

1 the company level with the Contigen issue.

2 I think this can be dealt with, with labeling.
3 The great majority of urogynecologists and urologists in the
4 United States are trained, and I would just leave it that
5 the product should be used by physicians trained in the use
6 of bulking agents.

7 DR. DEITRICK: I would agree with that because if
8 you exclude the urogynecologists, there is not too many
9 local gynecologists doing this. Secondly, they are usually
10 curtailed somewhat by the delineation of privileges in their
11 local hospital bylaws.

12 DR. DIAMOND: Unless it's done in the office
13 procedure room.

14 DR. DEITRICK: Those same gynecologists probably
15 would not venture into that, but, yes, there is all kinds of
16 people.

17 DR. HAWES: My thought would be that it should be
18 done by people who are trained in therapeutic cystoscopy and
19 any further, quote, unquote, "training," can be handled by
20 booklets, videos, et cetera.

21 DR. N. KALLOO: I agree. In the labeling, it
22 should say somebody who is trained in therapeutic
23 cystoscopy.

24 DR. DONATUCCI: I agree with Dr. Kalloo's comment,
25 and I think the majority of the panel feel that this can be

1 handled in the labeling with a statement saying that it
2 should be used by people familiar with therapeutic endoscopy
3 although we have dissension.

4 DR. A. KALLOO: Okay. The final question is: Are
5 the proposed "Directions for Use" accurate and
6 comprehensive?

7 DR. FOOTE: Yes.

8 DR. HUNTER: Yes.

9 DR. DIAMOND: I am going to have to pause as I
10 read through it again after all of today's discussions.

11 DR. A. KALLOO: Ms. Newman.

12 MS. NEWMAN: I think they are accurate, but we
13 don't get to talk about the patient information brochure, I
14 guess, is my question.

15 DR. A. KALLOO: No. The patient information
16 brochure -- what is the question? I am sorry.

17 MS. NEWMAN: I just wanted to comment on something
18 that I want them to put in, we can't do that?

19 DR. A. KALLOO: Sure. Do you want to make a
20 comment?

21 MS. NEWMAN: They have got to say that -- they
22 don't answer the question will I feel pain, and I want them
23 to answer that question. It isn't answering that question
24 on this brochure. Okay?

25 DR. A. KALLOO: Okay.

1 DR. VERTUNO: Yes.

2 DR. STEINBACH: Yes.

3 DR. BENNETT: Yes.

4 DR. DEITRICK: Yes.

5 DR. HAWES: Yes.

6 DR. N. KALLOO: Yes.

7 DR. DONATUCCI: Yes.

8 DR. A. KALLOO: Can you summarize?

9 DR. DONATUCCI: I think the summary of the panel
10 is the answer to the question is yes.

11 DR. A. KALLOO: Now, Dr. Donatucci, if you can do
12 a complete summary of the panel's recommendations.

13 DR. DONATUCCI: I think the summary concerning the
14 five questions raised, basically, in the labeling we wish to
15 see that the indication to be for intrinsic sphincter
16 deficiency in patients over 21 years of age with a further
17 statement saying that there are no data in the pediatric
18 population, there is few data in men, and we have no
19 specific data concerning the safety in women in pregnancy.

20 It was felt that the post-approval study is
21 adequate as designed, however, we want you say on the
22 effectiveness side, further information on the patients with
23 Grade III incontinence, and on the safety side, segregated
24 data looking at the pediatric population, women of
25 reproductive age and also in men, and the directions for

1 labeling are adequate as presented to the panel -- let me
2 rephrase that -- directions for use are adequate as
3 presented to the panel.

4 DR. A. KALLOO: Physician training?

5 DR. DIAMOND: Yes. And it was felt that the
6 physician training issue would be handled also in the
7 labeling with the statement that the device should be used
8 by physicians familiar with therapeutic endoscopy.

9 DR. A. KALLOO: Thank you.

10 Before we take a vote, if anyone wishes to address
11 the panel, please raise your hand and you may have an
12 opportunity to do so.

13 MR. SEGERSON: Dr. Kalloo, before you go into
14 that, I would like to make a clarification. We outlined
15 five specific areas that we wanted you to address, but we
16 are also asking you to deliberate and make recommendations
17 on the whole premarket approval application.

18 So, if there is any issue that you would like to
19 raise, we would like to hear them especially if it affects
20 your recommendation on safety and effectiveness.

21 DR. A. KALLOO: Could you repeat specifically,
22 other than the five questions, what would you like us to do?

23 MR. SEGERSON: You are not limited to those five
24 questions. When Diane brought up that other issue, I just
25 wanted to let you know that you are welcome to bring up

1 anything else that is of concern.

2 DR. A. KALLOO: Panel, here is your chance. If
3 there are issues that you are concerned about other than the
4 five questions that we were asked, here is your chance.

5 DR. HUNTER: What is the shelf life?

6 DR. A. KALLOO: There is a question with respect
7 to the shelf life. If one person can come up to the podium,
8 please.

9 DR. HUNTER: Six months?

10 MS. PETERSON: Our current shelf life is at six
11 months.

12 DR. HUNTER: Temperature problems, storage?

13 MS. PETERSON: None.

14 DR. HUNTER: Obviously, we are going to make this
15 less expensive than the alternatives, please.

16 DR. A. KALLOO: Any other issues or questions?

17 MS. NEWMAN: The thing about the patient brochure
18 again, I think you need to answer the question will I
19 experience pain, because I don't think you are answering
20 that, and I do think that women experience pain even if it
21 is from the anesthetic, and you, evidently your adverse
22 effects was over time.

23 The other question I just was wondering, why did
24 you do it with PVR less than 100, where we in the AHCP, we
25 used a higher number. Was there any reason, you just wanted

1 to be real safe? And whenever you talked about acute
2 retention, then, what was it, a total not able to void, or
3 what did you see then?

4 DR. SNYDER: To answer your first question, some
5 definitive number has to be ascribed to bladder volume.
6 There has never been a study which associates post-void
7 residual with disease state, and so somebody who carries a
8 post-void residual of 250 cc, who goes to the bathroom once
9 every four hours, and has no urinary tract infection nor any
10 deterioration of renal function is a perfectly normal person
11 although a finding of elevated post-void residual is
12 present.

13 So, one needs to just remove the patients who are
14 the neurogenics, and we created 100 cc as being a very
15 critical, and overly critical number to make sure that we
16 weren't anywhere near patients who had neurogenic bladders.

17 MS. NEWMAN: Then, when you did your acute
18 retention, what were your figures there then?

19 DR. SNYDER: Acute retention was actually defined
20 somewhat loosely. It included the patients who completely
21 could not urinate and the patients who felt, that they had
22 the sensation of incomplete bladder emptying.

23 Had we used a pure diagnosis or a pure symptom
24 complaint of urinary retention, absolute no urination, our
25 numbers for urinary retention would have been much, much

1 lower, but we included the patients in a sense of fairness
2 who said, you know, I just don't feel like I empty my
3 bladder well, and I feel like I have to go to the bathroom
4 again in 15 minutes as urinary retention.

5 So, we tried to actually be very critical on our
6 post-procedural results.

7 DR. A. KALLOO: Thank you. Any other comments or
8 issues?

9 [No response.]

10 DR. A. KALLOO: Before entertaining a motion
11 recommending an action on this PMA, Mary will remind the
12 panel of our responsibilities in reviewing today's premarket
13 approval application and of the voting options that are open
14 to us.

15 MS. CORNELIUS: Before you vote on a
16 recommendation, please remember that each PMA has to stand
17 on its own merits. Your recommendation must be supported by
18 the data in the application or by publicly available
19 information. You may not consider information from other
20 PMA's in reaching your decision in this PMA.

21 The Medical Device Amendments to the Federal Food,
22 Drug, and Cosmetic Act, as amended by the Safe Medical
23 Devices Act of 1990, allows the Food and Drug Administration
24 to obtain a recommendation from an expert advisory panel on
25 designated medical device premarket approval applications

1 that are filed with the agency.

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

6 Safety is defined in the Act as reasonable
7 assurance, based on valid scientific evidence that the
8 probable benefits to health (under the conditions on
9 intended use) outweigh any probable risks.

10 Effectiveness is defined as reasonable assurance
11 that, in a significant portion of the population, the use of
12 the device for its intended uses and conditions of use (when
13 labeled) will provide clinically significant results.

14 Your recommendation options for the vote are as
15 follows:

16 1. Approval - if there are no conditions
17 attached.

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

24 3. Not approvable. The panel may recommend that
25 the PMA is not approvable if the data do not provide a

1 reasonable assurance that the device is safe, or, if a
2 reasonable assurance has not been given that the device is
3 effective, under the conditions of use prescribed,
4 recommended, or suggested in the proposed labeling.

5 **Panel Deliberations and Vote**

6 DR. A. KALLOO: We will now consider the panel's
7 report and recommendations concerning approval of P980053
8 Advanced UroScience Durasphere indicated for the treatment
9 of stress urinary incontinence due to intrinsic sphincter
10 insufficiency together with the reasons or recommendations
11 as required by Section 515 Part C(2) of the Act.

12 The underlying data supporting a recommendation
13 consists of information and data set forth in the
14 application itself, the written summaries prepared by the
15 FDA staff, the presentations made to the panel, and the
16 discussions held during the panel meeting, which are set
17 forth in this transcript.

18 The recommendations of the panel may be approval,
19 approval with conditions that are to be met by the
20 applicant, or denial of approval.

21 Dr. Donatucci, will you summarize the panel
22 discussion and make a motion?

23 DR. DONATUCCI: Yes. In summary, the panel finds
24 that there is a favorable risk-benefit analysis for the
25 Durasphere implant; that the indications for Durasphere

1 implant should be in patients with intrinsic sphincter
2 dysfunction over 21 years of age, with further
3 qualifications that there are minimal data in men and no
4 data available in the pediatric age group and reproductive
5 women; that the device should be used by physicians who are
6 familiar with therapeutic endoscopy; further, the panel
7 feels that the post-approval study is adequate as designed,
8 but would like to see specific data in terms of
9 effectiveness on patients with Grade III incontinence and
10 specific data in terms of safety in the pediatric
11 population, the male population, and women of reproductive
12 age.

13 Finally, I would like to move that the panel
14 approve the PMA with the conditions as I have just
15 summarized.

16 DR. A. KALLOO: Will all those voting members in
17 favor of approval with the conditions as stated by Dr.
18 Donatucci, raise their hands.

19 Before you vote, I need someone to second the
20 motion by Dr. Donatucci.

21 DR. HAWES: Second.

22 DR. A. KALLOO: Good. Now, may I have all the
23 members who are in favor of the motion as proposed by Dr.
24 Donatucci to raise their hands, please.

25 [Show of hands.]

1 MR. SEGERSON: Would you announce the count?

2 DR. A. KALLOO: Can you raise your hands once
3 more?

4 [Show of hands.]

5 DR. A. KALLOO: Eight in favor of approval of the
6 motion.

7 DR. DIAMOND: Seven. You can't vote, I don't
8 think, unless there is a tie.

9 DR. A. KALLOO: Seven then in approval.
10 How many members in denial of the motion that has
11 been set forth?

12 [One hand raised.]

13 DR. A. KALLOO: One.

14 Dr. Diamond, could you put forth your reasons for
15 denial?

16 DR. DIAMOND: Sure. In principle, I agree with
17 most of the statements that were reviewed. I find, though,
18 that I cannot vote for approval with that inclusion of males
19 in that group, when just reading from what it says, there
20 has not been a reasonable assurance that the device is
21 effective in that group, and not only is there only a
22 paucity of data of effectiveness or of safety, but even in
23 the introduction that the company has provided to us, the
24 very last sentence is that based on anatomical and
25 etiological differences, it is expected that treatment

1 outcomes would be gender specific.

2 So, despite lack of efficacy data, the company's
3 acknowledgment and presentation to us that there is
4 difference in mechanisms, the vast majority of the members
5 of the panel have recommended that it be approved for use in
6 men.

7 I would rather see it not be approved for use in
8 men and let a physician decide to do that if he or she so
9 chooses.

10 Other than that, I think the safety profile, the
11 efficacy profile is equivalent to the control group, and
12 would be in favor of its approval.

13 DR. A. KALLOO: Starting with Dr. Hunter, could
14 you please give your reasons for approval as we go around
15 the panel.

16 DR. HUNTER: The safety and efficacy was supported
17 by the data. I continue to be impressed by what a good job
18 our agency people do in preparing the information for us,
19 and I think it was a well done study, and I think that what
20 the labeling issue does, it states that there is not enough
21 information on men, women of childbearing age, and pediatric
22 patients. So, you are not saying that it is approved for
23 that use or that group, and you are not telling people how
24 to practice medicine either.

25 DR. DIAMOND: A point of information. If the

1 product is approved, is that not approving it for those
2 groups?

3 DR. A. KALLOO: We are making recommendations to
4 the FDA. This is the recommendation.

5 The next voting member.

6 DR. VERTUNO: I think the safety has been
7 demonstrated. I also think efficacy has been demonstrated.
8 I think the remaining questions can be adequately handled in
9 the labeling.

10 DR. STEINBACH: I think the safety and efficacy
11 has been demonstrated.

12 DR. BENNETT: The only comment I have is
13 concerning the male issue. I think that physicians who
14 don't treat males with post-prostatectomy incontinence
15 should probably not be making decisions on issues related to
16 that disease, which is very specific.

17 There are many males who respond to bulking
18 agents, and denying them what is really the only option --

19 DR. A. KALLOO: I am sorry, Dr. Bennett. Are you
20 a voting member?

21 DR. BENNETT: I am not a voting member.

22 DR. A. KALLOO: The comments are just for the
23 voting members who approve. Sorry.

24 DR. BENNETT: I am sorry.

25 DR. DEITRICK: I agree with the other panel

1 members that approve.

2 DR. HAWES: I agree, as well. I think safety and
3 efficacy has been shown, and I am comfortable with the male
4 issue.

5 DR. N. KALLOO: I agree with the others, and just
6 to sort of bring in what Dr. Bennett said, I think that if
7 you have a person, even though it is not necessarily
8 approved for that person, but it might be the safest and
9 best option for that patient, whether they are a male or a
10 pediatric patient, and the safety and efficacy profiles have
11 been good based on the data that we see, I think that that
12 should be up to the physician and the patient to discuss,
13 and it should be an option.

14 DR. DONATUCCI: I voted approval because, one, I
15 think the safety and efficacy data as presented warrants
16 such an approval, with the qualification that we have
17 minimal data in men.

18 I would also say the reason I am comfortable with
19 that is because this is not the first bulking agent.
20 Urologists have vast clinical experience with bulking agents
21 in the radical prostatectomy patient, and so the physicians
22 who will be using it in that population are familiar with
23 limitations of bulking agents in that population.

24 So, I don't feel that there is an undue -- I
25 really feel there is no risk really in going ahead the way

1 we have done.

2 DR. A. KALLOO: Based on the majority position,
3 the recommendation of the panel is that the motion is
4 carried with the stipulations as stated by Dr. Donatucci.

5 This concludes the reports and recommendations of
6 the panel for Advanced UroScience Durasphere.

7 Thank you.

8 We will have a 10-minute break before we move on
9 to the second portion of the session.

10 [Recess.]

11 DR. A. KALLOO: Welcome back. I would like to
12 call to order for this session of the meeting to discuss
13 revisions to the Draft Guidance for Preparation of PMA
14 Applications for Testicular Prosthesis.

15 I would like to note for the record that the
16 voting members present constitute a quorum as required by 21
17 C.F.R., Part 14.

18 We will begin the open committee discussion with
19 John Baxley presenting the recommendations for revisions to
20 Draft Guidance for Preparation of PMA Applications for
21 Testicular Prosthesis.

22 Mr. Baxley.

23 **Open Committee Discussion**

24 **John H. Baxley**

25 MR. BAXLEY: Good afternoon. I am John Baxley, a

1 biomedical engineer in the Urology and Lithotripsy Devices
2 Branch. I am before you today to present some preliminary
3 thinking within the agency regarding changes to our clinical
4 data recommendations for testicular implant PMAs.

5 We currently have a guidance document in effect
6 regarding PMA submissions for testicular prostheses, the
7 clinical data recommendations contained within that guidance
8 are general to any design.

9 The aim of my presentation this afternoon is to
10 propose clinical data recommendations for three particular
11 designs of testicular implants: solid elastomer, elastomer
12 shells filled with saline, and elastomer shells filled with
13 silicone gel.

14 The goal of developing these design-specific
15 recommendations is to establish clinical testing
16 recommendations which are least burdensome to manufacturers,
17 and at the same time sufficient to demonstrate the safety
18 and effectiveness of each of these particular device
19 designs.

20 Before proceeding further, I want to emphasize
21 that the information being presented are only our
22 preliminary thoughts, which have not yet evolved to the
23 stage where they can be written down as draft guidance to
24 the industry or public.

25 Therefore, since these thoughts are in the infancy

1 of their development, I eagerly and openly invite the
2 panel's comments on this matter. I also want to note that
3 we are only proposing changes to the clinical testing
4 section of the guidance document.

5 A significant portion of this document addresses
6 preclinical testing regarding material chemistry, toxicity,
7 and mechanical characteristics, which we do not intend to
8 alter substantially. After today's recommendations, we will
9 develop and issue a draft guidance document for public
10 comment following the agency's internal "Good Guidance
11 Practices" as a Level 1 document. We hope to have this done
12 in the fall. Ultimately, we foresee this updated guidance
13 document supplanting the March 1993 guidance that is
14 currently in place.

15 Before jumping into our proposed clinical testing
16 scheme for testicular prostheses, I feel that it is
17 necessary to understand the regulatory history of these
18 devices as well as the clinical recommendations section of
19 our current guidance document.

20 After the Medical Device Amendments in 1976,
21 testicular prostheses were classified into Class III. By
22 law, this classification meant that FDA would eventually
23 require testicular implant manufacturers to submit safety
24 and effectiveness information regarding their device in PMA
25 applications unless the device is first down-classified.

1 These devices were not down-classified, so in
2 January 1993, FDA issues a proposed regulation calling for
3 PMAs. Following publication of this proposed regulation,
4 FDA issued the March 1993 guidance document of which you
5 each have a copy, and presented it to the panel in April.

6 Although the proposed regulation and the guidance
7 document were applicable to all device designs, both
8 documents contained detailed testing recommendations
9 specific to the silicone gel-filled design as this was the
10 predominant type of testicular implant on the market at that
11 time.

12 After reviewing the comments received on the
13 proposed rule and noting that no petitions for down-
14 classification were received, FDA issued a final regulation
15 in April 1995 requiring PMAs for all testicular implants.

16 At the same time, however, each manufacturer
17 ceased production of their testicular prosthesis. Since no
18 PMAs were received, there have been no legally marketed
19 testicular implants in the U.S. since 1995.

20 Although several companies have since proposed
21 clinical investigations of new testicular implant models
22 that do not contain silicone gel, these trials were either
23 not started or proceeded much slower than expected due, in
24 part, to difficulties in applying the clinical
25 recommendations of the March 1993 guidance with its heavy

1 emphasis on silicone gel-filled designs.

2 With this regulatory history in mind, let me
3 briefly describe the clinical study recommendations of the
4 March 1993 guidance document.

5 The clinical study objectives recommended in the
6 guidance are to demonstrate the safety and effectiveness of
7 the testicular implant when used for cosmetic replacement of
8 a missing testicle.

9 The document recommends that safety be evaluated
10 through assessment of all complications related to the
11 implant, including any potential material-related adverse
12 events. The guidance document primarily discusses this
13 issue of "material-related adverse events" in terms of the
14 potential toxicity of silicone gel and polyurethane foam
15 coating. Unlike silicone gel, however, polyurethane foam
16 was only briefly used as a coating of testicular prostheses,
17 after which it was discontinued following reports of
18 increased infection and tissue reaction.

19 Regarding the effectiveness endpoints, the
20 guidance document recommends evaluation of the implant's
21 cosmetic effect, either by the physician or patient, as well
22 as assessment of the patient's "psychological well-being,"
23 which is more appropriately referred to today as "quality of
24 life."

25 As for study design, the guidance document only

1 recommends that studies be prospective using an appropriate,
2 concurrent control population. Likewise, specific sample
3 sizes are not stated; rather, the document states that the
4 number of patients enrolled should be statistically
5 calculated.

6 The recommended follow-up duration prior to PMA
7 approval is five years or physical maturity, whichever is
8 later.

9 Post-approval follow-up is also recommended,
10 although the sample size and duration of follow-up are not
11 specified. The recommended objectives for this post-
12 approval study are to assess the rates of any longer long-
13 term complications, such as rupture, revision, and material-
14 related adverse events.

15 Lastly, the guidance document makes general
16 recommendations to manufacturers on the design of an
17 epidemiological study to evaluate the connection between
18 testicular implants and material-related and other long-term
19 adverse events, which could be submitted either in support
20 of PMA approval or in lieu of the stated post-approval study
21 recommendations.

22 Having summarized this background information, I
23 would like to go over the proposed changes to the guidance
24 document's clinical study recommendations. In general, our
25 proposed changes involve the following concepts:

1 First, development of design-specific clinical
2 recommendations. As stated at the outset of this
3 presentation, we would like to device clinical study
4 recommendations for each of the specific designs that
5 manufacturers are most likely to propose for market.

6 Two designs that we believe are likely to come
7 before the agency are solid elastomer implants and saline-
8 filled designs. Although silicone is the elastomer material
9 that we would most likely expect to see used in each of
10 these designs, other polymers could be potentially be used.

11 The third design that we believe should be
12 included in our revised guidance document is the elastomer
13 shell filled with silicone gel. While we currently don't
14 have an indication that manufacturers are interested in
15 pursuing PMA approval of the gel-filled design, we feel that
16 it should be considered since this was the dominant design
17 during the seventies and eighties and is still used abroad.

18 Since polyurethane coatings were rarely used in
19 the past, we will not specifically address them in the
20 revised guidance document. At this point I want to briefly
21 make a distinction between the solid and the gel-filled
22 devices.

23 In designing the solid device to feel as natural
24 as possible, some manufacturers use a softer consistency
25 elastomer for the implant's core, which is less cross-linked

1 than the external surface of the device. Since at some
2 degree of cross-linking the distinction between a soft
3 elastomer and a gel blurs, our future guidance will define
4 the minimum material characteristics that can be considered
5 a solid elastomer.

6 For the purposes of today's discussion, however, I
7 propose that we just assume that any material used in a
8 solid device will not flow in the event of implant rupture,
9 whereas, a gel filler material will.

10 The second general concept is reliance on the
11 literature. We have reexamined the available literature on
12 testicular implants to determine what is and what is not
13 known regarding the safety and effectiveness of each of the
14 various designs.

15 While published information is not sufficiently
16 complete to support either PMA approval or down-
17 classification of any particular device design, there is a
18 significant amount of information regarding the surgical
19 technique and short-term risks and benefits which can be
20 included in each PMA as supplementary information to confirm
21 the validity of the clinical results.

22 The last general concept in these recommendations
23 is that patients should serve as their own control. Since
24 there is no alternative treatment for cosmetic replacement
25 of a missing testicle, baseline control should be

1 recommended for the clinical evaluation of all device
2 designs.

3 Now, for the specifics. For PMA approval of the
4 solid elastomer prosthesis, we proposed manufacturers submit
5 data on 50 patients followed for a minimum of six months.
6 Since there is information available in the literature
7 regarding the implantation technique and acute effects of
8 solid and gel-filled testicular implants, and assuming that
9 this information is equally applicable to the solid design
10 that I described earlier, which we believe it is, the
11 objectives of this study would be to simply confirm that the
12 proposed device requires similar surgical technique and has
13 a comparable short-term adverse event profile.

14 Of course, if the implantation procedure or
15 clinical results deviate significantly from those reported
16 in the literature, a larger clinical trial will be needed to
17 sufficiently characterize this information for the labeling.

18 Following approval, we recommend that the
19 manufacturer collect one-year follow-up data on 50 patients
20 to assess the incidence of adverse events after the early
21 post-implantation period, such as erosion or migration.

22 For the saline-filled testicular implants, we
23 recommend that PMA approval be based on a minimum of 100
24 patients followed for six months. As with the solid design,
25 the objectives of this study should be to confirm that the

1 implantation technique and short-term adverse event profile
2 is similar to that described in the literature for gel-
3 filled and solid devices.

4 However, since the saline-filled device will
5 likely require unique device handling, filling, and
6 implantation procedures, and could potentially be associated
7 with different rates of rupture or other adverse events as
8 compared to the gel-filled and solid designs reported in the
9 literature, we believe that 100 patients should be followed
10 to provide higher statistical confidence for each measured
11 endpoint than what we are currently recommending for new
12 solid implants.

13 Again, if the reported results deviate
14 significantly from the literature, a larger clinical trial
15 should be performed. Following approval, we recommend that
16 the manufacturer collect five-year follow-up data on 100
17 patients to assess the rates of long-term adverse events,
18 primarily rupture and revision.

19 Alternatively, the manufacturer could choose to
20 maintain a patient registry to record information on the
21 rates of rupture and revision. We believe that these
22 additional post-approval study recommendations are warranted
23 due to the absence of published information on saline-filled
24 testicular implants.

25 For approval of a silicone gel-filled testicular

1 implant, we recommend that PMAs contain the results of 100
2 patients followed for 12 months. As with solid devices, the
3 study objectives should be to confirm that the implantation
4 technique and short-term adverse event profile are similar
5 to that described in the literature.

6 However, since this design carries the additional
7 risk of rupture with associated potential material-related
8 adverse events as compared to the solid design, we believe
9 that a minimum of 12 months of follow-up data should be
10 obtained premarket.

11 As with the proposed study design for saline-
12 filled devices, we believe that the proposed sample size of
13 100 patients is necessary to provide adequate statistical
14 confidence for the key safety endpoints.

15 Following approval, we recommend that the
16 manufacturer either follow 250 patients for 10 years to
17 document the rupture, revision, and long-term adverse event
18 rates, or maintain a patient registry to record this
19 information for all patients.

20 The objectives and follow-up duration proposed for
21 these post-approval recommendations are designed to
22 precisely evaluate the rate of rupture and the effects of
23 subsequent release of silicone gel into the body, and is
24 consistent with the agency's post-approval study
25 recommendations for breast implants.

1 The remainder of our clinical study
2 recommendations are relatively straightforward. As in the
3 current guidance document, we believe that the effectiveness
4 of the testicular implant is best evaluated by physician
5 assessment of the cosmetic effect, and assessment of patient
6 satisfaction and quality of life.

7 However, we recognize that assessments of patient
8 satisfaction and quality of life are typically only valid
9 for adults and older teens. Therefore, for younger
10 subjects, this information may need to be obtained from
11 parents or guardians and analyzed separately.

12 We still plan to recommend that the safety of the
13 testicular implant be assessed through analysis of all
14 reported adverse events. However, we propose removing the
15 recommendations on the design of epidemiological studies, as
16 they would not be practical to perform due to the limited
17 numbers of patients receiving this implant.

18 This concludes my presentation. At this point I
19 would like to turn the discussion of these proposed changes
20 to the panel. But before I do so, let me take this
21 opportunity to answer any questions regarding my
22 presentation.

23 DR. A. KALLOO: Any questions?

24 DR. DONATUCCI: Let me ask you first you said
25 earlier that you hadn't changed the -- I was there in March

1 of 1993, and I remember the preclinical testing
2 requirements, which were rigorous. I have two questions.
3 One, fortunately, six years have passed, there is a large
4 body of data now, and the anxiety attendant to 1993 has
5 subsided to a certain extent.

6 If the material is the same as the same material
7 that is used for the breast implant for example, do they
8 have to repeat all that stuff?

9 MR. BAXLEY: Referencing the biocompatibility
10 data, for instance, of the material in another application,
11 that was used in another --

12 DR. DONATUCCI: I mean it is just a different
13 anatomic site, it's the same thing, but it's a different
14 anatomic site.

15 MR. BAXLEY: Right, we would consider whether that
16 was valid to do, and would probably take that
17 biocompatibility data or take that assurance of
18 biocompatibility based on approval of some other
19 application. That is certainly an option.

20 DR. DONATUCCI: Secondly, we heard earlier a
21 presentation from FDA about the registry. There is a lot of
22 experience with the gel-filled prosthesis. How many adverse
23 effect complaints relative to rupture of a testicular gel-
24 filled prosthesis have come in to FDA over the 20 years that
25 they were available?

1 MR. BAXLEY: There are on the order of tens, not
2 many, relative to, say, the adverse event reporting for
3 breast implants.

4 DR. DONATUCCI: A final question. Is the process
5 that led to classification as Class III, they were included
6 in the 1976 law because they were an implant basically, a
7 permanent implant, in 1976, all of them were automatically
8 Class III with the provision that at some point, FDA would
9 ask for a PMA. Is that how --

10 MR. BAXLEY: Yes, but it wasn't just because it
11 was an implant. There were specific risks raised regarding
12 adverse tissue reaction that were raised by the panel that
13 classified the device.

14 DR. DONATUCCI: But you also said that no requests
15 for reclassification arrived. Does that mean there is a
16 mechanism to ask for reclassification?

17 MR. BAXLEY: Yes, a device that is in Class III
18 can be down-classified regardless of whether it was pre-
19 amendments or not. I mean this device existed prior to
20 1976, which is why it is a pre-amendments device.

21 DR. DONATUCCI: But you can't do that, that has to
22 come at a request of someone?

23 MR. BAXLEY: That is a petition from the public,
24 which could include --

25 DR. DONATUCCI: Does it have to be for an existing

1 device? In other words, do the people who had a device at
2 that time have to request that this should be reclassified,
3 or is it a category of devices?

4 MR. BAXLEY: Oh, no, you request the category, not
5 one particular.

6 DR. BENNETT: John, have you had any --

7 MR. BAXLEY: Oh, and FDA can initiate a
8 reclassification, too.

9 DR. DONATUCCI: You can initiate it.

10 MR. BAXLEY: The case of the lithotripter that you
11 heard about last year, that was FDA initiated.

12 DR. A. KALLOO: How did you get to the sample
13 sizes?

14 MR. BAXLEY: Sample sizes are based on the comfort
15 level with the confidence intervals on the adverse events
16 that we would expect to see from the literature, so for a 5
17 percent adverse event rate, we know the confidence interval,
18 and that is a comfort level on that confidence interval.

19 DR. BENNETT: John, has the FDA been in contact
20 with the one company that used to make testicular prostheses
21 or is this an internal process?

22 MR. BAXLEY: Right now this is right off the
23 press, and so it is before we have put it out for public
24 comment. The public comment will follow immediately after
25 this.

1 DR. BENNETT: I mean if there is no interest from
2 the point of view of the sole manufacturer, isn't it just
3 kind of a -- or are you looking to the future?

4 MR. BAXLEY: We are looking to the future and are
5 hopeful this will stimulate interest.

6 DR. HAWES: Assuming these are done now, what is
7 happening now?

8 DR. DONATUCCI: They are not done now.

9 DR. HAWES: They are not done. There have not
10 been any done since 1995.

11 DR. BENNETT: If the child or an adult wants a
12 testicular implant today, they go to Europe.

13 DR. HAWES: Are you serious?

14 DR. DONATUCCI: That's not entirely true. We, at
15 one of our grand rounds recently, presented a product that
16 is a silicone block that can be used as a testicular
17 prosthesis coming from Europe. I forget the company that
18 makes it.

19 DR. FOOTE: I would like to make a comment on
20 that. My partner put one in, and will never put in another
21 one. It just doesn't feel real.

22 DR. DONATUCCI: Fine, but I was referring to Alan
23 that you don't have to go to Europe, Europe has come here,
24 and as I understand it, because it is not a "testicular
25 prosthesis," but a silicone block, it doesn't fit into this

1 discussion today. It's semantics.

2 DR. BENNETT: So, Jenelle, what do you do?

3 DR. FOOTE: My partner had an experience in using
4 one of these things, and it didn't feel real, it felt like a
5 rock.

6 DR. BENNETT: Like the old ones used to feel.

7 DR. FOOTE: Yes.

8 DR. DONATUCCI: In fact, Alan they have already
9 been shaped.

10 DR. FOOTE: Yes, they are shaped, but it doesn't
11 feel good.

12 DR. HAWES: So, we went from 4,000 per year before
13 1995, to zero, none.

14 DR. BENNETT: Yes.

15 DR. N. KALLOO: I did a literature search, and in
16 Ontario, they are using them, and they actually were
17 reviewing their data, old data, this is from '93, but they
18 are doing some old data, and they used the gel-filled, and
19 they actually had rupture in those, who had significant
20 trauma, so they sort of went over their profile for rupture,
21 and a lot of these were in transsexuals, male and female,
22 and one was in a bicycle rider, and another was in somebody
23 who did various things to excite himself.

24 So, they ruptured under extreme conditions. Now,
25 there is an article that is from the Netherlands, from

1 Amsterdam, that came out in February, and they are using the
2 -- which one are they using -- I believe they are using the
3 solid ones, but with sort of the less cross-linking, which
4 makes them softer, but they have had no evidence of any
5 complications whatsoever, but they are still being used, but
6 not in this country, because -- you know, Canada and Europe.

7 DR. STEINBACH: The problem with devices of this
8 kind is we have trouble convincing the public and maybe
9 ourselves that there is any benefit -- I am just saying, so
10 this is what I am saying, that he is proposing not a
11 controlled trial where it's just, you know, how you felt six
12 months ago, to how you feel now.

13 I think we really ought to allow the manufacturers
14 to be creative as to what might be a control group. One
15 suggestion I will toss out, and I certainly wouldn't require
16 it, is that if it was like a jock strap, you know, that was
17 purely external, and was not an implant, might serve as a
18 control group.

19 DR. DONATUCCI: In terms of satisfaction you mean?

20 DR. STEINBACH: Yes.

21 DR. DONATUCCI: Obviously not in terms of safety.

22 DR. STEINBACH: But in terms of satisfaction, and
23 because of the perception in the public, I mean there will
24 be adverse events, and do the benefits justify it.

25 DR. DONATUCCI: I would say first there is a

1 population out there that is waiting for something. I get
2 calls frequently, requests frequently for this, so there is
3 a demand out there. However, it is low, and in a sense, we
4 talked earlier today, FDA mentioned kind of an orphan device
5 equivalent to an orphan drug, and this is essentially that
6 situation because there is a demand, but it's not that
7 large, never will be.

8 DR. A. KALLOO: I wonder, too, about the numbers
9 that you are requesting, is this going to be doable with the
10 amounts of the population. I have no idea. I guess it's a
11 question I am putting to the urologists.

12 DR. DONATUCCI: Is the study doable from a company
13 point of view or from just accrual of patients?

14 DR. A. KALLOO: Just accrual of patients.

15 DR. DONATUCCI: I think, yes, I mean 50 patients
16 is doable.

17 DR. HUNTER: Yes, it's doable.

18 DR. A. KALLOO: I guess we should go on to the
19 clinical presentation, and then consider more questions.

20 Next, Dr. Naida Kalloo will give a status report
21 on current management of testicular implants and will lead
22 the discussion of the FDA charges.

23 **Naida Brooks Kalloo, M.D.**

24 DR. N. KALLOO: I want to start this off by saying
25 that a lot of people will know a lot more than me about all

1 this stuff, and this is less than 24 hours notice that I am
2 doing this, so I just wanted to sort of make that clear, and
3 again, a lot of this will be repetitious.

4 As I mentioned before, implants were first
5 introduced in the sixties, and were introduced as rock-hard,
6 solid silicone rubber tips to give a prosthesis that went
7 over like a lead balloon.

8 Then, over time this gel-filled testicular
9 prosthesis was introduced in 1972 by Dow Corning. There
10 have been several cross-linking changes made between '72 and
11 '88, and there are at least four other companies that make
12 them - Mentor and some other ones that were making them at
13 that time.

14 The indications for a prosthesis in the
15 prepubertal population would be a person who is born without
16 a testicle, perinatal torsion, some intersex disorders that
17 require gonadectomy because of the risk of tumors later on,
18 tumors, both benign and malignant, and then post-surgical
19 atrophy after hernia repairs and after orchidopexies.

20 Post-pubertally, patients who have Klinefelter
21 syndrome, who have very small, hard testicles like them
22 replaced for something that is more appropriate, and female
23 to male transsexual operations, peripubertal torsion, and
24 again for tumors.

25 In most cases, the surgical procedure is either an

1 inguinal, an inguinal scrotal, or a scrotal approach for
2 implanting the procedures or implanting the testicular
3 prosthesis.

4 Complications from historical data, from the
5 literature, include wound infections, discomfort from the
6 devices, inadequate size at puberty for those who are
7 implanted prepubertally, rupture again with extreme force,
8 wound dehiscence, and extrusion through a dehisced wound.
9 Also, I would include on here migration to an extrascrotal
10 position.

11 In 1992, right around the same time that we were
12 going through all the hoopla with the breast implants, the
13 AUA had a position paper and basically indicated that
14 silicone, gel-filled testicular prostheses should not be
15 used, however, they stated that the use of silicone
16 elastomer-filled implants may be considered when the
17 benefits to the patient outweigh the possible risks.

18 Right about the same time, Dow Corning suspended
19 their production of testicular implants right after the AUA
20 had their position paper.

21 Now, in the literature again, mostly associated
22 with breast implantations, they were concerned about
23 systemic disorders, and in the literature, there is
24 absolutely no evidence that testicular implants are
25 associated with any systemic abnormalities. There is one

1 paper again, like I mentioned before, in Ontario, there were
2 34 males. There was a mean follow-up of at least five years
3 postoperatively, and there were no systemic disorders noted
4 that could be related to the silicone.

5 Again, in the current literature, again, from the
6 Netherlands, in February, an article mentioned that they use
7 the silicone elastomer envelope of highly cross-linked
8 semisolid medical grade, silicone elastomer filling, and
9 none of the patients had any complications from that.

10 In those that were ruptured, they mentioned
11 various ways of identifying the rupture with both ultrasound
12 and MRI, and they went into a lot of those details, but what
13 they found is that, unlike the gel-filled prostheses before,
14 these prostheses did not spill the contents either with
15 rupture or with puncture of the envelope.

16 In essence, I think right now, people are being
17 very creative with how they are putting in testicular
18 implants. I know that Dr. Kogan, who is sort of the liaison
19 with the AAP, is doing a mentor-sponsored study, and they
20 are supposed to come up with about 267 patients, but with
21 all the problems going on, they are unable to get the
22 adequate numbers to get those patients for approval.

23 So, that is one thing that is actually going on
24 right now. Other than that, I know that plastic surgeons
25 often use tissue expanders, and those are silicone based,

1 that you fill with water.

2 DR. A. KALLOO: Any questions?

3 DR. DONATUCCI: So, there is a trial ongoing at a
4 single site in the pediatric population?

5 DR. N. KALLOO: That is my understanding based on
6 information that I received today, but I have put them in
7 with tissue expanders, that are used by plastic surgeons,
8 and you can get them to shape them any way you want to, and
9 you just call the company, and they will shape them in an
10 ovoid shape, and you fill them with saline.

11 I have done it for people who want two big
12 testicles, and I have had no complications. Of course, that
13 is anecdotal, and I have put them in sort of a peripubertal
14 male who was, you know, sort of a petite type of male, and
15 was always being pushed around, was always being kind of
16 knocked around, and his level of self-esteem came up tenfold
17 once he had a matching pair because then he wasn't, you
18 know, One Eye, and all the other sort of things that he
19 mentioned he was being called.

20 So, I think you are going to get a lot of
21 anecdotal studies about that, but certainly I don't think
22 any one place is going to have a large number of these
23 particular patients, especially with those indications.
24 There just isn't one place that has a lot of them.

25 If anybody has anything about the status, you are

1 more than welcome to bring it up. That is certainly all
2 that I have available.

3 **Open Public Hearing**

4 DR. A. KALLOO: Does anyone outside the panel wish
5 to address the panel? Please raise your hand.

6 DR. HOLEBRUE: I am Dr. Logan Holebrue [phonetic]
7 from the American Urological Association. I am Chairman of
8 the Health Policy Council and former President of the AUA,
9 and I have no financial interest in any of the companies that
10 manufacture any of these, and neither have I spoken to any
11 of the industry representatives. I might also add that the
12 AUA has not revisited this issue since its pronouncement
13 back in 1993.

14 I would like to make several points. First of
15 all, we applaud the Food and Drug Administration in its
16 efforts to protect the public and to assure efficacy in the
17 various products it reviews. It is extremely important,
18 first, to do no harm.

19 The second point I would like to make is that this
20 is a very rare condition, and a study that was advocated
21 here would have to be a multi-center study, indeed, I would
22 suspect it would have to include every children's hospital
23 in this country.

24 It would be a multi-year study. I don't know how
25 many of these operations would be performed a year were

1 there prostheses available. Neither do I know how many were
2 performed back when they were available. A figure of 4,000
3 a year has been bantered around. I think those are the
4 production and sales. My own hospital would have an array
5 of different sizes on the shelf because what is suitable in
6 size for a six-year-old would not be suitable for a 21-year-
7 old, and what would suit a 21-year-old would, of course, be
8 grotesque in the scrotum of a 6-year-old.

9 So, there are lots of sales. I don't know how
10 many implants there are, we simply have no data. Now, I
11 have a feeling that given the minimal number of these
12 implants that are going to be done in a year, even if there
13 were to be approval, I wonder if any company or companies,
14 plural, would be interested in embarking on such a study
15 given the meager numbers of sales available.

16 I am not in industry. I don't know that I can
17 answer that question. I simply raise it.

18 I think there is serious question whether the
19 cost-profit ratio would be such that they would want to fund
20 and embark upon and support a study of this magnitude
21 involving so many different centers, which is always costly,
22 and over so many years, which is also costly.

23 Now, having said all of that, I would be very
24 happy to go back to the AUA and to ask our board of
25 directors to reevaluate the position it put forward in 1993,

1 and perhaps we should do that.

2 I think that the facts having been stated, as I
3 have just given them, I think we all have to admit that no
4 young man or young male child dies because they have an
5 empty scrotum, but I think that, on the other hand, there
6 are emotional issues involved, and we all know that young
7 children and young adolescents compare the appearance of
8 genitalia, we know that, and the young man with an empty
9 scrotum I am sure is at considerable psychological
10 disadvantage amongst his peers.

11 So, having said these things, I think that this is
12 an open issue, and I think we have to therefore balance the
13 risks of these devices. If we know of anecdotal situations,
14 if we -- I was interested to hear that there were 10 cases
15 reported of problems, I would certainly like to know what
16 those were. I would love to see that data.

17 We have to balance the risks of this versus the
18 potential psychological benefit we glean of a young man and
19 children who are in need of this procedure. It is a very
20 small number, and very honestly, I would think that the
21 study proposed here would probably be near nigh to
22 impossible, and I doubt that industry would ever be
23 interested in funding it.

24 You might ask industry. I don't represent them,
25 so I don't know.

1 Thank you very much.

2 DR. A. KALLOO: Thank you.

3 **Open Committee Discussion (Continued)**

4 Any questions from the panel with regards to this?

5 DR. DONATUCCI: To anyone?

6 DR. A. KALLOO: Yes.

7 DR. DONATUCCI: I have one more question to the
8 FDA. If these devices, say, the saline-filled testicular
9 implant is essentially the same as a saline-filled breast
10 implant except that it's a different size and it is placed
11 in a different anatomical location, what issues are
12 different about putting the same prosthesis that is already
13 approved for placement underneath the skin of the chest
14 wall, demand a clinical trial when it's placed in the
15 scrotum? Is there a substantial difference in the potential
16 risk in terms of materials and rupture? I just don't see
17 it, and that's why I am asking.

18 MR. BAXLEY: Well, we want certainly the labeling
19 or its directions for use be able to be clear enough that a
20 physician knows how to put it in, and there are no reports
21 in the literature of this version of a device to give you
22 that information. That is one thing in our minds.

23 Another thing is we like the labeling to tell the
24 physician and patient what likelihood it has of rupturing,
25 which means that you probably would have to get a

1 reoperation, not being satisfied with a ruptured implant.

2 DR. DONATUCCI: But the data from the chest wall
3 is not sufficient for this scrotum?

4 MR. BAXLEY: No, because its rupture rates depend
5 on its geometry, and it is also dependent on location, being
6 in an area which I guess a child, who is rough in playing,
7 could very easily break it. It's hypothetical, but in this
8 area, it seems like it might, because of the anatomic
9 location, might have different forces received.

10 DR. DONATUCCI: But you couldn't gather that data
11 by postmarket? I mean record ones that were ruptured.

12 MR. BAXLEY: Yes, and what we are proposing is to
13 study the patients premarket for six months, and probably
14 not have any rupture data in that time period, and then
15 postmarket, get the rupture data, and the option is we are,
16 at least at present, equally open to the ideas of post-
17 approval follow-up with that patient population, of a
18 specific patient population, or a patient registry, which
19 doesn't include follow-up, but tracks all patients.

20 DR. N. KALLOO: I would like to just address that.
21 There is an article here, this one from Amsterdam, from
22 February of '99, and what they are mentioning is that -- I
23 will just read this one paragraph -- "As opposed to the
24 subpectoral location of many prostheses, the scrotum is said
25 to offer a position with low tension, low friction, and

1 lower temperatures. Testicular prostheses are also more
2 mobile, allegedly making them potentially less vulnerable to
3 pressure injury. These factors may contribute to the lack
4 of demonstrated implant failure."

5 So, they are actually suggesting that the scrotum
6 is actually an advantageous place. Now, certainly, if you
7 are performing extreme acts, like bicycle riding and things
8 like that, then, you certainly might put it at risk, but I
9 think the two cases that they mentioned were actually
10 extreme cases.

11 DR. BENNETT: I see a representative from AMS in
12 the room. Is there anyone here from Mentor? I mean again,
13 there are none being made in the United States. Is there
14 any interest from any company here to revisit the issue vis-
15 a-vis down-classification or whatever?

16 DR. A. KALLOO: Please state your name and
17 affiliation.

18 MR. PURKATE: My name is Bobby Purkate [phonetic].
19 I am from Mentor Corporation. I am the Senior Vice
20 President for Science and Technology.

21 To answer your question, yes, we do have interest
22 both on the saline testicular as well as the solid
23 elastomer. Currently, we have completed a clinical study,
24 about 100 patients, on the saline testicular, and on the
25 solid elastomer, we do not have any clinical data, but we

1 have extraordinary amount of preclinical data, which we
2 believe would be sufficient to show the safety and
3 effectiveness. So, we are very interested.

4 DR. BENNETT: But you haven't discussed this with
5 the FDA?

6 MR. PURKATE: We have opened the dialogue with
7 John Baxley and Don St. Pierre. They are pretty familiar
8 with what we have. We are continuing to work with it,
9 hopefully, we will bring the data to them for their review
10 very shortly, and we will take it from there.

11 DR. A. KALLOO: I think I would like to move on
12 and look at the specific questions that the panel will be
13 asked.

14 The first question is: Does the panel believe
15 that the proposed scheme for stratifying the clinical
16 testing recommendations for the testicular prosthesis by
17 solid, saline-filled, and silicone gel-filled designs is
18 clinically sound?

19 Question 2. Should adult and pediatric patients
20 be analyzed as separate cohorts, or are the general issues
21 of safety and effectiveness sufficiently similar to permit
22 these two populations to be pooled for analysis?

23 The third question is: Does the panel believe
24 that the proposed pre-/post-approval follow-up
25 recommendations are necessary and sufficient to demonstrate

1 the safety and effectiveness of the three testicular
2 prostheses designs currently being considered?

3 So, those are the three questions and what we will
4 do is I will pose each question to each of the panel
5 members, and Dr. Kalloo will summarize the panel comments at
6 the end.

7 The first question, we will start with Dr. Foote,
8 if you could please comment.

9 Does the panel believe that the proposed scheme
10 for stratifying the clinical testing recommendations for the
11 testicular prosthesis by solid, saline-filled, and silicone
12 gel-filled designs is clinically sound?

13 DR. FOOTE: Yes.

14 DR. HUNTER: Yes, but I think it's a waste of time
15 for the last one, because of the lawyers.

16 DR. DIAMOND: Yes.

17 MS. NEWMAN: Yes.

18 DR. VERTUNO: Yes.

19 DR. STEINBACH: Yes.

20 DR. DEITRICK: Yes.

21 DR. HAWES: Yes.

22 DR. DONATUCCI: Yes.

23 DR. N. KALLOO: Yes, and I think the consensus is
24 yes.

25 DR. A. KALLOO: The second question is: Should

1 adult and pediatric patients be analyzed as separate
2 cohorts, or are the general issues of safety and
3 effectiveness sufficiently similar to permit these two
4 populations to be pooled for analysis?

5 DR. FOOTE: I would pool the analysis of the adult
6 and the pediatric populations. I don't think there is going
7 to be a whole lot of difference in regards to how they do.

8 DR. HUNTER: Ditto.

9 DR. DIAMOND: I would think they could be pooled.

10 MS. NEWMAN: I agree.

11 DR. VERTUNO: Yes.

12 DR. STEINBACH: No, I think children behave
13 differently than adults, and may stress them more.

14 DR. N. KALLOO: I am sorry. Would you repeat what
15 you said?

16 DR. STEINBACH: I think the children are more
17 likely to put them to higher mechanical stress.

18 DR. DEITRICK: Yes, I agree they could be pooled.

19 DR. HAWES: I think they could be pooled.

20 DR. DONATUCCI: I think they can be pooled, and in
21 response to your comment, again, we do have prior clinical
22 experience, and it just wasn't an issue.

23 DR. N. KALLOO: And personally, I think they can
24 be pooled. There are very few things that they are going to
25 be doing that really put that much stress -- they are so

1 mobile, and they are so little.

2 DR. A. KALLOO: And the summary?

3 DR. N. KALLOO: In summary, I think the majority
4 have agreed that they can be pooled.

5 DR. A. KALLOO: Question 3. Does the panel
6 believe that the proposed pre-/post-approval follow-up
7 recommendations are necessary and sufficient to demonstrate
8 the safety and effectiveness of the three testicular
9 prostheses designs currently being considered?

10 DR. FOOTE: In regards to the recommendations, I
11 guess my only concern was that, as I recall, for the solid
12 prostheses, it was recommended that a size 100 was used, but
13 for the other two, was it 250? Am I correct?

14 MR. BAXLEY: No, it was 50 for solid.

15 DR. FOOTE: 100 for the saline and for the gel.

16 DR. N. KALLOO: 250 at 10 years for the gel.

17 DR. A. KALLOO: Postmarket.

18 DR. FOOTE: 250 postmarket. Yes, that's fine.

19 DR. HUNTER: It's either acceptable or I would
20 simplify it to a registry only. I think that is more
21 realistic.

22 DR. DIAMOND: I am not sure you can really assess
23 effectiveness in this sort of model, but in view of the
24 small number of patients, I think it probably is going to be
25 the most realistic and best that you are going to be able to

1 do in any reasonable amount of time. I would be in favor of
2 it the way it was proposed.

3 MS. NEWMAN: I think it's fine.

4 DR. VERTUNO: Yes.

5 DR. STEINBACH: I still would like to see some
6 kind of control group for effectiveness.

7 DR. N. KALLOO: Would that be psychosocial
8 effectiveness?

9 DR. STEINBACH: Yes.

10 DR. BENNETT: I have no problem with the early
11 follow-ups, but I would eliminate totally the post-approval
12 studies. I think they are unrealistic and past history
13 would indicate that they need -- there is not requirement
14 especially if the only thing that you are really concerned
15 about is rupture. I think that that information can be
16 gleaned within the first few years.

17 DR. DEITRICK: I agree with the proposal as it is.

18 DR. HAWES: I think the study is sufficient and
19 can demonstrate safety and efficacy. I would agree with Dr.
20 Hunter. I would just simplify the follow-up to a registry,
21 and not require a formal study.

22 DR. DONATUCCI: The way I look at the post-
23 approval studies, 5,100 and 250, it seems like there is
24 still some concern long term about gel-filled prostheses.
25 Again, I question whether, in an adult population, the fact

1 that it is placed in the testicle and leaks in the scrotum
2 as opposed to leaking in the body wall, would make any
3 difference in the long-term toxicity, and I think there are
4 data already about the toxicity of gel in an adult
5 population.

6 Now, I don't think we have any information about
7 the risk of leakage of saline gel in the pediatric
8 population. It just doesn't exist as far as I know. I am
9 not necessarily overly concerned, but the way you stratify
10 that, 1,500 and 250, says to me that you are still more
11 concerned about the gel-filled prostheses than the other two
12 in the potential toxicity of the gel.

13 I just wonder whether that needs to be a fear in
14 the scrotum as opposed to any other anatomic location in an
15 adult given the data that we have available.

16 I would say, I have to agree I think the registry
17 would probably be the most logical way to handle that.

18 DR. N. KALLOO: I think that a summary would
19 indicate that the majority would say yes, that the proposed
20 pre- and post-approval follow-up recommendations are
21 sufficient to demonstrate safety and effectiveness of the
22 three types with the caveat that they should probably be
23 reduced to a registry, and again, other comments would be
24 that there should be a control group for psychosocial
25 effectiveness, that again, the post-approval studies are

1 probably excessive, and the registry would probably address
2 those issues.

3 DR. A. KALLOO: Before I ask the panel to vote on
4 whether they agree with this or not, would you like to have
5 the summaries restated? No.

6 Those in agreement with this final consensus, if
7 you could raise your hands, please.

8 [Show of hands.]

9 DR. A. KALLOO: Unanimous.

10 Mary, do you want to read the letter?

11 MS. CORNELIUS: I would just like to read into the
12 record some comments sent to me by Dr. Kogan.

13 Dr. Stanley Kogan, representing the Urological
14 Section of the American Academy of Pediatrics, submitted a
15 letter to the agency that will be added to the panel record.

16 To summarize Dr. Kogan's comments, he states there
17 is a need for a legally marketed testicular implant in the
18 United States and would like the FDA to ensure that this
19 device is available to patients who are in need.

20 I have one final comment before we adjourn.
21 Please leave your books on the table and put your trash in
22 the trash can before you leave.

23 DR. A. KALLOO: This concludes the meeting. I
24 would like to thank all the members of the panel and the FDA
25 for making this a very successful day.

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The meeting is now adjourned.

[Whereupon, the meeting was adjourned at 3:08

p.m.]

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C E R T I F I C A T E

I, **THOMAS C. BITSKO**, the Official Court Reporter for Miller Reporting Company, Inc., hereby certify that I recorded the foregoing proceedings; that the proceedings have been reduced to typewriting by me, or under my direction and that the foregoing transcript is a correct and accurate record of the proceedings to the best of my knowledge, ability and belief.

A handwritten signature in black ink, appearing to read 'T.C. Bitsko', is written above a horizontal line.

THOMAS C. BITSKO