

1 DR. CHANG: I reiterate previous
2 discussions that complications presented and listed
3 rigorously pursued are due to the device, patients'
4 response to the implant, as well as surgical
5 technique, and the data shows that these implants are
6 reasonably safe and effective.

7 CHAIRMAN WHALEN: Thank you.

8 Dr. Burkhardt.

9 DR. BURKHARDT: Yes on both counts. I
10 would also say that the deflation rate that is
11 recorded here is almost certainly biased in the form
12 of being too high because patients who have deflation
13 are much more likely to return to the operating
14 surgeon.

15 CHAIRMAN WHALEN: Thank you.

16 Dr. Bandeen-Roche.

17 DR. BANDEEN-ROCHE: You can pretty much
18 duplicate my comments from yesterday. Let me say that
19 the study in term -- I had to weigh the study with the
20 other evidence. The study has very, very many well
21 done points, but some substantial limitations
22 including no randomization, a lot of loss to follow-

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1 up, and no control group.

2 What I can come down on is I would repeat
3 that given everything together, I think there's a
4 reasonable assurance of safety in terms of drastic
5 events.

6 Limited effectiveness in terms of increase
7 in body size and aspects of body image. The
8 improvements in self-esteem were significant, but not
9 very large.

10 And finally, the troubling area is in
11 complications and events that I don't know where to
12 place relative to safety or effectiveness. The
13 epidemiologic long term data is weakest in this area,
14 and so I would certainly qualify my -- I think that
15 adequately qualifies my response.

16 CHAIRMAN WHALEN: Thank you.

17 Dr. Boykin.

18 DR. BOYKIN: Yes. I believe it's
19 reasonably safe and effective.

20 CHAIRMAN WHALEN: Thank you.

21 Dr. Blumenstein.

22 DR. BLUMENSTEIN: Effective, safety --

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1 safe, provided the characterization of risks and
2 sorting out all of the events and so on can be done
3 appropriately.

4 CHAIRMAN WHALEN: Thank you.

5 Dr. Li.

6 DR. LI: I'll defer to my statistician
7 colleagues for the effectiveness answer, and I'll go
8 -- I'll answer safe on two conditions, one, that the
9 surgeons would agree that the leakage and rupture rate
10 is one that they believe is a reasonably acceptable
11 level, and two, that the manufacturers' testing, once
12 it's complete, will preclude or identify or insure
13 that there isn't a size or thickness or design
14 dependence on the final mechanical testing.

15 CHAIRMAN WHALEN: Thank you.

16 Dr. Witten, in regard to question number
17 two, as it relates to augmentation patients, the
18 consensus of the panel is within the definition of
19 reasonably safe and effective come to agreement that
20 it is, indeed, reasonably safe and effective with some
21 editorial caveats perhaps being added that the
22 effectiveness as it was studied and designed is

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1 perhaps not quite as good as it may have been, and in
2 regard to safety, encapsulating all of the comments we
3 have made about complications, events, "bad things,"
4 that that be taken into account.

5 Does that answer FDA's question?

6 DR. WITTEN: Thank you.

7 CHAIRMAN WHALEN: Thank you.

8 Question number three, as projected is the
9 same question as number two, but for the population of
10 reconstruction patients rather than augmentation
11 patients.

12 And, Ms. Brinkman, if you would please
13 being.

14 MS. BRINKMAN: I think my comments will be
15 the same as for augmentation. The sad part of all of
16 this is that the number of patients that are used for
17 reconstruction to study and then the large number of
18 patients lost to follow-up gives us smaller sample
19 sizes than I would like to see, I suppose than all of
20 us would like to see.

21 Again, to look at the statistics for
22 complications and rupture rates are of concern. I

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1 think that, again, we'll look at that; that patient --
2 in labeling, that physicians and patients certainly
3 need to know all of those things.

4 As far as effectiveness goes, again, it's
5 a real concern, and I said this yesterday, that we
6 look at these perceptual measures, and effectiveness,
7 if you had -- if I had an implant and I had it for a
8 reason to change the size of the breast and it
9 deflated, I don't think I would consider it very
10 effective.

11 CHAIRMAN WHALEN: Dr. Robinson.

12 DR. ROBINSON: The effective, yes;
13 reasonably safe, yes.

14 CHAIRMAN WHALEN: Ms. Dubler.

15 MS. DUBLER: Yes on both.

16 CHAIRMAN WHALEN: Dr. Morykwas.

17 DR. MORYKWAS: Yes, on both.

18 CHAIRMAN WHALEN: Dr. Chang.

19 DR. CHANG: It's reasonably safe and
20 effective.

21 CHAIRMAN WHALEN: Dr. Burkhardt.

22 DR. BURKHARDT: Yes on both counts.

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1 CHAIRMAN WHALEN: Dr. Bandeen-Roche.

2 DR. BANDEEN-ROCHE: Same comments for
3 augmentation, except that I would say that for
4 effectiveness with the exception that many patients
5 seem to be satisfied, the other aspects of
6 effectiveness were not well demonstrated by the data
7 in the PMA.

8 CHAIRMAN WHALEN: Dr. Boykin.

9 DR. BOYKIN: Yes on both.

10 CHAIRMAN WHALEN: Dr. Blumenstein.

11 DR. BLUMENSTEIN: Same comments as the
12 previous question.

13 CHAIRMAN WHALEN: Dr. Li.

14 DR. LI: Same comments on the previous
15 question, although I would encourage the sponsor that
16 if there is a higher incidence of deflation in this
17 particular patient group, that they should try to
18 understand that from a more biomechanical and
19 engineering and stress and material standpoint.

20 CHAIRMAN WHALEN: Thank you.

21 Ms. Domecus.

22 MS. DOMECUS: Yes on both.

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1 CHAIRMAN WHALEN: Dr. Witten, in regard to
2 question number three as regards reasonable safety and
3 effectiveness for the population of reconstruction
4 patients, it is the consensus of the panel that the
5 caveats pretty much as were entered for the prior
6 question, that indeed the answer is yes to both
7 points.

8 DR. WITTEN: Thank you.

9 CHAIRMAN WHALEN: Thank you.

10 Moving then to question number four, as
11 projected and due to its length I won't necessarily
12 read the entire question, but this has to do with the
13 population of patients who represent for revision and
14 evaluating safety and effectiveness in regard to that
15 population and should there be data collected in a
16 post approval study.

17 Dr. Robinson.

18 DR. ROBINSON: I can't imagine why
19 something that's acceptable for augmentation and
20 reconstruction would not be acceptable for revision.
21 So my answer would be it is acceptable.

22 And addressing the question whether the

1 sponsor should evaluate the safety and effectiveness
2 of this as a condition of approval, I would say no.

3 CHAIRMAN WHALEN: Ms. Dubler?

4 MS. DUBLER: I would agree it shouldn't be
5 a condition of approval, and what puzzles me about
6 this is that the data are so misleading. If
7 reconstruction usually is a two part process, then the
8 data should reflect that. Then that second part is
9 not a revision. It's what was anticipated, and it's
10 a very -- it's not useful to have the data collected
11 and reported in the way they are now, and I don't know
12 if that's an FDA problem or a sponsor problem, but it
13 would certainly be more helpful to think about it in
14 that other way.

15 I think given that, I think data would be
16 useful, but it isn't a condition of approval.

17 CHAIRMAN WHALEN: Thank you.

18 Dr. Morykwas.

19 DR. MORYKWAS: Well, I agree that the data
20 would be useful, but it's not required.

21 CHAIRMAN WHALEN: Dr. Chang.

22 DR. CHANG: My answer is no to the

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1 question should they be required to -- should this be
2 a condition of approval.

3 CHAIRMAN WHALEN: Thank you.

4 Dr. Burkhardt.

5 DR. BURKHARDT: No. Further investigation
6 on this line should not be a condition for approval,
7 and furthermore, I'm not sure that this is even an
8 appropriate category for indication, as an indication
9 for use. I think that it should be dropped.

10 CHAIRMAN WHALEN: Thank you.

11 Dr. Bandeen-Roche.

12 DR. BANDEEN-ROCHE: Yeah, I think I agree
13 with my colleague, Dr. Burkhardt. I think it would be
14 useful to collect post follow-up data to give better
15 information to patients about what to expect.

16 CHAIRMAN WHALEN: Dr. Boykin.

17 DR. BOYKIN: I agree.

18 CHAIRMAN WHALEN: Dr. Blumenstein.

19 DR. BLUMENSTEIN: I concur.

20 CHAIRMAN WHALEN: Dr. Li.

21 DR. LI: Concur^{**}.

22 CHAIRMAN WHALEN: Ms. Domecus.

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1 MS. DOMECUS: I don't think it should be
2 a preapproval requirement. I think it would be useful
3 in a post approval setting to understand that the
4 complication rates are higher or lower for a second
5 operation so that can be provided to patients.

6 CHAIRMAN WHALEN: Ms. Brinkman.

7 MS. BRINKMAN: Agreed.

8 CHAIRMAN WHALEN: Dr. Witten, in regard to
9 question number four, the panel feels that this should
10 not be a condition that such data be collected, a
11 condition for approval should approval be recommended,
12 and that furthermore, surprise, surprise, a bunch of
13 academics feel such data might be useful.

14 (Laughter.)

15 DR. WITTEN: Thank you for that message.

16 CHAIRMAN WHALEN: Question number five,
17 with its three subcomponents, has to do with the
18 increasing cumulative rates for a complication for
19 both populations of patients, and we are asked to
20 address regarding those three subpoints what minimal
21 duration of follow-up, ^{**}type of visit, active or
22 passive, and which types of complications should be

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1 assessed, and we begin with Ms. Dubler.

2 MS. DUBLER: I'll use this opportunity to
3 make a comment on what has frustrated me throughout
4 yesterday and today, which is it seems impossible to
5 determine, given the way we're presently framing
6 questions whether it is the device or the surgical
7 technique that lies at the heart of some of these
8 complications and problems, and I think that's just a
9 critical issue to begin to get a handle on.

10 I think in terms of the long term adverse
11 effects we ought to follow up for as long as we can
12 until we see some improvement. I'm especially
13 concerned as others are with the leakage and the
14 deflation, and it seems that the sponsor is interested
15 and focused on those issues, and I would hope that
16 some data would emerge over the follow-up that would
17 give us some sense of how the improvement of technique
18 or of the device itself might help the patients in
19 whom it's implanted.

20 I think active visits are always better if
21 we can do it, and I think the ^{**} complications should be
22 assessed are by and large the ones we've noted, but

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1 only the ones that are really complications: the
2 second scheduled visit to the surgeon for
3 reconstruction is not, I think, a complication, and
4 it's misleading to label it in that way.

5 CHAIRMAN WHALEN: Dr. Morykwas.

6 DR. MORYKWAS: Well, for Part A, I think
7 the ten year follow-up is recommended before should be
8 followed, again, an active visit whenever possible is
9 the best, but realistically there's not a real
10 probability, although I think now with the Internet
11 and the ability to track some people and do searches,
12 phone tracking of some of these patients or phone
13 interviews of some of these patients might be possible
14 especially as the technology increases.

15 And I'll agree with Ms. Dubler that for
16 the type of complications that should be assessed,
17 they really should be the complications, just not the
18 nipple reconstructions and tatoosings and some of the
19 other items that currently are listed as
20 complications.

21 CHAIRMAN WHALEN: Dr. Chang.

22 DR. CHANG: Ten year follow-up is

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1 recommended. Passive; active, if possible, and the
2 four that were examined in the LST study, infection,
3 capsular contracture, severe, failure of device, and
4 decisions for explant, I believe.

5 CHAIRMAN WHALEN: Thank you.

6 Dr. Burkhardt.

7 DR. BURKHARDT: I believe that a five year
8 follow-up on the current studies is entirely adequate.

9 CHAIRMAN WHALEN: Thank you.

10 Dr. Bandeen-Roche.

11 DR. BANDEEN-ROCHE: I believe that a
12 longer term follow-up is necessary to try to
13 characterize some of these events that are not
14 leveling out sufficiently over time.

15 I would agree with the other people on the
16 panel who said, you know, active if possible, passive
17 if that's what's is feasible, but I think it's worth
18 thinking about for the future, for post market
19 surveillance, designing a system to do our best job of
20 identifying people and not losing them to follow-up.

21 I don't know ^{**} what that would be, whether
22 it would be a registry system or what have you, but

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1 it's worth thinking about.

2 CHAIRMAN WHALEN: Dr. Boykin.

3 DR. BOYKIN: I would also encourage the
4 ten year follow-up if at all possible. I think the
5 active visit should be encouraged. This may not be
6 realistic for the long term, and the complications, as
7 Dr. Chang mentioned, I think, would capsulize it.

8 CHAIRMAN WHALEN: Dr. Blumenstein.

9 DR. BLUMENSTEIN: I concur.

10 CHAIRMAN WHALEN: Dr. Li?

11 DR. LI: I concur also with the -- I'm not
12 sure where to add this. So I'll just throw this out
13 now and you can decide where it should go.

14 One thing I think is missing, I guess,
15 from my particular interest, is that as leakage and
16 deflation are one of the key reasons for bad things,
17 Dr. Blumenstein, that I'm surprised that that isn't
18 tracked in the database somehow, for instance, like
19 the model or the volume or the size or the placement.

20 That kind of information should be readily
21 available when someone comes in for a deflation or
22 rupture, and should be tracked and probably is going

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1 to be the start of the only way we're going to find
2 out this is a device related complication or if it's
3 surgical, it would be a step in the right direction.

4 CHAIRMAN WHALEN: Ms. Domecus.

5 MS. DOMECUS: I don't think any of this
6 should be a preapproval requirement. Post approval,
7 I think it should be ten year follow-up, active or
8 passive, and I think all complications should be
9 followed.

10 CHAIRMAN WHALEN: Ms. Brinkman.

11 MS. BRINKMAN: I agree that there needs to
12 be a ten year follow-up. Obviously active is much
13 better. I would like to see some sort of post market
14 surveillance. I would love to see the FDA take some
15 sort of lead in a national registry of some type.

16 Obviously only complications that are true
17 complications should be assessed. It interests me in
18 the fact that pain has been brought up a number of
19 times, and although I believe that sometime that's
20 difficult to measure, we do measure it, and I'd like
21 to see that talked about in follow-up studies.

22 CHAIRMAN WHALEN: Dr. Robinson.

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1 DR. ROBINSON: Maxine stole all of my
2 comments. We apparently agreed yesterday ten years
3 was the appropriate amount of follow-up. I'm still
4 skeptical and myself would vote for a minimum of five.

5 Type of visit, as yesterday, I would hope
6 would be active if possible and would re-echo what
7 several people have said. I think the only answer
8 really is a transplant -- I mean an implant registry.

9 The third thing, the complications.
10 Again, to re-echo, being the last in line here, they
11 have to be redefined as to what really is a
12 complication, and the complications with these
13 implants appear to be local. So they should be local
14 complications assessed.

15 CHAIRMAN WHALEN: Thank you.

16 Dr. Witten, in regard to question number
17 five, it is the majority opinion of the panel that
18 there be a ten year follow-up with a minority opinion
19 suggesting five might be sufficient. Clearly it is
20 the desire of the panel that active follow-up be the
21 means employed. However, ^{**}there's acknowledgement
22 pragmatically this may not be able to be achieved, and

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1 so passive should be as a back-up at the least.

2 And in regards to complications, they,
3 indeed, should be followed, defined by the
4 sophisticated Chicago statistical terminology of "bad
5 things," which might best be defined by the four that
6 were in the LST study.

7 DR. WITTEN: thank you.

8 CHAIRMAN WHALEN: Thank you.

9 Going to question number six, this deals
10 with three issues that were not part of the sponsor's
11 study design to answer and whether or not we should
12 make conditions of approval any one of these three,
13 and they have to deal with interference of the ability
14 of treating mammography to detect cancer in women with
15 implants; interference with lactation; and any effects
16 there may be upon offspring of women with implants.

17 Beginning on these three points with Dr.
18 Morykwas.

19 DR. MORYKWAS: Well, we did have limited
20 discussion today just on the interference with
21 lactation and did not discuss the other two items, but
22 I believe all of the PMAs are supposed to say

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1 separately some of our discussions, I guess can come
2 into our scientific expertise from yesterday, and I
3 would just say that, no, they should not be a
4 condition of approval for further studies.

5 CHAIRMAN WHALEN: Dr. Chang.

6 DR. CHANG: The first item, I think, is
7 best deal with labelings. My answer is no.

8 CHAIRMAN WHALEN: And the other two?

9 DR. CHANG: Global answer is no.

10 CHAIRMAN WHALEN: Oh. Sorry. Thank you.

11 Dr. Burkhardt.

12 DR. BURKHARDT: I think further
13 quantification on these issues is unnecessary.

14 CHAIRMAN WHALEN: Thank you.

15 Dr. Bandeen-Roche.

16 DR. BANDEEN-ROCHE: No, there should not
17 be a condition. Further surveillance for problems in
18 these areas is recommended.

19 CHAIRMAN WHALEN: Dr. Boykin.

20 DR. BOYKIN: I would say not.

21 CHAIRMAN WHALEN: Dr. Blumenstein.

22 DR. BLUMENSTEIN: Not as a condition of

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1 approval, but I would encourage the use of novel
2 mechanisms to collect these data, not necessarily
3 under the sponsor, but the FDA maybe working with the
4 sponsor, possible use of insurance providers and
5 managed care databases.

6 CHAIRMAN WHALEN: Dr. Li.

7 DR. LI: I'll defer to my colleagues.

8 CHAIRMAN WHALEN: Ms. Domecus.

9 MS. DOMECUS: No to all three as a
10 condition of approval. I think number three should be
11 studied post approval, and I just want to clarify my
12 comments. Yesterday when we talked about this, I
13 thought we were talking about post approval. So I
14 didn't mean to imply this number three should be done
15 pre-approval.

16 CHAIRMAN WHALEN: Ms. Brinkman.

17 MS. BRINKMAN: Not as a condition of
18 approval, but I do believe there needs to be ongoing
19 data collection in all of these areas.

20 CHAIRMAN WHALEN: Dr. Robinson.

21 DR. ROBINSON: No, no, and no, other than
22 there needs to be in the consent process strong,

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1 definitive wording about the potential problems in the
2 small number of patients with mammography and how to
3 resolve it.

4 CHAIRMAN WHALEN: And Ms. Dubler.

5 MS. DUBLER: No, they should not be
6 conditions of approval, but I would like actually all
7 of these issues raised in the consent process to draw
8 women's attention to the fact that there are concerns
9 for some people on some levels.

10 CHAIRMAN WHALEN: Thank you.

11 Dr. Witten, in regard to question number
12 six, the panel is unanimous in not feeling that any of
13 these issues need to be a condition for approval,
14 should that be decided upon.

15 However, that is not to diminish the
16 importance of any of these issues, and all need to be
17 taken into account as regards consent issues,
18 potentially labeling issues, and it would be desirable
19 to accumulate data upon them.

20 Does that answer the question?

21 DR. WITTEN: Thank you.

22 CHAIRMAN WHALEN: And the final question,

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1 again, as last night -- seems like just a few hours
2 ago -- we will not go around the entire table, but
3 we'll solicit opinions about it, and this has to do
4 with implications for what the sponsor need do in
5 terms of physician training.

6 Ms. Dubler.

7 MS. DUBLER: This actually lets me raise
8 a point that became irrelevant, but interests me a
9 lot, and that is the sales reps. If we're talking
10 about all the people who participate in the discussion
11 of information and the shading of information and the
12 spin on information, my guess is that the sales reps.
13 are up there as players.

14 I'm very concerned that dealing with
15 surgeons is like herding cats, but I think that's just
16 simply an unacceptable place to stop. It may be like
17 herding cats, and we may have to cage a cat now or
18 then. I'm not sure what the right metaphor is, but it
19 seems clear that surgical practice has an enormous
20 effect on whether these are safe and effective.

21 And, therefore^{**}, I would think that the
22 sponsor, perhaps with the help of the FDA, all people,

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1 all sponsors, all companies that make these have to be
2 very clear to women who are choosing a procedure that
3 surgical technique is very important, and I'm not
4 sure, again, what role these sales reps. play, and my
5 guess is that their discourse departs from the written
6 word.

7 And, therefore, there's a mythology about
8 how these things work, which goes in addition to the
9 data that describes how they work, and I don't know
10 what to do with that, but it interests me as a
11 problem.

12 CHAIRMAN WHALEN: Thank you.

13 DR. BURKHARDT: I'll comment on that.
14 Surgeons are used to spin from representatives. It's
15 part of the business, and we understand it.

16 My greatest concern is not the spin that
17 is directed at the surgeons, but the spin that is
18 directed at the potential final user, in other words,
19 the pre-augmentation patient who does not have a frame
20 of reference with which to judge it.

21 CHAIRMAN WHALEN: Dr. Blumenstein.

22 DR. BLUMENSTEIN: I wonder. The concern

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1 about the sales force is, I think, a good one. I'm
2 wondering if the sales force might be tempted to
3 market these devices to people who aren't qualified in
4 order to --

5 CHAIRMAN WHALEN: Dr. Witten?

6 DR. WITTEN: I think these are important
7 issues, but I think the question at hand is really
8 whether or not there's data in the PMA that tells us
9 something about, you know, what kind of instruction
10 should be provided at the surgeons that would optimize
11 the use of these products.

12 So although I think, I mean, these are
13 useful concerns, but I don't want to go into a
14 discussion right now about, you know, their marketing.
15 What we want to focus on is assessment of the product.

16 So I'd like to know if someone has a
17 comment about the state of that.

18 DR. CHANG: Well, I would say one of the
19 useful information that we received were Dr. Leroy
20 Young's comments regarding multifactorial causes of
21 capsular contracture, and there are specific
22 techniques that are more perhaps important, better

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1 disseminated during residency training, but there will
2 be physicians other than plastic surgeons who are
3 putting these devices in, and so part of education may
4 be in physician's letter or the package insert note to
5 the physician, whoever that person might be, other
6 than a plastic surgeon to try to minimize the
7 potential side effects, to minimize formation of
8 capsular contracture.

9 So my comment directly to this regarding
10 the sponsor is consideration of that kind of education
11 for those who would not have the benefit of a plastic
12 surgery residency training in trying to minimize
13 capsular contracture.

14 And, yes, there will be many non-plastic
15 surgeon physicians putting these devices in.

16 CHAIRMAN WHALEN: Dr. Witten, in regard to
17 the issue at hand in question number seven, there is
18 clear concern among panel members in view of the data
19 that was presented to us that there are factors
20 inherent in the complications or bad things that
21 result from some of these insertions that relate more
22 to the physician than inserts and how that physician

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1 inserts than necessarily to the actual manufactured
2 device.

3 And in that regard, there is a general
4 sense of concern and perhaps there should be an effort
5 in conjunction between FDA and sponsor to improve the
6 educational process for the physicians who are to
7 insert these things.

8 DR. WITTEN: Thank you.

9 CHAIRMAN WHALEN: Thank you.

10 Having completed the FDA questions, we
11 will now proceed to the second open public hearing.

12 All persons who address the panel are
13 asked to speak clearly into the microphone as the
14 transcriptionist is dependent upon this means of
15 providing an accurate record of this meeting.

16 The instructions from the morning still
17 apply as regard to remembering to disclose if anyone
18 is paying for your trip or accommodations; if you have
19 any financial ties to industry or health professional
20 societies. We would also have you disclose whether
21 you're a witness or party to any lawsuits related to
22 breast implants or whether you derive any of your

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1 income from medical procedures involving breast
2 implants or symptoms attributed to breast implants.

3 Speakers in this session have been pre-
4 informed that they have ten minutes each, and in this
5 session we only have time for scheduled speakers. The
6 first speaker is Dr. Patricia Lieberman.

7 DR. LIEBERMAN: Hi. I'm going to help you
8 out by not taking my full ten minutes.

9 My name is Dr. Patricia Lieberman. I'm a
10 staff scientist at the National Center for Policy
11 Research for Women and Families.

12 My answer to the four questions is no.

13 Members of the advisory panel, yesterday
14 you expressed strong concerns about the high
15 complication rate in the Mentor PMA. Today's PMA
16 shows even worse problems. As a person who believes
17 in the mission of the FDA and feels strongly that the
18 public deserves an FDA that protects its interest, my
19 one message to you is that you should make a decision
20 based on the science and on the understandable science
21 that's presented to you.

22 McGhan presented preliminary four year

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1 data that looks appreciably worse than the data at
2 three years. The presenter explained that the numbers
3 would likely decline when the data set was completed,
4 but what evidence is there that outcomes, such as
5 capsular contracture, leakage and deflation,
6 replacement or removal, would level off after three
7 years?

8 Indeed, these effects have not leveled
9 off. There is every reason to think that they would
10 continue to increase.

11 It seems to me that the FDA would never be
12 taken seriously again if they approved a device with
13 a complication rate that's steadily increased every
14 year and reaches 60 percent for augmentation patients
15 and 84 percent for reconstruction patients by the
16 fourth year.

17 And the finding that revision patients
18 experience similarly high complication rates only two
19 years after the revision surgery compared to the four
20 years in the previous study is also troubling. What
21 will those numbers look like at four years and beyond?

22 When we talk about giving patients

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1 informed consents, how do these complication rates
2 gibe with the one to two percent yearly failure rate
3 that Dr. Spears and other doctors present to their
4 patients?

5 The high dropout rate would likely
6 underestimate the rate of complications because women
7 who have problems may seek help elsewhere. It's been
8 our experience that women who are displeased are less
9 likely to return to their doctor, especially if their
10 doctor tells them that the problem is not related to
11 their implants.

12 Just as important are the proportion of
13 women reporting pain which should be unacceptable to
14 you. If a woman has been in pain for four months,
15 it's possible that she shouldn't be included as a
16 complication. Unfortunately, she could have one, two
17 or even ten complications subsequent to that reporting
18 of pain after that, and with this data analysis we
19 would have no way of knowing.

20 All complication rates increase over time.
21 They are not stable. New problems are occurring.
22 Look at pain. It increases over time. It doesn't

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1 stabilize after one month or even one year.

2 Yesterday one of the panel members
3 suggested that safety could be defined as not causing
4 death. I don't think that's an appropriate standard
5 for these devices. While we are concerned that breast
6 cancer patients should have choices whenever possible,
7 I do not believe that breast cancer patients need to
8 have the choice of different manufacturers of saline
9 implants. If none of the data are reassuring and
10 truly prove safety, it would be helpful to guide
11 consumers by only allowing the safest ones to remain
12 on the market.

13 If McGhan wants to continue to sell these
14 products, they should improve it.

15 One additional note. Yesterday many of
16 you expressed the desire that additional research be
17 required before approving the Mentor implants. There
18 are precedents for that, most notably silicone gel
19 implants.

20 Before the FDA decided to restrict
21 silicone gel implants because of their high failure
22 rate and lack of safety data, it had decided to allow

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1 the implants to remain on the market while the
2 manufacturer conducted additional studies.

3 Yesterday Celia Witten implied that this
4 was not an option to you, but she was apparently
5 mistaken.

6 That being said, I do not believe this is
7 the appropriate choice here. The McGhan device should
8 not remain on the market. They are harming women.

9 Thank you very much for this opportunity
10 to provide testimony.

11 CHAIRMAN WHALEN: Thank you.

12 Just so everyone in the room knows, there
13 are going to be two more speakers who have up to ten
14 minutes each. There will then be time for summations
15 by FDA and the sponsor maximally ten minutes each,
16 which FDA probably may not utilize, but I'm sure the
17 sponsor will, and we will then vote before we break
18 for lunch.

19 DR. BANDEEN-ROCHE: Dr. Whalen, could I
20 please make a comment first that directly addresses
21 what the first -- what this speaker just said?

22 CHAIRMAN WHALEN: All right.

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1 DR. BANDEEN-ROCHE: Very, very briefly.

2 CHAIRMAN WHALEN: Okay.

3 DR. BANDEEN-ROCHE: I would just like to
4 say the speaker was referring to me. I believe that
5 the context and the intent of my statement was grossly
6 mischaracterized by what was just said, and it's also
7 inaccurate because both death and systemic
8 complications, including CTDs, et cetera, was included
9 in my initial characterization.

10 But I believe that the spirit of my
11 comments, whether I technically divided them into
12 safety and efficacy, was not at all consistent with
13 the comment that was just made.

14 CHAIRMAN WHALEN: Thank you.

15 The next identified speaker is Dr. Harold
16 J. Brandon from Washington University.

17 Dr. Brandon.

18 DR. BRANDON: Mr. Chairman, members of the
19 panel, ladies and gentlemen, my name is Harry Brandon,
20 and my background is mechanical engineering. I'm an
21 associate research professor in plastic surgery and
22 mechanical engineering.

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1 All of my travel expenses, except laundry
2 and dry cleaning, will be paid for by the Breast
3 Implant Research Fund established at Washington
4 University. I will pay my own cleaning and dry
5 cleaning.

6 Part of my salary is also established from
7 our gift fund to investigate breast implants.

8 Dow Corning has contributed unrestricted
9 gifts to our gift fund. I also have a PSEF grant to
10 study failure mechanisms of breast implants.

11 My answer to questions three and four is
12 no.

13 This morning we'll consider an analysis of
14 some breast implants from the Washington University
15 Implant Retrieval Program. Our studies conducted in
16 our breast implant research project, which is part of
17 plastic surgery research and supported by plastic
18 surgery, mechanical engineering, and materials
19 research lab, chemistry and earth and planetary
20 science.

21 We have over 1,000 breast implants in our
22 inventory made by all of the major manufacturers.

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1 About 20 percent are saline implants. The implants
2 range -- the explants, rather, have implantation times
3 which range from a few months to 32 years.

4 A few of the pertinent objects relative to
5 this study determine the changes that occur in the
6 properties of breast implants as a function of
7 implantation time, and to determine the factors and
8 mechanisms that contribute to breast implant failure.

9 To help us answer these questions, we are
10 conducting a series of analyses and experiments on
11 controls and explants.

12 Here are some of the implant shell
13 properties we measure. To conserve time we'll only
14 consider a few of these properties. I'll start off by
15 reviewing some of the data related to silicone gel
16 explants, to demonstrate material durability and
17 variability due to different types of implants.

18 We have found that the strength
19 characteristics of silicone gel breast implant shells
20 can vary considerably according to implant type and
21 lot to lot variability. For example, for a SILASTIC
22 I control shell made by Dow Corning, the strength can

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1 vary by a factor of three, from 356 to 1080 psi, and
2 the range in strength from a minimum SILASTIC I
3 control to a maximum SILASTIC II can vary by a factor
4 of five.

5 The importance of these data is that to
6 quantify the effect of implantation on an explant, one
7 needs to compare an explant with a lot managed control
8 or the control range of the same type of implant. So
9 that's the message.

10 This figure gives us the tensile strength
11 of all SILASTIC I implant shells as a function of
12 implantation time that have been published in the
13 literature to date. We have 15 controls plotted at
14 time zero and 60 explants with implantation times out
15 to 28 years.

16 These studies were conducted at five
17 different research facilities.

18 There's a lot of scatter in the data.
19 However, the explant data fall within the range of the
20 control. The scatter is primarily associated with the
21 lot to lot variability and different testing
22 techniques.

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1 Statistically speaking, there is no
2 significant change or degradation of the properties as
3 a function of implantation time out to 28 years of
4 implantation.

5 This figure gives us the tensile strength
6 for all published data related to SILASTIC II implant
7 shells. We have -- the longest implantation time for
8 SILASTIC II is about 13 years.

9 We have 53 controls of 34 explants, the
10 data again obtained at five different research
11 facilities.

12 I might add that for the SILASTIC I about
13 half of the explants were intact. The other tact
14 failed. For these, the newer generation, 30 of the 34
15 were intact. We have found no difference in the shell
16 strengths or the implant properties as a function of
17 whether or not the implant was intact or failed.

18 Again --

19 DR. BURKHARDT: I'm sorry to interrupt.
20 These are gel filled implants?

21 DR. BRANDON: ^{**} These are gel filled,
22 SILASTIC I and SILASTIC II, yes. These behave

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1 differently. SILASTIC II behaved differently in that
2 there is an initial decrease in the properties
3 associated with the implantation process, and after
4 that, from a statistical standpoint there's no
5 effective long term implantation.

6 Now we'll look at the saline control and
7 explant shells which we've tested. We'll have four
8 different manufacturers: Simaplast, Heyer-Schulte,
9 Mentor, and McGhan.

10 The implantation times range from 5.5
11 years out to 23 years. We had only one Simaplast
12 explant in our inventory. It was intact. For the
13 remaining three manufacturers, we chose explants that
14 had the longest implantation times of those we've
15 tested so far.

16 Also for each manufacturer one of the
17 explants was chosen as failed and the other as intact.

18 We've only tested a limited number of
19 controls. The controls that we have shown here give
20 the strength range in the controls for all of the
21 controls we've tested thus far.

22 This is a Simaplast explant. It was

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1 manufactured in France. It has 23 years of
2 implantation time. It was intact. We believe it's
3 the longest explant -- it's the explant that has the
4 longest implantation time of any saline implant that
5 is being tested and analyzed.

6 There is a Heyer-Schulte explant. It had
7 22 years of implantation and was intact on
8 implantation -- on explantation, rather. This, we
9 believe, has the longest implantation time of any
10 saline implant manufactured in the United States.

11 And last, we have an intact McGhan implant
12 with six years of implantation.

13 This figure summarizes the tensile
14 strength data for all of the explants and controls,
15 and I'll explain this busy plot. We have data for the
16 four manufacturers, Simplast, Heyer-Schulte, Mentor,
17 and McGhan.

18 The boxes give the range and the strength
19 of the data from the minimum value we've measured to
20 the maximum value. The open boxes give the control
21 data and the cross-hatched boxes give the explant
22 data.

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1 To really qualitatively explain the
2 difference, we can do this because -- well, no, let me
3 reverse that a little bit.

4 In order to quantitatively explain the
5 effect of implantation, we need to compare an explant
6 with a lot match control, as I said, or the expected
7 range in the controls. We don't think we can do that
8 with our data.

9 We can, however, make a qualitative
10 assessment in comparing the controls and the explants,
11 and based on that type of a comparison, the explant
12 data for the Heyer-Schulte implants fall below the
13 control data. The explant data for the Mentor are
14 slightly above the range, and for the McGhan slightly
15 below the middle of the range.

16 The Simaplast explant with 23 years of
17 implantation has the tensile strength. So we see no
18 large scale degradation in the shell property for long
19 term implantation.

20 Next we're going to consider analysis of
21 some failed explants. This is a Heyer-Schulte implant
22 that failed after 21 years of implantation. The

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1 failure occurred in a crease or a fold or a wrinkle at
2 the outer perimeter. We can see that the actual
3 failure was a straight line in the crease. It appears
4 as a straight line, anyway.

5 SEM analysis, this is an SEM microgram or
6 micrograph, rather, which shows that the line is
7 actually jagged and not straight as one would see with
8 a scalpel cut. Micron scale is shown on the lower
9 right-hand side of the photograph.

10 Higher magnification shows how the
11 material was torn apart in the crease.

12 Next we have a failed McGhan explant which
13 failed after three years of implantation time. Again,
14 the failure occurred in a fold in the outer perimeter,
15 and in that region we can see two wear marks and a
16 very small break in the shell occurred between those
17 two wear marks, and with a .2 millimeter break.

18 This is an SEM micrograph of that
19 fractured, failed region. It consisted of a small,
20 .06 millimeter hole with cracks propagating from that
21 hole.

22 We have also seen this feather type of a

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1 wear pattern emanating from a crease in a saline shell
2 that was explanted from Spain and had six years of
3 implantation.

4 Our last failure analysis is for an
5 explant that failed in England after three months of
6 implantation and it was sent to us for analysis. It
7 was thought to have failed because of manufacturing.

8 We discovered on the inside of the shell
9 this triangular cut. If you look at a typical suture
10 anneal you see a --

11 CHAIRMAN WHALEN: Could you please
12 conclude, Dr. Brandon.

13 DR. BRANDON: -- a similar cut with a tip
14 of the suture needle, and we induced this cut in the
15 shell and concluded that the failure was not due to
16 manufacturing, but due to a suture anneal cut at the
17 time of implantation surgery.

18 In conclusion, saline implants have
19 remained intact up to 23 years in vivo. Implant
20 failure is not the result of large scale shell
21 degradation. Failure occurs in folds, and these
22 should be minimized whenever possible.

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1 CHAIRMAN WHALEN: The last speaker is Dr.
2 Wendy Anne Epstein.

3 DR. EPSTEIN: Good morning, and thank you
4 for the opportunity to address the issue of safety and
5 efficacy of saline breast implants.

6 My name is Dr. Wendy Anne Epstein, and I'm
7 a practicing physician in the teaching faculty at New
8 York University Medical Center. I paid for my own
9 travel to and from Washington. I consult for Avon
10 skin care products, evaluating their product safety.
11 I have never been involved with any lawsuit relating
12 to breast implants, and I do not receive any income
13 from surgery or care related to breast implants.

14 In 1992, at the age of 37, I was
15 unexpectedly widowed with two small children. I chose
16 after that to have saline breast implants. Mentor
17 1600 saline implants were implanted under my pectoral
18 muscles using the transaxillary approach.

19 Having breast implants made me feel more
20 comfortable as I put my life back together. I have
21 since remarried.

22 As a physician with breast implants, I've

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1 reviewed the literature, spoken to physicians
2 performing mammographies, and have seen many examples
3 of breast implants over the course of clinical
4 practice. This winter I helped a friend and her
5 husband through a mastectomy and saline implant
6 reconstruction.

7 I am convinced that submuscularly placed
8 saline breast implants are preferable with respect to
9 cancer detection and aesthetics.

10 My primary concern was to have the least
11 impact on future cancer detection. Since all types of
12 breast implants will impede mammography to some
13 degree, I urge you to recommend that all women obtain
14 a baseline mammography before any breast implantation.

15 Compression. For women with breast
16 implants, mammograms are easier to interpret when
17 there's less compression of the overlying breast
18 tissue. Breast implants placed under the pectoralis
19 muscle compress the breast tissue significantly less
20 than implants placed directly under the breast and
21 above the muscle.

22 Only inflatable saline breast implants can

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1 be placed beneath the pectoral muscles. Silicone
2 breast implants are always prefilled and, therefore,
3 cannot be inserted under the pectoralis muscle.

4 Radiolucency. The more radiolucent an
5 implant is, the less it interferes with mammography.
6 All types of saline implants allow better cancer
7 diagnostic surveillance compared to silicone implants
8 because they are significantly more radiolucent and,
9 therefore, do not obscure mammographic image of the
10 breast the way silicone liquid implants do.

11 Calcification. High density mammographic
12 calcifications indicative of calcium phosphate may be
13 a consequence of the breast implant or a nearby
14 carcinoma. Calcium deposits can form around both
15 saline and silicone implants.

16 With subpectoral saline implants, the
17 implants and their surrounding calcifications are the
18 farthest away from the natural breast tissue and least
19 likely to obscure mammography.

20 Contracture. The formation of a fibrous
21 capsule around a breast ^{**}implant causes distortion by
22 compression the overly breast tissue, which impedes

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1 mammography and spoils the aesthetics of the breast.
2 All implants have some type of silicone rubber
3 envelope. The main difference between silicone and
4 saline implants is what they are filled with.

5 Liquid silicone can lead to a nonspecific
6 foreign body reaction and fibrosis. Liquid saline
7 cannot. Therefore, saline implants, whether placed
8 submammary or subpectoral, have a lower incidence of
9 capsular contraction compared to liquid silicone
10 filled implants.

11 Subpectoral saline implants have the
12 lowest risk of capsule formation, and this is because
13 the pectoral muscle contractions produce constant
14 motion of the implant inhibiting capsule formation.
15 Because saline and particular submuscular saline
16 plants have less chance of forming a fibrous capsule,
17 breasts stay softer and more supple, and mammography
18 is less obscure.

19 Aesthetics and function. There can be
20 nerve damage and loss of nipple and breast sensitivity
21 from the insertion, trauma, and/or pressure from any
22 implant. This leaves a woman with dyschesia or

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1 numbness, both of which can be disconcerting.

2 Over many months to years there can be
3 recovery of sensation, and I have experienced this
4 myself. Endoscopically got at transaxillary or
5 transumbilical insertion enables saline implants to be
6 placed under the pectoralis muscle without cutting
7 into the breast or nipple.

8 Because the skin of the breast is not cut,
9 there is less direct nerve damage and nipple
10 sensitivity. There are also no scars on the breast or
11 nipple.

12 When saline implants are placed under the
13 muscle, there's less compression of the overlying
14 breast tissue. Aesthetically the breasts remain more
15 supple, pliable, and more natural feeling.

16 When implants compress breast tissue in
17 the submammary location, the breasts feel harder and
18 less natural.

19 Children's health. Based upon testimony
20 and publications that I have presented, I and other
21 physicians and scientists delivered before the IOM
22 last year claims alleging adverse effects of breast

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1 implants on a woman's children are just not valid.

2 There are some disadvantages to saline
3 implants. Saline implants can be placed, as I
4 mentioned, above or below the pectoralis muscle. The
5 major disadvantage of the initial subpectoral
6 placement of the implant is that it requires general
7 anesthesia.

8 However, if a subpectoral saline implant
9 ruptures, the implant may be replaced within about 24
10 to 48 hours with only local sedation, provided there
11 is preservation of the tissue pocket beneath the
12 muscle.

13 Deflation. It's clinical more evident
14 with saline implants. However, if a saline implant
15 ruptures, only sterile saline is liberated to the
16 body. Saline, a natural body component is eliminated
17 through the urine. The well know therapeutic benefit
18 of microdroplet liquid silicone in the diabetic foot
19 or soft tissue repair of scars and wrinkles can become
20 a complication when large volumes of liquid silicone
21 are liberated by ruptured silicone implants.

22 When two silicone implants rupture, two

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1 and a half cups of liquid silicone is released. The
2 silicone remains in the body.

3 While silicone has been shown not to cause
4 any systemic illness, this volume of liquid silicone
5 can cause local complications, including palpable
6 breast lumps and granulomas in and around breast
7 tissue confounding mammographic interpretation.

8 Noise. Rarely, but even if two cc's of
9 air is trapped within the saline implant, this can
10 result in a postoperative noise or sloshing sound in
11 the saline implants.

12 Aesthetically, you can feel the wrinkles
13 of a saline implant under the breast as the bag is
14 thicker than that of silicone implants. This is less
15 apparent with submuscular placement of the implants.

16 With submuscular saline implants, when you
17 flex your pectoralis muscles, the implant and the
18 overlying breast tissue is deformed by the muscle
19 contraction. Both will return to native shape upon
20 relaxing your muscles. This can be embarrassing for
21 women, and I've experienced it, during certain
22 exercises.

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1 breast implants have the lowest risk of obscuring
2 mammography, are the most biocompatible. I can
3 personally attest to the positive impact on a woman's
4 appearance and self-esteem in our culture.

5 Once again, I thank you for the
6 opportunity to speak today.

7 CHAIRMAN WHALEN: Thank you.

8 A question, Dr. Epstein, if you don't
9 mind. Would you recommendation about considering a
10 routine baseline mammogram pre-insertion be
11 irrespective of the age of the patient having the
12 insertion?

13 DR. EPSTEIN: Yes. I thought a lot about
14 that, and your question is my question. It's my
15 opinion, yes, because once the implants are in, there
16 are many changes that go on the mammography. For time
17 constraints I didn't mention you also sometimes get
18 little lymph nodes around just having the surgery.
19 There's calcification around the implant, and I think
20 that if a person is going to undergo the procedure,
21 you'll never have another chance to look at that
22 native breast again, and I think it is in the best

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1 interest of all women if they're going to undergo this
2 procedure to have a pre-mammography.

3 CHAIRMAN WHALEN: Thank you.

4 DR. EPSTEIN: Thank you.

5 CHAIRMAN WHALEN: I'd like to thank all of
6 you for taking time out of your schedules this morning
7 to testify at the panel meeting.

8 Is there any further comment from anyone
9 in the FDA?

10 DR. WITTEN: No. Thank you.

11 CHAIRMAN WHALEN: Is there any closing
12 comment from the sponsor?

13 DR. DUHAMEL: My comments will be very
14 brief.

15 I want to thank the panel for the
16 thoughtful consideration of the data that we
17 presented, and we look forward to discussing with the
18 FDA the remaining issues based on the recommendations
19 that you made today.

20 Thank you.

21 CHAIRMAN WHALEN: Thank you.

22 MS. BRINKMAN: Dr. Whalen, may I say

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1 something?

2 CHAIRMAN WHALEN: Ms. Brinkman.

3 MS. BRINKMAN: I'm fully aware that this
4 is not an FDA issue, but it's my opportunity to say
5 this to those of you that I have your ear.

6 I know that this is a very difficult issue
7 for everybody here, and I know that we all want to be
8 responsible professionals and make good decisions with
9 appropriate data using good science.

10 The one thing I do want to point out
11 thought. As a representative of consumers is that we
12 also use responsible promotion and marketing of what
13 we do. Both companies, both Mentor and McGhan, have
14 running full page ads in magazine to teenage girls,
15 and I as a consumer representative find this
16 deplorable in the fact that I'm not sure -- and I
17 realize we have free country and free choice -- but we
18 sit here as professionals worried about consumers,
19 worried about long term safety, worried about
20 reoperation, and then look at a new market.

21 And I hate to think that -- and actually
22 these full page ads say nothing about whether there

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1 are side effects or what to be concerned about or what
2 kinds of cautions one should use, and as a
3 representative of consumers, I find that not
4 acceptable, and I realize it's not an FDA issue, but
5 I said it.

6 CHAIRMAN WHALEN: Well, the only thing I
7 would add is when we're going to be talking about
8 labeling tomorrow morning, it is most certainly an FDA
9 issue and one that I'm sure will occupy a significant
10 portion of the time that we have to discuss it.

11 Dr. Krause will now read to us the voting
12 instructions.

13 DR. KRAUSE: The following are the panel
14 recommendation options for pre-market approval
15 applications. Medical device amendments to the
16 Federal Food, Drug and Cosmetic Act, as amended by the
17 Safe Medical Devices Act of 1990, allows the Food and
18 Drug Administration to obtain a recommendation from an
19 expert advisory panel on designated medical device
20 pre-market approval applications that are filed with
21 the agency.

22 The PMA must stand on its own merits, and

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1 your recommendation must be supported by safety and
2 effectiveness data in the application or by applicable
3 publicly available information.

4 Safety is defined in the act as reasonable
5 assurance, based on valid scientific evidence, that
6 the probable benefits to health under conditions on
7 intended use outweigh any probable risks.
8 Effectiveness is defined as reasonable assurance that
9 in a significant portion of the population the use of
10 the device for its intended uses and conditions of use
11 when labeled will provide clinically significant
12 results.

13 Your recommendation options for the vote
14 are as follows.

15 The first option: approval with no
16 conditions.

17 The second option: approvable with
18 conditions. The panel may recommend that the PMA be
19 found approvable subject to specified conditions, such
20 as physician or patient education, labeling changes,
21 or a further analysis of the existing data.

22 Prior to voting, all of the conditions

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1 should be discussed by the panel.

2 Not approvable. The panel may recommend
3 that the PMA is not approvable if the data do not
4 provide a reasonable assurance that the device is safe
5 or if a reasonable assurance has not been given that
6 the device is effective under the conditions of use
7 prescribed, recommended or suggested in the proposed
8 labeling.

9 Following the vote, the chair will ask
10 each panel member to present a brief statement
11 outlining the reasons for their vote.

12 CHAIRMAN WHALEN: Thank you, Dr. Krause.

13 Is there a motion?

14 Dr. Boykin.

15 DR. BOYKIN: Mr. Chairman, I would like to
16 make a motion that the panel recommend approval with
17 condition on the PMA submitted by McGhan.

18 CHAIRMAN WHALEN: The motion is made that
19 we recommend that this be approvable with condition.

20 Is there a second?

21 PARTICIPANT: ** Second.

22 CHAIRMAN WHALEN: With the second to that

1 motion being made, Dr. Boykin, would you like to
2 suggest any first of those conditions?

3 DR. BOYKIN: One condition that I would
4 recommend for discussion with the panel is the post
5 approval continued evaluation of revision surgeries
6 for the augmentation of reconstructed patient; that
7 the revision category be dropped; and that these
8 changes following augmentation or reconstruction be
9 placed in those respective categories.

10 CHAIRMAN WHALEN: The slight difference we
11 are going to proceed with from last evening is, number
12 one, rather than my advancing failing memory for any
13 of these amendments, we are going to have a scribe
14 which will write down and project such amendments.

15 And, number two, we are going to vote upon
16 each amendment as we discuss them rather than
17 cataloging all amendments and then voting.

18 So the amendment -- the condition, rather,
19 is stipulated that the category of revision be
20 abolished and that there simply be the two categories
21 of augmentation or reconstruction. Is there any
22 further discussion of that condition?

1 Dr. Bandeen-Roche.

2 DR. BANDEEN-ROCHE: My only concern is
3 that will it lessen the information that goes to
4 patients. In other words, if revision is not listed
5 as a specification, will there therefore be no data on
6 post revision outcomes?

7 DR. BOYKIN: Actually I'm hoping it will
8 improve the data. Right now when you look at the
9 revision category, you can't tell who had an
10 augmentation or reconstruction that went into that
11 group. They've broken it down that perhaps 25 percent
12 of it was augmentation patients, but by pushing it
13 into the other two columns, you'll know exactly
14 everything that's happened to the augmentation patient
15 or the reconstruction patient.

16 In terms of reoperations, the capsular
17 formation, et cetera, I think it will be a clearer
18 evaluation of the data.

19 CHAIRMAN WHALEN: Dr. Blumenstein, any
20 comments statistically on that?

21 (No response.)^{**}

22 CHAIRMAN WHALEN: Seeing no other comments

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1 on this particular condition, would all those in favor
2 signify by raising their hands?

3 (Show of hands.)

4 CHAIRMAN WHALEN: Thank you.

5 It is unanimous that that condition be a
6 part, and for anyone who wonders why two of our
7 members did not raise their hands, they are nonvoting
8 members. It's not that they're disinterested in the
9 conditions.

10 DR. BOYKIN: I have one other condition.

11 CHAIRMAN WHALEN: Dr. Boykin.

12 DR. BOYKIN: I would also like to
13 recommend that changes in the product labeling and
14 marketing information concerning the proposed
15 advantages of the anatomic device designed by McGhan
16 be revised to reflect the absence of clinical data or
17 delete it completely.

18 CHAIRMAN WHALEN: On the condition that
19 the labeling's flash marketing as regards the anatomic
20 device be either revised or eliminated, is there
21 further discussion?

22 (No response.)

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1 CHAIRMAN WHALEN: Seeing none, those in
2 favor of that condition please raise their hands.

3 (Show of hands.)

4 CHAIRMAN WHALEN: It is unanimous.

5 Dr. Boykin, have you any further
6 conditions?

7 DR. BOYKIN: There may be others. I don't
8 have them.

9 CHAIRMAN WHALEN: Dr. Burkhardt.

10 DR. BURKHARDT: In fairness to the
11 sponsor, I think that should be eliminated pending
12 studies that establish a reasonable scientific
13 probability that that is, indeed, the case.

14 CHAIRMAN WHALEN: Would you accept that,
15 Dr. Burkhardt, as editorial comment to be a part of
16 that process?

17 DR. BOYKIN: Sure, yes.

18 CHAIRMAN WHALEN: Thank you.

19 MS. DUBLER: Dr. Whalen.

20 CHAIRMAN WHALEN: Ms. Dubler.

21 MS. DUBLER: I just want to be certain
22 that all issues of labeling are still available for

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1 our discussion tomorrow.

2 CHAIRMAN WHALEN: Dr. Witten.

3 DR. WITTEN: Anything specific about this
4 product that you think needs to go in the label we
5 should talk about now. If there are some general
6 issues, in other words anything specific as it relates
7 to this product should be brought up now.

8 MS. DUBLER: I actually have a list of
9 issues that I want to raise about how the data are
10 presented in the label. I don't think that's
11 appropriate for this discussion, is it?

12 DR. WITTEN: No, if it's just how people
13 are going to be informed or how it's going to look,
14 but in terms of what information on this product goes
15 in, we should talk about it now. But if it's
16 generically how things should appear in the label --

17 MS. DUBLER: Well, I was --

18 DR. WITTEN: -- that could be discussed
19 tomorrow.

20 MS. DUBLER: I would like some of the
21 percentages that we're comfortable really do reflect
22 complication rates in the label, but I want that with

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1 all of the products.

2 So I think there is a general that the
3 labels in general do not reflect the data that we
4 have, and the data are not presented in ways that give
5 women a good sense of what real risks are there.

6 DR. WITTEN: I think those will be good
7 discussion items for tomorrow.

8 MS. DUBLER: Fine. Thank you.

9 CHAIRMAN WHALEN: Dr. Blumenstein.

10 DR. BLUMENSTEIN: I have three conditions:
11 that there be long term active follow-up with a focus
12 on informative sensoring as we discussed during NAFDA
13 (phonetic) questions.

14 CHAIRMAN WHALEN: And we will take each
15 one at a time.

16 Is there any further discussion on the
17 condition that there be long term follow-up with a
18 focus on active sensoring?

19 Dr. Change would like you to define long
20 term chronologically. How many years?

21 DR. BLUMENSTEIN: Ten years.

22 DR. ROBINSON: Could we just change it to

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1 appropriate statistical analysis?

2 CHAIRMAN WHALEN: I'm sorry?

3 DR. BLUMENSTEIN: Could we just singe it
4 to appropriate statistical analysis?

5 CHAIRMAN WHALEN: Would you accept that as
6 an --

7 DR. BLUMENSTEIN: Well, actually what I
8 really want to say is that this is a point of
9 negotiation between the FDA and the sponsor, and the
10 FDA hears us when we suggest ten years, but that they
11 be --

12 CHAIRMAN WHALEN: So you would --

13 DR. BLUMENSTEIN: -- told that it be
14 flexible.

15 CHAIRMAN WHALEN: That the condition be
16 long term follow-up, deferring the definition of long
17 term to the FDA.

18 DR. BLUMENSTEIN: Right. They know them
19 a lot better about how to do this than we do.

20 CHAIRMAN WHALEN: Any further discussion
21 on that condition?

22 (No response.)

1 CHAIRMAN WHALEN: Seeing none, those in
2 favor please signify by raising your hands.

3 (Show of hands.)

4 CHAIRMAN WHALEN: In favor? Everybody
5 here was in favor? I'm sorry. I didn't look to my
6 left.

7 It is, indeed, unanimous.

8 Dr. Blumenstein.

9 DR. BLUMENSTEIN: Redo the risk
10 characterization analysis with appropriate statistical
11 methodology and appropriate classification of bad
12 things, events, and attributions.

13 CHAIRMAN WHALEN: Any further discussion
14 of that condition?

15 (No response.)

16 CHAIRMAN WHALEN: Seeing none, in regards
17 to the condition to redo the risk characterization
18 analysis, dot, dot, dot, all those in favor please
19 signify by raising your hands.

20 (Show of hands.)

21 CHAIRMAN WHALEN: It is unanimous.

22 Dr. Blumenstein.

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1 DR. BLUMENSTEIN: The last one, provide
2 analyses quantifying the degree of informative
3 sensing and the quality of life risk and follow-up
4 data.

5 CHAIRMAN WHALEN: Any further discussion
6 on that condition?

7 DR. BANDEEN-ROCHE: Dr. Whalen.

8 CHAIRMAN WHALEN: Dr. Bandeen-Roche.

9 DR. BANDEEN-ROCHE: I have one that I
10 think might well fall within this category. It's in
11 terms of characterizing the population. The
12 representativeness of the sample as a whole also was
13 not very well demonstrated, and some analyses to
14 characterize the sample and to argue its
15 representativeness relative to data in the literature
16 would be useful. Mentor did this.

17 CHAIRMAN WHALEN: Suggesting analysis of
18 the present data set, not --

19 DR. BANDEEN-ROCHE: Right.

20 CHAIRMAN WHALEN: -- a new data set.

21 DR. BLUMENSTEIN: And that could be folded
22 in.

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1 DR. BANDEEN-ROCHE: Right.

2 DR. BLUMENSTEIN: That could be folded
3 into this condition.

4 CHAIRMAN WHALEN: Very well. Any further
5 discussion on that condition?

6 (No response.)

7 CHAIRMAN WHALEN: Seeing none, all those
8 in favor please signify by raising your hands.

9 (Show of hands.)

10 CHAIRMAN WHALEN: It is unanimous.

11 That's all you have, Dr. Blumenstein?

12 DR. BLUMENSTEIN: That's it.

13 CHAIRMAN WHALEN: Any other panel members
14 have any other conditions?

15 PARTICIPANT: I do.

16 CHAIRMAN WHALEN: I'm sorry. Dr. Bandeen-
17 Roche.

18 DR. BANDEEN-ROCHE: The reason that I
19 brought up the issue of CTD and systemic disease is
20 because there was lack of external consistency
21 relative to the whole package that we received, and
22 there was also an internal inconsistency in that the

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1 data that were up on the projector were not consistent
2 with the data that was in the booklet or that FDA
3 projected.

4 And so as a condition, I would just state
5 that that be absolutely clarified and characterized
6 with respect to the nature of conditions and not just
7 one lump category.

8 CHAIRMAN WHALEN: A condition then as to
9 clarification of nature of conditions.

10 Is there any further discussion?

11 Seeing -- Dr. Bandeen-Roche, can you put
12 that in a sentence to be projected?

13 DR. BANDEEN-ROCHE: There was some
14 confusion in the CTD data in that what was up on the
15 screen today did not agree with what was in the
16 booklet or with what FDA put up on the screen. That
17 needs to be clarified.

18 CHAIRMAN WHALEN: That there be
19 clarification of the CTD data.

20 DR. BANDEEN-ROCHE: Yes.

21 CHAIRMAN WHALEN: Dr. Li?

22 DR. LI: A condition of the mechanical

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1 testing --

2 CHAIRMAN WHALEN: Excuse me.

3 DR. LI: Sorry.

4 CHAIRMAN WHALEN: We haven't voted on that
5 one yet.

6 DR. LI: Oh, I'm sorry.

7 CHAIRMAN WHALEN: I thought you were
8 commenting upon that.

9 DR. LI: I'm sorry.

10 CHAIRMAN WHALEN: Is there any further
11 comment upon that?

12 (No response.)

13 CHAIRMAN WHALEN: Seeing none, those in
14 favor, please raise their hands.

15 (Show of hands.)

16 CHAIRMAN WHALEN: That is unanimous.

17 Dr. Li.

18 DR. LI: My conditions of the mechanical
19 testing are a reiteration of what I said before. I
20 believe they should test the component with the
21 thinnest wall and the highest potential for failure.
22 I think they need to work with the FDA to agree on an

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1 acceptable fatigue test and fold flaw test.

2 And it turns out that they actually have
3 submitted a procedure for looking at the explants in
4 your PMA, but there was no follow-up data collection
5 on that. So I guess my condition -- hold that for a
6 second condition. I'll leave that for the mechanical
7 testing.

8 CHAIRMAN WHALEN: In regard to the
9 condition that -- in regards to mechanical testing,
10 that with the thinnest wall and highest potential for
11 failure be tested, and that there be dialogue between
12 FDA and sponsor to come to agreement on acceptable
13 fatigue and fold flaw testing.

14 With no further discussion, those in favor
15 please raise their hands.

16 (Show of hands.)

17 CHAIRMAN WHALEN: Thank you. It's
18 unanimous.

19 Dr. Li.

20 DR. LI: The next condition was that the
21 sponsor complete and follow their standard operating
22 procedure for looking at their explanted devices,

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1 perhaps including on that procedure a tabulation of
2 the model and wall thickness of these devices.

3 CHAIRMAN WHALEN: With no further
4 discussion, the condition that there be completion and
5 following of the SOP by the sponsor on their explants
6 with emphasis on their thickness.

7 All those in favor, raise their hands.

8 (Show of hands.)

9 CHAIRMAN WHALEN: It is unanimous.

10 Anything further Dr. Li? Does any other
11 panel member have any condition?

12 (No response.)

13 CHAIRMAN WHALEN: We, therefore, come to
14 the motion, which is that we recommend as a panel to
15 the FDA that this be approvable with the conditions
16 that we have voted upon.

17 Would all those in favor please raise
18 their hands and keep them up for a moment?

19 (Show of hands.)

20 CHAIRMAN WHALEN: It is, indeed, unanimous.

21 Before announcing that decision, I would
22 ask to go around the panel and have everyone briefly

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1 tell us why they voted the way they did, beginning
2 with Dr. Li.

3 DR. LI: The effectiveness stems by
4 agreement of my colleagues that there is effectiveness
5 and it does clearly help certain patient population,
6 the safety issue apparently is one that's acceptable
7 risk weighed again by my surgical colleagues, and I
8 presume they'll go along with that so long as there's
9 some mechanical testing and product evaluation to
10 insure that that level of safety does not decrease at
11 best or worst in the future.

12 However, I can't help but do anything but
13 beg you to understand the failure mode of deflation
14 and leakage and address and make that better. It'll
15 help the patients, and if you could solve that
16 problem, it'll help your commercial activity.

17 CHAIRMAN WHALEN: Dr. Blumenstein.

18 DR. BLUMENSTEIN: I found it effective,
19 and I feel that with the conditions and so on that
20 we'll be able to have a package insert that will
21 adequately reflect the risks.

22 CHAIRMAN WHALEN: Dr. Boykin.

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1 DR. BOYKIN: I believe the product is
2 effective. I think we've collected some meaningful
3 information which will be related to the patients and
4 make informed consent a meaningful situation.

5 CHAIRMAN WHALEN: Thank you.

6 Dr. Bandeen-Roche.

7 DR. BANDEEN-ROCHE: I hope it's been clear
8 in my comments yesterday and today that I do have
9 substantial concerns about various aspects of these
10 data. Doing the best I could, I think that the best
11 weighing of all the evidence that I saw of risk and
12 benefit is to approve conditional on being able to
13 provide reasonable assurance that women are fully
14 informed to weigh the risks and benefits.

15 CHAIRMAN WHALEN: Thank you.

16 Dr. Burkhardt.

17 DR. BURKHARDT: I believe the studies are
18 very well done, that the products are effective, and
19 that they are reasonably safe.

20 CHAIRMAN WHALEN: Thank you.

21 Dr. Chang.

22 DR. CHANG: I believe the sponsor has been

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1 very thorough in examining the data and follow-up
2 especially for the clinical studies, and they've shown
3 that this product is effective and safe. I have no
4 doubt that there will be a lot of care given in
5 providing informed consent and enough information to
6 prospective patients regarding these devices.

7 CHAIRMAN WHALEN: Thank you.

8 Dr. Morykwas.

9 DR. MORYKWAS: I also agree that the
10 device is effective and has been proven to be
11 reasonably safe, and given the conditions that they
12 still have to fulfill, given the thoroughness of their
13 presentation, I have no doubt that they will work very
14 hard on those conditions.

15 CHAIRMAN WHALEN: Thank you.

16 Ms. Dubler.

17 MS. DUBLER: I think the product is
18 sufficiently safe and effective for us to approve it.
19 I think the challenge in discussing the informed
20 consent process will be to recognize what we now have
21 from empirical studies as the defects of the informed
22 consent process and try, in fact, to create a process

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1 that will give a woman sufficient objective data to be
2 able to discuss it with friends, relatives, and other
3 physicians to reach a conclusion.

4 CHAIRMAN WHALEN: Thank you.

5 And finally, Dr. Robinson.

6 DR. ROBINSON: Even using QO -- quality of
7 life measures which I think we all would agree are
8 imperfect at best, the product appears effective to me
9 and is reasonably safe, and I suspect when the
10 complication rate is properly defined, it will be even
11 safer than it appears now.

12 CHAIRMAN WHALEN: Thank you.

13 The recommendation of the panel then is
14 that the pre-market approval application for saline
15 filled breast prostheses from McGhan Medical be
16 recommended as approvable with the conditions that we
17 voted affirmatively upon.

18 The FDA has generously allotted 30 full
19 minutes for lunch, and so we will see you back here in
20 a half an hour.

21 (Whereupon, at 1:15 p.m., the meeting was
22 recessed for lunch, to reconvene at 1:45 p.m.)

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1 A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

2 (1:56 p.m.)

3 CHAIRMAN WHALEN: Good afternoon. We now
4 will have the first open session.

5 All persons addressing the panel are asked
6 to speak clearly into the microphone as the
7 transcriptionist is dependent upon this means of
8 providing an accurate record of this meeting.

9 The instructions from the morning still
10 apply. Please remember we ask that you disclose if
11 anyone is paying for your trip or accommodations, if
12 you have any financial ties to industry or health
13 professional societies.

14 We also ask that you disclose whether or
15 not you're a witness or party to any lawsuits related
16 to breast implants or whether you derive any of your
17 income from medical procedures involving breast
18 implants or symptoms attributed to breast implants.

19 The identified speakers for the first
20 session of the afternoon would first be Dr. James
21 Baker.. Dr. Baker has ten minutes.

22 DR. BAKER: Could I have the first slide,

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1 please?

2 Mr. Chairman, members of the panel, I'm
3 Dr. James Baker, clinical professor of plastic
4 surgery, University of South Florida, representing the
5 Aesthetic Surgery Education and Research Foundation.

6 The foundation is a not for profit
7 organization dedicated to enhancing patient care in
8 aesthetic plastic surgery through dedicated research.
9 The foundation has paid my travel and accommodations
10 for this hearing.

11 I have more than 30 years' experience in
12 breast implant development and clinical use. However,
13 I have no financial interest or obtain no compensation
14 from industry or health professional societies. I am
15 not a witness or a party to a pending lawsuit relating
16 to breast implants.

17 As a Board certified plastic surgeon, I do
18 derive a portion of my income from surgical procedures
19 involving breast implants.

20 Since the introduction of breast implants
21 in the early 1960s, despite^{**} social and cultural
22 changes, the demand for this self-directed

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1 modification and body image has persisted.

2 The benefits of cosmetic breast
3 augmentation are ultimately psychological, sexual and
4 social. They include decreased self-consciousness and
5 heightened self-confidence. These benefits are
6 supported in scientific literature.

7 In the present deliberations on cellulite
8 implants, our foundation encourages the FDA to avoid
9 making any distinction between women seeking breast
10 implant surgery for reconstruction following
11 mastectomy, and women seeking cosmetic breast
12 augmentation.

13 Both groups of women have psychological
14 needs that require the continued availability of
15 breast implants. Both groups are entitled to the same
16 right to make decisions about their preferred body
17 image, and both groups are entitled to the same level
18 of informed consent prior to undergoing surgery.

19 My presentation today focuses on the
20 psychological issues of breast augmentation. Breast
21 augmentation has proven to be a safe and efficacious
22 procedure, but as with any surgery, it is not risk

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1 free. However, it is critical for this panel to
2 recognize that the benefits of augmentation are real
3 and important to our patients and outweigh the risk.

4 Women seeking cosmetic breast surgery have
5 been described as self-conscious about the size of
6 their breast, and this may produce low self-esteem and
7 even negatively affect social, sexual, and family
8 relationships.

9 Just like the women who have lost their
10 breast due to cancer, the cosmetic patient finds the
11 option of an external prosthesis or a padded bra
12 unacceptable. Only a prosthesis implanted beneath the
13 skin can effectively be incorporated into the
14 patient's own body image.

15 The insertion of implants changes the
16 breast size and appearance. A 1994 study at
17 Washington University showed the average increase was
18 two cup sizes.

19 This same study of 112 women who underwent
20 breast augmentation over a 12 year period included
21 patient interviews to assess psychological benefit.
22 The results of these interviews suggest that surgical

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1 intervention had a dramatic impact on most of the
2 patients. Eighty-six percent of the women reported
3 decreased self-consciousness. Eighty-eight percent
4 said they felt heightened self-confidence, and 95
5 percent said they felt better about themselves
6 following surgery. Eighty-six percent reported being
7 completely satisfied or mostly satisfied with their
8 postoperative results, and 95 percent said that
9 augmentation surgery had met their expectations.

10 The strongly positive nature of these
11 responses is especially impressive in view of the fact
12 that this study was conducted at the height of the
13 controversy and criticism of breast implants in the
14 media.

15 In my own 30 years' experience in plastic
16 surgery, I find that patients seeking augmentation are
17 realistic about their expectations. They do not
18 expect major changes in their health, social life, or
19 marriage. They just want to look better and feel
20 better about themselves, and the research confirms
21 this.

22 Importantly, however, in the Washington

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1 University study 42 percent reported that sexual
2 function was improved, an unexpected benefit.

3 In 1974, I published a study with Dr.
4 Irving Kolin, assisting clinical professor of
5 psychiatry at the University of Florida, on the
6 psycho-sexual aspects of breast augmentation. This
7 study included 142 women who had undergone breast
8 augmentation during the previous six years.

9 The average woman in this study was
10 typical of breast augmentation patients today. She
11 was married, in her early 30s, with two children. The
12 interviews reveal that most of the patients in our
13 study developed feelings of inadequate sexual
14 development during adolescence when they compared
15 their own breast size with that of their friends.
16 Nearly 90 percent reported feelings of self-
17 consciousness; 65 percent had moderate to strong
18 feelings of inadequacy.

19 From this study, the case history of
20 Denise, age 30 and married with two children, is quite
21 representative of augmentation population in general.
22 I will share her case history with you because for

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1 many of these women, the experience is too personal to
2 discuss in a public setting.

3 When counseled for surgery, Denise
4 explained that she wanted to look better in clothing
5 and feel attractive without a padded bra, which
6 increased her feelings of inadequacy and deception.
7 She clearly stated she wanted normal, well
8 proportioned breasts, not large ones.

9 Her adolescence was marked by feelings of
10 inadequacy when she became aware of the difference
11 between her own breast development and that of her
12 peers. Even after marriage, self-consciousness
13 inhibited her sexual expression.

14 She felt embarrassed when seen without
15 clothing and would engage in sexual relations with her
16 husband only in the dark.

17 She recalled feeling very pleased by the
18 increased breast size during her two pregnancies and
19 feeling deflated, as she called it, after she stopped
20 nursing.

21 It is important^{**} to note that Denise's
22 husband had not encouraged the surgery. In fact, he

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1 was against it. Nevertheless, at six months after
2 surgery, she described sexual relations with her
3 husband as being more satisfactory than before
4 surgery.

5 She described being proud of her body and
6 no longer required that intimacy take place in the
7 dark.

8 Tactile exploration of the breast
9 following augmentation surgery mimics the normal
10 experience of self-discovery in infancy, and it allows
11 for incorporation of the implant into the body image.
12 In our study we found that implants were incorporated
13 into the patient's body image within a six week period
14 if no complication occurred.

15 When a complication did occur,
16 incorporation was delayed, but also accomplished once
17 the complication cleared.

18 Feelings of increased adequacy after
19 breast augmentation were reported in 84 percent of the
20 women in our study. Almost 80 percent reported an
21 increased interest in intimacy with their partner.
22 Over 50 percent reported greater sexual fulfillment.

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1 These changes are viewed as lasting. Our
2 study has a six year follow-up following surgery.

3 We have been raised in a society based in
4 Puritan ethic. It is often reflected in the attitude
5 that physical attractiveness is highly desirable as
6 long as one doesn't have to do anything artificial to
7 achieve it.

8 These attitudes are a major reason why
9 happy patients who have undergone breast augmentation
10 are sometimes reluctant to go public with their
11 experience. For these women, breast augmentation is
12 a private matter. They have long ago successfully
13 incorporated their implants into their body image.
14 They have left behind the feelings of inadequacy or
15 dissatisfaction that led them to seek surgical remedy.
16 They have no desire to revisit these feelings.

17 The many thousands of women who are happy,
18 satisfied augmentation patients are quietly living
19 their lives as mothers, wives, career women, or
20 leaders in our society. These women are more than
21 capable of determining for themselves the risk and
22 benefit of surgery.

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1 Our priority now must be to make
2 absolutely certain that all women seeking breast
3 implant surgery have the opportunity to understand the
4 facts about this operation. Fully informed patients
5 must be our number one goal.

6 The Aesthetic Surgery Education and
7 Research Foundation is here to participate in a public
8 education effort concerning the risk and benefits of
9 saline filled implants. We share the goal of better
10 informed patients because we know from experience that
11 the informed patients are happier patients, even when
12 complications arise.

13 We were anxious to lend our expertise in
14 plastic surgery education and research to this effort,
15 and we ask the panel and the FDA to include us in the
16 development of effective education material.

17 Thank you.

18 CHAIRMAN WHALEN: Are there any questions
19 for Dr. Baker?

20 (No response.)

21 CHAIRMAN WHALEN^{**}: Thank you.

22 We have some further time for public

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1 comment. While two other individuals have identified
2 themselves to speak, Ms. Zuckerman and Pierce, I
3 understand they want to go in the second session and
4 not the first. If that's incorrect, please raise your
5 hand.

6 All right. Is there anyone else that
7 wishes from the public to address the panel? If so,
8 please raise your hands.

9 (No response.)

10 CHAIRMAN WHALEN: Very well. We are now
11 going to consider to the open committee discussion and
12 review of the pre-market approval application.

13 I would like to remind all public
14 observers at this meeting that while this portion of
15 the meeting is open to your public observation, as
16 public attendees you may not participate except at the
17 specific request of the panel.

18 We are now ready to begin with the
19 sponsor's presentation for which you will have, if you
20 need it, up to one hour.

21 MR. HAWK: Thank you, and good afternoon.

22 We're here today to present the PMA for

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1 Poly Implant Prosthesis from Toulon, France, which is
2 sold here in the United States by PIP America.

3 The presenters today will be myself, Rick
4 Hawk, President of PIP America; Dr. George Burdock,
5 who's a toxicologist, who will present the preclinical
6 testing; Dr. Ioana Carabin, who's a medical consultant
7 who has long history in plastic surgery; and Dr.
8 Jefferson Goudeau, who is a practicing surgeon in
9 France.

10 Before we start I'd like to give a little
11 history of PIP. In 1991, PIP was established as a
12 breast implant manufacturer. In 1992, PIP began
13 marketing prefilled saline breast implants
14 internationally.

15 In 1996, PIP established a direct United
16 States operation and began marketing products under a
17 510(k), which made them substantially equivalent to
18 products currently on the market.

19 In 1997, PIP received the ISO and CE for
20 both manufacturing and products.

21 In the year 2000, PIP is an established
22 breast implant company. It's the third largest

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1 manufacturer in the world of breast implants, selling
2 products in 35 countries. We have over 35,000
3 prefilled saline implants sold domestically here in
4 the United States to date, with 521 MDRs reported to
5 date.

6 And you can see what those MDRs there are.
7 The most important thing to note off of that slide is
8 that's less than one and a half percent of adverse
9 events reported with the implant to date.

10 PIP sells its implants in both textured
11 and smooth and high profile and standard profile.
12 This gives the surgeon and the patient the option to
13 choose which implant is going to give them the best
14 results.

15 Some characteristics of the PIP implant.
16 The PIP implant is a prefilled implant. Thus, we've
17 eliminated the valve and valve leakage. With it being
18 prefilled, we've also been able to reduce
19 interoperative handling of the implant. There's no
20 preparation needed. It eliminates contamination
21 during filling, and also reduces surgical time.

22 As we begin to talk about the clinical

1 information, I'd like to keep some things in the
2 forefront of your mind, which is what -- valid
3 scientific evidence is what is relied upon to make
4 decisions, and I'd like to just go over that here.

5 Valid scientific evidence is evidence from
6 well controlled investigations and studies, studies of
7 objective trials without match controls, well
8 documented case histories conducted by qualified
9 experts, or reports of significant human experience
10 with a marketed device.

11 PIP's valid scientific evidence. We have
12 a U.S. clinical study today that we'll discuss. It's
13 both prospective and objective in its reporting. We
14 have a French clinical study which is also both
15 prospective and objective in its reporting.

16 We also discuss the U.S. surgeon case
17 survey, which is a report of significant human
18 experience with a marketed device.

19 We'll also be discussing preclinical
20 testing. As you can see, some of the tests we'll
21 discuss here, but what I'd like to put into your mind
22 as well before we start our presentation on the

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1 preclinical and the clinical, just for your thought
2 processes, is the data that PIP will show today about
3 the product shows that the product is safe and
4 effective for both augmentation and revision, which
5 are the indications that we are pursuing today.

6 PIP is asking the panel the help us, in
7 formulating labeling based on our data for both
8 patients and surgeons, to allow them to make an
9 informed decision.

10 Dr. Burdock.

11 DR. BURDOCK: Thank you, Rick.

12 Back me up one, will you please? Thank
13 you.

14 Obviously I can't be trusted with much
15 technology.

16 My name is George Burdock. I have a Ph.D.
17 in toxicology, and I'm a Diplomat of the American
18 Board of Toxicology. I am a consultant in toxicology
19 and have my own consulting company in Florida.

20 My task here today is to discuss the in
21 vitro and in vivo studies which demonstrate the
22 biocompatibility and safety of this elastomer. There

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1 are a number of studies, most of which on this list I
2 will be discussing this afternoon.

3 The first of this list or on this list of
4 in vitro studies is the hemolysis assay. First, the
5 silicone elastomer is extracted in saline and the
6 whole rabbit blood cells. There are both positive and
7 negative controls. It's incubated for an hour. The
8 sample is centrifuged and the supernatants examined
9 for hemolysis.

10 The results from this assay indicate there
11 was no hemolysis and the conclusion thereby being it's
12 not hemolytic.

13 In the cytotoxicity assay, again, the
14 elastomer is extracted, added to mouse fibroblast
15 cells, and they're examined microscopically at 24, 48,
16 and 72 hours. The results indicated that both the
17 positive and negative controls performed as expected.
18 Therefore, the assay works.

19 Secondly there was no evidence of lysis or
20 toxicity with the elastomer. Conclusion: no
21 cytotoxicity.

22 A chromosomal aberration study was also

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1 conducted here. Human lymphocytes are gathered and
2 cultured, the elastomer extracted, positive and
3 negative controls run in parallel, and have the assays
4 receive the activation system. This is necessary
5 because some clastigens (phonetic), genotoxins and
6 mutagens as well, need a metabolic activator, and this
7 is done using homogenized mouse liver.

8 These cultures are continued and then
9 stopped in metaphages and cultures seen, and the cells
10 are fixed, stained, and examined microscopically. The
11 results indicated that the positive and negative
12 controls, again, performed as expected, and the
13 elastomer was negative. There were no chromosomal
14 abnormalities with or without the activator.

15 Conclusion: there is no chromosomal
16 aberration with this elastomer.

17 Mutagenicity assay using the Ames test was
18 also conducted. Here the elastomer is again
19 extracted, this time with saline, and it's added to
20 five different strains of salmonella typhomerium.
21 These five strains comprise all the known mechanisms
22 for genotoxicity or mutagenicity. They essentially

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1 cover the waterfront.

2 The extracts, as I said, were added to the
3 salmonella along with control substances, and of
4 course, half the plates received the metabolic
5 activating system for those genotoxins that need
6 activation. The plates are incubated for 48 to 72
7 hours and the revertant colonies counted.

8 Results indicated that the positive
9 controls are positive. Therefore, the assay works.
10 The extract had no increase in number of mutant
11 colonies, the conclusion thereby being the elastomer
12 is not mutagenic.

13 Following up on this, we're initiating a
14 carcinogenicity study designed in collaboration with
15 the FDA. We'll be using the P-53 transgenic mouse,
16 and the results will be submitted to the agency.

17 Other in vivo studies include an
18 irritation study in the guinea pig or an extract of
19 the elastomer is given intradermally and topically to
20 the guinea pig and the sites examined at 24 hours.
21 Again, there were no untoward findings. There was no
22 erythema, no edema, the conclusion thereby being the

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1 material was not irritating.

2 This is followed up with a sensation assay
3 in the guinea pig using the guinea pig maximization
4 test. Again, an extract of the elastomer is used for
5 the induction phase, which is an injection followed by
6 a topical application, followed then by a rest period
7 of two weeks, and then a challenge phase in which the
8 extract is applied topically under occlusion to get
9 best absorption.

10 The challenge sites are read at 24, 48,
11 and 72 hours. The results indicated there was no
12 edema, no erythema, and no untoward reactions.
13 Therefore, this substance is not sensitizing.

14 Another in vivo study is the
15 intracutaneous toxicity test where the elastomer is
16 extracted both with saline and oil, and two rabbits
17 are injected intracutaneously along the flanks.
18 They're observed at the intervals of four, 24, 48, and
19 72 hours. The criteria evaluated again is erythema
20 and edema or any adverse reactions. There were no
21 difference in the treated controlled scores.
22 Therefore, there is no intracutaneous toxicity.

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1 Systemic toxicity test was conducted in
2 mice. Again, there was an extraction using saline and
3 oil. The saline injected intravenously or the saline
4 extract and the oil extract injected
5 intraperitoneally, observations take place or take
6 place at four, 24, 48, and 72 hours, and the study
7 terminated at 72 hours. Criteria evaluated here are
8 mortality, body weight loss, and clinical
9 observations.

10 The results indicated there was no
11 difference between treated and controlled groups.
12 Therefore, there was no systemic toxicity.

13 Completed is a subcutaneous implantation
14 study in the rat. I'm sorry. This is underway. The
15 subcutaneous implantation study consists both of a
16 subchronic and chronic study. The subchronic lasts
17 for a total of 90 days and the chronic one year. The
18 control groups are implanted with a negative control
19 plastic and the test groups are implanted with
20 elastomer.

21 Test parameters^{**} taken here include body
22 weights, food consumption, clinical observations,

1 ophthalmologic exams, hematology and samples are taken
2 for clinical biochemistry, and at necropsy organ rates
3 will be taken and histopathology results will be
4 gathered. The results will be submitted to the
5 agency.

6 Concluding this preclinical data, it's
7 obvious that the elastomer is biocompatible. All of
8 the in vitro studies are negative. All of the in vivo
9 studies are negative. All of the findings are
10 congruent with the literature, the IOM report, and all
11 peer reviewed literature. The elastomer is safe.

12 And if I can quote from the IOM report,
13 review of toxicology studies of silicones does not
14 provide a basis for health concerns. Our findings are
15 congruent with this conclusion by the IOM.

16 Dr. Carabin will now be reviewing the
17 clinical data.

18 DR. CARABIN: Distinguished members of the
19 panel, colleagues, ladies and gentlemen, I'm Ioana
20 Carabin, and I am a medical consultant with Burdock &
21 Associates, Incorporated. ** I am a graduate of Mount
22 Sinai School of Medicine in New York. My training is

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1 in general surgery, head and neck and facial plastic
2 surgery at Cornell University and Mount Sinai Medical
3 Center.

4 I have been a practicing physician in New
5 York, Georgia, and Florida since 1991, and
6 incidentally, I'm fluent in three languages, one of
7 which is French.

8 In the next half an hour, I will give you
9 an overview of PIP's clinical studies and results that
10 demonstrate the safety and effectiveness of this
11 implant.

12 The cell compressed implant was first
13 introduced to the market in 1962 and has continued to
14 evolve in its physical and chemical composition and
15 design to present. Our presentation shows that the
16 safety and effectiveness of PIP prefilled saline
17 breast implants is determined through the following
18 studies:

19 Toxicological studies of which you have
20 already heard the data;

21 Ongoing U.S. clinical studies;

22 U.S. surgeon case experience survey;

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1 Two year prospective French clinical
2 studies;

3 And, of course, consistency of this data
4 with U.S. and global literature.

5 Complications that speak to the safety of
6 breast implants are those that require further and
7 significant medical and surgical intervention and
8 alter the desired cosmetic outcome.

9 Various complications from breast
10 implantation have been identified in the medical
11 literature. Some complications are associated with
12 the implant, while others can be surgically -- can be
13 due to surgical technique or can be iatrogenically
14 induced.

15 Other so-called complications are just
16 anticipated postoperative findings in a defined
17 postoperative time.

18 Specific complications could arise either
19 from an implant failure or from damage to the implant
20 during the procedure such as micropuncturing as
21 reported by Rapaport in '97.

22 As presented by Freeman in '67 and Mladick

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1 in 1993, differences in surgical technique have been
2 identified as playing an important role in explaining
3 the frequency of the infection, hematoma, capsular
4 contracture or other complications whose reported
5 rates in the medical literature vary greatly.

6 PIP prefilled saline breast implants have
7 been marketed in the United States since 1996.

8 PIP clinical data for the PMA is comprised
9 of three separate studies: a prospective U.S. study,
10 a U.S. surgeon case experience survey, and a
11 prospective two year French study.

12 The U.S. clinical studies have been
13 ongoing since December of 1997, and they have been
14 prospective. Indications for the implantation are, as
15 you see, two of them: augmentation and revision
16 surgery. Contraindications for the implantations are
17 certainly more numerous, and I would leave this up for
18 you to read, and these were definitely part of the
19 protocol.

20 The total number of patients that entered
21 the study were 392, and that is tabulated as of
22 October '99. The large majority underwent

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1 augmentation, and then certainly 60 of them underwent
2 revision as you see.

3 While there are numerous types of
4 acceptable surgical incisions, our protocol evaluated
5 these four: surgical placement focused on
6 subglandular and retropectoral. The study focused on
7 these two. As you already know, surgical placement
8 has safety relevance primarily because of its effect
9 on contracture development which lessens the need for
10 additional surgery and possible complications.

11 As described in the IOM report of June
12 '99, sufficient evidence exists to conclude that
13 submuscular versus subglandular placement of the
14 implant is associated with a lower incidence of severe
15 contracture.

16 In a study of saline implants, Cocke in
17 '94 reported 44 percent noticeable firmness in
18 subglandularly placed implants compared to 19 percent
19 in submuscularly placed implants.

20 PIP has two types of implants: textured
21 and smooth. A number of clinical trials have
22 supported the association of texturing with less

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1 severe capsular contracture.

2 One study designed primarily to evaluate
3 the role of infection in contracture development
4 determined that texturing had significant contracture
5 controls for saline implants of a particular
6 manufacturer. This was reported by Burkhardt and
7 Eades in '95.

8 An earlier study designed to evaluate on
9 the microbial effects of submammary augmentation
10 compared textured and smooth saline implants and
11 reported respectively two percent and 40 percent Class
12 III and IV contractures. This was reported by
13 Burkhardt and Demas in '94.

14 As far as follow-up is concerned, again,
15 this was tabulated as of October 15, '99. The numbers
16 are as you see, and the 24 months follow-up were due
17 December '99. That data has been collected and is
18 presently being analyzed.

19 After breast implantation, short follow-
20 ups appear to be a common occurrence, and it has been
21 identified and reported in the literature. Mladick in
22 '93 and Burkhardt in '88 indicate that part of the

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1 problem may be due to the fact that augmentation
2 surgery is performed in a young and mobile population,
3 making adequate recall and follow-up difficult.

4 Our clinical studies have evaluated a
5 number of complications. Certainly the most dreaded
6 ones are capsular contractures, and as you see, these
7 are the numbers for capsular contracture Grade III,
8 for augmentation and revision, and these are for Grade
9 IV.

10 While foreign body reaction is intrinsic
11 to human physiology, contracture is in excess of
12 fibrosis that may go beyond the patient's usual
13 biological response, influenced by local and poorly
14 understood factors.

15 The contracture of the fibrous connective
16 tissue of the capsule can lead to discomfort and loss
17 of cosmetic result, and while undesirable, it is a
18 common complication of the surgery.

19 Capsular contractures Grade III and IV are
20 essentially cosmetic problems, but are associated with
21 safety to the extent that they lead to reoperation,
22 things like open capsulotomy and explantation, with

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1 those anesthetic and operative risks, in addition to
2 the realm of postoperative complications seen
3 otherwise.

4 In general, reported data seems to support
5 a lower frequency of contracture around saline
6 implants compared to gel and this was demonstrated by
7 the IOM report of June '99. Compared to PIP's data,
8 the medical literature reports higher incidences of
9 capsular contracture Grade III and IV both for
10 augmentation and revision surgery.

11 For example, Capozzi in '96 reported a 3.4
12 percent incidence. Lavine in '93 reported a 6.1
13 percent incidence, and for revision, the McGhan series
14 in 1990s reported an 8.8 percent incidence, and as you
15 see, our revisions are zero.

16 Certainly in revision cases, because of
17 the nature of the procedure, increased contracture
18 formation is anticipated, something that obviously we
19 did not see in our study.

20 Well, I'm sorry I gave away my next slide,
21 but this demonstrates that we had a zero percent
22 incidence of hematoma, seroma, infection, delayed

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