Exhibit 13

UNITED STATES OF AMERICA

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FOOD AND DRUG ADMINISTRATION

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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

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RADIOLOGICAL DEVICES PANEL

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MEETING

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TUESDAY, DECEMBER 10, 2001

The Panel me t at 8:30 a.m. in the Walker/Whetstone Rooms of the Gaithersburg Holiday Inn, Two Montgomery Village Avenue, Gaithersburg, Maryland, Dr. Minesh P. Mehta, Chairman, presiding.

PRESENT:

MINESH P. MEHTA, M.D.	Chairman
HARRY K. GENANT, M.D.	Member
GEOFFREY S. IBBOTT, Ph.D.	Member
ALICIA Y. TOLEDANO, Sc.D.	Member
PRABHAKAR TRIPURANENI, M.D.	Member
EMILY F. CONANT, M.D.	Temporary Voting Member
REGINA J. HOOLEY, M.D.	Temporary Voting Member
MARILYN R. PETERS, M.N., M.P.H.	Non-Voting Consumer Representative
ERNEST L. STERN	Non-Voting

Industry
Representative

ROBERT J. DOYLE

Executive
Secretary

PRESENT FROM FDA:

NANCY BROGDON
HARRY F. BUSHAR, Ph.D.
JOHN C. MONAHAN
ROBERT A. PHILLIPS, Ph.D.
WILLIAM SACKS, Ph.D., M.D.
STANLEY STERN, Ph.D.

SPONSOR REPRESENTATIVES:

JOHN BRENNA
KARLEEN CALLAHAN, M.D.
KEVIN HUGHES, M.D.
ELIZABETH NELSON
YURI PARISKY, M.D.
STEVE RUST, Ph.D.
LYNN SATTERTHWAITE

C O N T E N T S

C O N T E N T S (CONTINUED)

mammography.

Along with that, we have approved supplements for Soft Copy Imaging for the Digital Mammography Systems.

All of the PMAs that we have have summaries of safety and effectiveness. If anybody on the Panel is interested in any of these, if you would just drop me a line or leave me a note, I will be glad to send them to you, so you can see what our basis for approval was.

Thank you. Any questions?

CHAIRMAN MEHTA: Any questions for Dr. Phillips?

(No response.)

No? Thank you, Dr. Phillips.

At this time Mr. Doyle would like to make some introductory remarks.

MR. DOYLE: Thank you, Dr. Mehta.

Pursuant to the authority granted under the Medical Devices Advisory Committee charter, dated October 27th, 1990, and as amended August 18th, 1999, I appoint the following individuals as voting members

of the Radiological Devices Panel for the meeting of December 10th, 2002. These individuals are Emily F. Conant, M.D., and Regina J. Hooley, M.D.

For the record, these individuals are special government employees and consultants to this Panel under the Medical Devices Advisory Committee. They have undergone the customary conflict-of-interest review and have reviewed the material to be considered at this meeting. This authorization is signed by David W. Feigal, Jr., Director, Center of Devices and Radiological Health.

Now for the conflict-of-interest, the following announcement addresses conflict-of-interest issues associated with the meeting and is made part of the record to preclude even the appearance of an impropriety.

To determine if any conflict existed, the agency reviewed the submitted agenda and all financial interests reported by the Committee participants. The conflict-of-interest statute prohibits special government employees from participating in matters that could affect their employer's financial

interests. However, the agency has determined that participation of certain members and consultants, the need for whose services outweighs the potential conflict-of-interest involved, is in the best interest of the government.

Therefore, waivers have been granted to Drs. Regina Hooley, Geoffrey Ibbott, and Prabhakar Tripuraneni for their interest in firms that could potentially be affected by the Panel's recommendations. The waivers allow them to participate fully in today's deliberations.

Dr. Hooley's waiver involves stockholdings valued between $25,001 to $50,000 in the parent of a competing technology manufacturer.

Dr. Ibbott's waiver involves a consulting arrangement with a competing technology firm. For this unrelated consulting services, he receives less than $10,000 a year.

Dr. Tripuraneni's waiver involves an unrelated consulting agreement with a firm that has a financial interest in a competing technology manufacturer. He receives less than $10,000 a year

for this service.

Copies of these waivers may be obtained from the agency's Freedom of Information Office, Room 12A-15 of the Parklawn Building.

We would like to note for the record that the agency took into consideration other matters regarding Drs. Ibbott, Mehta, and Tripuraneni. They reported interest in firms at issue, but in matters not related to today's agenda. The agency has determined, therefore, that they may participate fully in all discussions.

In the event that the discussion involves any other products or firms not already on the agenda for which an FDA participant has a financial interest, the participant should excuse him or herself from such involvement, and the exclusion will be noted for the record.

With respect to all other participants, we ask, in the interest of fairness, that all persons making statements or presentations disclose any current or previous financial involvement with any firm whose products they wish to comment upon.

If anyone has anything to discuss concerning these matters, please advise me now, and we will leave the room to discuss them.

(No response.)

Seeing none, I will proceed.

The FDA seeks communication with industry and the clinical community in a number of different ways. First, FDA welcomes and encourages pre-meetings with sponsors prior to all IDE and PMA submissions. This affords the sponsor an opportunity to discuss issues that could impact the review process.

Second, the FDA communicates through the use of guidance documents. Towards this end, FDA develops two kinds of guidance documents for manufacturers to follow when submitting a pre-market application.

One type is simp ly a summary of information that has historically been requested on all devices that are well-understood in order to determine substantial equivalence.

The second type of guidance document is one that develops as we learn about new technology.

The FDA welcomes and encourages the Panel and industry to provide comments concerning our guidance documents.

I would also like to remind you that the next two meetings of the Radiological Devices Panel are tentatively scheduled for February 4th and March 20th next year. You may wish to pencil these dates on your calendar, but please recognize that these dates are tentative at this time.

Thank you.

MS. BROGDON: Excuse me, Mr. Doyle. You said March 20th for the next meeting?

MR. DOYLE: May. Did I say March? Oh, excuse me. Thank you. May 20th.

CHAIRMAN MEHTA: Thank you for the correction, Nancy.

Thank you, Mr. Doyle.

The first item on our agenda today is a presentation by Dr. Stanley Stern from the Office of Surveillance and Biometrics. Dr. Stern will discuss the development of amendments to the U.S. Radiation Safety Standards for diagnostic x -ray computed tomography.

recommendation for care of all patients receiving a negative IR test result be similar to the recommendation for care of a mass that is assigned a mammographic category of 3 or a BIRADS 3. That is short-interval followup is recommended in order to establish the stability of the findings.

This is the proposed indication for use, and I would now like to turn this over to Dr. William Sacks to discuss the clinical study.

DR. SACKS: Just for those of you who don't know me, I'm a radiologist and used to be a physicist. So I have some familiarity with numbers as well.

I want to stress a number of aspe cts of the device that I will enlarge on as I go on. First of all, this is a new type of thermographic device. Secondly, it's an adjunct to mammography. Thirdly, it renders a positive or negative result, as you have seen, and that is based, as the company has explained, on an index-of-suspicion score.

It is intended for women on their way to biopsy only. It is, furthermore, intended for women

on their way to biopsy who have mammographic masses only, and the intended use is to save biopsies of lesions that turn out to be benign.

The points I am going to cover are what the BCS is and is not intended to do; how the device does it. Then I'm going to have Dr. Bushar give the clinical trial results, and I will come back and make some assessment of those results and, finally, a few labeling issues that we would like the Panel to consider.

Before I start on what the BCS is and is not intended to do, I want to make a clear distinction in the minds of the Panel between a device and its intended use. It is very important to keep that in mind as we go on. One and the same device can have a number of different intended uses, and, indeed, for any given intended use, there may be one or more devices that will satisfy that use.

We will be talking predominantly about the clinical trial. A clinical trial is always designed based to demonstrate that the particular chosen intended use of the device is safe and effective. So

it will always be an underlying issue here that we are talking about the company's intended use for this device.

Now in case any of you come here with any baggage or prejudice from the past about breast thermography, I want to make a clean break with that. Historically, it has not had the sensitivity and specificity to either replace screening mammography or to be a complementary screening test; that is, it hasn't had the sensitivity or specificity to be a screening test.

However, the BCS is a new type, as I said, of thermographic device, and it is new in two ways. One, it uses a new application of technology which lies predominantly in the cooling of the breast with the fan, and that enlarges the temperature contrast between malignant tissue and benign tissue, it is thought. The reason for that is that the benign tissue will cool, whereas the malignant is fed by angiogenesis and has a higher metabolic rate, will not cool as fast.

So that if you were to track the time

course, as this device does, over the cooling, the contrast between malignant and benign tissue would be enhanced. So that is one aspect that is new.

The second one is that it targets a different group of women from that which conventional thermography in the eighties tried to target. In the eighties the attempt was to make this a screening device that, hopefully, would replace mammography or at least work alongside it for all women screened. This device, however, targets, as you have heard, and as I myself have mentioned, a subgroup of screened women.

I've already mentioned that, that the cooling is the issue here, and the different group of women is the ones whose screening tests, mammography and/or palpation, along with other factors, indicate a need for biopsy.

So it is not intended as a screening device -- that's very important -- and it's neither, therefore, a replacement nor a complement to screening mammography, but rather as an adjunct, and, in particular, an adjunct to mammography, not to clinical

palpation, as was hoped at the time of the original protocol, but to mammography, and, indeed, only for women on their way to biopsy and only for those with mammographic masses.

Let me say a few words about the difference between a complementary test and an adjunctive test. These are somewhat confusing concepts, and adjunctive is itself probably the most confusing.

Let me say something about complementary tests to begin with. A test that's complementary to a screening test is used on all persons screened; that is, it is itself a screening test, and, therefore, its results may by themselves determine the next step in clinical management.

Complementary screening tests, therefore, are on equal footing with each other. One easy example is screening mammography and clinical examination. Women over 40 get annually, should get annually, a clinical palpation as well as screening mammography. If either one of these shows need for a biopsy, such as a palpable mass, even if it's

invisible on the mammogram, then the clinical examination will be the thing that will decide the woman's clinical management.

If, on the other hand, there is nothing to palpate, but the mammogram shows a suspicious finding, the woman will still go on and get further workup. So these two exams are complementary to each other because either one by itself can determine the next step.

Adjuncts, on the other hand, are subordinate to the index screening test; that is, the screening test to which they are adjuncts. They can be subordinate in one of two ways or both.

They are either not used on all the persons screened, and I will come back to the examples in a second, or if they are used on all the persons screened, their results do not by themselves determine the next step in clinical management. Let me give you examples of each of these.

The BCS itself is the first type. It is not used on all persons screened. However, on those on whom it is used its results do generally by

themselves, or will, or it is intended that, its results will determine the next step in clinical management; namely, whether or not the woman goes on to biopsy or not.

In a sense, it is inherent in the nature of the device, which is a black box that pops out a number, you can't make a judgment, the company has stressed. You have no -- it is not a visual issue of the image itself; the device gives you a number. So insofar as it does, you are forced to listen to the device.

Now you are not forced to do what the device tells you, but if you do, it is not a -- let me put it this way: If you have a woman that you really think needs a biopsy and you subject her to this test, and this test gives you a negative result and you decide to send her to biopsy anyway, my suggestion is, don't do the test. There's no point in having done it. You could have foreseen that ahead of time.

Another example of an adjunct of this type is the ultrasound of solid breast masses, as it is being done by a growing number of people, Stavros and

others, and so on. It is used only on a subgroup of those who go through mammography or palpation, and it may by itself determine whether the woman needs a biopsy or not, if you happen to use ultrasound in that fashion for solid masses. Extra-mammographic views are another example, and so on, and even biopsy itself.

Now the other type, the results by themselves don't determine the next step in clinical management, even if they are used on all the women screened -- and a perfect example of that is a mammography computer-assisted diagnostic system. It is used on everybody, but it is the radiologist who decides, after it points out places, "Have you looked here, here, and here," whether or not to do something about that.

So those two types of subordination, either one of those or both will throw a device into an adjunctive status.

The intended use -- and I stress it again -- the intended use, as currently intended, of the BCS is to confirm the need for biopsy or change a woman's

clinical management. If it is changed, it is to be changed from biopsy only to short-term followup, not to come back in a year for the next screen.

Thereby, it can only decrea se the number of biopsies, and in statistical language that means it can only increase the specificity. It cannot increase the detection of cancers as it is currently intended to be used and as the trial was conducted. That is, it cannot increase sensitivity.

An advantage of the particular selection of target population -- that is, only women on their way to biopsy -- is that device false positives, and I define a device false positive as a woman who has a mass that is benign but gets a BCS-positive result. It's that simple. Such device false positives have no impact on clinical management. After all, these are women who were on their way to biopsy anyway, and if you get this positive result, you will simply go on and do what was recommended in the first place. Therefore, there's no impact upon clinical management.

We would like the Panel, during the discussion this afternoon, to consider an issue as to

whether they have any concern over the potential psychological impact of a positive mammogram followed by a false positive BCS result, that is, on a woman who does not, in fact, have cancer. Let me just say a word about that.

If I were to get a mammogram based on which a recommendation that I get a biopsy was made, my main fear would not be of a biopsy procedure; it would be that I had cancer. Now I'm offered a test that says we can do one other test that may obviate the need for a biopsy, and if I get a positive result from that test, now I'm a little more convinced that I must have cancer, even though -- and it can be explained to women, and this is what we want you to discuss, whether labeling or anything like that needs to be addressed -- is your chance of having cancer zoomed from about 20 to 23 percent. I mean, you're still overwhelmingly not likely to have cancer, even though both tests were positive, but this is a subject that one of our questions will be designed to ask you to discuss.

Is the BCS an alternative to biopsy? In

80 to 85 percent of women who obtain the test, it will end up being in addition to biopsy. Only 15 to 20 percent of such women will end up not getting a biopsy in addition, at least not immediately.

How does the BCS do this? This is somewhat repetitious, but it is good to hear a little redundancy when so much information is being thrown at you.

It calculates an index-of-suspicion score for the region of interest selected by the radiologist, and the radiologist bases that selection on the mammographic location of the mass. The device then compares whatever that number is, which ranges from zero to a hundred, with the determined threshold that was determined by the company during their training set of the first 700 -- a slight detail there, but Dr. Bushar will talk about that -- but, roughly, the first 700 out of the 2,407 patients, did some training and picked the threshold of 20.59 so as to keep a very high sensitivity.

If the IOS score for this woman falls below that threshold, the device will read negative

results, and that means change her path to biopsy to short-term followup. That is very similar to the BIRADS 3 category. If the IOS score is at or above the threshold, the device output will read positive, and that means just continue with the plan to biopsy.

There is a side effect, and that is that some cancer diagnoses may be delayed, and we can talk about that.

Now I would like to have Dr. Bushar give you some of the statistics here.

DR. BUSHAR: Thank you very much, Bill.

Good morning. My name is Harry Bushar. I'm the statistician who reviewed this PMA on the computerized thermal imaging Breast Cancer System 2100. I will be doing the statistical presentation. An outline of what I will be presenting is I want to discuss the clinical study protocol, including objective design, population, demographics, and evaluation, both effectiveness and safety, and then get into the actual PMA clinical study and what was done there in terms of effectiveness and safety.

And, finally, continue to move on to

alone sensitivity, indicates exploration which requires confirmation, which requires new data. The sponsor's attempt at Bonferroni adjustment to make sense out of putting all of the data together by widening the confidence interval estimates is not statistically-acceptable.

Thank you very much for your attention. I am going to turn the podium back over to Bill Sacks to continue with the clinical.

DR. SACKS: Before I do that, I just want to make a point about safety. We have heard that there were four adverse events out of 2,400, which is a very important aspect of safety, but there are two aspects of safety for any diagnostic device. It's not peculiar to this device.

That is the accuracy of the diagnostic output of the device also involves a question of safety. So as far as the adverse events were concerned, they were very few and minor, but from the point of view of the BCS output, we should focus on safety is more closely related to the question of sensitivity; that is, on cancers or the false negative

rate. In other words, how many cancers have their diagnoses delayed? Also, in the context of the psychological impact, the false positive rate also can be regarded as a question of safety.

Effectiveness is more closely related to the specificity; that is, its performance on the benign masses, because the intent, the intended use of the device is to save biopsies of benign masses.

Now let's look at what the clinical trial demonstrated. I am going to just summarize this briefly for the history of these again.

There were four relevant clinical submissions here: the PMA, Amendments 4, 5, and 7. After reviewing the PMA, the FDA sent a letter to the company listing a number of deficiencies, and the company's response was Amendment 4.

In Amendment 4, for their conclusions concerning the effectiveness, the company retrospectively selected from the PMA data one of two analytical indices, namely, sensitivity and specificity, as opposed to ROC curve comparison, and two of three lesion types at first, masses and

architectural distortion, and not microcalcifications.

In that same amendment, however, the revised labeling further deleted architectural distortion and referred to masses alone. So that was sort of both steps were involved in Amendment 4.

The FDA sent another deficiency letter, and the response was Amendment 5. Amendment 5 was offered as a test of the device in additional subjects. That's those 275, although not all of them were evaluable, additional subjects who had not previously been analyzed. That was because Amendment 4 had contained retrospective selections.

The company refers to this additional dataset as the "post-PMA." That is PPMA for short.

This amendment confined its analysis of the PPMA data, that is, the newly-analyzed data, just to the newly-chosen analytical index, namely, sensitivity/specificity, in the newly-chosen subgroup, masses. That was done before unvaulting that data. So as far as this data is concerned, that was prospectively done.

In addition to presenting data on a new

set of subjects, the amendment also contained an analysis, as you have seen, of the combined datasets from Amendment 4 and the PPMA.

Because of the retrospective selections in Amendment 4, the FDA asked the company to justify combining that data with the PPMA data, and the response was Amendment 7.

In Amendment 7 the company applied the Bonferroni correction, as you've heard, in an attempt to compensate for retrospective selection and the smallness of the additional PPMA sample.

Now, as we go through this, there are two overriding issues. One is the adequacy of the data, and the second is the interpretation of the data. That is, do they demonstrate safety and effectiveness of the device, assuming that we accept that the data is adequate?

On the question of the adequacy, a question that we will have the Panel consider this afternoon, and before that we will give you the questions as they are phrased more precisely. This is paraphrasing. Can the data from Amendment 4

contribute to the judgment of safety and effectiveness when it consists of retrospective selections? Is a Bonferroni correction applicable in this context? Are the data from the PPMA alone adequate for the judgment of safety and effectiveness?

In looking at the interpretation of the data, it is noteworthy for the following discussion that no formal hypotheses were explicitly put forward for testing either in the PMA or in the subsequent amendments, and let me hasten to add here that, to qualify as a testable hypothesis, there must be a quantitative criterion whereby either a point estimate may imply rejection or a confidence interval may entail exclusion.

There were two implicit hypotheses. One was that the ROC area for the device and mammography combined would exceed that of mammography alone with statistical significance.

The second was -- and this was derived from the training set of 700 subjects, of whom 150 were cancers, and the sensitivity of the device -- that is, the threshold for the device was set such

that 149 of those 150 cancers were positive, with one being negative, which is a sensitivity setting of 99.3 percent. There was an implicit hypothesis that the point estimate for sensitivity would be at least 99.3 percent in at least 75 percent of simulations with the data.

The protocol otherwise contained only non-quantitative statements of what the company hoped to achieve in the clinical trial. One example, quote, "The objective of the study is to determine if the BCS, when used in conjunction with clinical examination and/or diagnostic mammography, increases the ability of physicians to differentiate benign from malignant or suspicious breast abnormalities." But there is no quantitative criterion by which we can judge success or failure on this, except through ROC area comparisons, but those were dropped.

In the original PMA submission, the comparison of ROC areas failed to achieve statistical significance except, as Harry has shown you, as an artifact of too few points in the mammography alone curve. It was, therefore, not pursued in any of the

amendments.

In addition, the sensitivities failed to achieve a level of 99.3 with 75 percent confidence in any of the datasets. Here is a diagram that shows them. I finally get to use this pointer.

This is the upper righthand corner of an ROC plot. It is about a quarter in both dimensions. Mammography alone, because of this being the universe here is women on their way to biopsy based on mammography, was 100 percent sensitive. That is just an artifact of the choice of the universe here.

It was, similarly, zero percent specific. That is, there were no non-biopsied people here.

Now the PPMA -- I'm sorry, the original PMA point estimate with 187 cancers -- this "N" is just the number of cancers -- turned out to be 97.1 percent. For reference, this line here is the 99.3 percent level that was involved in that implicit hypothesis of trying to keep it above 149 out of 150. Its confidence limits are, as you see here, 94.1 to 98.8.

The next data was Amendment 4, where out

of this set of 187 were culled the 90 masses. It is the same as -- these 90 are part of this on the 97. In those 90 we got point estimate of 100 percent sensitivity. The higher confidence bound, of course, is also 100 percent because you can't go over that, and the lower one is about 96.7.

Because of the retrospective selection of these out of this group, the next set of data in Amendment 5 was the PPMA, of which there were 15 cancers. The point estimate there was 93.3 percent because one of those turned out to be negative, so 14 out of 15.

The confidence interval on this, because the number is so small, 15, is rather wide. Interestingly, the lower confidence bound is actually below the chance line.

When the two sets of data are combined, if you think it is valid to combine these two, you get a point estimate of 99.0, which is still below the 99.3, and its lower confidence limit is about 95.6. So that sort of displays all of the data in reference to that 99.3 implicit hypothesis.

The potential safety and effectiveness in the U.S. population as a whole -- this is a bit of a busy slide, but I'll walk you through it. The percent of U.S. biopsies that are potentially obviated by the BCS, if used on all eligible women, and we've seen these figures, and mine are very close to the company's, 1.3 million U.S. women biopsied each year, of which I use the number 45 percent; the company used 45.5.

Forty-five is not only a typical figure for the country at large, but happened to be exactly the percentage in the used data combining the PMA and the PPMA; 45 percent of them were cancer. So I used that figure. That's about 585, which is very close to -- Steve Rust gave you a figure that was 591,000, very close -- of which 80 percent, roughly, are benign. That's about 468,000, of which 15 to 20 percent, using the various ranges of specificity that we got for the device, which would be 70,000 to 94,000, would be BCS-negative and, therefore, save the biopsy.

So 70,000 to 94,000 out of 1.3 million is roughly 5 to 7 percent of the 1.3 million U.S.

biopsies would be obviated. That is if the BCS were used on all 585,000 women who are eligible; namely, mammographic masses on their way to biopsy.

In addition to saving biopsies on these benign masses, approximately 1 to 6 percent of the malignant masses -- that's, again, the range from the data -- and a half to 3 percent of all breast cancers, that is, not just of masses, might be delayed in diagnosis.

A couple of labeling issues involved the size of the mass and the depth of the mass. We are going to ask you for some discussion on this this afternoon.

The size of the mass: The effect of small lesion size on device sensitivity was difficult to evaluate since only 2 out of the 105 cancers in the two combined sets were smaller than 5 millimeters. Here are the figures for how they fell. This is different from the figures that Karleen Callahan gave you, but she was including the ones that we didn't have the data for. This is just the two combined, Amendment 4 and PPMA data. Only two of the malignant

masses were less than a half a centimeter, 5 millimeters. So it is hard to make any statement about it.

With the chosen threshold, there was no definite effect of lesion depth on BCS result, but, as the mammographers here know, the effect of lesion depth is difficult to evaluate because depth is not easily gauged on the mammogram. Worse yet, we are imaging women in a position in which the breast is pendulent. It is a fairly mobile structure. Depth is variable. A given lesion has different depths in the breast, depending on the position.

Therefore, we really have difficulty from this data making any judgments or conclusions about depth. However, one should realize that, just from the physics of the situation and the physiology, that the deeper the lesion, the less effect a cancer will have on contrast of temperature on the overlying skin. So that might affect device sensitivity, but we can't make any statement about it.

Conclusions then: In summary, only 4 out of 2,407 subjects had an adverse event, all minor. In

that regard, the device seems safe.

There were no explicit, quantitative hypotheses. There were two implicit, quantitative hypotheses. Neither hypothesis was fulfilled. Most of the data was selected retrospectively. Bonferroni correction we feel is not applicable in this context, in part because there were no hypotheses; therefore, no alpha levels to protect, and so on. But if you did use the correction to widen the confidence limits with the point estimates already below the implicit hypothesis of 99.3, that doesn't help keep them above it.

Finally, using the trial results, if the BCS were in general use in the U.S., it would obviate 5 to 7 percent of the 1.3 million biopsies a year, and approximately 1 to 6 percent of these obviated biopsies would turn out to be malignant and their diagnoses would, thus, be delayed.

The people who are still awake will notice this 1 to 6 percent is not the same figure as 1 to 6 percent I gave before because one was looking at the percent of malignants that would be negative and this

is looking at the percent of negatives that would be malignant. It turns out that the diagonal members of the 2x2 table are about the same, so these figures come out to be the same, or perhaps it's not so coincidental.

Thank you.

CHAIRMAN MEHTA: I think, before we leave for lunch, I would like to remind you that the open Committee deliberations will resume at 1:00 p.m., but the Panel members are requested to be back here at 12:30 for a Panel-members-only Closed Session from 12:30 to 1:00 p.m.

(Whereupon, the foregoing matter went off the record for lunch at 12:00 noon and went back on the record in Closed Session at 12:36 p.m.)

enter into the radiology community. Through the product maturation process controlled by radiology, you brought it to where it is today.

I am just very concerned, and I share the same sentiment that Dr. Parisky did, and I thank you.

CHAIRMAN MEHTA: Any further comments from the sponsor? It is an opportunity to tell us anything additional that you might want to at this time.

(No response.)

Mr. Doyle will address the Panel.

DR. PHILLIPS: We will now move to the Panel's recommendations concerning PMA P010035.

The medical device amendments to the Federal Food, Drug, and Cosmetic Act, referred to as "the 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 pre-market approval applications, PMAs as they're often called, 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.

Safety is defined in this case, in the Act, as reasonable assurance based on valid scientific evidence that the probable benefits to health under conditions of intended use outweigh any probable risks.

And effectiveness is defined as reasonable assurance that in a significant portion of the population the use of the device for its intended uses and conditions of use, when labeled, will provide clinically-significant results.

Now your recommendation options for the vote are as follows, and there are three of these:

Approvable. That's straight approval if there are no conditions attached.

Then approvable with conditions. This Panel may recommend that the PMA may be found approvable subject to specified conditions, and these include physician or patient education, labeling changes, or further analysis of existing data. Prior to voting, all of the conditions should be discussed

by the Panel.

And the third, 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 if a reasonable assurance has not been given that the device is effective under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

If you should vote for non-approvable, the Panel will have to indicate what steps the sponsor may take to make the device approvable.

CHAIRMAN MEHTA: Would anyone on the Panel like to make a motion?

DR. TOLEDANO: I'll do it. I move for approvable subject to specified conditions. Do you want the conditions?

CHAIRMAN MEHTA: Is there a second?

(Motion seconded.)

CHAIRMAN MEHTA: Is there discussion of the main motion?

DR. CONANT: I'm still concerned that, not that there hasn't been some wonderful data and

My opinion is, my very thoughtfully-considered opinion is that, with reanalysis of the current data in an exploratory manner, and with knowledge that already exists, we can establish a high probability of effectiveness for this device.

So that's why I make the recommendation of approval subject to conditions.

CHAIRMAN MEHTA: Is there any other discussion on the main motion?

(No response.)

If not, let's proceed to vote on the main motion, which was approvable with conditions.

All those members in favor of the motion for approval with conditions raise your hands, please.

(Show of hands.)

MR. DOYLE: Three.

CHAIRMAN MEHTA: For the record, we count three.

DR. CONANT: Can we try that again after we talk about the conditions?

MR. DOYLE: No.

DR. CONANT: Okay. I just thought I would

ask.

DR. TOLEDANO: May I ask you a question of clarification?

CHAIRMAN MEHTA: Yes.

DR. TOLEDANO: Okay. In previous meetings when we have recommended approval subject to specified conditions, those specified conditions have reflected only changes in the labeling.

My understanding from what Mr. Doyle has just stated is that the conditions can include further analysis of existing data, and I just wanted to confirm that.

MR. DOYLE: That's correct.

CHAIRMAN MEHTA: I think that finishes the vote.

So is there anybody else who wants to make a different motion?

I was assuming that those who didn't raise their hands were against, but we need to clarify that that's really the case.

So all those members who are not in favor of the motion please raise your hands.

(Show of hands.)

MR. DOYLE: It's three to three. So you can see there's a tie vote, so the Chair can now vote.

(The Chair votes no.)

MR. DOYLE: Now I guess we need another motion.

CHAIRMAN MEHTA: We need a second motion at this point. Does anybody want to make a second motion?

DR. HOOLEY: I motion that the PMA is not approved because there are significant questions on the efficacy of the study and how it was performed and omissions in the clinical reality of how we work up breast masses.

CHAIRMAN MEHTA: Is there a second?

DR. CONANT: I second.

CHAIRMAN MEHTA: Is there discussion on this main motion? Go ahead, Alicia.

DR. TOLEDANO: May I discuss? One of the most difficult things that I have learned over three years being on this Panel, and previous experience with the Panel, is the difficulty of separating out

the effectiveness of a device from what happens once the device is released into market.

I think that, as we make our motions and as we make our votes, we need to be considering the device itself.

CHAIRMAN MEHTA: Any further discussion of the main motion?

(No response.)

If not, let's proceed to vote on the main motion.

All those members in favor of the motion, which is for disapproval raise your hands.

(Show of hands.)

That's three.

All those members against the motion for disapproval please raise your hands.

(Show of hands.)

That's three.

I guess I get to cast the vote for disapproval.

What we are going to do at this point is we're going to poll all the voting members for the

reasons for their recommendations, and we will also ask the industry and consumer representatives for their comments on the recommendations.

As part of your comments, specific statements regarding what it would take to obtain approval would be very useful at this point, specifically for the FDA and the company.

So perhaps we can just start at one end of the table and go around. Prabhakar, we can start at your end.

DR. TRIPURANENI: The reason I was in favor of approving with conditions is it is a relatively non-invasive machine, hardly any invasiveness. The patient comes in for ten minutes and then gone.

I think it does have its utility, and I think we have probably seen the first wave of these things. I think as the data gets finetuned a little more, as the clinicians get more experienced on the machine, the company gains more experience, I think they can finetune the data a little bit more. Perhaps presumably in the real clinic at this point somebody

will get a mammogram followed by ultrasound, and probably this IR imaging at this point in time.

So, for all those reasons, even though the data is not as clean as I would like to see, but, once again, with all the vagaries of doing a clinical trial, being a clinician, I was in favor of doing this.

Now that officially the Panel has recommended, once again I abide by the Panel's majority disposition at this point in time that this is not approvable, but I think my own bias is that the second clinical trial, if there is going to be one -- I presume there will be one -- will be take the real-life situation such as a mass, perhaps followed by ultrasound and followed by this machine in some shape or form, basically, directly going right to what to do to get the final approval to be done.

Thank you.

CHAIRMAN MEHTA: Mr. Stern, do you have comments?

MR. STERN: Had I been able to vote, I would have voted with the doctor (referring to Dr.

Tripuraneni). I believe that if some tens of thousands of women in America can be spared the psychological trauma, thanks to a negative reading with the BCS 2100, I'm for the PMA.

CHAIRMAN MEHTA: Geoff?

DR. IBBOTT: Well, I voted in favor of the first motion, but, like Dr. Tripuraneni, I'm quite comfortable with the approval of the second motion.

I have concerns, as you know, about this device. I am not concerned that any significant number of women will be injured or hurt by this device, but I do have the concerns that have been mentioned about the psychological effects of the results, but I also have the concerns that not very many women will be positively impacted by the use of the device. It is only a small number of women whose course of therapy appears likely to be changed, based on the data that have been presented.

As you know, I have concerns about the physics of the device, the reproducibility from a physics and engineering point of view, and quality assurance issues, and the concern about the procedure

that was used to set the threshold for the IOS. I think that can be done better, perhaps with the existing data, perhaps not, but it does need to be done.

DR. HOOLEY: I think that a future study should be a prospective study which better characterizes the definition of mass, whether the mass is just clinically detected by only mammography or seen with ultrasound. I think the omission of ultrasound in the characterization of masses is significant, and I think that that should be addressed in the future.

DR. CONANT: I certainly look forward to this because I think it is a promising device, and I certainly do want to cut down unnecessary biopsies. However, I am concerned that a real-life population is women with masses felt on exam, not seen mammographically. I think in the case of the data presented this was an artificial exclusion.

I think that the power with a prospective study will be very convincing, and I look forward to that data. So I am very optimistic, but I am

concerned about implementation in real life, and if this was to go out now, what it could be used for, masses, and that that is not as defined as it could be and I think should be, what a mass is.

I am also very interested in refining threshold for the IOS based on masses alone for this indication, rather than on all different lesion types, and moving forward to test that as a hypothesis.

The talk about sensitivity again confuses me because the sensitivity is 100 because our population is incoming with mammographic masses. Again, that is not reality. It goes back to the definition of a mass, and a mass on an exam, a physical exam, and I think that is a very important population to address. So the sensitivity part, I'm really looking forward to the improvement in your specificity that I think you may show us in the future.

Oh, the reproducibility of the exam which would be shown, hopefully, by inter- and intra-reader studies, I look forward to that data.

CHAIRMAN MEHTA: I think the sponsor has

done an excellent job of building what looks like an exciting device. I think they mounted a clinical trial that was very broad, which in its original design had very limited quantitative analysis built in, which I suspect in hindsight was a statistical error.

It had a variety of concerns in terms of trial design, such as, for example, the inclusion of 600 patients, and then somehow 2,400 showed up, and then we were told maybe there was supposed to be 3,000, but, sorry, there's only 2,400, but, oh, by the way, it's not 600 per institution.

Then not all data were analyzed. There were many, many exclusion criteria, and eventually a subgroup was identified where it appears that there may, in fact, be up to a 15 to 20 percent benefit in terms of potentially delaying or avoiding biopsies, or at least allowing these patients to be screened closely.

This appears to be a finding in a subset of patients. In fact, if, indeed, this device is going to benefit this group of women, then a properly-

designed clinical trial in this subset of women should be conducted to verify that this was not artificial finding as a consequence of this broad study, but a real benefit in these women.

After all, we are talking about a target population of half a million women. Before we allow a half million women to be subjected to this, let's be absolutely sure that this benefit is real. And that's the reason I voted for disapproval.

DR. TOLEDANO: So it's my turn now. I made a motion to approve subject to conditions, and those conditions, as I brought up in my request for clarification, I greatly wish I could have stated those conditions before we took the vote. Unfortunately, that's not allowed.

I did bring up something in the clarification, that the conditions could be different from the usual things that we see approval with conditions, change the labeling.

And I appreciate all the issues that have been brought up about clinical practice and I value everybody's opinions and their experience. But when I

look at this, what I see is somebody who has a product that could work, and I see data that shows that it probably does work, and the data may not have been gathered in the optimal way, and it may not have been analyzed in the optimal way, but I, honest to goodness, believe that if you go out and collect new data in the optimal way and analyze it in the optimal way, you're going to come up with the same answer.

To me, that doesn't mean sending somebody back to the drawing board. To me, that means saying I think we're going to come up with the same answer, approvable subject to conditions.

Look at your data the right way. Go through the literature. Go through your physics. Tell me what you think is going to happen. And if you can prove to me that your device is going to be effective, get your approval and do a post-market study.

So that was the reason for my motion. Unlike my esteemed colleagues, who I have really come to enjoy, I am not comfortable with the recommendation to disapprove.

DR. GENANT: I basically agree with the comments made by our Chairman. I thought that he captured my own feelings about this issue very, very well.

Perhaps, in addition, maybe I would just comment. To the sponsors, I think that you have a very exciting technology, and there are definitely great possibilities.

I think it represents a refinement and a substantial advance over earlier work that was done with thermography and that has kind of lingered under a cloud for some many years. I think you have the opportunity now in designing prospectively a study that will address the various issues that we have raised and will bring to the larger community somewhere down the road, hopefully, not too far down the road, a technology that will, in fact, bring benefit to women in this particular setting.

MS. PETERS: If I was able to vote, I would have voted for the PMA with conditions, approval of the PMA with conditions.

It is an adjunct therapy. It is not used

as screening, which would make it what I think some of that would really be necessary for. But I think with its being non-invasive, that with education and some of the additional changes in looking at the data, it would make it very good.

MR. DOYLE: Before we adjourn for the day, I would like to remind the Panel members that they are required to return all materials they were sent pertaining to the PMA itself. Of course, the list of Panel members and agendas, and so forth, you're welcome to keep.

Any materials you have with you may be left at your table. Any others that you may not have brought, you can send back to me at the FDA as soon as possible. Thank you.

CHAIRMAN MEHTA: At this point I would like to thank the speakers and the members of the Panel for their preparation and participation in this meeting.

I would also like to thank the sponsors for being here to present the data to us, and to all the members for attending.

Since there is no further business, I would like to adjourn this meeting of the Radiological Devices Panel. Thank you.

(Whereupon, the Committee was adjourned at 3:35 p.m.)