the referenced scientific articles provide sufficient information to warrant approval of the requested change in Indications for Use for the non-CARTO sensor equipped catheters.

So I think in terms of comment, we've covered this a couple of times, and I think my recommendation would be that where at all possible, if we can leverage this data for similar catheters without creating new safety issues, that would be a very good thing to do from an industry point of view.

DR. ZUCKERMAN: Okay. Just a point of clarification, just like the FDA gives guidance, our industry and consumer representatives give important guidance from their perspectives, but for these key Panel questions, the Agency benefits most from just the regular clinicians and statistician discussing the impact of these questions.

DR. BORER: Okay. Dr. Fleming, your clinical experience would not -- well, maybe it will. What do you think about this? Do we have enough information here to extrapolate?

DR. FLEMING: I'm not so sure that we do, that we can extrapolate the catheters that do not have the ability to map, generating maps. I think we discussed this earlier about the fact that the best

results, at least from your point of view, were obtained when you could map and you could track with the catheter and so on. So I'm not clear that that data can be generalized to the other non-map catheters.

DR. JEEVANANDAM: I agree. I don't think the information can be or the recommendation can be generalized to the navigation system. My only caveat to that would be the uni versus bidirectional catheter, and perhaps they could do an engineering analysis, and if the stiffness and everything is very, very similar, the diameters are similar, maybe we can get one approved on the basis of the monodirectional catheter, but I think the other ones without the mapping system probably need to be compared to the catheter that was used in this study.

DR. BORER: Dr. Karasik.

DR. KARASIK: I would agree. I think we just have to comment on the data that we have. I don't think that the other data, you know, I don't think we should really look at using the other data in the literature on the other catheters to support this particular application.

DR. BORER: John.

DR. ZUCKERMAN: Excuse me. Dr. Karasik, as

an electrophysiologist though, could you comment on Dr. Jeevanandam's last point about an appropriate dataset might be developed for a bidirectional catheter?

DR. KARASIK: Well, I do think from a handling perspective, we would like to know whether the handling characteristics of the catheter are the same as the unidirectional. The unidirectional catheter is kind of stiff as it is. So I'm not, you know, I've not used the bidirectional. So I can't comment on it specifically, but I think that you could probably acquire some clinical data with it fairly easily. I don't think it would have to be a big deal, but I would prefer to limit what we do here to what we have in front of us.

DR. BORER: Dr. Somberg.

DR. SOMBERG: Well, as I said before, I think it's the site of lesions and how they're constructed and their anatomical array and how you go about that. There's this CARTO system. There's another system out there I've just learned, a guidance system that may be different. Do they have to do a study with that? Then you have, you know, echo ultrasound procedures for guidance and other procedures as well, and you have the classic, and

some people do the best work with a classic loop or Lasso. So I think this is in the electrophysiology specialist literature, and they will go back and have meetings on how they do this and how they don't, and I do think that it should be said in the package insert with this device that the data was done with using this catheter and this system.

However, if you're able to make certain lesions that will interrupt the initiation and sustaining of PAF, that is up to the individual investigator how they go about doing that. And I think otherwise, we will be so incremental in this field that we will be, you know, we will have to have so many Panel meetings and bogged down with so many things, it's just going to be impossible. So I don't think that is the way devices are usually approved and developed in the United States.

DR. BORER: David.

DR. NAFTEL: I think on this one I'm interested bystander.

DR. BORER: Judah.

DR. WEINBERGER: Just a footnote to what Val said, and that is since the primary concern for the bidirectional catheter is one of safety, I think an appropriate acute dataset could be gotten just by

getting estimates on safety alone, seven day acute safety on a set of patients who had the bidirectional catheter used. I don't think it's an efficacy question about that particular catheter. The other ones present both safety and efficacy questions, and I think that would be more circumspect.

DR. BORER: David, I think you've already commented on this, but for the record, do you want to reiterate?

DR. SLOTWINER: Yeah, I do. You know, I feel obligated to look at the data that's only included here, and not to extrapolate to other catheters with or without the mapping system. However, having used many catheters, I don't truly believe that the risk with the other catheters is likely significantly different, and I don't think that it would require extensive clinical trials to demonstrate equivalency. Perhaps a relatively small study at experienced centers looking at safety for the bidirectional limited endpoints for efficacy, perhaps pulmonary vein isolation with a navigation system.

So I think that the bar to accept to these other catheters should be much lower than it is to approve this catheter, but I think in terms of what

we can say today, we have to limit it to the data before us.

DR. BORER: Dr. Kelley.

DR. KELLEY: I would agree. I would be hesitant to recommend approval without a navigation system, but I wonder if the company can tell us just how different the bidirectional catheter is. Does it have an extra pull wire? So is it stiffer? Is it not stiffer? Somebody ought to know that, I would bet.

DR. YAROSS: We have previously provided data to the Agency that from both bench and animal testing, to demonstrate the equivalent performance, equivalent handling, of the bidirectional to the unidirectional, and --

DR. KELLEY: Does it have an extra pull wire?

DR. YAROSS: Yes, there are two pull wires. We though have characterized the stiffness within a standard classic bench setup as well as provided animal data to the Agency to address the issue of, you know, potential for perforation and --

DR. KELLEY: But there is one more wire than in the unidirectional catheter?

DR. YAROSS: That is correct.

DR. KELLEY: Okay.

DR. BILAZARIAN: I would say again that I think the approval with the electroanatomical mapping is appropriate but not the others, and in deference to Mr. Halpin's comments, I certainly don't want to put an inappropriate burden on industry, but it seems like one of the concerns was the inability to recruit for this trial, and I would think that there would be no burden in recruiting for a trial using the robotic system. It seems like it would be a very easy trial to recruit for, a trial comparing a robotic system versus a non-robotic system.

DR. YAROSS: I think our question would be, you know, from the standpoint of least burdensome, can the question be satisfactorily answered from bench and animal data, and in the past we have argued to the Agency and they have accepted that argument for two other indications that these questions can be addressed through bench and animal data, and I think Dr. Eloff had a comment.

DR. ELOFF: Yes. Dr. Kelley, I was the lead reviewer also for the bidirectional steering catheters, and without giving away too much detail on the internal workings of them, they use the same pass/fail criteria for stiffness for both the

unidirectional and bidirectional steering catheters. There were some modifications made with the addition of a pull wire and subtraction of some other stiffness materials within the tip that made those two buckle force measurements equivalent in those. And that was part of the basis for approval in both the ventricular tachycardia and atrial flutter indications for that device.

DR. BORER: I agree with everyone who has said that the navigation system is what we're looking at here and that we really cannot extrapolate beyond that, and I don't care how many other techniques may be used by different people in different laboratories. I haven't seen any data and I don't know how good those are. I know how good this is.

With regard to the bidirectional, my comment was going to be, except you've done it already, that I would be willing to accept bench data about the physical characteristics of the catheter, and I would leave it to the FDA to determine whether the bidirectional and the unidirectional catheter are sufficiently similar in their physical characteristics so that we needn't have a concern about the use of one or the other because David pointed out and others have that, you know, if there

really is a difference in being able to point in one direction rather than two, you can just point in one direction with the bidirectional catheter. So I would be willing to be guided by the bench data that the FDA could analyze for that issue. But, for the other issues, the catheter that's automated, magnetized, and the navigation system, I think we're approving this catheter with the navigation system, and we really can't go beyond that.

Is that sufficient for this?

DR. ZUCKERMAN: That's very helpful.

DR. BORER: D. Okay. Why don't we move around here. Dr. Fleming, have you done one yet?

DR. FLEMING: That would be D, right?

DR. BORER: Yes.

DR. FLEMING: Okay. The study protocol allowed enrollment of patients who failed a class II/IV antiarrhythmic drug, AAD, rate control therapy, in addition to patients who failed a class I/III AAD, membrane active drugs. Of the enrolled patients, 16 percent, 26 of 167, failed only rate control therapy.

Please discuss whether the trial provides sufficient experience in a population that has failed only rate control therapy such that the indication statement should include patients that have failed

only rate control medical therapy.

Well, since I'm not much of an expert on these medications, I may need to defer that to those on the Panel who are.

DR. BORER: Okay. Why don't we go then to Dr. Jeevanandam.

DR. JEEVANANDAM: Well, I mean the efficacy here was symptomatic atrial fibrillation, and if you just give rate control medication, then you're basically allowing the patient to stay in atrial fibrillation. So you don't expect them to convert to the sinus rhythm.

On the other hand, I don't know if you want to put that into a label, you know. You're going to have to select which drug to give to which particular patient. So I don't know if this trial provides sufficient experience to say that patients need to be tried on membrane active drugs before they get a surgical or catheter ablation.

DR. BORER: Dr. Karasik.

DR. KARASIK: So, no, the trial doesn't provide sufficient experience in a population that's failed only rate control therapy; however, I would just say that I was taught not to do subset analyses in trials that were not powered to look at such

subsets, and you have to consider the whole population, the population as a whole, which is that we believe the therapy is effective.

But given that, I would not offer this therapy to patients who only failed rate controlling therapy except in extraordinary circumstances.

DR. BORER: John.

DR. SOMBERG: Well, I agree with your personal choices here, but I think the study said class I and class III drugs that failed in class II and IV. So we're taking the whole study as a whole, and therefore I would go along with that.

I think if we say that they failed antiarrhythmic drugs and are symptomatic PAF, then this population makes sense. There are people who have just failed class II or IV drugs who they don't want to take them, who have problems with the more reasonable ones that may want to go about this.

So once again, I think we don't want to be too prescriptive in the discussion and take what the protocol says.

DR. BORER: Okay. David, do you want to say anything about this or do you want to --

DR. NAFTEL: I agree with Dr. Somberg.

DR. BORER: Okay. Spoken like a true

statistician. Judah.

DR. WEINBERGER: I don't think we really have any specific guidance that we -- the study doesn't give us sufficient guidance on this question. It's a labeling issue. I think that this is a place for reasonable clinical judgment.

DR. BORER: David?

DR. SLOTWINER: Yeah, I agree. I think that just as the guidelines for the treatment of AF permit ablation as first line therapy occasionally, if somebody cannot tolerate rate control and doesn't want an antiarrhythmic drug. I think we should leave it vague, and I think that we shouldn't be too specific. So I would leave it the way it is.

DR. KELLEY: Yeah, I would agree. I don't think we know. I mean if you look at the chart, there's only 20 patients that had actually finished the 9-month follow-up. So I don't think we have those data, but I don't know how practical it is as far as labeling to get into all that.

DR. BILAZARIAN: I agree that it does not provide sufficient experience, but I would not change the label.

DR. BORER: You know, I guess it seems like it's unanimous here, but I would urge that if the

indication section reflects the way the trial was done, which is not unreasonable, but at least a statement has to be provided about how little we know about rate control alone as a basis for doing this, about the success in people who have failed rate control alone. It does look like it's different from those who have failed antiarrhythmic drugs. In fact, if you took out the rate control alone, we're not talking about 47 versus 18 anymore in the United States. It's looking much better.

But anyway, I think at least the label has to reflect what we know and what we don't know about treating people just for rate control failure.

Okay. Looking around the table here, I think we've -- have we finished with this one? Is this okay?

DR. ZUCKERMAN: No, we need to go onto E.

DR. BORER: Oh, we will, but I just wanted to know if D was okay.

DR. ZUCKERMAN: Yes.

DR. BORER: We can't do E without D. Looking around the table here, does anyone have any additional recommendations regarding the device labeling that we haven't discussed? Dr. Kelley.

DR. KELLEY: I would just agree with what

you just said. It would not be unreasonable to say that we don't have the information. We have information only on patients who failed class I or III or we don't have it on ones that failed rate control, and I think that would be reasonable.

DR. BORER: It looks like everybody is all thought out here on these issues. Do you have specific questions before we get to the post-approval study that you were thinking of?

DR. ZUCKERMAN: Yes. In the current IFU, I don't think the sponsor has really described the fact that this is not a cure for atrial fibrillation and that anticoagulation should be maintained. So that's one point we'd like your viewpoint on.

The second point is, in the clinical studies section, we are obligated to describe clearly what happened during this clinical trial and would like some suggestions for how we can appropriately describe the U.S. versus OUS results.

DR. BORER: Okay. I think we've had a couple of opinions about the first part but nothing about the second. Does anybody want to provide an opinion on these issues? First of all, the fact, you mentioned, Judah, and so did John, the issue of anticoagulation and specifically the fact that this

isn't a curative procedure.

DR. WEINBERGER: I think that was implicit in my request to label this as for treatment of symptoms. I don't think that there's any expectation. Certainly, there's no data to suggest that anticoagulation should be in anyway altered by this therapy. I think that what you can say is that, and I think this is probably a reasonable thing to say in the IFU, is that the data does not support alteration of anticoagulation therapy recommendations for this patient population. So that way you're not saying whether they must be if they haven't or, you know, you don't want to be in the business of deciding who should be anticoagulated. I mean that's a separate decision, and this therapy doesn't seem to alter that decision.

DR. BORER: Does anybody want to add to that or does anyone disagree with that? David.

DR. SLOTWINER: No, I agree entirely. I think the label should say the decision regarding appropriate anticoagulation should be made independent of the decision whether or not to perform an ablation.

DR. BORER: And would anyone disagree with the earlier suggestion that this has to say somehow

that this has not been shown to cure atrial fibrillation? John.

DR. SOMBERG: I think it's gone too far to say it does cure or doesn't cure. I mean that was not what this is about. And saying symptomatic is going to be confusing on people, you know -- you have to state that anticoagulation, in my mind, should be continued. It is reasonable to continue anticoagulation. I think coming from what I heard at the AHA, et cetera, on this quite extensively, there is no data to support without a randomized clinical trial, stopping anticoagulation. So why should we say maybe it's reasonable, it's this, it's that. I think just continue anticoagulation, and if people want to disagree with that, they have to have some evidence to do that.

DR. BORER: Dr. Kelley.

DR. KELLY: But, see, not all these patients are going to be anticoagulated, whether they get an ablation or not depending on the CHADS score. So if you have somebody, a young healthy person with one atrial fibrillation, the physician may elect not to anticoagulate them regardless.

DR. SOMBERG: You're absolutely right. The lone atrial fibrillation is an excepted group. So

maybe you have to say anticoagulation should be continued following standard clinical practice or something like that. Then I agree.

DR. BORER: Okay. I think you get the sense of the committee here. Okay. Any other additional recommendations that anyone has or that you want us to talk about?

DR. ZUCKERMAN: How should the U.S. versus OUS results be described in the clinical section?

DR. BORER: David, how would you like to say something here?

DR. NAFTEL: A couple of things. First of all is I'm looking at the indications for use on figure 1, and so that shows the overall results that we've all focused on, and just as a small thing to keep from getting in a trap, it does say that it shows the Kaplan-Meier survival curve and then what's being shown is not survival, and I know --

DR. ZUCKERMAN: Excuse me. Dr. Naftel is on page 21 of the label.

DR. NAFTEL: So I know we all say Kaplan-Meier survival curves, but you'll confuse people. I'd call it Kaplan-Meier curve or freedom from event curve, but I wouldn't use the word survival because it's not survival.

Okay. So now to get to your question, you know, we've danced around the issue totally as to whether or not we can pull that one hospital with the rest or the OUS with the U.S. We've totally danced around it because we haven't needed to answer it because we were fine when we exclude those. So we never answered the key question, are the data poolable? We've never answered that because we haven't had to until now that you bring it up.

So it seems to me there are two choices. Either show the curves just like they are with the combined data and say it's poolable or show that one site with the wonderful results, which I would not be comfortable in showing here. So given that I'm not willing to show that wonderful curve, I personally would just go ahead and pool the data, show this curve, and let it go. That's my suggestion.

DR. BORER: John.

DR. SOMBERG: Well, I knew we would find a difference between us.

DR. NAFTEL: You're supposed to say you agree with me.

DR. SOMBERG: Well, I agree you should show the poolable data, but I would say one site had a higher performance, and I would show that data versus

the other sites as well. I think it would be very misleading and maybe disheartening for both patient and clinician who aspired to this great mental -- results when it's not obtainable for all the other centers of excellence across the U.S. I don't know if you have to go into it's OUS and U.S. sites or what have you, but I think there is a distinct difference between these two groups, and it gives a very false impression by combining them and not saying anything else because they're not going to have the benefit of all this discussion we've had here all day. I think it's been a very important discussion.

DR. BORER: They can read it in the Federal Register.

DR. JEEVANANDAM: I completely agree with John. I think it would be a little deceptive to put that data in there, considering the fact that one site changes that from 72 percent to 47 percent. So I think we need to get a reality check in there.

DR. BORER: Yes.

DR. KELLEY: Could you put it in and then just say, you know, results vary from whatever percent to 100 percent depending on many factors, including experience and patient population.

DR. BORER: You could.

DR. SOMBERG: That's going too far because, you know, we've -- that it's experience and patient population, but I think you wouldn't want to necessarily want to put it in the IFU.

DR. KELLEY: Well, many factors which may include.

DR. SOMBERG: Yeah, something like that. But I mean you can't just say in my opinion, you know, the results are 70 versus whatever that they have varied.

DR. JEEVANANDAM: I mean one way to get around there I guess is to have -- if you want to streamline this, you can have that one graph, and then you could have a graph that says all centers, and you can have another graph that says U.S. centers only.

DR. BORER: David.

DR. SLOTWINER: I think what I would consider doing is showing all the centers together and then the outside U.S. centers and the U.S. centers and just make a note that there was a difference. I think the reason is speculation. Our speculation isn't going to be any better than somebody else's, and just leave it at that. Let them

see the difference.

DR. BORER: Any other?

(No response.)

DR. BORER: I would suggest that this curve is just fine, but I do think that there has to be a mention of the variability of the data, whether it would be in the form of a small table which would be one way to do it or a few narrative lines that describe the variability, the high, the low, the average, whatever. I wouldn't put in a lot of graphs. I think the data are what they are. They were pooled. We've heard several statistical opinions that suggest that that's not a terrible thing to do. So I would leave it at that. I would put in the one graph as it is, and I would add something, table or narrative, small, underneath about the variability of the results.

I just don't think there are enough -- we have enough data to do much more than that.

Okay. Is that okay on that one?

DR. ZUCKERMAN: Yes.

DR. BORER: Okay. Let's move on then to post-approval study. Dr. Somberg.

DR. SOMBERG: The premarket clinical data has provided evidence regarding the safety and

effectiveness of this device in the acute phase and up to 12 months post-ablation. The study was performed at recognized centers of excellence. The purpose of ablation therapy is to produce a permanent Change to the structure of the heart, generally thought to be a non-regenerative organ. One clinical site performed prophylactic application of a right atrial, cavotricuspid isthmus (CTI) lesion that was not done in the remaining clinical sites and that site had higher effectiveness results 12 months post-ablation compared with the remaining sites.

Please discuss the appropriate trial design for determining the procedural safety profile in a broader patient and provided population. Please comment on what may be an appropriate hypothesis, endpoint, duration of follow-up, and control group.

Well, before I came in here, I thought that might be a very important difference between OUS 1 and the other sites. I think you must have deference to people who have a procedural familiarity with this and pathophysiologic knowledge that I don't. And specifically, correct me if I'm wrong, Dr. Wilber, you felt that that was not a case given a whole series of data that I don't want to be repetitious here on.

But needless to say, I think that would certainly be one thing that I would collect in a post-approval study. And I think what's most needed is not a small study of 100 or 200 patients that tries to study some of these questions in maybe a slightly different population, et cetera, but I think what is needed is really a much larger study to give us an understanding of some of these issues which will only come out with greater numbers of patients.

Therefore, I think the most important thing is a registry that looks at the next 500 to 1,000 patients that are followed for the next 2, 3, 4, and hopefully even 5 years, which the sponsor did say they were willing to go out for 5 years. So I think the more patients we get into this, the more sites we get would be helpful, and we would ask questions like the right atrial lesion question, the significance of pulmonary vein stenoses because I want to know what happens to 20 to 30 to 40 percent lesions over time. I mean that may be significant or it may have, you know, it may over address or stay the same. So questions of that nature and also try to see what happens when you do this ablation. If they don't have repeat symptomatic episodes, many doctors will stop anticoagulation and see the frequency of late

term events as well. So I think that would be very useful.

That's not to exclude, you know, a smaller directed study that might be in heart failure patients, for instance, comparing heart failure patients versus the patients with reserved ventricular function, but I would not want to limit it to, if you just do 150 patients again, and you have 20 in a group that has cavotricuspid isthmus ablation, I don't think we'll have, you know, 5 years from now we'll have the same thing, that the group is too small, we can't make a comparison, et cetera, et cetera.

DR. ZUCKERMAN: Okay. Dr. Somberg, those were very helpful initial comments, but if I could ask you and the other Panel members to become a little bit more focused regarding some of the safety and longer-term efficacy questions, and to help you out, I would suggest you go back to FDA slides 103 and 104. I think it gets to the core of the matter.

On slide 103, the sponsor is suggesting an equivalence registry with a non-inferiority delta of 9 percent when the expected rate is 11 percent, et cetera, if you'd just review those slides.

DR. NAFTEL: May I ask a point of

clarification?

DR. ZUCKERMAN: Yes.

DR. NAFTEL: I understand sort of, post-approval studies, postmarket surveillance, and then the whole MDR process. So I understand these studies a bit, but what I've never quite been clear on is we're calling this a trial, a trial design for the post-approval study. And what I'm not clear on is will there ever be a decision? Are we just learning stuff or is there actually a point in time, like will there be aggressive patient enrollment? Would it be treated just like the premarket? And at some point, would people get together and say you made the endpoint or you didn't, and would there be some action after that.

DR. ZUCKERMAN: Yes, to all of the above. So again, FDA has a significant responsibility to regulate products throughout the total product life cycle. That includes both the premarket and the post-approval evaluation of data. The challenge always is to figure out what that balance is, what is the amount of data that's needed for a device to get on the market, and then post-approval, what type of surveillance is necessary.

Now, I can appreciate some of your

comments, Dr. Naftel, that there's a general sense that sometimes post-approval commitments are not carried through, et cetera. In general, I would summarize that as the old FDA/CDRH.

If one looks at the performance of both the industry and FDA over the last few years with respect to the drug eluting stent post-approval studies, carotid stent studies, AAA studies, these trials, and here I'm defining a post-approval trial as one with a hypothesis and a sample size, et cetera, are taken extremely seriously. As many know, when the problems cropped up with both AAA graphs and drug alluding stents, we brought this data back to an Advisory Panel for significant discussion. We also have the ability to include these important real world data as supplemental information in our label.

So this is an important part of the total regulatory process that we're asking Panel member comment on.

DR. NAFTEL: And if I may say, I did not intend to be critical. I am aware of this history. I'm more commenting on the slides for the proposed study. It sounds a little, if I may use the technical term, looser than the premarket study. Like I'm not quite seeing where the action plan is in

the slides we saw on the postmarket study.

DR. ZUCKERMAN: Well, those are the comments that you and others need to give both the Agency and the sponsor, because as we've perhaps talked about today, atrial fibrillation is a large public health problem. This is potentially not just an evolutionary device approval, but a transformational device approval, and the Agency has a responsibility to construct with the sponsor an appropriate post-approval surveillance mechanism, hence our concern with this question.

DR. BORER: John.

DR. SOMBERG: Well, I was just going to follow up on what Dr. Zuckerman was asking me, and I just thought that you asked me to refer to those two pages in the FDA slide, and I don't agree with that study. I mean it's 145 patients. I mean that caused me to get short of breath and diaphoretic even though the air conditioner is on.

So, no, I think that's wrong. I would want to have a follow-up on an adequately sized population, and I'm not here, and I'm probably never prepared to tell you what an exact, you know, but you have people that do that very, very well, but I want to know about what's the consequence of pulmonary

vein stenosis. I want to know what's the consequence of CTI lesions, and I want to know what's the -- and I would personally, I don't know if the rest of the Panel wants to have anything to do with this, but I would like to know because I think there will be wide use of the catheter regardless of what the label is, with or without a navigation system.

So I would want to have those things answered and maybe, maybe you want to answer in this type of format or maybe it's a specific study, but what happens in people with 40 percent or below ejection fraction who will utilize this as well, or that might be a separate study. It probably should be.

DR. SLOTWINER: Can I ask a question, Dr. Borer? I don't know what the limitations of what we can ask for are, but this has become the predominant ablation for electrophysiologists. This makes up I think the most common ablation now, and that's probably going to increase exponentially.

Is there a way to request information that's scalable to the use of the catheter and with the distribution of the catheter? I'm very curious to have the real world experience rather than 20 centers of excellence experience, and is there a way

to get information based upon where the catheters are distributed and sold and the patients that they're used in, using that as the primary method for determining who and how many patients would be included.

DR. ZUCKERMAN: Yes, I would ask everyone to look at slide 98 from the FDA presentation. I think what you're getting to, Dr. Slotwiner, is that we can't ask for everything under the sun. These are the five general areas where the Agency has regulatory authority. I think what you're pointing to is a study that gets better at real world community performance in study centers that are traditionally not the highest enrolling sites, et cetera, but please elaborate.

DR. SLOTWINER: No, that's exactly what I'm interested in. The smaller centers, perhaps not the training centers where there may just be one person doing these studies, with or without a mapping system, and looking at the complications and the efficacy, and the long-term success. I realize it will be burdensome to follow-up patients for many years, and I think five-year follow-up will be very valuable. And there are obviously many studies ongoing now to look at atrial fibrillation ablation

in many subsets of populations, but I would hope that what we could ask for would be something to track the actual use of this catheter if it's approved, and efficacy and safety primarily in the population that you would give it approval for.

DR. BORER: Dr. Bilazarian.

DR. BILAZARIAN: Yeah, I guess my guidance as a clinician would be that I'd be willing to accept less data points but in a larger dataset. Dr. Yaross said that this catheter, 70,000 units have been sold since 2005, and Dr. Calkins has told us this is the most frequently performed ablation. So that means 35,000 of these catheters have been sold for atrial fibrillation. So that's about 10,000 catheters per year, so to propose a 150 patient follow-up study I think is very concerning, doesn't make me short of breath, but maybe diaphoretic.

So I guess I would love to see a much larger dataset of several hundred, 500 patients with seven day follow-up and then vital status annually with an EKG, as sort of a baseline, minimum amount of data would at least give us a forward looking idea of the safety acutely and adding to it the other suggestions that that could be mandated in both high volume and lower volume centers, and I think that

that would be not very burdensome for industry and should be very easy to accomplish based on the numbers that I just cited.

DR. BORER: Can I, just in the interest of time, suggest a straw man and then everybody can shoot at it. Based on the comments we've heard and my own reading of this dataset, I think it's fine to have, to begin with, with hypothesis testing, but I think there are two separate components to what's needed.

Number one is more data, which means basically an observational study, a registry, and then there are a couple of specific questions that need to be asked that really only can be answered if there is a true experimental design incorporated into the study.

So I would suggest that, number one, we do need a registry. I would have said given the number, just as Dr. Bilazarian said, with the number of units being sold, I don't want to make this terribly burdensome financially for the company because that wouldn't be reasonable, but I think between 500 and 1,000 patients can be followed with the number of units being put in. I would make it a five-year follow-up with annual reporting. I think that we

would want to know the following specific pieces of information at the outset and during the follow-up. Number one, the pre-procedure experience of the users, and it goes without saying that with FDA concurrence, the sites that are involved in this follow-up should be a variety of sites, high volume academic, lower volume community, wherever the stuff is being sold.

The pre-procedure experience of the operator needs to be known. The pre-operative formal training and use of the device, yes or no. The indication for which the procedure was done. Whether or not the patient is in heart failure and whatever the class is. What the ejection fraction is. I'm not suggesting that one must do a trial, but I think we could get some observational data that might be helpful here. The number of ablations that was performed and the pulmonary vein size at the outset of study.

The outcome events would be pulmonary vein size, atrial fibrillation recurrence with whatever kind of follow-ups seems reasonable each year, be it a 24-hour tape or some other means of follow-up, and that could be variable, and the number of heart events, the number of major adverse cardiovascular

events that have occurred.

That would be the registry that I think would not be overly burdensome. I think a trial with an experimental design would need to be done to determine the importance of the lesions that are placed with the catheter, whether -- specifically I'm interested in knowing what the right atrial lesion does and what the results are if the company wants to get extension of approval of the nav system versus non-nav system catheters. I think those need to be studied in trials, those two things, and the rest in a registry.

So that's what I would suggest should be the post-approval mandate.

Now, everybody's heard that, and if you want to shoot at it, add to it, detract from it, throw something at me, it's okay. Now's the time.

(No response.)

DR. BORER: I don't see anybody saying anything. Do we need specific requests of people around the table?

DR. ZUCKERMAN: No, I think that's a very helpful general approach, but I do have several follow on questions. Number one, the longer-term follow-up is going to be extremely important. We've

suggested out to five years, and this is a question specifically for Dr. Naftel. The sponsor with their post-approval study has suggested a usual frequentist design. Given that we want to be able to detect longer term signals more quickly, more efficiently, would you recommend thinking about a Bayesian design for this large post-approval study?

DR. NAFTEL: That's a great question. You know, now it really could be Bayesian design with an informative prior. You could build something based off of the current study. I could go either way. I'd love to hear what Laura and Dr. Berry had to say, but that certainly could tighten it up if you were willing to do that.

DR. BORER: Can I just make a point here. I mean, you know, what I've suggested is an observational study and a Bayesian design so you can telescope the conclusions would be great I think. I mean, you know, if it's reasonable, but again I don't think it has to be a hypothesis testing study. I don't think you need a benchmark. What's acceptable in terms of risk is going to be determined by what happens in terms of efficacy, and both of those kinds of data are going to be obtained from this kind of study. I would see the registry largely as a label

refining exercise. Of course, if one saw some -- happening, then that could lead to removal of the approval of the device. But I don't think it needs to be set up with an a priori hypothesis that you're going to have X event rate, not Y event rate. I don't think we're at that point yet. I don't think we know enough. But the Bayesian design business might get us to some number a lot faster than just straight observation.

DR. ZUCKERMAN: Okay. And that handles our second key question, which is really what control are you going to compare it to, and given the lack of data out there, it sounds like you're suggesting just qualitative descriptive statistics at various time points.

DR. BORER: That's exactly what I'm suggesting, yeah.

DR. NAFTEL: If I just may make one comment because I run three registries and I know the pain, we always say with our registries that we do everything we can to make them mimic a FDA clinical trial. So I kind of like your idea of refining the indications for use, and I like everything you're saying. I just wouldn't want anyone to interpret it as it can be a loose, crummy registry. It still has

to have the same standards of follow-up and still has to be as if it were a clinical trial, maybe fewer data points, maybe fewer -- but it still has to be a serious effort, not just a crummy old registry.

DR. BORER: And having said that, wherever the thing is done, it's got to be consecutive series, you know. There can't be any selection. I mean it's got to be a consecutive series.

Yes, I'm sorry.

DR. ELOFF: Dr. Borer, in your straw man, you didn't mention specifically the procedural safety. I was wondering if you could comment on that aspect.

DR. BORER: Oh, I'm sorry. That's wrong. When I discussed heart events and atrial fibrillation recurrence, what I meant was the whole series of major adverse cardiac events and anything that we think is important. The seven-day results are certainly very important. Just as they were done in the trial, one would like to record those, but further out, you know -- and AF recurrence to me seem to be the key issues and pulmonary vein size. So that means some kind of imaging is going to have to be done on a periodic basis in these patients.

DR. ELOFF: Would you continue to recommend

that the seven-day adverse event rate be captured in a registry or go with the sponsor's recommendation that there actually be a hypothesis test related to the post-approval study?

DR. BORER: Again, I don't think we have enough data to set up a hypothesis that's reasonable. I think we need more data. There are just a few hundred patients who have been studied. We need a more stable point to estimate. I would think that's what we've got to do.

DR. ZUCKERMAN: Okay. Good.

DR. BORER: Does anyone else want to say anything about that? Disagree, agree, enhance, tear down.

(No response.)

DR. BORER: No. Okay. Well, if that's the case, then guess what we're up to. Voting.

MR. SWINK: Not yet.

DR. BORER: Sorry. I missed my script. So sorry. My fault.

Second open public hearing of this meeting. We were supposed to do that at 3:30 and I didn't. Does anyone wish to address the Panel? If so, please come forward to the podium and state your name, affiliation, and indicate your financial interest, if

any, in the device being discussed today or any other device.

(No response.)

DR. BORER: I don't see anyone coming forward. I think we have nobody.

At this time, we will not take a 15-minute break. Are there any further comments or clarifications from the FDA, Dr. Eloff or Dr. Zuckerman?

DR. ZUCKERMAN: No.

DR. ELOFF: No, thank you.

DR. BORER: Okay. Are there any other comments or clarifications from the sponsor?

DR. YAROSS: In the interest of time, I'll be brief. Just a few short clarifications. First of all, on the issue of anticoagulation, the sponsor has not been proposing any statement about cure and agree that the trial is silent on anticoagulation and are perfectly happy to have that so addressed in the labeling.

One issue that came up a couple of times, I'd just like to clarify for the record, during the discussion, there was a statement that for the U.S. subjects, there was less than a 1 in 2 chance of being AF free at 90 days. Just to clarify, that was

the probability of being a chronic success per the protocol. The actual point estimate for being AF recurrence free was, in fact, 62 percent and not 47 percent.

DR. BORER: Thank you for the clarification.

MS. YAROSS: There was a comment a couple of times about an eight-hour procedure. In fact, the median procedure time was between three and four hours, and then finally as for the post-approval study design, we recognize that our trial that we initially proposed was small. It was consistent with what we had agreed upon with the Agency for our two prior approvals for this, but we, of course, will work with the Agency to respond to the Panel's recommendations.

And with that, I want to thank the FDA again and the Panel for their great deliberative process and the excellent recommendations. Thank you.

DR. BORER: Thank you for the very nice presentation.

Okay. We will now move onto the voting. The industry and consumer representatives do not vote, and I only vote only if there's a tie.

We're now ready to vote on the Panel's recommendation to FDA for this PMA. Mr. Swink will now read the Panel recommendation options for premarket approval applications. Mr. Swink.

MR. SWINK: The Medical Device Amendments to the Federal Food, Drug and Cosmetic Act, as amended by the Safe Medical Devices Act of 1990, allows the Food and Drug Administration to obtain a recommendation from an expert advisory panel on designated medical device premarket approval applications that are filed with the Agency. The PMA must stand on its own merits, and your recommendation must be supported by safety and effectiveness data in the application or by applicable publicly available information.

The definitions of safety effectiveness and valid scientific evidence are as follows:

"Safety as defined in 21 C.F.R. Section 860.7(d)(1) - There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probably benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probably risks."

"Effectiveness as defined in 21 C.F.R. 860.7(e)(1) - There is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results."

"Valid Scientific Evidence as defined in 21 C.F.R. 860.7(c)(2) - is evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use. Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions, are not regarded as valid scientific evidence to show safety or effectiveness."

For the Panel, your recommendation options

for the vote are as follows:

1. APPROVAL - If there are no conditions attached.

2. APPROVABLE with conditions - The Panel may recommend that the PMA be found approvable subject to specified conditions, such as physician or patient education, labeling changes, or a further analysis of existing data. Prior to voting, all of the conditions should be discussed by the Panel.

3. NOT APPROVABLE - The Panel may recommend that a PMA is not approvable if the data do not provide a reasonable assurance that the device is safe or the data do not provide a reasonable assurance that the device is effective, under the conditions of use prescribed, recommended, or suggested in proposed labeling.

Following the vote, the Chair will each Panel member to present a brief statement outlining the reasons for his or her vote.

Thank you.

DR. BORER: Are there any questions from the Panel about the Voting Options before I ask for a motion?

(No response.)

DR. SOMBERG: I would like to make a

motion.

DR. KARASIK: I'm sorry. Are you going to tell us exactly what we're voting on? Are we voting on one catheter, five catheter? Can you --

DR. BORER: Let me finish reading first. I'd like to direct the Panel to the voting procedure flowchart in your folder. It's in color. Let the record show it's four colors.

In the context of this flowchart, I think you'll be able to make a recommendation specifically answering your question. So --

DR. KARASIK: Okay.

DR. BORER: -- perhaps that's the way we'll go ahead. Can I ask for a motion from any Panel member, either approval, approvable with conditions, and then the conditions like the one you just suggested might be stated, or not approvable, and I see a hand. I thought I saw a hand. Yeah, Dr. Somberg.

DR. SOMBERG: Unless you want to make the motion.

DR. BORER: No, no, I can't make the motion. You have to make the motion.

DR. SOMBERG: No, no, my colleague at the other end.

DR. BORER: David make the motion.

DR. SOMBERG: I'll defer to David. It was his --

DR. SLOTWINER: I move that it's approvable with conditions.

DR. BORER: Okay. Any second?

DR. SOMBERG: I second.

DR. BORER: Okay. Let's discuss the main motion. You suggested with conditions. Can you state the conditions?

DR. SLOTWINER: Yes, I think the conditions are limited to the catheter studied with the navigation system studied.

DR. BORER: Okay. Any second for that?

DR. SOMBERG: Can I just ask a point of clarification?

DR. BORER: Yes.

DR. SOMBERG: I thought you were going to go for the bidirectional as well?

DR. SLOTWINER: Well, I think that that is something I really need to turn to Dr. Zuckerman to give guidance. I think that -- I feel obligated to stick to the information that we're provided, although I understand that the catheter may have exactly very safe physical characteristics that have

been tested in an animal lab and the FDA may feel that that's equivalent, but I don't feel that we have enough information to make that decision.

DR. ZUCKERMAN: Okay. Let's take a step back here and, Jim, you need to help Dr. Borer here. Please go back to the flowchart. There is an approval with conditions motion. Does the Panel first need to vote on Dr. Slotwiner's general approval?

DR. BORER: Sorry. Okay. We have a motion --

DR. ZUCKERMAN: Dr. Slotwiner, you want to be as specific as possible regarding what device you're talking about. Maybe you can rephrase it.

DR. SLOTWINER: Okay. So I move to approve with conditions approve the ThermoCool catheter unidirectional with navigation catheter in conjunction with the CARTO mapping system for ablation of lone symptomatic paroxysmal atrial fibrillation.

DR. BORER: Okay. Do we have a second?

UNIDENTIFIED SPEAKER: I second it.

DR. BORER: We have a second. Okay. Any discussion of this motion?

DR. SOMBERG: If there are additional --

DR. BORER: We'll get to conditions in a minute.

DR. SOMBERG: Okay. Fine.

DR. BORER: We're just discussing this motion.

DR. SOMBERG: That's fine.

DR. BORER: Okay. Then I'd like a show of hands? Can I do it that way or do I have to ask everybody to say it on the record?

UNIDENTIFIED SPEAKER: (Off mic.)

DR. BORER: Okay. We're now voting for the approvable with conditions.

MR. SWINK: Okay. It's been moved and seconded, and we're going to vote on approvable with conditions, and we're voting on the first condition which David Slotwiner could paraphrase again.

DR. SLOTWINER: Yeah, the condition is that the catheter being approved is the unidirectional catheter with navigation used in conjunction with the CARTO mapping system as the data reflects it's presented to us today.

DR. BORER: Okay. Can we do that by hand or --

MR. SWINK: And that's being seconded.

DR. BORER: That's been seconded. Okay.

Can I have a show of hands all in favor?

(Show of hands.)

DR. BORER: Let the record show the vote is unanimous in favor of that motion.

So now we need to determine the conditions. Is there a motion for a second condition? We have a first condition. Is there a second condition?

DR. SOMBERG: I would like to have a physician education program for providing training in the use of the catheter and the navigation system obviously.

DR. BORER: Okay. Is there a second for that motion?

DR. SLOTWINER: Yes, I second it.

DR. BORER: Okay. Any discussion?

DR. BILAZARIAN: I would ask if Dr. Zuckerman can advise us. Should we be specific about that, or I guess the modification essentially to your motion would be to restrict its use to physicians who are not previously experienced, but obviously physicians who are experienced shouldn't be restricted or required to undergo a physician education program.

DR. BORER: May I ask, Dr. Zuckerman, do you want us to micromanage this?

DR. ZUCKERMAN: No. We need to appreciate the broad strokes.

DR. BORER: Yeah. So the motion, not that what you're suggesting wouldn't be done, but it's been moved that we should vote in favor of a training program, and it's been seconded. Is there any discussion about that particular motion?

(No response.)

DR. BORER: If not, then can I see a show of hands for those who approve?

(Show of hands.)

DR. BORER: Okay. Once again let the record show that the vote is unanimously in favor of that condition.

Is there a motion for another condition? Dr. Somberg.

DR. SOMBERG: I would move that we request that the registry be established to look at the problem or a registry be established and be adequately powered to look at questions of what atrial isthmus ablation, pulmonary vein stenosis and operator experience in the success or failure of the ablative technique.

DR. BORER: Is there a second for that?

DR. SLOTWINER: I second it.

DR. BORER: Okay. There is a second. Any discussion?

UNIDENTIFIED SPEAKER: I'm sorry. I didn't quite under Dr. Somberg's condition. Can you restate that please?

DR. BORER: Yeah. What he's suggesting is that there should be a registry established to look at the impact of the isthmus lesion being performed.

DR. WEINBERGER: In the right atrium.

DR. BORER: In the right atrium.

DR. SOMBERG: Well, I made a mistake. I said left. I meant right, yeah.

DR. BORER: And what were the other aspects of your registry?

DR. SOMBERG: Experience of the operator and pulmonary vein stenosis and its long-term consequences.

DR. BORER: Okay. There's been a second. Is there any discussion?

(No response.)

DR. BORER: If I may, I'd like to offer a discussion point. I don't believe that the isthmus lesion can be studied with a registry. I believe that needs a hypothesis test with an experimental design. I think that the registry really is required

to deal with the whole panoply of outcomes that I mentioned earlier in the summary statement that I made, that I won't repeat because you've got them, and I don't think we have the time to go through them one by one. But I'd suggest, if you would accept it, John, to modify what you said to deal with the registry issues and the registry and the issues like the lesions that are placed and nav versus no nav.

DR. SOMBERG: Well, the isthmus ablation issue, I mean I'm not against the study as well on that, but if you have let's say 500 patients or 1,000 patients and 100 of them or 150 have isthmus ablation and they have a success rate of 100 percent, and the other group has a success rate of 30 percent, that would be very useful in a large number. If you did 100, you know, if you start a 100 patient study and, you know, you may have very great difficulty in getting this done or not, you may not ever get to see this.

So I would like to see those questions asked in a registry. I'm not precluding setting up a study for that or what have you, but, you know, you can do this type of work with registry data as well.

DR. BORER: Okay.

DR. SOMBERG: Not as well, of course, but

you can get some inclination. So -- am I wrong on that, Jeff? I mean if you want to insist, I'll drop it, but --

DR. BORER: No, I'm not insisting on anything. I'm just asking. I don't think that in a not well-controlled study you can get rigorous results, but if you want to, you know, if that's the motion you want to make, that's it. Can I ask who is in favor of that motion?

DR. NAFTEL: Can we discuss it?

DR. BORER: Oh, yes. Yeah.

DR. NAFTEL: A registry, just the word, it's still loose enough that we're leaving a lot of room for FDA to work with the company within the confines of saying registry, and I think that's a good thing, but I mean these are recommendations and you work with them, right?

DR. ZUCKERMAN: That's correct.

DR. NAFTEL: Okay. Thank you.

DR. BORER: Okay. Then perhaps it should be broadened to -- we've had a motion in favor of a registry that could include any number of items.

DR. ZUCKERMAN: Okay. I believe we need to vote on Dr. Somberg's recommendation.

DR. BORER: Well, that's it. That's his --

DR. ZUCKERMAN: Okay. As stated.

DR. BORER: As stated, okay. Can I have a show of hands, those who favor the motion as it's stated?

(Show of hands.)

DR. BORER: Okay. We have one, two, three, five. Those opposed?

(Show of hands.)

DR. BORER: One. Abstaining?

(Show of hands.)

DR. BORER: One. Okay. So that motion passes.

Any other conditions? Would anybody like to make another motion? Dr. Somberg.

DR. SOMBERG: Well, I propose that consideration be given to a study looking at patients with ablative procedure with a left ventricular ejection fraction below 40 percent comparing patients, and I don't want to try to do the protocol here, but it could be drug therapy. It could be analogous to this protocol, drug therapy versus intervention, or it could be, you know, different types of intervention.

DR. ZUCKERMAN: Okay. Just for a point of clarification, Dr. Somberg, and you can make any

motion you'd like, that would generally be a new indication for use in a new IDE study as opposed to, you know, being incorporated in this particular PMA package.

DR. SOMBERG: Yeah, I hear your point. The trouble is without recommending there should be a study, there's going to be this issue, and there's going to be extrapolation from above 40 percent to below 40 percent. So I'm just saying that whether it be within the confines of a registry or a new study or a new IDE and PMA, that's a very important question to answer, but with that said, I'll withdraw my motion and leave it to you to discuss with the sponsor.

DR. BORER: Okay. Or would you like to perhaps suggest that these issues that you raised be considered within the registry. You want information on these issues. Ejection fractions --

DR. SOMBERG: Well, I'm not sure we can recommend that we have an off-label data collection.

DR. BORER: It's not off-label.

DR. SOMBERG: I thought we approved it for --

DR. BORER: No.

DR. SOMBERG: Okay.

DR. BORER: We didn't say anything at all in the approval with conditions yet out excluding people below a certain ejection fraction. In our prior discussions, we said we need more data. I don't think we said anything exclusive.

DR. SOMBERG: Okay. Then I recommend that we collect this data either in a registry, this data being data of the success and safety of the device in patients with ejection fractions below 40 percent, in either a registry format or a controlled study that may require an IDE and a new PMA.

DR. BORER: Okay.

DR. SOMBERG: Is that acceptable, Dr. Zuckerman?

DR. ZUCKERMAN: Anything you say is acceptable.

DR. BORER: Do we hear a second for that motion?

DR. KELLEY: I'll second it.

DR. BORER: Okay. Any discussion?

(No response.)

DR. BORER: Okay. Well, I would suggest that the several issues that were raised be included in the registry and we not get into control trials of that particular sort here, but I don't know if

anybody agrees with that or not. Can I hear from anyone else?

(No response.)

DR. BORER: Okay. If not, we have this motion on the table. All in favor?

(Show of hands.)

DR. BORER: Okay. We have a majority of people voting in favor of the motion to have either/or but look at the ejection fraction issue.

I assume, but I shouldn't assume, that you also intended the heart failure issue to be assessed or no? No, John, in your motion.

DR. SOMBERG: You want to clarify? You mean in other words people with -- I made the motion with people with ejection fractions under 40 percent but you could --

DR. BORER: With or without heart failure.

DR. SOMBERG: Yeah, that's right.

DR. BORER: Okay.

DR. SOMBERG: And I don't think that's necessarily -- I'm not concerned about, you know, symptoms of heart failure. I'm concerned about a quantitative total because this study was everyone above 40 percent.

DR. BORER: Okay. So that's been voted

upon and approved.

Are there any other conditions that anyone would like to suggest?

(No response.)

DR. BORER: Am I allowed to suggest a condition?

DR. ZUCKERMAN: Yes.

DR. BORER: Okay. I would like to suggest that a postmarketing study specifically assessing the nav versus non-nav catheters needs to be performed and that needs to be a controlled study. I won't suggest the design, the specifics of the design, whether it's non-inferiority or something else, but I would suggest that that needs to be done and that in addition, the right atrial lesion, yes or no, plus the standard pulmonary vein isolation needs to be studied in an experimental design format, those two things.

DR. WEINBERGER: We didn't approve a non-nav catheter.

DR. BORER: No, no, I know we didn't. But that's why I'm suggesting that it needs to be known if the sponsor wants to extend to it.

DR. ZUCKERMAN: I'm sorry. I don't understand that recommendation, Dr. Borer.

DR. BORER: We were asked to -- well, okay. I'll retract that. That's true. We're suggesting approval of one item. If the sponsor wants approval of another item, then they can think of the other studies. I'm sorry. I take that back.

DR. ZUCKERMAN: Yes.

DR. BORER: So let me just recommend the assessment of the right atrial lesion with the pulmonary vein isolation, yes or no, in an experimental design format. So that would be a condition that I would recommend.

DR. SOMBERG: I second the motion.

DR. BORER: Okay. Any discussion?

(No response.)

DR. BORER: If not, can I see a show of hands those who approve?

(Show of hands.)

DR. BORER: It looks like we have a unanimous approval.

Are there any other conditions that anyone would like to suggest?

(No response.)

DR. BORER: I don't see any. So we voted on the main motion already I believe, did we not?

Okay. It has been moved and seconded that

the Biosense Webster PMA Application P030031 for the NaviStar ThermoCool Irrigated RF Ablation Catheter is found approvable with the conditions the Panel has just voted one.

DR. ZUCKERMAN: Dr. Borer -- Jim, can you please help him. Now, we have to vote on the main motion with the conditions.

MR. SWINK: We're doing that.

DR. ZUCKERMAN: Okay.

DR. BORER: That's the next sentence.

DR. ZUCKERMAN: Sorry.

DR. BORER: We will now vote on the main motion with a show of hands. With a show of hands --

MR. SWINK: (Off mic.)

DR. BORER: Okay. With a show of hands, please indicate if you concur with the recommendation that the above-stated PMA be found approvable with conditions, and I'm going to read to you the conditions.

First, that the approval is for the unidirectional catheter with the CARTO mapping device only.

Second, that a physician education program should be provided, and that will have to be defined better with the FDA.

Third, that a registry needs to be established to obtain a variety of types of information which we discussed.

Fourth, that specifically data need to be obtained in patients with ejection fraction less than 40 percent with or without heart failure, clinical heart failure.

And, fifth, that a specific assessment in experimental design format of the CTI lesion plus the pulmonary vein isolation lesion should be performed postmarketing.

Those are the five conditions that we are voting on together with the main motion. Can I see a show of hands in favor of approval with those conditions?

(Show of hands.)

DR. BORER: And it unanimous.

DR. ZUCKERMAN: Excuse me. For the record, is Dr. Somberg still here?

DR. BORER: It's unanimous of those who are here, but Dr. Somberg has had to leave. Do I have to state the names? It's unanimous. I don't have to.

The decision is that everybody voted for it.

It is the Recommendation of the Panel to

the FDA that the Biosense Webster PMA P030031 for the NaviStar ThermoCool Irrigated RF Ablation Catheter is approved with the previously voted upon conditions, which I've just summarized.

I'm now going to ask each Panel member to state the reason for his or her vote, and we'll start with our primary reviewer, Dr. Slotwiner.

DR. SLOTWINER: Well, I think this will add a very important tool to the electrophysiologist's tool kit, the one we've been using today, but this will give us more support and the ability for the sponsor to improve training and spread the use of this catheter, which I think will be very beneficial for our patients. I hope that we quickly can extend the indications to include the other catheters which I think will be safe and effective, and so I look forward to having that data.

DR. BORER: Dr. Kelley.

DR. KELLEY: I voted with a reasonable assurance of safety and efficacy.

DR. BORER: Dr. Bilazarian.

DR. BILAZARIAN: I agree that the safety and efficacy are acceptable for approval.

DR. BORER: Dr. Weinberger.

DR. WEINBERGER: I'd like to congratulate

the sponsor. In this space, it was really difficult to do this kind of trial, and I think that they did a very admirable job.

DR. BORER: Dr. Naftel.

DR. NAFTEL: A lot of times trials like this are very difficult to understand. The statistics get so contorted. I just want to compliment both the sponsor and the FDA on making it accessible and understandable. It still took work on our part, but I thought the presentation was good, and I felt like the safety was just fine and the effectiveness was quite good.

DR. BORER: Dr. Karasik.

DR. KARASIK: I thought that the data supported the efficacy of the catheter. The safety profile was okay.

DR. BORER: Dr. Jeevanandam.

DR. JEEVANANDAM: I agree. I think the study supported the safety and efficacy.

DR. BORER: Is Dr. Fleming here? We would like a statement from him. Okay. Mr. Halpin.

MR. HALPIN: I'd just like to congratulate the sponsor and the FDA on doing a very good adaptive design trial and what appears to be a very tough category to enroll patients in. Thank you.

DR. BORER: If I had been allowed to vote, I would have voted in favor because I believe the sponsor demonstrated the efficacy and acceptable safety for the device, and that it provides a useful tool and benchmark for patients with a particularly difficult problem to resolve. So I think that this is a very good thing.

I would like to thank the Panel and the FDA and the sponsor, and I'd like to ask Dr. Zuckerman if he has any final comments.

DR. ZUCKERMAN: I'd like to sincerely thank Dr. Borer and the Advisory Panel. The advice given today was excellent and will be well utilized by the Agency.

DR. BORER: Thank you. This meeting of the Circulatory System Devices Panel is now adjourned.

(Whereupon, at 5:38 p.m., the meeting was concluded.)

C E R T I F I C A T E

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

CIRCULATORY SYSTEM DEVICES PANEL

November 20, 2008

Gaithersburg, Maryland

were held as herein appears, and that this is the original transcription thereof for the files of the Food and Drug Administration, Center for Devices and Radiological Health, Medical Devices Advisory Committee.

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