

1 for consideration, presentation at NASB.

2 As I might have mentioned, we have a  
3 substantial interest from our heart failure group in  
4 this device and restitution of maintenance of sinus  
5 rhythm. The clinical question which is very  
6 interesting is because of the common incidence of  
7 atrial arrhythmias in patients with heart failure, who  
8 are those that stand to benefit from atrial arrhythmia  
9 suppression and who are those that are expressing the  
10 atrial arrhythmias in epiphenomenon of the clinical  
11 outcome of the heart failure. That's something we're  
12 working aggressively with.

13 But we've accumulated 18 patients with  
14 ejection fractions of under 30 percent how have Class  
15 2 or Class 3 heart failure within the context of this  
16 study and actually a couple who have gotten the device  
17 for standard indication which is acceptable VT/VF  
18 indication.

19 If you look at their progression, New York  
20 Heart Association Class, 16 of the 18 are at stable or  
21 better class with an average follow up of 9 months,  
22 nine and change. The ejection fraction has stabilized

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1 or improved in 14 of those patients. One patient  
2 progressed without a change in ejection fraction to  
3 transplant. That was a patient who died after  
4 transplant.

5 And so I think, if anything, that for us  
6 we're not concerned about a promotion of mischief with  
7 this device. What we're concerned about is  
8 elucidating the heart failure patient in whom atrial  
9 arrhythmia control will benefit them. That's really  
10 where we're at with the device.

11 DR. STANTON: Cindy, in answer to your  
12 question, ejection fraction was not tracked during the  
13 trials as part of the protocol.

14 DR. TRACY: Okay. I think at this point  
15 we should break for lunch and let us regroup here in  
16 one hour.

17 (Whereupon, at 11:53 a.m., the meeting was  
18 recessed, to reconvene at 1:00 p.m., Tuesday, December  
19 5, 2000.)  
20  
21  
22

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A F T E R N O O N   S E S S I O N

1:02 P.M.

1  
2  
3           DR. TRACY: At this point we're going to  
4 resume the open committee discussion and I'm just  
5 going to ask the Panel Members if there are any  
6 additional questions that they would like to ask  
7 before we move on to addressing the FDA questions.

8           Mr. Dacey?

9           MR. DACEY: Yes. I want to bring a little  
10 bit of a consumer perspective to this, I hope. I'm in  
11 general agreement with the reviewers' comments on the  
12 patient labeling issue and I went through the material  
13 myself. After spending so many years in patient  
14 education, it was a difficult transition for me to  
15 make myself, but there was a time when patient  
16 education was words on paper and then it became words  
17 and pictures on paper and then we moved it down to the  
18 5th grade level.

19           But as we're seeing more evolution of  
20 technology that requires not just patient monitoring,  
21 but patient activation at home, I think patient  
22 education now has a component that's called skill

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1 training and I would like to see not in just this  
2 example, but other examples where it's acknowledged  
3 that patients across the whole socio-economic spectrum  
4 receive skill training because oftentimes patients  
5 don't want to know how the thing works, but they have  
6 to know how to make it work. And very often some of  
7 the best teachers are other patients. So there's an  
8 opportunity here for some support adjunct where like  
9 the two patients who were at the podium could help  
10 other patients understanding and using such devices  
11 and bringing a great deal of more comfort to it. But  
12 I do urge you to consider skill training as a  
13 component of patient education and not just more words  
14 on paper. And then of course, when you get to the  
15 words and pictures on paper, keep it as simple as  
16 possible because the better educated people will ask  
17 more questions, but you want to capture the folks who  
18 may not be asking the questions and that's the only  
19 point I'd like to make.

20 DR. TRACY: Mr. Jarvis, did you have any  
21 comments?

22 Anybody else on the Panel? Then we'll

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1 move on to the questions the FDA posed to the Panel.

2 DR. KRUCOFF: Can I ask for clarification?  
3 Are we going to follow questions along what we were  
4 handed out or along the slide set?

5 DR. TRACY: I think --

6 MR. DILLARD: Jim Dillard. And Doris may  
7 add a few comments also, but what we have done is we  
8 gave you the full questions, Doris gave you the full  
9 questions in the first go around so you at least got  
10 the full context of where we're coming from. What  
11 we're going to show you now is the abbreviated version  
12 that just has the couple of sentences that are really  
13 the meat of the question. So I would refer back to  
14 the longer version of the handout that we gave you  
15 today that has all the slides, page 8. And if you go  
16 past page 8 to page -- at the beginning of page 13,  
17 that's actually what you will see on the overheads or  
18 actually from the computer images right now. But all  
19 they are are the last piece of each one of those  
20 questions so that we could fit them all on one slide.  
21 So if you want the long version you can look back a  
22 couple of pages.

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1 DR. TRACY: While they're getting that set  
2 up I'm just going to go ahead and read those things  
3 real quick so we're on the same page.

4 In evaluating device safety, Medtronic  
5 reported 3 and 6 month complication pre-survival  
6 results were lower when compared to adverse event  
7 results from previous ICD studies. In addition, four  
8 patients had a stroke during the course of the study.  
9 The risk of stroke, possibly as a result of frequent  
10 cardioversions raises an important issue when  
11 evaluating safety of atrial shock therapy. Please  
12 discuss the clinical significance of the  
13 complication-free survival results and the occurrence  
14 of stroke in assessing the safety of the Jewel® AF for  
15 the new indication of treating patients with atrial  
16 tachyarrhythmias.

17 MS. TERRY: That last portion is number 1.

18 DR. TRACY: That last portion is number 1.

19 MS. TERRY: Yes. Please discuss the  
20 clinical significance of the complication-free  
21 survival results and the occurrence of stroke in  
22 assessing the safety of the Jewel® AF for the new

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1       indication of treating patients with atrial  
2       tachyarrhythmias.

3                   DR. TRACY: If I can just start by saying  
4       I believe that we've discussed that in detail so far  
5       and I think we all have some concerns about it. My  
6       attempt at some type of solution would be some type of  
7       labeling that would indicate that would suggest a  
8       course of anticoagulation in keeping with published  
9       guidelines for anticoagulation and I would also go  
10      even a little bit further and recommend some type of  
11      labeling that would indicate that the device be  
12      deactivated in the event that a stroke has occurred  
13      until an appropriate period of time has passed before  
14      another shock could be delivered.

15                   DR. KRUCOFF: Krucoff. I for one would  
16      like to see some data that the strokes go away when  
17      anticoagulation is rigorously followed and would even  
18      wishfully like to see in a cohort of patients well  
19      matched in whom the device is not applied that this  
20      outcome looks similar to this group of patients. But  
21      that may be hard to do.

22                   I would at least like it a post-marketing

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1 or some sort of additional data that would make us all  
2 feel more comfortable, I hope, that when rigorous  
3 anticoagulation is applied, the strokes go away.

4 DR. TRACY: So I think there are three  
5 parts to that, our answer to that. That we do want  
6 some guidelines printed in the labeling and we do want  
7 -- I would like to see the device deactivated, a  
8 warning in there that the device should be deactivated  
9 after a stroke has occurred, if a stroke does occur.

10 DR. SIMMONS: Or TIA?

11 DR. TRACY: Good point, or TIA.

12 DR. HARTZ: Yes, because that one patient  
13 had a TIA and then went home and came back with a  
14 stroke and it says "on Coumadin" but we don't know  
15 what the INR was so TIAs also.

16 DR. TRACY: And a post-market surveillance  
17 for the occurrence of stroke.

18 DR. KRUCOFF: What about the patient  
19 activator, should that also have some sort of warning  
20 that the patients would be educated too, that if they  
21 feel symptoms consistent with a stroke to not use  
22 their activator and to notify their doctor or

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1 something along that line?

2 DR. TRACY: Yes. I think that would be  
3 appropriate to something in the patient education.

4 MS. TERRY: Number 2. Given the choice of  
5 controls, do the clinical results of the Jewel® AF  
6 only study demonstrate device safety for the intended  
7 patient population?

8 DR. SIMMONS: They may not demonstrate  
9 significant danger, but I'm not sure they demonstrate  
10 safety. That's an interesting question.

11 DR. TRACY: I think that the preamble to  
12 this question was the fact that this was a comparison  
13 between the ventricular defibrillator, the control  
14 that was chosen in this particular study was the  
15 ventricular defibrillator versus this device. So if  
16 the question is dealing with does it show safety  
17 compared to the ventricular defibrillator, I think  
18 that the answer is yes, it appears to have safety  
19 equivalent to the ventricular defibrillator. If the  
20 question is more global, is there a safety compared to  
21 some other patient population. We don't have  
22 information to state that.

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1 DR. KRUCOFF: Well, I think key, Cindy, is  
2 compared to a patient population with atrial  
3 fibrillation who meet the entry criteria for the use  
4 of this device on a-fib only, does this data set  
5 demonstrate safety. That, to me, would be the central  
6 theme of the question.

7 MR. DILLARD: Jim Dillard, I just thought  
8 I would read, just for everybody's benefit because I  
9 know this happened in training yesterday, but --  
10 because you're really hitting on the two points that  
11 are important for this question. One, let me just  
12 read what safety is defined as again.

13 Safety is defined as reasonable assurance  
14 based on valid scientific evidence that the probably  
15 benefits to health, under conditions of use, outweighs  
16 any probable risks.

17 So I think it is worthwhile for both of  
18 the discussions based on the control that was chosen  
19 for this particular study, but also realize that the  
20 ultimate focus of this question is going to have a  
21 direct impact on what you're going to say about the  
22 safety of the product when you actually go to your

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1 vote. So I don't want to sweep that under the rug.  
2 That's certainly where this particular question is  
3 aimed.

4 DR. HARTZ: Jim, can we separate out?  
5 This question specifically relates to the device and  
6 most of our discussion has centered on the fact that  
7 some of the safety issues are not necessarily related  
8 to the device, so can we answer this question very  
9 specifically in relation to the device?

10 MR. DILLARD: Jim Dillard. I would like  
11 you to answer it very specifically for the device,  
12 number one, but also noting which I think you have  
13 already done in your discussion the other safety  
14 considerations that FDA should factor into their  
15 overall decision.

16 DR. TRACY: The main benefit to health  
17 that's been demonstrated has been symptomatic.  
18 There's no claim here for mortality or certainly no  
19 claim for decreased CVA, but there are no other  
20 therapies that could possibly make that claim for the  
21 treatment of atrial fibrillation, so I would say that  
22 given what the device is trying to do, it's my

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1 impression that safety has been demonstrated.

2 Any other comments?

3 DR. SIMMONS: It's a little frustrating.  
4 I wish I had some better answer. I guess I can't  
5 argue -- I guess I won't argue with that statement.  
6 I'm not sure the data are there. I'm just not sure  
7 the data is there.

8 Like I said before, I don't think that  
9 there's enough -- there's a lot of smoke in here, but  
10 there's no real gun that we found.

11 DR. TRACY: No clear clot.

12 DR. SIMMONS: Or clot.

13 (Laughter.)

14 And it's disturbing. It's worrisome, but  
15 I don't think we found anything in our discussions  
16 that make me feel like that in a general population of  
17 atrial fibrillation patients that this device poses a  
18 tremendous risk. If we really apply it to a narrow  
19 group and we only let Dr. Schwartzman take care of the  
20 patients.

21 DR. TRACY: This seems to me to be an area  
22 where post-market surveillance is going to be

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1 important, very important looking at not only the  
2 stroke risk but other risks.

3 DR. KRUCOFF: Can I just get some  
4 clarification on -- is there an onus for proof? I  
5 mean as a safety issue, is the onus for the data to  
6 show a smoking gun? Or is the onus for the data to  
7 show that this is safe?

8 MR. DILLARD: Jim Dillard. I guess you're  
9 looking for the specific regulatory comment on that.  
10 Let me say there isn't an absolute answer to that. I  
11 mean obviously by the language of how we judge safety,  
12 there's a lot of fuzzy words in there. Probably  
13 benefits, under the conditions, outweighs any probable  
14 risks. And so I think it's really -- this is where a  
15 large portion of clinical judgment does come into play  
16 here. I think we generally look at it as their needs  
17 to be a demonstration of safety, not sort of the  
18 corollary which I think has been discussed here over  
19 the last few minutes which is you're concerned, but we  
20 haven't really found the major gun behind why it is  
21 that we have these concerns. I think we do need to --  
22 eventually, I think, as this will generate the

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1 ultimate sort of question and the vote, you'll need to  
2 go through and try to give your clinical impressions  
3 about what you think those benefits are and certainly  
4 try to weigh those against what you think the probably  
5 risks are and I think that's really what clarifies  
6 safety.

7 DR. LASKEY: But the absence of an  
8 appropriate set of controls precludes making an  
9 informed decision.

10 I don't think we can judge safety in a  
11 vacuum. We can give you our clinical gestalt and if  
12 that's what you want, that's what you'll get, but we  
13 need to do more than that based on the information  
14 we've been given and I don't think that you can assess  
15 the safety of X without having an appropriate  
16 comparator. So the issue is is this an appropriate  
17 comparator? And if not, then I think everything else  
18 needs to be qualified.

19 DR. KRUCOFF: But you know, I guess one of  
20 the reasons it kind of finally motivated me to go in  
21 this direction was some of the things that Mike said  
22 about could you reasonably design a study to find the

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1 significant difference that this company could do that  
2 would actually show us that there was really a  
3 difference there and is there benefit and without  
4 absolute proof of significant harm -- and we know  
5 defibrillators save lives. As we said before, you  
6 might even make a comment that some of those patients  
7 with VT/VF in this study they got the device for their  
8 a-fib, may have had their lives saved because of the  
9 device, so we didn't even talk about that.

10 I guess that was kind of what motivated me  
11 is that I can't -- if you're saying that you want more  
12 proof, how would you get the proof? I don't think you  
13 can. This may be as good as you can get and you have  
14 to use your sort of clinical judgment and say probably  
15 benefit outweighs risk. That's the best I can say and  
16 I don't have proof. And I may not be able to get the  
17 proof I want.

18 DR. TRACY: I would agree with that. I  
19 think that would be how I would sort of put it  
20 together. I'm not sure that we could -- I made sort  
21 of the facetious comment earlier that the -- if you  
22 did have a control study that the disease process

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1 would probably kill the patients before you could get  
2 to the end of the study, get enough recruitments in to  
3 define the difference in death and stroke. I just  
4 think it's impractical. I think we're stuck with the  
5 data that we have and with historic knowledge of the  
6 behavior of atrial fibrillation and the problem I  
7 think we're struggling with is that I think there were  
8 two types of populations, one that was much sicker  
9 than the other and I think that's confusing some of  
10 our analysis here that I think is not clearly coming  
11 through in the data as it was presented, but just  
12 teasing it out, the deaths and the EFs of 20 percent,  
13 somebody gets a transplant and so on and so forth. I  
14 think that's part of what's confusing us. But that,  
15 in fact, is the type of population that a-fib is,  
16 everything from the 20 year who appears to be pretty  
17 healthy but has intolerable AF to the 65-year-old,  
18 70-year-old person with a bad ventricle who requires  
19 some additional treatment.

20 So I would still stand by given what we  
21 have, our knowledge of the entity and the control that  
22 we did have that safety has been demonstrated.

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1 DR. KRUCOFF: Well, one thing that could  
2 be done would be to take the data that already exists  
3 and stratify it a little bit so that it would be a  
4 little clearer, that the people who did suffer adverse  
5 outcomes were the higher end risk on a basis of  
6 descriptors which could be done with the existing  
7 data, were not presented, were available at least in  
8 the materials that I reviewed. That, to me, would be  
9 one of at least supporting the interpretation that the  
10 adverse outcomes were related to underlying disease  
11 rather than to the device.

12 I think if it didn't stratify out that way  
13 that to construct a subsequent clinical trial that  
14 would not take multiple years to complete, that would  
15 not be definitive on every endpoint, but for  
16 reassurance purposes at least with regard to safety,  
17 would be -- would add significant information, could  
18 be done as sort of an adjunct.

19 I think one thing that would help a lot  
20 would be just to stratify these data in a presentation  
21 that would allow you to see is it the high risk  
22 substrate patients who really suffered complications

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1 as opposed to not.

2 DR. DOMANSKI: I'm actually concerned  
3 though about going on a data drudging operation. I  
4 don't know that we're really going to gain much from  
5 that. I doubt that you're going to be all that much  
6 more assured by looking more and more at these data.  
7 There are only four events that we're talking about  
8 with these strokes and I think you've got out of it  
9 what you can.

10 I'd quit now. I'd make a decision based  
11 on what you've got.

12 DR. LASKEY: Is it possible to get stroke  
13 which hopefully is zero or death in 7219? Can we at  
14 least -- because what we're looking at here is device  
15 related safety as distinguished from major adverse  
16 clinical events, definition of safety, so what's  
17 driving the device-related safety here are the lead  
18 failures which are soft endpoints if you will. Maybe  
19 there's another way to get to this other clinically  
20 important -- can you compare 7219 with death and  
21 stroke versus this one?

22 DR. STANTON: Well, the mortality data is

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1 there. The Kaplan-Meier curves show the 7219  
2 mortality versus this. And to reiterate, I did walk  
3 through the case scenarios of each of the deaths and  
4 the ejection fraction in four of the five cases that  
5 we had EFs was in the 20 to 40 percent range.

6 For strokes, we had the four strokes in  
7 this study, three of whom were not taking Coumadin at  
8 the time. We don't have a stroke rate here for the  
9 7219D right now.

10 DR. TRACY: I think we could ask that  
11 there be some further data given that would indicate,  
12 particularly the deaths. There's no way around the  
13 fact that a couple of these strokes occur because of  
14 interruption of anticoagulation. One was surgical and  
15 one was a surgical complication. There's no way  
16 around that and getting more information isn't going  
17 to help us think about that. But the deaths, as I  
18 recall the EFs they were more in the 20 to 30 range,  
19 so I think that we could ask for some kind of an  
20 analysis of risk of death related to ejection fraction  
21 within the population. I think that might be a  
22 reasonable request to make.

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1 DR. KRUCOFF: And the 11 VT/VFs?

2 DR. TRACY: And the 11 VT/VFs. On to  
3 number 3.

4 MS. TERRY: Based on these effectiveness  
5 results, please discuss whether you believe the  
6 potential benefits of atrial tachyrrhythmia termination  
7 and prevention therapies outweigh the risks of  
8 implanting the Jewel® AF in the intended patient  
9 population.

10 DR. TRACY: We didn't spend too much time  
11 discussing specifically the AT tach -- atrial  
12 tachyrrhythmia termination and prevention therapies.  
13 My impression is that they're sort of there. They  
14 don't seem to be harmful. They may be helpful. They  
15 probably could get better with further you know  
16 iterations of it.

17 The only place where I have again, a very  
18 strong concern is the use of the antitachy in a  
19 patient who has undergone an A-V node ablation. That,  
20 I think, somehow should be put as a warning in the  
21 labeling, a warning in the patient handbook, a warning  
22 plastered on everything and if possible, a warning

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1 built into the programmer.

2 DR. STANTON: It is. Can I make a  
3 comment? I apologize. We did get some information.  
4 I want to clarify what I previously said about that.

5 There is a warning on the programmer. It  
6 comes up with ATP is programmed to the two maximal  
7 number of pulses and this is what it says, "caution,  
8 atrial pacing therapies are delivered with no back up  
9 bradycardia pacing or detection in the ventricle.  
10 Initial number of pulses should not be set to large  
11 values in ventricular-paced dependent patients." And  
12 the typical ATP duration is 3 seconds.

13 DR. TRACY: I'm happier.

14 DR. STANTON: Okay.

15 DR. TRACY: Any other comments? Renee?

16 DR. HARTZ: The beginning of that  
17 statement is Medtronic reported that the reduction in  
18 AT/AF frequency when atrial prevention therapies were  
19 programmed ON versus OFF was not statistically  
20 significantly different from zero. So I don't know  
21 how we could possibly say that it was effective for  
22 this use.

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1 I would agree with you.

2 DR. TRACY: And I think that that probably  
3 when we get to the labeling issue, that needs to be  
4 pretty clear in the labeling that this statistically  
5 was not different. I think we have to be pretty clear  
6 on that.

7 Any other comments on that particular  
8 question?

9 Number 4.

10 MR. DILLARD: Jim Dillard, can I just ask  
11 for one clarification just to make sure I get it? Can  
12 you go back?

13 So should the take home be for us, just so  
14 I make sure I have this one very clear, which is you  
15 believe that based on the effectiveness results, that  
16 and we put it in terms of safety kinds of wording  
17 which is the potential benefits or probable benefits  
18 outweighs the risk of the implantation of Jewel® AF  
19 that really safety of these particular kinds of  
20 features you feel is reasonable enough to include in  
21 the particular product which is what I would take just  
22 from your discussion and I just want to make sure that

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1 that's in effect what you're saying.

2 DR. TRACY: Yes. I think that the safety  
3 of it, the effectiveness is marginal. There does  
4 appear to be some people who benefit from it, so there  
5 is some effectiveness to it and that with the warnings  
6 that are either in place or will be put into labeling  
7 more clearly that the effectiveness outweighs the risk  
8 involved, it is safe enough to go ahead with that.

9 MR. DILLARD: Great. Thank you.

10 MS. TERRY: The clinical experience from  
11 the Model 9464 Patient Activator is being used to  
12 support approval of the downsized Model 9465 Patient  
13 Assistant. Given the experience, do you have comments  
14 or concerns regarding the clinical use and labeling of  
15 the Model 9465?

16 DR. TRACY: The Model 9464 was used in  
17 some patients though wasn't it?

18 MS. TERRY: No.

19 DR. TRACY: It was not at all?

20 MS. TERRY: No.

21 DR. SIMMONS: It would have been  
22 interesting to see one of these things. I mean if you

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1 just read the description, if you just read the  
2 description it is a little daunting. The Patient  
3 Assistant has two buttons, blue and red. One that  
4 queries and one that enables. Also four LEVs, red,  
5 yellow, green, blue, therapy pending, AF present, no  
6 AF present and contact your physician will depend on  
7 what color lights up.

8 DR. DOMANSKI: Yeah, but you know it's  
9 reasonable to support, Tony, that you ought to have --  
10 you may have to have a patient with a reasonable level  
11 of intelligence to do this and you know what, if you  
12 can't -- if you're not smart enough to do it, then you  
13 shouldn't get the device.

14 DR. SIMMONS: Right.

15 DR. DOMANSKI: That's kind of a  
16 physician-dependent thing. I don't think I'd beat  
17 them half to death on that one.

18 DR. SIMMONS: Right, not everybody can get  
19 every device. You might beat their engineers up a  
20 little bit. I don't know.

21 DR. KRUCOFF: Do we have documentation  
22 that the electrical specs on these things are the

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1 same? I mean it's going to transmit a signal to the  
2 permanently implanted device with the same strength of  
3 signal or do we have any sort of specs?

4 DR. TRACY: Maybe we could get some  
5 clarification provided.

6 MR. SHETH: We actually chose -- I'm  
7 sorry, I'm Nirav Sheth, Medtronic engineer on the  
8 Patient Activator, Patient Assistant. We have the  
9 same requirements for the 9464 and the 65 in terms of  
10 the functional telemetry of the implantable device.  
11 So that's the question that was asked, right?  
12 Telemetry performance?

13 DR. KRUCOFF: And Jim, are these  
14 specifications that FDA would review prior to making  
15 a final decision?

16 MR. DILLARD: Jim Dillard. Yes. Yes. I  
17 think one of our concerns really was here and I think  
18 it was brought out in a lot of the discussion is  
19 number one, based on the patient, those are two very  
20 different size devices, the ergonomics and how a  
21 patient actually uses it as well as would there be any  
22 clinical difference even though based on

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1 specifications there doesn't appear to be any  
2 difference.

3           Would your expectation clinically be that  
4 we either need to test that, number one, or there's a  
5 specific question that you might see between the two  
6 of them that otherwise couldn't be answered with bench  
7 kinds of concerns and I think we wanted you to discuss  
8 that just to see if there was anything that maybe we  
9 hadn't thought of.

10           DR. TRACY: Does the sponsor have a  
11 comment there?

12           MR. SHETH: Yes. We actually shared some  
13 of the same concerns you mentioned in terms of the  
14 simplicity of the device and we did some testing with  
15 the representative, not patients, but representative  
16 of humans in the age group, 50 or 60 years old, both  
17 lefthanded, righthanded, some with hearing aids, some  
18 with acuity, glasses, everything was included in terms  
19 of getting a real perspective of what a person could  
20 feel if he doesn't have any familiarity with the  
21 device or AF or anything and everything indicated that  
22 this is a good design from an ergonomic perspective.

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1                   We learned one thing is that the specific  
2 training aspect where they press a button and then put  
3 on the device and move it around, that's the only  
4 aspect which didn't come naturally to them if they  
5 didn't have any kind of training up front. So we took  
6 that to our designing team and had a special patient  
7 card developed showing a sequence of instructions in  
8 terms of how to use it right from doing this, putting  
9 on the device and doing that. And actually working on  
10 even better and more simple and clean patient and  
11 physician instructions for specifically that aspect.

12                   DR. HARTZ:     Could I ask a general  
13 question, maybe this is illegal, outlandish or both,  
14 but is it appropriate to ask two patients since  
15 they're such a valuable resource what their feelings  
16 are about the activator? Or is that not allowed at  
17 this point?

18                   MR. DILLARD:   Jim Dillard, no, I think as  
19 a Panel you can certainly, with the okay from your  
20 chairperson, you could certainly do that, number one.  
21 It's not illegal or outlandish.

22                   And number two, there has been and one of

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1 the other pieces of data that we look at occasionally  
2 are things like preference testing and/or some other  
3 human factors kind of testing based on patients or  
4 representative patients. And I think that is a piece  
5 of data that we generally will factor in when we have  
6 something that certainly is in the hands of the  
7 patient and I think it was more of an attempt here to  
8 just see based on your discussion if there was any  
9 other real clinical concerns that you might have that  
10 we hadn't thought about and so if there aren't, that's  
11 okay also, but I think we wanted to put that on the  
12 table.

13 DR. DOMANSKI: I would say, you know, of  
14 course, whether it's illegal or outlandish, I think to  
15 take two paid individuals who are highly educated,  
16 giving a testimonial, brought here by Medtronic is a  
17 meaningless exercise.

18 MR. DILLARD: Jim Dillard. I think your  
19 chair will have to make up her mind on that.

20 DR. TRACY: I think as we pass this device  
21 around I would rather have the large device personally  
22 because I would lose the smaller device and I'm sure

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1       there are people who would rather have the smaller  
2       device because it would fit in their pocket easier.  
3       So I think if all things are equal and bench testing  
4       has indicated that the device is functioning  
5       equivalently well, then I don't see the need to have  
6       a clinical trial to evaluate the equivalence of these  
7       two hand-held devices as long as we're assured by  
8       bench testing that they are equivalent.

9               So as much as I appreciate the folks being  
10       here, I'm not sure that we need to bring them up at  
11       this time.

12               What's the question mark for?

13               MR. SHETH: It's actually an enhancement  
14       we're planning for future implantable devices where  
15       the patient can check if he's in AF without having to  
16       find out the hard way, I guess, in terms of getting a  
17       shock which is the only option we have right now with  
18       the 9464. So we'll have two separate -- one is to  
19       check if you're in AF and the other to give a therapy  
20       when you are.

21               DR. HARTZ: I love this because of the  
22       size. I might try to open my car with it, but it's

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1 not self-explanatory.

2 DR. TRACY: It gets back to Mr. Dacey's  
3 comment about patient education and instruction, hands  
4 on instruction. Very important.

5 MR. DACEY: Excuse me, when I have it in  
6 my hand, of course, the first thought I had was it was  
7 like a key chain and I remember how often I lose my  
8 keys, but when I mentioned skill training, this is a  
9 one on one experience. This is where a person, an  
10 educator, could be the physician, nurse, takes a  
11 patient and goes through it step by step as often as  
12 necessary and then comes back and does it again later.  
13 And is constantly updating the learning curve for the  
14 patient until the patient arrives at this comfort zone  
15 where they can -- like glucose monitoring for  
16 diabetics. And that's why I also mention there's a  
17 role here for the patients themselves to be supportive  
18 to new patients in that very, very same role.

19 DR. STANTON: I think those are very good  
20 points and we'll certainly act on those. I want to  
21 emphasize many of you know that there are other  
22 devices out there that are patient activated. There

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1 are various pacemakers. There's the implantable loop  
2 recorder, etcetera, but your points are very  
3 appropriate.

4 DR. TRACY: Okay. Question 5. Given the  
5 proposed new Indications for Use for the Jewel® AF and  
6 the likelihood that the patients will be healthier  
7 than the ICD patient population, please discuss  
8 whether you believe that the potential benefits of  
9 implanting the Jewel® AF in patients with atrial  
10 tachyarrhythmias outweigh the possible risk associated  
11 with the implantation and therapies of the device.

12 DR. DOMANSKI: I'm not sure that's the  
13 question. Their study doesn't answer that question.  
14 What it does answer is that it's effective in  
15 terminating atrial fibrillation. I don't think --  
16 their data simply don't address this issue at all.  
17 But they do address the question of whether you can  
18 terminate a-fib. It's effective for that, but to say  
19 it's effective for that would go beyond their data.

20 DR. TRACY: So you're saying we really  
21 can't answer this question?

22 DR. DOMANSKI: Not No. 5, but I think --

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1 I mean I think the device is effective in terminating  
2 a-fib and I think it's reasonably safe. I don't want  
3 anyone to misunderstand, but to say that it's  
4 clinically beneficial would go beyond the data. They  
5 simply haven't addressed the issue with the kind of  
6 study they've got.

7 DR. TRACY: So you have a non-answer from  
8 the Panel.

9 DR. HARTZ: I think the answer to the  
10 question is yes. We sort of discussed that under 1  
11 and 2.

12 MR. DILLARD: Let me -- Jim Dillard -- let  
13 me maybe try to throw something out a little bit  
14 different here. One of our concerns certainly is the  
15 status of the patients compared to the ICD patient  
16 population and I think it's an issue that's been  
17 talked about here quite extensively about whether it's  
18 a healthier patient population, whether it should have  
19 been a healthier patient population and what the data  
20 actually tells us.

21 I think, and again, a number of your  
22 discussions centered around if it's really the

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1 specific patient population that was targeted here and  
2 if there's a labeling that can be worked on about the  
3 really specific sort of high risk, drug-refractory  
4 patient population that we're talking about here which  
5 I think you've been talking about, that perhaps this  
6 question in terms of a broader patient population is  
7 not as appropriate, I think based on your discussions  
8 and so I only say that as maybe it's not as important  
9 based on your conversations.

10 DR. TRACY: Yes, I think we've sort of hit  
11 the issues from different directions and I think this  
12 question becomes a little bit, perhaps less important  
13 in light of the other discussions.

14 MS. TERRY: Please comment on whether you  
15 believe the Jewel® AF provides adequate AF prevention  
16 and/or treatment therapy for this patient population,  
17 and whether you believe that the therapies,  
18 particularly atrial shock therapy, may be poorly  
19 tolerated in some patients.

20 DR. TRACY: I think the evidence that they  
21 have provided suggests that it does provide adequate  
22 therapy. Whether it provides -- I'm not so sure about

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1 prevention. It depends on what you're talking about  
2 in terms of prevention. The anti-tachy or the pacing  
3 algorithms to prevent atrial fibrillation appear to be  
4 not significantly beneficial to the patient. However,  
5 the shock therapy in combination with the anti-tachy  
6 and high frequency burst does seem to be effective at  
7 terminating atrial fibrillation.

8 There was very little comment made to  
9 patients to indicate that they both have to do  
10 something to steel themselves to prepare for receiving  
11 the shock, yet they do go ahead and deliver shocks to  
12 themselves and based on the quality of life  
13 indications, it would appear that it is  
14 well-tolerated. It may be poorly tolerated in some  
15 patients, yet given the fact that 80 percent of the  
16 devices were intact and active at two years, I would  
17 say that the answer is that it is tolerated well  
18 enough.

19 Any other discussion on that point?

20 MS. TERRY: Please provide your clinical  
21 impression of these potential intention-to-treat  
22 failures and discuss how this clinical information

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1 should be presented in the Jewel® AF's Instructions  
2 for Use labeling.

3 DR. SIMMONS: Here again, I think it's  
4 going to matter when we get around to defining what  
5 the indications for the device are. It's  
6 unfortunately true that this device doesn't have a  
7 rate responsive mode if the patient is going into  
8 atrial fib. you're going to have patients drop out  
9 because they need VVIR. You're going to have patients  
10 drop out because they need A-V node ablations.  
11 Unfortunately, I think the best you can do in this is  
12 to say if we try to narrow the patient population  
13 that's going to end up getting the device, then you  
14 can minimize those kinds of unfortunate implants that  
15 aren't going to be helpful, but I don't think they're  
16 completely avoidable.

17 DR. TRACY: I would agree with that  
18 comment. Any other comments on that question?

19 MR. DILLARD: Jim Dillard. Can I ask for  
20 just a little bit further discussion about based on  
21 what we saw in this particular study, how would you  
22 present that information and do you think it's

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1 important to present that information in the clinical  
2 section of the instructions for use?

3 DR. HARTZ: It's difficult to see a no  
4 atrial capture, in other words, used as effective as  
5 an intention to treat.

6 DR. SIMMONS: Oh yes.

7 DR. HARTZ: If we had a huge study, maybe,  
8 but with 140 some --

9 DR. SIMMONS: I mean you cut on this guy  
10 with the intention of putting this device and weren't  
11 able to do it. That's an intention to treat. He's  
12 got a scar and a possible infection and pneumothorax  
13 and I mean sure, there are patients who don't get the  
14 device, may have been poked around with more than the  
15 other ones.

16 DR. DOMANSKI: You know, as a methodologic  
17 matter, I mean if you randomize somebody to something,  
18 that's it. With an intention to treat analysis --

19 DR. HARTZ: This was not a randomized  
20 trial.

21 DR. DOMANSKI: That's true, but if you  
22 analyze something by intention to treat, you got to

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1 analyze by intention to treat. You may not use that  
2 analysis, but you can eliminate things selectively.

3 DR. TRACY: I think it would probably be  
4 reasonable to request that that information be clearly  
5 stated in the labeling.

6 DR. SIMMONS: Where would you put it? Is  
7 it part of the indications or is it part of the  
8 warning or is that what you're asking?

9 MR. DILLARD: Well, that is one thing I'm  
10 asking. I generally -- what we would do is we would  
11 do is take the clinical information and we would  
12 develop a clinical section, clinical trial section to  
13 the instructions for use where we would particularly  
14 concentrate on the effectiveness data. We would also  
15 have a separate section that talked to the adverse  
16 event information and the safety data. And so I think  
17 part of the question is should we really put in all  
18 the intention to treat patients in the instructions  
19 for use. Is it important to very openly talk about  
20 all of those patients or do we take a subset sort of  
21 analysis and really focus on that and labeling?

22 DR. TRACY: No, I think they should be

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1 included there. I think they do provide information  
2 about why it might not work out, if you have a patient  
3 that you feel is a candidate. What might be the  
4 pitfall. So I do think it's important to put it in  
5 there, in the clinical, somewhere in the clinical  
6 section. I don't think it's a warning, but I think  
7 it's something in the clinical section.

8 MS. TERRY: The Jewel® AF System is  
9 intended to provide pacing, cardioversion and  
10 defibrillation for treatment of patients with  
11 symptomatic, drug-refractory atrial tachyarrhythmias  
12 and/or life threatening ventricular tachyarrhythmias.  
13 Please provide your clinical impression of Medtronic's  
14 proposed Indications for Usage and comment on whether  
15 they are clinically appropriate for the Jewel® AF  
16 indicated population.

17 DR. TRACY: I would say that we have not  
18 -- we spent some time talking about the difference  
19 between focal atrial tachycardia, but we realize that  
20 in the patient population that was included there were  
21 -- if you add it up, certainly some of these people  
22 had more than one of these arrhythmias so the

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1       likelihood is that a patient on one day will have  
2       a-fib and another day atrial tach and another day  
3       atrial flutter. So I think to state it that it's for  
4       atrial tachyrrhythmia it's probably fair, although I do  
5       have some concern that that might lead people to want  
6       to put it in for PAT. I don't know, Tony is shaking  
7       his head as though he might be able to suggest better  
8       wording than that.

9               DR. SIMMONS: I just don't think there's  
10       any evidence. I'm sorry, I think it should say atrial  
11       fibrillation.

12              DR. CRITTENDEN: I would agree with that  
13       as well. I think that we really show is efficacious  
14       was the atrial shock therapy and the others were kind  
15       of minimally effective.

16              DR. SIMMONS: I mean I agree that there  
17       are some atrial fib. patients who have atrial flutter  
18       that you'll be able to use the atrial tachyrrhythmia  
19       function for, but if they've got pure atrial flutter,  
20       they shouldn't get a defibrillator. If they've got  
21       a regular SVT they shouldn't get a defibrillator.  
22       They should have atrial fib. before they get this

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1 defibrillator.

2 DR. KRUCOFF: And that doesn't exclude any  
3 of the patients who are included here. The common  
4 denominator was atrial fibrillation. Some of them  
5 also have flutter. Some of them also have other  
6 atrial tachyrythmias, but it would seem like the  
7 indication common denominator would be atrial  
8 fibrillation.

9 DR. TRACY: I wouldn't argue with that.  
10 That might avoid inappropriate implants if we just  
11 asked them to say atrial fibrillation, recognizing  
12 that there will be other atrial tachyrythmias in that  
13 patient population.

14 DR. SIMMONS: I wish I could figure out a  
15 way to throw in there something like Mike was talking  
16 about, but I just can't seem to do it, multiple drug  
17 refractory -- or serious drug refractory, but I don't  
18 see any way to do it because lots of time if you do  
19 start with amiodarone as your drug of choice on your  
20 first drug, then you're talking about a 30 or 40 day  
21 washout period and you don't really have any  
22 enthusiasm and you give the drug anyway and I just --

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1 I can't think of a way to phrase it that would be  
2 different.

3 DR. TRACY: I think we're kind of stuck  
4 with that because once you've tried and failed  
5 amiodarone you're not real enthusiastic about doing  
6 other things and I think we're just sort of stuck with  
7 calling it drug refractory, but I would agree that we  
8 can request that it would be changed to atrial  
9 fibrillation rather than atrial tachyrrhythmia and I  
10 think it's also, since the device and/or life  
11 threatening ventricular tachyarrhythmias is also a  
12 reasonable thing, but if there is the and/or part,  
13 then certainly the defib. therapy has to be programmed  
14 on and one of the deaths was, in fact, a VF, well,  
15 actually the guy didn't even get the device implanted,  
16 so that's part of the intention to treat where that  
17 does have to be put in there somewhere.

18 DR. CRITTENDEN: Tell me if I'm splitting  
19 hairs, but I was impressed with the conversation both  
20 by the representatives from the sponsors and from the  
21 Panel about how we should really restrict this to a  
22 tiny niche limited cohort, right subgroup, etcetera by

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1 changing for treatment of patients versus  
2 cardioversion and defibrillation for treatment of  
3 patients with -- say should be limited to patients  
4 with. I think it's a little strong, but maybe it's  
5 just a semantic thing and not important, but -- should  
6 be limited to instead of for treatment of.

7 DR. SIMMONS: Where are you at? I'm  
8 missing this.

9 DR. CRITTENDEN: It says "Indications for  
10 Use". "The Jewel® AF System is intended to provide  
11 pacing, cardioversion and defibrillation" and now I'll  
12 substitute my words, it should be "limited to patients  
13 with" instead of "for treatment of".

14 DR. TRACY: It just adds a little bit of  
15 additional burden to the physician to look at it and  
16 say this is a limited indication.

17 I'm not -- I know why you're saying that.  
18 I'm not sure that -- I really don't think that the  
19 door is going to open and hundreds of people are going  
20 to walk in demanding this device.

21 I'm not sure that's necessary. I think  
22 this is going to find its own niche, but I'd be

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1 interested in whether the rest of the Panel feels that  
2 they want to try to pass that message that be careful  
3 who you put this in by changing that wording.

4 Do people feel that's important?

5 DR. HARTZ: I do because we don't have the  
6 additional safety information on the whole implant and  
7 the way Dr. Crittendon states this is really does  
8 limit it to a few number of implants for some period  
9 of time. That can always be changed. I think it's a  
10 very good point.

11 DR. TRACY: It should be limited to.

12 DR. HARTZ: It's been our fear all along  
13 with this device is just wide open use and of foreseen  
14 strokes, not because of the device itself, but because  
15 of the implant. It might be nice to limit this right  
16 now to what we're talking about.

17 DR. TRACY: All right. Then it seems to  
18 be the sense of the Panel that we'll recommend they  
19 change the wording to say "should be limited to."

20 Were there other questions from the FDA?

21 (Pause.)

22 At this time I'd like to open for an open

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1 public hearing, if there are any additional comments  
2 from the members of the public here today?

3 (Pause.)

4 Did the sponsor have any additional  
5 comments that they would like to make at this time?

6 DR. STANTON: Just a quick comment. I  
7 appreciate all the discussion on the labeling and we  
8 agree with most of the comments that were made. The  
9 only one that I would like to just ask Jim to consider  
10 is the comment about "limited to" aren't all  
11 indications limited what the indication is.

12 MR. DILLARD: Jim Dillard. I think  
13 there's probably many different ways to interpret that  
14 and I think what we will take is under consideration  
15 based on what the Panel recommendation was, probably  
16 even more broadly than the wording that they gave us  
17 to take a look to see if there isn't a better way to  
18 sort of hone in on the specific patient population  
19 that means something to them as clinicians which I  
20 think we will work very closely with Medtronic to try  
21 to do that. So I think it's an important point for  
22 both of us to take home, not necessarily the identical

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1 wording, but the issue, I think came through loud and  
2 clear, so I appreciate that.

3 DR. TRACY: Did the FDA have any  
4 additional comments?

5 MR. DILLARD: No, thank you.

6 MS. MOYNAHAN: Okay, I'd like to read  
7 through the voting options.

8 The Medical Device Amendments to the  
9 Federal Food, Drug and Cosmetic Act, as amended by the  
10 Safe Medical Devices Act of 1990 allows the Food and  
11 Drug Administration to obtain a recommendation from an  
12 expert advisory panel on designated medical device  
13 pre-market approval applications that are filed with  
14 the Agency.

15 The PMA must stand on its own merits and  
16 the recommendation must be supported by safety and  
17 effectiveness data in the application or by applicable  
18 publicly available information. Safety is defined in  
19 the Act as reasonable assurance based on valid  
20 scientific evidence that the probable benefits to  
21 health under conditions on intended use outweigh any  
22 probable risks. Effective is defined as reasonable

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1 assurance that in a significant portion of the  
2 population, the use of the device for its intended  
3 uses and conditions of use when labeled will provide  
4 clinically significant results.

5 Your recommendation options for the vote  
6 are as follows:

7 1. Approval, if there are no conditions  
8 attached.

9 2. Approval, with conditions. The Panel  
10 may recommend that the PMA be found approval subject  
11 to specified conditions such as physician or patient  
12 education, labeling changes or a further analysis of  
13 existing data. Prior to voting, all of the conditions  
14 should be discussed by the Panel.

15 3. Not approval. The Panel may recommend  
16 that the PMA is not approvable if the data do not  
17 provide a reasonable assurance that the device is safe  
18 or if a reasonable assurance has not been given, that  
19 the device is effective under the conditions of use  
20 prescribed, recommended or suggested in the proposed  
21 labeling.

22 Following the voting, the chair will ask

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1 each Panel Member to present a restatement outlying  
2 the reasons for their vote.

3 DR. TRACY: I'd like to ask for a motion  
4 regarding approval or disapproval of this device.

5 Tony, it's your prerogative if you'd like  
6 to --

7 DR. KRUCOFF: Cindy, just before we start  
8 the motion and I apologize, maybe I'm just tired, but  
9 can I ask one more time for help with the definition  
10 of what we are calling safety? Safety is the  
11 reasonable assurance --

12 MS. MOYNAHAN: Do you want me to re-read  
13 the definition?

14 DR. KRUCOFF: Okay.

15 MS. MOYNAHAN: Safety is defined in the  
16 Act as reasonable assurance based on valid scientific  
17 evidence that the probable benefits to health under  
18 conditions on intended use outweigh any probable  
19 risks.

20 DR. KRUCOFF: So we're talking about  
21 putting this device in patient population with  
22 intractable atrial fibrillation as having been

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1 demonstrated as safe in the data we were presented  
2 today?

3 DR. SIMMONS: Do the benefits outweigh  
4 probable risk?

5 DR. TRACY: Don't worry, Mitch, you'll  
6 have a chance to make some comments when it comes time  
7 to vote.

8 Any motion --

9 MR. DILLARD: I might say just one thing  
10 to that for Dr. Krucoff's sake. The safety from a  
11 regulatory perspective is not an absolute. What we're  
12 not saying is the device is absolutely safe and/or  
13 absolutely effective. There is the definitions  
14 associated with them which certainly give some leeway  
15 for interpretation, but I think in both of the cases  
16 for both safety and effectiveness, I think the  
17 terminology reasonable here and probably weigh heavy.  
18 And so I think you need to from your own perspective  
19 take a look at the data and think in your own mind  
20 whether or not you think that it's been reasonably  
21 demonstrated and whether or not there's probably  
22 benefits associated with the product and they outweigh

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1 the probable risks. I think that's really what it  
2 comes down to and there's no absolute, so I don't want  
3 everybody to agonize over it completely. That's what  
4 we have to deal with.

5 DR. SIMMONS: Well, I am still agonizing.

6 (Laughter.)

7 I guess I'm going to recommend approval  
8 with significant conditions and do I have to list the  
9 conditions now?

10 MS. MOYNAHAN: If that's a motion, we need  
11 a second and then we'll go through each of the  
12 conditions independently and can discuss them.

13 DR. CRITTENDEN: I second the motion.

14 DR. TRACY: Okay, we'll get the conditions  
15 hammered out now and then we'll vote on your motion  
16 and then we'll vote on each condition separately.

17 DR. DOMANSKI: Suppose they disapprove it?  
18 If the Panel disapproves it then --

19 DR. TRACY: Then we wouldn't vote on the  
20 conditions. Is that format-wise okay to vote now or  
21 do we want to hear the conditions before we vote?

22 MR. DILLARD: Jim Dillard. I think it's

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1 customary to go ahead and kind of go through the  
2 conditions. If you can get consensus on the  
3 conditions, then go ahead and take the whole motion  
4 with the conditions would be the preferable way.

5 DR. TRACY: Okay, then I'm going to take  
6 a stab based on the notes, unless Tony, you have some  
7 burning desire to come up with the conditions? I  
8 think that the conditions that we have talked about is  
9 that there must be a warning added for -- in the  
10 warning section there must be some statement made  
11 referring to an anticoagulation protocol that is  
12 consistent with current guidelines .

13 There must also be a more specific  
14 warning, the current warning about A-V node ablation  
15 does not state specifically that during antitachy  
16 pacing there is not brady backup. That has to be  
17 reworded so that's very specifically stated.

18 Those would be two within the warning  
19 section.

20 There has to be a statement added that  
21 clearly indicates the marginal efficacy or the not  
22 significant efficacy of the pacing algorithms.

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1           There has to be clear -- I think there has  
2 to be a clear indication of the lead or pertaining to  
3 the lead dislodgement and we really did not explore  
4 that, but it has to be at least clearly stated that  
5 there is a fairly significant amount of lead  
6 dislodgement.

7           The other condition would be that we would  
8 request that the wording be changed from atrial  
9 tachyrrhythmia to atrial fibrillation.

10           We also requested additional information  
11 from the sponsor regarding the -- some stratification  
12 on the deaths as pertains to the underlying heart  
13 condition.

14           DR. KRUCOFF: Deaths, strokes, VF?

15           DR. TRACY: I'm sorry, yes. Deaths and  
16 VT/VF.

17           I think we've addressed, but just to be  
18 sure that there are adequate warnings on the  
19 programmer and elsewhere about the antitachy pacing  
20 and the absence of brady backup.

21           There has to be a very clear patient  
22 education program and commitment to basically one on

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1 one training for the use of the patient activator.  
2 And there has to be some warning regarding the device  
3 being deactivated if there's been a TIA or CVA to  
4 prevent a recurrent shock in close temporal proximity  
5 to neurologic event.

6 I hope somebody wrote those down.

7 DR. SIMMONS: What about -- is it in here,  
8 I didn't see it. I was just flipping through real  
9 fast trying to find it. Is there a warning about that  
10 there must be VF testing and that adequate  
11 defibrillation thresholds for ventricle must be  
12 achieved prior to leaving the device in atrial fib.  
13 only? Is that in there somewhere in the morning  
14 section?

15 DR. TRACY: I missed it.

16 DR. SIMMONS: I couldn't find it here just  
17 now.

18 DR. TRACY: I missed it if it is there.  
19 If it's not there, it should be there.

20 Where there any others that I've forgotten  
21 and from the discussion?

22 DR. KRUCOFF: Cindy, when you mentioned

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1 anticoagulation did you mention getting some  
2 post-market data that will be reassuring that the  
3 strokes actually do disappear when anticoagulation is  
4 properly conducted?

5 DR. TRACY: Right, and we would like a  
6 postmarket surveillance, however, to be sure that the  
7 risk of stroke is not inordinately high or that the  
8 risk of death is not somehow higher, so the specific  
9 things that we would think should be followed would be  
10 stroke, VT/VF and death.

11 DR. LASKEY: Do you want to now specify  
12 the number of patients to be followed?

13 I think we should.

14 MR. DILLARD: Jim Dillard. If you have  
15 some suggestions about -- what would be really  
16 important is if you would have suggestions about what  
17 it is we should look at in that either surveillance or  
18 post-approval study. That's the most important  
19 because then I think it would be appropriate to do  
20 some reasonable statistical calculations about how we  
21 actually answer those issues.

22 The other just while I have the mike for

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1 one more second, one of the other things at least I  
2 thought I heard was potentially some surveillance  
3 about the lead, the higher lead complication rates and  
4 I don't know whether or not you think it would be  
5 reasonable to try to roll both of those into either  
6 the same study or the same surveillance effort, but if  
7 I could get some comments on that, that would be  
8 helpful.

9 DR. TRACY: Yes, as you were making the  
10 first part of your comment, I remember that was one of  
11 the issues that we wanted to follow up on. It seems  
12 that there may be configurations. If there is no  
13 difference in the defibrillation threshold between  
14 different lead configurations and one lead  
15 configuration has a significantly higher chance of  
16 dislodgement than another, then it seems like  
17 information we should be able to track over time. So  
18 I think that following lead configuration and tracking  
19 that against dislodgement would be appropriate. So  
20 there would really be then VT/VF, deaths, stroke and  
21 lead configurations versus dislodgement.

22 DR. SIMMONS: And thresholds.

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1 DR. TRACY: And defibrillation threshold.

2 DR. SIMMONS: The other thing that we did  
3 talk about was maybe in the information section and  
4 not in that warning, but just in the information  
5 section that in this trial, the 6973A did not  
6 significantly reduce defibrillation thresholds.  
7 There's no proven benefit to the 6973A in reducing  
8 defibrillation thresholds.

9 MR. BROWN: I'm sorry, I have one piece of  
10 information which may be relevant about the 37A.  
11 While it did not decrease defibrillation thresholds,  
12 we do have an analysis which indicates that shock  
13 efficacy was superior with the 37A than without it.  
14 That is a statistically significant difference. The  
15 margin is about 90 percent GEE with versus 80 without.

16 DR. SIMMONS: Is that in here somewhere?

17 MR. BROWN: No, that is information that  
18 was requested afterwards.

19 DR. TRACY: Then I think what we said has  
20 to hold because we don't formally have that  
21 information available to us.

22 Mitch, you look like you have a comment

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1 there.

2 DR. KRUCOFF: Yes, just regarding Jim's  
3 question on numbers. I think there are two kinds of  
4 numbers we should consider for post-market  
5 surveillance. One would be a number of patients. The  
6 other would be a number in time and the actuarial  
7 curves, in fact, while not significantly different at  
8 the follow-up reported potentially could continue to  
9 separate. So one option would be simply to ask for  
10 on-going surveillance of the patients who have already  
11 been enrolled in the data reported to see again over  
12 time what the behavior of the actuarial curves is and  
13 the other would be in a consecutive post-market array,  
14 if we're looking for appropriate anticoagulation  
15 therapy and its impact on stroke rate, as a total  
16 first pass I would simply say in a reasonably  
17 similarly sized cohort to the original trial, about  
18 140, 150.

19 DR. TRACY: I think there might be enough  
20 things that we're asking for, some statistical  
21 investigation is needed here.

22 Can I have a motion to accept these

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1 conditions as listed above?

2 (Motion moved and seconded.)

3 DR. TRACY: All in favor, aye? Keep your  
4 hands up.

5 MS. MOYNAHAN: That's 7 in favor.

6 DR. TRACY: Okay. Now we can take a vote  
7 on the initial approval with conditions. All in  
8 favor?

9 MS. MOYNAHAN: Seven for.

10 DR. TRACY: Okay, now I think we have to  
11 vote on each of the conditions independently or can we  
12 vote in package form?

13 MR. DILLARD: You could take them in  
14 package and if you can get lucky and get them all,  
15 that's great.

16 DR. TRACY: Okay, let's try for the  
17 package deal. All in favor of the package deal of  
18 conditions as stated above?

19 MS. MOYNAHAN: That's seven in favor.

20 DR. TRACY: That's pretty amazing.

21 (Laughter.)

22 DR. TRACY: The meeting is now closed and

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1 thank you very much.

2 DR. SIMMONS: You don't need a motion?

3 MR. DILLARD: Thank you very much Panel  
4 Members. I appreciate it and thank you also the  
5 sponsor.

6 Thank you for bringing all your requisite  
7 individuals to answer our questions.

8 (Whereupon, at 2:05 p.m., the meeting was  
9 concluded.)

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CERTIFICATE

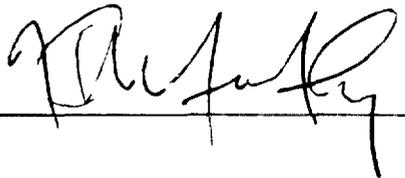
This is to certify that the foregoing transcript in the  
matter of:                   Circulatory System Devices Panel of the  
                                  Medical Devices Advisory Committee

Before:                    DHHS/FDA/CDRH

Date:                      December 5, 2000

Place:                     Gaithersburg, MD

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



A handwritten signature in cursive script, appearing to read "R. L. F. J. R.", is written above a horizontal line.