CHAIRPERSON CANADY: Could we then rephrase that, further analysis of existing data for completion purposes?

DR. EDMONDSON: A rhetorical question. And what if it can't be answered?

CHAIRPERSON CANADY: Then that decision will be made.

DR. PIANTADOSI: I have a rhetorical answer.

(Laughter.)

I am totally confident that the Agency has heard the concerns and that they will make an appropriate decision with the additional analyses and data clean up.

CHAIRPERSON CANADY: Any other comments regarding that amendment?

DR. NUWER: Well, I have a concern that it's a whole unforseen set of circumstances that could arise if the company gives data of a certain sort and then that leads to further concerns and it sort of rolls on month after month and this gets stretched out for a long time without any sense of closure to it.

DR. ZAMORANO: Well, basically, we have said that somehow we say which patients are the ones that will be the indications, but they think it should be maybe stated which are the ones should not be considered. For example, patients that are responding to therapy, for example, it's not recommended for patients that are currently responding to levodopa. It's not for patients with dementia.

CHAIRPERSON CANADY: We have to be a little careful because almost all of these patients were responding to levodopa, but had some relatively negative effect of levodopa.

DR. ZAMORANO: Right.

CHAIRPERSON CANADY: So I'm not sure responsiveness, per se, is the right term.

DR. PIANTADOSI: We have criteria from the protocol. There were exclusion criteria in the protocol. They're not reflected though in the thoughts behind these questions and maybe it would be enough to point to those or state and crafted from the exclusionary criteria as contraindications.

CHAIRPERSON CANADY: Well, maybe we could

DR. PIANTADOSI: I would add to that also that I'd be comfortable not voting on this personally, that I think the Agency has heard the discussion and the concern and knows what to do and I'm perfectly comfortable with that if people decided that they don't want to vote on it explicitly.

CHAIRPERSON CANADY: Dr. Hallett, what is your pleasure, it's your amendment?

DR. HALLETT: I would be happy to withdraw it as long as it's done.

(Laughter.)

CHAIRPERSON CANADY: Any additional amendments? Dr. Zamorano?

DR. ZAMORANO: I think we all have the concern that something like this gets approved. I think tomorrow every patient with Parkinson's disease is going to notify a surgeon to get bilateral stimulation. It should be labeled by the sponsor in some way contraindication or it's not advised in such and such patients.

CHAIRPERSON CANADY: This is the brass nuts part. You've got to say which patients.

say the exclusion criteria of the protocol should be part of the labeling.

DR. MASSAQUOI: Question. Is it essential that things be made a contraindication versus a statement that says safety and/or effectiveness has not been established in a certain group?

CHAIRPERSON CANADY: Okay, that could be done.

DR. MASSAQUOI: In the situation where you don't know explicitly one or the other and there's not an overriding --

DR. ZAMORANO: Or it's not advisable in patients without saying it's a contraindication.

CHAIRPERSON CANADY: Since that group wasn't studied.

DR. ZAMORANO: Uh-huh.

CHAIRPERSON CANADY: We could say that safety was not established in this group and include the excluded population from the protocol. Is that acceptable to you or not?

DR. ZAMORANO: My concern is mostly with

the patients that are currently in good -- that are well controlled with medical treatment, those patients because they will know that this exists, this bilateral stimulation, they will go and try to have this procedure and I think we need to provide some means that it doesn't happen. And we know it will happen between different colleagues, some get more excited about doing this bilateral stimulation and --

CHAIRPERSON CANADY: I think that that group is excluded by the statement in the first one which is only those patients who are advanced, and only those patients who are not adequately controlled was part of the original label. So I think we've covered that group.

DR. ZAMORANO: Yes. I think we covered it, but I don't know if we could add some second --

CHAIRPERSON CANADY: Is there additional people that you wish to include in that?

DR. EDMONDSON: No, I think we really do need a contraindication label that's clear. The exclusion criteria for the study is not, will not match one to one with what we really need. For

example, patients over 75 are excluded in the study. We probably don't want to include an age contraindication or maybe we do want to say, I mean it's understood that Parkinson's occur in adults anyway, so an age limit or consideration is not necessary.

Secondary Parkinsonism, I think using levodopa responsive Parkinsonism is an important point, so excluding secondary Parkinson's patient would not be appropriate in the contraindication label.

CHAIRPERSON CANADY: Dr. Fessler?

DR. FESSLER: At this point all we really know is that this has been somewhat effective in patients with advanced Parkinson's who are responsive to levodopa, but are now losing their responsiveness. We don't know anything else and we really can't say it's contraindicated for conditions we don't know that it's contraindicated. That has to be a medical decision that has to be the doctor.

DR. EDMONDSON: However, when you put it in someone who is demented, quite demented -- so, you

know, I think we still need some sort of guideline.

CHAIRPERSON CANADY: I need your recommendation.

DR. EDMONDSON: Number one, it is contraindicated in patients with dementia. Number one, that it is contraindicated in patients with coagulopathies. Number three, I don't know if you want to say -- I mean that would include folks with advanced hepatopathies and other potential coagulopathies. I think that's it.

CHAIRPERSON CANADY: A second? For that amendment that it would be contraindicated in dementia and in coagulopathy. Second?

[No second.]

I will entertain other amendments.

DR. WALKER: Can we change the wording to safety and efficacy has not been evaluated -- and done the same way.

CHAIRPERSON CANADY: A second for that? A second for the amendment, "safety and efficacy has not been demonstrated in dementia and in coagulopathy."

DR. HALLETT: Well, coagulopathy --

CHAIRPERSON CANADY: Just dementia? What is your --

DR. HALLETT: There are certain exclusion criteria in this particular protocol. I mean coagulopathy and secondary drug-induced Parkinsonism, previous intracranial neurosurgical procedures, demand pacemakers, substance abuse, things like that which should be or could be considered exclusion criteria.

And then there are some other ones in which we just don't have the information such as age, so that one could say that safety and efficacy have not been demonstrated for patients older than age 75 or perhaps some other things. But then there are other situations --

CHAIRPERSON CANADY: I need to know at this point in time those things.

(Laughter.)

This is no longer general conversation.

DR. HALLETT: Right.

CHAIRPERSON CANADY: So we can say the exclusion criteria of the protocol. And whatever you

might wish to add to that or subtract from that.

DR. HALLETT: Okay, but I would think that we could say exclusion criteria are the ones that can be taken directly from the protocol.

CHAIRPERSON CANADY: So safety and efficacy has not been demonstrated under the excluded criteria. Is there a second for that amendment?

DR. PIANTADOSI: I second that, yes.

CHAIRPERSON CANADY: Conversation regarding this?

Call for the vote then. Dr. Walker?

DR. WALKER: Yes.

CHAIRPERSON CANADY: Dr. Zamorano?

DR. ZAMORANO: Yes.

CHAIRPERSON CANADY: Dr. Hallett?

DR. HALLETT: Yes.

CHAIRPERSON CANADY: Dr. Edmondson.

DR. EDMONDSON: Yes.

DR. NUWER: Yes.

DR. MASSAQUOI: Yes.

DR. FESSLER: No.

DR. PIANTADOSI: Yes.

CHAIRPERSON CANADY: Additional amendments?

DR. PIANTADOSI: I have a question.

CHAIRPERSON CANADY: Yes sir.

DR. PIANTADOSI: Is the panel going to make any recommendations generically about safety?

CHAIRPERSON CANADY: If you would then so amend them, yes sir. Anything you want us to say needs to be said now.

DR. PIANTADOSI: Well, let me just raise the generic concern and see if one of my clinical colleagues can put it into better words. Many times labeling reflects the serious adverse events with approximate frequencies that they occur and I wonder out loud if anybody considers them to be clinically important enough that they should be put in the label and that the physicians contemplating the use of the device should be informed directly through the label about their frequency.

CHAIRPERSON CANADY: I need some wording.

DR. HALLETT: Could I just ask a question about that? For all of the other uses for DBS, has

that already -- does that type of statement exist or not?

CHAIRPERSON CANADY: I can't answer that. I don't know.

DR. HALLETT: For example, for the indication for DBS of the thalamus for tremor, do we have that type of statement in the labeling?

CHAIRPERSON CANADY: Dr. Witten?

DR. WITTEN: I will just say that in general for PMA, in the label there's a description of -- the safety issues are described, but if there is some -- the safety issues from the study are described. But if there's some particular things that should be highlighted in some way, you know, those would be good to note. But otherwise, just in the general for any PMA --

CHAIRPERSON CANADY: That will happen.

DR. WITTEN: We note safety and there's a safety table in the label. But if there's any concerns about what needs to be said or what to do or suggestions like that, you could --

CHAIRPERSON CANADY: Obviously,

hemiparesis is the major one.

DR. PIANTADOSI: That would satisfy my --

CHAIRPERSON CANADY: Other amendments. Okay.

DR. ZAMORANO: I wonder if there is a way this panel can introduce an amendment related to the training of the physicians when to perform the procedure.

CHAIRPERSON CANADY: What is your amendment?

DR. ZAMORANO: I don't know how to phrase it, but basically, I mean related to the training of the -- need to be highly trained in this procedure, the physician.

CHAIRPERSON CANADY: I think it's an issue that we have -- that we need a specific statement as to how to add the two amendments.

DR. ZAMORANO: It could be a recommendation to the sponsor that to establish a mechanism for the training or to establish a criteria.

CHAIRPERSON CANADY: The concern I have regarding that is that it's not clear that that falls

within the industry's purview to establish that is the concern in terms of how we go about establishing that. You might want to have a statement on the labeling regarding the concern that it be performed by physicians who are trained specifically in this procedure.

DR. ZAMORANO: Right.

CHAIRPERSON CANADY: I think that would be an amendment we could make.

DR. ZAMORANO: Maybe it could be related to the other one that we said, the potential complications of this procedure is so and so and so and that required a highly trained physician to perform this procedure.

CHAIRPERSON CANADY: Should we say that we would recommend specific training in this procedure be made available for physicians?

DR. ZAMORANO: That would be a good recommendation.

CHAIRPERSON CANADY: Would that be an acceptable version of y our amendment? Is there a second for that?

DR. HALLETT: Could you say it again once more?

CHAIRPERSON CANADY: Specific training in this procedure should be made available for physicians.

DR. HALLETT: Could we say that specific training in the procedure is recommended for physicians?

CHAIRPERSON CANADY: Yes, we surely can.

DR. WALKER: I'll second that.

CHAIRPERSON CANADY: Second?

DR. WALKER: Yes.

CHAIRPERSON CANADY: Any more comment? Vote. Dr. Walker?

DR. WALKER: Yes.

CHAIRPERSON CANADY: Dr. Zamarano?

DR. ZAMORANO: Yes.

DR. HALLETT: Yes.

DR. EDMONDSON: Yes.

DR. NUWER: Yes.

DR. MASSAQUOI: Yes.

DR. PIANTADOSI: Yes.

CHAIRPERSON CANADY: Other comments, amendments?

DR. MASSAQUOI: One amendment. Third from the last item. Regarding the increase in duration and quality of on time and decreases the duration of off time without mentioning the severity of off time unless -- I didn't --

CHAIRPERSON CANADY: You wish to exclude severity?

DR. MASSAQUOI: Yes, severity of off time.

CHAIRPERSON CANADY: Is there a second?

DR. MASSAQUOI: I just don't recall the data off hand. Maybe if someone could remind me. I just didn't recall that as being established that during the periods when people were off that they were less severe --

DR. NUWER: I thought that was established. It was part of the data that was presented.

The severity in the off was not that much different from the on before implanted.

DR. MASSAQUOI: Okay, fine, I'll withdraw.

Thank you.

CHAIRPERSON CANADY: You withdraw that. Any other amendments?

Okay, now I'd like to take a vote on the major motion which is approvable with conditions. The conditions are the conditions that we have voted on. This would also be your opportunity to make a comment regarding the entire -- we should vote first and then the reasons?

CHAIRPERSON CANADY: Dr. Walker?

DR. WALKER: I'll vote yes. Thirty seconds of comment, running a multicenter clinical study of 22 bright and innovative principal investigators, especially neurosurgeons is probably something like herding cats.

CHAIRPERSON CANADY: Neurosurgeons, of course, take offense to this.

DR. WALKER: I think the sponsor did a good job in this and I think that by approving this today the panel is making a big contribution to what's available to Parkinson's patients.

CHAIRPERSON CANADY: Dr. Zamarano?

DR. ZAMORANO: Yes, a very brief comment. I think this is an excellent possibility to offer to some of the patients and I think with the condition that we have outlined it makes good step, the approval.

CHAIRPERSON CANADY: Dr. Hallett.

DR. HALLETT: I vote yes. I think the most important reason is the prolongation of the on effect which gives rise to a better lifestyle for the patients.

CHAIRPERSON CANADY: Dr. Edmondson?

DR. EDMONDSON: I vote yes and I'll say ditto to my predecessors.

CHAIRPERSON CANADY: Dr. Nuwer?

DR. NUWER: I vote yes and add that I think that the improvement int he patients' clinical status outweighs the methodological flaws in the matter before us.

CHAIRPERSON CANADY: Dr. Massaquoi?

DR. MASSAQUOI: I vote yes and I'll just ditto and also say that it does seem that despite the methodological problems, there was an incredible

amount of work that was done and it was headed all in the right direction, I think.

CHAIRPERSON CANADY: Dr. Piantadosi?

DR. PIANTADOSI: I'll vote yes with no additional comment. Thank you.

CHAIRPERSON CANADY: Then the motion passes with conditions as outlined. I believe that's the end of the meeting.

Any other comments the panelists would like to make?

DR. COHEN: Yes, I'd like to make a comment as a patient. I'm pleased with the outcome and that I'm glad we stuck close to the data and I'm glad that we approved this treatment.

CHAIRPERSON CANADY: Dr. Witten?

DR. WITTEN: I'd like to thank the panel and everyone else who participated today.

(Applause.)

CHAIRPERSON CANADY: The meeting is adjourned.

(Whereupon, at 5:39 p.m., the meeting was concluded.)

CERTIFICATE

This is to certify that the foregoing transcript in the matter of: Neurological Devices Panel of the Medical Devices Advisory Committee

Before: DHHS/FDA

Date: March 31, 2000

Place: Rockville, MD

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