

1 being done, and then they'll come to your institution
2 for five times. I guess what is the learning curve,
3 and do they have any information on the learning curve
4 with doing this procedure?

5 DR. NOLLER: We'll ask them in a minute.

6 Yes.

7 DR. SOLOMON: This is amazing technology,
8 but it's very complicated, and very few people have
9 been trained in the physics of ultrasound, physics of
10 MRI, the interactions of tissue and the physiology.
11 It's very cutting edge, and I think the training,
12 especially for safety purposes, is absolutely critical
13 because there can be a lot of damage that's done. I
14 have no doubt that we're seeing very good safety
15 results in this continuing study that they are having
16 that there haven't been skin burns, for instance. And
17 that's terrific and it comes from experience of the
18 women and men who are performing the procedure. But
19 I think it's very important that there's a lot of
20 training, and that there's a lot of follow-up in
21 several cases in the beginning so that people are
22 prepared to do this appropriately and safely.

1 DR. NOLLER: Other comments? Yes.

2 DR. HAYES: I was going to say, we need to
3 include the training for the role of the nurse
4 specifically.

5 DR. NOLLER: Yes.

6 DR. HAYES: And also in follow-up to
7 someone else's comment, what was magical about the
8 number five times from the physician?

9 DR. NOLLER: Could we hear from the
10 sponsor about the learning curve? Do you have data to
11 support one session followed by up to five at a site,
12 and then being proficient in doing it?

13 DR. TEMPANY: I'd like to speak to that in
14 two parts, and I think if you talk about the training
15 that we have designed, and how we ourselves in the
16 trial --

17 DR. NOLLER: Please. We have read the
18 training, so don't repeat what we already have,
19 please, but new information we'd be happy to hear.

20 DR. TEMPANY: Well, you've asked about why
21 five, and I think five or ten treatments could be
22 observed at a treatment site, and then the simulations

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1 - one of the key things that I think is going to be
2 very helpful here is that we have the ability to play
3 the treatments that have already occurred, and show
4 those to trainees, to people who are going to be
5 learning how to do the procedure, so they can see
6 individual sonications and direct it, and how to
7 change or angle the tilt. So there's a lot that can
8 be learned ahead of time before you actually are
9 involved in doing primary treatment yourself through
10 either virtual or simulated learning techniques.
11 Those are things that I think that are tools that we
12 have at our disposal for many facilities. Certainly,
13 in the Boston area, we have a simulation center which
14 trains people on how to manage codes, for example, in
15 a radiology suite or an operating room. And we have
16 video playback of how you responded under pressure, so
17 we can obviously learn a lot from these simulation
18 tools. I think this particular device and the way
19 that it records everything that occurs lends itself
20 very nicely to that type of training.

21 Going back to our experience and how we
22 learned this procedure, and how the 600 patients

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1 across the world have been treated by different people
2 in different sites, I think there is a relatively fast
3 learning curve. Certainly, radiology imaging is an
4 important part at the beginning of it. It's not
5 necessary to learn all of the MR physics, nor is it
6 necessary to be proficient in ultrasound physics.
7 There are certain basic principles that can be taught
8 in the beginning. Interpretation of the images, all
9 of the imaging modalities that I have been involved in
10 in my career, I think MRI is one that's relatively
11 easy for people to learn, because if you know anatomy,
12 you know MR imaging. You can see things so incredibly
13 clearly. It's not like learning ultrasound, which I
14 still have struggles with. So from that perspective,
15 I think the learning curve is relatively quick, and
16 certainly the experience that we've had with the
17 safety problems, such as the skin burn or the nerve
18 are very easy to train and teach people about. And I
19 think with the mitigating factors that we put into
20 place, I think it will be relatively easy.

21 It might be useful to hear from another
22 radiologist who learned a lot from a prior experience

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1 and his use at the first site, as well, so I'd
2 introduce Dr. Hesley.

3 DR. NOLLER: Please limit it to answering
4 the question that was asked.

5 DR. HESLEY: Okay. I'm Gina Hesley. I'm
6 from the Department of Radiology at the Mayo Clinic.
7 My travel and accommodations are paid for by
8 InSightec, but I operate under the Mayo Clinic
9 Foundation guidelines and institutional review board
10 there.

11 Our site did join, after significant
12 experience was obtained by other institutions. We
13 benefitted significantly from the training. We had,
14 first of all, classroom training, followed by that we
15 went and actually did a mock setup with a phantom
16 where all of us, our technologist, a nurse, study
17 coordinators, radiologists, and the gynecologists were
18 invited, as well, to participate in the setup of a
19 patient and do phantom experiments. After that, the
20 company did come for a limited number of treatments to
21 help us in our learning curve of how these treatments
22 operate, some things that we might encounter.

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1 As far as skin burns, we never encountered
2 any skin burns. We joined a study after those kind of
3 features were identified, and so from the very
4 beginning we were shaving all our patients. We were
5 making sure that we cleaned them off with alcohol no
6 matter what the circumstances may be. As far as also
7 movement, we secure our patients down similar to what
8 Dr. Tempany does. And I would also say from our
9 experience with the nerve injury, we as well
10 benefitted from that. We joined later on. We already
11 knew some of the things to be aware of by that time.

12 DR. NOLLER: Okay. Thank you. Are we
13 ready for Question 9? This deals with post market
14 study. Under current FDA guidance patients from the
15 pivotal study are scheduled to be followed for a total
16 of three years after the procedure, one year pre-
17 market, and two years post market, and up to 250
18 patients to be enrolled in the continued access
19 setting are scheduled to be followed for a total of
20 three years after the procedure.

21 Two questions. Is there a need for
22 additional post approval studies or other post market

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1 measures? Number two - If so, what is the purpose of
2 such studies, and what are the key elements of the
3 study design? Discussion. Dr. Diamond.

4 DR. DIAMOND: I would think it would be
5 very important to gain additional knowledge about
6 whether the improvements that they have seen could be
7 increased by treating larger portions of the fibroids
8 or by more of the fibroids, so that hopefully patients
9 could get better and longer lasting benefit. And if
10 we go with what Dr. Spies told us earlier about having
11 to get complete infarction of the fibroid, with the
12 amount of treatment now it's probably not very likely
13 to happen in those situations, so I think that would
14 be a valuable study to conduct.

15 DR. NOLLER: Other comments. Dr. Brown.

16 DR. BROWN: I would just emphasize again
17 my point about the lack of diversity in your studies
18 that going forward I would like to see a post market
19 study that specifically recruited the population that
20 has a very high incidence of disease, and to make sure
21 that there are no unexpected findings in a population.
22 For example, maybe different or different ethnicities

1 have higher percentage of calcified fibroids or things
2 like that, so I think that should be a key component
3 of any post market study.

4 DR. NOLLER: Dr. Roberts.

5 DR. ROBERTS: Well, I think it's important
6 that the patients that have already been enrolled in
7 the study be followed, but I think we have to be
8 really careful about expanding what the sponsor has to
9 do in terms of enrolling new patients, and following
10 these patients for three years. Now that's an
11 enormous amount of work and expense, and quite
12 frankly, I'm not sure that it's appropriate to have
13 the sponsor do that. I think that that's a study that
14 needs to be done. I think there is going to be
15 presumably people out there that can make a good
16 career out of doing those kinds of studies, and I
17 would certainly encourage them to be done. But I
18 think we really do have to be careful about putting an
19 enormous burden on the sponsors. We're already asking
20 them to follow the patients that have been enrolled in
21 the pivotal study. They're already being asked to
22 follow the patients that are being enrolled in the

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1 continued access study for three years. I think
2 that's important. I think it needs to be done, but I
3 wouldn't agree with asking them to do a whole other
4 study on other patients.

5 DR. NOLLER: Dr. Brill.

6 DR. BRILL: Well, since this our time for
7 a wish list, this is also directed at the FDA itself.
8 One of the problems with these quality of life
9 instruments is that most of these things are surrogate
10 measurements, and there's no question that the symptom
11 severity score is mostly menstrual in nature, but
12 there are some pressure and physical phenomena
13 integrated into that score.

14 Why objectification and menstrual blood
15 loss was not included in the study, I don't know. But
16 surely we can add this to whatever is forthcoming.
17 It's going to objectify some of this information and
18 take it out of the realm of the discrepancies that
19 occur with quality of life instruments. And I would
20 highly suggest we consider that.

21 DR. NOLLER: Others?

22 DR. MILLER: I think at some point, and

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1 I'm not sure exactly where to do this, because this is
2 a uterine-sparing procedure, and because it's being
3 done in a reproductive age population, the issue of
4 potential pregnancy following the use of this
5 technology is going to come up, and there needs to be
6 some provision for how that's done. If it's done by
7 registry or some other way, but if this technology is
8 going to be successful, it's going to be considered as
9 an adjunct to enhanced fertility for those people who
10 have large fibroids and want to conserve their uterus.

11 DR. NOLLER: Yes.

12 DR. WEEKS: Jonathan Weeks. I'd like to
13 see some of the sponsor's data on uterine volumes.
14 You've got stored images on uterine volumes in
15 patients over time. Again because in many cases
16 you're selecting a fibroid to treat, or two of a
17 number of fibroids to treat, and I think there may be
18 a correlation between total uterine volume and how
19 well a patient does. If they've got several more
20 fibroids that couldn't be treated because of the 150
21 CC, let's say limitation, then those patients may be
22 more likely to fail in the other procedures down the

1 road.

2 DR. NOLLER: I guess we didn't ask any
3 specific questions there. So now what I would like to
4 ask the panel is, are there questions that you have
5 that have not been asked of the sponsor either before
6 lunch or as we went through the questions? Seeing
7 none, I will ask the sponsor to close.

8 DR. STEWART: Thank you very much, Mr.
9 Chairman. This is Elizabeth Stewart. I know it's
10 been a complicated technology to try to grasp all the
11 subtleties, and I appreciate everyone's perseverance.

12 I'd like to go back, first of all, and just look at
13 the efficacy data since there were questions raised
14 about dropouts. I think that Dr. Spies information
15 gave us much more context to put our primary efficacy
16 endpoint in, and did describe an endpoint.

17 In the letter it was raised that there as
18 loss to follow-up along the six month study. There
19 was actually no loss to follow-up. We had 109
20 patients, and we know exactly where each of them went
21 during the six month trial. And it seems like from
22 the discussion that the concern has not been with the

1 efficacy that was demonstrated at six months, but
2 instead the efficacy at 12 months. Can we go on to
3 the next slide.

4 It's a complicated slide and I know that
5 it's somewhat confusing. But again, we started with
6 109 patients. We had 91 who continued. There were 9
7 patients who we did contact and talk to, but declined
8 to come in for official 12 month follow-up. However,
9 if any of these patients had alternative treatments
10 they did end up here, so if they did report to us they
11 had a hysterectomy, a myomectomy, a uterine artery
12 embolization, that information was captured. So it
13 was really only 9 patients who we didn't have follow-
14 up on. The 9 patients that were non-evaluable, we did
15 again have information on, but may not have fallen
16 exactly on the window of evaluation.

17 And in fact, if we look at the patients
18 going to alternative therapies, I don't think we can
19 characterize this as falling apart. We did have 23
20 patients going on to alternative therapy out of 109,
21 but as the uterine artery embolization data suggests,
22 these are all women who very well could have gone on

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1 to hysterectomy, and so in essence, we've had around
2 75 to 80 percent of people who have not elected to go
3 on to therapy. And can you just go to the next slide.
4 No, one more, please.

5 Again, looking at the symptom severity
6 score, again we see that we start at a marked level of
7 symptomatology. We come down substantially, and I
8 think it's important to note at this 12 month time,
9 this represents 61 patients for whom we had actual
10 values, and all of the rest of the 109 had zeroes
11 added into it. So I think that this under-represents
12 the symptomatology or the symptom improvement that
13 we're seeing.

14 Three other questions I think that have
15 been directed regarding the clinical issues are
16 patient diversity, and we recognize that that is
17 important issue. In fact, in Boston we specifically
18 tried to recruit minority women through various
19 publications that cater to the minority community. I
20 think we were hampered in this effort by certain sites
21 that had no minority representation in their
22 demographic area, and I think that's an important part

1 for moving forward.

2 We have talked about the intended
3 practitioners tangentially, and I think that it is
4 important to recognize that there is a lot of input
5 that needs to go into this in terms of radiographic
6 decision making, gynecologic decision making. And
7 that's why we view this technology as a true
8 partnership. And that at this point in time of its
9 evolution, it absolutely requires a radiologist and
10 gynecologist to be working together.

11 I think what we see for the distant future
12 is that there will be specific individuals doing this
13 kind of therapy, just like every gynecologist on the
14 staff is not doing hysteroscopic surgery, and every
15 radiologist is not doing interventional procedures.
16 And we may move to a model very much like high risk
17 ultrasound where people can come through an MFM
18 background, or they can come through a radiology
19 background and meet the same needs.

20 I think your point about potential
21 pregnancy is very important. In fact, right now the
22 company is sponsoring a trial outside the U.S. to look

1 at women who want future fertility and following them,
2 and we have extensively discussed a registry for U.S.
3 cases when and if we get to that point.

4 I'd like to turn things over to Clare
5 Tempany at this point so she can address a couple of
6 the issues related to the more technical aspects of
7 the procedure.

8 DR. TEMPANY: Thank you. There were two
9 other sets of questions really relating both to bowel
10 gas and structures in the distal field. And I think
11 that a lot of the simulations and modeling have shown
12 you that the bowel gas issue really reflects the
13 ultrasound wave, that there's been no evidence of
14 damage to anybody, none of the patients have
15 experienced any problems or side effects related to
16 injury to bowel.

17 We have not done a bowel preparation,
18 which came up as well, which is a good question, for
19 several reasons. Simply, because there didn't appear
20 to be an indication that anybody was having bowel
21 symptomatology either during or after the procedure in
22 any way. And also, because if you give a bowel

1 preparation what happens unfortunately is you
2 stimulate extensive peristalsis and cause a lot of
3 motion. And so this, of course, will blur the thermal
4 imaging during the procedure. So we felt it probably
5 wasn't indicated clinically, and it would also detract
6 from our ability to monitor the therapy as it was
7 ongoing.

8 The other question I think was about the
9 far field, and the nerves and the bone, and I think
10 that we've answered that several times, and I hope
11 that that's been addressed completely. And if there
12 is anything else, please feel free to ask. But I do
13 want to say that only five out of 600 patients have
14 had problems there, and it's really less than 1
15 percent, so this is a relatively small number, and
16 certainly something we've learned extraordinarily
17 from. And I think that we have very good mitigating
18 ways to get around this problem.

19 Somebody else asked a question about
20 conscious sedation and would that be included in our
21 training. We feel that conscious sedation is part of
22 standard hospital staff privileging and for procedure-

1 based medicine, physicians are all required in my
2 hospital certainly, and many hospitals, they are
3 required to undergo conscious sedation training
4 directed by the Department of Anesthesiology. We
5 would hope that would continue to be part of it. The
6 sponsor doesn't feel that training in conscious
7 sedation would really be their expertise, and we would
8 request the hospitals in their staff privileging
9 processes would do that.

10 We would certainly include training with
11 a nurse and a physician during the treatment as we
12 talked about earlier about the communication and the
13 role of medication certainly in monitoring it. And I
14 think Dr. Wood's point about requiring it to be light
15 to ensure continued communication will certainly be
16 included in our training, so I hope those addressed
17 the remaining questions.

18 DR. STEWART: Elizabeth Stewart. Just to
19 sum up, I think that the risk benefit ratio of this
20 treatment is very favorable. I think there have been
21 concerns about the comparability of the groups to
22 assess safety, but I think the safety of the treatment

1 is clear. And I think it has provided an effective
2 means of therapy for many women who wouldn't choose
3 any other treatment modality, that the investigators
4 and the company are all committed to not only
5 continuing on with our experience, but improving and
6 learning. And in effect, we really have been carrying
7 on our post market study for the past year, and have
8 treated 89 patients to-date to try to optimize
9 treatment and extend benefit. And we look forward to
10 continuing to understand better how this treatment can
11 be optimized to give more benefit to more patients.

12 DR. NOLLER: Thank you. Does the FDA have
13 any closing statement? Okay, panel members, your
14 attention, please. Dr. Whang will now read us our
15 instructions.

16 DR. WHANG: We will now move to the
17 panel's recommendations concerning PMA P040003. The
18 medical devices amendments to the Federal Food, Drug,
19 and Cosmetic Act, the Act as amended by the Safe
20 Medical Devices Act of 1990, allows the Food and Drug
21 Administration to obtain a recommendation from an
22 expert advisory panel on designated medical device

1 pre-market approval applications, PMAs, that are filed
2 with the agency.

3 The PMA must stand on its own merits, and
4 your recommendation must be supported by safety and
5 effectiveness data in the application, or by
6 applicable publicly available information. Safety is
7 defined in the Act as reasonable assurance based on
8 valid scientific evidence that the probable benefits
9 to health outweigh any probable risk.

10 Effectiveness is defined as reasonable
11 assurance that in a significant portion of the
12 population the use of the device for its intended uses
13 and conditions of use will provide clinically
14 significant results.

15 The recommendation options for the vote
16 are as follows. Approvable, if there are no
17 conditions attached. Approvable with conditions, the
18 panel may recommend that the PMA be found approvable,
19 subject to specified conditions, such as physician or
20 patient education, labeling changes or further
21 analysis of existing data. Prior to voting, all of
22 the conditions should be discussed by the panel.

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1 Not approvable - the panel may recommend
2 that the PMA is not approvable if the data do not
3 provide a reasonable assurance that the device is
4 safe, or if a reasonable assurance has not been given,
5 that the device is effective under the conditions of
6 use prescribed, recommended, or suggested in the
7 proposed labeling. If the vote is for not approvable,
8 the panel should indicate what steps the sponsor may
9 take to make the device to approvable. You will find
10 a handout summarizing the voting procedure in the blue
11 folders and in the packets that were handed out this
12 morning at the table.

13 DR. NOLLER: All right. I would now like
14 to ask if anyone would like to make one of the three
15 possible motions, approve, approve with conditions or
16 not approved. Dr. Roberts.

17 DR. ROBERTS: I move approve with
18 conditions.

19 DR. NOLLER: Is there a second? There is
20 a second. Next we will then discuss conditions before
21 we vote on that motion. Anyone like to add a
22 condition? Dr. D'Agostino.

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1 DR. D'AGOSTINO: Can I ask a question?
2 This is accelerated approval or something like that.
3 Does that --

4 DR. NOLLER: I can't hear you.

5 DR. D'AGOSTINO: I'm sorry. This is an
6 accelerated approval?

7 MS. BROGDON: It's an expedited --

8 DR. NOLLER: It's expedited.

9 DR. D'AGOSTINO: It's an expedited
10 approval, so that just --

11 MS. BROGDON: It's an expedited review.

12 DR. D'AGOSTINO: Review. Okay.

13 MS. BROGDON: And that need not affect
14 your recommendations. It affects the timing of our
15 review and decision making.

16 DR. NOLLER: Anyone want to add a
17 condition? Dr. Roberts.

18 DR. ROBERTS: Well, I would just add the
19 conditions that I believe that we spoke about in terms
20 of the indications for use, and the --

21 DR. NOLLER: Please be a little more
22 specific.

1 DR. ROBERTS: I'll be specific. That the
2 indications for use contain information regarding the
3 study itself that was used for the approval, that it
4 contain the indications for the procedure, that it
5 contain the indications for use, contain the
6 parameters that were used in performing the procedure,
7 and include the contraindications. And specifically,
8 that it include the importance of minimizing the
9 possibility of nerve damage by indicating what the
10 mitigations should be to try and avoid that. And I
11 would further put in the conditions that the patient
12 information include the possibility of nerve damage
13 and that the patient information, which I assume the
14 FDA will do anyway, that the patient information be
15 written in such a way that it's understandable.
16 There's certain, I've forgotten now the terminology
17 that's used for creating ones with the appropriate
18 reading level, but that it be geared for anyone who
19 might be coming in to get th is procedure, that they
20 can understand it.

21 DR. NOLLER: Is there a second to that
22 condition?

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1 DR. ASCHER: Second.

2 DR. NOLLER: Second. Discussion of the
3 condition. Now let me reread what I have. The
4 indications for use include information concerning the
5 pivotal study, the indications for the procedure, the
6 parameters used for performing the procedure, the
7 contraindications for the procedure, the importance of
8 attention to the mitigating factors to decrease nerve
9 damage, and that the patient information include the
10 possibility of nerve damage, and be rewritten to the
11 FDA standard of educational level. Discussion of that
12 condition.

13 DR. BROWN: Can I add something to it, or
14 it has to be a totally separate motion? It relates to
15 --

16 DR. NOLLER: Well, let's discuss what you
17 would want to add.

18 DR. BROWN: The part about expanding the
19 segment on training, that I would also add that the
20 training --

21 DR. NOLLER: Well, why don't we add that
22 as a separate condition.

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1 DR. BROWN: Okay.

2 DR. NOLLER: Any other -- if not, then
3 we'll vote on that condition. Everybody understand
4 the condition? Okay. Everyone can vote yes, no, or
5 abstain. We'll start at this end of the table. Dr.
6 Wood, are you a voting member? I forget who votes and
7 who doesn't.

8 DR. WOOD: Yes, I am, and yes, the vote.

9 DR. NOLLER: Yes.

10 DR. ASCHER: Yes.

11 DR. NOLLER: Yes.

12 DR. MILLER: Abstain.

13 DR. NOLLER: Abstain.

14 DR. HAYES: Yes.

15 DR. NOLLER: Yes.

16 DR. SAMULSKI: Yes.

17 DR. NOLLER: Yes.

18 DR. JANIK: Abstain.

19 DR. NOLLER: Abstain.

20 DR. CRUM: Yes.

21 DR. NOLLER: Yes.

22 DR. BROWN: Yes.

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1 DR. NOLLER: Yes.

2 DR. NOLLER: I vote yes.

3 DR. WHANG: You don't vote.

4 DR. NOLLER: Oh, I don't vote. That's
5 right.

6 DR. ROBERTS: Yes.

7 DR. NOLLER: Yes.

8 DR. HILLARD: Yes.

9 DR. NOLLER: Yes.

10 DR. BRILL: Abstain.

11 DR. NOLLER: Abstain.

12 DR. D'AGOSTINO: Yes.

13 MR. WEEKS: Yes.

14 DR. NOLLER: That motion carries. Now
15 other conditions? Dr. Brown.

16 DR. BROWN: That the essential prescribing
17 information and labeling be modified that the training
18 segment of such labeling is expanded to indicate more
19 specifically the steps that are required in training,
20 including the classroom time, the phantom lab practice
21 to be attended by all personnel involved, and in the
22 subsequent on-site supervision provided by the

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1 company. That that paragraph just be expanded to
2 include all of those things.

3 DR. NOLLER: Is there a second to that
4 condition?

5 MEMBER: Second.

6 DR. NOLLER: Second. Discussion of that
7 condition. Hearing no discussion, we'll vote on that.
8 Dr. Wood.

9 DR. WOOD: Yes.

10 DR. NOLLER: Yes.

11 DR. ASCHER: Yes.

12 DR. NOLLER: Yes.

13 DR. MILLER: Abstain.

14 DR. NOLLER: Abstain.

15 DR. HAYES: Yes.

16 DR. NOLLER: Yes.

17 DR. SAMULSKI: Yes.

18 DR. NOLLER: Yes.

19 DR. JANIK: Abstain.

20 DR. NOLLER: Abstain.

21 DR. CRUM: Yes.

22 DR. NOLLER: Yes.

1 DR. BROWN: Yes.

2 DR. NOLLER: Yes.

3 DR. ROBERTS: Yes.

4 DR. HILLARD: Yes.

5 DR. BRILL: Abstain.

6 DR. D'AGOSTINO: Yes.

7 MR. WEEKS: Yes.

8 DR. NOLLER: That motion also passes. Are
9 there other conditions? Dr. Diamond.

10 DR. DIAMOND: I would like the group to
11 discuss whether or not there ought to be a need to
12 conduct a small randomized --

13 DR. NOLLER: I'm sorry, we really only
14 discussion motions, so if you'd like to make a motion.

15 DR. DIAMOND: Well, I can't make a motion.
16 That's why I was planning something for discussion.

17 DR. NOLLER: You can't make a motion.

18 DR. JANIK: I can make a motion, can't I?
19 Yes. I would like to make a motion that we add a
20 small line to my study to look at efficacy between
21 either the sham study or UAE.

22 DR. NOLLER: Do I hear a second?

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1 MEMBER: Second.

2 DR. NOLLER: Second. Now we can discuss
3 it, and Dr. Diamond can discuss.

4 DR. DIAMOND: I think I probably have made
5 my point fairly well before as to why I think it would
6 be necessary. I think actually, though, it would also
7 be beneficial to the company to have objective data
8 where they could show to practitioners who will have
9 patients come in to see them, and have hard data to be
10 able to show this would be a benefit to the patients
11 where they have a control group, who end up I would
12 expect with high degree or failures in a very short
13 period of time. So I think actually it would be to
14 their benefit to conduct such a study.

15 DR. WHANG: I'd like to make the point
16 that you cannot -- I don't know if you mean the pre-
17 market or post market study. You cannot require a
18 pre-market study as part of a condition of approval.
19 If you think additional pre-market studies are
20 required, then you would have to consider recommend
21 not approvable, and list this as a reason for not
22 approvable.

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1 DR. BROWN: Question. But you can
2 recommend it as a post market study.

3 DR. NOLLER: I have a problem with the
4 word "small". I don't know what that means.

5 DR. JANIK: Well, because if it is
6 randomized your end number for statistical
7 significance will inherently be small, so it won't
8 have to be large.

9 DR. NOLLER: It depends on the --

10 DR. DIAMOND: But if it's not adequately
11 pallid, it would just leave us in a quandary.

12 DR. NOLLER: Dr. Roberts.

13 DR. ROBERTS: I would speak very strongly
14 against this. I think that we've been presented with
15 a study. We have to decide either it's a good enough
16 study that we vote approval or it's not. And if it's
17 not, it's not. And if it is, then it is. But to tell
18 the sponsors that well, gee, we really like your
19 study, and we think that we're going to approve it,
20 but we really want you to do something else I think is
21 wrong, and I think we can't do that. I just don't
22 think that's the right thing to do.

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1 I think that we can encourage the
2 investigators, we can encourage the company to think
3 about the fact that they would be much better in terms
4 of their marketing or selling this thing or whatever,
5 that they go ahead and this would be a great study to
6 do as some kind of a randomized study with something
7 else. But I think in terms of saying that this is
8 either approved or not approved, we can't -- I would
9 speak very, very strongly against this. I don't think
10 it's the right thing to do.

11 DR. NOLLER: Ms. Mooney.

12 MS. MOONEY: I just would like to agree
13 with Dr. Roberts in terms of the distinction here, and
14 again remind the panel of Dr. Whang's comments in
15 terms of the definitions. The threshold here for
16 safety and efficacy is reasonable assurance. And I
17 think clearly there's a lot to be learned and gained
18 by additional studies, but in terms of the
19 approvability of this application, I think it's
20 important to stay focused on the reasonable assurance.
21 And I think again we've debated the merits and
22 limitations of the control that was used, but in terms

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1 of the company demonstrating that its met its
2 endpoints, I think that's been clear with a fair
3 margin, so I think it is important, as Dr. Roberts is
4 pointing out, to make a clear distinction.

5 DR. NOLLER: Dr. Janik.

6 DR. JANIK: I think that a number of us
7 are concerned about the endpoints, if they were agreed
8 upon with the FDA, but I think there are a number of
9 us that have insecurities if efficacy is truly
10 demonstrated here, that I think we need more
11 information to really confidently say that is the crux
12 of the problem.

13 DR. NOLLER: Dr. Wood.

14 DR. WOOD: I was just going to say that
15 scientifically a sham study makes great sense, and it
16 would be great to see. But ethically, I'm not sure,
17 and to put it passed five IRBs, conservative ones may
18 not approve it given the data available. And I, for
19 one, would probably not feel comfortable going to a
20 patient and saying you may or may not be treated,
21 although if you are treated it might help you, albeit
22 short-term efficacy.

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1 DR. NOLLER: Dr. Brown.

2 DR. BROWN: I would just say I think the
3 problem is not with the safety, but with the efficacy
4 and depending on how this vote goes, if this is voted
5 not to do the study, I am going to make another
6 condition about what's specified about the endpoints
7 in the information because I think that that's -- if
8 you're not going to do something else, I think it has
9 to be very clear to the people reading this booklet
10 what the endpoint was, and exactly what it was, and
11 not lead them to think something else. Specifically,
12 I think all the comparisons to hysterectomy then need
13 to come out. You need to just say it shows this 10
14 point change, period.

15 DR. NOLLER: Dr. Brill.

16 DR. BRILL: Just to accelerate things.
17 Grace, are you suggesting a pre or a post market
18 study?

19 DR. JANIK: I would suggest pre-market.

20 DR. BRILL: So it's not really germane to
21 where we are right now in the motion, because we're
22 here with conditions, so I think it's going to have to

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1 follow our discussion.

2 DR. MILLER: As a point of order, just for
3 clarification for myself, can we be at a point in
4 discussing conditions if we haven't decided approval
5 or disapproval?

6 DR. NOLLER: Yes.

7 DR. MILLER: WE can be? Okay.

8 DR. NOLLER: Yes, that's what we do.

9 DR. BROWN: But just a point of
10 clarification, so you're talking about a pre-market
11 study, then you have to wait and vote down the
12 approval with conditions, and then --

13 DR. NOLLER: Right. I was just going to
14 make that point.

15 DR. MILLER: That's my point.

16 DR. NOLLER: Ms. Mooney, you were next.

17 MS. MOONEY: Yes. Just again to emphasize
18 Dr. Brown's point. There is a lot of latitude the
19 panel has in terms if adding wording to the
20 instructions for use, the training. They can clearly
21 spell out what data were generated in this trial, and
22 what data were left unanswered for subsequent study.

1 So again I think the key is the reasonable assurance
2 in that threshold in terms of deciding whether
3 something should be pre or post market.

4 DR. NOLLER: Dr. Diamond.

5 DR. DIAMOND: I was just going to say, in
6 as much as what is now being discussed is approval
7 with conditions, Dr. Janik may want to think about
8 suggesting the study at this point as a post marketing
9 study, although it sounds like her ultimate goal and
10 her ultimate desire might be to have as a pre-approval
11 study.

12 DR. JANIK: That would be my primary goal,
13 though I would take it as a secondary.

14 DR. NOLLER: I understood your motion to
15 be for a post market study. Is that correct? Was
16 that your motion?

17 DR. JANIK: My motion would be for a pre-
18 market study, so that can't be --

19 DR. NOLLER: We can't consider that here
20 then. So we will no longer discuss that condition.
21 Any other conditions? Yes.

22 MR. WEEKS: Yes, Jonathan Weeks. Again,

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1 I think the sponsor should evaluate their data on
2 uterine volumes, and to be sure that there's no strong
3 correlation between larger uteri and failed therapy;
4 specifically going in to get hysterectomies or second
5 procedures.

6 DR. NOLLER: Is there a second?

7 DR. BROWN: What was the motion? I'm
8 sorry.

9 DR. NOLLER: The motion is for the sponsor
10 to evaluate the current data on uterine volume.

11 DR. BROWN: And that would be reviewed --

12 DR. NOLLER: And relate it to success or
13 failure of the procedure.

14 DR. BROWN: And that would have to be
15 reviewed by the FDA and put in this --

16 DR. NOLLER: Do we have a second?

17 DR. BROWN: I'll second it.

18 DR. NOLLER: Okay.

19 DR. BROWN: So my question would be then
20 that information would be provided by the sponsor to
21 the FDA, and that would ostensibly be included in this
22 packet.

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1 DR. NOLLER: Is that what your motion was?

2 MR. WEEKS: Yes.

3 DR. NOLLER: Okay. Discussion of that
4 motion. If not, we'll vote. Dr. Wood.

5 DR. WOOD: Yes.

6 DR. ASCHER: Abstain.

7 DR. NOLLER: Abstain.

8 DR. MILLER: Abstain.

9 DR. NOLLER: Abstain.

10 DR. HAYES: Yes.

11 DR. NOLLER: Yes.

12 DR. SAMULSKI: Yes.

13 DR. NOLLER: Yes.

14 DR. JANIK: Abstain.

15 DR. NOLLER: Abstain.

16 DR. CRUM: Yes.

17 DR. NOLLER: Yes.

18 DR. BROWN: Yes.

19 DR. NOLLER: Yes.

20 DR. ROBERTS: No.

21 DR. NOLLER: No.

22 DR. HILLARD: Yes.

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1 DR. NOLLER: Yes.

2 DR. BRILL: Abstain.

3 DR. D'AGOSTINO: No.

4 MR. WEEKS: Yes.

5 DR. NOLLER: We have to count this one.

6 Motion carries. Are there other conditions?

7 DR. D'AGOSTINO: What was the count on the
8 vote?

9 DR. NOLLER: Seven yes, two nos, four
10 abstain. Other conditions?

11 DR. MILLER: I would move that the company
12 provide some strategy for handling future pregnancies
13 beyond this procedure in the event that this
14 technology is approved. That there be either a
15 registry or some other strategy that they can work out
16 with the FDA to capture that information, because
17 there will be pregnancies following the use of this
18 technology.

19 DR. NOLLER: Is there a second to the
20 motion?

21 MEMBER: Second.

22 DR. NOLLER: Second. Discussion?

1 DR. ROBERTS: Are you saying that the
2 company has to follow every single patient that comes
3 into the study with the idea that at some point they
4 might become pregnant, and that somehow they're going
5 to recognize that?

6 DR. MILLER: I'm saying that there are
7 many pharmaceutical companies who release medications
8 knowing that they may not be safe in pregnancy, but
9 establish mechanisms for following those patients, so
10 that information can be understood over time.

11 DR. ROBERTS: But I don't --

12 DR. NOLLER: There are various ways to do
13 that, and probably the simplest is just to create a
14 registry with a telephone number that you call if you
15 have a patient that becomes pregnant with this. It's
16 not a great way to do it, but it's a way to do it.
17 Ms. Mooney.

18 MS. MOONEY: Another option that sponsors
19 will sometimes be asked to do is put something
20 explicit in the labeling that says the effects are
21 unknown or have not been studied, so that's another
22 option to consider.

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1 DR. NOLLER: Will the FDA do that
2 automatically? Yes. Okay.

3 MS. BROGDON: Yes.

4 DR. NOLLER: Yes.

5 DR. BROWN: We already heard the sponsor
6 say they expressed a strong interest in creating a
7 registry, so I move for specifically saying they
8 should create a registry with an 800 number, and that
9 be part of the labeling package.

10 DR. NOLLER: That would restrict them to
11 one way. The notion is that they would work out some
12 way, a registry would be one possibility. Clearly,
13 you wanted it a little more open-ended than registry.
14 Is that correct?

15 DR. MILLER: Correct. I'm open to some
16 mechanism.

17 DR. NOLLER: Further discussion? Let's
18 vote.

19 MS. MOONEY: I'm sorry. Can I just ask,
20 you said the FDA would do that anyway?

21 DR. NOLLER: No, they would add the
22 precaution don't do this in a pregnant woman.

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1 MS. MOONEY: Oh, okay.

2 DR. NOLLER: Are we ready to vote? Dr.

3 Wood.

4 DR. WOOD: Abstain.

5 DR. NOLLER: Abstain.

6 DR. MILLER: Approve.

7 DR. NOLLER: Approve.

8 DR. HAYES: Yes.

9 DR. NOLLER: Yes. Dr. Samulski.

10 DR. SAMULSKI: Yes.

11 DR. NOLLER: Yes.

12 DR. JANIK: Yes.

13 DR. NOLLER: Yes.

14 DR. CRUM: Yes.

15 DR. NOLLER: Yes.

16 DR. BROWN: Yes.

17 DR. NOLLER: Yes.

18 DR. ROBERTS: No.

19 DR. NOLLER: No.

20 DR. HILLARD: No.

21 DR. NOLLER: No.

22 DR. BRILL: Abstain.

1 DR. NOLLER: Abstain.

2 DR. D'AGOSTINO: No.

3 DR. NOLLER: No.

4 MR. WEEKS: Yes.

5 DR. NOLLER: Yes. The motion passes; 7
6 yes, 3 nays, 3 abstain. Are there other conditions?
7 Hearing none --

8 DR. BROWN: Wait. I'm sorry. I think I
9 need to make a motion that within the description
10 about the results of the pivotal study, that it just
11 be made clear what the primary endpoint was, the 10
12 point range on the scale. And to make sure to give
13 the appropriate references. There may be there's more
14 up-to-date references that we were given today that
15 could be included here to look at validating the
16 questionnaire that the clinician could turn to, that
17 that reference that we heard about in the public
18 testimony also be included here. And if the other one
19 gets published before this gets done, that one would
20 be included also that talks about the validation of
21 this questionnaire.

22 DR. NOLLER: Is there a second?

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1 MR. WEEKS: Second.

2 DR. NOLLER: Second. I understand this
3 condition to be that in the patient information?

4 DR. BROWN: No, the prescribing
5 information.

6 DR. NOLLER: The prescribing information
7 there be a description of the results of the pivotal
8 study, particularly the endpoints, and the appropriate
9 references. Is that correct?

10 DR. BROWN: Right, but they update,
11 because there are now some new references that aren't
12 currently in here.

13 DR. NOLLER: Discussion? If not, we'll
14 vote. Dr. Wood.

15 DR. WOOD: Yes.

16 DR. NOLLER: Yes.

17 DR. ASCHER: Yes.

18 DR. NOLLER: Yes.

19 DR. MILLER: Abstain.

20 DR. HAYES: Yes.

21 DR. NOLLER: Yes.

22 DR. SAMULSKI: Yes.

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1 DR. NOLLER: Yes.

2 DR. JANIK: Abstain.

3 DR. NOLLER: Abstain.

4 DR. CRUM: Yes.

5 DR. NOLLER: Yes.

6 DR. BROWN: Yes.

7 DR. NOLLER: Yes.

8 DR. ROBERTS: Yes.

9 DR. NOLLER: Yes.

10 DR. HILLARD: Yes.

11 DR. NOLLER: Yes.

12 DR. BRILL: Abstain.

13 DR. NOLLER: Abstain.

14 DR. D'AGOSTINO: Yes.

15 DR. NOLLER: Yes.

16 MR. WEEKS: Yes.

17 DR. NOLLER: Yes. The motion carries.

18 DR. WOOD: Could I add a motion for --

19 DR. NOLLER: Five conditions. You have --

20 what?

21 DR. WOOD: Can I add a motion?

22 DR. NOLLER: Another condition? Yes.

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1 DR. WOOD: Yes, another condition. The
2 prescribed information include more information on
3 scaring. It just says does not have extensive
4 scaring, just that no information has been obtained on
5 previous C-sections.

6 DR. NOLLER: I'm sorry. I can't hear you.

7 DR. WOOD: Something about there not being
8 any data on the history of C-sections prior to use.

9 DR. NOLLER: So the information,
10 prescribing information include more data on scars and
11 specifically data on -- mentioning that there are no
12 data on Caesarean sections.

13 DR. WOOD: That's easily accessible. It's
14 available in the database and looking through charts.
15 In the pivotal studies we looked back and see how many
16 had C-sections, so they can determine whether those
17 patients had scars that potentially unfocus the beam.

18 DR. NOLLER: So to include the statement
19 either that there is no information on C-section
20 scars, or to present the actual data.

21 DR. WOOD: Yes.

22 DR. NOLLER: Is there a second? Second?

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1 Discussion? Let's vote. Dr. Wood.
2 DR. WOOD: Yes.
3 DR. NOLLER: Yes.
4 DR. ASCHER: Yes.
5 DR. NOLLER: Yes.
6 DR. MILLER: Abstain.
7 DR. NOLLER: Abstain.
8 DR. HAYES: Yes.
9 DR. NOLLER: Yes.
10 DR. SAMULSKI: Yes.
11 DR. NOLLER: Yes.
12 DR. JANIK: Abstain.
13 DR. NOLLER: Abstain.
14 DR. CRUM: Yes.
15 DR. NOLLER: Yes.
16 DR. BROWN: Yes.
17 DR. NOLLER: Yes.
18 DR. ROBERTS: Yes.
19 DR. NOLLER: Yes.
20 DR. HILLARD: Yes.
21 DR. NOLLER: Yes.
22 DR. BRILL: Abstain.

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1 DR. NOLLER: Abstain.

2 DR. D'AGOSTINO: No.

3 DR. NOLLER: No.

4 MR. WEEKS: Yes.

5 DR. NOLLER: Yes. The motion carries.

6 Are there other conditions? Yes.

7 DR. JANIK: I think I'm going to go back
8 and put it in again, just let me go through. I'd like
9 to make a motion to put a post market randomized study
10 between this technique and a sham, or uterine RA
11 embolization, sponsor's choice.

12 DR. NOLLER: Sufficiently powered.

13 DR. JANIK: Sufficiently powered, with one
14 year follow-up.

15 DR. NOLLER: Is there a second?

16 DR. BROWN: Second.

17 DR. NOLLER: Second. Is there a
18 discussion? Dr. Roberts.

19 DR. ROBERTS: I don't know. I guess I
20 feel like the only one that sort of looks at what it
21 costs to bring one of these products to market. And
22 quite frankly, I mean I've seen this happen in other

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1 panels where basically people spend enormous amounts
2 of dollars, millions of dollars to bring something to
3 market that they present the data on the study. Our
4 job is to look at that data and to decide whether or
5 not they've done an appropriate job. And if they
6 haven't done an appropriate job, then I think it's --
7 I have no problem with voting it down and saying go
8 back and do another study, and come back and see us
9 again sometime. But I think to say well, we're going
10 to approve it, but we really want you to do another
11 study - quite frankly, I don't think it's fair to the
12 sponsor.

13 I think if in the community there's a
14 feeling that this is not really a good technology, and
15 we don't have the data for it, don't refer your
16 patients to get it. That's one way that the market
17 will speak. I just think it's the wrong thing to do,
18 and I think it really puts a burden on the sponsors to
19 -- they work out a deal with the FDA in terms of
20 deciding ahead of time what their study is going to
21 be, and they carry it out. And then to come back and
22 say well, you know, we kind of like it, and it's

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1 pretty good, but we really want you to do something
2 else - I just think is wrong.

3 DR. NOLLER: I'm going to read the FDA
4 guidance before any further discussion. This guidance
5 says that post approval studies may provide additional
6 information about an approved device. However, the
7 safety and effectiveness must be demonstrated before
8 approval. The results of a post approval study should
9 not be expected to change the approval status of the
10 device. Dr. Brill.

11 DR. BRILL: I think those guidelines speak
12 for themselves, so there's no further reason to
13 discuss this. If we mistrust the data, then we should
14 disapprove and move forward.

15 In addition to that, if we do either pre
16 or post market study, I think it's misnomerous for us
17 to compare it to uterine artery embolization. And
18 where you're talking about total myoma treatment, and
19 a change in menstruation from probably some change in
20 the endometrium itself, the selective myoma treatment,
21 so I think we need to intellectually separate these
22 procedures, and not in any way consider them

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1 equivalent.

2 DR. NOLLER: Additional discussion? Let's
3 vote. This vote, if you vote aye, it is for a post
4 market randomized study. If you vote nay, it's the
5 condition is not approved. Dr. Wood.

6 DR. WOOD: No.

7 DR. NOLLER: No.

8 DR. ASCHER: No.

9 DR. NOLLER: No.

10 DR. MILLER: No.

11 DR. NOLLER: No.

12 DR. HAYES: No.

13 DR. NOLLER: No.

14 DR. SAMULSKI: No.

15 DR. NOLLER: No.

16 DR. JANIK: Yes.

17 DR. CRUM: No.

18 DR. NOLLER: No.

19 DR. BROWN: No.

20 DR. NOLLER: No.

21 DR. ROBERTS: No.

22 DR. NOLLER: No.

1 DR. HILLARD: No.

2 DR. NOLLER: No.

3 DR. BRILL: No.

4 DR. NOLLER: No.

5 DR. D'AGOSTINO: No.

6 DR. NOLLER: No.

7 MR. WEEKS: No.

8 DR. NOLLER: No. Condition number 7 is
9 defeated. Are there additional conditions?

10 DR. BROWN: One more.

11 DR. ROBERTS: I move approval.

12 DR. NOLLER: More conditions. Dr. Brown,
13 and then Dr. Wood.

14 DR. BROWN: Also, I think under a separate
15 heading other than training, there should be a bullet
16 about who would be doing the procedure, and this blurb
17 about describing this joint multi-disciplinary
18 partnership between radiologists and gynecologists,
19 and that should be in the central prescribing
20 information and all of that labeling information, so
21 that that comes across very clearly that it requires
22 that, so that you do not have -- they have the

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1 appropriate people working together.

2 DR. NOLLER: Is there a second? Hearing
3 no second. Dr. Wood. Did you have another condition?

4 DR. WOOD: Okay. Yes. It would be nice
5 to have in the prescribing section --

6 DR. NOLLER: I can't hear you. I'm sorry.

7 DR. WOOD: It would be nice to have in the
8 prescribing section a sentence on deep sedation or
9 lack of continuous patient feedback could increase
10 risk for nerve injury.

11 DR. NOLLER: Is there a second. Second.
12 Discussion? The condition is that the prescribing
13 information include the statement that deep sedation
14 or general anesthesia may increase the risk to the
15 patient. Did I get it right?

16 DR. WOOD: Lack of feedback for whatever
17 reason.

18 DR. DIAMOND: I would think that would
19 have to be worded that we don't know whether deep
20 sedation would cause that, because I don't know that
21 we were presented any data to demonstrate that.

22 DR. WOOD: Well, we've been presented with

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1 data that the patients -- we've been presented with
2 the suggestion that patients who feel this electrical
3 twinge and the sonication is stopped, and the latest
4 50 or so cohort have had less risk of -- less severe
5 nerve damage, so that would imply that this is true.

6 DR. NOLLER: Ms. Mooney.

7 MS. MOONEY: Perhaps it could be worded to
8 reflect what we heard from the clinicians in terms of
9 make sure you maintain continuous and adequate
10 feedback with the patient.

11 DR. WOOD: Sounds good.

12 DR. NOLLER: Do you accept that?

13 DR. WOOD: Yes.

14 DR. NOLLER: Okay. Any other discussion?

15 For that condition, Dr. Wood.

16 DR. WOOD: Yes.

17 DR. NOLLER: Yes.

18 DR. ASCHER: Yes.

19 DR. NOLLER: Yes.

20 DR. MILLER: Yes.

21 DR. NOLLER: Yes.

22 DR. HAYES: Yes.

1 DR. NOLLER: Yes.

2 DR. SAMULSKI: Yes.

3 DR. NOLLER: Yes.

4 DR. JANIK: Yes.

5 DR. NOLLER: Yes.

6 DR. CRUM: Yes.

7 DR. NOLLER: Yes.

8 DR. BROWN: Yes.

9 DR. NOLLER: Yes.

10 DR. ROBERTS: Yes.

11 DR. NOLLER: Yes.

12 DR. HILLARD: Yes.

13 DR. NOLLER: Yes.

14 DR. BRILL: Yes.

15 DR. NOLLER: Yes.

16 DR. D'AGOSTINO: Yes.

17 DR. NOLLER: Yes.

18 MR. WEEKS: Yes.

19 DR. NOLLER: Yes. It passes. Finally, a
20 unanimous one.

21 DR. WOOD: Point for discussion. Is there
22 -- can we discuss now? No, only motions.

1 DR. NOLLER: We can only discuss motions
2 at this point.

3 DR. WOOD: Motion for discussion. No,
4 motion that we consider the statement the mechanism of
5 effect is not entirely understood or something softer
6 than that, if anyone has any suggestions, when we're
7 discussing the pivotal trial and the quality of life
8 improvement.

9 DR. NOLLER: Could you -- I don't quite
10 understand that.

11 DR. WOOD: Just something to reflect the
12 fact that we don't know exactly why these patients
13 have the effect, have the quality of life improvement
14 that they have. And I'm not sure it belongs in the
15 prescribing section. And I guess this is more of a
16 discussion point than a motion.

17 DR. NOLLER: Perhaps by raising it, the
18 point has been made.

19 DR. WOOD: Yes.

20 DR. NOLLER: And you can withdraw it.

21 DR. WOOD: Sure.

22 DR. NOLLER: Okay. Other conditions?

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1 Hearing none, we will now vote on approval with the
2 seven conditions we approved. And we can now discuss
3 that motion before we vote. Motion to approve with
4 conditions, and it's the seven that we just voted on.
5 No discussion. Let's vote. If this passes, then
6 we're finished for the day. If not -- well, almost.
7 If not, then we consider possible other motions. Dr.
8 Wood.

9 MS. MOONEY: Dr. Noller, I think one of
10 your voting members stepped out. I don't know if you
11 --

12 DR. NOLLER: Okay. Let's start. We'll go
13 real slow. Dr. Wood.

14 DR. WOOD: Yes.

15 DR. NOLLER: Yes.

16 DR. ASCHER: Yes.

17 DR. NOLLER: Yes.

18 DR. MILLER: No.

19 DR. NOLLER: No.

20 DR. HAYES: Yes.

21 DR. NOLLER: Yes.

22 DR. SAMULSKI: Yes.

1 DR. NOLLER: Yes.

2 DR. JANIK: No.

3 DR. NOLLER: No.

4 DR. CRUM: Yes.

5 DR. NOLLER: Yes.

6 DR. BROWN: Yes.

7 DR. NOLLER: Yes.

8 DR. ROBERTS: Yes.

9 DR. NOLLER: Yes.

10 DR. HILLARD: No.

11 DR. NOLLER: No.

12 DR. BRILL: No.

13 DR. NOLLER: No.

14 DR. D'AGOSTINO: No.

15 DR. NOLLER: No. We have one more vote to

16 come. And, Dr. Weeks, we're voting on the motion to

17 approve with conditions or not. And we're around to

18 you.

19 MR. WEEKS: Yes.

20 DR. NOLLER: Yes. The motion passes 8

21 ayes, 5 nays, no abstentions. The final piece of work

22 I believe now is that we need to go around the table

1 and everyone is to state how they made their decision
2 to vote yes or no, and we will include the non-voting
3 members, the consumer representative, and the industry
4 representative. Dr. Wood. I'm not really picking o
5 you by starting with you.

6 DR. WOOD: This can be short, I assume.

7 DR. NOLLER: This should be very short.

8 DR. WOOD: Yes. I think they've shown
9 enough short-term efficacy and the safety issues have
10 been addressed adequately with the mitigating
11 circumstances.

12 DR. ASCHER: I would concur that they put
13 out their hypothesis, and they proved both safety and
14 efficacy for the limited scope that they were looking
15 for.

16 DR. MILLER: I wasn't convinced that
17 effectiveness was demonstrated. I had less problem
18 with safety, and a problem for the mitigating factors,
19 but I wasn't convinced by the efficacy work.

20 DR. HAYES: I voted yes because the safety
21 and efficacy, and also with the conditions it's going
22 to contain.

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1 DR. NOLLER: Dr. Samulski.

2 DR. SAMULSKI: The pivotal data wasn't
3 strong enough. The pivotal data, I think, wasn't
4 strong enough.

5 DR. NOLLER: The pivotal data wasn't
6 strong enough.

7 DR. JANIK: I voted no. I have concerns
8 of efficacy. I think safety is adequate. And the
9 concerns are that its only a very short-term that's
10 been demonstrated. In fibroids it needs to be at
11 least a year to warrant the risk.

12 DR. CRUM: I think it's safe. I think
13 it's efficacious, and I think that with the
14 restrictions that the FDA has placed, that only a
15 small percentage of the fibroid can be treated, and
16 yet patients have a satisfaction level after one year
17 of 72 percent speaks very strongly in favor of this
18 technology. And this gives the patient a choice, and
19 I think that's what -- that's the desirable thing of
20 this technology.

21 DR. BROWN: I voted yes. I didn't think
22 there was any question about the safety. I think my

1 efficacy concerns were answered by limiting that the
2 efficacy was proving their really first hypothesis
3 about the 10 point difference.

4 DR. NOLLER: Dr. Roberts.

5 DR. ROBERTS: I think that they satisfied
6 their endpoints. I think particularly given the fact
7 that they were limited in terms of the amount that
8 could be treated and still met those endpoints
9 probably speaks fairly strongly to the technology.

10 DR. DIAMOND: I think the technology
11 itself is very exciting, and I think it has lots of
12 potential for the future. I think the company has
13 done a great job in working through many of the safety
14 issues. I remain concerned about efficacy, and
15 whether or not the benefit that they saw in the
16 primary endpoint could be placebo effect, as it has
17 been in other trials which have looked at pain in
18 women for the length of follow-up that have been shown
19 here.

20 DR. HILLARD: I remain unconvinced about
21 the efficacy and the quality of life change of 10
22 points. I think my concerns about safety have been

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1 answered and addressed.

2 DR. BRILL: Well, I believe the device is
3 safe. I'm somewhat saddened by the design of the
4 study which I think probably is feedback to the FDA,
5 as well as to the sponsor, for the efficacy suffered
6 for lack of a control group. I don't think there's
7 any question about that.

8 I'm not convinced that this particular
9 instrument has been validated. And despite the fact
10 that it's the best thing we have to use, we truly
11 haven't used it that much to say in fact these
12 surrogate measures equal change necessarily.

13 I have concerns about the fact that
14 there's no algorithm as far as how fibroids are
15 treated, and it is somewhat random, and define in
16 inspiration by nature. And to reflect what Dr. Spies
17 said in his presentation, that at least the efficacy
18 of uterine artery embolization seems to be dependent
19 upon the ability to completely treat the myoma.

20 In this case, it's been presented to us
21 that, in fact, this is only partial treatment. And if
22 we go with that logic then, in fact, we should have

1 sub-optimal treatment.

2 DR. D'AGOSTINO: I'm unconvinced by the
3 efficacy data. It's a composite score. I really
4 don't know what's driving it, and I'm very concerned
5 also about the 12 month data. And it wasn't 70
6 percent, it's only 40 percent. It didn't make the
7 anticipated 50 percent that they were looking for,
8 over 50 percent having a better than 10 point change,
9 so I think the efficacy data is very problematic. The
10 safety data looks all right.

11 DR. SOLOMON: I'd like to commend the
12 company for what's really an incredible engineering
13 feat that's taken many, many years to accomplish. The
14 complexity in the MRI and the focused ultrasound
15 brought together to do a completely non-invasive
16 therapy is really amazing. But that complexity
17 emphasizes the point that training is really going to
18 be critical from a safety point of view, and that's
19 the area that I really recommend that they work and
20 emphasize with all the people being involved.
21 Otherwise, there could be some serious complications,
22 so congratulations.

1 DR. WEEKS: I was convinced about safety.
2 I struggled quite a bit with the efficacy question,
3 and how to sort of juxtapose my concerns against some
4 of the constraints that the sponsor was under.
5 Ultimately, I think the number of motions to improve
6 the patient brochure and training, and physician
7 instructions swayed me to vote yes.

8 SPEAKER: I commend the company for giving
9 women another choice for a problem that has troubled
10 them for a long time. I think you have met the burden
11 of proof as far as safety and efficacy. I think you
12 discussed probably at more length the study design
13 issues, but I don't think that should separate what
14 really happened as far as the safety and efficacy.
15 There were study design issues, so be it.

16 I think you have done a good job, vis a
17 vis the FDA of balancing two very critical functions;
18 and that is the patient's safety and do no harm, as
19 well as the innovation that we are continually asked
20 to look at, so I think we met that burden.

21 I remain concerned about the training, and
22 I think it should be beefed up as far as what has been

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1 discussed today here with the physicians, both
2 radiology and gynecology, as well as the other
3 discipline of nursing. Nursing would be the watchdog
4 in that room, since there is no machine that will shut
5 off the heat source. It will be the communication
6 pattern, and with that in mind, that is the classic
7 role for the nurse. So please make sure that that is
8 adequately included in all your materials.

9 MS. MOONEY: I have no additional
10 comments.

11 DR. NOLLER: Well, Panel, our work is done
12 for the day. I want to commend you on doing your
13 reading ahead of time, and dealing very fairly with a
14 complex issue, and we're now adjourned. Oh, please
15 leave all your materials on the table, and they'll be
16 picked up and destroyed.

17 (Whereupon, the proceedings in the above-
18 entitled matter went off the record at 4:45 p.m.)

19
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21
22

CERTIFICATE

This is to certify that the foregoing transcript in the
matter of: Obstetrics and Gynecology Devices Panel

Before: DHHS/PHS/FDA/CDRH

Date: June 3, 2004

Place: Gaithersburg, MD

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


