finish. Next one please.

This is the distribution of months when the first data become available. There were a number of centers that provided data beginning in October and then there were a splattering of others that provided data as time goes on. The maximum number of centers I think that we have data from at the present time or at least through the month of April is 25. Next one. Next slide.

This is the take home message, the bottom line from the data we've been collecting. Number one, there's no macro effect. The data are not sufficient to consider the possibility of minor effects or minor regional effects. Unfortunately there are a few data before and after implementation and implementation was staggered among the blood centers that were studied and there were a few seasonal effects. The next slide.

This one shows the number of red cells that were released. These are units of blood, not what was collected, but what was released for use. This is the available blood supply and the losses are already taken out here. Some of those loses I think will be discussed in a minute. These are total because O positive and O negative are almost

always in short supply everywhere. We've got those scattered on here. As you can see, there's no particular trend and most years I think there tends to be a dropoff in November, December and January, a beginning increase and here you have the March increase that is common. Next one please.

This is the inventory. These are inventories that are collected on the first and third Wednesday of each month so that they will be spot checked as they come along. I should have mentioned earlier that although there are different centers represented at each one of these points, I have normalized the data to the maximum number of centers that provided that kind of data. So there presumably reasonably comparable within the confines of ability of that kind of extrapolation. There were relatively few centers done in this area. So I'm not sure that I believe those figures and these don't show any particular trend. Next one please.

In order to try and look at the before and after, I took an average of the release for distribution of red cell products over the entire time that a particular center provided information. I then took each month as a percentage of that average so that five months before they implemented,

11 centers collected 102 percent or released for distribution 102 percent of the average for the entire period of time. The mean before was 100 percent. The mean after was 99.2 percent and I don't think that one can make much of a trend out of that. This one which looks like it may be lower represents only two centers. So I wouldn't place a lot of value on that. This information is graphed on the next slide, and although it looks as if it's going down, I think it's probably at the present point fluctuating. We'll continue to look at this as time goes on. Next one.

It was I think a year ago when this was discussed at this committee meeting. It was pointed out by one or two discussants that the apheresis platelet supply would be more effected than the whole blood supply. We are collecting data on the release of apheresis platelet products each month. These are the data normalized to 22 centers that provided the information and that information is graphed on the next slide and you can see there's really no particular trend in the available of platelets either. Actually the majority of people, as you will recall from an earlier slide, implemented the UK deferral in March. So we may not

have seen the entire effect of it yet. I think that's the last one. Thank you.

DR. BROWN: Continuing this same subject, Marian Sullivan will now tell us about the effect of UK deferral data on the blood supply.

DR. SULLIVAN: Good afternoon. As you heard from Dr. McCurdy, the National Blood Data Resource Center in cooperation with the National Heart, Lung and Blood Institute recently began the collection of monthly data from a sample of U.S. Blood Centers primarily to allow the timely monitoring of the blood supply.

In addition to the supply related information that we're collecting for NHLBI, we recognized a well-timed opportunity to capture data regarding the deferral of donors with a history of travel to or residence in the UK immediately following implementation and over time. These are the data that I will present today.

In addition, 26 Blood Centers, an enhanced stratified random sample of U.S. Blood Centers were invited to participate with modest compensation. The sample is representative of all Blood Centers which collect at least 25,000 units of whole blood annually. Despite the size of the

sample, it represents 34 percent of national monthly Blood Center whole blood collections. Operational data submitted monthly to the NBDRC by the 10th day of the subsequent month and at this point, the data base covers the period from October 1999 through April 2000.

This slide illustrates the catchment or collection area for all of the Centers in the sample.

To further characterize the sample with respect to the percent of first time donors, the median is 19.7 which is just below the national average and the range extends from six to 55 percent. And the median of the donation interval between donations for repeat whole blood donors is 180 days or two donations per year.

This graph illustrates the distribution of the month of implementation of the UK travel deferral for the 26 Centers in the sample. As you can see, although there are a few Centers implemented immediately after the recommendation in August of last year, more than 50 percent implemented in either March or April of this year.

The cumulative deferrals for the sample are shown on this slide building from a total of 286

in October to a total of 2,500 exactly, not rounded, by the end of April.

The UK deferral data that we have collected thus far represent 57 total Center months of deferral. For example, if Center A reported referral data for four months and Center B for six months, together they total 10 Center months of deferral.

The total number of donors deferred as we saw is 2,500. The total whole blood collections for the 57 Center months for which we have deferral data were 746,433. If we calculate deferrals as a percent of whole blood collections overall, we come up with a 0.33 percent and this ranged between Centers from a low of 0.4 percent to a maximum of 0.95 percent.

The Blood Centers were asked to provide a breakdown of deferred donors by whole blood versus apheresis. Only 11 of the Centers has managed to do this. Of the 2,500 deferrals, 1,290 were whole blood donors, 57 were apheresis donors, primarily platelet apheresis we can assume and the remaining 1,153 were unspecified and will be treated as whole blood donors in this analysis.

Similarly, only 11 of the Centers were

able to distinguish first time from repeat donors. Of the 1,290 whole blood donors deferred, 425 were reported as first time, 865 is repeat and again 1,153 were not specified and will be treated as first time donors in the analysis.

We prepared a geographic analysis of deferrals overall by collapsing some of the U.S. Public Health Service regions, the standard breakdown of the 10 regions. We have collapsed the New England and Mid-Atlantic Region to create a Northeast Region with an overall deferral rate of 0.31 percent. The Mid-Atlantic region has been untouched and has an overall rate of 0.41 percent. East North Central and West North Central were collapsed, have the lowest rate, 0.13 percent. Similarly, East South Central and West South Central, the combined rate 0.48 percent and the Pacific and Mountain areas combined have a deferral percentage of 0.29 percent.

The only difference between regions that's statistically significant, between the Northeast and the South Central, the pi of 0.3, but there are a lot of factors that can affect this and probably best not to read too much into that. Okay.

The monthly deferral for each Center

will vary somewhat with the time elapsed post implementation. Plotted on this slide are the donors deferred per 1,000 donations for the first 30 days post implementation, the next 30 days and so on. This pattern will continue to develop as many of the centers have only just completed the one or two months of deferral and will be influenced strongly by first time donor rates at the centers as well as other factors.

I have made an approximation of the minimum number of components lost annually as a result of the deferral of just these 2500 donors. the 57 apheresis donors would be expected to donate and average of 12 times per cent and on the average, each platelet apheresis unit provides the equivalent of six units of platelet concentrates resulting in 4,104 platelet units.

865 repeat whole blood donors that date on an average for our sample twice per year times 1.8 components processed from each whole blood unit. Now this factor is based on our 1997 database from the Nationwide Blood Bank and Utilization Survey and it's a little lower than what is typically given, but it may be a little low for many of the individual Blood Centers, but overall, the national

average I believe that 1.8 is the more accurate factor to use here. So that's 1.8 components processed from each whole blood unit, would yield 3,114 components.

First time donors at a minimum, if they're successful may donate only once resulting in 765 component units from the 425 donors.

And the unspecified donors we have to assume are first time whole blood donors would yield at least 2,075 additional components for a minimum total number of components lost before laboratory screening of 10,058. This would be about 1.2 percent of the total number of components expected to be generated annually by this sample of Blood Centers. That would be about 8.5 million components absent any additional deferrals that these Centers will experience over the remainder of deferral year one.

Okay. Just as there were limitations on the REDS survey data that had been presented to estimate potential deferral loss, so too there are limitations on the actual on-site deferral data that I have presented. Most importantly there has been to my knowledge no assessment of self-deferrals which are likely to be considerable given the media

attention to this issue and preinterview materials and even letters distributed by many Blood Centers.

The breakdown of total deferred donors for apheresis and repeat whole blood donors is incomplete and may result in an underestimate of product loss. And our Blood Center sample may not be representative of other U.S. Blood Centers with respect to this particular donor characteristic.

In conclusion, we've seen a total of 2,500 donors were deferred at 26 Blood Centers between October and April, that repeat donors account for two-thirds of whole blood donors deferred and we suggest that the discrepancy between expected and actual on-site deferrals may indicate the substantial self-deferral is occurring.

I'd like to acknowledge those individuals who are contributing to the collection and analysis of the monthly monitoring data from the NBDRC, the NHLBI and at all of the participating Blood Centers in the sample. Thank you.

DR. BROWN: Thank you very much, Marian. We have now come to that moment when the grand public has an opportunity to comment, and we have at least four individuals, two are deferred from an earlier time period. So perhaps we can hear from

them in turn now. Either Kay Gregory or Dr. Christopher Healey, whoever wishes to speak first.

MS. GREGORY: Thank you. Let me tell you first a little bit about the American Association of Blood Banks. It's a professional society for over 9,000 individuals involved in blood banking and transfusion management and represents roughly 2,200 institutional members, including community and Red Cross blood collection centers, hospital based blood banks, and transfusion services as they collect, process, distribute, and transfuse blood and blood components and hematopoietic stem cells. Our members are responsible for virtually all of the blood collected and more than 80 percent of the blood transfused in this country. For over 50 years, the AABB's highest priority has been to maintain and enhance the safety and availability of the nation's blood supply.

The AABB is grateful for the attention of the FDA and the TSE Advisory Committee on this issue. We have few formal comments to make at this juncture, having clearly stated in the past our position on the issue of deferral of donors for potential BSE exposure.

You have just heard the report from the

National Blood Data Resource Center on the effect of the current UK deferral on the national blood supply. We would like to reiterate the limitations of this data which NBDRC has already stated. We believe that substantial self-deferral is not reflected and will never be reflected in the deferral statistics.

Pre-implementation publicity was significant. Also m any centers provided written materials or displayed posters to apprise potential donors of the new deferral criteria before they even registered to donate. Some centers even sent out letters to inform donors of the new deferral criteria so they would not make an unnecessary trip to donate.

Finally, many centers did not implement the deferral until April and donors who donated prior to April will not be reflected in the deferral statistics until they return to try and donate. The recorded rates of deferral which Marian has discussed should be understood in this context. We also remind the Committee that a number of donor deferrals does not equate to the number of units of blood. The survey data suggests a disproportionate loss of frequent repeat donors in the recorded

deferrals which only amplifies produce loss particularly for platelet apheresis.

Tomorrow you're going to be discussing leukoreductions. So I just want to say just a word about that. Sorry, I got ahead of myself.

A recommendation for deferral of donors from other BSE endemic countries with lower incidence and prevalence of BSE than the UK, will necessarily further shrink a marginal blood supply and complicate the donor screening process. Although it is not possible to predict the effect nationwide, we do know that extension of the deferral can have dire consequences on the adequacy of the blood supply in the New York metropolitan area. The New York Blood Center, for example, collects 150,000 red blood cells a year from sites under their FDA license but the sites are located in Holland, Switzerland and Germany.

Now let me go on to talk for just a second about leukoreduction. With regard to protection of the blood supply from TSEs using leukoreduction, the data are inadequate to assess effectiveness. Since, however, universal leukoreduction is the stated goal of the FDA for other reasons, the issue is moot from an operational

standpoint for blood collection facilities and transfusion services. However, we request the Committee, if you find the argument for leukoreduction for this indication to be credible, to communicate formally this opinion to the Health Care Financing Administration as further justification for upward adjustment of blood intensive reimbursement rates so that universal leukoreduction does not represent an unfunded FDA mandate. Thank you.

DR. BROWN: Thank you, Dr. Healey, and now Kay Gregory please. That was Kay Gregory. Now Dr. Healey please.

MR. HEALEY: Thank you for the opportunity to address you and I appreciate the title of doctor. However, I am not a doctor but thank you.

My name is Chris Healey and I'm the Director of Government Affairs for ABRA. ABRA is the trade association and standard sitting organization for the source plasma collection industry. ABRA represents almost 400 plasma collection companies or plasma collection centers across the country and responsible for almost 10 million liters of plasma collection in the U.S. each

year.

Back in February of 1999, we did a quick donor survey to try and get our hands around what the impact of the UK donor deferral may be and you see the data here from this slide. Almost 2,000 donors were surveyed at 12 centers. Almost four percent indicated that they traveled to the UK since 1980 and almost one percent had said they spent six months or longer there. The reasons as you see here are primarily military duty and some leisure travel as well.

After doing this impact assessment, we went back and tried to see what the actual impact was and we had some preliminary new data. If you'd put the next slide please.

We went to two companies who implemented the UK deferral early on. One company, AUC implemented it back in October and Company B implemented in January. Although they are only two companies, they represent more than a quarter of all the collection centers across the country, Company A having 50 collection centers that contributed to these data, and Company B having 67. Company A was able to get some estimate of the potential new donor loss as a result of the UK deferral criteria and

they estimated that to be about 8.5 percent. Some of the factors that go into this 8.5 percent are those that Marian Sullivan mentioned and Kay Gregory mentioned as well, a lot of self-deferral. A number of source plasma donors are actually telephoned screened before coming in. So there's a substantial new donor loss there as well. So we know it's in this neighborhood but this is not a hard number if you will.

Since implementing in October, Company A had 132 qualified donors, that is repeat donors, that were deferred on the basis of the UK deferral and 6,000 units or prior donations of source plasma was implicated from those donors. So you see an average of 45 units implicated per deferral. What's striking to me about this slide is that Company B had a substantial similar experience with an average of 40 units per deferral. They had 22 qualified donors at 67 centers that were deferred. Next slide please.

So based on those numbers of units implicated in the deferral, we tried to estimate what the total loss of donations may be. This is meant only to be a range. So some of the assumptions we made here are the 40 to 45 units per

deferral or per donor, roughly .5 to 1 percent of new donor loss. That's based roughly on the .85 percent estimate in new donor loss in the previous overhead. And then we've estimated that there are approximately 500,000 to 1,000,000 new donors each year, that some donors retire their donation history, their donation life and we get new donors on. So based on those assumptions and the prior data, you can see that the lost donations per year are estimated to be 100,000 to 500,000 and based on our total collections, we see a loss estimate of 1 to 4.5 percent as a result of the UK deferral. Next overhead.

To put this in a little bit of context, here's some of the other factors impacting source plasma supply. We've seen overall a seven percent loss of new donors from '97 to '99. That's a surrogate estimate based on use of a deferral registry that ABRA maintains and it's used to check new donors for prior deferrals. So we've seen this trend there. In addition, we've seen collections down almost 10 percent and Dr. Epstein was kind enough to tell me it's actually nine percent from 11 million in 1998 to 10 million in 1999. Some of the reasons they gave were not enough time in scheduling

and the length of the process which are issues unrelated to what's before the Committee, but I wanted to put the donation loss into context here.

That's it. Thank you.

DR. BROWN: Thank you very much, Mr. Healey. I think we have two doctors who are now scheduled and both from Canada, excuse me, one from Canada and one from Quebec. The first is Dr. JoAnne Chiavetta from Canadian Blood, I don't know what the S stands for here, but in any case, she is the Canadian representative from perhaps it's the Canadian Blood Services. Is that close?

DR. CHIAVETTA: Yes. I'm JoAnne Chiavetta, and my talk will be in English. Basically Hema-Quebec and CBS, we did our surveys just as you all did in the U.S., and I'll tell you a little bit about what we find in our deferrals. Okay. Next slide. I've just got a few words on each.

Basically in CBS, we surveyed 8,000 donors. We have 21.8 percent of our donors say that they had been in the UK since 1980. Very similar to the REDS study, we found that there were 2.5 percent who reported in the survey now, reported more than six months in the UK. So we calculated our loss

based on the survey and we would lose about 17,000 units from the 700,000 that we collect each year. Next please.

So we did a few things to try to minimize what we expected to be quite a loss. We sent a letter to all donors telling them about the UK travel deferral and its implementation and we set up a toll free number. Next please. Sorry.

And then after we did that we began the deferral on September 30th. The criteria was a cumulative time of six months or more in any UK country since 1980. Next.

And then we got about 900 or so calls as a result of that letter, and as it happened, of those people, we actually got 5,000 calls but I won't go into that because lots of donors called to find out how they could get their donor card, but anyway, when we took the calls that were regarding the CJD criteria, we actually had to defer 79 percent of those that called in because they did indeed understand the deferral and were not eligible to donate at all. And then during our first month of implementation, just very similar to REDS, we found that only 1.3 percent of the donors that finally showed up were deferred based on their

travel history. And our deferral rate has dropped steadily to 0.2 percent by the end of April of this year. Now obviously people are self-deferring. Next please.

We found also, not like our survey, this proves my survey wrong and that's not so good, but we found that the deferrals in the clinic were higher .65 percent of first time donors, whereas in the survey we found that there was a much higher rate of long term donors that would have been deferred. We think, of course, that this is due to self-deferral. Next please.

We basically ended up with 1/12 of the donor loss that we estimate but the big problem is that we're worried that not only your people who should not donate not coming back, but people that may, you know, may imagine that they're not eligible based on the UK think or are annoyed at us about the UK thing, and we're beginning a survey. Next please.

We're beginning a survey where we can actually look at that, where we're contacting donors who have lapsed since the deferral survey by phone and asking them some questions. I don't have those results yet, but this is for Hema-Quebec.

They also implemented their survey on the 30th of September, and their deferral was a little more stringent than ours. Their deferral is cumulative time of 30 days since 1980. Each of our services try to salvage as much blood as possible in our deferral and as it happens, their numbers allow them to only lose what they hoped wouldn't be anymore than three percent with a 30 day deferral, whereas we had to go all the way to six months to achieve that. Slightly less than three percent I meant to say.

Okay. So there were three percent of donors in their survey, and during the first month, a third of that were actually deferred for UK travel, and as in CBS and in the U.S., that rate is dropping and, of course, this suggests that people are self-deferring. Last slide.

So basically the only concern we have is that we are losing people because of misunderstandings and the only way we can find that out is through the surveillance or the survey that I mentioned to you to find out what's happening to our lapsed donors and hopefully the right people are saying I won't donate and the right people are saying I will continue. That's all I have to say.

DR. BROWN: Thank you, Dr. Chiavetta. Dr. Marc Germain from Hema-Quebec.

DR. GERMAIN: Thank you, Dr. Brown, and good afternoon. My name is Marc Germain, and yes, I'm a French Canadian, but this is only a statement about my ethnic background, not a political statement whatsoever.

I am the co-director of Microbiology and Epidemiology at Hema-Quebec and today I'm speaking on behalf of both the Canadian Blood Services and Hema-Quebec which are the two blood operators in Canada. What I would like to do is to try and explain very briefly the way in which the Canadian transfusion ad agency have tried to assess the exposure of Canadian blood donors to beef products originating from the UK but consumed elsewhere, that's outside of the UK. Obviously this is in the context of the evolving variant CJD epidemic and particular with regards to the increasing number of cases in France.

When the decision was made to apply the deferral criterium for donors who traveled to the UK, it was assumed that the potential exposure to BSE was mostly confined to the UK territory simply because that's where the bulk of the cases of BSE

had occurred. However, we were all aware that this assumption was not totally accurate and that's because untold quantities of beef and beef products had been exports from the UK prior to the ban in 1996. However, at that time, no good data existed to substantiate the level of exposure to UK beef in other European countries. If I could have the first overhead.

Now since then, we've had access to data that could help us to define this potential exposure. This is the data regarding UK exports and obviously the data can be far more detailed than that but for the sake of simplicity, I'm only showing the number of live bovine exports for the time period mentioned there. And these countries represents 95 percent of the total UK exports during that period and Dr. Will went over that material this morning. So I won't take too much time. But that did not say much about the actual relative exposure to British beef in each of these countries and until very recently, we didn't have any way to figure out what that exposure could have been but that's until the French authorities very recently released some information and some information that you heard this morning actually, to the effect that

prior to the embargo about between five to 10 percent of the beef and beef products eaten in France came from the UK and it seems that this information is pretty reliable since it came from two different sources within the French government.

Now obviously other countries also imported UK beef and we do not know exactly the extent to which these beef products contributed to the overall beef consumption in these countries. If I could have the next overhead please.

Now what we try to do is to roughly estimate this simply by extrapolating the combined data from the UK exports and also the French data on internal consumption of these products in trying to assess the potential exposure in these other countries. And what we determined is that France and the Netherlands are the two countries where the most important potential exposure to UK beef might have occurred. You recognize the five to 10 percent figure here for France and for the Netherlands, we estimate that it may be as high as 17 percent.

Now in our analysis we kept only these two countries, the Netherlands and France, because they represented the most significant potential exposure to UK beef and also taken together these

countries would represent approximately 80 percent of the total beef exports from the UK.

Using the information from the surveys that we conducted in early '99, both by CBS and Hema-Quebec and that you heard about on blood donor travel habits, we then tried to evaluate the impact of various deferral criteria, on one hand the number of donors that would be lost because of these criteria and also the reduction in the overall burden of exposure of our donors to beef and beef products.

Now obviously the scenarios can be quite varied because now we have three countries to look at simultaneously and you'll see the possibility of these are quite varied a little bit later. And as is true with all of these analyses, we have to make quite a number of assumptions and I don't have time to go through all of them, but let me point out maybe the two most important ones if I could have the next overhead.

First we assumed, and this is number five here, we assumed that the risk of acquiring vCJD in a country exposed to UK beef, and that's not new, is directly proportional to the amount of time spent in that country but it is also discounted by a

favor which corresponds to the proportion of the total beef consumption that was of UK origin. Now just to give you an example, someone who visited France for a duration of 10 months would be considered to have a risk which is equivalent to someone who visited the UK for one month.

Now another important assumption was that the contribution of homegrown if you wish or indigenous BSE in countries other than the UK was considered to be negligible. Now this is not to say that indigenous BSE does not pose any risk at all, but it's just to recognized the fact that in comparison with beef from the UK origin, that this contribution was minimal. So we didn't include that in the analysis, and I'll let you read the other assumptions which are quite self-explanatory. Next overhead please.

Now I don't have time to go through these details of this analysis and basically it's the same procedure that you were told about regarding the American data. I must point out that in our survey, we had detailed information on each of the countries that we decided to look at. In other words, we knew for a given donor the duration of time spent in each of these countries for the

period at risk.

Now I think it's important to point out some interesting features on this analysis. First, the current deferral of criteria, and this is one month for Hema-Quebec and six months for CBS, both achieve a reduction in the total burden of exposure which is in the order of 65 percent. It's about the same. It's almost by chance I should say. It really depends on which criterium we chose and the travel habits of our respective donor population. And that's not something new is the fact that the impact of any given criterium very much depends on the travel habits of the population to which it is applied. For example, in Quebec, if we were to add to our current deferral criterium the criteria that people who had traveled to France for six months or more would be deferred, this would affect approximately an additional two percent of our donors and this is listed here, two percent of our donors and it would reduce the total burden of exposure to UK beef by almost 20 percent which is negligible whereas the same criteria for CBS would only affect half a percent of donors but at the same time the burden of exposure would be reduced by less than two percent.

Now finally I'd like to remind you that these numbers are at best rough approximations. They're based on numerous assumptions. However, I think they could provide some basis to help in the decision on any specific course of action with regards to the evolving nvCJD situation.

In the end, any decision to upgrade the current criterium will depend on obviously several factors including the impact on exposure reduction but more importantly I guess on the capacity of each blood agency to compensate for yet another loss of donors and as JoAnne Chiavetta explained to you earlier, I think it's important to remind everyone that one of the guiding principals in the decision to defer donors at risk for BSE exposure was to try to minimize other potential and quite real risks in the face of a purely theoretical risk and one of these real risks being the shortage of blood. That's all. I want to thank you.

DR. BROWN: Thank you very much. That actually concludes the -- yes, there's a question from the floor or a comment. Paul Holland.

DR. HOLLAND: Thank you. Paul Holland, Sacramento Blood Center. I didn't realize you had to sign up to speak in the open session. I wanted

to make two quick comments and a suggestion.

As you've seen, at least I felt reassured by the data today that there is not a great deal of increased theoretical risk that is going to be helped by deferring more donors from other European countries and the United Kingdom. Contrary to the numbers, I can tell you from a regional blood center that traditionally has an excess of donors and we actually help many other centers and having put the UK deferral or UK deferral criteria into place on April 17th, the last possible moment, we are struggling to maintain our area blood supply and are having trouble helping other people.

But if you do decide to make some additional recommendations to the FDA regarding additional deferrals because of people who have been to Europe and have been exposed to BSE in those countries, either from their cattle or from British beef products, then I would recommend or suggest that you ask our FDA, our Department of Agriculture and our Fish and Wildlife Service to get together and work out what I've called the BBME scale to be supplemented by the USVME scale. BBME stands for the British Beef Monthly Equivalents and we work out

a system whereby we calculate for each country and for a period of time, the risk of exposure to British beef or BSE in those cattle, but we should also supplement this with the US Venison Monthly Equivalent scale because of the chronic wasting disease in our elk and deer.

My point is, this is going to become very complex. We are asking important serious questions of our donors regarding risk of AIDS and Hepatitis and to dilute that important thing with now asking about other travel history in other countries and trying to figure out some measure or risk theoretical which we're going to diminish by deferring them, and potentially impacting our blood supply, I urge you not to make further recommendations regarding deferring more donors for this theoretical risk because of travel to other countries which have far less theoretical risk from their own cattle or from British beef than from the impact of the UK deferral. Thank you.

DR. BROWN: Thank you, Mr. Holland. Are there any other comments from the public?

In that case, we have about 15 minutes for discussion before the break and then following the break, we have about an hour for further

discussion and vote.

If you've looked at the sheet, there are about 20 questions we've been asked to respond to, and therefore what I would like to do after, well, perhaps the next 15 minutes we can use for general questions if there are any, and then what I'd like to do is limit the discussion to each of the three questions and vote on each of these three questions after a short discussion focused on those questions. So that what we'll do now is if you have any questions at all, now is the time to ask them. We'll have the break, we'll come back and then we'll have further discussion and voting as a integrated procedure rather than just 40 minutes of discussion and then taking votes on question after question after question.

Any questions from the Committee about anything they've heard today? Yes.

DR. KATZ: Yeah. Paul, you might be the best person to answer this, but one of the linchpins of risk assessment that we're all engaged in mentally here is the incubation period, variant CJD. The cases that have been reported to date are all in 129 homozygotes and is there not animal data that would suggest that heterozygotes or other

polymorphisms at that site might change the incubation period? I'm trying to get at, is there any way that we can take any solace in the apparently flat epidemic curve in Great Britain?

DR. BROWN: I'm not sure I'm the best person to answer it. If I say bad things, Bob Will can correct me. There is evidence, a lot of evidence to indicate that incubation periods in both naturally or iatrogenically acquired and acquired CJD are shortened by codon 129 homozygosity. The fact that 100 percent of patients with new-variant disease tested have all had a homozygote codon 129, to me is the single most distressing fact about the entire outbreak. It could be good news but it could also be very bad news. The good news would be if only homozygote genotypes were susceptible. In that case at a minimum half the British population will survive.

On the other hand, I doubt that there's going to be an absolute block in the infection by BSE based on homozygosity and that in due time we may see heterozygotes and the troubling matter is that if homozygotes in BSE and new-variant truly are the short incubation period subset, we therefore might be looking at an extensive and large epidemic

when the heterozygotes begin to kick in. And that's just a plain old fashioned unknown. Bob, you agree that those are the options and we really can't predict.

DR. WILL: (Nods.)

DR. BROWN: Yes. Linda.

DR. DETWILER: I was just going to give an example on sheet, and again I know in cross species you don't always have the same rules that apply, but a codon 136, you do have incubation influence with the valene homozygotes being usually shorter incubation, allonene homozygotes being longer, and the heterozygotes being in the middle. However, at 171 it appears that arginine homozygotes, right now there's only been one reported in the world and that was in Japan. And so in the sheep model, again if you're arginine homozygote at 171, it appears to at least preclude, you know, stops clinical disease.

DR. BROWN: Bob.

DR. WILL: Am I allowed to ask an unrelated question?

DR. BROWN: As our guest, yes.

DR. WILL: Thank you. I'm interested in what the last two or three speakers were saying

about the disadvantages of deferring donors in relation to loss of blood supply, but one other last issue I think presumably must occur is that if you are a blood donor and you're told you're no longer allowed to donate because of the risk of new-variant CJD, there's a possibility that that might cause a great deal of concern to such individuals, and I wonder if any of these surveys there's evidence that the donor population have been caused anxiety and whether there's been any evidence of depression or anything of that sort in this particular population. I think it's an important consideration.

DR. BROWN: Yeah, I'm sure the answer is yes, but you will want to verify that from the floor.

DR. CHIAVETTA: I don't know about everywhere else, but I do know that we certainly have not had instance of that. Our nursing department is very good about that. The other thing that I didn't report on and I'm not completely done with the analysis, but we did focused interviews and that's a half interview on blood donors. Now mind you these are blood donors--that have come in, but this was before the vCJD survey, and there really was minimal concern for themselves plus the fact

that 40 percent of our blood donors believed we already tested for CJD. So I don't know whether we're just dumb in the west of Canada, but whether that would be true in Quebec. I don't know, but in fact, we were very shocked at that.

There is an analogy for this and that, of course, is HIV and I think there's a variety of experiences with HIV across the country. I don't really know what happens in the U.S. I've been in blood banking for 16 years and I just don't understand why people don't seem to get more concerned, but I've done, I can't tell you how many surveys over the years, and I've never really seen significant amounts of that in people that are generally healthy otherwise.

DR. GIULIVI: I could answer from the surveillance of the CJD from Canada and from the connections that we've put in with the Public Health from the federal and the provincial about Canada in concern. There was an increase of psychological consults in Canada, not that much, about one percent more. There was an increase of neurological consultations due to our surveillance because the calls came to us and then we had to refer them to neurologists, about three percent over the overall,

and the calls that we got in Health Canada, we got about 30,000 calls and we had to screen them and their concern was not the donation of blood, but the concern of eating the beef and their coming down with the disease and we had to explain that.

DR. LEITMAN: I'm the Medical Director of a smaller donor center. We have a population of 2500 whole blood donors and 1500 platelet apheresis donors. We implemented April 17th, and we deferred 17 so far, three platelet apheresis and 14 whole blood donors. The majority were quite distressed. They asked to speak to the Medical Director or another physician in at least half the cases and I spoke to numerous numbers of at least seven or eight of such donors, and I finally had to explain that as a perception of increased safety, an unmeasurable gesture almost on the part of advisory committees of the appearance of increased safety because there was no documented risk, just a theoretical risk, but presenting actual data was just too hard for them to understand. But it's quite distressing.

DR. BROWN: Yes, in my experience the most typical reaction is anger. They get furious, rather than depressed.

DR. LEITMAN: We direct that at the FDA

and then they understand.

DR. BROWN: Other questions?

DR. SAYERS: Yes. Paul, I'd like to follow up on that one too. The reactions, and I'm almost reluctant to talk about this because in a quasi scientific group here, it's difficult to talk about issues that don't have units and measurements. But when you speak to donors that have been deferred, I agree with Susan. Their response, and we had 215 individuals deferred so far, in the first five there were two individuals who had been them donated 250 apheresis platelets during their donation history, but the gambit of the experience ran from dismay to duration. So the point that you made was one that was well taken, and I think we're inclined to forget when we talk about the table here, the donor deferral for some individuals becomes a socially stigmatizing event because donor deferral is associated with Hepatitis, with HIV and it's not associated with tourism, and the individuals who try and explain to their spouses that they have been permanently deferred are often at a difficult point in being able to say something sensible because we cannot in return answer their question with confidence when the pose the question,

"Well, why am I deferred and what is the risk for my sexual partner? What should I tell my physician? What should I be telling my dentist? How can I get tested? What is my prognosis?" I don't think we should lose sight of that when we're trying to enhance safety. We can't be doing it even at the risk of further alienating individuals who originally came to blood programs intent on exercising their altruism.

DR. BROWN: Yeah, thank you, Merlin.

DR. KATZ: Paul.

DR. BROWN: Yes.

DR. KATZ: On the theory that enough anecdotes make data --

DR. BROWN: I just wanted to say, Merlin, this is a fully scientific group, not quasi.

DR. SAYERS: What category does that fall into, Paul?

DR. KATZ: My experience is with about 100 deferrals for this now. Ours is essentially identical to what Susan describes. I think there are a few depressed people. There is a large plurality of extraordinary confused individuals and a quarter that are just flat mad. There is not truth to the rumor that I've given Jay Epstein's

phone number and e-mail address, however. The only thing that I found more difficult in, I don't know, 15, 18 years in blood banking, is explaining an HIV false positive is harder, but that's the only thing.

DR. BROWN: Yeah, this touches on the phenomenon or the issue that comes up time and time and time and time again, for this kind of deferral, for another kind of deferral, for anything that goes on in our field, it's always involved in a process of continuing education and in time, people do understand that decisions are made because we can afford to make them or their conservative to a point where they're not necessarily realistic but we find that the trade off warrants the precautions, but it certainly doesn't happen overnight and it requires just constant explanation and education. Yes.

DR. HOLLAND: Yes, Paul Holland. Just to echo it another way, you're trying to reassure these people that they're really okay, and they're not at risk. They're not to worry about this, but you can't donate blood. Well, that's a very mixed message, and they go away, angry, upset, frustrated, disappointed, and there's this lingering doubt in their mind. There must be something wrong with me. Otherwise, they would let me donate blood, and it's

very hard to dispel that in these people because they cannot donate blood. In fact, you've told them they permanently are out, but don't worry about it, you're really okay.

DR. BROWN: One way I guess that you could mollify this is to point out and emphasize the fact that this very likely to be temporary and that we're not sure what's going on, but we're trying to be as safe as we possibly can and maybe in four months or eight months when the situation shakes out, everything's going to be okay again. And that's true. That's not lying to them. That's telling them exactly what's going on.

DR. HOLLAND: Yes, but we use the polite term here deferred. The real term is rejected and these people whether you reject them for four months or eight months, it's very difficult to get them back. You've rejected them.

DR. BROWN: Well, yeah.

DR. HOLLAND: And do we really have hope in four months or eight months that this is going to turn around. I doubt it.

DR. BROWN: I don't know about getting them back, but my definition of deferred is temporary rejection.

DR. LURIE: I'm not somebody who is in the position of having to relay this message to anybody, but I will make two observations. One is that the fraction of people who will defer, will be rejected, will decline over time because there's an end on it, 1996, and you can't continue to accumulate years of travel from now on out. So as people get older, the fraction of people affected by this will go down from 2.2 percent. That's a maximum estimate.

Second is that inevitably any problems on a sort of psychological behavioral level that are encountered will be worse right now, where people are coming for the first time and encountering this new regulation for the first time, and over time, people will be better educated and it will become less of a problem.

DR. BROWN: Yes. Go ahead.

DR. EWENSTEIN: Well, let me make a comment about the current discussion and then ask a question of Dr. Giulivi. You know if they weren't blood donors and they just came to our medical office with this question, I'm not sure what we would tell them. I mean we've posed this in sort of, you know, here's this poor altruistic donor. If

you're a resident of the UK, right now you're still living with a lot of uncertainty. This epidemic may be flat. This epidemic may explode. I don't know what a physician or a psychiatrist is telling his patient in the UK right now about how much to worry.

Now you have a patient or a donor in the United States who has a fraction of that risk but it's a measurable fraction of that risk as best we can tell. He's lived there 10 years, not 20 years. You know, to tell that person you have absolutely nothing to worry about, that epidemic in the UK has nothing to do with your 10 year visit, may be just as disingenuous as anything else we can tell them until we know more about the scope of the epidemic. So it's really not a donor deferral questions. It's what do you tell people in the UK and who have been in the UK for a long time. If we knew what to tell them, we would be much clearer about what to tell our donors.

The question I had which is not totally off the track, for Dr. Giulivi, was whether there was any sensitivity analysis done on those projections? Obviously there must have been some. There were a lot of hypotheses, a lot of variables, obviously built into the model, and I was wondering

if you could identify for us where the greatest impact or what variables would have the greatest impact on those graphs that you showed us particularly the ones that showed the probability of acquiring disease based on length of stay in various countries.

DR. BROWN: Tony, your response will conclude this discussion.

DR. GIULIVI: Sure. Yes. Sensitivity by using the Monte Carlo Analysis and the most sensitive one was the amount of beef imported to a country, the assumption, you know, how much was imported and how much, you know, the amount of beef contamination, how much will that express into exposures. Okay. That was the most sensitive. The second one was the variant CJD, you know, the incidence that we used as a proxy in the 60 cases divided by the population and we did analysis there. That was the second variable that was more sensitive.

DR. EWENSTEIN: Are you saying that the number, because it's almost a straight line.

DR. GIULIVI: But it humps. The way you saw it, it humps and then it goes that way, okay. That's the way the graph is just done.

DR. EWENSTEIN: At about two years it was about 10 to the minus five.

DR. GIULIVI: That's right.

DR. EWENSTEIN: That's right. So at 20 years it would only be 20 to the minus four which would be sort of the entire exposure period --

DR. GIULIVI: Right.

DR. EWENSTEIN: -- for a UK resident. So obviously this model is sort of centered around a total risk for a UK resident of 10 to the minus four.

DR. GIULIVI: You could look at it that way, yeah.

DR. EWENSTEIN: So I'm wondering, you know, sort of off of that, you know, what other things that you have to hypothesize about, for example, the incubation period --

DR. GIULIVI: Yeah, we ignored that. Remember that? We just said that anybody that was exposed who will come down with the disease, that's how we went around that and it was a big discussion and when we presented this to our Advisory Committee TSE over that issue and, you know, it took about two hours to express what we have done there.

DR. BROWN: Thank you, Tony. We'll now

break for 15 minutes, and I will reconvene at five minutes past 4:00 sharp.

(Whereupon, the foregoing matter went off the record at 3:46 p.m. and went back on the record at 4:03 p.m.)

DR. BROWN: We'll reconvene now and Dr. David Asher will read the first question which the Committee is going to design. Can we all reconvene please? Dr. Asher.

DR. ASHER: Thanks, Paul. I won't reiterate the full charge, but I just want to remind the Committee that the most important thing that we'd like to do is to entertain advice on whether the FDA deferral policy should change, and in so doing, we ask you to compare the risk from people incubating new-variant CJD because of residence in the UK with that risk for people who are resident in France and other BSE countries recognizing that in the past we have realized that there's no possibility of achieving a zero risk and we don't expect that now.

Finally, we ask you to consider any policy change in the context of the risk that that change in policy would have, that is the loss of product, potential loss of product and the loss of

repeat donors with its potential benefit. We do ask that you keep the implications for the blood supply in mind.

That having been said, we can turn on the overheads and I'll read the questions one by one.

Question 1: Do the Committee members believe that available scientific data on the risk of transmitting CJD and new-variant CJD warrant a change in the current FDA policy regarding deferrals of blood and plasma donors and product retrievals? And we ask you to comment on this. Thank you.

DR. BROWN: On this first question, the vote when it comes, a yes vote will indicate that the Committee believes a change is warranted, and a no vote will leave the present policy intact.

What I would like to do now is to let you know how I'd like the votes to be made in terms of format, and I use as a precedent the U.S. Congress. We can discuss and you can justify what you are going to do because you probably already know what you're going to do in advance of the vote. The vote itself, there are so many questions that the votes themselves will be a strictly yes, no or abstain. There will be no discussion for your vote

at the time of your vote and I will call your name and you will vote and I will reiterate how you voted. So the first vote is up now for discussion. Not a vote. If there is discussion before we vote on this question, we should do it now. Yes, Susan.

DR. LEITMAN: First, I want to thank the FDA for revisiting this on a yearly or more often basis and giving us the opportunity to answer exactly this question. I would vote yes, it is time for change but not perhaps change in the direction that is going to be indicated by the questions following the initial question.

I was very influenced this morning by Dr. Jay Epstein's comments to us to urge us to consider the marginal increase in safety, the marginal theoretic increase in safety of deferring individuals who have resided and traveled in France for any period of time based on the recent three cases and that those three cases, his discussion was very open, constitute perhaps five percent in France of the risk in the UK. So in the next year we may see three more cases and a couple of years after that we may see one case in the Netherlands based on consumption of risk material, oral consumption of risk material from Britain.

The risk to individuals who have resided in those countries, in France and the Netherlands, who have resided, who have lived, who are citizens of those countries and travel there, is much, much greater than any American who's traveled to those areas. Residing and inhabiting and again being citizen of those countries, one's risk for variant CJD is much greater than a traveler to that area because this disorder has never been reported, there's no epidemiologic data in support of a traveler being at risk in terms of disease having occurred.

So if one wants to proceed with that logically since we voted last year, the majority voted to defer individuals who have traveled, you'd have to defer individuals who are citizens of those countries because the risk is greater than that of the traveler. So the whole system is illogical. What we established last year sets the precedent for more votes that are positive to increase, to add marginal increases in safety that have overwhelming consequences to the donor population here.

My suggestion is to revisit the entire question of who should be deferred, if anybody should be deferred, for travel or residency to the

countries that we've been discussing this morning, and I have a suggestion, and I'll stop there. I know it's very long, which is that the true risk and the documented risk is in citizens of those countries who have lived there their lives or most of their lives, the youngest age being 14, I suggest that we should defer individuals who have spent 10 or greater years which means they have to had been residents of the countries we're talking about during the period from 1980 to 1996. The individuals that fit into that category will understand immediately why they're being deferred. They would not have the feelings that we've discussed at length early this morning. And I feel I could justify that, your questions says, available scientific data. I could justify that on the basis of available scientific data. I don't think I could justify anything else on that basis.

DR. SCHONBERGER: Do you mean all BSE countries?

DR. LEITMAN: I think that's open for discussion. You could sharp shoot and say UK, Netherlands and France, which I think are the highest risk, 80 percent.

DR. SCHONBERGER: Loosening for the UK?

DR. LEITMAN: Loosening, yes. Loosening for the UK to include other countries and I'm not sure, I think that's open to discussion.

DR. BROWN: The only thing I would say, Susan, is that the current policy would certainly apply to citizens. I mean they have lived there more than six months.

DR. LEITMAN: It refers to individuals who are at theoretic risk?

DR. BROWN: No, no, but I mean just in terms of clarifying travelers versus citizens, as the FDA guidance now exists, it automatically takes care of citizens. So they would be deferred because they've lived in, unless they're citizens of Great Britain and were born in an airplane.

DR. LEITMAN: No, that's true, but my new proposed deferral would capture the population that's truly at risk, the greater than 10 year.

DR. BROWN: Yeah, no, right. I just want to clarify that citizens are already excluded. Yes. Linda.

DR. DETWILER: I just had a question of Dr. Leitman because this came up during the break here. You said Netherlands and France I believe. What was that based on? Was that based on the

Canadian?

DR. LEITMAN: It was. It's also in our written materials. The French report went through that as well.

DR. DETWILER: Okay. One of the things I think that I've heard Bob say before, Bob Will, is that again the muscle meat is not what we think is the source. It's the CNS incorporated into this mixed meat and so I would caution looking at carcass beef moving on to any country as risk material. I know we did studies here and looked at products and what not, and you have things that you barely know that there's meat in it and it's all kind of mixed products, and they're the high risk material and that's very, very difficult to capture. I know just looking at the United States and trying to put all these fire walls up at the port because it's in things like spaghetti sauce. And they are the things that I think are risks but it's hard to get the data on that versus the carcass beef which probably is a lot lower risk.

DR. BROWN: Yes. Go ahead.

DR. HOLLINGER: Well, I'd like to reiterate a little bit of what Susan said. Last year I also voted no on this issue anyway and I

haven't really seen anything that's changed my mind at the present time, and I will probably vote yes for a change, but a change primarily to eliminate the deferral as I felt last year. There were two votes last year that separated this Committee from advising. Somehow I think it's nine to seven or 11 to nine, something like that, for and against.

The fact is that as I see it, the surveillance is excellent in Britain and also appears to be in France as well, and there seems to be somewhat of a lag time, and if you take the data in which there are 60 cases now in 60 million people, it's about one out of a million, and we suspect perhaps there will be more cases but even if it's one out of 300,000 and the risk then in France is five to 10 percent of that, you're looking at one out of three to six million, and then you have to tie into that, and I think the risk to people who have traveled there from the United States to Britain for six months or more, that the risk would be even much less than that and then we're talking about the theoretical risk for which there is no data that this could be transfused and associated maybe, but that's a risk that hasn't even occurred in Britain yet and which I think would precede what

one would see in the United States or perhaps even in France. So from my standpoint, I still see nothing that has changed my viewpoint, a donor deferral for six months and travel to the United States from a citizen of the United States anyway is valid.

On the other hand, I think that what Susan has said about deferring people who have lived in Britain, whether it's five years, 10 years or a period of time, it would make them more like a resident of that country seems justified.

DR. BROWN: I remind the Committee that the first question has to do only with the United Kingdom only. We're not talking in the first question about any other country than the United Kingdom. That comes up in the second question. Larry.

DR. SCHONBERGER: My recollection is that we discussed this issue for the United Kingdom in part because the United Kingdom government itself had barred its own residents from being part of the donor population for plasma products. I think it would be a poor precedent for us to change what we did last time without their being at least some more data than what I've heard that the situation in the

UK has changed markedly towards the better. It is true that last time I had voted for like a three or five year duration before we would screen, but I sensed from the rest of the Committee that they wanted to go down to a much tighter level of control. Now that we've done that, I would feel the need for something more substantial than what we've heard, to say that the situation in the UK, you know, is much better than it was when we last voted. The most important data perhaps that we had was the absence of the curve shooting up of the uppy curve in the UK but I got the sense from Bob that he doesn't take too much reassurance from that yet. It hasn't gone on long enough particularly if you look at those models. There's still a substantial maximum possibility of the numbers of cases and then the other somewhat reassuring at least was that survey of the tonsils and appendices which didn't have any positives but the data we saw from that, it still was consistent with an outbreak of as much as 150,000 people and I don't even think we were thinking of numbers that large when we voted last time for imposing this particular screening criteria. So I'm going to end up probably voting no for this particular question.

DR. BROWN: Yes.

DR. CLIVER: Requesting a clarification of the Chair's clarification. If on question one the ultimate vote is no, does that trigger a reconsideration? I mean is there an option of de-escalation as well as escalation from this? It's not clear that anything further would follow from a note vote.

DR. BROWN: That's right. A vote of no is status quo with respect to the United Kingdom.

DR. CLIVER: I'm sorry. I meant a vote of yes, does that leave the option of de-escalation? -- follow up in prospect, just yes or no?

DR. BROWN: Well, maybe the FDA would like to respond, but the question as asked allows a change of any sort.

DR. CLIVER: Yeah. Your interpretation is just the UK was the intention.

DR. BROWN: Yeah, right. But with respect to the first question, it's in either direction with respect to the UK. Forget everything else and think about the UK for this question.

DR. LEITMAN: Paul, that's not what's on the screen. If you look at the title of the screen --

DR. BROWN: Yeah, unfortunately it's not what's on the screen, but it's in the questions that are written. The question as written, and I'm sorry about the disparity, do the Committee members believe that available scientific data on the risk of vCJD warrant a change in the current FDA policy regarding deferrals of blood and plasma donors based on a history of travel or residence in the UK? Yes.

DR. LURIE: Just procedurally, it doesn't seem wholly logical to me that those of us who would like to see things weakened from the status quo should be voting in the same direction of those of us who would like to see things strengthened compared to the status quo. So I'll leave it to you to sort out but I'm not sure we should be voting in that fashion.

I think Larry's summary of the developments since the last meeting are helpful with just one exception which the data on deferrals, the donor deferral data, and what we see is that the number of in effect documented deferrals is vastly lower than what was initially predicted. Now that might be due to some self-deferral, but what that amounts to is in effect that 95 percent of deferrals were self-deferrals. I say this because there was a

predicted 2.2 percent decrease in the number of donors or the number of units I guess it was and instead we saw about .11 percent decrease in the number. So it's five percent. That amounts to five percent. 95 percent must have deferred themselves. That seems high to me. But regardless, the number that really matters is what the inventory looks like, and Dr. McCurdy had data that were relevant to that. He showed that the inventories by and large safe.

The only data that I see that are really new are reassuring data that show that what we did appears to have done no harm.

DR. BROWN: I'll make a comment also and that is I think the Committee last year, the Committee decision was a reasonable one. It was not based on any satisfactory scientific evidence for the magnitude of the potential risk. It was based on a position of maximum conservatism viewed against the context of its disadvantages and I think nothing has happened in the year since that decision was made to warrant a change. The epidemic could explode and we can reevaluate this.

In fact, I think it probably worthwhile, David, to let everyone know that there is a

committee which you have established in the FDA to reassess the situation with respect to BSE and new-variant CJD in Europe on at least a six month and I think probably a four month basis.

DR. ASHER: The FDA has made a commitment to the Surgeon General that issues both of risk and of effect on the blood supply will be revisited at least every six months, and I must say that that commitment affected the decision to convene this meeting of the TSE Advisory Committee.

I can't restrain myself from commenting that I was struck today by the fact that the single Irish case of new-variant CJD had been a resident in the United Kingdom for six years.

DR. BROWN: I'm prepared to call a vote on this first question if the Committee agrees. Susan.

DR. LEITMAN: In Larry's analysis of things that have changed and have not changed since last year, he didn't include one critical point which is documentation of transfusion transmission and lack of evidence in this case I think is substantial evidence against transmission especially in the, I'm not sure if my number is right, the six individuals who donated 30 components or something

like that, 12 of which were actually transfused and traced. It's short, a small number of data, small number of points, small number of recipients and not a very long follow up period, but again there's no evidence whatsoever of transmission through transfusion.

DR. BROWN: I agree with Susan. It's a point against. I probably don't put as much weight on it as a point against as she does, but such as it is, Bob Will himself qualified it properly. Most of the transfusions have occurred within the past three or four years. We certainly have experimental evidence from monkey experiments indicating that low level infectivity transmissions with no species barrier can take six, eight and 10 years. So I don't think the negative is really a massive argument.

DR. EWENSTEIN: Thank you for saying that. I was going to say something very similar. I don't think there's any conclusion that can be drawn from the transfusion data. I think the risk of transfusion transmission for variant CJD could be 50 percent right now looking at the data and given an invariably fatal disease. I don't think any blood banker here would accept that as a risk or it could

be zero, but I think we're exactly where we were at the last vote and I think it would not be good form in the absence of new data as quasi scientific as the last set of data might have been to change our position.

DR. BOLTON: Paul.

DR. BROWN: Yeah.

DR. BOLTON: I'd just like to say I voted against the ban, the deferral last time and if we were starting fresh, I would like to see a longer time period. Being in the position that we are now, I think it would be extremely unwise to relax the deferral conditions and then later perhaps have to come back and tighten them again. So I would vote against the change.

DR. BROWN: Let's put it to a vote. Dr. Schonberger.

DR. SCHONBERGER: No.

DR. BROWN: Dr. Detwiler.

DR. DETWILER: No.

DR. BROWN: Dr. Leitman.

DR. LEITMAN: Yes.

DR. BROWN: Dr. Lurie.

DR. LURIE: No.

DR. BROWN: Dr. Ewenstein.

DR. EWENSTEIN: No.

DR. BROWN: Dr. Belay.

DR. BELAY: No.

DR. BROWN: Dr. Tramont. I have your name written poorly here.

DR. TRAMONT: That's right.

DR. BROWN: Is it? Good. Tramont.

DR. TRAMONT: Yes.

DR. BROWN: Dr. Bolton.

DR. BOLTON: No.

DR. BROWN: Dr. Hollinger.

DR. HOLLINGER: Yes.

DR. BROWN: Dr. Brown votes no. Ms. Walker.

MS. WALKER: No.

DR. BROWN: Dr. Piccardo.

DR. PICCARDO: No.

DR. BROWN: Dr. Hoel.

DR. HOEL: No.

DR. BROWN: Dr. Burke.

DR. BURKE: No.

DR. BROWN: Dr. Cliver.

DR. CLIVER: No.

DR. BROWN: Dr. Ferguson.

DR. FERGUSON: No.

DR. BROWN: Dr. McCurdy.

DR. McCURDY: No.

DR. BROWN: Dr. McCullough.

DR. McCULLOUGH: No.

DR. BROWN: The vote is --

DR. FREAS: Two yes votes.

DR. BROWN: Sixteen no.

DR. FREAS: Three yes votes. Three yes votes.

DR. BROWN: All right. So the vote is 15 no votes and three yes --

DR. FREAS: Just for clarification of the record, Dr. Leitman voted yes, Dr. Tramont voted yes and Dr. Hollinger voted yes. Is that correct? Three yes votes.

DR. BROWN: So the Committee votes 15 to three in favor of status quo for question 1.

And now we come to the more guisy question, question 2. David. Do the following questions reflect exactly the language on the written, do you know?

DR. ASHER: To simplify the questions sometimes, one drops out important things. Considering the current scientific data on the risk of new-variant CJD and the potential impact on the

blood supply, should FDA recommend deferral from blood or plasma donation for persons with a history of travel or residence in France? And there are four contingent questions.

DR. BROWN: Let's just work on that one. So the question is does the Committee feel that any kind of deferral policy should be inaugurated with respect to residents and travelers to France, just irrespective of time of deferral. Just the question, should there be any initiative with respect to deferral? Comments, questions, yes.

DR. BURKE: My answer is no, it should not and my assessment of the data is that if there is any risk associated with living or being in France, that it is substantially less than that in the UK and it's probably on the order of magnitude of 1/20 of the risk of being in the UK during that same time period, and if we balance those benefits and risks about deferral of donors in the United States, on this one I think that we come down on this side, that there is no significant risk benefit.

DR. BROWN: Let me charge in here. I've just written out for myself and then I won't probably say anything for the rest of the meeting.

I heard that.

I think that any deferral policy based on national BSE incidence is impossibly complicated and, two, qualified by incomplete data for anybody to make any rational decisions. I think contaminated beef is responsible for new-variant CJD. I note that in France the incidence of new-variant CJD is one-tenth to one-twentieth, one-twentieth actually of what it is in the United Kingdom, and that fits perfectly the postulated exposure to imported beef from the UK which is about one-twentieth of that of the UK. If the UK exposure of six months would be equivalent therefore in a very simple minded way to a French exposure of about six to 12 years, and I think the proportion of donors resident in France for 12 years or more is too small even to bother asking the question and that residence in other countries would be even longer, and I recognize that the epidemic in the UK could explode and thus needs a regular periodic reassessment, but on the basis of this very straightforward and perhaps simple minded reasoning, I would and will be voting against any other deferral policy at this time.

Other questions? Other comments?

DR. HOEL: I would continue with that analysis and say if you feel you need more conservatism, then you'd probably do better on a risk benefit basis of tightening the British requirement as opposed to have any requirement on France which I'm against changing at this time, the British.

DR. BROWN: Bob.

DR. ROHWER: I think we should keep in mind that the measures that we have implemented so far can at best mitigate but never eliminate the risk from this type of exposure and in fact, the way it's been implemented, we built in a 10 percent risk of exposure because we were only claiming to eliminate 90 percent of the risk at the six month exposure. So any incremental change is not going to benefit us to add an increment to that 10 percent.

Furthermore, from my perspective anyway, the danger from these exposures is not so much from the rare possible transmission from a primary exposure of a donor to a recipient, but rather the worry that variant CJD may be more virulent than CJD especially with respect to blood borne infectivity and the concern that the epidemic might be expanded through the pooling of blood and blood products.

And from that point of view, I feel like the better thing we could do with respect to the French situation is to learn from the French and do what they've done.

I feel that one of the smartest things we could do is to expend our limited ability to defer people, to defer people who have received human-derived biologicals in the past from giving blood in the first place, and I'd rather see the whole argument focused in that direction than on the deferral of people who have traveled to these countries because if there's a lesson that we can learn from the BSE epidemic, it was that when the feed ban was put in place, it worked. It had a very dramatic effect in arresting that epidemic and bringing it back to a low level, and an exactly analogous thing in the human population is our use of human-derived biologicals. We're not cannibals per se but we do use these products that we get from each other and we have this same type of interspecies, intraspecies exposure to each other via these products, and I would argue again, I argued for this the last time we met, but I'd like to bring it up again here, that building this type of fire wall from the people who are perhaps and we

don't know how big this cohort might be, what the prevalence rate might be, but building a fire wall between us and the people who are already exposed to this disease and incubating it seems to me to be the most sensible thing we can do to protect ourselves from the expansion of this epidemic.

DR. BROWN: Thank you. Any other questions or comments? Then let's put the second question to vote. Larry.

DR. SCHONBERGER: I just wanted to add. I find myself in agreement with you, Paul, and wanted to also mention, I don't know how others reacted, but I'm not quite as assured that our votes last time have not had some negative consequences. What we've heard so far is, you know, no shortage, not apparent decrease and as you say, you know, the reserve seems to be fine, but a lot of what was implemented is relatively recently implemented and I didn't get a sense that we have had enough time yet to truly evaluate the consequences of what we've already done, and I'd like to see a little bit more time pass to evaluate that before changing the system again.

DR. BROWN: Paul.

DR. McCURDY: Since the variant CJD has

apparently come from BSE, it would seem to me that despite your comments about the difficulty of knowing what's going on with BSE, that that frequency in a country may be more important than variant CJD and I think that the message I got today was that the major surveillance for BSE, prospective, active surveillance is in UK and Switzerland, and not much anywhere else. That is they're doing careful studies in Switzerland. I think they're doing analyses of brain tissue from a large number of cattle to determine what their frequency is.

DR. BROWN: Other comments or questions? Yes.

DR. TRAMONT: Larry, I'd like to get back to what you were just saying. You said that you wanted more time to see what the impact of the decision last time had and I presume you mean on the incidence of CJD, right?

DR. SCHONBERGER: No, no, no. I meant on the negative consequences to the blood supply. In other words, many of the blood banks implemented the screening just recently, like April and we haven't had data to show what in my just, you know, the true impact of that necessarily. What we did

see was reassuring. It looked like smaller than what we expected and so on and I'm just saying that I'm not sure that I want to shake the system up again at this point for the extra 10 percent benefits until we are more at comfort that what we've already done doesn't have a bigger consequence than what we heard today.

DR. TRAMONT: So that if it did have a bigger impact, you would want to go back and look at the original question. Is that the logic --

DR. SCHONBERGER: Well, I certainly would not want to aggravate it by adding a new requirement for screening, you know, adding another one or two percent on top of something --

DR. TRAMONT: I see.

DR. SCHONBERGER: -- that I'm not sure is as benign as we heard today.

DR. BROWN: Shall we put question 2 to the vote? Question 2 again, a no vote represents a status quo. A no vote represents a vote that the FDA is not being recommended to initiate any new deferral policies with respect to France. A yes vote indicates that you feel that the FDA should consider deferral policies to France. No vote, status quo; yes vote, start thinking about France.

Dr. Schonberger.

DR. SCHONBERGER: No.

DR. BROWN: Dr. Detwiler.

DR. DETWILER: No.

DR. BROWN: Dr. Leitman.

DR. LEITMAN: No.

DR. BROWN: Dr. Lurie.

DR. LURIE: Yes.

DR. BROWN: Dr. Ewenstein.

DR. EWENSTEIN: No.

DR. BROWN: Dr. Belay.

DR. BELAY: No.

DR. BROWN: Dr. Tramont.

DR. TRAMONT: No.

DR. BROWN: Dr. Bolton.

DR. BOLTON: No.

DR. BROWN: Dr. Hollinger.

DR. HOLLINGER: No.

DR. BROWN: I vote no. Dr. Brown votes no. Ms. Walker.

MS. WALKER: No.

DR. BROWN: Dr. Piccardo.

DR. PICCARDO: No.

DR. BROWN: Dr. Hoel.

DR. HOEL: No.

DR. BROWN: Dr. Burke.

DR. BURKE: No.

DR. BROWN: Dr. Cliver.

DR. CLIVER: No.

DR. BROWN: Dr. Ferguson.

DR. FERGUSON: No.

DR. BROWN: Dr. McCurdy.

DR. McCURDY: No.

DR. BROWN: Dr. McCullough.

DR. McCULLOUGH: No.

DR. BROWN: The vote is 17 to one, retaining a status quo position with no recommendations for the FDA to inaugurate a deferral policy with respect to France. By that vote, you have passed go again and have no truck with subset A, B, C and D, and we now proceed to question 3.

DR. ASHER: Question 3 is comprised again of a main question and four contingent questions. The main question is Should FDA recommend deferral from blood or plasma donation for persons with a history of travel or residence in BSE countries other than the UK and France?

DR. BROWN: I expect question 3 can be disposed of fairly quickly, but if there's comments and questions about it before we vote on it, we have

time. Question.

DR. EWENSTEIN: Let me just make one comment. I think, and I know it's not the question before us exactly, but I think that it would be important for the Committee to recommend that all countries who are at potential risk do what they can within certainly the human population, if not the animal population, to try to institute the sort of surveillance programs that we've seen in some of the presentations today because I think we just don't have any data from some of these countries, and I suspect we're all going to say in the absence of data, that we're not going to change the status quo which is okay. But I think we should recognize the fact that we are really blind in a lot of these places right now.

DR. BROWN: I think that's a good point, and I think it's good that it's put on the record that we're making this vote not to dismiss our concept of potential risk and Dr. Detwiler has done a lot of work and will I'm sure be burdened in the future to no end but, yeah, this should not be a signal to Europe to indicate that we're unconcerned.

DR. LURIE: Paul, speaking personally which is the only way I can, I'm not as comfortable

as you are, Paul, and some other people on this Committee are in poo pooing the cattle data. I think that the numbers of CJD cases remain very small. Even in France, we're talking only about three cases. That does not reassure me that the number might not be higher or might not soon be higher. The same is true for zero cases. So I still think that the cattle data are in some ways constructive and in particular I'm worried about the situation in Portugal where whatever the artifact of surveillance might be, there is almost a doubling of the rate of infected cows per million cattle over the last several years to a point that the rate is now half of what the rate is in Britain at present. So I'm quite concerned about that. Fortunately, Portugal is a country to which the amount of travel is very limited and so the impact upon the blood supply of the restriction of Portugal I think would be low.

DR. BROWN: Yeah, I think your comments and your comments are that both sides of the same coin, and I agree with both of you. And I wasn't poo pooing by the way. I simply said that on the basis of what we now know and all of the qualifications that go into these estimates, that

it's simply not possible scientifically speaking to make estimates of risk based on what we now know about cattle and BSE, and therefore there's no point in making a policy on essentially totally incomplete information for most of the countries. I looked at it as a practical matter, not to imply that. Fundamentally the most important thing is in fact the number of infected cattle around Europe. So we're in complete agreement. Are we not?

DR. LURIE: Stated that way we are but I guess you're certainly right that we can't move from the number or rate of infected cattle to make an estimate of risk. I think that's true. What we're really doing is we've established in the previous time a kind of bench mark of sort of a risk that as I'm quantified as it was is still in some sense unacceptable resulting in some kind of a restriction. So the question is where does the risk lie relative to that, and for that I don't think that the human data are particularly helpful when you're dealing with small numbers. So I look to the cattle data and as limited as they are, I think they provide some suggestions that are quite worrisome and in particular in Portugal. Anyway, that's probably the other side of the same coin.

DR. PICCARDO: Pedro. Dr. Piccardo. I agree we are very concerned with Portugal, but it's hard to believe that Spain is not reporting BSE if Portugal is reporting so much. So I think that -- of course, I have no proof of what I'm saying. What I'm saying is the analysis of the situation in the cattle in Europe is something that is very critical and Spain is one country in which I would like to keep an eye on.

DR. LURIE: Right, but the rate of Portugal is no less than they estimate it to be I think. I mean if anything, they're underestimating it due to poor surveillance. So it may not tell us, but Spain, God knows what's going on there.

DR. BROWN: Well, that's exactly the point he's making.

DR. LURIE: Well, yeah. I'm talking about Portugal though.

DR. BROWN: No, but I mean in comparison if you're going to say, well, Portugal is bad news because it's got 300 cases but we're not doing anything about Spain because they haven't got any, it's exactly what we were saying. It's impossible to establish a policy based on this variability of knowledge of BSE from country to country.

A vote on question 3. As in the first two questions, a no vote is a vote against establishing any deferral policy for other countries in Europe. A yes vote says the FDA should start thinking about deferral policies for other European countries. Dr. Schonberger.

DR. SCHONBERGER: No.

DR. BROWN: Dr. Detwiler.

DR. DETWILER: No.

DR. BROWN: Dr. Leitman.

DR. LEITMAN: No.

DR. BROWN: Dr. Lurie.

DR. LURIE: Yes.

DR. BROWN: Dr. Ewenstein.

DR. EWENSTEIN: No.

DR. BROWN: Dr. Belay.

DR. BELAY: No.

DR. BROWN: Dr. Tramont.

DR. TRAMONT: No.

DR. BROWN: Dr. Bolton.

DR. BOLTON: No.

DR. BROWN: Dr. Hollinger.

DR. HOLLINGER: No.

DR. BROWN: Dr. Brown votes no. Ms. Walker.

MS. WALKER: No.

DR. BROWN: Dr. Piccardo.

DR. PICCARDO: No.

DR. BROWN: Dr. Hoel.

DR. HOEL: No.

DR. BROWN: Dr. Burke.

DR. BURKE: No.

DR. BROWN: Dr. Cliver.

DR. CLIVER: No.

DR. BROWN: Dr. Ferguson.

DR. FERGUSON: No.

DR. BROWN: Dr. McCurdy.

DR. McCURDY: No.

DR. BROWN: Dr. McCullough.

DR. McCULLOUGH: No.

DR. BROWN: Again we have a vote of 17 against and one vote yes.

We will reconvene tomorrow morning. Before we do, I ask anybody on the Committee if they would like to say anything further before we adjourn today. Susan.

DR. LEITMAN: I'd like to make one comment. I wrote it down so I'd make sure I got it straight. The Committee's vote suggests that it believes that traveling --

DR. BROWN: I didn't hear you. Start again.

DR. LEITMAN: The Committee's vote today suggests that it believes that traveling, an American who travels for six, seven, eight months or so, as little as that, in the UK constitutes a greater potential threat to the safety of the American blood supply than an individual who has lived 30 to 50 years in France. The data on confirmed cases of variant CJD in residents of France versus confirmed cases in travelers to England does not support this view.

DR. BROWN: I think the logic of your reasoning is impeccable.

DR. BURKE: I don't. I disagree.

DR. BROWN: I don't. I think -- well, go ahead.

DR. BURKE: And the reason is that the number of individuals, there's a policy here. Do you put a policy in place for how many individuals? Do you put a policy in place for the five or 10 or 20 people? No, you don't. You put a policy in place for a large number of people. So the practical applications side of the policy is, well, it isn't just a simple risk benefit of calculating

the numbers. There's also the impact of implementing a policy and you do that for a sizeable number. You don't do that for a small number.

DR. BROWN: There was another -- yes. Jeff.

DR. McCULLOUGH: Another point that was made earlier that I'd just like to get very clearly into the record, Dr. Schonberger mentioned and I think the blood bank transfusion medicine people here would agree that it is too early to determine the impact of this present deferral policy on the blood supply and that while I don't mean to speak in favor of altering because I voted not to do that, I just think we need to be very clear that it is premature and we want to see, we want to watch the experience to determine what effect this really will have.

DR. BROWN: Is it built in by the way? I maybe missed a beat earlier. Is this evaluation of impact on the blood supply ongoing? It's not going to stop. It is ongoing. Okay. Linda.

DR. DETWILER: Just one other comment for Dr. Leitman is that the FDA's deferral on blood was a time period in the UK which is now it's between '80 and '96. So it's not ongoing. So it's

not people that are ongoing after '96, and it was the highest risk period of time in a country that had magnitudes of infection in their pipeline. So I think there is a difference between that versus on the continent.

DR. BROWN: And won't we all feel better if, well, not all of us, the people in the UK won't feel better, but if by any chance the UK does explode with several hundred cases in the next year and we had decided to relax everything today, we would be very sorry a year from now. Very well. When is the -- yes, Ernest.

DR. BELAY: Just for the record, I think we should also formally say that this policy should be revised periodically as more data becomes available for France and also other European countries.

DR. BROWN: Okay. When do we reconvene tomorrow, Bill?

DR. FREAS: Tomorrow morning we reconvene at 8:30 in the morning.

DR. BROWN: Same as this morning.

DR. FREAS: The same as this morning, according to the Agenda, here.

UNIDENTIFIED PERSON: Can we leave our

things here?

DR. FREAS: They may clear the tables tonight. So we ask you if you want to save anything, you take whatever you want to save today with you. I also would like to make one announcement because some members won't be with us tomorrow. We are currently setting up another meeting of this Committee to meet jointly with the Vaccine and Related Biological Products Advisory Committee on July 27th, and in a couple of weeks we'll have the topics and more information available and if you look at the next to the last page of your Agenda, it gives the telephone number for the Advisory Committee Information Line, and that's where we'll post the announcement to the public. Thank you.

DR. BROWN: Thank you very much, all members of the Committee, those of you who are leaving, we'll hope to see you again at the next meeting.

(Whereupon, the foregoing matter went off the record at 4:51 p.m., to reconvene tomorrow, June 2, 2000, at 8:30 a.m.)

C E R T I F I C A T E

This is to certify that the foregoing transcript in the matter of: MEETING

Before: TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES ADVISORY COMMITTEE

Date: JUNE 1, 2000

Place: GAITHERSBURG, MARYLAND

represents the full and complete proceedings of the aforementioned matter, as reported and reduced to typewriting.

Rebecca Davis