

1 see it.

2 The other issue which is of tremendous
3 importance to the industry in general is this whole
4 question of surrogate endpoints, and this is related
5 to the first point. Once you have largely
6 significantly reduced the really terrible clinical
7 outcomes, obviously mortality, to the point where that
8 the incidence of mortality is very low, it is only
9 possible basically -- and other very important,
10 obvious clinical endpoints -- it is very difficult
11 under those circumstances to power studies, to do
12 studies that can possibly show differences in those
13 endpoints unless you do tens of thousands, thousands
14 of patients at a time, which as just a practical
15 matter is impossible for companies to do.

16 As a result, we look at surrogate
17 endpoints, and you know, the issue really becomes in
18 the final analysis is it reasonable to expect that a
19 particular surrogate endpoint that we choose is
20 reasonably likely, particularly where you have at
21 least some causality, where you can understand the
22 causal relationship of the surrogate to a particular

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1 clinical outcome; is it reasonably likely that this
2 surrogate endpoint is going to translate in the larger
3 population that we won't be studying, but we will be
4 treating to a real clinical benefit?

5 I think that has to be kept in mind. In
6 addition, I think the last point is with respect to
7 the types of analysis that we do, the argument was
8 made about why we need to have intention to treat
9 analyses.

10 Intention to treat analysis is very, very
11 difficult to do in a surgical study. It is very easy
12 to do that in a pharmaceutical study where usually the
13 endpoint doesn't require a surgical follow-up. You
14 can look at the patient, as a question, take a blood
15 test or something, and you have an answer.

16 Here we're asking patients in cardiology,
17 in surgery to undergo additional procedures. In those
18 cases it is very, very difficult to guarantee 100
19 percent follow-up. So then the question becomes: in
20 the absence of that kind of follow-up is it possible
21 to make a reasonable judgment, again, about what
22 likely really happened here?

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1 And, again, unlike a case where -- the
2 anutrol (phonetic) case that was presented -- where
3 the loss to follow-up population clearly had a
4 terrible outcome, i.e., 26 percent death rate, the
5 population here that we have been able to follow or
6 that the company has been able to follow who have been
7 lost to follow-up, the data that is available that Dr.
8 Roy has asked about indicate that a significant number
9 of those people did not come back to the study because
10 they had a good follow-up, and I think that has to be
11 considered.

12 When you put that all together, you end up
13 with a situation where both on an intention to treat
14 basis you end up at worst, which is the worst possible
15 analysis, with a null result, a null result.

16 Sorry. My mouth is dry.

17 CHAIRMAN WHALEN: I'm sorry. I'll have to
18 ask you to summarize since it's usually a two to three
19 minute comment period.

20 MR. LASSERSON: Oh, I'm sorry. I didn't
21 know what the time limit was.

22 You're getting no result in the worst case

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1 and a positive result in the evaluable population,
2 which I think is a reasonable case to look at.

3 Thank you for listening.

4 CHAIRMAN WHALEN: Thank you.

5 We reserve the right to have you testify
6 to Congress about excellent results when they talk
7 about the Institute on Medicine report though.

8 Thank you.

9 One of our panelists, Dr. Levy, has to
10 leave very shortly. We are going to try to proceed to
11 a vote expeditiously, but not without due process.

12 I would ask now if the FDA has any final
13 comments before the sponsor does and before we then
14 proceed to a vote.

15 MR. DILLARD: Jim Dillard.

16 I'm looking over to our team here, and I
17 don't see anybody jumping up for additional questions.
18 I think at this point I don't have any either.

19 I think that you've clarified a number of
20 the issues for us, and I think that gives us a sense
21 of how to look at this data and some other things that
22 are going to be important.

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1 I only wanted to perhaps make one comment
2 on the surrogate because I think it's important here
3 to make one statement, which is there have been other
4 adhesion barrier products that have come before this
5 panel that have also come before the agency, and we
6 have looked at and we have focused on surrogate
7 endpoints, and I think that the agency has been
8 willing in these cases to primarily focus on surrogate
9 endpoints, and we have made decisions on that.

10 So just based on the last comments that
11 were being made, I just wanted to set the record
12 straight that what we have not been asking for is an
13 absolute demonstration of a clinical endpoint before
14 a product goes to market, but reasonable assurance of
15 safety and effectiveness of the products.

16 CHAIRMAN WHALEN: Thank you.

17 Anything else from the FDA?

18 MR. DILLARD: No.

19 DR. HORBOWYJ: I guess I just have -- Roxi
20 Horbowyj -- a question to Dr. DeMets, that I
21 understand the pooling.

22 When we looked at the patients that had

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1 adhesiolysis, and I understand I'm looking at just the
2 piece of the whole population; it's really just my own
3 clarification here. When you looked at the patients
4 who were in Europe, whether they were treated with
5 control or investigational device, their both scores
6 and incidence of adhesions went down from baseline,
7 whereas in the U.S. they went up.

8 And when you were talking about pooling,
9 is that the kind of -- are those opposing trends that
10 then you would say at least in that subgroup as an
11 example -- I'm not really saying overall here -- would
12 be non-poolable or I was just trying to understand how
13 you were interpreting poolability.

14 DR. DeMETS: Well, the point I was trying
15 to make is that if you have interaction, you have
16 interactions for two reasons. One is just the size of
17 the effect is different, and that wouldn't be
18 surprising I mean across sites, across centers,
19 rather, in this case or across any other subgroup one
20 might think of.

21 Where you begin to worry is if you have
22 this qualitative interaction where it's going in one

1 direction in one group and opposite in the other.
2 Now, that doesn't mean you wouldn't because as I
3 pointed out you expect a little of that just by
4 statistical theory says it must happen. Some will go
5 positive; some will go negative. You hope that the
6 majority are going in the direction you think.

7 It doesn't mean you wouldn't pool all of
8 those sites, but you should begin to start worrying
9 when you see qualitative interaction.

10 DR. HORBOWYJ: So in the case where in
11 Europe we have for both groups?

12 CHAIRMAN WHALEN: And really just as a
13 reminder, we're talking about a period of comment
14 here, not a period of question, and I want to keep
15 that difference focused upon.

16 Does the sponsor have any final comments?

17 MS. KEYPORT: Yes, we do. How much time
18 do we have?

19 CHAIRMAN WHALEN: Fifteen minutes.

20 DR. diZEREGA: Thank you, Dr. Whalen.

21 What we'd like to do is address what we
22 think is the primary issue that is left before us this

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1 afternoon, and that's the one of the clinical
2 significance. We've talked about the numbers and the
3 scoring systems, and I think we're all clear on the
4 utility of these things, their strengths and their
5 limitations, but what does it all mean actually to the
6 patients?

7 What I'd like to do is three things, if I
8 may. Our two clinicians, between them they have the
9 largest experience with this device. I'd like them
10 individually to comment to you as what this device
11 means to them, and then I'll close with a direct
12 response to the panel to give them a sense of what the
13 differences actually relate in terms of utilization of
14 the surrogate for clinical outcomes.

15 First, Dr. Alan Johns.

16 DR. JOHNS: Thank you very much.

17 Just a couple of quick comments. Dr. Levy
18 and Dr. Roy and I have been working at least the last
19 five, maybe ten years since we finished medical school
20 -- maybe a little longer than that -- to try to
21 perfect surgery.

22 (Laughter.)

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1 DR. JOHNS: And thus far we haven't been
2 successful. Those of us that have been able to do
3 these second looks over the years are absolutely
4 astounded at the number of adhesions that we get.

5 Those that don't do the second looks,
6 every surgeon in the room think that they're God's
7 gift to surgery and they don't get adhesions, and they
8 happen.

9 So I'm not so certain that if a product
10 will decrease in adhesion by one percent or five
11 percent or whatever, if it reduces it that's what's
12 important.

13 My partner had a bowel obstruction from a
14 single adhesion that a little small bowel looped
15 around, a single adhesion. If that had been an
16 adhesion that was stopped by a product, that mattered.

17 So I can't say that one adhesion or its
18 lack thereof may or may not have a clinical outcome,
19 but it certainly may, and I think we can't discount
20 that possibility unless we have data that shows
21 otherwise.

22 Thank you.

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1 DR. diZEREGA: Thank you, Dr. Johns.

2 Dr. Thornton, please.

3 DR. THORNTON: I would just like to make
4 some important comments. As a woman's health care
5 provider who's treated women from the complications of
6 adhesions postoperatively, such as infertility, in
7 chronic pelvic pain, and as a surgeon who's had the
8 opportunity to reoperate on patients who are suffering
9 from adhesive disease and see the complications that
10 arise, such as bowel injury, prolonged surgical time,
11 I think that this is an important day for women's
12 health care.

13 And the reason why I say that is for two
14 important reasons. One is that if you look at the
15 data and, you know, you don't look at the numbers, as
16 a surgeon who has done these studies, I know that this
17 works. It does reduce adhesions.

18 And, second, it's very easy to use. The
19 products that we have available today are very
20 difficult to use, and because they're so difficult to
21 use, surgeons will not use them because they think it
22 will prolong their time in surgery, and it's difficult

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1 to use.

2 And I think now as we're progressing, as
3 obstetricians and gynecologists, being primary care
4 providers, we have to deal with preventive medicine,
5 and any time that we can reduce the incidence of
6 adhesions no matter how large or how small it is, I
7 think that's the first step in preventive medicine and
8 reduction of chronic pelvic pain and infertility.

9 And as far as a clinician's point of view,
10 when we were talking about this intent to treat, we're
11 all talking about numbers, but when you're the
12 physician who's taking care of these patients and you
13 have the patient who's four and a half weeks pregnant
14 and she tells you that she doesn't want to come back
15 for a second look, how can you say that she has a poor
16 outcome, or the patient who's back to work, she's
17 doing well and doesn't want to take time off from her
18 job to come back to have a second look? How can you
19 say that that's a poor outcome?

20 I just think this is a great day in
21 women's health care, and it would be a crime if this
22 isn't approved because this is something that will

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1 benefit the GYN surgery.

2 Thank you.

3 DR. diZEREGA: There's been discussion
4 about a consistent response in the effectiveness of
5 the device, different types of surgical procedures,
6 different types of adhesions, and different anatomical
7 locations. I think that's clear.

8 I would like to remind the panel that
9 there is also consistency between and among
10 investigational sites. As Dr. Johns indicated, the
11 size of these individual balloons, all referring to
12 investigational sites, represents their relative
13 number of patients contribute to the study, and all of
14 those that are above the line show that the product is
15 effective, a very consistent response.

16 Next slide, please.

17 As Dr. Dillard has -- as Jim Dillard has
18 indicated, the standard of these types of studies is
19 necessarily surrogates. Dr. Roy and I have discussed
20 pregnancy. Of course we have no pregnancy data or we
21 would have presented it. We wish we could do such a
22 study. We cannot.

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1 We wish we could do a pain study. We
2 cannot. It's even more confounding. So where we're
3 left with moving medicine forward in this area is with
4 surrogate endpoints.

5 The surrogate endpoint that was chosen for
6 this study, as we've discussed, are the scoring
7 systems. The scoring systems are not about means. I
8 think that's a very important point that has been made
9 in the discussions about nonparametric tests. I
10 remind myself of the Time magazine's Man of the
11 Century, Albert Einstein. Someone asked him once
12 about means. He said, "Well," he said, "if I put one
13 hand on the stove and one hand in the freezer, I'm
14 feeling okay."

15 There's more to this type of categorical
16 analysis than means, and I think the AFS score or its
17 extension into the modified AFS score is a very good
18 surrogate endpoint for doing adhesion prevention
19 studies.

20 Now, how did that turn out in our
21 particular situation? And then I relate that to the
22 question that a number of you are asking, and that is

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1 the clinical significance of having fewer moderate or
2 severe adhesions.

3 Let me remind the panel that the main
4 benefits from this device can be shown. If you look
5 at the minimal and mild adhesions, at second look
6 laparoscopy there are certainly more of those in the
7 treatment than the control, but perhaps more
8 importantly, the moderate and severe adhesions.

9 The patients that ended up with moderate
10 and severe adhesions, as you can see, there were a
11 total of three of those in the active and a total of
12 17 of those in the control. Now, these numbers are
13 most certainly different. The table is different
14 statistically. I don't think that's the issue.

15 The issue is: does this have any clinical
16 relevance? Is having a moderate or severe adhesion
17 clinically more important than having a minimal or
18 mild adhesion?

19 Next slide, please.

20 In terms of the absolute patient numbers,
21 first, what about totally adhesion free? I think
22 having no adhesions is better than having adhesions,

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1 and you can see that quite clearly the product was
2 effective in increasing the number of patients who had
3 no adhesions, and we're talking about a large number
4 of sites throughout the abdominal cavity.

5 Now, what about the patients who had
6 moderate or severe? As I had mentioned, these are the
7 differences: three to five times more patients.
8 Three to five times more patients were spared a
9 moderate-severe outcome from the adhesive disease
10 perspective if they received the active.

11 I'll get back to the "so what" of that in
12 just a moment.

13 The worst of all, of course, are the
14 severe patients. These patients have no chance of
15 becoming pregnant spontaneously. Most of the moderate
16 patients don't either, but quite clearly these
17 patients would be considered a surgical failure.
18 INTERGEL reduced the chance of our surgery failing.
19 I think that's clear.

20 Now, what about the clinical correlate to
21 all of this? May I have the last three slides one at
22 a time, please?

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1 We talked about pain. Dr. Roy asked me
2 about pain. Dr. Levy has talked about pain. What is
3 the evidence that there is a use to these surrogate
4 endpoints?

5 Well, let's look at pain, and, Cathy, if
6 you could raise that just a little bit.

7 This particular study is from Stout.
8 Stout is representative of the group in North Carolina
9 that has spent years studying pelvic pain. As Dr.
10 Levy correctly pointed out, pelvic pain has many
11 etiologies, some of which happen to relate to adhesion
12 formation. The most common interperitoneal pathology,
13 the most common interperitoneal pathology that's
14 associated with pelvic pain is adhesion formation.

15 So what Stout did was to find if there's
16 a way to quantitate this in terms of doing clinically
17 meaningful studies. He used the AFS score. He
18 assessed patients preoperatively as to their pain in
19 this prospective study, and you can see those that had
20 elevated AFS scores had pain compared to those who did
21 not have pain, quite clearly a difference in an
22 outcome based on AFS score.

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1 What about pregnancy? Pregnancy, two
2 studies. First, it's a large study, over 200
3 patients. It's from Japan. These investigators did
4 AFS score evaluations at the time of surgery. They
5 did what they could to repair the pelvic cavity from
6 a reconstructive point of view irrespective of whether
7 the patient had minimal, mild, moderate or severe
8 adhesions, and then they allowed the patients to
9 conceive spontaneously.

10 Who got pregnant? Who got pregnant were
11 the patients with minimal and mild adhesions.

12 Who did not get pregnant? And perhaps
13 this is the more important point. Who had failed
14 response to surgery? Those patients with the moderate
15 and severe adhesions, the very patients that INTERGEL
16 is reducing three to five times the frequency of. You
17 can see the benefit to the patients in terms of real
18 pregnancy.

19 And my last transparency comes from
20 someone I think is known very well to all of the
21 gynecologists here, Victor Gomel. When Victor Gomel
22 was the Chairman at his Department of OB-GYN, he did

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1 a prospective study that asked the very question that
2 Dr. Levy and Dr. Roy are asking, and that is how can
3 we use a scoring system to predict clinical outcome.

4 The use of the surrogate for pregnancy is
5 shown in Gomel's study very clearly. Lumping together
6 with AFS score the mild and the two lowest adhesion
7 scoring groups with the moderate and severe, you can
8 see in this study of almost 100 patients a very
9 different response, and all of these things are, of
10 course, statistically significant, but a very
11 different clinical response. Having bad adhesions
12 gives bad outcomes to surgical therapy. I think
13 that's what INTERGEL adhesion prevention solution is
14 all about.

15 And I think we've shown that, and I think
16 the benefits to the patient are very clear.

17 Thank you.

18 CHAIRMAN WHALEN: Thank you.

19 Dr. David Krause, our Executive Secretary,
20 will now read the voting instructions for the panel.

21 DR. KRAUSE: "The medical device
22 amendments to the Federal Food, Drug, and Cosmetic

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1 Act, as amended by the Safe Medical Devices Act of
2 1990, allows the Food and Drug Administration to
3 obtain a recommendation from an expert advisory panel
4 on designated medical device pre-market approval
5 applications that are filed with the agency."

6 The PMA must stand on its own merits, and
7 your recommendation must be supported by safety and
8 effectiveness data in that application or by
9 applicable, publicly available information. Safety is
10 defined in the act as "reasonable assurance based on
11 valid scientific evidence that the probable benefits
12 to health under conditions on intended use outweigh
13 any probable risks."

14 Effectiveness is defined as "reasonable
15 assurance that in a significant portion of the
16 population the use of the device for its intended uses
17 and conditions of use when labeled will provide
18 clinically significant results."

19 Your recommendation options for the vote
20 are as follows:

21 Approval, if there are no conditions
22 attached.

1 Second choice, approvable with conditions.
2 The panel may recommend that the PMA be found
3 approvable subject to specified conditions, such as
4 physician or patient education, labeling changes or a
5 further analysis of existing data.

6 Prior to voting all of the conditions
7 should be discussed by the panel.

8 Third choice, not approvable. The panel
9 may recommend that the PMA is not approvable if the
10 data do not provide a reasonable assurance that the
11 device is safe or if a reasonable assurance has not
12 been given that the device is effective under the
13 conditions of use prescribed, recommended, or
14 suggested in the proposed labeling.

15 CHAIRMAN WHALEN: Thank you.

16 And as a reminder, our consumer and
17 industry representatives are non-voting members.

18 Is there a motion?

19 DR. EDMISTON: I move that we vote.

20 (Laughter.)

21 CHAIRMAN WHALEN: I'm all for voting, but
22 I think we have to vote on one of the three stipulated

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1 possibilities as either approvable, not approvable, or
2 approvable with conditions. So the motion would need
3 to contain one of those elements.

4 DR. EDMISTON: I move that we look at the
5 approvable motion first.

6 CHAIRMAN WHALEN: The motion as approvable
7 has been made. Is there a second?

8 (No response.)

9 CHAIRMAN WHALEN: Seeing no second, the
10 chair will entertain an alternative motion.

11 DR. EDMISTON: I think I misspoke. You're
12 just looking at the actual three choices?

13 CHAIRMAN WHALEN: One of those three
14 choices can be made, and if seconded, we will then
15 vote upon it.

16 DR. EDMISTON: You do not want to discuss
17 whether the product was approvable or not. Excuse me.
18 The wrong motion.

19 CHAIRMAN WHALEN: So is there a motion
20 other than approvable, since there was no second to
21 that?

22 DR. LEVY: I'll move that the device be

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1 nonapprovable.

2 CHAIRMAN WHALEN: There is a motion made
3 that the device is not approvable. Is there a second
4 to that motion?

5 DR. EDMISTON: Now that I understand it,
6 I'll second it.

7 CHAIRMAN WHALEN: The motion has been made
8 and seconded that the premarket approval application
9 for the INTERGEL adhesion prevention solution from
10 Lifecore Biomedical, Incorporated be recommended as
11 not approvable.

12 Will all those voting members in favor of
13 that motion raise their hands?

14 (How of hands.)

15 CHAIRMAN WHALEN: As the voting is not
16 unanimous, I would identify those if you would
17 continue to raise your hands if you're in favor of
18 that motion.

19 Those in favor of that motion are Dr.
20 Levy, Dr. Edmiston, Dr. McCauley, Dr. Talamini, and
21 Dr. DeMets.

22 Those opposed to that motion -- you can

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1 lower your hands. Thank you -- those opposed to that
2 motion are Dr. Roy and Dr. Davis.

3 I need to go around the panel now and ask
4 that each of you identify the reasons that you voted
5 as you did, and continuing in our circular fashion,
6 with the exception asterisk that I will go to Dr. Levy
7 since she has to leave.

8 DR. LEVY: At the moment I have issues
9 with the infection rate. The studies that are ongoing
10 that we have not seen yet with respect to the safety
11 of the product, and based on the fact that I don't
12 have that safety information, I feel that at the
13 present time that the product is not approvable.

14 Secondly, given the language of our
15 mandate, which is that a significant proportion of the
16 population will benefit and that that benefit
17 outweighs any potential risk, when we're talking about
18 infertility patients, I have issues that the infection
19 may outweigh the probable or possible benefit of a
20 small reduction in the number of adhesions, and those
21 are my problems with the PMA as the data currently
22 exists for this panel.

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1 CHAIRMAN WHALEN: Thank you.

2 And it follows from what you just said,
3 but as we are discussing it, would you please discuss
4 what you feel would make this approvable since it has
5 been voted as not approvable?

6 Thank you.

7 Dr. Roy.

8 DR. ROY: The reason I was going to vote
9 approvable with conditions, and in a way, some of
10 those conditions I'm concerned about what Dr. Levy
11 said as well, but I think that at the present time
12 with the information at hand it seems to be safe, but
13 I'm not sure because of the differences in conclusions
14 according to the analysis whether I can be persuaded
15 that the subset analysis would indicate a certain
16 group for whom it would be effective, and I think I
17 probably can if I had enough time to look at the data.

18 So I think that I would -- the reason I
19 was going to vote approval with conditions is to have
20 a chance to determine what those subset patient
21 populations would be.

22 CHAIRMAN WHALEN: Dr. McCauley.

1 DR. McCAULEY: I agree with Dr. Levy. I
2 think the safety data is incomplete, and I think
3 that's a -- particularly the infection data is a major
4 issue for this particular PMA. So from the standpoint
5 of safety, based on a PMA that we currently have, I
6 cannot in good conscience vote for approval.

7 In terms of effectiveness, I think also
8 that there's considerable amount of controversy
9 concerning the scores as it relates to clinical
10 effectiveness, that that's a major issue, and I don't
11 think that based on what we've seen here that
12 clinically it is effective in terms of helping these
13 patients reduce pain or improve their fertility.

14 There was one comment made by one of the
15 surgeons saying that a small bowel obstruction can be
16 -- that one can develop a small bowel obstruction from
17 a single band, and I agree with that. So that doesn't
18 mean that a reduction in the number of adhesions in
19 these areas is going to lead to any significant
20 clinical benefit.

21 CHAIRMAN WHALEN: Dr. Talamini.

22 DR. TALAMINI: On the safety side, I have

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1 concerns with the current application in that there is
2 still outstanding data regarding safety that we don't
3 have in hand, and I believe there are hints in the
4 data that we do have suggesting that there may be
5 safety issues.

6 On the efficacy side, I do have trouble
7 with the surrogate and the conclusion that that
8 surrogate reflects clinically significant results.
9 For me the next step would be endpoint studies
10 including pregnancy, abdominal pain and bowel
11 obstruction, which we already have a population in
12 hand with the current patients that have been studied,
13 and there would also be the potential for expansion of
14 studies to additional patients and populations.

15 CHAIRMAN WHALEN: Dr. DeMets.

16 DR. DeMETS: To follow that, I'm one of
17 those who is skeptical and pessimistic about the use
18 of surrogates. Two things are required for a
19 surrogate. One is to be predictive of the therapy
20 being effective.

21 And, second of all, it must capture all of
22 the things that could go wrong because if your

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1 surrogate doesn't capture that, you could think you're
2 doing well, but you would be doing harmful things
3 downstream, and there's many examples in drugs and
4 biologics for that, and I think there are examples in
5 devices, as well.

6 So, one, I'm skeptical about the
7 surrogates that were used even if you can sort out the
8 interpretability and analyzability of it.

9 And, second of all, there is a long term
10 safety. So actually I was more convinced by the last
11 presentation about pain and pregnancy. If that's
12 true, first of all, you in fact could do a pain and
13 pregnancy study, and if you had it it seems like you
14 would clinically nail it down.

15 So for those reasons.

16 CHAIRMAN WHALEN: Thank you.

17 Dr. Davis.

18 DR. DAVIS: I voted against disapproval
19 because I think it is approvable with stipulations.
20 There is a hint in the data that it is effective
21 potentially for patients who have adhesions and who
22 have a lot of adhesions. It seems that this is part

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1 of the population that the manufacturer is interested
2 in, and so then it comes back to the question of was
3 the study designed to look at that, particularly
4 excluding the patients with many adhesions. That
5 would seem to be then the target population.

6 And then I guess at that point, that's
7 coming back to a new clinical study which I think
8 means actually I've said I'm effectively voting to
9 disapprove it.

10 CHAIRMAN WHALEN: Dr. Edmiston.

11 DR. EDMISTON: Now that I've got my focus
12 completely back, let me make a couple of comments.

13 First of all, there's a smoking gun.
14 We've seen in the past couple of years compounds
15 approved by the FDA in which you went back and looked
16 at the data and there were some smoking guns, in
17 particular, liver abnormalities in particular to an
18 antibiotic that's just been pulled in the past year.

19 Had we looked at that a little more
20 closely we may not have approved that compound.

21 When I see the WBC levels going up, I'm a
22 little bit suspicious, especially in a relatively low

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1 risk patient population, and we really didn't address
2 why those WBCs were increasing. We would probably
3 hypothesize why they are, primarily because of the
4 foreign nature of the body, but what I'm concerned
5 about is the impact of a device like this on the
6 peritoneal immune systems because, after all, that's
7 what I'm interested in studying.

8 It's true 95 percent of our patients have
9 a wonderful outcome, but five percent of them, five to
10 eight percent develop nosocomial infection, and one of
11 which is surgical site infection of which a
12 significant number of those are organ space
13 infections.

14 And I am concerned that at this point the
15 PMA is being submitted without complete animal data.
16 In light of that, I have a concern about safety.

17 My issue about efficacy was not quite so
18 resolved when I came here, but it's fairly resolved
19 now in light of the comments that have been made by
20 our distinguished panel and individuals who are much
21 more knowledgeable on this area than I am.

22 If the sponsor is willing to change their

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1 labeling to limit the use of the compound in women who
2 are undergoing surgical procedures for infertility,
3 that might be a valid consideration, but with the
4 current indication, I would be highly skeptical of
5 approving this compound in light of the gaps that
6 exist in the current data.

7 CHAIRMAN WHALEN: Thank you.

8 I would like to thank all of the members
9 of the panel for their time and expertise; thank Dr.
10 David Krause, our Executive Secretary, and Mr.
11 Dillard.

12 The meeting is adjourned.

13 MR. DILLARD: Dr. Whalen, I'd also like to
14 add one thing. I apologize.

15 Just a thank you from the FDA for all of
16 your hard work and your time, and we appreciate it,
17 and thank the audience, too, for their participation.

18 Thank you very much.

19 (Whereupon, at 3:51 p.m., the meeting was
20 concluded.)

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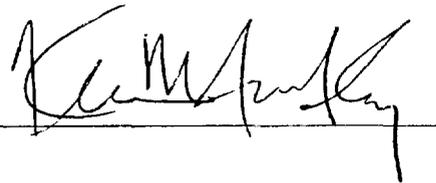
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Before: FDA Medical Devices Advisory Panel

Date: January 12, 2000

Place: Rockville, MD

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Kenneth M. Anthony