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MEDICAL DEVICES ADVISORY COMMITTEE

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GENERAL AND PLASTIC SURGERY

DEVICES PANEL

+ + + + +

MEETING

+ + + + +

Thursday, March 2, 2000

+ + + + +

The meeting was held in the Ballroom, Gaithersburg Holiday Inn, Two Montgomery Village Avenue, Gaithersburg, Maryland, at 8:00 a.m., Dr. Thomas V. Whalen, Chairman, presiding.

PRESENT:

THOMAS V. WHALEN, M.D., Chairman

JOSEPH V. BOYKIN, JR., M.D., Voting Member

PHYLLIS CHANG, M.D., Voting Member

KAREN BANDEEN-ROCHE,** Ph.D., Temporary Voting Member

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PRESENT (Continued):

BRENT BLUMENSTEIN, Ph.D., Temporary Voting
Member

BOYD BURKHARDT, M.D., Temporary Voting Member

NANCY A. DUBLER, LL.B., Temporary Voting Member

STEPHEN LI, Ph.D., Temporary Voting Member

MICHAEL J. MORYKWAS, Ph.D., Temporary Voting
Member

JOHN S. ROBINSON, M.D., Temporary Voting Member

MAXINE F. BRINKMAN, R.N., Consumer

Representative

CINDY DOMECUS, Industry Representative

DAVID KRAUSE, Ph.D., Executive Secretary

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P-R-O-C-E-E-D-I-N-G-S

(8:05 a.m.)

DR. KRAUSE: Can everybody take their seats? I'd like to start the meeting.

Good morning. It's nice to see that some people are able to get up after yesterday's late hour. I'd like to welcome you all here.

We're ready to begin the second day of the 56th meeting of the General and Plastic Surgery Devices Panel.

My name is David Krause, and I'm the Executive Secretary of the panel, and I'm also a biologist and a reviewer in the Plastic and Reconstructive Surgery Devices Branch.

I'd like to remind everyone that you are requested to please sign in on the attendance sheets which are available at the tables just outside the doors. You can also pick up an agenda there, a meeting roster, and information about today's meeting and also information which tells you how to find out about future meetings of this panel and other panels.

Before turning this meeting over to Dr.

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1 Whalen, I'm required to read two statements into the
2 record: the deputization of voting members, temporary
3 voting members, and the conflict of interest
4 statement.

5 Pursuant to the authority granted under
6 the Medical Devices Advisory Committee charter, dated
7 October 27th, 1990, and as amended August 18th, 1999,
8 I appoint the following individuals as voting members
9 of the General and Plastic Surgery Devices Panel for
10 this meeting on March 2nd, 2000: Karen Bandeen-Roche,
11 Brent Blumenstein, Boyd Burkhardt, Nancy Dubler,
12 Stephen Li, Michael Morykwas, and John A. Robinson.

13 For the record, these individuals are
14 special government employees and consultants to this
15 panel or other panels under the Medical Devices
16 Advisory Committee. They have undergone the customary
17 conflict of interest review and have reviewed the
18 material to be considered at this meeting.

19 The statement is signed by Dr. David W.
20 Feigal, Jr., the Director for the Center for Devices
21 and Radiological Health. **

22 The second statement I'm required to read

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1 is the conflict of interest statement. The following
2 announcement addresses conflict of interest issues
3 associated with this meeting and is made a part of the
4 record to preclude even the appearance of impropriety.

5 To determine if any conflict existed, the
6 agency reviewed the submitted agenda and all financial
7 interests reported by the committee participants. The
8 conflict of interest statutes prohibit special
9 government employees from participating in matters
10 that could affect their or their employer's financial
11 interests.

12 However, the agency has determined that
13 participation of certain members and consultants, the
14 need for whose services outweighs the potential
15 conflict of interest involved is in the best interest
16 of the government.

17 A waiver has been granted for Dr. Stephen
18 Li for his interests in a firm at issue that could
19 potentially be affected by the committee's
20 deliberations. The waiver allows this individual to
21 participate fully in the panel's deliberations. A
22 copy of this waiver may be obtained from the agency's

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1 Freedom of Information Office, which is in Room 12A-15
2 of the Parklawn Building.

3 We would like to note for the record that
4 the agency took into consideration certain matters
5 considering Drs. Burkhardt, Chang, Li, and Michael
6 Morykwas.

7 Dr. Li reported a current interest in a
8 firm at issue, but in matters not related to the
9 panel's agenda. Therefore, the agency has determined
10 that he may participate fully in today's
11 deliberations.

12 Drs. Burkhardt, Chang and Morykwas
13 reported past related involvements with firms at
14 issue. Since these are past involvements and there
15 are no continuing financial interests, the agency has
16 determined that these panelists may also participate
17 fully in today's deliberations.

18 In the event that the discussions involve
19 any other products or firms not already on the agenda
20 for which an FDA participant has a financial interest,
21 the participant should excuse him or herself from such
22 involvement, and the exclusion will be noted for the

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1 record.

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

7 Thank you.

8 At this point I'm going to turn the
9 meeting over to Dr. Whalen, the chair.

10 CHAIRMAN WHALEN: Thank you, Dr. Krause.

11 Good morning. My name is Dr. Thomas
12 Whalen. I'm a pediatric surgeon from Robert Wood
13 Johnson Medical School in New Jersey.

14 Today the panel will be making
15 recommendations to the Food and Drug Administration on
16 two pre-market approval applications. I would like to
17 note for the record that the voting members present
18 constitute a quorum as required by 21 Code of Federal
19 Regulations, Part 14.

20 Before we proceed to the open public
21 hearing, in follow-up to some of yesterday's
22 activities, I'd turn the microphone over to Dr.

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1 Witten.

2 DR. WITTEN: Yes, thank you.

3 I just have three brief comments. One is
4 a correction to or clarification to something that I
5 said yesterday, which is that the 180 day review time
6 frame is 180 days from the date that the PMA is filed,
7 not 180 days from the date of the call for PMAs.

8 Some people came up to me after the
9 meeting yesterday and had calculated already and said,
10 "Doesn't that mean our time is up already?"

11 The second thing I want to mention is that
12 as we discussed, the PMAs today that are going to be
13 considered, I want to remind the panel and everyone
14 else that each PMA needs to stand on its own. So each
15 PMA is discussed separately from the PMAs before.
16 We're considering them individually, not as a group.

17 And the third thing I want to mention is
18 just the role of the public comments during this panel
19 process, and although the data to be considered for
20 safety and effectiveness for each PMA is the data in
21 the PMA and the scientific knowledge of the panel
22 members, we certainly value the public comments for

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1 sharing their perspective on important issues and
2 concerns.

3 And of course, these types of concerns can
4 be factored into the discussion as the panel did
5 yesterday.

6 Thank you.

7 CHAIRMAN WHALEN: Thank you, Dr. Witten.

8 We will now proceed with the morning's
9 first open public hearing session of the meeting. All
10 persons addressing the panel are asked to speak
11 clearly into the microphone, as the transcriptionist
12 is dependent on this means of providing an accurate
13 record of this meeting.

14 At this time, Dr. Krause has some
15 instructions for those who will be testifying before
16 the panel.

17 Dr. Krause.

18 DR. KRAUSE: Thank you, Dr. Whalen.

19 I have some instructions for those of you
20 who will be testifying to the panel this morning. We
21 are requesting that all persons making statements
22 during the open public hearing of the meeting disclose

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1 whether they have financial interest in any medical
2 device company or if their trip to this meeting has
3 been paid for by someone else.

4 Before making your presentation to the
5 panel, in addition to stating your name and
6 affiliation, please address the following four
7 questions. I will read the questions into the record
8 now so that rereading by all presenters will not be
9 necessary.

10 The questions are as follows:

11 Question one, has your travel and/or
12 accommodations been paid for or will they be
13 reimbursed by someone else? If so, please state who.

14 Question two, please indicate whether you
15 have financial ties, including grants or other
16 compensation with industry of health professional
17 societies.

18 Question three, please indicate whether
19 you are a party to or witness in a pending lawsuit
20 related to breast implants.

21 And finally, question four, do you derive
22 a portion of your income from surgical procedures

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1 using saline filled implants or from treating patients
2 with complaints that they believe are related to
3 saline filled implants?

4 I don't think we need any other further
5 special instructions because today's public testimony
6 times will be short. I think we'll have Ann Marie
7 Williams will be helping you out and kind of directing
8 you to the podium when your time to speak comes. So
9 we can go with that for now.

10 Thanks.

11 CHAIRMAN WHALEN: Thank you.

12 At this time only one individual has made
13 prior arrangements to speak at this first open hearing
14 session. I would then ask that Ms. McCloud come
15 forward and present your testimony to the panel, and
16 you have ten minutes, ma'am.

17 MS. McCLOUD: Oh, I was told I only have
18 five minutes, but thanks for ten.

19 CHAIRMAN WHALEN: This group says ten. So
20 if you want to talk about the Redskins or something,
21 go ahead.

22 (Laughter.)

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1 MS. McCLOUD: Maybe we should.

2 I'm Liz McCloud. My travel arrangements
3 have been paid for by my husband and in part by my
4 support group, Silicone Survivors of the World, New
5 Mexico.

6 My answer to your remaining questions is
7 no.

8 Thank you all for giving me your attention
9 after the late night last night. I appreciate your
10 effort, and I'm impressed to see you all here.

11 Seventeen years ago, I decided to have a
12 unilateral breast reduction because one breast was
13 substantially larger than the other. My doctor told
14 me that breast reduction was complicated, relatively
15 dangerous, and unlikely to yield a good aesthetic
16 result. He persuaded me to have augmentation of the
17 smaller breast with a subpectoral implant.

18 Just as my doctor promised, I was very
19 pleased with the result. I remained pleased with the
20 result for several years. The pain following the
21 surgery and thereafter seemed a very small price to
22 pay for the benefits of looking good and feeling

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1 normal.

2 My implant, however, ruptured while I was
3 playing volleyball at a company picnic. It felt like
4 my breast had split open. The flush of fluid made me
5 feel almost like I had wet my pants in front of my
6 boss and all my co-workers. I was mortified and
7 terrified. I went and sat under a tree by myself
8 until I felt well enough to drive home.

9 Yesterday when I heard the man from Mentor
10 tell this panel it would take about three times the
11 force of an automobile accident to rupture his
12 implant, it sounded remarkably like what my plastic
13 surgeon had told me all those years ago.

14 Another thing I wondered about yesterday
15 is whether local pain is considered by you to be an
16 issue of product safety or of product efficacy. I had
17 capsular contracture for many years, and it really
18 hurt. The pain varied from shooting pains, cramps,
19 throbbing, radiating pain, burning, et cetera. It
20 remained predictable only that it was relentless, ever
21 present.

22 When I moved my arm, the muscle under the

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1 implant pressed it almost like a fist into the tender
2 tissue that was always inflamed and painful. I
3 devised all manner of ways to try and look normal
4 while I supported the painful breast to keep it from
5 jolting with pain each time I took a step walking or
6 every time I made a sudden movement.

7 My arm became reflexively tied to my
8 breast as a protectant. A hug caused agony since
9 compressing the breast caused the most pain of all.
10 I began to flinch whenever I saw anyone come near me
11 to give me a hug.

12 Lifting, stretching, dancing, swimming,
13 skiing, cleaning, and even riding hurt my breast. I
14 started avoiding the pain by avoiding the many
15 activities that induced it. Without really noticing
16 it, I was slowing becoming practically sedentary, and
17 I had lost a huge part of my enjoyment of life.

18 When I was considering explantation in
19 1994, I sat down naked in front of the mirror, and I
20 finally realized the implant had made my smaller
21 breast look truly deformed where it had previously
22 simply been a question of the sizes not matching. The

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1 implanted breast was hard, misshapen and altogether
2 unnatural looking. The breast adversely affected my
3 appearance, my self-esteem, my posture, my movement,
4 and my health and well-being. It had become for me a
5 little bundle of agony.

6 The only benefit the device still offered
7 as far as I could tell was to give me the appearance
8 that my breasts were the same size when safely tucked
9 into a brassiere.

10 I remembered having that same benefit
11 using an external prosthesis from the time I was a
12 teenager.

13 I had the explant surgery in 1994, and my
14 breast still hurts six years later every single day
15 and every single night. It's the first thing I notice
16 when I get into bed.

17 My arm still jumps to protect the breast
18 from being jostled and bumped, and I can tell you that
19 this pain was absolutely caused by the implant because
20 I had the situation where one breast was left in its
21 natural state and one breast was implanted. I have
22 the opportunity for direct comparison.

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1 Now, I recognize that my testimony may be
2 disregarded by this panel because it is anecdotal, and
3 I understand that isn't considered very reliable or
4 scientific, but I don't see my experience or that of
5 other women as being statistically acceptable risks.
6 We're real people who endure these real experiences.

7 We all know even from the evidence
8 presented today that rupture, capsular contracture,
9 and local pain are common, uncontroverted consequences
10 of using these devices. For me the implant clearly
11 caused deformity and injury to previously health
12 tissue and to a previously more healthy life.

13 I would ask you to take my case and cases
14 like mine into account when you're looking at all of
15 the three things that I understand you will look at:
16 the safety. I feel that my implant was unsafe. It
17 lasted only three years. I thought it was a lifetime.
18 It harmed me. That says to me it's unsafe.

19 The efficacy. I didn't feel it was
20 effective for the intended use. It was designed to
21 right a physical abnormality, and it created far more
22 abnormality than it had ever been designed resolve.

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1 It also deflated, which would affect the
2 efficacy of the device if you were considering such a
3 thing.

4 And finally, I would say that you would
5 have to look at my case to question the need for such
6 a device. I have had it out now for these six years,
7 and I have found out that I didn't need it. I wasn't
8 really talked to about the possibility of maybe
9 getting some counseling about body image or maybe
10 having another option. My surgeon really discussed
11 with me either making the big one little or the little
12 one big, but somehow they needed to be even.

13 And when I went to try to get an explant,
14 I went to a number of surgeons and had to fight like
15 cats and dogs with them to say, no, I didn't want to
16 throw good, healthy tissue in the trash to make them
17 even, and, no, I didn't want another implant. I just
18 wanted to get back to my natural state.

19 And so I would just ask you guys to really
20 look at all of these three things as much as you can
21 with some kind of human context.

22 And I thank you so much for doing your

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1 best. Thanks.

2 CHAIRMAN WHALEN: We'd like to thank you
3 for taking time out of your schedule in order to
4 testify to the panel.

5 DR. BURKHARDT: May I ask a question?

6 CHAIRMAN WHALEN: Would you entertain a
7 question, ma'am?

8 DR. BURKHARDT: Some of your history was
9 not entirely clear to me. After your implant ruptured
10 and you felt this saline release, did you then proceed
11 to have another implant inserted?

12 MS. McCLOUD: No, sir. I had a double-
13 lumen device. So I had saline on the exterior, and
14 when that ruptured, I still had the silicone.

15 DR. BURKHARDT: I understand. Thank you.

16 MS. McCLOUD: Okay. Thanks.

17 CHAIRMAN WHALEN: Is there another
18 question?

19 No. Thank you again, ma'am.

20 We do have some additional time for
21 testimony. If there is anyone who wishes to address
22 the panel, would you please indicate by raising your

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1 hand?

2 Sir, if you would come forward and
3 identify yourself.

4 DR. YOUNG: My name is Leroy Young, and I
5 represent the Plastic Surgery Educational Foundation.

6 I would like to address you from the
7 standpoint of the -- thank you, Jim. As I said --

8 CHAIRMAN WHALEN: Mr. Young.

9 DR. YOUNG: Yes.

10 CHAIRMAN WHALEN: I'm told that you had
11 already been a scheduled speaker for the second public
12 session. Is that so or not?

13 DR. YOUNG: Well, I didn't realize that if
14 that was true. When I talked to the people out front,
15 they told me I was the second speaker, and that's why
16 I was up at this point.

17 CHAIRMAN WHALEN: You were the second
18 speaker in this afternoon, in the second session, I
19 mean?

20 DR. YOUNG: I don't care. Whichever works
21 best for you.

22 PARTICIPANT: He can just do this now.

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1 CHAIRMAN WHALEN: Please proceed, and
2 please do answer the questions at the beginning that
3 have been posed.

4 DR. YOUNG: Yes. As I said, I represent
5 the Plastic Surgery Educational Foundation.

6 For some reason it won't advance on page
7 up, Steve. Sorry.

8 Yes, as I said, I represent the Plastic
9 Surgery Educational Foundation, and that institution
10 has paid for my travel and accommodation here.

11 I currently have no ties to any of the
12 industry that's involved in this. In the past I have
13 received research funding and have served as
14 consultants to manufacturers and societies.

15 I am currently an expert witness in a
16 single malpractice lawsuit that involves a breast
17 implant. I derive a portion of my income from breast
18 surgery, and I treat both patients seeking implants
19 and patients who perceive that they have problems with
20 breast implants.

21 The Plastic Surgery Educational Foundation
22 is the educational and research arm of the American

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1 Society of Plastic and Reconstructive Surgery. The
2 PSEF sponsors and endorses educational courses and
3 symposia, many of which are related to breast surgery
4 and breast implants.

5 The PSEF solicits funds for research and
6 plastic surgery in related areas.

7 Activities that the PSEF sponsors that are
8 related to breast implants are the attempt to form a
9 breast implant registry, to form a device and
10 retrieval analysis program, to try to develop better
11 devices and understand the shortcomings of the current
12 devices, and the ASTM subcommittee on plastic surgery
13 and reconstructive devices.

14 Issues related to saline filled breast
15 implants which we have reviewed as part of the PSEF
16 review of saline breast implants are listed here.
17 Obviously the time precludes our discussing all of
18 them, but in view of some of the things that were
19 discussed yesterday, I would like to comment on
20 several issues, one of which is capsular contracture.

21 One of the ^{**}things that I think is
22 important to understand is that capsular contracture

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1 is multi-factorial. It's related to the surface
2 properties of the implant, the position in which the
3 implant is inserted, whether or not antimicrobial
4 irrigation is used.

5 I think you can see from yesterday that
6 the comments about revisional patients, patients who
7 have more complicated histories and have had multiple
8 procedures are more likely to have problems with this.

9 And I also think that technique,
10 particularly minimizing the amount of manipulation and
11 touching of the implant is important. So that the
12 thing to understand is that it's multi-factorial.

13 If one goes through the literature, you
14 can see that there's a wide range of rates of capsular
15 contracture listed, and it's important to see the
16 effect of where the implant is positioned.
17 Subpectoral implantation almost always has a lower
18 incidence of capsular contracture regardless of
19 whether it's augmentation or reconstruction.

20 It's also interesting to note that
21 individuals who have a long^{**} experience, an extensive
22 experience with saline filled implants tend to report

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1 lower incidences of capsular contracture than surgeons
2 who have less experience and surgeons who don't adhere
3 to rigid techniques.

4 Dr. Mladick has had about a 20 year
5 experience with this, and after converting to
6 subpectoral position and no touch technique has a very
7 low incidence of Grade III and Grade IV capsular
8 contractures.

9 Again, when you see a lot of the
10 literature isn't really clear what was done because
11 they've either used both positions, in some instances
12 both textured and smooth devices. That makes it very
13 hard to make a rigid interpretation of exactly what
14 went on, but when you use only one device and you put
15 it in a submuscular position and you use a no touch
16 technique, again, the incidence seems to be much
17 lower.

18 And interestingly with saline filled
19 devices at least for augmentation, I would say that
20 there capsular contracture rate tends to stay more
21 stable as opposed to a gel filled implant where gel
22 bleed can contribute to ongoing inflammatory

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1 processes.

2 The other issue that got a lot of
3 attention yesterday was deflation, and again, I want
4 to point out that deflation can be both device related
5 and technique related. Examples of device related
6 features are fold flaw failure, valve and patch
7 problems, technique related issues or fill volume, the
8 type of incisions used, and not being cautious in
9 avoiding surgical injury to the device.

10 If one reviews the literature on
11 deflation, you can see that it ranges from very low
12 numbers like one to four percent up to higher numbers,
13 but in general, if you really go through this
14 literature, the modern literature related to modern
15 devices, the failure rate seems to range between one
16 and four percent per year.

17 And, again, it's important to understand
18 that these technique related issues, such as the fill
19 volume of the implant are important. In these two
20 studies here, when either the recommended nominal
21 volume, fill, was used or it was overfilled, the
22 deflation rate was much lower than when the device was

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1 under filled.

2 What can you do to minimize deflations?
3 Use an adequate fill volume. For example, if you need
4 400 cc's of volume, then pick a 350 cc implant and
5 fill it to at least 400 cc's.

6 Use an adequate incision so that you don't
7 damage the implant while you insert it, and voice
8 injury to the implant with manipulation with
9 instruments, such as when you're closing the wound.

10 Sometimes there comes at tradeoff between
11 aesthetics and minimizing deflation because the more
12 you inflate the device, the more rigid the device
13 becomes. I think it's clear to me, having done
14 research in this area for a long time, that it's easy
15 to make a device that would never fail. You just have
16 to make a solid rubber implant.

17 However, a solid rubber implant is not
18 aesthetic. So we need a balance between a thick
19 shelled device that is overfilled, versus a device
20 that is capable of producing a soft breast which has
21 natural shape and feel. **

22 I believe it is possible to achieve all of

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1 these goals, but we need further research to
2 accomplish that.

3 Reoperation is also a big issue here, and
4 it's, again, device and technique dependent. Some of
5 the device features that contribute to this are
6 capsular contracture, deflation, implant palpability,
7 and skin wrinkling, whereas technique issues are
8 asymmetry, bleeding, infection, and size changes.

9 You can minimize the risk of reoperation
10 by obtaining an adequate informed consent, the use
11 preoperatively and interoperatively of sizers and
12 photographs, antimicrobial irrigation, a no touch
13 technique, smooth implants, putting an implant in a
14 subpectoral position, use an adequate fill volume,
15 measure the width of the breast as a surrogate of bra
16 cup size, and evaluate patients in a sitting position
17 intraoperatively.

18 Note that only one of these issues is
19 device related.

20 We've looked at patient satisfaction
21 preoperatively and postoperatively using a five point
22 scale. As you can see, preoperatively most patients

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1 are either completely or mostly unsatisfied with the
2 size or shape of their breast, whereas postoperatively
3 that's just reversed. Ninety-eight percent of the
4 patients are mostly or completely satisfied.

5 We've also looked at anatomical impact
6 using a variety of measures, include bra cup size,
7 suprasternal notch to nipple distance, inframammary
8 crease to nipple distance, internipple distance,
9 breast width, and in circumference measurements.

10 When you look at the results of this, you
11 can see that there are minimal changes in the
12 suprasternal notch to nipple distance, internipple
13 distance, or the circumference at the inframammary
14 crease, whereas there are significant differences in
15 the inframammary crease to nipple distance, which must
16 be taken into account if you're going to use an
17 inframammary incision, the circumference at the
18 nipple, and the width of the breast in inches.

19 In conclusion, we feel that saline filled
20 implants are safe. They produce anatomical changes
21 which are predictable. The patient's satisfaction is
22 high. Our experience and review of the literature, we

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1 feel the rupture rate is more like one to four percent
2 per year.

3 Complication rates vary among
4 investigators, and are both technique and investigator
5 dependent.

6 What do we need in the future? We need a
7 better informed consent because we've heard from a
8 number of people who say they didn't feel like they
9 were adequately informed.

10 We need a breast implant registry that
11 will allow us to retrieve devices that can then be
12 analyzed to determine the mechanism of failure, the
13 changes in properties that will allow us to evolve
14 better devices.

15 We obviously need to link this to device
16 retrieval and analysis. We need clear definitions of
17 what reoperations are and why they occur among
18 researchers. We need to ongoing research for better
19 devices and better techniques, and we need a multi-
20 disciplinary device forum.

21 Thank you.

22 CHAIRMAN WHALEN: Thank you.

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1 I'm sure there are questions. Dr.
2 Burkhardt.

3 DR. BURKHARDT: I have a question, Dr.
4 Young. In your experience, how frequently have
5 patients, prospective patients, turned down breast
6 implant surgery after being given what you would
7 consider adequate informed consent?

8 DR. YOUNG: Well, in the State of
9 Missouri, we have a mandated policy that we have to
10 give every patient the FDA information booklet on
11 breast implants, and that they have to have five days
12 to review that before they can have surgery.

13 I haven't had a single patient turn down
14 surgery having been given that booklet.

15 DR. BURKHARDT: In your experience, can
16 you give us some idea of how many patients actually
17 read that booklet and whether they remember those
18 precautions retrospectively after surgery?

19 DR. YOUNG: They all tell me they read it.
20 Now, i didn't sit in the room while they read it.
21 They seemed to understand the issues when I asked them
22 questions about it because I don't rely solely on the

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1 booklet. I give them what I consider my informed
2 consent while they make their initial office visit,
3 and I go through all of these features like, you know,
4 the position, various positions of the implants,
5 whether to have a textured or a smooth implant, and
6 all of these issues such as carcinogenicity, altered
7 mammography, capsular contracture, rupture, bleeding,
8 infection, the whole litany of things that we've gone
9 over.

10 And then I give them the booklet to go
11 home and read, and then I say, "Do you have any
12 questions?"

13 And typically the answer is, "No, I've
14 read through it. You told me this. I think I
15 understand it."

16 DR. BURKHARDT: Thank you.

17 DR. BOYKIN: I have a question.

18 CHAIRMAN WHALEN: Dr. Boykin.

19 DR. BOYKIN: I'd just like your opinion on
20 the use of warranties by manufacturers for implants
21 and if you feel this is a positive step for them and
22 how it might relate to any future litigation or if

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1 there are some clauses that might prevent that, how
2 that might be effective.

3 DR. YOUNG: Well, I think there are two
4 things that can be done to significantly improve this.
5 One is I think a device registry program should be
6 linked to the patient having to return the card that
7 we've made up to the central area to inform them that
8 they've had a problem in order to get a free implant
9 to replace one that deflates.

10 And I think that will enhance compliance,
11 and almost every EQUAM (phonetic) country has a breast
12 implant registry. Holland and Germany have very
13 successful implant registries working along these
14 lines.

15 The other thing that I think that in terms
16 of warranting issues, I think it would behoove the
17 manufacturers to incorporate what might be sort of an
18 insurance policy that may be a premium to attach to an
19 implant that would say not only will you get a
20 replacement implant, but the cost of the surgery to
21 remove the old implant and ^{**}put back the new device
22 will be covered by this insurance plan.

1 That in my experience would eliminate many
2 of the dicey issues that evolve between the patient
3 and the physician. It also would encourage the
4 patient to return to the original physician to get the
5 surgery, and not that that's necessary or good
6 essentially, but it would probably enhance our
7 understanding of failure rates and complication rates,
8 which would be good.

9 CHAIRMAN WHALEN: Dr. Chang.

10 DR. CHANG: Dr. Young, in your opinion,
11 who should maintain this registry?

12 DR. YOUNG: I have no doubt that that
13 should be maintained by organized plastic surgery. If
14 the manufacturers maintain it, we'll never get the
15 information. If the FDA maintains it, we probably
16 will get less compliance, and it may be treated as
17 proprietary evidence, and by not wanting to do the
18 right thing, but by the rules that they have to work
19 under, they may not be able to make that information
20 as available to the surgeons who are the direct then
21 respondents to the patients.^{**}

22 Because I think as plastic surgeons our

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1 primary response needs to be to the patient, and if we
2 have access to that data, we can disseminate the
3 information rapidly and respond to it.

4 CHAIRMAN WHALEN: Ms. Dubler.

5 MS. DUBLER: Thank you, Dr. Young.

6 That was a very interesting presentation,
7 and I wish you could comment on the following. We had
8 some discussions yesterday, which I'm sure you heard
9 about legislating surgeons, surgical technique, and
10 telling surgeons what to do, and there was the
11 majority of the panel who thought that was neither
12 feasible nor a good idea.

13 And yet surgical technique and departures
14 from good surgical technique seem, in fact, to be
15 quite important in untoward, unpleasant, negative
16 results.

17 What do you do?

18 DR. YOUNG: Well, unfortunately, as I
19 believe Dr. Burkhardt pointed out, we are limited in
20 our ability to control who performs these procedures.
21 In a university, such as ^{**}where I work, we have very
22 set policies and very set rules and deviation from

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1 those rules results in consequences.

2 Unfortunately as I understand it the
3 restriction of trade rules are such that we can't say
4 to people, "You have to follow this cookbook."

5 I think that what we can do is that in
6 residency training and in continuing medical
7 education, we can emphasize the importance of what we
8 know about these issues of using the best techniques,
9 and I think we need to emphasize what's gone on here;
10 that there are places where complication rates are
11 clearly too high. There's information that we don't
12 understand, and we need to do research to figure that
13 out.

14 And there are things that if you go down
15 this path, you will have some of these problems, and
16 you should not do that.

17 Now, as you probably know, dealing with
18 physicians is a little bit like herding cats. You can
19 open the door for them, but they won't always go
20 through. But I think those are the issues that we can
21 do, and I think we have to have peer pressure to say,
22 you know, when you misbehave, you know, you get dealt

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1 with.

2 MS. DUBLER: Well, I think that's an
3 interesting answer. I think it's inadequate, given
4 the recent IOM report on mistakes and negative health
5 effects, and perhaps what we should be doing is
6 alerting patients to the fact that there are
7 differences in techniques that lead to differences in
8 outcomes, and perhaps giving the patients more
9 information to query their prospective surgeons.

10 Might that be useful?

11 DR. YOUNG: I think it would be.
12 Obviously the President is moving in this direction
13 with relation to hospital related injuries and
14 complications. Maybe we will come to something like
15 that where there is a rating card, you know. They've
16 done that in the East Coast with cardiac procedures,
17 and there haven't been a significant increase in
18 litigation, and the death rate has dropped
19 significantly under those circumstances.

20 So I think that things like that probably
21 deserve a proactive look and maybe it may be something
22 that we should explore in a limited setting in maybe

1 one geographical area before we decide to implement
2 something on a national scale only to find out we went
3 in the wrong direction or need to modify it.

4 MS. DUBLER: Thank you.

5 CHAIRMAN WHALEN: Thank you, Dr. Young.

6 There will be a further period of public
7 comment later in the morning if there is anyone else
8 who wishes to address the panel.

9 MS. DUBLER: We've received some slides
10 and write-ups from people who testified top the panel.
11 Would it be appropriate to ask if those slides could
12 be made available to the members of the panel?

13 DR. YOUNG: I'll be glad to give you this
14 and a whole lot more if it'll help you.

15 (Laughter.)

16 CHAIRMAN WHALEN: Thank you.

17 We are going to be proceeding to the open
18 committee discussion, and I would like to ask that the
19 sponsor start to come forward for their presentation.

20 I'd like to remind public observers at
21 this meeting that while this^{**} portion of the meeting is
22 open to your public observation, as public attendees

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1 you may not participate unless there is a specific
2 request from a member of the panel.

3 When the sponsor is ready, please feel
4 free to proceed with your presentation.

5 DR. ESCHBACH: Mr. Chairman, distinguished
6 members of the panel, my name is Scott Eschbach. I'm
7 the President and CEO of McGhan Medical Corporation.

8 For 25 years McGhan Medical has been a
9 developer, manufacturer and marketer of medical
10 devices to the aesthetic medicine market.

11 Since 1990, we have been collecting data
12 on our saline filled implants, and in December of 1994
13 began working with the agency to develop the state
14 submission of data for support of our PMA.

15 Today is the culmination of that activity.
16 Contained in the more than 30 volumes of our
17 application are both preclinical and clinical results.
18 We will present a brief overview of these data,
19 focusing the large majority of our allotted time on
20 the clinical outcomes.

21 We are pleased to present these data, and
22 I would like to express our gratitude and our

1 appreciation to the more than 4,400 patients and over
2 400 physicians who participated with us in these
3 studies.

4 Leading our presentation today is Dr. Ray
5 Duhamel, Vice President of Regulatory and Clinical
6 Affairs.

7 Joining Dr. Duhamel is Dr. Scott Spear, a
8 plastic surgeon at Georgetown University who will
9 provide some clinical assessment of the study outcomes
10 concerning quality of life and patient satisfaction
11 will be addressed by Dr. Marie Pletsch, a practicing
12 plastic surgeon in Northern California.

13 I thank you in advance for your
14 consideration.

15 Dr. Duhamel.

16 DR. DUHAMEL: Thank you, Scott.

17 My name is Ray Duhamel. I have been
18 involved in implant biology and biomaterials research
19 both in the academic world and in the industrial world
20 for over 20 years.

21 I'm pleased today to present the outcome
22 of our McGhan Medical studies over the course of the

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1 last five years or so and in some cases for longer
2 than that. We will be presenting our results in three
3 areas: preclinical studies. I will present an
4 overview of the clinical studies, and then we will
5 concentrate on the data from the core or pivotal
6 clinical studies, which will be a joint presentation
7 by myself, Dr. Spear and Dr. Pletsch.

8 I will take just a few moments just to
9 tell you about the preclinical testing that was
10 performed because we think the bulk of our time should
11 be spent on the clinical data.

12 We have addressed all elements of the
13 guidance. McGhan Medical and FDA over the last
14 several years have worked very closely and have been
15 in frequent communication about various issues to
16 bring to completion the requirements of the FDA as
17 stated in the guidance. We have completed 15 of 17 of
18 the tests that were described in the summary results
19 of the preclinical data.

20 There are two remaining issues that are
21 incomplete that are what I would characterize as a
22 dispute among scientists about the way to apply

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1 certain methodologies and the way to interpret the
2 resulting data.

3 We are still discussing those two areas,
4 namely, fatigue and fold flaw testing, with the
5 agency, and we believe that these issues can be
6 successfully resolved with a focused attention and
7 resolved in short order and come to some resolution
8 about how to proceed.

9 Just to state very briefly the situation
10 as we see it regarding fatigue and fold flaw, we are
11 talking here about preclinical data on the benchtop.
12 However, we must recognize that we have actual in vivo
13 data regarding reliability. The clinical data
14 demonstrate that the cumulative device rupture rate is
15 2.7 percent for augmentation and 4.6 percent for
16 reconstruction at three years, and that's a reality
17 against which discussions of some of the subtleties of
18 the in vitro testing need to be kept in perspective.

19 With regard to the type or the cause or
20 the primary modality of failure of devices in clinical
21 use, we have examined over 200 explants in a
22 controlled manner and concluded that the largest cause

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1 of failure is due to fold flaw.

2 Now, this does not require a great deal of
3 testing. It requires simply informed inspection of
4 the devices, and it's something that the surgical
5 community has learned a long time ago, and that is
6 that fold flaw, although it is an event mediated or
7 event triggered failure, does not apply to devices who
8 don't have a fold, which don't have a fold, but when
9 they do have a fold, there is a process that takes
10 place that may eventually lead in a failure of the
11 device either as a pinhole or as a tear.

12 And this can be readily observed simply by
13 looking at the devices as they are returned.

14 The cause of folds is indeterminant, but
15 may be procedure related or patient specific, and they
16 come about by a variety of means which our clinicians
17 would be better prepared to discuss.

18 Now I'd like to turn to an overview of the
19 clinical studies. Before discussing the prospective
20 multi-center trials, I just want to make a comment
21 about the retrospective studies that we and other
22 manufacturers are asked to support and that were

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1 presented yesterday. So I won't go over them again.
2 That's the SEER study and the study by Dr. Cunningham.

3 I do wish to point out, however, that in
4 the case of the SEER study, because of the time frame
5 in which the patients that were included in that study
6 were collected and the time frame in which McGhan
7 Medical devices were available that we are going to
8 discuss today, there were virtually no McGhan Medical
9 devices in the SEER study, and a very small proportion
10 of McGhan Medical devices in the Cunningham study.

11 Now, let's turn to the four prospective
12 multi-center trials. Prospective, I think, is the key
13 word about the nature of these studies, and they are,
14 of course, all open label studies.

15 The AR-90 study is a study that included
16 both silicone and saline devices, and of course, I'll
17 restrict my few comments on that study to the saline
18 devices.

19 There were two arms to the study. There
20 was a moderate size population of augmentation
21 patients, and there was a very small reconstruction
22 group which might be characterized as a pilot study.

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1 Certainly we regard the study and so did
2 the FDA in 1994 and made that very clear they
3 considered these studies to be preliminary, and we in
4 McGhan Medical in '94 in consultation with the FDA did
5 develop protocols for what were to be the pivotal
6 studies, and these studies I'll talk about in a
7 moment.

8 Those studies supersede the AR-90 study,
9 and I will not present any data from the AR-90 study
10 this morning, although that data is available and is
11 presented in the PMA.

12 The second study is referred to as the
13 LST, large, simple trial. The two manufacturers on
14 the market in '95 were asked to carry out a large
15 trial, to collect safety data on four very specific
16 complications to an endpoint of one year, and I will,
17 in a very summary way, give you the results of that
18 study.

19 Our focus, however, through the rest of
20 this presentation will be primarily on what we call
21 the pivotal or the core studies. They were run under
22 two separate protocols, one protocol for the

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1 augmentation patient, one protocol for the
2 reconstruction patient.

3 So they were entirely different studies,
4 although they were quite similar in the nature of the
5 protocol, the way the data was collected. There were
6 some differences, but they were separate studies.

7 These studies were, as I said, developed
8 and designed in consultation with the FDA and approved
9 under a 1994 agreement prior to initiation.

10 This is the status of those four
11 prospective studies. The enrollment dates you can
12 see. The duration of the studies, the planned
13 duration of the studies in the protocol, were five
14 years for AR-90, one year for LST, and five years for
15 both of the pivotal studies.

16 The first two are completed. The pivotal
17 studies are ongoing, and we're currently in a four
18 year follow-up period. The three year data are
19 complete. All patients have traversed the three year
20 follow-up, and the data have been analyzed.

21 The four year follow-up, we are in it and
22 no patient at the moment has traversed the four year

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1 follow-up period. Therefore, no patient is
2 noncompliant. We are collecting data in that follow-
3 up period.

4 I think the operative word here about the
5 studies is that they were designed to a protocol of
6 five year follow-up, and so an important point to make
7 is that all of the data that is being presented here
8 is based upon active follow-up. This is patients
9 coming into their follow-up visit and receiving a
10 physical exam.

11 This depicts the size of the studies in
12 terms of patient enrollment. The AR-90 study, as I
13 said, had two arms, and note the reconstruction arm
14 only had 25 patients, a total of 493.

15 The LST had a grand total of 2,855
16 patients and is the only study in which there was a
17 cohort that was a revision position that was enrolled
18 at enrollment as a specific cohort.

19 That data is the only data in the
20 presentation that is directed specifically at LST,
21 with the exception of within the pivotal studies those
22 patients who became revision patients because of the

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1 need to explant and replace or explant devices.

2 We recognize that the LST data do not meet
3 the time requirements nor the size requirements of the
4 other indications, and that question will be put to
5 you in terms of what to do about that, and I'm sure
6 you will be provided advice.

7 One way to deal with that, as you
8 discussed yesterday, is in the labeling.

9 The A-95 study had 901 patients, the R-95
10 study 237, and the grand total was 4,486 patients on
11 which data were collected.

12 Excuse me just a moment. My lips were
13 about to stick together here.

14 This shows the status in terms of
15 compliance. You can read those figures for the top
16 three studies. Let me focus on the pivotal studies
17 which will be the subject, as I said, of the rest of
18 the presentation.

19 The guidance document states that the PMA
20 is to be based upon a minimum of two year data with 80
21 percent compliance, at least 80 percent compliance.
22 As you can see, we were well over that at two years,

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1 but we have completed three years with 80 and 88
2 percent compliance, respectively.

3 Now, this is adjusted compliance.

4 The demographics of the patient
5 populations in the augmentation and reconstruction
6 studies are depicted here. The largest difference is
7 the age of the patients. The reconstruction patients
8 are not unexpectedly approximately 15 years older in
9 terms of the median than the augmentation patients.

10 In both studies, the patients are
11 predominantly Caucasian.

12 These are the device styles or designs
13 that were included in these studies, and you can see
14 the styles listed in terms of two key characteristics
15 of the device design. One characteristic is the
16 surface structure described as either textured or
17 smooth, and the other is the profile or shape, which
18 we refer to as anatomical or round.

19 If you look at the distribution of those
20 devices within the two studies, you can see that for
21 reconstruction patients the devices were -- 98 percent
22 of the devices were textured, and within that group,

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1 the vast majority, 87 percent, were anatomical.

2 In the augmentation group, you can see
3 that smooth, round devices were a significant
4 proportion of the devices used in addition to the
5 textured devices.

6 I might point out on that slide, if you
7 look at the bottom row on the styles listed there, the
8 style 68 and the style 60, the style 60 is a valve
9 with a -- is a device with a leaf valve design, and
10 all the other devices have a diaphragm valve design.

11 We are not seeking approval for the leaf
12 valve design. It's been stated that we notified the
13 FDA of that and we ceased marketing that device in
14 1999. However, we actually stopped manufacturing that
15 device many years earlier, and we're mainly
16 distributing that device to physicians who had
17 patients already with that device, and we're using
18 them for replacement.

19 Implant placement, very different between
20 the two groups. Reconstruction patients, 98 percent
21 of the devices were implanted submuscularly. One
22 percent subcutaneous reflective of prophylactic

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1 mastectomy.

2 In the augmentation group, you can see
3 again that the submuscular is predominant, but there
4 were a very significant number of patients with
5 subglandular placement.

6 Here I'll present the occurrence of breast
7 cancer. This, the issue of breast cancer and the
8 issue of connective tissue disease has been addressed
9 by studies better designed than this one to address
10 them, but nonetheless, we will report on the incidence
11 that was observed in these studies.

12 In the augmentation study, there was only
13 one post implant report of breast cancer 27 months
14 after surgery. In the reconstruction group, who all
15 had breast cancer or, with the exception of the
16 prophylactic mastectomy patients, there were 19 post
17 implant reports and the various categories of whether
18 they had breast cancer alone or metastasis as well or
19 metastasis alone are depicted in the bottom of the
20 slide.

21 Connective tissue disease, again, the key
22 issues there have been addressed elsewhere in more

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1 definitive studies than this study was ever designed
2 to accomplish. Nonetheless, we report on the CTD
3 information that was collected.

4 The methodology of connective tissue
5 disease reporting in this study was primarily by
6 patient self-reports. It was a form, a questionnaire
7 that had a list of connective tissue diseases
8 described which the patients could check off or they
9 might report it in some other way at an office visit
10 and that was collected.

11 Whenever a patient self-reported a
12 connective tissue disease, then the principal
13 investigator was asked to follow up to confirm the
14 patient's self-report with the diagnosing physician.

15 Needless to say, you might think that
16 that's an easy task, but it's not. But we put a lot
17 of effort into having our investigators do that, and
18 they did it. They put in considerable effort into
19 attempting to define whether the diagnosis was correct
20 or not.

21 These are the reports that were obtained
22 with regard to connective tissue. There were -- you

1 can read that for yourself, but I think the two key
2 points on the slide.

3 The very high rate of incorrect reporting
4 of connective tissue disease. The patient would
5 report the disease, but upon final examination, it
6 would turn out that the patient was incorrect. In
7 some cases we never could determine whether they were
8 correct or not, and that was characterized as
9 uncertain.

10 If you look at those with confirmed
11 diagnoses in the bottom panel, there was only one
12 patient in the augmentation group, none in the
13 reconstruction group, who had a confirmed diagnosis
14 with also a definitive onset post implant.

15 There were three patients and one,
16 respectively, with an indeterminant onset, which we
17 are still attempting to complete and determine.

18 Now we'll turn to the local complications.
19 As I said earlier, the local complications are
20 collected by physical examination and office visit.
21 The primary way in which we will present the data will
22 be by patient, although for certain complications of

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1 interest we'll present the by device complication as
2 well.

3 The two types of presentation will be life
4 table analysis, Kaplan-Meier, of cumulative risk of
5 first occurrence of the complication for which we did
6 develop, and we won't show them here, but we did
7 develop and in the tables we have the 95 percent
8 confidence intervals, and we believe that that is in
9 many ways the worst case presentation, and it is the
10 presentation that would be most informative about two
11 patients who are considering breast implant surgery
12 with these devices.

13 We'll also present the noncumulative
14 prevalence or frequency of occurrence of a
15 complication at each follow-up visit. I will present
16 for certain complications the time course to
17 illustrate not only the time course but the
18 methodology used.

19 The major complications, those that were
20 included in LST, would be presented, as well as the
21 secondary surgery, and we present secondary surgeries
22 as both implant related or distinguishing between

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1 implant related and procedure related.

2 We'll also then -- at that point I'll turn
3 the podium over to Dr. Spear, who then will present
4 the rest of the local complications, in fact, the
5 entire series, and provide clinical explanation and a
6 clinical perspective on the breakdown, you'll notice
7 on that slide, of the implant replacement, removal,
8 the reasons for implant removal and what they mean
9 clinically and the types of secondary surgery, both
10 implant and procedure related.

11 Before going over the data on the pivotal
12 studies I will present just one slide on the LST, and
13 I think the key point to take away from this slide, I
14 think, is that at least three of those complications
15 listed there, that the revision complication rates are
16 somewhere in between the augmentation and
17 reconstruction.

18 And you can make of that what you will,
19 but it's at least in part some reflection of the fact
20 that we have two populations in the LST group, those
21 who came into the group as augmentation, primary
22 augmentation, or primary reconstruction.

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1 Now, let's focus on the pivotal studies.
2 I'm going to spend some time on this infection slide
3 by patient to illustrate the mode of presentation so
4 that we can then speedily go through the remaining
5 time course presentation.

6 The reconstruction patients or
7 reconstruction risk among patients is pointed out in
8 blue, and reg is augmentation, and you can see the
9 rate is very much higher for reconstruction. That's
10 a pattern that you'll see for many of the
11 complications, but not all, repeated.

12 We also have for the point of information
13 in the middle of the figure a block that gives you the
14 three year rates by device, which is in some cases of
15 more interest than others, but it does give you the
16 flavor of the difference between the by patient rates
17 and the by device rates.

18 The bottom panel shows the prevalence
19 rates, and so if we look at the shape of the
20 cumulative curve, you can see that for this
21 complication most of the **rates are occurring very
22 early at the zero to four weeks and then some more at

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1 six months, but then that pretty much levels off, and
2 that's more dramatically illustrated perhaps by the
3 prevalence rates where you can see the spikes are very
4 high early on, and then there are virtually none.

5 Actually in these studies there were
6 virtually no infections at the later periods. In the
7 AR-90, I will make one comment about in that study
8 there were some infections that came about at later
9 years, but in those cases they seemed to be associated
10 with a secondary surgical procedure.

11 A similar presentation for capsular
12 contracture, now you see a different time course.
13 There is a more gradual increase. The increase is
14 still taking place, but the slope of the cumulative
15 curve has definitely flattened out quite a bit, and
16 you can see that even or as clearly in the prevalence
17 rates, where you can see that they're decreasing
18 slightly.

19 One thing I hadn't pointed out in the
20 infection slide, but I will now, is that sort of the
21 open figures, and the four**year reflects that we are
22 still -- those are interim data, and they are --

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1 patients are still coming through the interval, as I
2 said earlier, and so we expect that those rates will
3 actually come down because the patients who have
4 experienced the complications, of course, are already
5 recorded, and the remaining patients presumably will
6 have fewer complications. So that's the typical
7 pattern that we would see.

8 So we expect as the interval is completed
9 that those will come down. Those are interim data,
10 and so our focus is on the three year data, and we
11 think it's the three year data that should be the
12 subject of the labeling.

13 Here we have leakage deflation, and that's
14 an interesting combination of terms. You would think
15 deflation should be the primary factor, but we had
16 data which we took very conservatively. If the
17 clinician reported leakage or reported deflation, then
18 both of them smack of failure of the device, and so
19 they're lumped together with no need for
20 corroborating physical evidence.

21 If the clinician said it leaked and it
22 deflated, then that's how it was scored. You can see

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1 that those rates are going up. They are going up.
2 There's no apparent -- there is something of a
3 flattening, but of course, it's too small to tell.
4 There certainly is no acceleration taking place in the
5 rate of this at the third year, and you can see that
6 equally well in the bottom panel.

7 One interesting point here is that on the
8 by patient rates, the rates for augmentation and
9 reconstruction, virtually identical. On the device
10 rates, there is something of a difference, but not the
11 large difference that you saw yesterday.

12 We can't quite explain that, although we
13 believe and, in fact, we have no reason to expect that
14 something that is entirely due to the structure of the
15 device should differ between reconstruction and
16 augmentation patients. We have no explanation for
17 differences, and, in fact, we don't have any
18 significant differences to explain.

19 This is a slide of implant replacement and
20 removal. Now, this is listed here as a different
21 complication, but, in fact, it's an accumulation of
22 the leakage deflation numbers that you saw in the

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1 previous slide on which are superimposed other
2 explantations with replacement primarily, but some
3 without replacement, and I'm going to stick with the
4 time course here, and very soon Dr. Spear will come up
5 and talk to you about the various types of reasons for
6 explantation and replacement and give you a
7 perspective on what they mean clinically.

8 Again, you can see the time course is
9 interesting, and that certainly appears to have
10 flattened out, and as I said, the interim data are
11 what they are right now, and we expect them to come
12 down.

13 Here we have secondary surgery. Now we're
14 talking about a different type of complication. This
15 is one where there's been clinical intervention in the
16 form of the surgery.

17 Dr. Spear will tell you about what that
18 means. What we have done here is divided the rates
19 into implant related, which you see on this slide, and
20 on the next slide you will see the non-implant or what
21 might be termed procedural related secondary
22 surgeries.

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1 The very dramatic difference there between
2 reconstruction and augmentation will be explained
3 further by Dr. Spear, but it's primarily planned
4 nipple procedures that are included in the total, and
5 you can make a judgment as to whether that should be
6 treated as a complication or not.

7 Now, I'll turn the podium over to Dr.
8 Spear for the clinical explanation.

9 DR. SPEAR: I'm trying to get away from
10 computer illiteracy, but it's a slow process.

11 Mr. Chairman and panel members, let me
12 begin by thanking you and the sponsor for the
13 privilege of presenting this much awaited and
14 important data before you today.

15 I'm a paid consultant to this company and
16 a practicing plastic surgeon at Georgetown University
17 Medical Center. I have no expenses for attending this
18 meeting since I live locally.

19 I personally hold a small amount of stock
20 in a related company, but I'm not a party to any
21 litigation. However, I do occasionally serve as an
22 expert witness for patients, physicians, and

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1 manufacturers.

2 Finally, I'm also involved in the clinical
3 practice of plastic surgery of the breast, which
4 includes cosmetic breast surgery and reconstructive
5 surgery for congenital breast deformities, as well as
6 acquired breast deformities, such as seen with breast
7 cancer.

8 Saline filled breast implants are just one
9 of many tools that are available to me and to my
10 patients to solve their medical problems. Yet they
11 are very valuable devices which can correct problems
12 not correctable by other devices or techniques.

13 I use these devices virtually every day to
14 help a variety of women, including doctors, lawyers,
15 judges, FDA staff, friends, family, and neighbors. I
16 want to emphasize that while I believe these devices
17 have great value, they also have risk, but in
18 perspective, all of the other devices, drugs, and
19 procedures that I use have risks, too, many of them
20 far greater, in fact.

21 As a surgeon it is my responsibility to
22 help my patients decide what treatment is best based

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1 upon an intelligent risk-benefit analysis. By and
2 large, the women that I consult with every day are
3 smart, well informed, careful to make wise decisions.

4 I think it is important to leave these
5 women options and choices. For many years I've
6 informed these women that the likely failure rate of
7 these devices is approximately one to two percent per
8 year, and armed with that and other similar realistic
9 information, the vast majority had made the decision
10 to proceed with the surgery.

11 With that said, let me begin with the
12 presentation. Let's look at the issue of implant
13 replacement or removal.

14 The reality is in these studies that
15 nearly all the devices removed were replaced. Among
16 the augmentation patients, fully 122 out of 132
17 devices were replaced and only ten devices were not
18 replaced.

19 In a reconstruction study, 17 out of 62
20 devices were not replaced, whereas 45 were replaced.
21 Clearly, the vast majority of implant removals were,
22 in fact, replaced.

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1 What was the cause for implant replacement
2 or removal? For augmentation patients, the highest
3 frequency of occurrence was for change of size or
4 style of the device. Other common reasons were
5 leakage and deflation and capsular contracture.

6 Likewise, of the 62 devices removed among
7 reconstruction patients, the most common reasons were
8 capsular contracture, again, change in size or style,
9 and leakage and deflation.

10 But a significant number of these
11 reoperations of the device were not, in fact,
12 medically indicated, but rather a matter of
13 preference.

14 In addition to implant replacement or
15 removal, there were other operations which were
16 implant related secondary surgeries, but these were
17 generally minor office procedures, such as scar
18 revision and aspiration, and generally did not
19 constitute major operative reinterventions.

20 Non-implant related secondary surgery,
21 such as removal of skin lesions or cysts, occurred in
22 only two percent of augmentation patients. There were

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1 far more non-implant related secondary surgeries in
2 the reconstruction patients, but these were primarily
3 planned secondary procedures done as part of the
4 reconstructive process, such as nipple reconstruction,
5 and certainly should not be construed as a
6 complication of the device.

7 I will now present data for each of the 23
8 complications for which clinical data was collected in
9 this study. Some of these complications were assessed
10 using severity ratings. It is our position that only
11 the moderate, severe, and very severe assessments are
12 medically and clinically significant. Therefore, we
13 are presenting the complications in that context.

14 The next three slides, including this one,
15 deal with all 23 of the complications we tracked in
16 these studies. It was an exhaustive review of all the
17 possible complications we could expect.

18 The first slide lists eight implant
19 related complications. Of these, the three with
20 medical and clinical significance are capsular
21 contracture, leakage or ^{**}deflation, and implant
22 extrusion.

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1 The other complications are, in reality,
2 more cosmetic than medical in nature.

3 The second graph, second bar graph here,
4 depicts eight procedure related complications and are
5 by definition related to the procedure, not the
6 device. Examples include things here such as
7 hypotrophic scarring, skin paresthesia, infection,
8 seroma, tissue necrosis. These are not specific to a
9 device. These are more specific to having had any
10 operation on the breast.

11 And the following graph depicts seven
12 additional procedure related complications, all of
13 which occurred in less than ten percent of patients.
14 These included a skin rash, delayed wound healing,
15 lymphadenopathy, others, basically very low level of
16 incidents of minor complications which, again, are
17 more likely related to just having had a procedure not
18 specific to the device.

19 Before I introduce Dr. Pletsch, I would
20 like to finish by saying in my opinion as a clinician
21 with 30 years of clinical** experience, the number of
22 significant medical complications is, in fact, quite

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1 small and it's probably, in my opinion, best
2 represented by the percentage of implants that were
3 reoperated for medical reasons.

4 This risk-benefit ratio, again, in my
5 opinion represents a very reasonable risk for the
6 benefits of this device.

7 Thank you.

8 Let me now introduce Dr. Marie Pletsch,
9 who will introduce the effectiveness data.

10 DR. PLETSCH: Thank you, Dr. Spear.

11 Mr. Chairman and panel members, I'm a
12 Board certified plastic surgeon practicing in Santa
13 Cruz and Monterey, California. I am here to present
14 the McGhan effectiveness studies.

15 McGhan is paying for my travel expenses to
16 be at this meeting, but I do not have any financial
17 connection with them.

18 I was previously employed by another
19 company as a medical monitor for their saline studies,
20 but no longer have any affiliation with that.

21 I'm a member of the American Society of
22 Plastic Surgeons, the American Society of Aesthetic

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1 Plastic Surgeons, and a member and past president of
2 the California Society of Plastic Surgeons.

3 I am not, nor have I been a party to
4 litigation regarding breast implants. I have been a
5 witness many times in litigation regarding silicone
6 gel breast implants, but never saline implants.

7 I derive a portion of my income by
8 implanting saline breast implants.

9 There may be arguments regarding the
10 safety of any medical device. While I believe that
11 saline filled implants are safe, there is no doubt in
12 my mind that they are effective.

13 Having practiced plastic surgery for over
14 30 years, and having inserted breast implants since
15 the 1960s, these studies merely confirm what I already
16 knew about the effectiveness of breast implants. I
17 believe that effectiveness studies would show
18 essentially the same results for any breast implant
19 with some minor differences.

20 The augmentation patients want to look
21 better and feel better about themselves. The
22 reconstruction patients want to be restored to as near

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1 normal as possible, and the reconstruction helps them
2 forget their cancer.

3 I especially know the feelings of the
4 reconstruction patients since I am one of them myself,
5 having undergone bilateral reconstruction following
6 breast cancer surgery, having four procedures from
7 1998 to 1991. I would opt for as many procedures as
8 was necessary to make me feel better about myself, and
9 if I had the choice of no implants because of concerns
10 for safety and having to have multiple surgeries, I
11 would choose the latter.

12 Plastic surgeons who do this surgery know
13 how helpful breast implants are in augmentation and
14 reconstruction. We did not need any studies to know
15 that, but some people who do not do the surgery need
16 studies to convince them.

17 So we welcome the confirmation which
18 studies provide and hope that the studies will dispel
19 any more doubt on this topic.

20 The 1995 augmentation study measured
21 change in bra cup size.** Bra cup size was also
22 measured in the '95 reconstructive study, post implant

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1 only, and the '95 augmentation and the reconstructive
2 studies measured quality of life using validated
3 standardized psychological tests.

4 The studies showed that bra cup size
5 increased in 96 percent of patients. Both
6 augmentation and reconstruction patients completed an
7 eight page questionnaire before surgery and again at
8 six months, one year, and three years postop.

9 The scores were compared to U.S.
10 population data for same age females. Four general
11 areas were studied: patient's concept of physical
12 health, emotional health, self-esteem, self-concept
13 and satisfaction.

14 In contrast to the data you saw yesterday,
15 we covered general health and emotional questions in
16 addition to self-esteem and satisfaction.

17 The next six bar graphs summarize the
18 results of the quality of life studies. In a general
19 way the first two slides document answers to general
20 health questions. The next two document results that
21 are related more directly to the feeling about the
22 breast themselves, and the last two relate to the

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1 satisfaction derived from the breast implants.

2 The results parallel what some of the
3 consumer speakers yesterday described. One speaker
4 spoke of having been a self-confident person before
5 augmentation, but being self-conscious about her
6 appearance, specifically in relation to her breasts
7 and how that affected how she felt about herself.

8 She had difficulty articulating the
9 difference between the general self-confidence and the
10 lack of confidence in her appearance in reference to
11 her breasts. I think this may explain why the quality
12 of life studies are not entirely what is expected from
13 what we experience with these patients clinically. We
14 do see a very marked improvement in self-confidence.

15 Unfortunately, there were no control
16 groups. So it's difficult to interpret the general
17 health results. Using medical outcome studies, 20
18 items health survey, and the SF-36 status survey,
19 self-concepts of pain, general health, physical role
20 limitation, and physical functioning were measured.

21 The reconstruction patients had a higher
22 score three years postop than preop, and were higher

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1 than the U.S. general female population.

2 The augmentation patients had a
3 significantly higher score preoperatively than the
4 U.S. population and had a small decrease in their
5 scores postoperatively, but still remained higher than
6 the U.S. population. These patients are significantly
7 healthier in all respects than the U.S. female
8 population.

9 The reconstruction patients had an
10 increase in all perceptions from preop to postop when
11 role emotional, role functioning, social functioning,
12 mental health, health perceptions, and impact of
13 health on social functioning was tested. The
14 augmentation patients had a very high score in all of
15 these areas preoperatively and a very small decrease
16 postop.

17 Again, these are very healthy patients in
18 the beginning. So any change tends to go toward the
19 norm.

20 Self-esteem, self-concept, which we spend
21 so much time and money on trying to achieve from
22 childhood, is easily achieved with augmentation

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1 patients. Feeling physically appealing, physically
2 adequate and desirable, all increase significantly.
3 They even increase or remain the same for
4 reconstruction patients.

5 The Tennessee self-concept physical scale
6 and Rosenberg's self-esteem showed minimal changes for
7 both augmentation and reconstruction patient in
8 general areas, but when the questions were
9 specifically addressed, the scores increased:
10 physically appealing, physically adequate, and feeling
11 desirable.

12 General scores for body esteem, total,
13 weight, and physical condition, decreased or remained
14 the same for both reconstruction and augmentation
15 patients. However, attractiveness body esteem
16 increased for augmentation patients.

17 Personal life, a slight increase for
18 reconstruction and no change for augmentation, but
19 there was marked increase in satisfaction concerning
20 breasts in general, how well the breasts matched, and
21 sexual interest for both reconstruction and
22 augmentation patients.

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1 For augmentation patients, satisfaction
2 increased markedly for breast symmetry, shape, size,
3 texture and natural feel. These items were examined
4 only postop in reconstruction patients, but the scores
5 were high, and in the area of breast shape, size, and
6 texture, there were higher scores than for
7 augmentation patients preoperatively.

8 Overall, patient-physician satisfaction at
9 three years was 95 percent for both patients and
10 physicians for augmentation, and 88 percent for
11 patients and 89 percent for physicians for
12 reconstruction.

13 Few, if any, surgical procedures come near
14 these figures.

15 In summary, saline implants demonstrate an
16 excellent risk-benefit ratio which is reflected in the
17 high satisfaction rates and a relatively low clinical
18 significant complication rate.

19 And now I'll turn the podium back to Dr.
20 Duhamel, who will conclude the presentation.

21 DR. DUHAMEL: We've presented our data and
22 the conclusions to be drawn from the data have been

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1 ably presented by my colleagues at the podium. So I
2 will not recap that data. I will simply state that we
3 believe that the data presented provide reasonable
4 assurance of safety and effectiveness and serve as an
5 appropriate basis for approval of this PMA.

6 And we thank you very much for your
7 attention.

8 CHAIRMAN WHALEN: Thank you.

9 Are there questions of the panel for the
10 sponsors?

11 Dr. Boykin.

12 DR. BOYKIN: Yeah, the first question I
13 have refers to the LST study where we had three
14 groups, augmentation, reconstruction, and revision,
15 and I'd like to know a little bit more about the
16 revision group.

17 Where did they come from? I'm assuming
18 they're either augmentation or reconstruction
19 patients. Can you tell us how that broke down?

20 DR. DUHAMEL: I can tell you in an
21 approximate way. I think that is one of the key
22 points about revision patients, and that is that they

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1 are extremely heterogeneous group, and so your
2 question could extend to were they primarily
3 augmentation or were they revision or it could extent
4 to which device did they have. Is this their second
5 or their third revision, et cetera, et cetera?

6 And that was not collected in that study.
7 The approximate numbers I believe, I think were in the
8 range of 20 to 25 percent, were reconstruction
9 patients as primary implants, and the rest were
10 primarily augmentation.

11 Having said that, the age or the length of
12 time from the definition of, you know, the original
13 surgery varies enormously. It could be a year. It
14 could be 20 years. Very, very heterogeneous in terms
15 of their history.

16 DR. BOYKIN: That particular group is
17 interesting because you also show that they had a
18 higher deflation rate than either the augmentation or
19 the reconstruction patients, and I was curious as to
20 why that happened.

21 DR. DUHAMEL: The large number of
22 patients, but it's followed to one year. So it's only

1 part of the story.

2 I think the answer has to be we don't
3 know. The data, the groups on which we have key
4 information or the ones that we presented at least, we
5 followed them out to three years.

6 DR. BOYKIN: Were there any indications
7 about the group that experienced deflation that might
8 help the surgeon in terms of planning the operation?

9 DR. DUHAMEL: In that particular group?

10 DR. BOYKIN: Well, just in what you've
11 presented so far.

12 DR. DUHAMEL: I think at this point I have
13 to turn to Dr. Spear to give us a clinical
14 perspective.

15 DR. SPEAR: Are we on?

16 Could you ask that question again?

17 DR. BOYKIN: Any specific demographics or
18 characteristics about the deflation group that would
19 help the surgeon in planning the procedure?

20 DR. SPEAR: I think it's important to look
21 at this deflation data very carefully. In fact, we
22 did so since yesterday, and to me the most compelling

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1 part of the data is the low number.

2 So if you're talking about two percent of
3 devices over three years, it's hard to draw
4 conclusions for very small incidents or problems. So
5 even referring to the LST, which is not a major part
6 of the presentation this morning, all three
7 experiences were actually very similar.

8 I mean, the revision group was a little
9 higher than the augmentation or reconstruction, but
10 they're all between three and five percent. So I
11 think in terms of statistical validity I wouldn't make
12 a big deal out about the fact that one was three and
13 one was five in one year. That is probably more
14 artifactual.

15 But I think in terms of surgical technique
16 the answer is no. I don't think surgical technique at
17 least in this sample is an issue because we're looking
18 at very low deflation rates. So it's hard to pull out
19 a surgical technique issue in terms of that, and we
20 were very surprised in contrast to the presentation
21 yesterday that our reconstructive and our augmentation
22 patients had about the same deflation rate, and those

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1 were vastly different operations.

2 So, again, it would tend to argue against
3 the surgery procedure per se for being the cause of
4 the deflation.

5 DR. CHANG: Dr. Spear, do you have any
6 conjecture of why the reconstruction patients,
7 although not significant, was higher? You said 2.7
8 compared to 4.6 percent.

9 DR. SPEAR: I don't know. I think, you
10 know, as a scientist I'd want to see more data and
11 longer follow-up and see whether, you know, that
12 actually meets the criteria of statistical validity
13 and the difference between the 2.4 and the four. It
14 may not, in fact, be statistically significant. I
15 think they're both low numbers.

16 DR. DUHAMEL: I would like to perhaps make
17 a comment on that point because here we are making
18 comparisons between augmentation and reconstruction.
19 There was no formal analysis to compare them. They
20 were different groups. There was never any intent to
21 analyze them. **

22 We juxtaposed the results because it does

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1 have some informative value, but we have run no
2 statistical tests of significance on any of those
3 numbers.

4 DR. CHANG: Dr. Duhamel, of the explanted
5 devices that you were able to examine, you stated most
6 were due to fold flaw. What percentage -- do you have
7 data in terms of what percentage you felt was due to
8 the valve leakage?

9 DR. DUHAMEL: Well, okay. This could take
10 some time to explain. Let me try to make this fairly
11 simple. It actually is simple, but we have to go
12 through a few assumptions first.

13 The first one is that when we examine
14 explanted devices, we're not exactly examining the
15 virgin device, if that's the correct term, but the
16 device as it was clinically. Surgeons have to remove
17 that device, and what do they do to remove that
18 device?

19 Well, Dr. Spear could probably discuss it
20 in detail, what his colleagues and he himself does,
21 but at the very least they have to remove the saline,
22 and sometimes -- and certainly that would involve

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1 reentering the valve. Sometimes it is done very
2 simply, perhaps more often by just simply puncturing
3 the shell.

4 And then after that, for reasons of
5 safety, the devices are sterilized, usually steam
6 sterilized, which means if they went through the valve
7 and then they either have to open the valve again
8 during the steam sterilization or this time seriously
9 puncture the cell or it will literally explode in the
10 autoclave.

11 And then when it arrives at our facility
12 for the safety of our employees, we sterilize it
13 again. So now it goes to the lab for observation, and
14 so what kinds of observations can you make.

15 You can actually make some very
16 intelligent observations, but you have to take into
17 account that you've got to attempt to distinguish
18 between what happened in all of this travail that the
19 device experienced and what you have in front of you.

20 In the case of malfunction of the valve,
21 we have some nondestructive ways of evaluating whether
22 the valve functions, and we have a certain number of

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1 devices that in the lab the valve does not appear to
2 be functioning well.

3 However, we also retain, we also get back
4 a number of devices who have not failed, which have
5 not failed structurally. They were removed because of
6 capsular contracture or they were removed for choice
7 for a whole variety of reasons, but they were not
8 structurally -- they did not fail structurally or leak
9 clinically.

10 And the frequency of malfunctioning valves
11 in our hands in the laboratory among devices that had
12 no clinical failure and the ones that did is exactly
13 the same. So what we're seeing is something that
14 could well have been induced and certainly we don't
15 see any significant increase in one group or the
16 other.

17 So now my personal belief and our belief
18 is that, in fact, valve leakage is very rare. On the
19 other hand, you can look at the device and look at
20 where you have holes, and certainly a slice with
21 scalpel you can generally recognize by the fact that
22 it has what we term a sharp edged opening. This is a

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1 very fresh cut.

2 There are other failures that are usually
3 very time. They might only be a pin hole or they
4 might be a running line that we call smooth edge
5 openings. You can recognize them. They're a little
6 polished. They're a little smooth, very, very
7 localized along the line. Those are virtually always
8 on a fold, on a crease, and those we believe are of
9 fold flaw failure.

10 We see devices that have not failed that
11 have those creases and presumably if they had not been
12 explanted for something else at some point in the
13 future they may well have progressed to failure.

14 For a long time at least I didn't
15 understand the modality of that because there had been
16 great interest in abrasion, and we did tabor testing
17 and submitted the data.

18 Tabor abrasion testing creates in the
19 textured device -- it's very obvious -- a very flat
20 plane that eventually gets smooth. You wear away the
21 textured layer and you get down to the smooth.
22 Virtually never see that in an explanted device.

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1 So there isn't this kind of broad,
2 abrasion of the device that eats away at the entire
3 surface. It's extremely rare to even see any area
4 that shows that kind of abrasion.

5 So we undertook to model on the benchtop
6 something that would create what we were seeing in
7 these explanted devices, and we induced a fold. We
8 sort of kept it in place in fluid, and we sort of
9 moved it around a bit for X number of cycles, and lo
10 and behold we were able to induce something that
11 looked exactly like what we saw in returned devices.

12 And when we did that, and let me plug in
13 and I'll show you. You may have seen in the panel,
14 but , but this is a highly schematic cartoon of the
15 fold that we induce on the benchtop. You can see, if
16 you can figure that out, it's essentially bent back on
17 itself.

18 And in the lower right panel where we're
19 showing a little more detail, what we observe, what
20 happened in vitro -- we could see it -- is that the
21 fold is actually rubbing on the inside of the device,
22 on the other part of the shelf in juxtaposition to the

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1 other inside surface of the shell. That where it
2 erodes on the inside.

3 Eventually that erosion proceeds to a
4 pinhole or a rip and then it leaks. Now, that
5 surprised me at least because here we were spending
6 all of this time at an abrasion on the outside and
7 rubbing it back and forth and trying to figure out
8 what causes failure, and here what causes failure is
9 entirely different, and the particles that are
10 generated, they are generated inside the device. They
11 never get outside the device.

12 So the particles that we were measuring,
13 and you may have seen that we submitted preclinical
14 data on particles that were generated by the Tabor
15 abrader far in excess of anything that ever happens
16 clinically had nothing to do with this kind of
17 failure.

18 Now, that in numerical terms, in terms of
19 frequency, all I can tell you is that is the general
20 impression. What we did, what I did actually in one
21 time was say, "Give me 200** devices and let's look at
22 them and compare the ones that had failed and the ones

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1 that had not failed."

2 And this kind of failure was only evident
3 on, was only seen on the devices that had failed
4 clinically, and the occurrence of these slits, what we
5 call sharped edge opening, had nothing to do with
6 whether the device had failed.

7 When those thing occurred, now, those may
8 have clinical relevance. With due apology to our
9 plastic surgeons, there are some suspicions that
10 sometimes they may get nicked, and that might proceed
11 to a different modality of failure, but that's very
12 rare, and it's a supposition in any case.

13 So that's what we think is the main cause
14 of that type of failure.

15 DR. SPEAR: Could I say something about
16 the valve?

17 DR. DUHAMEL: Sure.

18 DR. SPEAR: From a clinical point of view,
19 I'm happy to hear what Dr. Duhamel would say. From a
20 clinical point of view, I think the surgeons believe
21 that valve failures are usually the things that show
22 up fairly early. So if we were going to try to guess

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1 about device failures and valves, we would say as a
2 sort of supposition that the devices that seem to leak
3 in the first 90 days we would be more suspicious of a
4 valve failure, whereas late failures are more likely
5 shell failures.

6 CHAIRMAN WHALEN: Dr. Li.

7 DR. LI: A general question. Is the
8 information regarding your analysis of the 200
9 explants in your PMA?

10 DR. DUHAMEL: It is in the PMA as a
11 statement and an interpretation, not --

12 DR. LI: But there's no protocol or
13 statement of analysis?

14 DR. DUHAMEL: There was no protocol.
15 There was no protocol. Now, what we presented in the
16 PMA was this, which was a proof of principle.

17 DR. LI: I'll get to that in a second.

18 DR. DUHAMEL: Right.

19 DR. LI: So although I applaud definitely
20 your looking at 200 retrievals, it was from a
21 scientific standpoint kind of just a very large
22 anecdote then in the absence of a standard protocol,

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1 for instance, to look for leaks elsewhere other than
2 on the fold where you would expect them to be.

3 DR. DUHAMEL: Absolutely correct.

4 DR. LI: Okay.

5 DR. DUHAMEL: All right.

6 DR. LI: Now, on this fold flaw
7 examination, as I read into the details, the reason
8 that perhaps you get the wear on the inside is that
9 you tested these devices that were essentially only
10 filled halfway, about 45 percent under fill; is that
11 correct?

12 DR. DUHAMEL: Right. We were trying --
13 let me give you a little bit of background to that.
14 There were many attempts to mimic that failure, and we
15 couldn't induce it. So we were looking at ways of
16 making this happen and see what it was.

17 DR. LI: I understand that, but Dr.
18 Burkhardt has taught me in the last couple of days
19 that these things are never under filled, almost never
20 under filled. So although you have created a
21 laboratory model to create a pinhole in a fold
22 somehow --

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1 DR. DUHAMEL: Right.

2 DR. LI: -- I'm actually not sure that
3 actually is the mechanism that actually occurs. In
4 fact, Dr. Burkhardt is right and, if anything, they're
5 overfilled and not under filled.

6 DR. DUHAMEL: Well, right, but the device
7 is telling you what happens in terms of at least what
8 appears to have happened. How what caused it --

9 DR. LI: Well, that tells me what happened
10 to --

11 DR. DUHAMEL: -- what caused it to happen
12 in the first place is a different question, and that
13 is how did the folds get there.

14 I will tell you that in the study here, we
15 did look at fill and the percentage of overfill and
16 under fill, and we defined overfill in terms of our
17 labeling. We have a stated range of fill we recommend
18 that it be filled.

19 We only had, I believe, nine percent or 11
20 percent, my recollection, but in that range, that were
21 overfilled, and those were ^{**}overfilled by approximately
22 five percent.

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1 We had a small number -- it might be
2 around three percent -- that would be under filled.
3 These are the ones you should be concerned about, and
4 those again were under filled by a small amount. They
5 were about no more than five percent.

6 We had no major rate of under filling, and
7 the under filling that did occur was close to the
8 range of appropriate filling. The numbers in AR-90 of
9 that type are very -- somewhat different at least to
10 the ones in the '95 studies reflecting a change in
11 attitude and change in practice among surgeons with
12 regard to overfilling and under filling.

13 DR. LI: Can I ask another question?

14 CHAIRMAN WHALEN: Please.

15 DR. LI: In a related area, on your
16 fatigue testing, I noticed in the details of the
17 fatigue testing and some of the tests you noted a loss
18 of volume of liquid and essentially had to go back in
19 and refill the implant during the test. Is that
20 really actually you've developed a model for leakage
21 in that regard or --

22 DR. DUHAMEL: Well, the --

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1 DR. LI: -- how do you explain a loss of
2 volume large enough to where you have to go in and
3 experimentally correct it?

4 DR. DUHAMEL: Well, we haven't developed
5 a model for anything. It is the property of silicone
6 that it does, in fact, let water through, and the
7 range was actually very small. It's only a few
8 percent, but periodically they would refill. It's not
9 a large amount.

10 Now, I recognize that you may think that
11 has some sort of clinical implication, but of course,
12 in the body there is no issue. The water --

13 DR. LI: Well, I was trying to -- well, I
14 guess I didn't -- I couldn't decide though from your
15 description where the water was coming out. Was there
16 a drip somewhere?

17 DR. DUHAMEL: No.

18 DR. LI: Was it just diffusion? Is that
19 what you're saying?

20 DR. DUHAMEL: It was just diffusion,
21 vaporization.

22 DR. LI: A semi-permeable membrane.

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1 DR. DUHAMEL: Yeah.

2 DR. LI: Interesting. Outside the body --

3 DR. DUHAMEL: You might -- I know that
4 there are at least some folks here who are familiar
5 with the fact that there have been devices with
6 relatively similar shells that were essentially filled
7 sort of in vivo by osmosis. You just fill the shell
8 with a high salt solution, and it will take in water.

9 Water can move through silicone. So in
10 open air, unsurrounded by -- it does move.

11 DR. LI: In your fatigue testing, what was
12 the endpoint? Was it just catastrophic rupture, the
13 first line of --

14 DR. DUHAMEL: Or runoff, or run-out.

15 DR. LI: Right, but it was a catastrophic
16 failure. It wasn't like a slow leak developed.

17 DR. DUHAMEL: No.

18 DR. LI: It would be okay and then all of
19 a sudden it would leak or --

20 DR. DUHAMEL: Yeah. Actually it was very
21 simple. There was some blue die, and if the blue die
22 came out, that was characterized as it failed, and

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1 actually it was characterized as failed whether or not
2 we could see the leak.

3 So if we saw a substantial amount and you
4 come in in the morning and there's a substantial
5 amount of blue puddling on the benchtop, it failed,
6 and that's how it was scored.

7 Most of the time it wasn't that, by the
8 way. Most of the time it actually was the frank
9 rupture, be it a pinhole or whatever, that would allow
10 the saline to come out or the water.

11 DR. LI: I guess the rest are really more
12 comments than questions. I just have one procedural
13 one. You tended to pick what you would refer to as
14 the smallest size --

15 DR. DUHAMEL: Right.

16 DR. LI: -- implant in most of your tests.

17 DR. DUHAMEL: Right.

18 DR. LI: Did the smallest implant also
19 coincide with the thinnest implant?

20 DR. DUHAMEL: Not at all. First of all,
21 we picked the smallest by actually doing some testing
22 and doing some consultation with biomechanical

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1 engineers, and even though I'm not an engineer, if you
2 take a 55 pound load and you put it on a big thing and
3 put it on a small thing, the small thing, given that
4 they're the same dimensions of the shell, is likely to
5 break.

6 DR. LI: Would not the worst case
7 scenario, however, been the smallest implant with the
8 thinnest wall?

9 DR. DUHAMEL: Correct. So now we have the
10 smallest implant, but there is no -- what I'm trying
11 to say is that there is no systematic aspect of our
12 manufacturing that causes any one size or style to be
13 thinner than the others.

14 DR. LI: In other words, the idea that
15 they're all -- what target -- oh, so the thinness
16 range that you specify is the thinness range that you
17 just get as a matter of course.

18 DR. DUHAMEL: We get as a matter of
19 course. Now, the course is interesting. These
20 devices are dip cast, and they're round. Some of them
21 are round. They're not truly round. They're an odd
22 shape of round. They're oblate, and others are more

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1 complicated structures.

2 And so now you dip them, and they go
3 through multiple dips, and every time they come out,
4 there's a pattern of the way in which the material
5 flows around the device, just like dip casting
6 catheters. And so the thickness is a function of the
7 viscosity and how it flows and how it's handled before
8 it finally cures, and then it fixes into place, and
9 then in a period of time you go into the next dip and
10 you keep going through that process.

11 There is variability in thickness, but as
12 a matter of fact, there's a very significant amount of
13 the variability is within the device. It's almost as
14 large as among devices in a lot, and the reason is
15 that there are areas that tend to be thicker than
16 others. That is not lack of control. That's the
17 nature of the process.

18 The ones that are thin, those are always
19 the thinnest ones generally, and we measure thickness
20 17 different places on the devices in recognition of
21 that. And so if you look ^{**}not at the whole variation
22 of thickness, but if you were focused, say, thickness

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1 at the radius and map that across devices, that's a
2 much narrower definition. That's a much narrower
3 distribution of thickness.

4 The lot release characteristics are to
5 take these 17 measurements and you look at the
6 thinnest one, and that is the one that defines whether
7 the device met the characteristics or not.

8 DR. LI: But correct me if I'm wrong, but
9 the ones in the test were not of the thinnest
10 possible.

11 DR. DUHAMEL: They were production runs.

12 DR. LI: Right.

13 DR. DUHAMEL: And they were produced
14 within. Now, even our spec. is rather wide, but we
15 tend to run, you know, at a much more narrow range
16 than the spec.

17 DR. LI: So when you give a range --

18 DR. DUHAMEL: Can I make one more point
19 about that?

20 DR. LI: I'm sorry. Go ahead. Sorry.

21 DR. DUHAMEL: However, when we examine the
22 results of the data for lot release, we do that on a

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1 distribution basis, take data that we have, do the
2 statistical magic of quality engineering and determine
3 what the confidence interval should be and whether or
4 not a device with that thinness was in the lot.
5 That's what determines whether the lot is passed or
6 not.

7 So to make devices that pass, we have to
8 be having a means. It's fairly high from the lower
9 end. Otherwise the variation would cost a lot to
10 fill.

11 DR. LI: I understand.

12 DR. DUHAMEL: It's difficult to
13 manufacture devices with a specific thickness.

14 DR. LI: I understand all of that, but in
15 the terms of testing and qualifying a device for
16 approval, I guess I don't see why it wasn't
17 straightforward to go through and pick the ones that
18 you measure, in fact, that are the thinnest category
19 and test those.

20 DR. DUHAMEL: Could have been done.

21 DR. LI: Okay.

22 DR. DUHAMEL: It could have been done.

1 They question is are the variations significant enough
2 to change our conclusions at the end of the day.

3 DR. LI: Right, and then when you give a
4 range, I guess it's like .014 to .02-something as your
5 range.

6 DR. DUHAMEL: Right.

7 DR. LI: Is the .014 like the drop dead
8 bottom thickness, that if you read any part of the
9 implant that's less than that it's rejected or is that
10 the average of the whole thickness as part of --

11 DR. DUHAMEL: We have a drop dead spec.

12 DR. LI: Okay. Sorry for the term. Maybe
13 lower acceptable limit. Sorry.

14 DR. DUHAMEL: Can we state what the
15 thickness spec. is?

16 PARTICIPANT: It's minimum 0.014 and for
17 (inaudible) 0.022.

18 DR. DUHAMEL: Okay.

19 DR. LI: I guess my question is: is that
20 an average thickness or is that the average --

21 DR. DUHAMEL: *No. That is the thinnest
22 point.

1 DR. LI: That's the thinnest point.

2 DR. DUHAMEL: The thinnest point of the
3 distribution, and here we don't do this business of
4 only monitoring. Here we take the distribution as it
5 is, which causes a very -- a spread beyond which you
6 observe in terms of the distribution. So it's a
7 rather rigorous statistical demand, but that
8 distribution must for the thinnest point achieve the
9 spec.

10 DR. LI: And maybe just a general
11 question. With all of the -- first of all, actually
12 let me congratulate you. Some of your testing is
13 extensive and quite clever. I have a little trouble
14 understanding what to do with the data, but I applaud
15 your efforts in this line.

16 (Laughter.)

17 DR. LI: Given that let's say, as a
18 thought experiment, we just accept your protocol and
19 approve as you are so that you have, if you will, a
20 standard set of tests that you would run on future
21 design or material change or whatever, what confidence
22 do you have in all of this testing that if you made a

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