efficiency of the leukofiltration.

DR. EWENSTEIN: Right, but I guess what I'm saying on the second point then is: when would you extrapolate from the little we know about the difference between variant CJD and classical? That you might expect more of a benefit with leukoreduction in the variant case than classical.

And I would admit that if you see nothing, no reduction in fresh plasma, then you're not going to see any reduction in the freeze-thawed, but if there are other TSEs where there is more propensity for leukocytes, then you might see a difference between the frozen and fresh plasma experiments.

CHAIRMAN BROWN: I think that's correct. I think that was the implication. There might be I don't think maybe a greater association rather than perhaps simply more of it. There may be a greater burden in the body of infectivity peripherally in new variant than in classical CJD. I think that's probably as far as you can push that at the moment.

Bob?

DR. ROHWER: Well, that's the point I was going to make. But that means the distribution could be the same. It's just the overall amount in all compartments goes up.

CHAIRMAN BROWN: I think we'll take our break now, and when we come back, we will go to a vote, and this will obviously have the advantage of giving anybody the opportunity to lobby for the next ten or 15 minutes.

It is now 10:56. At 11:10 we'll recommence.

(Whereupon, the foregoing matter went off the record at 10:53 a.m. and went back on the record at 11:10 a.m.)

CHAIRMAN BROWN: Will the committee please reconvene?

And, Dr. Asher, would you like to read our question again? Dr. Asher.

DR. ASHER: Okay. Let me read the first question.

Can leukoreduction be expected to reduce significantly the infectivity theoretically present in blood of persons during the course of Creutzfeldt-Jakob disease and new variant Creutzfeldt-Jakob disease? If so, for which components?

CHAIRMAN BROWN: I think that it's possible we should vote on the first question. This is a double question, and the answer to the second question is implied in the first. So I think the

committee should vote simply on the first question, which is: can leukoreduction be expected to reduce significantly the infectivity theoretically present in blood of persons during the course of CJD and VCJD?

Dr. Schonberger.

DR. SCHONBERGER: Insufficient information. No.

CHAIRMAN BROWN: Dr. Leitman.

DR. LEITMAN: I'd agree with that. Insufficient information. No.

CHAIRMAN BROWN: Dr. Lurie.

DR. LURIE: Insufficient information, No.

CHAIRMAN BROWN: Dr. Ewenstein.

DR. EWENSTEIN: No.

CHAIRMAN BROWN: Dr. Belay.

DR. BELAY: No.

CHAIRMAN BROWN: Dr. Tramont.

DR. TRAMONT: No.

CHAIRMAN BROWN: Dr. Bolton.

DR. BOLTON: No.

CHAIRMAN BROWN: Dr. Hollinger.

DR. HOLLINGER: Insufficient information. Abstain.

CHAIRMAN BROWN: Ms. Walker.

MS. WALKER: No.

CHAIRMAN BROWN: Dr. Burke?

PARTICIPANT: Not here.

CHAIRMAN BROWN: I'm sorry. Dr. Cliver.

DR. CLIVER: You've skipped Dr. Piccardo, but Cliver votes no.

CHAIRMAN BROWN: Oh, all right. You're on the corner there. I missed you. Sorry, Pedro.

Dr. Piccardo.

DR. PICCARDO: No, because of insufficient data.

CHAIRMAN BROWN: Dr. Cliver, did you vote already?

DR. CLIVER: Yes. No.

CHAIRMAN BROWN: You voted not. Yes, no, no? I know. I'm just --

(Laughter.)

CHAIRMAN BROWN: Dr. Ferguson.

DR. FERGUSON: No.

CHAIRMAN BROWN: Dr. McCurdy.

DR. McCURDY: No.

CHAIRMAN BROWN: And Dr. McCullough.

DR. McCULLOUGH: Insufficient information. Yes.

CHAIRMAN BROWN: And Dr. Brown votes insufficient information. Yes.

So the vote, we have only 15 voting members at the moment, and the vote is, therefore, 13 to two.

PARTICIPANT: With one abstention.

CHAIRMAN BROWN: Oh, who abstained? Oh, okay. In that case it is 12 to two and one abstention. Twelve and two is 14 and one is 15.

That concludes the committee's charge today, and we will now hear the Topic 3, which is simply an update on the regulatory status of processed -- oh, I'm sorry. There is one other thing because I guess as a formality I should have asked for anybody in the audience who wishes to speak on this issue and influence our vote.

(Laughter.)

CHAIRMAN BROWN: Seeing none, we'll proceed to Topic 3 and here there are just three items:

First, an update on the regulatory status of processed human dura mater. That will be a very short presentation by Dr. Durfor, the Office of Device Evaluation of the FDA.

And then once again I will ask whether there are any comments from the floor, following which we will adjourn.

Dr. Durfor.

DR. DURFOR: Good morning or afternoon. I'm not sure which at this point, but I do appreciate your time to give you an update of where we stand on human dura mater.

Next slide.

I'll just give you one slide of background and then a couple of comments about where we stand. Human dura mater at this time is an unclassified pre-amendments medical device. Pre-amendments means that it was in commercial distribution before the medical device amendments were enacted in 1976. Unclassified means that at this point in time it has not been classified as which risk category is a medical device.

In February of 1990, the Neurological Devices Advisory Panel, which is a component of the Medical Devices Advisory Committee of the FDA, met together and made a recommendation that it could be dealt with as a Class II medical device. I'll discuss this a little bit more in a minute, but that recommendation was never finalized.

The other piece of background information I bring to you is to remind you that about a year ago I met with you and reviewed with you the guidance document that we were putting out for preparation of

a pre-market notification application for human dura mater. This guidance document was based on the deliberations of this particular panel in both 1997 and '98.

Next slide.

So in September of last year, we convened the Neurological Devices Panel again. We felt that in the nine years between the last recommendation and 1999 a considerable amount of information had been developed in terms of the risks and the value of human dura mater.

That panel meeting met and was represented by this panel member, both by Dr. Piccardo, who is here with you today, and Dr. Penn, who was a temporary voting member on this panel when you were discussing issues of human dura mater in '97 and '98. So we tried to include the comments of this panel in that panel as well.

That panel met and, once again, made a recommendation that human dura mater could be viewed and regulated as a Class II medical device.

What does that mean? There are three classes of medical devices. Class II medical device is a device for which we understand the safety and effectiveness of the device, and it can be regulated

first using the general controls of a Class I medical device, which means that a manufacturer would be prohibited from either misbranding or adulterating a product. They would be required to follow GMPs. They would be required to use the medical device reporting requirements and other issues associated with the general control of medical devices.

In addition, Class II medical device means that the safety and risk of a product are sufficiently well understood that they can be controlled by special controls.

And the last bullet sort of gives you an idea of what those special controls are.

Next slide.

The panel, a component, once again, of finalizing the regulatory status of any product requires a recommendation from a panel. Part of the deliberations of that of that particular panel involved identifying special controls that would help us make sure that the product is both safe and effective.

During the panel deliberations, the following special controls were identified by the panel. Those were a careful donor selection, testing guidelines, post market surveillance, patient

registries, and device tracking.

Next slide.

After consideration of the literature, the comments of this panel, and the comments of the Neurological Devices Advisory Panel, the FDA agrees with that recommendation that human dura mater can be considered as a Class II medical device.

Part of our preparation efforts for the preparing the final rule for that classification involved the FDA identifying risks to health. We have identified the following risks to health with human dura matter. Those are infection, transmission of TSEs, CSF leak, and adverse tissue reactions.

Next slide.

We feel that the appropriate special controls for controlling these risks are the two following guidance documents which are available on the FDA Web page.

The first is the guidance for the preparation of a pre-market notification application for human dura mater, which once again I discussed with you last year, and the guidance on medical device tracking, which I'll say a little bit more about in a minute.

Next slide.

Just as a quick review, the guidance document for the preparation of a pre-market notification application for human dura mater has a variety of issues. It was an update to an existing document, and here are some of the key issues that were listed -- that are listed in that guidance document, which is, once again, available for public use on the Web:

Donor qualifications;

Histology of the brain from which the donor -- from which the dura mater is taken;

Issues associated with archiving; and

PrP RES testing when such a test becomes available.

There are also other issues that this panel recommended to us with regard to how dura mater should be processed, and then there are product characterization issues and record keeping and tracking.

Next slide.

The other special control that we are considering is the guidance document on medical device tracking. In December of 1998, FDA issued a tracking order for human dura mater. This particular regulation of the FD&C Act requires the manufacturer

to develop, implement, and periodically test a program that allows them to locate any patient that has been implanted with a medical device until the device is either explanted or the patient dies.

And this is not unique to dura mater. There are other track medical devices as well.

Next slide.

So in conclusion, at this point in time FDA is preparing a rule to classify human dura mater as a Class II medical device.

Thank you very much.

(Applause.)

CHAIRMAN BROWN: Thank you, Dr. Durfor.

Are there any comments or questions from the floor with respect to the presentation you just heard?

DR. SCHONBERGER: Yeah, just one.

CHAIRMAN BROWN: Just a second. If not --

DR. SCHONBERGER: No.

CHAIRMAN BROWN: You're not on the floor, Larry.

DR. SCHONBERGER: Oh.

CHAIRMAN BROWN: Yet.

(Laughter.)

CHAIRMAN BROWN: Dr. Schulman (phonetic).

DR. SCHONBERGER: I was just asking whether -- it said to track them until device explanation or death?

DR. DURFOR: Explantation. Did I spell that wrong?

CHAIRMAN BROWN: Yeah, that's good, Larry. I was wondering about that myself. What's a device explanation? Yeah.

DR. DURFOR: Explantation. I'd like to blame my secretary for that, but I made my own slides.

CHAIRMAN BROWN: Taken out. Is that what you're saying?

DR. DURFOR: Yes.

CHAIRMAN BROWN: Yeah, okay. Well, the Chairman is aware that as the committee has been realigned over the past year, like the Supreme Court it has moved from a somewhat conservative to a somewhat liberal position, but he thanks the members for their intelligent and expeditious attack of the problems that were before it today.

DR. LURIE: May I?

CHAIRMAN BROWN: Yes.

DR. LURIE: Just I'm happy to see that this Class II medical device thing is going forward, but really I think it's long overdue at a minimum that

this happen. It's now ten years since the Neurological Devices Advisory Committee recommended this, and it had to be reiterated nine years later.

So I hope that the next time we get an update that it will be truly completed because it's taken way too long.

CHAIRMAN BROWN: Thank you, Committee. I will see you again in the fall, if not sooner.

The meeting is adjourned.

MR. FREAS: Thank you, Dr. Brown.

(Whereupon, at 11:23 a.m., the meeting was concluded.)

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 2, 2000

Place: GAITHERSBURG, MARYLAND

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

Rebecca Davis