around those concepts, I would greatly appreciate it. Thank you.

CHAIRMAN CEDARS: Thank you. And if we can -- Nancy, do you need a vote on that for the --

MS. BROGDON: No. I think we have enough information. Thank you.

CHAIRMAN CEDARS: The sixth question has to do with the indication for use. I'm sorry, Ms. Mayer.

MS. MAYER: Just one point of clarification from Panel members. I am really not aware that there is agreed upon evidence that clinical breast exam is useless. As far as I know, there is a study that puts it on a par with mammography, a Canadian study.

So I would just like to ask anybody who is aware of the research to comment on that.

CHAIRMAN CEDARS: Does someone want to comment on that?

DR. SNYDER: Clinical breast exam is not useless. I mean, it is a very important part of the examination. It has never been, you know, really

shown to be a cancer screening tool. I like to try to keep that separate in my mind.

I make sure my patients understand that just having had a clinical breast exam, doing their own self-breast exam hasn't been shown to decrease their chances of dying of breast cancer. It is still an important thing for them to be doing, for their health care provider to be doing.

We find a lot of things other than cancers, and for the patient that we do feel a 2.5 sonometer mass -- I mean, it's important that we find that. But it gets down to what was already alluded to. You know, what we are looking for is something that is going to ultimately decrease the chances of our patients dying of breast cancer, and there I don't think the clinical breast exam has any scientific proven utility. Is that fair?

DR. BERRY: The study that Musa Mayer is referring to showed that clinical breast exam plus mammography is effective. Separating out the two is far from clear.

CHAIRMAN CEDARS: There are clearly

lesions detected on mammography that aren't palpated and palpable lesions, as you described, that aren't noted on mammograms. So it really is a combined diagnostic screening tool.

If we can go to question number 6, and again the indications for use are spelled out and reprinted under question 6.

The question for discussion is to comment whether the data provided and the discussion we have had today provides a reasonable assurance of effectiveness and safety to support this proposed indication. And if not, are there simple modifications.

We are specifically talking about the indication, and this isn't the vote for approval or nonapproval. This specifically has to do with the indication as written.

DR. SNYDER: You know, when I read what we are looking at, I think I totally agree with their first sentence, their first two sentences. The problem I am struggling with is what to do with a positive T-Scan result, and again as it was mentioned,

that is information that is in progress now and will be decided at a later date. But we have seen some reasonable evidence that the device detects electrical impedance changes in breast tissue that are associated with an increased risk of breast cancer.

DR. BERRY: I say no. I want to quote one of my heroes, Anna Guinlin. The truth is that modern medicine too often does things because they are possible, not because they are useful.

DR. ROMERO: I think the last sentence in the statement -- "The T-Scan evaluates women's risk of breast cancer at the time of exam, current risk and not lifetime risk." -- is something that we have had to be reminded about many times by the sponsor, and has pointed to our own confounding, maybe not intellectually but just in the conversation and our -- the words we have chosen to describe things.

The fact that it has had to be -- we have had to have been reminded of that is probably indicative that any patients or consumers, anyone who is thinking of this following or before or after this type of a screening exam might be confused about.

So to the extent that any clarification of that wording can go more in the direction of understanding by a lay public, I think, would be really good; because I can intellectualize this, but I think it gets back to the question about what women will come away with believing and thinking after they have either a positive or a negative result.

CHAIRMAN CEDARS: Additional questions regarding the indications for use?

DR. ROMERO: I'm sorry, I have a question. I know it was pointed out earlier by the FDA scientists that the indication does not make any mention of a recommendation or restriction with regard to post-menopausal women. I guess one might just say, well, you know, if you use the age cutoff of 40 and over proceeding -- or being advised to proceed to mammography, then maybe that deals with it. But I'm just -- I guess I wonder why, if the study -- the analyses were limited to pre-menopausal women, why that would not be included in the prescribing information or the indication?

CHAIRMAN CEDARS: Any questions or

concerns or issues about the absence of -- it doesn't specifically say annual, although that was intended in their -- Does that give you more comfort, less comfort? There was some discussion about that previously.

DR. TAUBE: I think it goes back -- The question as asked by the agency goes back to what we consider the definition of safety in this case, and whether that includes the downstream events that occur, even when -- you know, given that the device is being used appropriately, following all the instructions and so on, and the device is kept up to date and so on. But I think we could use data on how many examinations actually followed positive T-Scan results and how many biopsies this led to and how many positive -- let's say positive biopsies.

I mean, we have data that suggests this, but we don't have actual data, and so I think, if you were to say what data would help, I think having some follow-up data would help us assess the safety.

CHAIRMAN CEDARS: I think this question is asking more in terms of labeling rather than, as the

PMA currently stands, are you comfortable with the indications for use. Whether or not there need to be additional studies once we get to an approval vote will be relevant, but given the PMA as it now stands, the question at hand is really whether or not we feel that the information presented provided reasonable assurance of effectiveness and safety to support this indication.

DR. TAUBE: I don't think it does.

CHAIRMAN CEDARS: Okay. Yes?

DR. BERRY: Can I just address that? We have at the maximum 15 cancers and five assessments by the G-Scan. This would establish a new low for the FDA in terms of the level of evidence that they accept for effectiveness. I can't imagine that this provides reasonable assurance for effectiveness for the group that we are talking about, the CBE negative and family history negative.

CHAIRMAN CEDARS: Any other discussion? If not, I'd like to poll the panel on this question, and we will start with Dr. Romero. Oh, I'm sorry. Ms. George?

MS. GEORGE: One question I have on what you were talking about, Dr. Taube, was about the safety and effectiveness with going on, biopsy decision and stuff like that. Isn't the determination of biopsy a clinical determination based off of another medical device that has already been approved for its safe and effective use?

So I'm wondering why we would be imposing that criteria on the sponsor when that is not what they are saying. They are saying that this is just to support the clinical determination to go to another assessment tool which has already been determined safe and effective for making decisions for biopsies. Right?

DR. TAUBE: That's why I said it depends on how we are going to define safety, and it is my understanding that -- I mean, it's just like when you write informed consents for patients and you talk about taking a blood sample, and you say that the only risk -- like for a genetic test, and you say the only risk is the risk of venipuncture. That's not the only risk. The risk is the answer that you get and what

that leads to.

So I'm suggesting that safety is more than just whether or not you have allergies or burns or dermal effects.

CHAIRMAN CEDARS: And I think one of the other issues is this is going to be an increased number of women going for that screening procedure with a known risk. So given the low sensitivity or relatively low sensitivity of this compared to mammogram, you are going to be getting a lot of women going to mammogram potentially that wouldn't have otherwise. So there do become sort of downstream risks other than just the risk of the procedure itself.

MS. GEORGE: Okay, because I guess I was understanding that, based on listening to the clinical assessment, that mammograms were not risky. So the very next step is going for the mammogram, and then the determination of going to the biopsy then would be based off of the mammogram, which again has already been proven as a safe and effective device for making those decisions.

So I just wanted to make sure that we are properly compartmentalizing the thought process when we think about the safety and effectiveness.

DR. BERRY: The mammogram is -- It has been shown to be effective in decreasing mortality for women age 40 and older. But there are clear risks. I mean safe and effective -- There are associated risks, the same risks that we are talking about, the risks of biopsy, the risks of overtreatment, indeed of overdiagnosis. But on balance for women over 40, it has been shown to be effective. It has never been shown to be effective, and in fact never been addressed, for women in the thirties, in part because of the very low incidence and prevalence of disease that we are talking about in that age group.

CHAIRMAN CEDARS: Additional comments? If not, Dr. Romero?

DR. ROMERO: Okay. Just so I understand, I think our original comments were with regard to actual wording within the statement provided for indication for use. But then the question after it is whether the data provided with regard to effectiveness

and safety support the indication.

CHAIRMAN CEDARS: Those are correct. So the question is whether -- is the second one, because then the other one was could the wording be changed. But the first one is do you believe that the information provided by the PMA gives a reasonable assurance of safety and efficacy?

DR. ROMERO: Okay. Well, I would say no, particularly with regard to effectiveness, because with questions, quite critical questions, still unresolved with regard to the appropriate prevalence rate to include in the calculations, also questions about whether -- to the extent, or the weight that should be given to subgroup analyses, I think those are overwhelming in terms of their shedding doubt on the effectiveness.

CHAIRMAN CEDARS: Ms. Mayer.

MS. MAYER: I would have to say no.

CHAIRMAN CEDARS: Dr. Hillard?

DR. HILLARD: I would say no, given concerns about sensitivity and the harms and risks of false positives.

CHAIRMAN CEDARS: Dr. Taube?

DR. TAUBE: I have already expressed myself.

CHAIRMAN CEDARS: Dr. Snyder.

DR. SNYDER: I want to understand the question again that we are asking. Is it safety and effectiveness?

CHAIRMAN CEDARS: Safety and effectiveness.

DR. SNYDER: I have no concerns about safety. I think, again, that the company did hit the FDA pre-agreed upon guideline of showing effectiveness for use as a risk assessment tool. However, their study wasn't designed to support the second part of their proposed indication, which is to make any sort of clinical recommendation of what to do with that data, and so it is hard for me to understand exactly what effectiveness we are talking about.

Is it effectiveness in its use as a risk assessment tool or are we talking about effectiveness in decreasing the mortality of breast cancer, effectiveness in finding new lesions. So I'm sorting

those apart.

CHAIRMAN CEDARS: I think the primary efficacy endpoint was the increased recognition to identify a high risk group. So it is not -- There was no endpoint of effect on mortality, morbidity.

DR. SNYDER: But what I have been hearing is more than just that, you know, it's saying. Then what I'm saying is I think there is exciting data to suggest that it may be effective in risk assessment. I have no idea, though, what to do with that data, and I don't think, as stated, that it can be used to make -- as an adjunct to further clinical management. Am I making any sense?

CHAIRMAN CEDARS: So the initial -- The indication says it is a complement to clinical exam. So are you saying you think it does represent a safe and effective complement to that or that that's what you are still unsure about?

DR. SNYDER: Again, you know, it's worded differently in several places, but if it is -- I think they have shown data to suggest that it can be used as a risk assessment tool.

CHAIRMAN CEDARS: I'm sorry, I don't mean to put you on the spot. Okay, Dr. Miller.

DR. MILLER: I don't have any concern about safety. I think the effectiveness is buoyed by many of the things that we have spent the last hour and a half talking about, the confounding variables in the population, the small sample size. I think, when put to the question of should we recommend this --

CHAIRMAN CEDARS: That is not the question.

DR. MILLER: Well, but we are talking about whether or not we think it has met the standard, and I don't think it has met the standard of effectiveness.

DR. JIANG: I am concerned about effectiveness.

DR. GLASSMAN: I have no concerns about the narrow definition of safety. I think patients will not walk away with burns or anything else. I think that has been shown.

I am concerned about the effectiveness piece, because of all of the comments that have been

made previously.

CHAIRMAN CEDARS: Dr. Berry?

DR. BERRY: I agree with Dr. Glassman except for the woman in the suburbs.

CHAIRMAN CEDARS: Dr. Weeks?

DR. WEEKS: I also have concerns about effectiveness, and narrow definition of safety, I have no concerns.

CHAIRMAN CEDARS: Dr. Mortimer.

DR. MORTIMER: I have no problems with safety. I do have a problem with efficacy, and I also have a problem with recommendations for further workup.

CHAIRMAN CEDARS: I'm sorry.

DR. MORTIMER: I have a problem with recommendations for further workup, since I don't think we know what the right workup is with a positive score.

CHAIRMAN CEDARS: Dr. Goldberg.

DR. GOLDBERG: I have no problem with the safety. As far as the effectiveness, as it is said at least half a dozen times in the pack that this is a

risk assessment tool, and I think as far as addressing the issue of is this a risk assessment tool, I think they adequately did address that.

I think the effectiveness that some of us are talking about are going above and beyond the scope of this conversation.

CHAIRMAN CEDARS: Ms. George?

MS. GEORGE: I, like everyone else, feel it is a safe item. I think that they did hit their pre-agreed endpoints that were identified, and I think that it does meet the aspect of being a complement, and I think that all it is doing is it is another tool to help the doctors make further determinations, hopefully in a proactive manner, to help patients get the right care at the right time.

CHAIRMAN CEDARS: And I agree. I don't have any short term safety concerns. There are the concerns about downstream risk to patients of further diagnostics and biopsy, and my concern about effectiveness has to do with not whether or not the pooled data meets the designed cutoff of 2, but whether or not the data, particularly the enriched

population in the sensitivity arm, rises to a valid enough population pool that you are really hinging all your effectiveness data on that sensitivity pool.

So I still have concerns about both the enrichment and the differences between the two populations. So because of those issues, and the effectiveness really hinges on that sensitivity arm, I have some ongoing concern.

Nancy, do you need any further discussion on that?

MS. BROGDON: I think we have enough. Thank you.

CHAIRMAN CEDARS: Okay. We have a bit covered this. Number 7 is just the overall risk/benefit profile. Does anyone have any comments additionally? We did talk about risk/benefit on one of the previous questions. Were there any additional comments or any additional concerns, Nancy, that you had that we did not address already?

MS. BROGDON: I think we have enough. Thank you.

CHAIRMAN CEDARS: Okay. And any comment

about the draft labeling that has been recommended by the sponsor? Yes?

DR. ROMERO: I had a question. When I was looking through the labeling and there was reference to Appendices, the appendix for a patient guide -- The closest that I could come to that were a couple of pages on FAQs. Was that the patient guide or was I missing something?

CHAIRMAN CEDARS: Can I ask the sponsor, is there -- For the patient guide, was it anything beyond the frequently asked questions? No. That was it.

DR. ROMERO: Then my only suggestion would that it be more clear that that's the patient guide.

CHAIRMAN CEDARS: Dr. Mortimer?

DR. MORTIMER: I have problems with the recommendations, because I just don't -- If we knew that nipple aspirate fluids or that ductoscopy found things in these positive patients, I think I would feel more comfortable. I just don't think we know what the right recommendation is for these patients.

CHAIRMAN CEDARS: And that something you

would expect from the sponsor?

DR. MORTIMER: Well, as I read this, it sort of looks as though the recommendation is to do mammography or ultrasound, you know, obviously, leaving it up to the physician. But I don't think we actually know that that is the right thing to do. There may be other things that would be more worthwhile to do.

CHAIRMAN CEDARS: Any other comments? Dr. Snyder?

DR. SNYDER: Again, echoing the same thing I said before regarding indications for use -- and that is what, I think, Dr. Mortimer just alluded to -- is we don't know what the post-positive study recommendation should be.

The other thing, and it may just be that I am not finding it, but in their precautions they said that it has not been tested on lactating women, women who have undergone chemotherapy or women with recent biopsies, but they also excluded women with implants or any cosmetic surgery in their other studies. That would, obviously, have to be put in the precautions,

too.

CHAIRMAN CEDARS: Okay. Before we take a break, I would just like to give an opportunity to the industry rep, consumer rep, and patient rep to speak. So, Ms. George, do you have any additional comments? Okay. Ms. Mayer.

MS. MAYER: Perhaps something that Cindy Pearson said to us at the open public hearing I would like to underscore. That is none of us doubts that this is a real and urgent need that is being addressed, and I really do appreciate the hard work that the company has done to meet this need. But what I am left with is the feeling that something to address a real need, regardless of its urgency, is not necessarily better than nothing.

CHAIRMAN CEDARS: Thank you. Dr. Romero?

DR. ROMERO: Yes. I think most of my comments heretofore have been with regard more to my scientific background, but as the consumer rep maybe the thing I would like to highlight most is a comment that I made earlier on or a question that I asked, which had to do with the lack of racial and ethnic

diversity in the sample.

It is acknowledged -- It is actually very discouraging that it continues to be acknowledged like, yes, that would be really good to achieve, but we didn't, and without any further discussion even about what kinds of recruitment, sample recruitment or study design modifications would or should be made in order so that we are not in this situation again.

I haven't sat on many panels before today, but it seems like this is a recurring theme from just the work I do, the studies I review. You know, to be in the year 2001 and to be confronted with an application for a device that enrolled in the specificity or sensitivity arm -- I forget which is which -- but two and four percent respectively of Hispanics and African Americans and four and eight percent respectively of those groups in the other arm, I think, is abysmal.

We have 15 percent Latinos in this country, and we have about 14 percent African American women. We also know that breast cancer is disproportionately experienced at this point by women

of color.

So to be confronted with a study that has abysmal representation of those groups is beyond my comprehension at this point.

CHAIRMAN CEDARS: Thank you. If there are no comments, any comments from the FDA before we take a break?

MS. BROGDON: No comments. Thank you.

CHAIRMAN CEDARS: Okay. We will take a 15 minute break, and reconvene at 3:15, and again I would like to remind -- I'm sorry, at 3:30, and again I would like to remind the Panel members to not discuss the PMA during the break.

(Whereupon, the foregoing matter went off the record at 3:16 p.m. and went back on the record at 3:35 p.m.)

CHAIRMAN CEDARS: Now that we have responded to the FDA's questions, we will proceed with the second open public hearing of this meeting. Prior to the meeting, we have received four requests to speak.

I would like to remind the speakers, as

was mentioned today, to disclose any conflict of interest or relationship with the sponsor or their competitors, and I would also like to remind the speakers to a five-minute limit, please.

The first speaker is Dr. Carol Lee.

DR. LEE: I am Dr. Carol Lee. I am a professor of diagnostic radiology at Yale University, School of Medicine. I am also the Chair of the Breast Imaging Commission of the American College of Radiology, and I am Vice President of the Society of Breast Imaging, and I am here representing both of those organizations. I have no conflict of interest to disclose with either the sponsors nor their competitors.

I would like to thank the Panel for this opportunity to make some brief remarks, and I want to make these remarks as a representative of the breast imaging community, who has been intimately involved with issues concerning screening for a number of years.

There is no body of people who would welcome improved ways of screening for breast cancer

than the breast imaging community. However, I am struck in the discussion today and in going over the materials provided on how we have managed to separate the effectiveness or the efficacy of this tool with the downstream testing and the downstream consequences of the testing.

Identifying increased risk without a method, a proven method, of acting on this or without knowing how to proceed once the risk is identified, I think, is not in the best interest of our patients.

I have heard talk about what constitutes an ideal screening test, and I think that, certainly, the considerations associated with downstream testing need to be considered, including the specificity -- not only the sensitivity but also the specificity of downstream testing.

MRI has been mentioned, and it is well known that specificity of MRI is quite variable, and in some reports is as low as 37 percent. So that's a lot of false positives that we are dealing with and, when we are talking about anxious patients, there is nothing more anxiety provoking than an abnormal MRI

examination.

In addition, I think we need to talk about the demonstration of benefit of screening tests. I find, not being a statistician, the sensitivity figures not to be particularly compelling. I have heard talk of early detection and cure, but based on what I see presented, I don't know that the cancers that are being detected by the T-Scan are indeed small cancers, early stage cancers, less aggressive cancers, etcetera. There is no data on that.

Finally, I want to mention -- I want to remind all of us of the weight that the words FDA approved have with the public, and this is something that we in the breast imaging community have dealt with recently with other imaging modalities that are FDA approved but that are being used in ways that were probably never intended by the FDA.

We are considering -- You are considering this device in terms of its safety and its effectiveness. It is, I think, important for us to understand what effectiveness constitutes, and in the minds of the public, once a device is approved as a

screening tool, it implies that it can pick up early stage disease, and I don't think that has been demonstrated by the data presented here.

I am concerned as a breast imager with the uncertainty of how to deal with these positive T-Scans, the lack of direction and the lack of data and information on how to proceed once a woman has an abnormal test. Thank you.

CHAIRMAN CEDARS: Thank you. Dr. Platt.

DR. PLATT: Thank you very much to the Panel to allow me to make a few comments. I will first claim that I have served as a consultant to the company and working along with some of the investigators in my community. As such, I am a professor of OB/GYN at David Geffen School of Medicine at UCLA. I also run a private prenatal diagnosis program, understanding the whole area of screening, and as an aside, in some of my professional affiliations I also serve as the Chair of the Breast Ultrasound Foundation, which is a branch of the ARDMS. So I am very interested in the whole concept of breast diagnosis.

I think we all realize what the Panel has heard today, both from the sponsor and from your own overviews, breast cancer in young women are hard to find. It is very difficult. The anxiety of waiting for the breast mass to be felt is at best too late.

We are all searching for newer and more innovative methods to identify the breast cancers before it is felt, because we all realize, and we have heard it here today as well, that earlier detection does mean better care, better cures.

As such, T-Scan has shown to be effective, as set out by the objectives put forward by the FDA's discussions with the company and their proposals, as you have said here. It is not 100 percent sensitive. It is not 100 percent specific. We know of no screening test that would be that. Otherwise, it would not be a screening test.

I think the screening tests have to be used as such, as a balance between sensitivity and specificity, which indeed it is.

What T-Scan also provides, what this electrical impedance methodology will provide, is an

earlier opportunity, I believe, for patient education as well. All too often, patients wait. They feel. They deny. Here is an opportunity before they even feel a mass to at least have a screening methodology that will bring them to their health care provider whose responsibility it is to care for the patient and lead them and help them in a process of management.

T-Scan does not set forth what the cascade of treatment will be after a positive test itself, because there are professionals who have spoken here today with what we do when we have a positive test, what we do with a positive mammogram.

I think it is clear that the clinical problems are there. We are not going to solve them, but we are going to help identify these patients a lot earlier where there is nothing else.

We have heard the compelling stories of patients who have waited too long to come in for their diagnosis. We have heard the needs of our patient population before the age of 40 where we tell them, just feel the breast and do a Gail Model scoring, which we know is not totally effective.

We need to find something that meets those needs, and I believe that we are on the way with this T-Scan, which has met the FDA objectives, to make it available for us so that we can utilize it in clinical practice, as I have seen patients undergo this test not feel that anxiety when it is a red tests but rather feel that they now can go on to another methodology that has a proven value in clinical practice.

Like all new technologies, we will learn more as we use it more. If our hands are tied in the back and we cannot use it, we obviously will not go any further with this opportunity. I believe that T-Scan's approach is education. T-Scan's approach is really a screening methodology, and I think that we do understand that this is a screening methodology and we understand that we can go to all the degrees of testing that we want, we will never have it available for our patients.

I do believe that this will be something introduced into clinical practice that will help us, not hurt us. Thank you very much.

CHAIRMAN CEDARS: Thank you. Dr. Akin.

DR. AKIN: Good afternoon. I've been asked to read a letter into the record for you from a physician in Vienna. I understand that he has not received any compensation or have any interest with Mirabel.

This is Dr. Michael Fuchsjager, Associate Professor of Radiology, Department of Radiology at the Medical University of Vienna in Austria. This letter was written August 24, 2006.

"Dear Honorable Panel Members,

"As Associate Professor of Radiology at the Medical University of Vienna, I have been researching and publishing on electrical impedance technology, initially with the TS-2000 and currently with the T-Scan 2000 ED, since 1999. I wanted to help clarity some of the important issues that may be a source of confusion to those who have less experience with the technology and its application in the assessment of breast cancer risk in women age 30-39.

"In my opinion, the true clinical need for this device lies in the identification of cancers that

would otherwise be entirely overlooked. The T-Scan 2000 Ed targets patients who are not routinely offered mammography or other imaging, and by scanning the entire breast, identifies women who should be offered additional screening. In my department, we rely heavily on full film digital mammography, and we feel that this technology, which offers a sensitivity of approximately 70 to 80 percent in women age 30-39, is an efficient, safe and economically logical means for identifying breast cancer in women who would generally not be offered their first imaging exam for several years or more.

"Amongst my radiology colleagues, I have encountered some initial resistance to electrical impedance. I believe that a significant amount of concern may arise from the misconception that the device can be used instead of mammography or other accepted breast screening or diagnostic technologies. Thus, I should note that the device does not allow a patient who has a breast symptom or who is above age 40 to be screened with the T-Scan 2000 Ed device, and that the device does not offer a breast image of any

kind. Thus, expecting that electrical impedance scanning will compete with mammography is similar to expecting that a BRCA testing will compete with mammography. In fact, it is expected that significantly more at risk women will benefit from mammography and other imaging once the T-Scan 2000 ED is available.

"Another point that I have discussed with my colleagues is the sensitivity rate, which is lower than the sensitivity of mammography, ultrasound or MRI. The primary goal of a risk assessment tool, such as the T-Scan 2000 ED, designed for women who are mostly free of disease, is not to diagnose pathology but to help identify a smaller number of women who require additional imaging and follow up with tools that have a high level of sensitivity and offer a diagnosis. Returning to the BRCA analogy, only 5 percent of patients who have breast cancer also carry the BRCA germ line mutation. Thus, it could be said that the sensitivity of electrical impedance scanning is very low, but in fact, the technology is very valuable in identifying risk.

"Having studied EIS technology for a long time, I am pleased by the robust, stable and easy to operate characteristics of the T-Scan 2000 ED device, and I fully expect that once the device is in the hands of primary care and Ob/Gyn physicians, we, as radiologists will have a valuable opportunity to screen a cohort of women which are distinctly underserved by the current standard of care. I have been and remain highly supportive of this new application, as embodied in the T-Scan 2000 ED which is currently under your review.

"Yours sincerely, Michael Fuchsjager."

Thank you.

CHAIRMAN CEDARS: Thank you. Dr. Gur.

DR. GUR: My name is David Gur. I am a scientist, not a clinician. I am the Executive Vice Chairman of one of the largest departments of radiology in the country, and I had been in the past a consultant to the company.

I would like to address three issues that are related to a theme that has been going on through the day, and in a way are related to each other and,

hopefully, will at least affect your thinking for the next set of deliberations.

The first one is the transition between age 39 and 40. There has been a lot of discussion here about prevalence and how it affects both PPV and the ratio of -- yield or ratio of false positives to cancers detected.

I just want to remind the team and those who raised the issue of changing prevalence or incidence during the decade of 30-40 that indeed, if you just take a woman at the age of 40 where annual screening with mammography is an acceptable practice, her risk of having -- and you take away women with known risk factors, actually her yield is about one in 1000, not one in 400 or one in 300.

So the woman at the age of 39 may be one in 800 or 900. The woman at age 39 may be one in 1000. So the transition is not a large transition between those that we have standard acceptable practice. Those at the age group, at least at the higher end, or 40 we are talking about.

If you think about going to a .2 cases per

thousand and you accept for whatever you wish to the fivefold increase in relative risk by the company, then even at the lower end we are coming to risks that are comparable to a woman at the age of 40 without known risk factors in terms of yield.

So we just need to be careful when we start talking about specific ages and common practices that either we take averages everywhere or we consider the fact that your transition between a screening age and an unscreening age is a very smooth transition where the risk factor really changes very little.

The second point that I would like to make is related to case availability and case pooling in regard to age. Indeed, in this study the women we would like to find with the technology or any other technology are not those with palpable findings and/or known risk factor because of family history.

Unfortunately, in this group the company, in my opinion, was lucky that, for whatever reason, there were four cases that were available at the age of 30-39, because typically we have no mammography, and the only way they get imaging procedures that go

up to follow-up is because they have family history and/or palpable finding, and therefore, in order to study those cases that we would like to find earlier, we actually have to extend the age and find those cancers that are found by other diagnostic procedures rather than palpability or that are not being screened because of the fact that they have family history.

That is -- In the current environment, to be practical, that is the only way we can get the number of cancers, if you like, that we would like to study for the purpose of this kind of screening.

So the discussion of whether or not we have large enough set in the intended use, in common practice in the United States you would not find those cancers, because those that you do find are related largely to family history and/or palpability, because that is the only reasons why they follow up to diagnostic procedures.

The third issue that I would like to address is the issue of sensitivity and procedures downstream. The fact is that, as I said before, the issue of transition between age 40 and above and 39

and below have no big changes in sensitivity of the procedures that are downstream procedures that we do accept in our society as a diagnostic tool that is commonly practiced.

We do know that FFDM alone in this group age, and if you add common practice today that was not done during the DMIST studies that we all quote, you add computer aided diagnosis, CAD, to it -- we all know that its sensitivity is someplace between 70 and 80 percent, and if you think about the future when there are technologies that are being looked at such as imaging tomosynthesis and/or FFDM plus ultrasound, we know that this sensitivity will only improve.

These are all common practices that we do know the sequela and the responsibility associated with those diagnostic tools, and to assume that there is some kind of a transition that at the age 40-41 or 42 all of this sequela is okay in our society, but in age 39 or 38 or 35 it is unacceptable just for that matter, in my opinion, should be taken into account. It should be acceptable as well. Thank you.

CHAIRMAN CEDARS: Thank you.

Is there anyone else from the audience? We have time for one speaker just three minutes, please.

DR. GOLDSTEIN: My name is Dr. Steven Goldstein. I am a professor of obstetrics and gynecology at New York University School of Medicine. In that capacity I have a half-time private practice in gynecology. I am not being paid to be here. I have no financial interest in this company. I have been an investigator with the T-Scan device, and I have listened very carefully to the discussion today, and I would like to make the following comments.

I came here today as a clinician, not as a breast imager. Twelve thousand women 30-39 are diagnosed with breast cancer each year, and regardless of what percent of the total that is, it is 12,000 women, 12,000 women whose lives and whose families' lives are turned upside down. In fact, the physical and psychological aspects of such a diagnosis are almost unimaginable unless you are the one going through it.

So 12,000 cases of breast cancer in women

ages 30-39. We have already heard that there are 9,000 cases of cervical cancer in all women, and think of the time and resources to accomplish this success. But for all the talk these days about HPV and vaccines, the cervical cancer success story is really the result of screening, the Pap smear.

Don't believe for a moment that, when first introduced by Papanicolaou 60 years ago, its sensitivity and specificity was nearly as good as it is today.

Clinical use allows maturation and further refinement of virtually all medical technology, and I am confident the same would be true of electrical impedance, if given the chance.

So 12,000 women with breast cancer, 71 percent picked up by the patient herself, the death rate per case higher in these women than in older women, largely because these tumors are larger and more advanced.

Thus, I think we can all agree that clinical breast exam is extremely disappointing. I do them. I do them sitting in line. I do them very

carefully, and I think patients are relieved when I feel nothing. I think all too often she thinks that she is guaranteed to be okay and, obviously, all of us in this room know it is not as reassuring as we would like to think.

Twelve thousand women per year, 71 percent find it themselves. The clinical breast exam is just not effective, sadly. Obviously, we can all agree that we want to diagnose breast cancer in women 30-39. The real question for you to consider is whether the T-Scan device is capable of making enough of a dent in the problem without creating undue subsequent testing and undue anxiety.

So what about undue subsequent testing? We have heard, and I think it needs to be clarified, right now arbitrarily at age 40 I send my patients for mammography. I think we know it takes 300 or 400 mammograms to pick up one cancer. In a T-Scan positive woman, I will find cancer in one out of 136 or perhaps one out of 194, according to Dr. Yustein. Either way, it seems like this is appropriate utilization of resources.

What about undue anxiety? There is no question that any positive finding in a screening situation creates anxiety, whether it is a positive glucose challenge test in a pregnant woman, the positive nuchal translucency leading to the amniocenteses, and I do appreciate the question this morning that screening usually leads to a definitive diagnosis, but not always.

Women with an atypical Pap smear or a low grade SIL on Pap who have no lesion on colposcopy, do not end up with a definitive diagnosis. They may be reassured by the negative colposcopy and the negative biopsies, but then they go back into the usual pool of care, not unlike the T-Scan positive patient with negative follow-up imaging.

It is our responsibility as physicians to be sure that patients realize what this means before they enter into it. So, certainly, the counseling and explanation with the test is crucial.

I tell every patient before they agree to participate that, if the test is positive, they will get further evaluation, but the chances are about 99

out of 100 that nothing will show up. Then we will probably just watch them carefully. No one at that point has then declined. Remember, this is a risk assignment tool.

In closing, I stand here speaking for my patients as well as all those patients who will have breast cancer detected because of T-Scan when otherwise they would go undetected. Would higher sensitivity be better? Of course, it would. But I believe that identifying 5.3 percent of women who will have 26 percent of the cancers should be sufficient for you to allow me and other health care providers of women to utilize this service.

I appreciate your concerns, but isn't it up to individual physicians to make many of these decisions? I personally find much of the discussion about downstream concerns to be actually paternalistic. I would hope --

CHAIRMAN CEDARS: Excuse me. Could you summarize?

DR. GOLDSTEIN: I'm on my last sentence. I would hope that you would leave such decisions up to

individual physicians in consultation with their individual patients. Thank you.

CHAIRMAN CEDARS: Thank you.

I would now like the give the opportunity to the FDA first and then the sponsor for closing comments. Does the FDA have any final comments? No?

MS. BROGDON: No comments. Thank you.

CHAIRMAN CEDARS: No comments. Then I would like to give the sponsor an opportunity for final comments.

DR. GINOR: Good afternoon. At this moment you are preparing to vote. I spent six years with our physicians, statisticians, scientists, trying to do whatever possible to take on the monumental task of clinical breast exam improvement in women 30-39. Many of the things you said today, which were disparaging, are also true. It is very, very, very difficult to find a solution to this problem.

The proof is the fact that we haven't done so. All of the large companies, all of the well funded and large scientific attempts -- no one has yet found a way to assign risk in women 30-39 who don't

have pre-known risk factors into a group that requires screening.

I am a little bit perplexed. I am perplexed, because this is a study that met and exceed by more than 100 percent every single milestone. I am perplexed, because this is a study that assigns risk at a level greater than the level at which you currently offer mammography to your patients because of family history, one first degree, two first degree relatives, findings of ADH.

I am perplexed that we are willing to go back to CBE, because we are concerned about things like anxiety. Our job here today is not, as far as I understand the regulations, to evaluate mammographic sensitivity, MRI yield, etcetera.

Our goal, as far as I understood it, was to determine whether risk assessment as identified by this device does or does to identify patients 30-39 who are at a level of risk equal to our greater than twice the average, and in this case what was discussed later with FDA, equal to or greater than women above forty.

I really want you to take very, very seriously as you prepare to vote on this the thought that, while there are improvements that are necessary, and we are aware of that and we are actively working on that both in terms of development and research and both in terms of clinical studies, not allowing us to move forward means staying with clinical breast exam. It means maybe ductal lavage. It means maybe relying on family history which misses 90 percent of cancers. It means maybe just waiting until women are 40.

All the discussion today that circled on prevalence and incidence misses one critical component that I am sure all of you will understand in a moment. It is extremely unlikely that the SEER prevalence is correct in 30-39-year-olds, given the unbelievable jump, three to four times, according to some studies, that occur with the first mammograph.

There is no question that these women that we are picking up, three to four more on the first mammogram than on the second or the third had their cancers when they were 36, 37, 38, 39. They didn't get them when they turned 40. What they got at 40 is

a mammograph.

What we want to offer women is the opportunity to have nothing from 0-20 other than clinical breast exam, T-Scan from 30-39, mammograph moving forward or MRI or full field digital or whatever the mammography world agrees and the imaging world agrees is correct, once we have shown, as we have, that the level of risk for these patients is right.

You have to understand, feeling that we have not met our milestone in terms of the yield actually questions the entire way in which we currently refer women to imaging. If we refer 35-year-olds, 34-year-olds forward with two primary relatives with breast cancer, they are actually at a lower risk than what was demonstrated here.

I really do not think this would be a new low for FDA. This is a device that is safe. This is a device that was proven effective prior with another indication, and a device that has shown a very reasonable safety and efficacy. While it is imperfect and, hopefully, will get so, keep in mind what

mammography's results were when we approved it back when we did so.

I know that this may very well not change your mind, but I very much wanted to make sure that I put this on the record. I do appreciate all your time and the opportunity you gave me to do so. Thank you.

CHAIRMAN CEDARS: Thank you. The Panel will now move forward in deliberations and vote. Prior to this Dr. Bailey will read the Panel recommendation options for pre-market approval applications. Dr. Bailey.

DR. BAILEY: The Medical Device Amendments to the Federal Food Drug and Cosmetic Act as amended by the Safe Medical Devices Act of 1990 allows the Food and Drug Administration to obtain a recommendation from an expert advisory panel on designated medical device premarket approval applications that are filed with the agency.

The PMA must stand on its own merits, and your recommendation must be supported by safety and effectiveness data in the application or by applicable publicly available information.

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

Safety: There is reasonable assurance that a device is safe when it can be determined based upon valid scientific evidence that the probable benefits to health from use of the device for its intended uses and conditions of use when accompanied by adequate directions and warnings against unsafe use outweigh any probable risks.

Effectiveness: There is reasonable assurance that a device is effective when it can be determined based upon valid scientific evidence that in a significant portion of the target population the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results.

Valid scientific evidence: Valid scientific evidence is evidence from well controlled investigations, partially controlled studies, studies and objective trials without matched controls, well documented case histories conducted by qualified

experts, and reports of significant human experience with a marketed device from which it can be fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of the device under its conditions of use.

Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness.

Your recommendation options for the vote are as follows.

Approval: If there are no conditions attached.

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

The final is Not Approvable: The panel

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

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

Dr. Cedars.

CHAIRMAN CEDARS: Is there a main motion to recommend approval, approval with conditions, or not approvable by the panel?

DR. BERRY: I move that the device is not approvable.

CHAIRMAN CEDARS: Is there a second?

DR. MORTIMER: I second.

CHAIRMAN CEDARS: Is there any discussion on this motion?

In the absence of a discussion, I would like to take a vote, and we will need to poll the members. If I can have all those in favor raise their

hand. That is Dr. Mortimer -- Dr. Goldberg, yes; Dr. Mortimer, yes; Dr. Weeks, yes; Dr. Berry, yes; Dr. Glassman, yes; Dr. Jiang, yes; Dr. Miller, yes; Dr. Snyder, yes; Dr. Taube, yes; Dr. Hillard, yes. And that was all the members.

So none opposed. So that motion passes.

I need to have each member please state their reason for so voting. Dr. Goldberg. Please speak into the mike.

DR. GOLDBERG: I think that, based on what we spoke about as far as effectiveness, the anxiety factors and the small patient population sample and the short duration of follow-up. So I think there were several factors in that decision.

CHAIRMAN CEDARS: Dr. Mortimer.

DR. MORTIMER: I am going to go back to Don Berry's comment about the 15 patients. I just think there just are inadequate numbers.

CHAIRMAN CEDARS: Dr. Weeks.

DR. WEEKS: I am concerned about the decreased sensitivity or performance of the test in the U.S. population, and decreased specificity,

sensitivity among the small group of minorities that were studied.

I believe that the prevalence number of .0015 is questionable. When it comes to drawing conclusions about sensitivity, it is based on a total of 94, just 94 total cancer patients. Only 29 of those cases are in the U.S., and I am struck by the fact that 19 cases were lost from the U.S. because of technical difficulties. I understand why that happened, but I believe there could still be some bias introduced there.

The device is intended to be used in women who are 30-39 years of age with a negative clinical examination and negative family history for breast cancer. I understand all the reasons for the study design, but the sensitivity figures that the sponsor would use, 25 percent overall, about 10 percent in the U.S., include patients who had positive clinical breast examinations or positive family history.

So for all those reasons, I believe that we don't have evidence of effectiveness.

DR. BERRY: So I am concerned about what I

have already said many times, false positive rate. I am concerned about introducing additional procedures into this population that are not clearly shown to be beneficial.

The issue of the 2, the relative probability that the FDA agreed to -- you know, as I have said several times, I am concerned about that. I am concerned about the age effect. But even that -- I mean, with the uncertainty associated with the sensitivity and if you use some of the FDA's calculations of confidence intervals and restricting to the intended use population, even that, the confidence intervals drop below the level 2.

So I think 2 was not appropriate as the overall hurdle. I think it was much too low, but even that low hurdle was not achieved.

DR. GLASSMAN: My concern comes down basically to the small numbers. The 15 cancers, the disparities between the Israeli and the American population come down probably to small numbers. The prevalence number of 1.5 per 1,000 I have concerns about and, if it is lower, the positive predictive

value becomes a very poor number. But basically, I think the study just had to have more power to convince me that it was effective.

CHAIRMAN CEDARS: Dr. Jiang.

DR. JIANG: So one of the reasons I voted that way is because Dr. Berry said that relative risk of 2, in and of itself, it's not a great goal to achieve in this age group of women, because the prevalence is very small, to begin with. But given that we agree on that's the intended goal as a relative risk of 2, I still have a question whether we demonstrate that.

So I don't know if I can vote yes to the effectiveness. The reason I say that is because, if you look at the FDA's presentation, there were three studies. The specificity has a range, and there are various numbers of sensitivity. So there is great uncertainties of these values, and those values decide the relative risk.

So in my mind, I can't really decide what the relative risk is. Having said that, I think the device has great potential, and what you are trying to

do is great. The difficult thing here is defining the relative risk, and that is very difficult to measure. Sensitivity is very difficult to measure.

CHAIRMAN CEDARS: Thank you. Dr. Miller.

DR. MILLER: Yes. I would like to echo some of the things that have already been said, but I would also like to highlight some things that maybe haven't been said.

When I think in terms of the Israeli versus U.S. statistics, at least for myself, I don't view it as not in the U.S. and in the U.S. I view it as one of the sites that was studied which had very different characteristics than the other sites, and those differences led to potentially different interpretation, and I am concerned that the conclusions that are being drawn from the pooled study don't properly reflect the fact that there were such differences.

Secondly, in terms of safety I don't have any concerns about the actual application of the technology being immediately injurious, and I'm not -- I have some concerns about anxiety, but I am more

concerned about many unnecessary -- In the risk/benefit equation I am concerned about many unnecessary procedures being done to a population to identify just a few cases.

I think there is nobody on the committee that doesn't agree that there is a tremendous need for this technology and that we need something to assist this younger group of women to identify a cancer that needs to be identified, but if the cost of that is subjecting an undue number of women to potentially morbid procedures or at least painful procedures on a sequential basis, then that is not justifiable.

DR. SNYDER: It's going to take me a minute to get through this, but I am really enthralled by the fact that I really do think that I've seen data today that suggests that this really is -- has been shown to be a risk assessment tool.

My problem is that I don't know if it is a screening tool, and I don't know -- You know, there's some semantics in those two definitions, but my reason for not voting for approval or approval with just relooking at the existing data is I'm really concerned

that we don't have enough data to know what to do with these patients that we have identified as being at increased risk.

Even now, the patient that's got a positive family history, maybe two first degree relatives, I still -- if it's not a pre-menopausal patient, there's not good data to say that I would do anything differently in the 30-39-year-old age group. Well, again we have something that now just gives the patient another risk factor, another increased risk factor, but we don't have any data to direct us as to what to do because of that information.

I am very optimistic that, should further studies, ongoing studies, be done that will allow us to have some direction as clinicians what to do with this information, then we may achieve exactly what the company came here wanting to do today.

I think they are on the mark with the multi-institutional, multi-year study that is going on. It is going to answer the questions about the population that we are dealing with, that the FDA is responsible for protecting here in the United States.

It is going to be an ethnically diverse population. It is going to be a much larger group, and it is going to allow better sub-analysis of groups.

Maybe it's not just 30-39. Maybe it's 35. Maybe it is 38 with family history. I think those are the things that we need to be armed with as clinicians before we just start assigning an increased risk to our patients.

I really do feel like, you know, that the company will be letting down the women of the world if they don't pursue this data, because they may be coming right back at us with the answers to the questions that we have laid out for them today.

CHAIRMAN CEDARS: Dr. Taube.

DR. TAUBE: I think everything that I have to say has pretty much been said. My main issue is that I don't believe that the data are sufficient to draw a conclusion that this is safe and effective.

Again, we don't know what to do with the information, which is frequently a problem with risk factors. But since there isn't truly an intervention that we are aware will make a difference, it is hard

to support this.

CHAIRMAN CEDARS: Dr. Hillard.

DR. HILLARD: As a clinician, I would have loved to have been convinced that this device is the way to go to add benefit to what is not a good technique; that is, clinical breast exam. So I would like to have been convinced, as I think the panel members all would like to say.

I was not convinced as yet, and perhaps we will see in the future that this is a good technique. I think it is intriguing.

I have remaining concerns, as had been expressed by all of the panel members, related to the sensitivity and the poor positive predictive value and the harms of false positives. So I am -- I was unconvinced.

CHAIRMAN CEDARS: For the record, it is the recommendation of the Panel to the FDA that Mirabel Medical Systems PMA P050003 for the T-Scan 2000 ED be not approved. The motion carried unanimously with no abstentions.

Since the panel voted to recommend the PMA

as not approvable, we must now identify what the panel believes is needed to make the PMA approvable. Dr. Hillard, would you like to start that?

DR. HILLARD: My first answer, and I would reiterate, and I think the others would, too, numbers. More.

CHAIRMAN CEDARS: Increased numbers for the sensitivity arm or just increased numbers of cancers? Where would you like -- or just increased numbers for screening?

DR. HILLARD: Yes, for all of the above, also increased numbers in the subgroups that were mentioned, the groups looking at different populations, the ethnic minorities. I am concerned as well about issues related to BMI and differences in those populations.

CHAIRMAN CEDARS: Dr. Taube.

DR. TAUBE: I think I would also like to see some relationship -- I'd like to see more information on the type of tumors that are identified in the subsequent studies, so that if a woman is at increased risk and goes on to further studies and to

biopsy, what the nature of the tumor is, and then some outcome data, even if it is evaluation of historical data, treatment of younger women with cancer.

CHAIRMAN CEDARS: Dr. Snyder.

DR. SNYDER: I've already said my piece, I think, on that. I had one other issue. I'd like to see a little bit more on reproducibility, be it that we actually see the numbers in the patients that you did scan 30 times.

I think another big issue of the reproducibility is what is going to happen with a positive result in subsequent years. You know, that is again, I hope, going to come from the multi-year study.

CHAIRMAN CEDARS: Dr. Miller.

DR. MILLER: So, yes, I think there needs to be some better address of the performance of this technology among important ethnic groups. I think it would be worthwhile for the company to do some post hoc analysis that better defines why this one site, albeit out of the country, but this one site had very different performance characteristics for the

technology.

Then, you know, this is not my field of expertise, but there clearly is quite a bit of dispute about what the prevalence is in this population, and I don't know if there is a way to look at the SEER data or to get at a better prevalence, but it would seem to me that we would have come to better conclusions if there was better understanding about what the actual prevalence is in this group.

CHAIRMAN CEDARS: Dr. Jiang.

DR. JIANG: I want to cite one of Dr. Snyder's recommendations to study the consistency of the device, repeated scanning of the women. I think that is an important issue that has been alluded to but not specifically addressed here.

My main comment would be that the key measurement here is sensitivity and specificity. So specificity, I think, with larger studies or maybe independent studies is easy to assess. The problem is sensitivity, and I don't know how to do that. So I don't know what to recommend. I think that is a really difficult question.

CHAIRMAN CEDARS: Dr. Glassman.

DR. GLASSMAN: Again, larger numbers, particularly numbers of patients with non-palpable cancers, imaging detected cancers in the near-39-40 age group. I'm sure it will have to be with some enrichment, but that is really the group that the T-Scan is made for, is people with non-family history, non-palpable.

I could live with just non-palpable if you had a number of those cases and you could show that the T-Scan was effective and positive in patients with non-palpable cancer and negative in those without.

CHAIRMAN CEDARS: Dr. Berry.

DR. BERRY: So I agree with everything that has been said. I underline Dr. Glassman with respect to the last comment. If there is an intended population and intended use population, it ought to show sufficient data in that population.

Underlining Dr. Taube and Dr. Miller's earlier comment about what kind of cancers are we detecting this way: the ideal, of course, is to do a mortality study, but we have already seen in a much

more prevalent circumstance, the older women, that even with hundreds of thousands of women, there are controversies associated with the benefits of mammography because of a number of things, not the least of which is lack of compliance with either group. So that's out, but you could address that at least to some extent.

What kinds of tumors are being detected, and are they treatable? Are they ER positive as opposed to negative, more commonly than younger women? We certainly expect younger women and then African Americans to be many more ER negatives. That would be a very poor prognostic group, and if you are identifying that group, that would be an additional benefit.

I would -- We talked about false positives, and it would be nice to -- and the question to one of the company representatives as to how do you know there was no anxiety, and the response is, well, I observed that there was none.

I don't know that there are tools for measuring such, but something. You ought to be able

to -- I don't know, testimony or some sort of sample of the patients who are testing positive but, in fact, are found by mammography or otherwise not to have the disease, what the impact was on those patients; and if you could quantify that in some fashion, it would have the effect of alleviating at least some of the anxiety on the part of the panel.

CHAIRMAN CEDARS: Dr. Weeks.

DR. WEEKS: I agree with all the previous comments. I understand it is difficult to -- since asymptomatic patients without masses and without a family history don't generally get imaging studies, that is difficult. So I suppose as a compromise, I would be more interested in BRCA positive patients or positive family history negative clinical breast exam.

CHAIRMAN CEDARS: Dr. Mortimer.

DR. MORTIMER: I actually find fairly intriguing the number of positive scans that there are in this population, appreciating that it takes 10 to 20 years for a cancer to develop. So I'm sort of intrigued that those individuals who truly are positive by this scan have a consistent workup that

may determine if there really is something there initially and, further, to have follow-up on them.

I would also think it would be worthwhile if we could correlate the positivity with those histologies which are classified as benign in the briefing document, but really are not, because they are part of the continuum of normal duct tissue to the development of an invasive cancer. I think that would be very helpful.

CHAIRMAN CEDARS: Dr. Goldberg.

DR. GOLDBERG: Also, just to reiterate what we have said, I agree. I think the multi-year, multi-center studies would help to increase all the numbers across the board as far as number of cancers, increase in the number of cases in the sensitivity and specificity arms, as well as the ethnicity.

CHAIRMAN CEDARS: And I would like to ask the industry, consumer and patient representatives if they have comments. Ms. George?

MS. GEORGE: I understand everything that everybody has described and the concerns that they have all identified, and I think that, as an industry

rep and as having sat on that side of the fence more than once myself, I think one of the challenges that industry and the FDA are going to have is really defining the protocols and the endpoints ahead of time, because this is now the fourth panel that I have sat on where every time the group says more data, more data, more data.

There was a protocol. There was endpoints defined, and they were reviewed with the FDA, and I think that I'm sure that the sponsor feels that they, in fact, did meet those -- what was defined ahead of time. So I think that that is going to be a challenge for industry to deal with, and understanding what is the right number -- you know, how many. How many is appropriate, because you know, I don't know Mirabel, and I know we are not supposed to talk cost but, you know, some of the companies that have come here end up not being in business after, because they can't afford to keep going.

Then the other comment that I did -- I heard a lot of comments about clarity with regard to what the next step is going to be, and more of a

comment than actually expecting anything further is that I guess I wonder how all of you as clinicians make the decision whether it's ultrasound, mammogram, MRI, whether it is six months, whether it's 12 months, whether it's for the next three years, six months. So it's more of a -- I guess you are asking the sponsor to give you more definition there, but I don't think you want medical industry companies to tell you how to do your jobs.

CHAIRMAN CEDARS: Dr. Romero.

DR. ROMERO: I would just like to follow up on the comment made by Dr. Berry concerning measurement of anxiety. I know just from sort of looking across the room that sometimes there seemed to be, I think, some maybe frustration about how that might factor into an application that is very specifically about a device with very constrained or narrow focus in terms of what it is supposed to identify clinically, or with regard to risk. But it is a very important part, I think, of the larger picture when it comes to trying to affect health and medical status.

While admittedly and probably ideally, most of the focus in these conversations and deliberations is around clinical indicators and measurements, there are innumerable psychosocial measures. If you look at the social psychological literature, there are measures out there. This is not something that needs to be created de novo. They have been validated, and a lot of psychometrics have gone into development of measures around stress, anxiety and related phenomena.

What I would suggest from a design perspective is that this is something that need not be just observed, because that is very difficult to make -- that is very difficult to have reliable measurements with one person doing the observation, much less across multiple sites.

So to the extent that sponsors in the future can look into including measures, psychosocial validated measures, and include them in the clinical design, I think that would be ideal. The fact that those measurements can be made pre- and post-test, if you will, probably would produce findings that would

favorable across the board, and I will just give one scenario.

To the extent that a woman who gets a positive scan result, to the extent that that woman might be anxious, all of us might think, well, better to know and to be able to do something about it and deal with that anxiety. But if upon follow-up it turns out that there is presumably nothing to be anxious about, and a post-test measurement would be psychosocial measures has taken place, you would probably find that many of these women would then say that they are no longer anxious.

That is something we would all be happy about, because the screening test was utilized. A risk factor was or wasn't identified, and the anxiety concern that has been expressed among members of this group would then be shown to be transient and not a longstanding concern. Then we could probably put all of that to rest.

CHAIRMAN CEDARS: Ms. Mayer.

MS. MAYER: I don't know that I have much to add that hasn't been said. I am always looking for

tools that much more specifically can find high risk populations. So I am particularly interested in the classification of tumor types that are found by this tool in terms of future research.

The stage of the tumor, the size, node involvement, and particularly to look at it in terms of the R status, 2 status -- we might find that this is particularly a good tool to identify fast growing, very highly proliferative tumors, and that might guide the design of future research.

So whereas there are other tumors that might be so slow going that, in fact, waiting until age 40 might not make a difference in terms of overall survival, that's the kind of sort of patient specific information I think we need to find out.

CHAIRMAN CEDARS: I would like to ask Nancy Brogdon if she has anything to add.

MS. BROGDON: I would just like to thank all the panel members for your time in preparing for this meeting and for the travel here, and we know that is getting increasingly difficult.

I would like to thank you for your energy

and your expertise in your evaluations today. Thank you very much, and we wish you a safe trip home.

CHAIRMAN CEDARS: And I would like to extend my thanks to the panel as well, and I would like to ask you to leave all materials specific to this product on the table.

If you have completed your questionnaire, if you could leave that as well or send it back. It was in your initial patient -- or your product folder that was mailed to you. It was in the initial product folder.

With this, this meeting of the Obstetrics and Gynecology Devices Panel is now adjourned. Thank you.

(Whereupon, the foregoing matter went off the record at 4:38 p.m.)

- - -

Deleted: ¶