

1 DR. DOMANSKI: So I actually to be
2 honest have not really bought into your view
3 of that. That bothers me a little bit. I
4 mean actually these things do look related.

5 DR. MILAN: Really?

6 CHAIRMAN MAISEL: I'm going on --

7 DR. MILAN: Dizziness, atrial
8 flutter.

9 DR. DOMANSKI: It depends on what
10 causes the dizziness.

11 CHAIRMAN MAISEL: Let's have one
12 person speak at a time. So I think the sinus
13 node dysfunction, the ablation is remote from
14 the sinus node. So unless we're hearing some
15 reason why the ablation occurred near the
16 sinus node, I agree with Dr. Milan. It's hard
17 to put those together to me. Maybe you can
18 explain the difference in physiology about how
19 an ablation remote from the sinus node can do
20 that. Dr. Brinker.

21 DR. BRINKER: There are a bunch of
22 different issues here. One is that one reason

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1 for lumping all adverse events is that it can
2 be difficult to adjudicate things one way or
3 the other clearly. For instance, if the
4 patient got contrast material for any reason
5 during procedure they could develop
6 hyperthyroidism. Just sedation could cause
7 dizziness or some of these other problems and
8 then manipulating the catheter, they could
9 have bumped into the sinus node and caused
10 something that might keep them another day.

11 So I'm not opposed to lumping all
12 these together. But what I've heard time and
13 time again is the fact that most of these
14 aren't ever reported except for the tamponade
15 predominantly and the AV block as
16 complications of a procedure like this. So
17 when you hear from the experts about the
18 literature and Hugh was telling us about four
19 percent adverse events, they wouldn't count
20 most of these things, and they would settle on
21 a relatively high profile adverse events like
22 the heart block or cardiac perforation

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1 tamponade.

2 So I'm not dissatisfied with the
3 general definition. I think that the
4 objective performance criteria don't reflect
5 reality in this case and probably in other
6 cases and they should be rejected by us in our
7 deliberations.

8 CHAIRMAN MAISEL: Adam, do you have
9 a comment to make?

10 DR. LOTTICK: Yes. We have a thing
11 that I think ought to be considered in context
12 is that these COEs were developed for SVTs
13 like WPW and ABNRT apparently and what's the
14 average age of that population and what's the
15 average morbidity. Well, they are 20 year
16 olds. They're not 65 year olds and this is a
17 population of 65 year olds who have a lot of
18 comorbidity. So the acute respiratory failure
19 in this population is not a terribly
20 surprising outcome, whereas it would be a
21 terribly surprising outcome in a population
22 where the CEO was originally designed.

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1 So I think that's the other thing
2 that makes me think that this is not as
3 concerning a list of adverse events and I
4 agree with Dr. Milan. I'm not seeing -- most
5 of these issues are not things that are
6 attributable except through great stretches of
7 the imagination to the ablation procedure.

8 CHAIRMAN MAISEL: Mike.

9 DR. DOMANSKI: Let me just follow
10 up that. Actually, the thing that strikes me
11 about it looking at the whole thing from a
12 distance from kind of 20,000 feet, the thing
13 that's reassuring actually is whether you can
14 stretch your imagination or not and I can
15 stretch mine a little more apparently than
16 perhaps you can. But what you don't see is
17 you don't see a pattern. You don't see a
18 whole bunch of people with a tamponade and you
19 don't see a whole bunch.

20 These things look like stuff that
21 happens in procedures. But it seems very
22 random and it's pretty hard to put it together

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1 as being the fault of this catheter or its
2 technique for ablation. So I'm actually
3 pretty reassured, not for the reasons that you
4 guys suggest, but just because I don't see a
5 pattern of one type of bad complication.

6 DR. LOTTICK: Right. I can stretch
7 my imagination a fair amount, but I would put
8 a probability on mine like how likely is it
9 that the dizziness or the sinus node
10 dysfunction, etc., are related. Those are
11 relatively low likelihood relatedness and
12 therefore I would lump all of those and maybe
13 give one more adverse risk.

14 CHAIRMAN MAISEL: Clyde.

15 DR. YANCY: I appreciate the
16 practical relevance that we're bringing to the
17 review of these serious adverse events. But
18 just to remind ourselves that we had a pre-
19 specified endpoint that was a composite of all
20 serious adverse events and if we set the
21 precedent that we can readjudicate after the
22 fact and say "Well, it maybe is, maybe isn't"

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1 it really makes it very difficult going
2 forward when we see additional PMAs. So I
3 appreciate the practical considerations and
4 embrace most of them, but we still have a
5 process and this was pre-specified. The
6 number are above the threshold and I think we
7 still have to wrestle with that.

8 CHAIRMAN MAISEL: Sharon.

9 DR. NORMAND: Thank you. I guess I
10 would like to echo Dr. Yancy's statements and
11 again it's not that -- I don't have an
12 argument about how you combine these things.
13 That's not the issue. Nor do I have an issue
14 that bad things happen in this older group.
15 That's not the issue.

16 The issue is what happens, the
17 counterfactual, if they would have had
18 something else and that's what we need to
19 know. And I don't think we can make it up.
20 And gut reactions and clinical experience have
21 gotten us in trouble in the past by saying "I
22 think this is what should happen." So if

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1 we're going to reject the 2.5 percent because
2 it's old and apparently some people on the
3 panel feel that it shouldn't be lower than 2.5
4 percent, I do think we end up going on a very
5 slippery slope without having an objective,
6 scientific criterion to say "This is the
7 number that we need to meet in this type of
8 population with this treatment relative to if
9 they hadn't got this treatment and got
10 something else." That's how you judge
11 scientific evidence.

12 And so again, I also appreciate the
13 comments and people talking about these
14 things, but let's put the science back into
15 this and think about how do we do this
16 objectively. Of course, these bad things are
17 going to happen. We're going to have these
18 rates. That's not the point. The point is
19 relative to if they would have gotten
20 something else would this be more serious
21 adverse events and I don't care if you're
22 saying "Well, they're not all congregated down

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1 here or down there." The whole point is the
2 composite.

3 CHAIRMAN MAISEL: I think at this
4 point I will summarize the panel's feelings
5 regarding safety which is there is a diversion
6 of opinion regarding safety. Some people feel
7 that safety has been demonstrated although the
8 OPC was not met. Other people feel that
9 safety is not sufficient and as always, this
10 is a balance with effectiveness which we
11 haven't yet discussed and that balance we will
12 discuss a little later.

13 I think also a message might be it
14 might be time at some point for the FDA to
15 revisit these OPCs for atrial flutter
16 ablation. I think we probably got that
17 message about seven hours ago, but I'll state
18 it.

19 DR. ZUCKERMAN: We were thinking
20 about adding that as an additional question.
21 Thank you, Dr. Maisel.

22 CHAIRMAN MAISEL: Yes. John.

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1 DR. SOMBERG: I just wanted to say
2 that you might be able to reach a further
3 consensus if you wanted to by those who are
4 more rigid about maintaining the OPC criteria
5 whether flutter and fibrillation would be
6 considered. If you take two out of those,
7 what, six I think, you change the incidence so
8 markedly as to reduce it to the frequency of
9 adversity to where the OPC was.

10 CHAIRMAN MAISEL: Yes.

11 DR. SOMBERG: So I was just --

12 CHAIRMAN MAISEL: I think we could
13 spend time going through each individual one.
14 I think my sense is that people know where
15 they stand and we can revisit these issues if
16 we need to when we get to the balance of
17 safety and effectiveness. But let's move onto
18 question two which is the chronic
19 effectiveness results by the core lab
20 determination. The blinded core lab
21 adjudication of patient event recordings led
22 to a chronic effectiveness result of 81.6

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1 percent with a 95 percent lower confidence
2 bound of 74.7 percent. The pre-specified
3 chronic effectiveness goal was 90 percent with
4 a lower confidence bound of 80 percent.
5 Please discuss whether the chronic
6 effectiveness results based upon the core lab
7 determination demonstrate that there is a
8 reasonable assurance that the device is
9 effective for the chronic treatment of
10 isthmus-dependent atrial flutter.

11 We obviously spent a great of deal
12 of time this morning talking about this. We
13 talked about how we felt the core lab
14 determination, the consensus of the panel,
15 seemed to be that this was the most
16 appropriate determination based on the data we
17 had in front of us. It may not be the trial
18 design we would choose if we were choosing to
19 study the catheter, but of the things in front
20 of us this seems to be the best data or most
21 appropriate data.

22 There was a general consensus that

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1 the OPC may be somewhat outdated based on the
2 fact that it was on a small number of studies
3 of ten years ago. There was discussion that
4 there may be a little wiggle room in the OPC
5 and I'm interested in hearing more now
6 specifically on this data and based on our
7 discussion whether people feel that chronic
8 effectiveness based on the results of the core
9 lab has been demonstrated. Reasonable
10 assurance of effectiveness. John.

11 DR. SOMBERG: Well, prior to this
12 study, I'm not sure that there was other
13 information available when the OPC was done
14 with this type of core lab analysis. So
15 therefore, this is an add-on from the point of
16 the study to make it even more certain. They
17 made it more rigorous. They found some
18 episodes of atrial flutter which may or may
19 not be clinically relevant. So I think this
20 is one way to look at it, but it's not the
21 best way to look at it if we want to compare.

22 If you want to be scientific, the OPC had a

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1 clinical efficacy and this protocol does not
2 use the criteria the OPC was using.

3 So there is no way you're going to
4 be able to be very scientifically valid and
5 what I think is this is only aspect to base
6 efficacy on. There is the clinical
7 reevaluation as well and whether you like it
8 or not that might be the most comparable to
9 the OPC 90 percent.

10 CHAIRMAN MAISEL: So in pinning you
11 down a little bit, the question is about the
12 core lab determination. So how do you feel
13 regarding the chronic effectiveness results
14 based upon the core lab determination? Based
15 on that data, is there a reasonable assurance
16 that the device is effective? You know I
17 always do this to you.

18 DR. SOMBERG: Yes. I do think it's
19 -- and it's very commendable that Dr.
20 Scheinman went through all these tracings. He
21 must have had a very good time on that. But
22 I do not think that if -- what I was trying to

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1 say, and let me if I can say this precisely,
2 is if one wants to approve or disapprove this
3 drug based on comparison --

4 CHAIRMAN MAISEL: Device.

5 DR. SOMBERG: I'm sorry. You're
6 right. That's a throwback. I have to watch
7 myself. This device on the basis of the OPC,
8 then no. But I say that's not appropriate
9 because the OPC was not based on this core lab
10 type of analysis.

11 CHAIRMAN MAISEL: Okay. Other
12 comments regarding the chronic effectiveness
13 based on core lab data? David.

14 DR. SLOTWINER: Yes. I agree with
15 John. I think OPC are just not a reasonable
16 criteria to use and I think with the intense
17 monitoring that was observed at the core lab I
18 think it's not surprising that these many
19 arrhythmia were picked up but I think it is
20 effective.

21 CHAIRMAN MAISEL: Adam.

22 DR. LOTTICK: One of the points

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1 that Dr. Scheinman made that I think we may
2 want to reiterate is the fact that when you
3 see flutter tracings it doesn't mean you
4 actually have isthmus-dependent flutter and
5 one of the things that's frustrating to me is
6 that we don't have data. If you just do
7 random flutter tracings on people with a
8 history of AFib, what is the rate that you
9 will see flutter that's not isthmus-dependent
10 flutter?

11 So as the company did point out,
12 what this essentially has done is create a
13 lower limit. I think the efficacy of the
14 flutter ablation was probably somewhere above
15 what was seen with the core lab analysis
16 because we're including lots of strips of
17 stuff that's probably not isthmus-dependent
18 flutter. It's probably atypical flutter or
19 atrial tachycardia, but we have no idea how to
20 assess how much.

21 CHAIRMAN MAISEL: Norm.

22 DR. KATO: You know, again I have

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1 to be consistent with my first comments. I
2 think again the OPC was used as their
3 standard. The FDA and the sponsor went into
4 their clinical trials with their eyes open.
5 Again, to start to throw out certain standards
6 rightly or wrongly at this stage, I think, is
7 incorrect. I think you have to go forward and
8 the first conclusion is the OPC goal wasn't
9 met. Okay. Fine. Then how do you want to
10 interpret that? Then based on my read of, at
11 least my belief, how we're supposed to
12 interpret this is that chronic effectiveness
13 endpoint was not met as well.

14 CHAIRMAN MAISEL: Pam, do you want
15 to comment?

16 DR. KARASIK: Well, I think it was
17 very useful to hear about how the OPCs were
18 derived and the fact that they were derived
19 based on clinical determination and not weekly
20 TTM or event monitor transmissions. And I
21 think that has to play a little bit into how
22 we think about it and I think in some ways the

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1 sponsor should be commended on being willing
2 to be much more diligent in trying to find
3 asymptomatic even clinical recurrences.

4 I think it's very hard to ignore
5 Dr. Scheinman's input here. I mean, every
6 study should have Dr. Scheinman review all
7 their tracings. That's an enormous advantage
8 and I do think that the 81 or 82 percent
9 chronic success as determined by tracings is
10 very consistent with clinical practice in what
11 we see and when we take care of these
12 patients. And so I am perhaps a little more
13 willing to consider that the device does meet
14 a standard for chronic effectiveness.

15 CHAIRMAN MAISEL: Sharon.

16 DR. NORMAND: Like I said, you're
17 going to know I don't think it meets the
18 standard for clinical effectiveness and for
19 the reasons that Dr. Kato has mentioned. But
20 also, again, I understand comparing an OPC
21 that wasn't based on these readings. But when
22 I look at some of the sponsor's presentations

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1 there was a study, I believe, in the *American*
2 *Journal of Cardiology 2004* that used the
3 monthly event ratings. This was presented to
4 us and its success rate, its chronic success
5 rate, was 87 percent. So this study currently
6 that's using the same endpoint data collection
7 has a lower rate.

8 Again, I understand my colleague's
9 need to say the OPC used different data
10 collection and the sponsor went through a very
11 rigorous data collection that could identify a
12 lot of false positives. However, let's also
13 place that in context of the example of the
14 data that the sponsor presented that showed or
15 demonstrated in, as they said, a published
16 article where the success rate at six months -
17 -

18 DR. SOMBERG: Can you give us the
19 reference? With atrial flutters, it's rated
20 87 percent with monthly --

21 DR. NORMAND: Six month chronic --
22 Unless I'm misunderstanding. It was a study

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1 presented. They don't have unfortunately --
2 can I just --

3 DR. CALKINS: Can I just clarify
4 that because I wrote the study? So in that
5 study, as you said, it was 87 percent chronic
6 success with monthly event monitors. That
7 differs from this data because this data was
8 weekly event monitor tracings. So this was
9 three or four times --

10 DR. NORMAND: Okay. So --

11 DR. CALKINS: -- rigorous screening
12 for asymptomatic episodes.

13 DR. NORMAND: But the point being -
14 - Okay. Now we're going to cut it a little
15 finer. The point being is that who cares if
16 it's monthly versus weekly. But I guess the
17 broader point that the panel members were
18 bringing up is that the OPC is based on
19 clinical data. But I refer my panel members.
20 They don't have slide numbers, but on the
21 sponsor's page six, you will see the numbers
22 that they used again using monthly event

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1 recordings from a core lab where there is a
2 higher success rate than in the current study.

3 So, again, it's a slippery slope
4 that we're on. I would just like everybody to
5 look at all the information that's available
6 to us and that's been reported today.

7 CHAIRMAN MAISEL: So I think, Mike,
8 why don't we hear from you and then --

9 DR. DOMANSKI: I think the last
10 sentence is the operative one. We really need
11 to look at the whole picture. I think the
12 OPCs have really failed in a sense. I think
13 it's old data. I think the stuff that Dr.
14 Calkins presented really is again if one is
15 sort of using a little bit of clinical
16 judgment and since we don't have a control
17 trial but I think to try to put these OPCs on
18 top of this is frankly -- just doesn't work.
19 My sense is that it's pretty comparable to
20 what's out there and I was actually --
21 certainly didn't start out being noncritical
22 of it, but, gee, it seems pretty

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1 straightforward. It looks fairly effective.

2 CHAIRMAN MAISEL: So I think to
3 summarize the panel's feeling regarding the
4 chronic effectiveness results based on the
5 core lab determination a number of panel
6 members seem comfortable that it is a
7 reasonable assurance of effectiveness, of
8 chronic effectiveness, and some panel members
9 still have concerns. We will deal with that
10 balance of safety and effectiveness a little
11 later.

12 Question 3 is the chronic
13 effectiveness results, the post hoc clinical
14 determination. The post hoc clinical
15 determination analysis results in the
16 readjudication of some patients as chronic
17 effectiveness successes who were previously
18 adjudicated as chronic effectiveness failures
19 by the blinded core lab. They readjudication
20 was based on the investigator's comments, with
21 the final determination made by the sponsor.
22 Please discuss the value of the chronic

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1 effectiveness results based upon the post hoc
2 clinical determination. We discussed this at
3 length this morning.

4 I think the general consensus of
5 the panel is we find a clinical determination
6 to be an extremely important and valuable
7 assessment of devices outcome and patient
8 benefit. Unfortunately, the study design here
9 and the quality of the data are such that it
10 is not particularly helpful in this case in
11 making an assessment regarding the chronic
12 effectiveness endpoint. Does anyone have
13 anything to add to that summary?

14 So we'll move onto question four
15 which is the chronic effectiveness results,
16 additional data. A retrospective analysis of
17 111 sequential OUS subjects with atrial
18 flutter who were treated with CryoCor Cardiac
19 Cryoablation System was presented. Please
20 discuss the value of the OUS results in
21 assessing the chronic effectiveness of the
22 device.

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1 Again, we saw extensive data from
2 one institution, a world class institution.
3 Certainly, the results are reassuring
4 regarding the effectiveness. We didn't see a
5 lot of safety data. I'm not sure how we can
6 extrapolate that to the real world without
7 having a formal IDE with data collection
8 forms, etc. I think it's a little hard other
9 than it certainly doesn't raise any new
10 questions in my mind. Does anyone else have
11 comments regarding the OUS data for
12 effectiveness? Bram.

13 DR. ZUCKERMAN: Yes. Can you
14 clarify for me, Dr. Maisel, the 111 Maastricht
15 data? Was that done without sedation to those
16 patients?

17 CHAIRMAN MAISEL: We can get a
18 clarification.

19 DR. WELLENS: The answer is yes.

20 CHAIRMAN MAISEL: Yes.

21 DR. ZUCKERMAN: Okay. Can you
22 comment on the potential utility of having a

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1 considerable number of patients done without
2 sedation?

3 CHAIRMAN MAISEL: Well, I think
4 maybe we can take that with question five
5 which is the pain study and we can get into
6 the issues related to other potential benefits
7 of the device. Before we move onto that, are
8 there issues related to the OUS data? Clyde.

9 DR. YANCY: There is one issue
10 related to the OUS data that is in the context
11 of the earlier discussions and if you look at
12 the numbers, the similar number for chronic
13 effectiveness is 93 percent with the OUS data
14 and that compares to the prevailing 81 percent
15 based on the accepted metric that we have used
16 today. So it gets back to this issue of how
17 much wiggle room, to use your word, we're
18 willing to allow. That's a pretty significant
19 difference.

20 CHAIRMAN MAISEL: Again, that
21 effectiveness data does not involve event
22 monitoring for the OUS data. So we're back to

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1 the issues we dealt with before. There was
2 good post procedure monitoring, 24 hour Holter
3 monitoring at one, three and six months. So
4 different monitoring, certainly good
5 monitoring.

6 DR. NORMAND: But monitoring
7 nevertheless.

8 CHAIRMAN MAISEL: Yes. Your point
9 well taken. Certainly not just a clinical
10 endpoint without ECG monitoring.

11 DR. YANCY: The point being that if
12 that is best case scenario it gives us some
13 context for the current data.

14 CHAIRMAN MAISEL: Excellent point.
15 So let's tackle the issue that Dr. Zuckerman
16 raised and we can do it in the context of
17 question number five which is the pain study.

18 A published study in 14 patients compared the
19 perception of pain between RF ablation and
20 cryoablation with the CryoCor Cryoablation
21 System. The publication states that all seven
22 of the patients treated with RF perceived pain

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1 with at least one application and one of the
2 seven cryoablation patients perceived pain.
3 Please discuss the value of the pain study
4 results. And why don't we also discuss the
5 potential value for patients who may not need
6 or may not tolerate sedation and how that
7 might impact the clinical utility or the
8 clinical use of this novel device. Dr.
9 Somberg.

10 DR. SOMBERG: I thought it was
11 remarkable in that 111, I think, patients were
12 done without sedation at Maastricht. It's
13 remarkable. I think they're probably, and I
14 mean this with no disrespect, but I think that
15 would not be per se a labeling consideration
16 until it was in some way reproduced.

17 I notice there was no claim made
18 for the U.S. study on that basis that -- or at
19 least, I didn't see one on the same level.
20 But I think it's a very interesting hypotheses
21 generating data and it most likely is, you
22 know, a finding especially since that's the

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1 way they do their ablations right now. But I
2 think it's something that has to be worked on
3 a little bit more before it's recommended.

4 CHAIRMAN MAISEL: Jeff.

5 DR. BRINKER: I similarly don't
6 think that it should be taken into
7 consideration in our deliberations today for a
8 number of reasons. The first reason is while
9 it's a good thing not to have pain from any
10 procedure, my experience is patients that are
11 going to be in the cath lab for an hour or an
12 hour and a half maybe getting a needle stuck
13 in their leg just to numb it up sedation is an
14 important part of making their experience more
15 tolerable and even if I were to give a
16 procedure like cardiac catheterization which
17 is not associated with pain after the
18 insertion of the sheath I still sedate
19 patients. So I don't think people -- I don't
20 think that should be a consideration. There's
21 not an absolute mandate to have a non painful,
22 sedation free procedure right now and I don't

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1 think there's enough data to say that this
2 procedure should be done with without sedation
3 per se and I think it should be put on the
4 back burner.

5 CHAIRMAN MAISEL: So you raise an
6 excellent point that it's not just the patient
7 comfort during the burn or freeze. It's their
8 whole procedural experience. Perhaps we can
9 hear from some of the electrophysiologists
10 regarding their feelings. Pam, do you want to
11 comment?

12 DR. KARASIK: I had, actually, the
13 same question and concerns that you did and I
14 was going to ask whether or not you really
15 meant that patients lay on the table for three
16 or three and half hours with nothing other
17 than local anesthesia.

18 CHAIRMAN MAISEL: We're getting a
19 nod of the head.

20 DR. KARASIK: You must play really
21 calming music in the lab because I work in a
22 Veterans' hospital and my patients can barely

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1 lay still for half an hour. So I commend you
2 if you can really absent any intravenous
3 sedation. But I have the similar concerns.
4 It's a small sample size and I don't know that
5 we should consider that today.

6 CHAIRMAN MAISEL: Adam.

7 DR. LOTTICK: I want to raise an
8 alternative issue with regard to this which is
9 that my patients are lightly sedated. I can't
10 imagine my patient population holding still
11 for the relevant time period without some
12 sedation even if they are completely pain
13 free. But typically when the RF ablations
14 hurt them, it's when I get near the coronary
15 sinus ostium or near the inferior vena cava.
16 I don't see as much pain when I'm ablating
17 from the tricuspid valve back until I get
18 closer and that actually is kind of useful
19 clinical information to me. I know if my
20 catheter is falling down too far in the vein
21 when I start to see the patients experience
22 some discomfort. So I'm not sure how much of

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1 that -- it may be my sloppy technique. But
2 I'm not sure how much of an advantage that is
3 for this product.

4 CHAIRMAN MAISEL: David.

5 DR. SLOTWINER: I have sort of a
6 pretty different perspective from the other
7 people on the panel. I've used cryoablation
8 for flutter pretty much exclusively for the
9 last three years, two years, I guess, since
10 the larger tip is available. I know I'm not
11 supposed to --

12 CHAIRMAN MAISEL: Let the record
13 show that that's off-label.

14 DR. SLOTWINER: Yes. Off-label.

15 (Laughter.)

16 DR. SLOTWINER: But the difference
17 in pain perception is just remarkable. The
18 nurses dread when I pull out the other unit
19 because they have to sedate the patients so
20 much more and especially when we get down to
21 the IVC junction. It's not that I don't give
22 any sedation, but I think that the -- I don't

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1 know how to take this into account
2 scientifically because I realize it wasn't
3 part of the protocol. But I want to express
4 to the panel how important a benefit I think
5 the reduction in pain is with cryo. I think
6 it's a safety benefit and I --

7 DR. ZUCKERMAN: Dr. Slotwiner, your
8 experience using cryo is with a different
9 manufacturer's device. Correct?

10 DR. SLOTWINER: Correct.

11 DR. ZUCKERMAN: So I think we have
12 to assume worst case scenario that results are
13 not generalizable to the whole cryo
14 experience and would ask the panel not to take
15 those comments into effect.

16 DR. SLOTWINER: Okay. Fine.

17 CHAIRMAN MAISEL: Other than his
18 comments that he considers pain not to be an
19 important issue for selected patients. Are
20 there other panel members who feel that the
21 pain data we have in front of us or the
22 potential lack of need for sedation is an

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1 important issue that we have sufficient data
2 to consider in our deliberations? David.

3 DR. MILAN: I do give some weight
4 to these 111 patients who have been done
5 without any sedation or pain medication and I
6 do agree also that the vast majority of
7 patients who come for a procedure are going to
8 require some form of sedation even in the
9 absence of pain just to lie on the table and
10 undergo the procedure itself.

11 But there are those patients who
12 you think are high risk for even any kind of
13 sedation. I think that those patients would
14 be the ones where you would probably expect to
15 see or anticipate a safety benefit if there is
16 one there.

17 CHAIRMAN MAISEL: Okay. Mike, do
18 you have a comment?

19 DR. DOMANSKI: Yes. I thought the
20 data that actually were presented was pretty
21 compelling from the standpoint of patient
22 comfort and I suspect that the -- I don't

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1 think it's terribly important to the panel's
2 deliberation, but I think it's going to be
3 interesting to see how it finds its way in the
4 marketplace based on that.

5 CHAIRMAN MAISEL: Clyde, did you
6 have a comment?

7 DR. YANCY: I just wanted to remind
8 all of us that the stated benefit when we
9 posed the question for this technique over the
10 others was this ability to avoid significant
11 sedation. So I don't know that it's directly
12 applicable to our deliberations, but at least
13 it's tangentially important.

14 CHAIRMAN MAISEL: Other than the
15 catheter is not obligated to show a benefit
16 over any catheter ablation approved for atrial
17 flutter.

18 So let's move onto to device
19 labeling. One aspect of the premarket
20 evaluation of a new product is the review of
21 its labeling. The labeling must indicated
22 which patients are appropriate for treatment,

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1 identify the products potential adverse events
2 and explain how the product should be used to
3 maximize benefits and minimize adverse events.

4 Please comment on whether the
5 indications section identifies the appropriate
6 patient population for the treatment with the
7 device. Please comment on the remainder of
8 the device labeling as to whether it
9 adequately describes how the device should be
10 used to maximize benefits and minimized
11 adverse outcomes. Please discuss any
12 additional recommendations regarding the
13 device labeling.

14 I will start by saying this may be
15 the smallest print I've ever seen in a panel
16 pack regarding the device label. I agree with
17 Pam's earlier comments regarding the left
18 atrial comments. I mean, it's explicitly
19 stated in there regarding how to use the
20 device in the left atrium which is clearly not
21 appropriate for this panel pack.

22 I think I'd be interested in

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1 hearing from Linda regarding the need for a
2 patient manual or something regarding this
3 different technology. Is that not important
4 or relevant? What do you think?

5 MS. MOTTLE: Absolutely, it is.
6 Any kind of interventional thing needs an
7 overall explanation, understanding of the
8 procedure, potential complications and risks
9 and benefits. But I didn't see anything on
10 that.

11 CHAIRMAN MAISEL: Right. So I
12 think we'd like to see a patient manual that
13 explains ablation and cryo and why they are
14 there. Clyde, is your light on because you
15 want to say something?

16 DR. YANCY: John, I also think a
17 lot of things were mentioned about some of the
18 techniques, some of the ways, to utilize the
19 system and some of the don'ts and that wasn't
20 clearly stated as well as it could be. So I
21 think a more rigorous package insert is needed
22 or device explanation of use.

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1 CHAIRMAN MAISEL: So other labeling
2 issues. One question I had, I guess, was
3 regarding our concern about use in regions
4 where the device is not approved and I don't
5 mean geographical regions. I mean anatomic
6 regions.

7 I know it's a little beyond the
8 purview of this panel to talk about off-label
9 uses other than to make sure that the device
10 is used as intended. So are we happy just
11 saying it's intended for use in the right
12 atrium? Do we feel that something stronger
13 needs to be said about where it should not be
14 used? Adam.

15 DR. LOTTICK: Should there be any
16 kind of black box labeling like for things
17 like atrial fibrillation until there is
18 clinical data to demonstrate a benefit?

19 CHAIRMAN MAISEL: First, maybe we
20 can ask Dr. Zuckerman to explain for the panel
21 the different labeling options available for
22 information that we might want to provide to

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1 the consumer and then we can talk about the
2 appropriate level of warning if one is needed.

3 DR. ZUCKERMAN: Okay. I think Dr.
4 Lottick was referring to how we put in perhaps
5 a contraindication and a contraindication is a
6 pretty strong statement in our IFU and really
7 is dependent on having actual data that
8 suggests that when you do this procedure we
9 know that the patient will suffer significant
10 harm and that is something for the panel to
11 look at, the contraindications, but I doubt
12 that that would necessarily apply to Dr.
13 Maisel's question.

14 But on the other hand, given the
15 limited data that we do have on use of this
16 catheter in sites other than the right atrium,
17 the use of that language in warnings or
18 precautions to alert the user is something
19 that the panel can explore.

20 CHAIRMAN MAISEL: So other comments
21 regarding we just let it go with an indication
22 statement or whether we want something more.

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1 Dr. Kato.

2 DR. KATO: Well, I guess my thought
3 on this being somewhat a stickler for process
4 is that as an example, it says "The device is
5 indicated in patients 18 years of age or
6 older." The inclusion criteria for their
7 trials was age between 18 and 75. They also
8 added a statement about symptomatic atrial
9 flutter because I think we're going after
10 symptomatic relief, not just the fact that you
11 have it. Of course, we could debate that.

12 The other issues would be, and
13 again we can debate this too because I've been
14 reading some of the agency guidelines on this,
15 that medical management is considered to be
16 first line therapy even for atrial flutter.
17 So there may be some controversy still about
18 with all due respect to the experts from the
19 sponsor about whether catheter ablation is
20 first line or should we try medical therapy
21 first.

22 The other thing is that there were

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1 a number of exclusions which include things
2 like heart failure, congestive heart failure,
3 rejection fraction less than 30 percent and a
4 whole host of other exclusions which could
5 potentially, and again, I'm not an EP
6 specialist, alter the outcomes of using this
7 device out in the field. So I think that much
8 of what the sponsor has already stated in
9 their trials which was an inclusion/exclusion
10 criteria should really be placed into the
11 package insert and, in fact, I'm a little
12 surprised why it isn't.

13 CHAIRMAN MAISEL: Right. I think
14 that's an excellent point and certainly we
15 would expect the label to reflect the patient
16 population that was studied. The question
17 comes down and, Norm, you raised an excellent
18 question regarding the actual indication which
19 right now reads "The CryoCor Cryoablation
20 System's intended use is in the ablation of
21 isthmus-dependent atrial flutter in patients
22 18 years of age or older." I certainly would

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1 add the word "right" atrial isthmus to that
2 and the question becomes because the inclusion
3 criteria says symptomatic atrial flutter do
4 people have an issue with symptomatic atrial
5 flutter not being in there. I don't have an
6 issue, but do other people feel the word
7 "symptomatic" should be in the indication?
8 Okay. Doesn't seem to be an issue.

9 DR. KATO: So I just want to make
10 this clear. Our specialists on the panel are
11 saying that if you have any atrial flutter
12 identified by any 24 hour Holter monitoring
13 device or anything like that you should get,
14 and let's say between 18 and 75, ablated.
15 That's what you're saying.

16 CHAIRMAN MAISEL: No. We're saying
17 that it is a reasonable first therapy, a
18 first line therapy. It doesn't say "get this
19 therapy." It says, "If you choose this
20 therapy, it is reasonable to do."

21 DR. KATO: Okay.

22 CHAIRMAN MAISEL: So you could

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1 choose medical therapy or you could choose to
2 do it --

3 DR. KATO: That's fine.

4 CHAIRMAN MAISEL: Okay. Dr.
5 Somberg.

6 DR. SOMBERG: I think normally what
7 you have to consider that this is a highly
8 technical area and unlike many devices and
9 most drugs which are utilized by many
10 practicing physicians, this is a far more
11 limited area of the utilization and it's a
12 tool for a very, very specific subset of
13 patients. Most patients with atrial flutter
14 will not be seen by the expert or
15 electrophysiologist here in this group or
16 sitting over there. They're seen by
17 internists, general cardiologists and that's
18 why in many ways medical therapy is
19 recommended first.

20 But what I think is this is going
21 to be a skewed population and I'm more
22 concerned about warning the experts or passing

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1 on the pearls in the dos and don'ts in the
2 label as opposed to saying the word
3 "symptomatic" or "not symptomatic" because
4 that's not necessarily -- There's a very
5 specific group who has utilization of this for
6 very specific reasons. Sometimes the patient
7 will be symptomatic. Other times there will
8 be other considerations such as they said they
9 convert atrial fibrillation to atrial flutter
10 and then they want to treat the atrial
11 flutter. So it's a very technical area.

12 DR. KATO: Well, I understand that,
13 but I'm also concerned from a policy
14 perspective because a lot of different
15 entities, people and entities, are going to be
16 reading this and interpreting it in their own
17 fashion and that's why in order to try to
18 limit some of the variants in that
19 interpretation having broad guidelines means
20 that "Well, heck. Let's go ahead and do it."

21 There are other players in the
22 healthcare market who would tend to say "Well,

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1 you know what? This needs to be honed down a
2 little bit." So that's why I'm concerned
3 about it is that I think the more information
4 you have about in disclosing how the studies
5 were done, how you got optimal -- let's say.
6 Let's assume for a minute that the efficacy
7 rate is the optimal, is the best, rate you can
8 get. Well, then I think it's incumbent upon
9 the sponsor and the FDA to make sure this
10 information is passed on so that the provider
11 out in the field knows all the nuances of how
12 to get those optimal results.

13 CHAIRMAN MAISEL: Dr. Zuckerman.

14 DR. ZUCKERMAN: Yes. Just to
15 respond to Dr. Kato and to get the panel
16 focused where it would be useful for the FDA,
17 we're really interested in some of the big
18 picture ticket items and certainly I would
19 like to hear more comment on Dr. Maisel's
20 suggestion that the use of the word,
21 adjective "right atrium" be included in the
22 indications for use indications statement.

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1 But it's important to appreciate
2 that in that indications statement we're
3 looking for something that is not totally
4 proscriptive, that just identifies the
5 intended patient population and what the
6 device can do. That's not to say that we're
7 not very interested in describing the clinical
8 trial and the actual conditions of use.

9 What this label is presently
10 lacking is a clinical trial section which is
11 standard for labels where we appropriately put
12 all those things that Dr. Kato was talking
13 about and certainly the agency would proceed
14 to do that including I would like some
15 discussion about Dr. Normand's point that we
16 really should start with an N of 160 and
17 calculate those procedures success results at
18 six months also as a way of fully informing
19 the practitioner and patient. Dr. Maisel.

20 CHAIRMAN MAISEL: So I think we
21 covered some of these issues earlier, but let
22 me just ask then. Is there anyone who feels

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1 the word "right" should not be added? We're
2 talking about the right atrial isthmus to the
3 indication statement. Is there anyone who
4 feels that -- right now, it doesn't have the
5 word "right" atrium in there. Is there anyone
6 who feels that shouldn't be added?

7 (No response.)

8 CHAIRMAN MAISEL: Okay. And, Dr.
9 Zuckerman, what was your second point?

10 DR. ZUCKERMAN: Well, right now, the
11 one page IFU that's --

12 CHAIRMAN MAISEL: The chronic
13 effectiveness that Dr. Normand wanted to add,
14 I think we all feel that that would be a
15 welcome addition, although I'll give people an
16 opportunity. So we will report as was
17 suggested by the FDA statistician acute
18 effectiveness, chronic effectiveness as it's
19 been shown here, but also we can come up with
20 a term the uncensored -- that's probably --

21 DR. NORMAND: Chronic effectiveness
22 is not the right description, right? It's

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1 conditional on --

2 CHAIRMAN MAISEL: Conditional
3 chronic effectiveness and unconditional
4 chronic effectiveness and the label will have
5 to reflect --

6 DR. NORMAND: I think using --
7 calling the one that you have been calling
8 chronic effectiveness is misleading. So you
9 should do the multiplication to do the chronic
10 effectiveness which is the unconditional one
11 and call the chronic effectiveness as
12 conditional on acute effectiveness something
13 else. But it's very misleading.

14 DR. SOMBERG: I think that would be
15 misleading the other way because --

16 DR. NORMAND: No, it's not.

17 DR. SOMBERG: -- I don't think --
18 Well, you didn't hear my why but that's okay.

19 I'll tell you why anyway and that is because
20 I don't think the other types of studies were
21 done that way. So therefore, once again,
22 we're going to be comparing apples and oranges

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1 and when you're --

2 For instance, the study you wanted
3 to quote here, there's an 87 percent chronic
4 success rate and maybe I don't know that
5 particular study.

6 DR. NORMAND: That's right.

7 DR. SOMBERG: Was that done on the
8 conditional basis or was that a nonconditional
9 one?

10 DR. NORMAND: It's the conditional
11 one as we found out, but that's totally
12 misleading. So let me just make this --

13 DR. SOMBERG: No. The one --

14 DR. NORMAND: Let me just make the
15 following statement. Just because we've done
16 it in the past doesn't mean we should do it in
17 the future and I think we should be thinking
18 ahead. I understand doing a level playing
19 field, but if we've done something bad in the
20 past and misguided in the past, this is the
21 opportunity to move it forward in the right
22 direction.

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1 DR. SOMBERG: Well, that sounds
2 nice but if you give misinformation --

3 DR. NORMAND: We're not giving
4 misinformation.

5 DR. SOMBERG: Yes, we are because
6 what we're doing is we're going to have one
7 IFU that would give one information that the
8 chronic efficacy is, let's say, 67 percent
9 when you factor in that and the efficacy of
10 radiofrequency ablation is 90 something
11 percent. That would make a false basis of
12 comparison.

13 DR. NORMAND: And we'd better know
14 what we're comparing.

15 DR. SOMBERG: Unless someone was an
16 expert and went through this panel discussion
17 with a fine tooth comb, they wouldn't know
18 that.

19 DR. NORMAND: Someone is going to
20 decide this. It's not going to be you or I
21 right now. I think everybody knows our
22 understanding on this that it's totally

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1 misleading and it's not for us in this room --
2 it's for the patient, that's really
3 misleading.

4 DR. ZUCKERMAN: I think the FDA can
5 handle this with the sponsor. We appreciate
6 the problem and we are committed to truthful
7 labeling that's clear.

8 CHAIRMAN MAISEL: So I think a
9 sidelight from the message of Sharon and I
10 certainly agree with her point. I think it
11 would be nice to have a level playing field.
12 If there are other labels out there which
13 we'll leave to you that are misleading on the
14 basis of this discussion, it might be nice if
15 they all reflected the same information based
16 on the comments here today.

17 Any other device labeling comments?
18 Is training part of device labeling or is
19 that a separate issue? We can discuss it now.
20 So can we get a little more specific
21 regarding the training program that people
22 think, if any, that needs to occur for this

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1 device? We heard about CryoCor University.
2 Dr. Somberg.

3 DR. SOMBERG: It's hard to be
4 specific as we all know specifically what was
5 the training program done for the
6 investigators, but I'm saying at least the
7 training program that's done for the
8 investigators in this particular study should
9 provided and all the information that was
10 provided to them including panel, whatever
11 that device use, console use, and all that has
12 to be provided in detail to anybody who is
13 utilizing and the patient because we want them
14 all to be at the same level.

15 CHAIRMAN MAISEL: But let me give
16 you different levels of training. There is
17 the pamphlet. There is the DVD you might have
18 to watch. There is proctoring with a
19 physician present or someone who has used the
20 device. There is someone in person training
21 by a member of the industry. So which of
22 these things sound appealing to you?

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1 DR. SOMBERG: What was -- Can I ask
2 the question?

3 CHAIRMAN MAISEL: Please. Sure.

4 DR. SOMBERG: What was used? How
5 were the investigators trained?

6 DR. BAROLD: It was a site visit by
7 us and explaining the procedure and going
8 through what the potential risks/benefits of
9 the procedure where there were -- We have
10 PowerPoint presentation. We don't have a DVD.
11 We don't have a video. We don't have any of
12 that.

13 DR. SOMBERG: Well, you're not
14 going to want to make a site visit to
15 everybody who purchases the system probably.
16 So therefore, I think you're going to have to
17 come up with some audio-visual detailed
18 presentation, that would be my proposal, that
19 would sort of provide the training. Or I
20 might be mistaken. Maybe I'm wrong. Maybe
21 you do have to make the site visit on each
22 site that have purchased one and goes through

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1 a training program.

2 CHAIRMAN MAISEL: Dr. Brinker.

3 DR. BRINKER: I think they are
4 going to anyway to show the professional staff
5 how to set up the console which is a major
6 part of this and they have to be comfortable
7 in doing that and that's usually done with a
8 site visit. I think it goes without saying
9 that in the labeling and it probably says this
10 already, I don't remember, that this device
11 should only be used by experienced
12 electrophysiologists experienced in the
13 performance of ablation procedures.

14 CHAIRMAN MAISEL: I might remove
15 the word "electrophysiologist." Just say
16 "experienced physicians."

17 DR. BRINKER: Other people other
18 than electrophysiologists doing this in the
19 cath lab?

20 CHAIRMAN MAISEL: Well,
21 cardiologists who might -- I mean there are
22 other guidelines regarding performance

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1 criteria for cardioelectrophysiologists.
2 Other comments regarding training? Anyone
3 feel that an onsite visit should be required
4 or everyone is comfortable with -- are people
5 comfortable with the idea of a PowerPoint
6 presentation or a video or some audio-visual
7 component? Clyde.

8 DR. YANCY: I think Dr. Daubert
9 made the point that these are relatively newly
10 initiated sites that had a pretty avid uptake
11 of the methodology and you felt pretty
12 comfortable with that. Is that correct?

13 DR. DAUBERT: Yes.

14 CHAIRMAN MAISEL: David, did you
15 have a comment?

16 DR. SLOTWINER: Yes, I think as Dr.
17 Brinker pointed out the representative from
18 the sponsor are invariably present when staff
19 is instructed how to use it and I think that
20 having them present for the first several
21 procedures is reasonable but I don't think any
22 further training would be necessary.

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1 CHAIRMAN MAISEL: Okay. So I think
2 we have a good sense of what the panel thinks
3 regarding that.

4 Question seven is a risks and
5 benefits assessment. Please provide your
6 overall assessment of the risks and benefits
7 of the CryoCor Cryoablation System for the
8 treatment of isthmus-dependent atrial flutter
9 as demonstrated in the premarket approval
10 application.

11 We're not voting at this time. So
12 I just would more ask for general comments
13 regarding the issues of weighing effectiveness
14 and safety. We've talked about each one
15 individually. Mike.

16 DR. DOMANSKI: My sense again
17 looking at all of the data is there is a
18 reasonable demonstration of both safety and
19 efficacy for this catheter. I actually am not
20 left with any much in the way of residual
21 concern.

22 CHAIRMAN MAISEL: David.

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1 DR. MILAN: Can I ask a question
2 about the labeling? Is it going to be the
3 case that it's indicated for patients who
4 don't have congestive heart failure and an EF
5 less than 35 percent?

6 CHAIRMAN MAISEL: It's up to us to
7 decide, but as we last left it, the actual
8 indication statement is, it's indicated for
9 the treatment of right atrial isthmus ablation
10 and then the label would go on to describe the
11 indications and exclusion criteria from the
12 trials. So there would be a clinical trial
13 section that describe the type of patients on
14 which that indication statement is based.

15 DR. YANCY: The question is whether
16 or not that is sufficient particularly since
17 this unique patient population has a high
18 penetration of atrial arrhythmia and there
19 might be likelihood for practitioners to use
20 this technology in those patients.

21 DR. MILAN: And the reason, I
22 think, it's relevant to the next question is

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1 that this is pretty much the best case
2 scenario in it selected patients that were
3 fairly healthy as these patients go. And so I
4 think you wouldn't anticipate seeing the
5 safety go up if you went into a sicker
6 population and certainly --

7 CHAIRMAN MAISEL: So I think the
8 risk and benefit assessment in our vote today
9 should be predicated on the entry criteria and
10 the patients that are included in this trial
11 as presented in this PMA.

12 DR. MILAN: Okay.

13 DR. SOMBERG: That's also where the
14 post marketing may come in as well to assess a
15 broader population. I mean, one of the most
16 important is that there would be heart failure
17 patients with atrial flutter.

18 CHAIRMAN MAISEL: Other
19 risk/benefit comments? We'll obviously have a
20 vote in a little bit. But any -- We've heard
21 from a lot of people already regarding these
22 issues. So why don't we move onto the post

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1 approval study. If you recommend approval,
2 please discuss whether a post-approval study
3 should be performed to address any issues that
4 are unresolved but not essential to the
5 approval of the device. If so, please comment
6 on the major components of such a study.

7 I'd like to discuss this now
8 because even if we end up recommending non
9 approval, sometimes subsequent data to the FDA
10 may make a decision to approve. As we heard
11 earlier, our discussion of this does not mean
12 that anyone is particularly endorsing or not
13 endorsing approval. So do we need a post
14 approval study? If so, what are the specific
15 issues we want to address in such a post
16 approval study?

17 DR. YANCY: Can we go back to risk
18 for just one second because tamponade is not
19 specifically stated and that was observed in
20 the study? It has perforation or damage to
21 vasculature.

22 CHAIRMAN MAISEL: I think the label

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1 has to reflect all the indications, the
2 exclusions, the adverse events, the
3 effectiveness as we've discussed. So I think
4 the FDA is good at writing labels and we can
5 feel confident they will include all those
6 relevant issues. Sharon.

7 DR. NORMAND: One suggestion I
8 would make for a post approval study would
9 definitely be the inclusion of a concurrent
10 control group. I just don't think we can go
11 forward without having some information given
12 the discussion we had today not knowing what
13 the right rate should be and that would be to
14 everybody's benefit because if you end up with
15 a higher number we don't know if it's too high
16 relative to the current state-of-the-art. So
17 it's very difficult to go forward without a
18 contemporaneous control group and that control
19 group could be everybody who is getting
20 something else. It doesn't have to be
21 randomized. It just has to be proscriptively
22 followed.

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1 CHAIRMAN MAISEL: To answer what
2 question?

3 DR. NORMAND: To answer the
4 question about effectiveness, about chronic
5 effectiveness, about acute effectiveness. So
6 to answer the same questions that we're
7 looking at now as well as safety.

8 CHAIRMAN MAISEL: So obviously,
9 this packet needs to stand on the data in
10 front of us regarding approval. So let's
11 pretend for --

12 DR. NORMAND: I thought we were
13 talking about post approval study.

14 CHAIRMAN MAISEL: Post approval.
15 So the post approval study is not meant to
16 replace premarket information. So we have to
17 decide --

18 DR. NORMAND: And I still say --

19 CHAIRMAN MAISEL: -- on safety and
20 effectiveness now.

21 DR. NORMAND: So my --

22 CHAIRMAN MAISEL: So what specific

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1 -- Do you have issues with patient population,
2 meaning are you concerned about the
3 effectiveness and safety as it's rolled out
4 into a more general population?

5 DR. NORMAND: So perhaps I'm not
6 understanding the question. I thought you
7 asked about what would be the recommended
8 design for a post approval study. Is that the
9 question?

10 CHAIRMAN MAISEL: What should --
11 What issues should a post approval study be
12 addressing, if any, and what design should it
13 look like?

14 DR. NORMAND: And I just answered.
15 I'm not changing my answer and my answer
16 still is I think in a post approval study as
17 we found out in the past with other
18 experiences that we had not having the
19 concurrent control group bites you back and
20 this is the sponsor's benefit. I'm not saying
21 something that is detrimental. It's to the
22 sponsor's benefit, I would argue, and based on

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1 lots of experience, if there was any way to
2 get a concurrent control group that you could
3 collect that that would be very beneficial
4 because if anything happened, I know we're
5 saying it's approved, but if you want to look
6 at things in practice in terms of certain
7 sites that that's the right way to do it.

8 CHAIRMAN MAISEL: Other comments?
9 John.

10 DR. SOMBERG: Well, I agree with
11 what Sharon was saying here that the control
12 group is critical. But there's a broader
13 context here and what I would say if it's
14 approved and we have a post marketing study, I
15 think it's going to be essential to see how it
16 performs to a broader population. This is a
17 very narrow population. I'm not even sure why
18 it was so narrow, but it is and I think
19 patients with heart failure, overt heart
20 failure, low rejection fractions, also a
21 younger population, if there -- That's
22 arbitrary. What happens if you're 17? I

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1 mean, silly things like that. So a broader
2 population. So you go through almost all the
3 points there.

4 Also I think the time --

5 CHAIRMAN MAISEL: John, if I could
6 just interrupt. So all the things you just
7 mentioned are not in the indication statement.
8 They would have been excluded from this trial
9 and the sponsor is not necessarily obligated
10 to study off-label uses if they don't want to
11 study off-label uses. So I'm not disagreeing
12 with you, but are you concerned that the
13 device is going to be used off-label and you
14 want to understand how it's being used because
15 we can't -- the sponsor study.

16 DR. SOMBERG: Of course, I'm
17 concerned. I'm -- You're mixing apples and
18 oranges. Am I willing to approve it now and
19 then do I have concerns? Yes, if you want to
20 say that out loud right now. So given the
21 type of data we have there are certain
22 assurances of relative safety and efficacy

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1 here. But there's not enough for the long
2 term. So you want to do additional studies.
3 Without those additional studies, I'd be less
4 likely to feel that I have enough information
5 now. So I think by agreeing to a post
6 marketing study, it would be in the sponsor's
7 interest, one to increase the marketplace, two
8 to demonstrate safety and additional. There's
9 always a danger. The more you study you can
10 find out bad things.

11 But the worst danger is that bad
12 things happen and then you're held accountable
13 for them and you didn't study them. Then I
14 also think we should go out further than six
15 months to 12 months, but I think all that
16 data, all this broadening of all these areas,
17 would be irrelevant if you don't have a
18 control group.

19 CHAIRMAN MAISEL: So what are the
20 endpoints of such a study? Marcia, why don't
21 we hear from you?

22 DR. YAROSS: Yes. I'd just like to

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1 comment from the pragmatic standpoint.
2 Randomized control studies are hard enough to
3 do preapproval. Once a product is
4 commercially available, getting patients to
5 agree to be randomized to it --

6 DR. SOMBERG: I don't mean to
7 interrupt but I never used the word
8 "randomized."

9 DR. YAROSS: Then I may have
10 misunderstood what Dr. Normand was saying.

11 DR. SOMBERG: It's a registry. It
12 would be a registry.

13 DR. NORMAND: So what I would do
14 and again it's to the -- I'm arguing. It's to
15 the benefit of the sponsor to do this and you
16 may not want to be able to have to collect
17 data in patients that aren't using your
18 device. But it is a benefit if you just
19 prospectively collected data, let's say, at a
20 number of institutions. You roll it out. You
21 get information from patients who would have
22 been eligible and you might not need their

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1 sign-off. There's way to collect the data but
2 got another procedure. And that way at least
3 you have contemporary information about some
4 of the outcomes.

5 DR. YAROSS: Appreciate the
6 clarification. Thank you.

7 CHAIRMAN MAISEL: Dr. Zuckerman.

8 DR. ZUCKERMAN: Yes. The question
9 is a bit confusing, but if I could ask the
10 panel members to go to FDA slides page 20, the
11 slide on the bottom of the page. The first
12 question we have is in this situation, is
13 there a demonstrated need for post approval
14 study in general and can you please look at
15 the five bullets as to why we might require a
16 post approval study and if any panel member
17 could comment on whether they see something
18 lacking here that they would request that that
19 bullet be developed as a post approval study.

20 CHAIRMAN MAISEL: So I think we've
21 already heard about some of these bullet
22 points. We heard Dr. Somberg is interested in

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1 longer term performance. Are other people
2 interested in more than six month follow-up
3 and registry data?

4 We have a yes from Linda. Other
5 people concerned about just six month data?
6 So how long, if we were to collect data, how
7 long should the endpoint be? And do people
8 feel six months is long enough? David.

9 DR. MILAN: I think we keep coming
10 back to the same issue which is what are we
11 going to compare this data to if we collect it
12 at the 12 months. I think that's the struggle
13 we're having right now is we have some data
14 and we don't know what to compare it to. So -
15 -

16 CHAIRMAN MAISEL: So let's imagine
17 if it were post approval that there's a
18 registry and that we collect all comers
19 whether they've had this device or RF and it's
20 a consecutive series enrolled in a registry.

21 DR. MILAN: So if it's controlled,
22 then I think it would probably be useful.

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1 DR. DOMANSKI: You know, I'd like
2 to say a couple things about that.

3 CHAIRMAN MAISEL: Mike.

4 DR. DOMANSKI: I think it's hard
5 for us to sit here first of all and design in
6 its full detail a study and while my
7 enthusiasms in life generally run to doing
8 randomized trials, I'm a little worried about
9 being circumspect about taking the position
10 that longer is better. One of the
11 difficulties is with these patients, I'm not
12 so sure that some of the events that they have
13 down the pike are going to be so easily
14 attributable to this procedure which after
15 all, in any event, is relatively low risk and
16 again looking at the mechanisms by which it
17 would produce long-term problems, I guess, I'm
18 just worried about other things intervening in
19 these patients.

20 CHAIRMAN MAISEL: Are there people
21 who feel that post market study is not
22 necessary? That the data, that if the device

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1 is approved, we have the information we need?
2 David.

3 DR. MILAN: I'm not convinced that
4 post market study is necessary.

5 CHAIRMAN MAISEL: Anyone else?

6 DR. BRINKER: Well, I think it
7 would be nice to have post market study and
8 especially for unusual adverse events since
9 this is a different kind of technology and the
10 subgroup issues that we were talking about
11 before as well as real world community
12 performance because they're going to be out of
13 the strict indications that are here.

14 But I would like to just made the
15 difference that we shouldn't be asking the
16 sponsor to answer questions that may still
17 exist about flutter ablation in general. What
18 they're interested in and what we should be
19 interested in at least for now is this device
20 for flutter ablation. So the issue about how
21 long does an ablation last and things of that
22 nature is probably not specific or at least we

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1 don't have the indication to say it's specific
2 to the type of ablation beyond six months. I
3 think those other things like how it's used in
4 the community and rarer adverse events, we
5 only have 160 patients, would be interesting
6 and it could be done fairly easily.

7 CHAIRMAN MAISEL: Mike.

8 DR. DOMANSKI: Yes. I think Jeff
9 has really hit a point that makes a post
10 marketing approval study useful, but I would
11 constrain the way he said it. The business of
12 looking for unexpected, since it is a
13 different ablation technology, events is
14 probably done reasonably in a registry format
15 which strikes me as balancing reasonably
16 getting information that might be particularly
17 valuable with this device with not increasing
18 the burden on a manufacturer beyond what's
19 reasonable.

20 CHAIRMAN MAISEL: John.

21 DR. SOMBERG: I am somewhat
22 surprised because -- Well, I'm not actually.

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1 But there are many -- Let me take this back
2 and let me start again. There are many
3 committee members, panel members, here who
4 haven't sat on previous panels and I'll give
5 an example of stents. When registries were
6 created, registries weren't created long
7 enough and they weren't created to look at
8 certain situations. So I'll bring us to a
9 scenario.

10 The scenario is this device gets
11 approved. It's utilized and then at some
12 international meeting in Barcelona, someone
13 presents that at two years everybody who has
14 isthmus ablation with a cryoablation system
15 develops focal ventricular tachycardia. Did
16 we look out far enough? And it's on
17 especially patients who have low rejection
18 fractions. So there's a tremendous number of
19 people with low rejection fractions with
20 ischemic heart disease, recent ischemic
21 events, patients who were not in this type,
22 there's a small study.

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1 So I don't think it's an
2 unreasonable burden to ask a sponsor who did
3 not meet the performance criteria even though
4 there are all the problems we've discussed to
5 now go out and obtain an registry with a
6 comparative group, use the word "comparative"
7 not "control" group and follow it out for a
8 decent interval of time and not to do that
9 would be very upsetting to me.

10 CHAIRMAN MAISEL: I would just like
11 to clarify the difference between a permanent
12 implant and a catheter that is inserted to do
13 a procedure and then removed. But your point
14 is well taken and --

15 DR. SOMBERG: I'm sorry. But the
16 isthmus is now completely pathophysiologically
17 changed. There is a more irrevocable lesion
18 here than there is with a stent.

19 CHAIRMAN MAISEL: So your point is
20 well taken. I think what we're saying is it
21 sounds like the majority of the panel is
22 interested in post market data. Probably a

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1 registry would be okay. We want there to be a
2 good control. There will need to be a sample
3 size calculation based on what we're calling
4 rare, unexpected adverse events which is vague
5 and difficult.

6 DR. DOMANSKI: Yes, but I don't --
7 I think the problem is if your major concern
8 is looking for a pattern of rare events, then
9 there is no way that you're going to come up
10 with a control group that adequately powers
11 you to do that because, I mean, the size would
12 be enormous if you're looking for rare events.

13 So the registry format is probably no worst
14 than the control group.

15 If you're looking for more common
16 stuff, then you can do a control group. My
17 own thought is that the burden is higher than
18 it needs to be for that, but I don't feel that
19 strongly one way or another about that.

20 CHAIRMAN MAISEL: Clyde has been
21 waiting patiently.

22 DR. YANCY: No. I do think another

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1 reason to do this post marketing survey or
2 study understanding that we're talking about
3 going forward with it approved and we can't go
4 back and reimposing any questions of the
5 study. But we are looking at a safety signal
6 that's at least two times higher than the OPC
7 and we're trying to decide if there's going to
8 be any clustering and do recognize that it's a
9 different energy source and a different size
10 catheter. So I think to exercise appropriate
11 due diligence, we really should have that with
12 referable populations so we know what the
13 expectation would be.

14 CHAIRMAN MAISEL: So I might also
15 add that if the short-term safety is an issue,
16 then that's a shorter follow-up and so there
17 may be a different number of patients that
18 would be followed for that than for a chronic
19 effectiveness endpoint. Dr. Zuckerman.

20 DR. ZUCKERMAN: Yes. So, Dr.
21 Maisel, can you try to frame the panel
22 comments by using the four bullet points on

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1 the slide? What is the fundamental study
2 question? What are you trying out?

3 CHAIRMAN MAISEL: I think I've
4 heard two fundamental study questions. One is
5 the rollout to the real world community and
6 the performance of this device in the real
7 world. And one is the assessment of safety
8 endpoints because while many panel members
9 feel okay about the safety, it doesn't come
10 under the OPC and we'd like to be reassured by
11 that. So I think those are the fundamental
12 study questions.

13 The safety endpoints and method
14 assessment, I think, for safety, we'd be
15 looking at certainly for the short-term safety
16 we'd need quality, seven day outcomes similar
17 to what was done here. That means case report
18 forms and follow-up with patients at seven
19 days preferably by a physician office visit
20 and for acute and chronic effectiveness
21 endpoints and methods of assessment, again I
22 think we've been talking about follow-up

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1 similar to what we saw.

2 I personally don't have issues with
3 chronic effectiveness, although I think --
4 Does the panel want to know about chronic
5 effectiveness in the real world and, if so,
6 we're going to need to collect a lot of
7 demographic information and do a lot of
8 monitoring of patients? Is that what people
9 want?

10 DR. NORMAND: Well, I can say what
11 I want. I think that would be important
12 because if you're really going to answer the
13 question on how these devices are used in the
14 real world, you want the clinical endpoint
15 which is chronic effectiveness. And one could
16 figure out -- I mean, I'm sure the sponsor can
17 getting a real savvy person to design a study
18 that we're not going to design on the fly that
19 will figure this out that will find a cheap
20 way to collect the data and to add onto other
21 registries. We do it all the time.

22 CHAIRMAN MAISEL: And I think we're

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1 saying if we want real world community
2 performance we need to have some effectiveness
3 data and I think we're saying we'd like the
4 data and collection to be rigorous and it
5 might be a nice opportunity to also collect
6 some of that clinical data that we were
7 looking for and didn't have.

8 DR. SOMBERG: But you don't have to
9 have weekly or monthly monitoring. You could
10 have a recurrence of sustained flutter with
11 hospitalization, need for cardioversion,
12 easily defined and monitored clinical
13 endpoints.

14 DR. ZUCKERMAN: So the point would
15 be to get the chronic real world clinical
16 effectiveness data as perhaps Dr. Calkins
17 talked about this morning.

18 CHAIRMAN MAISEL: Correct. And I
19 think the duration of follow-up, it sounds
20 like for the effectiveness, would have to be
21 at least six months. I think the panel is a
22 little bit divided about longer. Some people

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1 want longer follow-up and others don't feel
2 that longer follow-up is necessary, six to
3 twelve month follow-up.

4 So at this point, why don't we take
5 a break. We will reconvene in 15 minutes at
6 3:45 p.m. Off the record.

7 (Whereupon, the foregoing matter
8 went off the record at 3:30 p.m. and went back
9 on the record at 3:45 p.m.)

10 CHAIRMAN MAISEL: Okay, why don't
11 we get started again? We will now proceed
12 with the second open public hearing of this
13 meeting. Is there anyone in the audience who
14 wishes to address the panel at this time? If
15 so, please raise your hand and come forward.
16 Seeing no one, we will close the open public
17 hearing portion of the meeting and we will
18 move onto FDA and sponsor summations, if any.

19 Does the FDA have any further comments they
20 wish to make?

21 DR. ZUCKERMAN: No, we don't.

22 DR. FARIS: I was about to say the

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1 same thing.

2 CHAIRMAN MAISEL: I got at least
3 three nos from the FDA. Is there any -- does
4 the sponsor have any additional comments
5 they'd like to make?

6 DR. BAROLD: Yes, and they are
7 going to be very brief. All right, first of
8 all, I do want to thank the FDA for working
9 very closely with us. And I want to thank the
10 panel today for taking the time out. I think
11 this has been a very valuable process for the
12 company. I think the panel process itself is
13 very valuable, especially when it applies to
14 new technologies.

15 I think it's difficult for you,
16 your decisions and that you are looking at
17 this device in a vacuum without having, you
18 know, full data on other devices of this
19 nature. I think it's also a credit to the
20 company, if I should say so, that we have such
21 esteemed experts that are willing to come and
22 speak for the product.

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1 I personally strongly believe that
2 there is a role for our device out there in
3 the marketplace and as a practicing
4 electrophysiologist, I want as many tools as
5 possible to be able to treat my patients.
6 And, you know, I do look forward to working
7 closely with the FDA to bringing this product
8 to market eventually and thank you again.

9 CHAIRMAN MAISEL: Thank you very
10 much. We are now ready to vote on the panel's
11 recommendation to the FDA for this PMA. Mr.
12 Swink will now read the panel recommendation
13 options for the pre-market approval
14 application. Mr. Swink?

15 EXECUTIVE SECRETARY SWINK: "The
16 Medical Device Amendment to Federal Food, Drug
17 and Cosmetic Act as amended by the Safe
18 Medical Devices Act of 1990 allows the Food
19 and Drug Administration to obtain a
20 recommendation from an expert advisory panel
21 on designated medical device pre-market
22 approval applications that are filed with the

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1 Agency.

2 The PMA must stand on its own
3 merits and your recommendation must be
4 supported by safety and effectiveness data in
5 the application or by applicable publicly
6 available information. The definitions of
7 safety effectiveness and valid scientific
8 evidence are as follows.

9 Safety as defined in 21 CFR Section
10 860.7, there is reasonable assurance that a
11 device is safe when it can be determined based
12 upon valid scientific evidence that the
13 probable benefits to health from use of the
14 device for its intended uses and conditions of
15 use when accompanied by adequate directions
16 and warnings against unsafe use outweigh any
17 probable risk."

18 Effectiveness as defined by 21 CFR
19 Section 860.7. "There is reasonable assurance
20 that a device is effective when it can be
21 determined based upon valid scientific
22 evidence that in a significant portion of the

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1 target population, the use of the device for
2 its intended uses and conditions of use, when
3 accompanied by adequate direction for use and
4 warnings against unsafe use, will provide
5 clinically significant results."

6 Valid scientific evidence as
7 defined is 21 CFR Section 860.7 is, "There is
8 evidence from well-controlled investigations
9 partially controlled studies, studies and
10 objective trials without match controls, well-
11 documented case histories conducted by
12 qualified experts and reports of significant
13 human experience with a marketed device from
14 which it can fairly and responsibly be
15 concluded by qualified experts that there is a
16 reasonable assurance of safety and
17 effectiveness of a device under its conditions
18 of use. Isolated case reports, random
19 experience, reports lacking sufficient details
20 to permit scientific evaluation and
21 unsubstantiated opinions are not regarded as
22 valid scientific evidence to show safety or

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1 effectiveness".

2 Your recommendation options for the
3 vote are as follows. "Number one is approval
4 if there are no conditions attached. Number
5 two, approvable with conditions. The panel
6 may recommend that the PMA be found approvable
7 subject to specific conditions such as
8 physician or patient education, labeling
9 changes or further analysis of existing data.

10 Prior to voting all of the conditions should
11 be discussed by the panel. Number three, not
12 approvable; the panel may recommend that the
13 PMA is not approvable if the data do not
14 provide a reasonable assurance that the device
15 is safe or the data do not provide a
16 reasonable assurance that the device is
17 effective under the conditions of use
18 prescribed, recommended or suggested in the
19 proposed labeling.

20 Following the voting, the Chair
21 will ask each panel member to present a brief
22 statement outlining the reasons for his or her

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1 vote". Thank you.

2 CHAIRMAN MAISEL: Thank you. Are
3 there any questions from the panel about the
4 voting options before we move onto the main
5 motion? Any questions regarding the voting
6 options? You can refer to your voting
7 procedure flow chart that is in your folder.
8 Yes, David?

9 DR. MILAN: Just to be clear, the
10 conditions in the approvable with conditions
11 wouldn't be limited just to post market
12 studies.

13 CHAIRMAN MAISEL: No, we can make
14 conditions on whatever we want to make
15 conditions on. Okay, so at this point, I will
16 entertain a main motion for a vote. David?

17 DR. SLOTWINER: I would move to
18 approve with conditions.

19 CHAIRMAN MAISEL: So we have a
20 motion from Dr. Slotwiner for approvable with
21 conditions. Do we have a second?

22 DR. SOMBERG: Second.

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1 CHAIRMAN MAISEL: Dr. Somberg
2 seconds. So at this point, we need conditions
3 for this approvable with conditions motion.
4 Is there anyone who would like to propose a
5 condition? John?

6 DR. SOMBERG: The first condition I
7 would propose is that the IFU be revised along
8 the lines we had discussed which was to
9 include a clinical trial section detailing the
10 inclusion/exclusion criteria of the study, the
11 study findings, the presentation of the
12 results and listing the acute efficacy,
13 chronic efficacy as interpreted with 140
14 denominator and 160 denominator and also with
15 an explanation that if one asked for acute
16 isthmus, non-conduction, there's -- what's the
17 word again, co -- there's an interaction, you
18 have to multiply one times the other and as we
19 discussed, as well.

20 And also, clearly, that the device
21 has not been studied in patients with severe
22 concomitant diseases such as congestive heart

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1 failure, et cetera. Another one I would say -
2 - okay, sorry.

3 CHAIRMAN MAISEL: Before we -- let
4 me try to summarize what you've said and then
5 we'll need a second on the motion. The first
6 condition is that the labeling be revised to
7 reflect our concerns that the clinical trial
8 section be included, that it include inclusion
9 and exclusion criteria results including acute
10 what I'm going to call for now but we don't
11 like the terminology, conditional chronic
12 effectiveness and unconditional chronic
13 effectiveness that reflects Dr. Normand's
14 concerns that we remove issues related to the
15 left atrium as we discussed earlier.

16 DR. SOMBERG: And the right atrial
17 mentioned as you had --

18 CHAIRMAN MAISEL: And that the
19 right atrial be added to the indication
20 statement. So basically condition one is the
21 labeling revisions that we discussed earlier.
22 Is there a second on Dr. Somberg's motion or

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1 condition.

2 DR. SOMBERG: Well, I'm the second,
3 Roberts' Rules of Order.

4 CHAIRMAN MAISEL: No, you seconded
5 the condition of approval. Now we need a
6 second on your condition.

7 DR. SOMBERG: Oh, I'm sorry, okay,
8 whatever.

9 CHAIRMAN MAISEL: Is there a second
10 on that condition?

11 DR. MILAN: Second.

12 CHAIRMAN MAISEL: Dr. Milan, okay.

13 We will now vote on that condition before we
14 move onto the next condition. And so we will
15 go around the table. What we are voting is
16 not on the entire motion. We are voting just
17 on Dr. Somberg's condition regarding the
18 labeling changes that we just spoke about. So
19 if you are in favor of that you will say, yes.

20 If you are not in favor, you will say no, and
21 if you want to abstain, you can abstain. I'd
22 like your name and your vote. We'll start

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1 with Dr. Domanski.

2 DR. DOMANSKI: I'll vote yes.

3 DR. BRINKER: Jeff Brinker, yes.

4 DR. SOMBERG: Yes, Somberg.

5 DR. KARASIK: Karasik, yes.

6 DR. KATO: Norman Kato, yes.

7 DR. YANCY: Yancy, yes.

8 DR. LOTTICK: Lottick, yes.

9 DR. SLOTTWINER: Dan Slotwiner, yes.

10 DR. NORMAND: Sharon-Lise Normand,
11 yes.

12 DR. MILAN: David Milan, yes.

13 CHAIRMAN MAISEL: Excellent, so
14 that condition passes. The first condition is
15 a labeling condition. Are there additional
16 conditions that people would like to add to
17 this motion. Dr. Somberg?

18 DR. SOMBERG: I think there should
19 be a training condition imposed and after
20 listening to my EP colleagues and they're
21 fresher in this area than I, I think it should
22 be in person, representatives training the use

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1 of the console system as well as face-to-face
2 discussion of the utility -- of the for want
3 of words, tricks of the trade for the catheter
4 manipulator as well.

5 CHAIRMAN MAISEL: We have a motion
6 for a training program that includes in person
7 training of the physician user of the device
8 and presumably the staff associated who will
9 also be using the device. Do we have a second
10 for that motion?

11 DR. SLOTWINER: I second that.

12 CHAIRMAN MAISEL: Okay, Dr.
13 Slotwiner seconds it. Any discussion on that
14 motion before we vote on that motion? So
15 let's vote on that motion. We've voting only
16 on the second condition of the training
17 program that we just heard about. Name and
18 vote, please, Dr. Domanski.

19 DR. DOMANSKI: Domanski, I'll
20 abstain.

21 DR. BRINKER: Brinker, yes.

22 DR. SOMBERG: Somberg, yes.

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1 DR. KARASIK: Karasik, yes.

2 DR. KATO: Kato, yes.

3 DR. YANCY: Yancy, yes.

4 DR. LOTTICK: Lottick, yes.

5 DR. SLOTWINER: Slotwiner, yes.

6 DR. NORMAND: Normand is yes.

7 DR. MILAN: Milan, yes.

8 CHAIRMAN MAISEL: So that is nine
9 nothing with one abstention. So that
10 condition also passes. Other conditions for
11 this main motion? I'm going to ignore you for
12 just a minute. Dr. Somberg, you're on a roll.
13 What's condition number three?

14 DR. SOMBERG: I actually --

15 CHAIRMAN MAISEL: Clyde.

16 DR. YANCY: Post-marketing study.

17 CHAIRMAN MAISEL: More specific,
18 please.

19 DR. YANCY: As we discussed,
20 hypothesis.

21 (Laughter)

22 DR. YANCY: And data.

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1 CHAIRMAN MAISEL: It's not going to
2 fly. No, seriously, more specific. What
3 specific post-marketing study are you --

4 DR. YANCY: Post-marketing study of
5 the application of this device with all others
6 that are being treated for a similar illness,
7 followed longitudinally with focus being on
8 near-term safety events, longer term adverse
9 events and general evidence of clinical
10 utility and experience.

11 DR. SOMBERG: Can I ask a
12 clarification? Is this a registry or a
13 randomized study?

14 CHAIRMAN MAISEL: Can you clarify
15 your --

16 DR. YANCY: This is not a
17 randomized control trial. This is an
18 observational exercise, registry is an
19 adequate word.

20 CHAIRMAN MAISEL: So let me try to
21 summarize your -- Dr. Normand?

22 DR. NORMAND: I just want to ask a

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1 clarification. And you meant to have some
2 comparison or not?

3 DR. YANCY: Which is not
4 inconsistent with the registry.

5 CHAIRMAN MAISEL: So just to try to
6 summarize the third motion, it's for a post-
7 market trial that's a registry of consecutive
8 patients to study short-term, near-term
9 safety, longer term adverse events, clinical
10 effectiveness in a real world population and
11 to incorporate the items we spoke about
12 before. Dr. Domanski.

13 DR. DOMANSKI: Yes, I don't think
14 you can say consecutive, though. I don't even
15 know what that means when we're all over the
16 country doing it.

17 CHAIRMAN MAISEL: Okay.

18 DR. DOMANSKI: I'd get rid of that
19 word.

20 CHAIRMAN MAISEL: Dr. Yancy, it's
21 your motion. What do you -- how do you feel
22 about the --

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1 DR. YANCY: I didn't use the word
2 consecutive.

3 DR. DOMANSKI: He didn't use the
4 word consecutive.

5 CHAIRMAN MAISEL: Okay, yes, I
6 added that word. So not consecutive, a
7 registry of patients with near-term safety,
8 long-term adverse event monitoring clinical
9 effectiveness powered to detect the issues
10 we've discussed.

11 DR. SOMBERG: Could the word in
12 patients with low ejection fraction and heart
13 failure be included? I mean, that's real
14 world but you can say, "Hey, you know, we're
15 doing everything else but that", and I think
16 that's a very important group to look at.

17 CHAIRMAN MAISEL: Dr. Yancy, it is
18 your motion.

19 DR. YANCY: I'm troubled with that
20 only because it technically is an off-label
21 use of the technology and I think the right
22 way to focus on heart failure and low

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1 injection fraction is with an appropriate
2 design prospective randomized study.

3 CHAIRMAN MAISEL: So the motion on
4 the table is a registry of patients with near-
5 term safety, long-term adverse event
6 monitoring, clinical effectiveness in a real
7 world population. So you want a registry of
8 patients --

9 DR. YANCY: Who are receiving this
10 according to the label indication.

11 CHAIRMAN MAISEL: So that's
12 different than real world. No, seriously,
13 it's different.

14 DR. LOTTICK: Could I seek
15 clarification? It seems to me that there may
16 be the rare individual out there who is
17 tempted to use this in an off-label fashion
18 and I would prefer to actually collect all the
19 data. So I'd rather have any usage of the
20 catheter followed because we're not
21 prescribing off-label use obviously but if
22 off-label use occurs, I think it's very

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1 important that we get information about
2 adverse consequences, et cetera.

3 DR. YANCY: I will be deliberate
4 only because I would not want the acquisition
5 of off-label data in a non-structured, non-
6 randomized way to suffice for a more
7 appropriate data set. So I will continue to
8 say that the registry experience should be
9 collecting a large denominator that reflects
10 the patients in whom the technology has
11 already been studied.

12 CHAIRMAN MAISEL: So the motion on
13 the table is for a registry of patients who
14 meet the current inclusion and exclusion
15 criteria with the features we've discussed.
16 Is there a second of that motion, of an on-
17 label registry? Is there a second for that
18 motion?

19 DR. DOMANSKI: I'll second.

20 CHAIRMAN MAISEL: Dr. Domanski. So
21 that doesn't preclude us from adding an
22 additional registry later if we want but --

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1 DR. BRINKER: Could I ask a
2 question?

3 CHAIRMAN MAISEL: Sure.

4 DR. BRINKER: So my understanding
5 of the labeling is for atrial flutter ablation
6 in patients over 18. Now, it's true that in
7 the labeling there will be this study
8 described but it doesn't proscribe a specific
9 sub-group in the labeling. Right?

10 CHAIRMAN MAISEL: So Dr. Yancy, can
11 you clarify your motion? Is it for people who
12 meet the inclusion and exclusion criteria of
13 this study that we've looked at, the pivotal
14 trial or is it for quote "on-label use right
15 atrial isthmus ablation?"

16 DR. YANCY: I think the registry
17 design should continue to reflect the patients
18 in whom these data were acquired. And the
19 indication and contra-indication statements s
20 they currently appear in the label, don't
21 adequately capture the patients in whom these
22 data were acquired. And so for this to be an

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1 appropriate registry and not a poor substitute
2 for a clinical trial, even if this gets
3 defeated, I think the right design is a large
4 denominator of the persons in whom these data
5 were originally acquired moving forward.

6 CHAIRMAN MAISEL: Okay, so just to
7 clarify -- Dr. Domanski.

8 DR. DOMANSKI: Yes, you know,
9 Clyde, let me sort of speak to the other
10 thing. I went through the stent thing and
11 what happens is there's a certain amount of
12 on-label use and off-label use. And I don't
13 think it would be encouraging off-label use to
14 say that it's a registry of all comers. And
15 what will happen is, the on-label stuff will
16 be picked up but we'll also get information
17 about other people, too.

18 So I take your point. It's not a
19 substitute at all. That said, we're kind of
20 going to end up throwing out the off-label
21 data if we do it that way. So I'd like to --
22 you know, I'd like to have you give that a

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1 little bit of thought and perhaps think about
2 altering the motion on that basis.

3 CHAIRMAN MAISEL: So right now we
4 have a motion that's been approved and
5 seconded for on-label registry only of
6 patients that meet this criteria. For us to
7 not vote on that, Michael, you can remove your
8 second if you wish.

9 DR. DOMANSKI: I'd like you to try
10 to amend it if you would. I don't want to
11 sound adversarial. I'm just trying to pick it
12 up.

13 CHAIRMAN MAISEL: No, my sense is
14 that Clyde -- I mean, I'll let Clyde speak for
15 himself. He said it three times and I think
16 I've heard it three times and I think we
17 should vote on it. Or if you don't feel
18 comfortable seconding it, then we can --

19 DR. DOMANSKI: Yes, I actually
20 think we should take all of the comers in that
21 situation. So I guess maybe I don't feel
22 comfortable if we feel really that constrained

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1 by it.

2 CHAIRMAN MAISEL: So can I take
3 that as you're removing your second, without
4 it being adversarial and --

5 DR. DOMANSKI: Yes, but I would
6 rather, just as a collegial thing have --

7 DR. YANCY: It won't hurt my
8 feelings.

9 DR. DOMANSKI: Okay, I remove my
10 second.

11 CHAIRMAN MAISEL: Okay, so does
12 anyone else want to second Clyde's registry
13 concept? So does anyone want to propose a
14 modified registry? Dr. Somberg?

15 DR. SOMBERG: I would like to
16 propose -- you're not going to let me get away
17 with this probably but I would like to propose
18 what Dr. Yancy had said but to take all
19 patients who undergo the procedure and -- or
20 to suggest inclusion of all patients who may
21 undergo the procedure as indicated.

22 CHAIRMAN MAISEL: So we now have a

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1 motion on the table for a registry of patients
2 for the issues that Dr. Yancy brought up; near
3 term safety, long-term adverse events,
4 clinical effectiveness, for all comers that
5 are receiving the therapy.

6 DR. YANCY: Real world --

7 CHAIRMAN MAISEL: Real world
8 experience, a registry of real world
9 experience. Do we have a second for that?

10 DR. DOMANSKI: I'll second that.

11 CHAIRMAN MAISEL: Dr. Domanski.

12 Any other discussion on that?

13 DR. SLOTWINER: I just have a
14 question. Do you include patients who are
15 eligible for flutter ablation if they get
16 treated with a different catheter as well?

17 DR. SOMBERG: Oh, yes, in fact
18 that's a good point because with a comparator
19 group and the appropriate follow-up which is
20 recommended at 12 months.

21 DR. DOMANSKI: Well, if you add a
22 comparator group then I withdraw my second.

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1 CHAIRMAN MAISEL: So the motion on
2 the table is for patients at an institution
3 undergoing the ablation procedure with any
4 catheter, atrial flutter ablation with any
5 catheter; is that what you're saying or are
6 you saying with this device?

7 DR. SOMBERG: No, I'm saying with a
8 registry that would evaluate -- have one part
9 of the study evaluating this device, one study
10 arm and comparing it to -- with a comparator
11 group to all other patients undergoing
12 ablation for atrial flutter.

13 DR. DOMANSKI: Okay, that's a
14 different motion than the one I seconded and I
15 won't second that.

16 DR. NORMAND: I will second that
17 one.

18 CHAIRMAN MAISEL: Okay, so let's
19 back up. So we have a second. We have a
20 second to the motion. Dr. Domanski removed
21 his second.

22 DR. SOMBERG: See, I had her in my

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1 back pocket there.

2 CHAIRMAN MAISEL: Dr. -- the motion
3 on the table, the condition on the table is
4 for a registry of all -- of patients
5 undergoing atrial flutter ablation with any
6 catheter and we want near-term safety, long-
7 term adverse events, clinical effectiveness
8 and Dr. Normand, you have seconded that
9 motion. Do we have other comments on that
10 motion? Adam?

11 DR. LOTTICK: I'd like
12 clarification as to what -- I mean, are we
13 asking for every patient in the country to be
14 put on the flutter ablation register?

15 DR. NORMAND: No, no.

16 CHAIRMAN MAISEL: No.

17 DR. LOTTICK: Are we saying each
18 institution that uses this catheter, all of
19 those? I mean, how is that designed?

20 DR. NORMAND: Here's the -- I
21 understand your concern and I think it's
22 difficult for this panel to sit down and write

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1 a detailed protocol. I think the spirit of it
2 is to have the sponsor collect data where
3 there is some sort of comparison group. It
4 doesn't have to be everybody and again, it
5 doesn't take a rocket scientist to think of a
6 judicious cheap design to get some sort of
7 comparison group.

8 The point of the matter is, is the
9 only one I'm going to agree to, and that's
10 just me, is one where there is some sort of
11 comparison group. Otherwise, we have no
12 information and we're in a vacuum and I've
13 lived through the stent as well. So that's
14 the problem.

15 CHAIRMAN MAISEL: Clyde.

16 DR. YANCY: And I've lived through
17 the stent as well and I can tell you that the
18 off-label data we collected was totally
19 uninterpretable and it created a false sense
20 of knowledge that was just noise. And as a
21 heart failure advocate now, this is a very
22 unique patient population and if we allow that

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1 patient population to be in any sort of data
2 base without doing this correct, that is not
3 justifiable.

4 DR. NORMAND: If I could say
5 something to Dr. Yancy, one of the things that
6 I'm -- I would suggest that the reason for
7 the comparison group is in order to have a
8 rate even in the -- really talking about the
9 on-label people right now, but a rate to
10 compare to something because we don't know if
11 that rate's going to be too high or too low.
12 So I'm not necessarily talking about all
13 patients but the point with the stent problem
14 that happened before we even met was that
15 there was a lot of issues about a bad event.

16 But it was in a vacuum. We didn't
17 know if that was too high or too low, and I
18 want to circumvent that by at least getting a
19 comparable population. I don't care what the
20 population is but there needs to be some sort
21 of comparable. Maybe it's the RF patients.
22 All I'm saying is that something like that

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1 would be helpful to gauge whether or not
2 there's a real problem or not.

3 DR. YANCY: And I agree completely.

4 My reason for pause is that it should be
5 restricted now to the population that we're
6 trying to mature. To generate more data in a
7 population about which we know nothing right
8 now, I think is not the right approach.

9 DR. SOMBERG: Yes, but can I just
10 say --

11 CHAIRMAN MAISEL: Dr. Somberg.

12 DR. SOMBERG: The reason I feel
13 strongly different, and I think we both have
14 concerns for the population that you're
15 discussing is, I think right now our RF
16 fibrillation is being used for people with
17 atrial flutter and with low rejection fraction
18 with or without symptomatic heart failure and
19 I think once this device is approved for
20 isthmus related atrial flutter that's
21 symptomatic, it will be used in that patient
22 population. And therefore, we will have no

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1 data and no ability to be able to judge
2 efficacy and safety.

3 Now, with saying that, I do not
4 think that's a substitution for a study that a
5 sponsor might bring forth that would get a
6 specific indication for that. But I'm afraid
7 in this world, those little indications, that
8 tiny slice of the salami may not be worth that
9 much.

10 CHAIRMAN MAISEL: Also I would just
11 comment that our asking to include those
12 patients in a registry does not necessarily
13 condone the use of that device in that patient
14 population. We're just trying to collect data
15 of what's going on out there. So we have a
16 motion on the table for a registry that Dr.
17 Somberg has described. It is for not just
18 this sponsor's device, but for patients
19 undergoing atrial flutter ablation with any
20 device near-term safety, long-term adverse
21 events and clinical effectiveness power to
22 detect the issues that we've discussed

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1 earlier, the sample size to be determined
2 later.

3 So that's been seconded. I would
4 like to vote on that condition only, the
5 registry we've just described and I'll start
6 with Dr. Domanski.

7 DR. DOMANSKI: I vote no.

8 CHAIRMAN MAISEL: Dr. Brinker?

9 DR. BRINKER: I vote yes.

10 DR. SOMBERG: Somberg, yes.

11 DR. KARASIK: Karasik, yes.

12 DR. KATO: Kato, yes.

13 DR. YANCY: Yancy, no.

14 DR. LOTTICK: Lottick, yes.

15 DR. SLOTWINER: Slotwiner, abstain.

16 DR. NORMAND: Normand, yes.

17 DR. MILAN: Milan, yes.

18 CHAIRMAN MAISEL: So we have seven
19 yeases, two nos and one abstention. That
20 condition passes. Any other conditions that
21 people would like to add to this motion of
22 approvable with conditions? David?

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1 DR. MILAN: Can I ask a question
2 about what happens to that registry data? I
3 mean, is it -- it's given to the FDA. Is it
4 made publicly available?

5 CHAIRMAN MAISEL: So it would be
6 classified as a post-approval study. That
7 comes under the purview of the FDA and the
8 public availability of that is subject to a
9 number of rules and regulations that are
10 beyond our control. Any other conditions?

11 DR. YANCY: Question.

12 CHAIRMAN MAISEL: You're sitting
13 right next to me.

14 DR. YANCY: I think Domanski did
15 that to my mike.

16 (Laughter)

17 DR. YANCY: But a question of
18 clarification; is it preceded for a
19 condition to be a request to initiate another
20 clinical trial in a different patient
21 population? Has that ever been addressed, do
22 you know?

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1 CHAIRMAN MAISEL: My understanding
2 is that it is --

3 DR. YANCY: Not to mandate it, but
4 to engage in forward looking discussion at
5 least about that?

6 CHAIRMAN MAISEL: No, I would
7 encourage us to save those remarks for our
8 post-vote commentary in which we will have an
9 opportunity to do.

10 DR. YANCY: I appreciate that.

11 CHAIRMAN MAISEL: Any other
12 conditions? So we will now vote on this
13 motion of approvable with the conditions. The
14 first condition is the labeling that we
15 discussed, adding a clinical trial section
16 inclusion/exclusion criteria, results acute
17 conditional chronic effectiveness,
18 unconditional chronic effectiveness, removing
19 the issues of left atrium. Adding right
20 atrium to the indication statement.

21 Condition two is training as we
22 discussed, in person training of the physician

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1 and lab staff and Condition three is the post-
2 market registry as we have discussed. So that
3 is the motion on the table. It's all or none.

4 You get to -- we vote on all of those
5 conditions or it's either yes, you wish to
6 approve with those conditions or, no, you do
7 not wish to approve with those conditions.
8 And we'll start with Dr. Domanski.

9 DR. DOMANSKI: Yes.

10 DR. BRINKER: Brinker, yes.

11 DR. SOMBERG: Somberg, yes.

12 DR. KARASIK: Karasik, yes.

13 DR. KATO: Kato, no.

14 DR. YANCY: Yancy, yes.

15 DR. LOTTICK: Lottick, yes.

16 DR. SLOTWINER: Slotwiner, yes.

17 DR. NORMAND: Normand, no.

18 DR. MILAN: Milan, yes.

19 CHAIRMAN MAISEL: So we have a vote
20 of eight to two in favor of approvable with
21 the conditions we outlined and now we'll go
22 around the table and hear from each individual

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1 regarding what your vote was and why you voted
2 that way. Mike?

3 DR. DOMANSKI: Well, I really -- I
4 think that there is a demonstrated reasonable
5 expectation that this device is safe and
6 effective, if one really looks carefully to
7 the data. I do think that the -- in the
8 future, the FDA should use a controlled trial
9 for this kind of study rather than these
10 parameters that don't require a control group.

11 I think there is a place for that kind of
12 parameter where the trial would have to be so
13 large that you could never introduce a device,
14 for instance, with valves.

15 It would be almost impossible to
16 run a trial at least for safety that showed a
17 difference, you know, of an appropriate size.
18 So I don't think there's no role for it, but I
19 think the role was clearly not here and I
20 think today's discussion demonstrated
21 remarkable limitations of the approach that
22 was used.

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1 With regard -- and the only other
2 thing that I would say is, my concern about
3 the post-marketing study is not so much that I
4 don't understand the usefulness of comparator
5 groups. What I'm concerned about is getting
6 meaningful ones and not asking people to get
7 data just so that they could say they got some
8 data. So that was the concern that I had. So
9 thank you.

10 CHAIRMAN MAISEL: Jeff.

11 DR. BRINKER: I think this is a
12 difficult situation for the FDA to present to
13 us, a scenario in which clearly the OPCs
14 weren't fully met and ask us to mediate
15 something which the gut feeling would be that
16 this is a good device for the purposes it's
17 being requested for use. So I think we've
18 done that and I echo all Mike's comments that
19 this is not a situation that the panel should
20 like to find itself in often. And that a
21 mechanism needs to be put into place which
22 evaluates OPCs before the beginning of a study

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1 and the wiggle room which one can operate in.

2 I think the panel did a good job,
3 as did the FDA and the company in presenting
4 their data and I think that the conditions of
5 approval are appropriate for the level of
6 information that we have now and expectations
7 to gain knowledge about its use in the future.

8 CHAIRMAN MAISEL: Thanks, Jeff.
9 John.

10 DR. SOMBERG: I voted yes because I
11 felt there was fairly good efficacy
12 information available. I was impressed by the
13 reports from outside the United States and the
14 expert center of the utility of this system.
15 I think there are great perils for a sponsor
16 to take when they don't have a control group
17 and I think this panel was most understanding
18 of those perils but it may not always be the
19 case. For the public good and also for the
20 sponsor's good, I think use of comparator
21 groups, controlled studies preferably
22 randomized, are essential.

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1 But what we did hear was we saw
2 some problems with maybe asking more efficacy
3 than has been asked before and some safety
4 issues but probably nothing that was related
5 to the actual catheter and device so
6 therefore, appropriate training, appropriate
7 IFU description of what has transpired and a
8 detailed real world post-marketing study will,
9 I think, give the FDA the tools it needs to
10 insure the public safety if everything was not
11 seen by this committee and the data
12 heretofore.

13 CHAIRMAN MAISEL: Thanks, John.
14 Pam?

15 DR. KARASIK: Can I just second
16 everything that's been said already? I do
17 believe that the sponsor showed that the
18 device meets reasonable safety and efficacy.
19 Although, like my colleagues, I have similar
20 slight reservations that I think the
21 conditions will help aswage. I do think that
22 post-marketing collection of information is

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1 very important to confirm what we -- you know,
2 what we suspect and what led me to vote for
3 approval. I'll just keep it at that.

4 CHAIRMAN MAISEL: Norm?

5 DR. KATO: I voted no not to
6 approve primarily because I felt that there
7 was insufficient evidence to satisfy the OPC
8 criteria which had been mutually agreed upon
9 by both FDA and the sponsor. I felt that to
10 basically ignore the criteria at this point
11 would be to allow the panel or allow actually
12 a panel decision or even an FDA decision to
13 occur that really wasn't evidenced based, that
14 it was much more subjective and I believe that
15 this is as I said before, a slippery slope of
16 modifying basically the success criteria by
17 which these devices are compared to.

18 I think that you know, if there was
19 a dispute among -- about the OPC criteria, you
20 know, I think that's one thing. I think that
21 in this situation, both the FDA and the
22 sponsor agreed upon the criteria. You know,

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1 there is no rule of law that says that you
2 have to choose a certain set of criteria.
3 That's up to the sponsor and the FDA, or even
4 to run a randomized control trial. And I
5 think that my -- I would hope that in the
6 future device companies would have -- use a
7 lot more scientific rigor and evidence to
8 prove safety and efficacy as opposed to coming
9 back and having this line moved around with a
10 lot of subjectivity.

11 CHAIRMAN MAISEL: Clyde?

12 DR. YANCY: My vote was yes because
13 ultimately we're here to serve patients and I
14 didn't see a very strong signal that this was
15 harmful or dangerous and I saw sufficient
16 evidence to suggest that it was likely
17 beneficial but no more beneficial than what's
18 there. I think on the aggregate the PMA is
19 not especially strong but I don't see any
20 reason to restrict good faith clinicians from
21 having access to a different technology to
22 attempt to help their patient population and I

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1 am sensitive to the issues of comfort and
2 freedom from distress. And I think those are
3 important constructs that we should respect.

4 I think the important issue here as
5 we go around the table goes back to the OPO.
6 There are only two ways that we can do these
7 device trials. We either have a concurrent
8 control population which you, the sponsors,
9 have convinced us is very difficult to do or
10 in its place, we use the criteria that we
11 struggled with today.

12 And if we make a call that this is
13 an unacceptable way of doing things and all of
14 us have to reconvene and start to re-evaluate
15 having prospective control groups, if we say
16 that this is the only way that we can acquire
17 sufficient data to move new technology
18 forward, then we have to respect the OPO and
19 OPC, you can tell I'm a transplant doc, and
20 find a better way to do this and make it
21 relevant.

22 I also am a little bit concerned

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1 that the clinical trial today was represented
2 differently than it was constructed. The
3 primary end point was clearly stated in the
4 trial but we requalified and redefined events
5 that effected the primary end point and I
6 think we have to be very careful with that
7 exercise and I would like to make the
8 strongest plea I can that you must uniquely
9 focus on the heart failure group.

10 My peers in the room that practice
11 electrophysiology are of the mind set that
12 they can do these invasive procedures in
13 patients with heart failure with relatively
14 little aggregate risk. My experience using
15 denominator patients with heart failure is
16 that they typically don't do very well when
17 they have RF ablation. I don't know how they
18 do with cryo ablation and I'm very concerned
19 that without some strong provisos focusing on
20 that patient population and without some
21 forward looking cryo HF experience, that we
22 stand the real risk of hurting a very

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1 vulnerable patient population.

2 So if the sponsor is responsible
3 and hears this argument, and accepts that
4 latitude we're giving them with this
5 permission, I would hope they would engage in
6 a good faith thought process and effort to
7 look specifically at heart failure patients.
8 I think that's very important.

9 CHAIRMAN MAISEL: Thank you. Clyde.
10 Adam?

11 DR. LOTTICK: Adam Lottick. I
12 voted yes. I'm very uncomfortable with
13 deviating from the previously agreed upon
14 OPCs. On the other hand, I think that the
15 basis for those OPCs was experience with
16 supraventricular arrhythmias that were
17 associated with different patient clinical
18 characteristics and were a fundamentally
19 different type of arrhythmia.

20 I think that we've also learned a
21 lot about what monitoring with event monitors
22 and other technologies that weren't available

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1 a few years ago means in terms of determining
2 recurrence rates of atrial arrhythmias. And
3 if I were determining the OPCs that we would
4 be using based on our current understanding of
5 flutter, I think that these criteria would be
6 met and, therefore, I voted yes.

7 CHAIRMAN MAISEL: Thank you.

8 David.

9 DR. SLOTWINER: Thanks. I won't
10 belabor the points too much. I think everybody
11 said what I was thinking but I voted yes
12 because I think it's a safe device and I think
13 it's effective and I think the OPCs are not
14 appropriate to compare this device to.

15 CHAIRMAN MAISEL: Sharon?

16 DR. NORMAND: I voted no. And I
17 voted no for several, I'll argue,
18 scientifically based reasons, not subjective
19 reasons. And those reasons related to the
20 fact that the safety end point was twice that
21 of the OPC. That's a fact. The second fact
22 is that the effectiveness end point didn't

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1 make it and more importantly, if we look at
2 numbers using the same type of data collection
3 instrument, it was 93 percent on an OUS study.

4 It was 87 percent in a study cited by one of
5 the study investigators, and it was only 81
6 percent in the current data that we have.
7 Those are numbers that are difficult to argue
8 with and I'm a little concerned -- let me
9 state it's my last time here so I guess I can
10 say whatever I want to say because I'm
11 leaving.

12 But I'm very concerned that
13 subjective opinion I feel, has caused a lot of
14 the votes today. And I'm very concerned about
15 that for patients. I think the public good is
16 at stake here. It's in terms of patients.
17 The data tell us that the safety is twice as
18 bad. The effectiveness end point wasn't met.

19 I can tinker with it in a thousand different
20 ways and come up with an answer I would like
21 to have if I was -- wanted that answer but
22 again, I have 25 years of experience in

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1 looking at scientific evidence for data and
2 clearly, the data do not support approval of
3 this device and, hence, my vote.

4 CHAIRMAN MAISEL: Dr. Milan.

5 DR. MILAN: I voted yes because in
6 the end I think the OPCs were -- the OPC for
7 effectiveness was probably too strict for
8 atrial flutter ablation and the best
9 comparator data for the alternative therapies
10 appear to be in the same range of efficacy for
11 this new proposed technology. I've already
12 stated my feelings about the safety which I
13 thought that the majority of the safety events
14 were not procedure or device related.

15 At the end of the day, I thought
16 both the safety and efficacy criteria were
17 met.

18 CHAIRMAN MAISEL: Linda, would you
19 like to comment?

20 MS. MOTTLE: I agree with Dr.
21 Normand. I am concerned. This was a PMA that
22 we're suppose to judge on its own merit. The

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1 wonderful expert opinion, diversity with your
2 OPC evaluations subjective, override of the
3 data. I am very glad that the committee has
4 put substantial conditions on the approval
5 vote, but it's of still concern.

6 Although as a consumer wanting to
7 have new novel devices available as treatment
8 options, particularly one that possibly has
9 indications for better safety with less pain.

10 But we have no data except for 14 patients on
11 that. So it's a little disconcerting that we
12 really didn't judge this PMA on its own
13 merits.

14 CHAIRMAN MAISEL: Marcia.

15 DR. YAROSS: I'd like to commend
16 the sponsor on what I thought was an excellent
17 presentation. I'd also like to commend the
18 panel because I think as we talked today, it
19 was clear that while studies can be designed
20 sometimes based on best guesses, many studies
21 don't turn out exactly as planned and that
22 there is a role for clinical judgment to be

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1 brought into the assessment of the study
2 outcomes. At the very beginning of the
3 meeting today, FDA talked about the fact that
4 the study did not meet the objective
5 performance criteria but that there were
6 important issues where clinical judgment could
7 be applied and I think that's what the panel
8 has done today. Thank you.

9 CHAIRMAN MAISEL: Thank you. I
10 would just like to add my comments that I
11 think one of the reasons that this device was
12 approved today was because of the superb job
13 that the sponsor did not only in their
14 presentations but in the conduct of their
15 clinical trial. While we had a lot of debate
16 over large number of safety issues, they were
17 only there because the DSMB cast a wide net
18 and gave us as much information as we could
19 have.

20 The follow-up data, although there
21 was some missing, to me seemed relatively
22 small and certainly smaller than other

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1 clinical trials that this panel has listened
2 to. So for me that was a major factor. I
3 think I can speak for myself that I had a lot
4 of confidence in the data that was presented
5 and I think you did a superb job.

6 I think we've debated a lot the
7 issues of the OPC. I think the clear message
8 from the panel is it needs further review and
9 discussion. I'm sure you'll take that under
10 advisement. I personally view those as a
11 dotted line in the sand and not a double
12 yellow line and I would like to think that
13 even if a device met the OPC but had some
14 issues that we would vote not approvable and
15 vice versa as in this case where it didn't
16 quite make the cut but at least a majority of
17 the panel feels that there is an important
18 clinical need for this device.

19 And it's been said by many people
20 on the panel that it's about the patients and
21 for me, as a practicing clinical
22 electrophysiologist, I'm glad that I might

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1 have this tool on the shelf to pull out in
2 certain cases. So, Dr. Zuckerman, do you have
3 what you need or do you want to address any
4 other issues today?

5 DR. ZUCKERMAN: No, this has been a
6 very helpful discussion and certainly, the FDA
7 has heard the panel's comments regarding very
8 careful considerations of clinical trial
9 design when dealing with electrophysiological
10 devices.

11 CHAIRMAN MAISEL: Thank you. Any
12 final comments from the sponsor?

13 DR. BAROLD: No, thank you.

14 CHAIRMAN MAISEL: Okay, at this
15 point, we will conclude this meeting of the
16 Circulatory System Devices Panel. We are
17 adjourned.

18 (Whereupon, at 4:32 p.m. the above-
19 entitled matter concluded.)

20

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