never detect almost with any surveillance system, but that the measures in place most likely would mean the disease would not last long and would not become established and would leave.

The other thing that we spent a lot of time on is looking at sources of potential human exposure. These are very hard to see but I can tell you the main sources of potential human exposure are consumption of brain, which is, of course, still legal in the United States, consumption of spinal cord, which is also legal in the United States and done, and then the third, and probably the largest source, is the consumption of advanced meat recovery product.

This is something I've heard mentioned around the table of MMR. In the United States at this point in time we now use something that is called AMR, advanced meat recovery. It works in a slightly different way but it has some of the same concerns in that a specific government either regulation rules, directives are not followed there is the potential for spinal cord which, of course, is one of the more infectious tissues, to be present in bones that go into an advanced meat recovery system.

These systems are used to extract the last bits of meat from a carcass after it has been treated

by hand, processed by hand. If that spinal cord goes into that system, some amount of spinal cord can contaminate that ultimate product. Those are the three main sources of exposure. We also did look at things like, for example, the potential for some contamination of edible meat through the splitting of a carcass because, of course, when a saw is used to split a backbone, the spine is in there -- excuse me, the spinal cord is in there and some amount of that spinal cord can be aerosolized. This, interestingly, is one of the few places where we actually had very good hard data from experiments that had been done in Europe looking at the amount of infectivity that would get onto a carcass following splitting and it is actually very, very low. We also assume that things like washing and further treatments wouldn't reduce this anymore. This still turned out to be a very, very small source of potential human exposure.

CHAIRMAN BOLTON: Dr. Gray.

DR. GRAY: Yes.

CHAIRMAN BOLTON: Can I interrupt for a second and just ask you I understand in the top part of the table that those numbers are numbers of animals for the most part. Is that correct?

DR. GRAY: That is correct.

CHAIRMAN BOLTON: "Potential human exposure," are those numbers of humans?

DR. GRAY: Oh, no. No.

CHAIRMAN BOLTON: What are those numbers?

DR. GRAY: Those are cattle oral ID_{50}s.

CHAIRMAN BOLTON: Oh, okay.

DR. GRAY: Thank you for making me say that. In many ways this can't be thought of as a risk assessment in that one of the things that we don't do is to make any kinds of predictions about the potential, for example, this introduction of 10 animals to lead to cases of variant CJD in the United States. This is because, frankly, there just are not sufficient data to make those kinds of predictions with any kind of accuracy or certainty at all.

Instead, what we do is track the amount of cattle oral ID_{50}s that could potentially reach the human food supply. Cattle oral ID_{50} is a unit that describes the amount of tissue from an infected animal that if given to another cow gives it a 50 percent probability of getting the disease.

In our model an animal with full-blown BSE, symptomatic, it has the disease, has 10,000 cattle oral ID_{50}s distributed through its brain, spinal cord, dorsal root ganglia, other tissues.

Those tissues then can potentially either be directly consumed as in brain or spinal cord consumption, or can contaminate human food and, in that case, our measure is the number of cattle oral ID_{50}s that could then be available for human consumption.

For example, you could think of these as sort of conservative estimates. For example, we have a category in our table of beef on bone. There what we are thinking about is the fact that there are certain cuts of beef in this country because we don't have something like a specified risk material ban that can contain spinal cord.

A T-bone steak can have a piece of spinal cord in there. That beef on bone category includes the chance that an animal with BSE was used to make that T-bone steak. Now, the reason that we call that potential human exposure is we're not saying that's going to be eaten. We're not saying that someone is going to eat that spinal cord. We're not saying that they are going to dig the dorsal root ganglia out of that particular piece of bone but it is there for potential human exposure.

DR. CLIVER: Does this imply at all that susceptibility of humans is comparable to cattle or just that relative risk from different tissues is

present?

DR. GRAY: This is much more useful for looking at the way in the relative risk, as you say, of different tissues, different products. For example, brain versus advanced meat recovery versus edible meat.

I said there really aren't good data for talking about the differential susceptibility. The best estimates from Europe, they make estimates that BSE may be -- excuse me, that the species barrier may be somewhere between 10 and 100,000. We sort of give that information in our report but we don't go further to say what this would mean.

For example, in the introduction of 10 sick animals over 20 years, our model estimates only about 35 cattle oral ID_{50}s reaching human food. It's a very small number and with a 10 to 100,000 species barrier, if that is, in fact, correct, you can put that in context.

In other words, you could put it in context to compare it perhaps to the UK situation where there might have been maybe a million sick animals and perhaps a number in that same general ballpark of cattle oral ID_{50}s that might have gone into the human food supply. But there aren't ways to

make accurate even sort of scientifically appropriate attempts at estimating vCJD cases. Thank you very much for bringing that up.

Are there other questions? I would encourage questions as we go along.

DR. JOHNSON: Yes. The group above that that are in ID_{50}s, when you say eliminated by rendering, you mean would be eliminated if you didn't render?

DR. GRAY: No. I'm sorry. There is a lot of information here that is explained in a lot of detail in the report. That particular line one of the things we do is assume that there is some reduction of BSE infectivity in the rendering process. For example, that particular line describes the number of all of the cattle oral ID_{50}s that go into the system from those 13 animals on average.

DR. JOHNSON: Oh, okay.

DR. GRAY: It's a way to sort of look at where things are going. How much of it is going out, for example, through the rendering process. There we sort of looked at -- there are different rendering systems used in the United States. They are used on different types of animals and we accounted for as much of that as we could with the data that were

available.

The other thing that I want to show you quickly is this is the time stuff. That was the stuff that let me say on average we don't see very many cases and we see relatively little infectivity reaching the human food supply. These are the sorts of data -- I guess you can't call them data. These are the results that let us say something about the time course of the disease and why it is that in these particular cases the disease appears to die out.

What we have here are the results if we import 10 infected animals. Along the bottom, and it doesn't seem to show up here and I hope it's on your handouts, are years starting at year zero, the year that we import those animals, and going out for 20 years.

For example, this bottom one shows the number of animals with disease. These are the total number of infected animals. These box plots indicate the -- the box is the 50th percentile, the top and bottom are the 95th percentiles, and the individual dots are some of the more extreme values.

The main thing to take away from this are the trends. In both of these cases the number of infected animals, this one is the probability that

there are any infected animals, and this one is the number of them that exist. Both of these go down and away, down and away.

This is the thing that is showing us that there is not enough transmission to keep the disease around. We get it. We get a few more sick animals but there is not enough transmission sort of for it to become established, again under the assumptions in the structure of our model. This is just a similar thing. You can look at those.

The other thing that we did was to look at -- we sort of said, well, 10 is a very arbitrary number. We actually chose it so that we had enough to look at so we had some idea of what would happen. We looked at also the importation of everywhere from one to 500 infected animals. In each of those cases we looked to see how many more infected animals would there be. You can see it is approximately proportional so that as you import more, you do get more cases. There's just more infectivity in the system.

For example, here is our 10 where you get about two. You can see it in this clump. For example, if you import 200 animals, you get an additional 100 sick animals roughly. In all of these

cases, again, the disease dies out. The more infectivity you put in, the longer it takes.

With one animal most of the time the disease just doesn't even take. That one animal sort of just doesn't -- its infectivity doesn't get to other animals or, if it does, it doesn't keep going and it goes out very quickly. If you put in 500 infected animals, or you can think of this as just putting in a lot of infectivity into the U.S. system, you get more cases. But even then, it goes away. It takes longer. The more infectivity you put in, the longer it takes to go away.

CHAIRMAN BOLTON: Does it bother you that you don't reach some threshold at which you begin to get a propagating epidemic? In your model -- let me ask at the same time a companion question, and that is if you plug in the UK 1979 type parameters and introduce 10 infected cattle, what does the model do in that case?

DR. GRAY: Well, we also modeled the United States going back and starting in 1980 and we used all of the sorts of assumptions there including no feed ban and widespread use of pneumatic stunning, fairly heavy rates of protein use and it goes bonkers. You get a huge number of cases.

Our model is perfectly capable of generating an epidemic. What really seems to be happening here is that there is just not enough of that transmission so, if you think about it, if 10 sick animals don't give rise to 11. A hundred sick animals aren't going to give rise to 101.

I mean, you still got a level of transmission between the sick animals and well animals that is far enough below that R0 to let something become established. No matter how many you put in it's not going to become established. It will take -- longer and longer to go away.

CHAIRMAN BOLTON: I hear echoes of the mid-1980s in the UK, or maybe the late 1980s where this epidemic was clearly not going to be a problem. I mean, I hear what you're saying about modeling the U.S. and I'm sure that your work is done and you would like to move on to other things. I would feel much more satisfied if I saw results from, as I said before, the UK parameters or something like them plugged in to see how well it models an actual epidemic that we know something about.

DR. GRAY: As I said, I'll show you in just a minute. I think I've got the data and if I don't, I can -- in fact, I have the report in the back

when we tried to do Switzerland.

CHAIRMAN BOLTON: Right. I've seen those in the summary.

DR. GRAY: Well, we can come to that, but we can mimic -- we underestimate the total number of clinical cases that were seen in Switzerland and there are a variety of reasons. Our model could have something that underestimates. It could be that we're not sure how much infectivity went into their system or when.

We also recently mimicked the time course which I find more satisfying. We mimicked their situation where they gradually tighten feed bans and their different risk management strategies and our time course very much follows the time course that they got. That gives us some competence again that what we've done is plausible.

I mean, we could be right for the wrong reasons and there is no way to tell that but we tried to do as many things as we can to at least establish that what we've done has some plausibility. That is sort of the best you can do in a situation where you cannot formally validate something.

DR. GAMBETTI: Are you prepared to say that the condition of the cattle industry and food

preparation in the United States is such that you never get epidemic no matter what?

DR. GRAY: I'm certainly trained as a scientist and I'm never comfortable saying never but I do believe that the likelihood, the chances of there being an epidemic are very, very, very small. They are actually getting smaller.

As I said, one of the main ways in which this disease is being spread in our model is through noncompliance with the FDA feed ban. There has to be a means for infectivity to get from a sick animal to others. As more is done to tighten up that feed ban or to remove that infectivity from the system, the likelihood that it's going to spread significantly goes down.

I will certainly never say never. I will certainly never say that we won't have a case of BSE. It's entirely possible that we will. It's entirely possible that we'll have a case of vCJD. I don't think based on the work that we've done that it's going to be something that is going to blow up into a major animal health and public health problem.

DR. BELAY: On the graph here what is the choice hold where the outbreak will be detected by current surveillance?

DR. GRAY: It is roughly -- if we look at the year 2000 -- let's see. There is a couple of nice graphs in the report in which we look at, for example, if spontaneous disease did exist. No, it's when we're looking at the importation of animals from the UK. We make some predictions of if something got in, what would it look like if it started back in 1980 and we've only had four years of a feed ban. There are some particular predictions from our model that are not consistent with the fact tha our surveillance system has not found the disease.

In 2000 it would be roughly -- see, the problem with this, this is the number of animals, not clinical animals. Roughly we assume that anything over --

Josh, is it on the order of 200, 250 clinical animals per year would have a very high probability of being discovered?

DR. COHEN: I believe that is correct.

DR. GRAY: Something like that. With 95 percent confidence we would likely detect a case for sure if there were 250 clinical cases in the United States. Something like that. We had a long discussion about that.

There are a lot of things that are very

uncertain here. This is not particularly helpful. You can look at the report. There are a variety of -- there are a number of parameters. There are a lot of things that we don't know very well. A lot of the ones that are most influential in our ultimate predictions have to do with compliance with the feed ban.

You can look in there and what turns out to be very, very important for us, and I find it very interesting, and it's what the folks in Europe have sort of been saying for a while and focusing on, is this potential for misfeeding. That is, is there the opportunity for someone to deliberately circumvent the feed ban by using feed containing ruminant byproducts.

For example, for chickens and feeding it directly to cattle. If that happens at any appreciable rate, that is a major breach of the feed ban that is a real potential problem for getting infectivity from a sick cow to some others.

If we look at some of the risk management options we looked at, we looked at a UK style ban on specified risk material in both human food and animal food. This said that in processing we are going to remove the brain, the spinal cord, the intestines, and take them out of both the animal food and the human

food supply.

What this does when we compare it and when we introduce 10 sick animals and follow this for 20 years and compare it to our base case of introducing 10 sick animals, it reduces the BSE cases by about 80 percent and it reduces potential human exposure by 95 percent.

Essentially almost the only thing that is left on potential human exposure is the possibility of microemboli that might be in blood that is used for human consumption and a little bit of that contamination from splitting. Of course, if we've taken brain and spinal cord out of both direct human consumption as food and their ability to contaminate food, for example, in advance meat recovery, we greatly reduce the potential for human exposure. For example, this is a step that has a pretty significant influence on both animal health and human health.

I mentioned that we looked at this question not rendering animals that die on the farm because --

Yeah?

DR. CLIVER: Finish your sentence.

DR. GRAY: Okay. You're anticipating. We notice that, in fact, a lot of animals who were dying

on the farm were dying of BSE. If they are going directly into rendering, that is a lot of potential infectivity that is then available for this potential cross-contamination, misfeeding, or other breaches in the feed ban.

We said what if you took that infectivity out? When we did that, it reduced the total BSE cases by about 70 to 80 percent. That is, there is just less infectivity available then for cross-contamination. And it reduced human exposure a little bit but that is mostly because it reduced the number of BSE cases.

This isn't something if you think about it that is taking animals anything out of the human food chain. It's just reducing the total burden of disease in the population.

DR. CLIVER: Now I would like to chime in.

DR. GAMBETTI: Fire away.

DR. CLIVER: I'm from California. Massive animal agriculture. As of the end of 2001 due to environmental and economic constraints, we were down to four renderers in the whole state. There are a lot of parts of California wherever the animal dies you cannot send it to rendering. Thanks to energy problems and so on, incineration is not an alternative

either.

We have a lot of covert burying, composting, things like that. We may not even have those four renderers much longer. Along with what Dr. Belay said earlier about compensation, we are to the point where the value of rendered product is so negative that farmers are having to pay dearly to get an animal taken off the farm even if they can find a renderer that will go all that way. It's not a question of banning rendering. I'm told there are states that don't have a renderer anymore. Whole states.

DR. GRAY: Yes, there are.

DR. CLIVER: It may not require a ban. It may take care of itself from that regard. I'm wondering whether the alternatives are really more salubrious.

DR. GRAY: Well, that's a very good question. We do know in some ways to be very, sort of, practical but not very pleasant about it, I mean, in some ways that is good because when animals are disposed of in ways that they can't reach either other animals or humans, it really reduces the possibility for the disease to spread.

However, we don't want to just be willy

nilly putting the stuff around the environment. One of the things that I know was going on, I don't know the details of it but I know that folks at USDA are actually looking into either alternatives to rendering or ways to encourage more rendering but in a way that those animals would be removed from the system trying to get at exactly this problem, that the value of rendered material has gone down so far it is very hard for people in a lot of parts of the country to even get dead animals off their farm.

DR. CLIVER: Well, I'm saying that to be the case in California. Hopefully none of them are susceptible but we have coyotes, cougars, and feral swine that are master recyclers and animals that aren't very, very deeply are liable to wind up recycled that way.

DR. GRAY: That's a very good point. I mean, it's something we really need to think about. Rendering does a very valuable service of removing a lot of this waste material from the system and we have to think about how we would replace that if that is not going to be an option.

Something that comes out from this that I think is actually important in the context of this feed ban issue also is that managing the risk up

stream, if you take the infectivity out of even what you think of as prohibited product, you greatly reduce the importance of -- this isn't the right way.

Compliance with the feed ban or lack of compliance is not as important if the stuff is not as infectious. This is kind of a way to beat noncompliance with the feed ban by taking the infectious material even out of prohibited product. Even if somebody does something they shouldn't, there is much less opportunity for spread. That was an observation that came out looking at these risk management options.

There are the results. You can look at them and you can compare these to the results that we got in our base case with just those 10 animals and see the difference that it made by either prohibiting rendering or implementing specified risk material ban.

Something that we spent a fair amount of time working on, frankly because we weren't comfortable in some ways with the way others had handled this, is this notion of animals who were imported into the United States from England in the 1980s.

We know that there were 334 animals that were brought in from England to the United States.