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ORTHOPEDIC AND REHABILITATION DEVICES PANEL
OF THE
MEDICAL DEVICES ADVISORY COMMITTEE

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THURSDAY,
JUNE 3, 2004

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*This transcript has not
been edited and FDA
makes no representation
regarding its accuracy*

The above-entitled meeting was conducted at 8:00 a.m., at the Gaithersburg Marriott, Salons A, B, C, D, 9751 Washingtonian Boulevard, Gaithersburg, Maryland, Dr. Michael J. Yaszemski, Panel Chairperson, presiding.

PANEL MEMBERS PRESENT:

- MICHAEL J. YASZEMSKI, M.D., Ph.D., Chairperson, Mayo Clinic Graduate, School of Medicine
- JANET L. SCUDIERO, M.S., Acting Executive Secretary
- MAUREEN A FINNEGAN, M.D., Voting Member, University of Texas, Southwestern Medical Center
- JOHN S. KIRKPATRICK, M.D., Voting Member, University of Alabama, School of Medicine
- KINLEY LARNTZ, Ph.D., Voting Member, Private Practice
- SANJIV. S. NAIDU, M.D., Ph.D., Voting Member, Pennsylvania State College of Medicine
- SALLY L. MAHER, Esq., Industry Representative, Smith & Nephew Endoscopy
- LEELEE DOYLE, Ph.D., Consumer Representative, University of Arkansas for Medical Sciences

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PANEL MEMBERS PRESENT: (cont'd)

MARCUS P. BESSER, Ph.D., Deputized Voting Member,
Thomas Jefferson University
CHOLL W. KIM, M.D., Ph.D., Deputized Voting Member,
University of California, San Diego
JAY D. MABREY, M.D., Deputized Voting Member,
University of Texas, Health Science Center
MICHAEL B. MAYOR, M.D., Deputized Voting Member,
Dartmouth Hitchcock Medical Center
CELIA WITTEN, M.D., Ph.D., FDA Division Director,
General Restorative and Neurological Devices

SPONSOR PRESENTERS:Morning:

TONI R. KINGSLEY, Ph.D., Zimmer, Inc, Warsaw,
Indiana
GREG MAISLIN, M.S., M.A., Biomedical Statistical
Consulting, Wynnewood, Pennsylvania
JAMES B. STIEHL, M.D., Medical College of Wisconsin
and Columbia and St. Mary's Hospital, Milwaukee,
Wisconsin
PETER S. WALKER, Ph.D., New York Medical Center, New
York, New York

Afternoon:

JOEL BATTS, Corin, USA, Tampa, Florida
JOSHUA JACOBS, M.D., Rush Medical Center, Chicago,
Illinois
BERNARD N. STULBERG, M.D., Cleveland Center for
Joint Reconstruction, Cleveland, Ohio

FDA PRESENTERS:Morning:

PETER G. ALLEN, M.S., Orthopedics Devices Branch

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Afternoon:

BARBARA D. BUCH, M.D., Orthopedics Devices Branch
PHYLLIS M. SILVERMAN, M.S., Orthopedics Devices
Branch

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

2 (8:01 a.m.)

3 DR. SCUDIERO: Good morning, everyone.

4 We're ready to begin this meeting of the
5 Orthopedic and Rehabilitation Devices Panel. I'm Jan
6 Scudiero, the Acting Exec Sec of the panel, while the
7 Exec Sec is on detail.

8 If you haven't already signed in, please
9 do so. I'm sure most of you already have.

10 I would like to announce that the
11 tentatively scheduled meetings for this panel are --
12 for the year 2004 remaining are August 12th and 13th,
13 and December 2nd and 3rd. Please monitor the Center's
14 web -- panel website for updated information on this.

15 Before I turn the meeting over to Dr.
16 Yaszemski I'm required to read two statements -- the
17 appointment to temporary voting status statement and
18 the conflict of interest statement.

19 Pursuant to the authority granted under
20 the Medical Devices Advisory Committee charter dated
21 October 27, 1990, and amended April 20, 1995, I
22 appoint the following as voting members of the

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1 Orthopedic and Rehabilitation Devices Panel for the
2 duration of this meeting on June 2nd and 3rd:
3 Marcus P. Besser, Ph.D., for June 2nd and 3rd.

4 Brent A. Blumenstein was deputized for
5 yesterday as was Fernando G. Diaz and -- were
6 deputized for yesterday. And for today Choll W. Kim,
7 M.D., Ph.D., Jay D. Mabrey, M.D., and Michael B.
8 Mayor, for the morning session.

9 For the record, these people are special
10 government employees and are consultants to this panel
11 or another panel under the Medical Devices Advisory
12 Committee. They have undergone the customary conflict
13 of interest review and have reviewed the material to
14 be considered at this meeting.

15 Daniel G. Schultz, M.D., Acting Director,
16 Center for Devices and Radiological Health, on
17 May 28th.

18 And now the conflict of interest
19 statement. The following announcement addresses
20 conflict of interest issues associated with this
21 meeting and is made part of the record to preclude
22 even the appearance of an impropriety. To determine

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1 if any conflict existed, the agency reviewed the
2 submitted agenda for this meeting and for all
3 financial interests reported by the panel
4 participants.

5 The conflict of interest statutes prohibit
6 special government employees from participating in
7 matters relating -- that could affect their or their
8 employer's financial interests. However, the agency
9 has determined that the participation of certain
10 members and consultants, the need for whose services
11 outweigh the potential conflict of interest involved,
12 is in the best interest of the government.

13 Therefore, waivers were granted for Drs.
14 Choll Kim and Jay Mabrey for their interest in firms
15 that could be affected by the panel's recommendations.
16 Dr. Kim's waiver entails consulting on a creditor's
17 unrelated product. Dr. Mabrey's waiver involves
18 consulting with an unaffected division of the
19 sponsor's firm on matters unrelated to today's agenda.

20 We would like to note for the record that
21 the agency took into consideration certain matters
22 regarding Drs. Maureen Finnegan, Choll Kim, John

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1 Kirkpatrick, and Jay Mabrey.

2 Each of these panelists reported current
3 or past interest in firms at issue, but in matters not
4 related to today's agenda. The agency has determined,
5 therefore, that they may participate fully in today's
6 deliberations.

7 In the event that the discussions involve
8 any other products or firms not already on the agenda,
9 for which an FDA participant has a financial interest,
10 the participant should excuse himself or herself from
11 such involvement, and the exclusion will be noted for
12 the record.

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

18 Thank you.

19 CHAIRPERSON YASZEMSKI: Thanks, Ms.
20 Scudiero.

21 Good morning. I'm Dr. Michael Yaszemski.
22 I'm the Chairperson of the Orthopedic and

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1 Rehabilitation Devices Panel. I'm an orthopedic
2 surgeon and a chemical engineer at Mayo Clinic in
3 Rochester, Minnesota. My areas of interest are spinal
4 surgery and polymeric biomaterials.

5 I'd like to note for the record that the
6 voting members present constitute a quorum as required
7 by 21 CFR Part 14.

8 At this meeting, the panel will be making
9 a recommendation to the Food and Drug Administration
10 on an OSMA-initiated reclassification proposal for
11 mobile bearing knee prostheses. We will also consider
12 a draft guidance on performance criteria for hip joint
13 prostheses.

14 Before we begin the meeting, I'd like to
15 ask our distinguished panel members who are generously
16 giving their time to help the FDA in the matter being
17 discussed today, and other FDA staff seated at the
18 table to introduce themselves.

19 Please state your name, your area of
20 expertise, your position, your institution, and your
21 status on the panel, whether a voting member, a
22 deputized voting member, consumer rep, or industry

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1 rep. Let's start to my left with Dr. Mayor.

2 DR. MAYOR: Thank you, Mike. Dr. Michael
3 Mayor from the Dartmouth Hitchcock Medical Center in
4 Hanover, New Hampshire. I'm an orthopedic surgeon and
5 the co-director of the Retrieval Laboratory at the
6 Dartmouth Thayer School of Engineering. I'm a
7 consultant to the panel and a voting member.

8 CHAIRPERSON YASZEMSKI: Thank you. May I
9 also mention, before we move on, that Dr. Mayor is a
10 former Chairperson of this panel.

11 Dr. Larntz?

12 DR. LARNTZ: Kinley Larntz. I'm a
13 statistician, professor emeritus, University of
14 Minnesota. And I'm now doing independent consulting,
15 and I'm a voting member.

16 DR. BESSER: Marcus Besser, associate
17 professor in the Department of Physical Therapy at
18 Thomas Jefferson University, but my background and
19 training was in mechanical engineering and
20 biomechanics. I am a deputized voting member.

21 MS. MAHER: Sally Maher, group director,
22 regulatory and clinical, for Smith & Nephew Endoscopy.

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1 I'm the industry representative.

2 DR. WITTEN: Celia Witten. I'm the
3 division director of the Division of FDA that reviews
4 orthopedic products.

5 DR. KIRKPATRICK: I'm John Kirkpatrick.
6 I'm an associate professor at the University of
7 Alabama-Birmingham in orthopedic surgery, and I have
8 a special interest in spine surgery. I am a panel
9 member.

10 DR. MABREY: Jay Mabrey. I'm at Baylor
11 University-Dallas. I'm a -- my area of specialty is
12 total joint replacement, wear debris, and particle
13 analysis, and I'm a deputized voting member.

14 DR. FINNEGAN: Maureen Finnegan. I'm an
15 associate professor at UT-Southwestern. I'm an
16 orthopedic surgeon, and I'm director of the Orthopedic
17 Research Laboratory, and I am a voting member.

18 DR. KIM: I'm Choll Kim. I'm an assistant
19 professor at the University of California-San Diego.
20 My clinical interest is in spine surgery. I'm the
21 director of the Spine Research Lab at UCSD.

22 DR. NAIDU: Sanjiv Naidu. I'm an

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1 associate professor of orthopedic surgery at Penn
2 State College of Medicine. My interests are in
3 orthopedic surgery and material science, and I am a
4 voting panel member.

5 CHAIRPERSON YASZEMSKI: Thanks, everybody.

6 Today the panel will deliberate on and
7 provide recommendations to FDA on a reclassification
8 petition for mobile bearing knee joint prostheses and
9 a draft guidance on performance criteria for hip joint
10 prostheses. Both documents were submitted by members
11 of the Orthopedic Surgical Manufacturers Association.

12 In the morning, after the open public
13 hearing, we'll first deliberate on the
14 reclassification petition. Representatives of OSMA
15 will present, followed by the FDA, then we'll have the
16 panel deliberation portion of the meeting, beginning
17 with an introduction of today's topic led by Dr. Mayor
18 and by Dr. Larntz.

19 After having a general discussion, the
20 panel will address the FDA questions. Then the ODE
21 classification/reclassification coordinator -- Ms.
22 Shulman -- will guide the panel on completion of two

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1 forms -- the reclassification questionnaire and
2 supplemental worksheet. The panel's vote on these two
3 documents will constitute our recommendation to the
4 FDA.

5 In the afternoon, we'll follow a similar
6 agenda for the draft guidance document. This is the
7 first industry group prepared draft guidance document.
8 After the open public hearing, representatives of OSMA
9 will again present, followed by FDA. In the panel
10 deliberations, Dr. Mabrey and Dr. Larntz will provide
11 their perspectives to start the panel deliberations.
12 There will be no panel vote on this topic.

13 Our response to the FDA questions will
14 constitute our consensus recommendations on the draft
15 guidance document.

16 We're now going to proceed to the open
17 public hearing. We ask at this time that all persons
18 addressing the panel speak clearly into the microphone
19 as the transcriptionist is dependent on this means to
20 provide an accurate record of the meeting.

21 I'll apologize ahead of time, if you
22 forget to this and identify yourself, then I'll ask

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1 you to do so when you come up to speak.

2 Ms. Scudiero will now read a statement
3 prepared for open public hearings.

4 DR. SCUDIERO: Both the FDA and the public
5 believe in a transparent process for information-
6 gathering and decision-making. To ensure such
7 transparency at the open public hearing session of the
8 Advisory Committee meeting, FDA believes it is
9 important to understand the context of any
10 individual's presentation.

11 For this reason, FDA encourages the open
12 public hearing speaker, at the beginning of your
13 statement, to advise the panel of any financial
14 relationship you may have with the sponsor, its
15 products, and, if known, its direct competitors. For
16 example, the financial information may include the
17 sponsor's payment of your travel, lodging, or other
18 expenses in connection with your attendance at this
19 meeting.

20 Likewise, the FDA encourages you at the
21 beginning of the statement to advise the committee if
22 you do not have any such financial relationship. If

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1 you choose not to address this issue of financial
2 relationships at the beginning of your statement, it
3 will not preclude you from speaking.

4 I would like to note for the record that
5 the American Academy of Orthopedic Surgeons has sent
6 a statement to the agency for the record of this
7 meeting, and it's signed by its President, Roger W. --
8 or Dr. Roger W. Bochohz. He stated that the
9 association is pleased to express support for the
10 reclassification petition for mobile bearing knees for
11 medical device Class III, intermedical device Class
12 II.

13 CHAIRPERSON YASZEMSKI: Prior to the
14 meeting, FDA received four requests to speak in the
15 open public hearing. We'll start now with these four
16 people, and I'll identify the amount of time allotted
17 for each of them. Just before the meeting started, we
18 had two additional requests, and we'll add two minutes
19 for each of those two people to come up, two minutes
20 apiece.

21 The first speaker will be Dr. Steve
22 Peoples, scheduled for five minutes. Dr. Peoples?

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1 Just to help all of the speakers as you're timing your
2 speech, I'll have the light go from green to yellow
3 when there's two minutes left.

4 DR. PEOPLES: Good morning. I'm Steve
5 Peoples, and I am an employee of DePuy. Thank you for
6 the opportunity to provide comments regarding this
7 reclassification petition.

8 You will hear this morning that the
9 sponsors of this petition believe that the information
10 supplied provides strong evidence of the safety and
11 effectiveness of mobile bearing knees and that the
12 risks associated with them are now adequately defined,
13 justifying reclassification.

14 The petition further proposes that FDA can
15 regulate these devices adequately under Class II
16 controls. You will also hear that the proposed
17 reclassification meets the least burdensome
18 requirement. However, least burdensome does not
19 preempt the underlying principle that the level of
20 control must be appropriate to the level of risk posed
21 by the device.

22 The petition offers clinical and

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1 laboratory data as justification for general
2 reclassification of mobile bearing knees and
3 identifies almost 50 different mobile bearing designs
4 as representing the spectrum of mobile bearing knees.

5 Basically, the proposed reclassification
6 would move mobile bearing knees from the current
7 requirement for valid scientific evidence of safety
8 and effectiveness provided via the pre-market approval
9 process to the level of Class II controls and
10 substantial equivalency under the Section 510(k) pre-
11 market notification process.

12 We believe that the petition fails to
13 justify a general reclassification and that an
14 examination of the information upon which the proposal
15 was based reveals why. And that reason is that the
16 vast majority of the mobile bearing clinical
17 literature and information presented as justification
18 for reclassification is in regard to a single total
19 knee system and a single unicompartmental device.

20 For example, 86 percent of the total knee
21 survivorship literature cited in the petition is on
22 the LCS mobile bearing knee system. Only two

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1 survivorship articles on two other total knee designs
2 are included, one of which -- the Accord knee --
3 deserves special comment.

4 Although the Accord design underwent
5 extensive preclinical laboratory and finite element
6 analyses, that testing did not predict the almost
7 50 percent failure rate encountered in actual clinical
8 use. Similar observations can be made in regard to
9 the clinical results reviewed.

10 The petition presents very limited data on
11 a limited number of total knee designs to substantiate
12 the safety and effectiveness of mobile bearing knees
13 as a generic type of device. And even this limited
14 data indicates that there is a very large variation in
15 revision rate from design to design.

16 The clinical outcomes information provided
17 is no different. And although IDE data on six total
18 knee mobile bearing designs is included in the review,
19 the vast majority of that data is a very short
20 followup and very small populations.

21 The petition clearly demonstrates what is
22 known today about mobile bearing knees, and in doing

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1 so also demonstrates what is not known. Absolutely no
2 clinical data is presented for over 60 percent of the
3 mobile bearing knee designs identified in the
4 petition, designs which presumably would be covered by
5 the proposed reclassification.

6 Regulations require that a proposed
7 reclassification describe how the new classification
8 will provide reasonable assurance of safety and
9 effectiveness. The petition proposes that the
10 controls already established for Class II fixed
11 bearing knees are sufficient.

12 However, most of the recommended special
13 controls are only standard or unvalidated non-standard
14 test methods. The petition offers no performance
15 criteria for these tests and provides no guidance on
16 the predicate control to be used, other than that it
17 be clinically successful, which the petition also
18 leaves undefined.

19 No recommendations are made to
20 specifically address significant polyethylene
21 performance issues, such as the effects of multi-
22 directional movement and cross-shear, or knee

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1 stability, which was the unpredicted mode of failure
2 of the Accord knee.

3 Both of these issues are unique to mobile
4 bearing design and cannot be evaluated or controlled
5 using methods employed for fixed bearing knees.

6 The significance of mobile bearing knee
7 kinematics and polyethylene wear, in relation to
8 mobile bearing design, was reported on at this year's
9 Orthopedic Research Society meeting. The authors
10 concluded, and I quote, "This study shows that minute
11 differences in mobile bearing prostheses may have a
12 major affect on their wear behavior."

13 The petition under consideration is
14 thorough, and it does employ sophisticated analytical
15 techniques. It is deep but very narrow. It is
16 essentially a review of the results of a single total
17 knee system and a single unicompartmental device that
18 the petitioners claim represents the safety and
19 effectiveness of mobile bearing knee designs in
20 general. We do not believe that such a generalization
21 is valid.

22 Your requirements for reclassification

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1 that you must consider and answer today are: does the
2 petition provide adequate and valid scientific
3 evidence that mobile bearing knees in general are safe
4 and effective and thus can be reclassified to
5 Class II? And does the petition identify the special
6 controls for Class II necessary to assure the safety
7 and effectiveness of these devices?

8 We do not believe that the petition meets
9 either of these requirements, and based on the limited
10 evidence provided in the petition and the significant
11 risk involved, general reclassification of mobile
12 bearing knees simply is just not justified.

13 Thank you.

14 CHAIRPERSON YASZEMSKI: Thanks, Dr.
15 Peoples.

16 The next speaker will be Dr. John Fisher,
17 also scheduled for five minutes. Dr. Fisher?

18 DR. FISHER: Good morning. My name is
19 John Fisher. I'm director of the Institute of Medical
20 and Biological Engineering at the University of Leeds.
21 I have 15 years' experience in wear testing of
22 artificial joints and run an academic laboratory with

1 over 100 stations of wear simulation capacity for
2 joint replacement.

3 Our work in the laboratory is supported by
4 government, by a range of different companies,
5 including DePuy, and DePuy is supporting my attendance
6 at this meeting.

7 CHAIRPERSON YASZEMSKI: Thank you.

8 DR. FISHER: The LCS rotating platform
9 mobile bearing knee is very special and unique. The
10 bearing design decouples motions and allows rotation
11 at the tibial tray, which then predominantly allows
12 linear motion at the femoral interface. Both these
13 motions are unidirectional, which has a substantial
14 reduction in polyethylene wear.

15 However, not all mobile bearings are the
16 same. Unconstrained bearings have multi-directional
17 motion, and, therefore, higher wear. That has been
18 shown by RADCA at two presentations this year and has
19 been confirmed in our own laboratory.

20 So wear is dependent on interfaced
21 kinematics and is design-specific. So are kinematics
22 the same, in fact, to the mobile bearing knees? Well,

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1 the clinical studies show the overall kinematics of
2 the whole joint, but what we must be concerned about
3 is the kinematics at the individual interfaces.

4 Mobile bearings are complex systems.
5 Motion -- individual wear interfaces -- is design-
6 dependent, and, therefore, cannot be predicted from
7 whole joint kinematics. Small changes in interface
8 kinematics can have a major effect on the wear in
9 mobile bearing knees.

10 Do lower contact stresses in mobile
11 bearing knees reduce wear? Lower contact stresses
12 certainly reduce the lamination fatigue failure, but
13 there is no increasing evidence that lower contact
14 stresses and larger wear areas actually increase
15 surface wear and micro and macro wear debris
16 generation.

17 However, this is not the case in rotating
18 platform designs, which have unidirection of motion
19 and, therefore, much lower wear than fixed bearing
20 knees. So, again, the effects of contact stress on
21 wear is design-dependent in mobile bearing knees.

22 Now let me turn to third body damage and

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1 wear debris. Mobile bearing knees are more prone to
2 damage and destruction by third body damage,
3 particularly on the tibial counterface. Particles get
4 trapped in that counterface and remain there for a
5 substantial period of time.

6 However, the wear that is produced by
7 third body damage is, again, design-dependent, as
8 linear scratches in rotating platform bearing knees do
9 not accelerate wear, whereas they would do in multi-
10 directional designs.

11 And what about wear debris? It is really
12 a very important issue. Is wear debris from mobile
13 bearing knees more reactive? There are significant
14 studies now in the laboratories and clinically that
15 shows that wear debris from fixed bearing knees is
16 larger and less reactive than debris from hips.

17 It has been speculated that mobile bearing
18 knee debris is more like hip debris. This may well be
19 the case in multi-directional designs due to cross-
20 shear as found in the head will produce fragmentation
21 of fibrils and smaller particles.

22 However, we've shown that with

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1 unidirectional motion the debris that is produced in
2 the polymer bearing is actually larger and less
3 reactive. So, once again, the reactivity of the
4 debris produced in mobile bearing knees will be
5 design-dependent.

6 Can we effectively determine wear? We all
7 know there are two separate standards for knee joint
8 simulators at the moment -- force control and
9 displacement control machines. And these have
10 produced different results in comparison to mobile
11 bearing and fixed bearing knees.

12 In our own laboratories, we developed a
13 special methodology for rotating platform design,
14 which allowed a combination of both force and
15 displacement control testing for the rotating platform
16 mobile bearing knee. This is not an ideal test
17 methodology, and it is not currently available in
18 other joint simulation systems.

19 Secondly, can wear be determined from
20 clinical measurements? It is not easy. Penetration
21 can be measured as reported in the knee study, but, of
22 course, volume depends on penetration and wear areas,

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1 and these are difficult to determine and compare.

2 The inherent nature of mobile bearing
3 knees introduces greater variability. Any bearing has
4 six degrees of freedom. Mobile bearing knees have 12
5 degrees of freedom. Meniscal bearings have 24 degrees
6 of freedom at four different interfaces. Meniscal
7 bearings also typically have smaller polyethylene
8 inserts, which are more prone to edge loading and,
9 therefore, cracking and fragmentation.

10 For the rotating platform LCS mobile
11 bearing knee, there is over 20 years' experience.
12 There are some serendipitous design features that have
13 resulted in low contact stress, low fatigue,
14 unidirectional interface motion, and a stable low-
15 wearing bearing.

16 Many of these design features have not
17 been replicated in other mobile bearing knee designs.
18 Not all mobile bearing designs are the same, and we do
19 not understand the result and impact of the numerous
20 design variables encountered in different mobile
21 bearing knees.

22 To conclude, the reclassification petition

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1 does not consider or address the effect of the
2 aforementioned design variables on the performance of
3 mobile bearing knees, and the special controls
4 proposed by the petition cannot assure us that the
5 various designs of mobile bearing knees are both safe
6 and effective.

7 Thank you.

8 CHAIRPERSON YASZEMSKI: Thank you,
9 Professor Fisher.

10 Our next speaker will be Dr. Doug Dennis.
11 Dr. Dennis? Dr. Dennis is scheduled also for five
12 minutes speaking time.

13 DR. DENNIS: I'm Dr. Douglas Dennis from
14 Denver. I serve as an adjunct professor in the
15 Department of Biomedical Engineering at the University
16 of Tennessee, medically direct the Rocky Mountain
17 Musculoskeletal Research Laboratory. I do serve as a
18 consultant for DePuy. They have provided my travel
19 expenses here.

20 Over the last 10 years, my laboratory has
21 received orthopedic industry support from many
22 different companies. It's a privilege to present.

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1 As I have reviewed the reclassification
2 petition, it is to reclassify all mobile bearing total
3 knees from Class III to Class II devices. Therefore,
4 I think this assumes that all available mobile bearing
5 designs will demonstrate similar efficacy and safety
6 as those designs that have been evaluated by pre-
7 market IDE studies.

8 There are many fears associated with
9 mobile bearing knees. These include the potential for
10 increased polyethylene wear, as you now have two
11 articulating surfaces on both the top and bottom side
12 of the bearing. It requires a more demanding surgical
13 technique. It is less tolerable of instability, as
14 demonstrated by Dr. Jack Burt and a 9.3 percent
15 bearing subluxation or spinout rate.

16 There are also fears about increased wear
17 that are created from tibial tray post bumpers,
18 etcetera, which try to control the boundaries of
19 bearing mobility. Therefore, all mobile bearings are
20 not the same.

21 There are numerous differences. Knee
22 kinematic patterns have shown various kinematic

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1 differences on both the top and bottom side of the
2 bearing. There are geometry differences of both
3 femoral and tibial components, and the bearing
4 stabilizing mechanisms of these various designs are
5 different.

6 My concerns about the petition primarily
7 are centered on the bottom side of the bearing as
8 underside motion pattern differences among differing
9 designs can be quite substantial, and, therefore,
10 create a potential for premature polyethylene wear and
11 periprosthetic osteolysis from increased undersurface
12 wear versus currently approved designs.

13 Another concern has already been mentioned
14 about the size of the microparticulate polyethylene
15 debris in mobile bearings. It is more similar to hip
16 replacement in that the particles are smaller, more
17 reactive. Will this result in more osteolysis,
18 particularly in designs which permit multi-directional
19 motion on the underside of the bearing?

20 If we look at some of these design issues,
21 as has been stated, in a rotating platform design you
22 have unidirectional motion patterns on the

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1 undersurface of the bearing. While there are many
2 designs that allow both rotation as well as antero-
3 posterior translation, these will, therefore, have
4 multi-directional motion patterns on the bottom side
5 of the bearing.

6 In the 1970s, Pooley & Tabor showed us,
7 when dealing with polyethylene, if this material is
8 exposed to unidirectional motion, the molecules align,
9 decreasing the coefficient of friction and the wear
10 rates, whereas with multi-directional motion patterns
11 you increase the shear forces and wear.

12 And this has been shown in multiple
13 studies since then, both by Wang and Marrs, which have
14 shown increased wear with multi-directional motion and
15 reduced wear when you have mono-directional motion
16 patterns.

17 Our previous speaker, in an elaborate
18 laboratory analysis studying undersurface wear, has
19 shown that unidirectional type of patterns
20 demonstrated .23 millimeters cubed per million cycles.
21 When exposed to multi-directional wear patterns,
22 nearly a 10-fold increase in wear.

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1 The last 10 years of my laboratory life
2 has been studying knee kinematics. We have done over
3 75 different knee kinematic studies, over 40 fixed and
4 mobile bearing designs. And to summate this 10 years
5 of work, we have found that knee kinematics vary
6 widely among differing fixed and mobile bearing
7 designs, and numerous adverse kinematic patterns have
8 been identified, which can adversely affect
9 polyethylene wear.

10 This has been shown in the study
11 previously mentioned this year at the ORS where minor
12 differences in kinematics have resulted in major
13 differences in wear, particularly when dealing with
14 unconstrained tibial bearings that have multi-
15 directional wear patterns. They had double the wear
16 rates versus those with unidirectional wear.

17 So, in summary, all mobile bearings are
18 not the same. I do think the petition clearly
19 demonstrates the safety and efficacy of a single
20 rotating platform design that demonstrates
21 unidirectional underside motion. It has been shown
22 that mobile bearing kinematics vary widely, which can

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1 affect polyethylene wear rates, inherent implant
2 stability such that precise surgical technique is
3 critical.

4 There are numerous laboratory studies that
5 suggest the potential of substantial increases in
6 polyethylene on the bottom side of the bearing if
7 multi-directional motion patterns are present, yet no
8 good long-term clinical data is available to document
9 the safety of this concept.

10 I think that it is wise for the committee
11 to proceed with caution in grouping all mobile bearing
12 total knees as Class II devices as only the rotating
13 platform concept has proven clinically successful.

14 Thank you.

15 CHAIRPERSON YASZEMSKI: Thanks very much,
16 Dr. Dennis.

17 Our next speaker is going to be Dr.
18 Ruddlesdin. As Dr. Ruddlesdin is coming up, I'd like
19 to note that we've been joined by another
20 distinguished panel member.

21 Dr. Doyle has kindly agreed on short
22 notice to serve as our consumer representative today,

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1 and I'd like to take the opportunity and ask her to
2 introduce herself. Ma'am, give your institution, your
3 area of expertise, please. And welcome.

4 DR. DOYLE: I'm LeeLee Doyle. I am the
5 assistant dean for faculty development and a professor
6 emeritus of OB/GYN and currently a professor of
7 maternal and child health at the University of
8 Arkansas for Medical Sciences College of Medicine.

9 I have a very personal interest in this
10 particular area, because I already have two hips that
11 have been replaced, and I'm looking forward to two
12 possible knee replacements. So I have spent a great
13 deal of time considering these things.

14 CHAIRPERSON YASZEMSKI: Thank you, and
15 welcome.

16 Dr. Ruddlesdin, you're scheduled for 10
17 minutes, and please begin.

18 DR. RUDDLESDIN: Thank you, Chairman.
19 It's a privilege to address this panel this morning.

20 My name is Cris Ruddlesdin. I'm a full-
21 time orthopedic surgeon working with the National
22 Health Service in the United Kingdom. I receive no

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1 remuneration from Corin, apart from my travel expenses
2 to come here today. My NHS organization has been
3 using Corin products from 1989, and we purchase these
4 products on a competitive tendering basis.

5 I think it is important to stress that
6 knee replacement is trying to replace a normal knee,
7 and for many, many years fixed bearing knees have
8 relied on either a hinge or a rotating device. But
9 they're trying to reproduce multi-directional knee
10 movement at one bearing surface.

11 The mechanics have been covered in some
12 detail by my colleagues, and I will not go into any
13 further detail beyond that.

14 The rotor-glide knee, as marketed by
15 Corin, first started life in 1977 as an experimental
16 design. It was first implanted in 1988 in clinical
17 patients. Over 20,000 of these joints have been
18 implanted worldwide to date, and the joint relies on
19 a polyethylene bearing, which both rotates and glides
20 anteriorly and posteriorly on the tibial tray.

21 I have a knee implant here, if the panel
22 wishes to see it. And if I can pass it around --

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1 CHAIRPERSON YASZEMSKI: Thank you, sir.
2 We'd like to do that.

3 DR. RUDDLESDIN: -- as I talk, you can see
4 how the implant works.

5 The tibia tray is a metal base plate with
6 two metal bullards, and this is a cross-section
7 through the knee. And the white is the polyethylene.
8 The polyethylene can rotate 12.5 degrees either side
9 of the midline and can glide backwards and forwards by
10 five millimeters. And, therefore, we are reproducing
11 the rotation of the knee as it achieves full
12 extension.

13 You will notice as the implant comes
14 around that it is fully congruous through 90 degrees
15 of flexion from full extension to 90 degrees of
16 flexion at the bearing surface between the femur and
17 the polyethylene insert. And this means that we have
18 very low point loading in that situation.

19 My personal experience over the last four
20 years -- I have implanted 119 joints in four years.
21 Prior to 2000, I had used the fixed bearing version of
22 the same knee marketed in the United Kingdom as the

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1 Nufield knee, and subsequently we changed to the
2 mobile bearing knee, mainly because one of my newly-
3 appointed colleagues got considerable experience in
4 this implant in Scotland. The only difference is that
5 the insert locks onto the pole shroud and being
6 constrained by them.

7 The average followup in my series is two
8 years. I have one gross dislocation, which I do not
9 blame on the implant. It was an overenthusiastic
10 surgical soft tissue release on my part, with a very
11 deformed knee, and this allowed the femoral component
12 to dislocate from the top of the polyethylene.

13 It is interesting that despite the fact
14 that his knee was grossly unstable that the
15 polyethylene bearing remained contained on his tibial
16 tray.

17 In a report in the Journal of Arthroplasty
18 in 1996, from the Solihol Group, they had 161 patients
19 with 171 knees, and this shows that the knee has been
20 in clinical use for the last 17 years. They had an
21 average followup of 3.1 years, which is relatively
22 short in orthopedic terms, because we don't expect to

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1 see problems, even in the worst design of joint, until
2 at least five years.

3 They had a series of complications, as you
4 would expect of any major joint replacement, but they
5 had no dislocations or spinouts of the inserts.

6 Further work from Stuart Brooks at Solihol
7 reviewed 136 patients between 1989 and 1991, and this
8 had a much longer followup -- minimum followup of
9 seven years and a maximum followup of nine years. Two
10 revisions for one loose femoral component and one
11 fractured insert in a knee which had been implanted in
12 extreme varus -- the other complications, again, as
13 expected in any major joint replacement.

14 Clinical data from Hayward's Heath
15 Hospital in United Kingdom shows a very large series
16 -- nearly 900 patients, who have been operated on in
17 the last 10 years with followup for five years or more
18 -- 13 deep infections, eight aseptic loosening, and
19 two gross dislocations, which yields a very low
20 percentage of 0.2 percent.

21 Since 1988, this knee has been implanted
22 using exactly the same instrumentation used in fixed

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1 bearing designs. So the discussion that these are
2 different types of knees is not valid.

3 Ligament balancing is equally important in
4 any knee, be it a fixed bearing or a mobile bearing
5 knee. A badly performed operation, whether it be
6 fixed or mobile, will fail, and I would put it to the
7 panel that a well prepared knee will survive whatever
8 the bearing type.

9 I have converted from fixed bearing to
10 mobile bearing, and I have found no difference in the
11 level of difficulty to implant either a fixed or a
12 mobile bearing knee. The Corin instrumentation is
13 extremely simple and straightforward. I think levels
14 of difficulty often relate to the instrumentation as
15 designed by the manufacturer.

16 A lot of discussion about the bone clips
17 and ligament balancing. These obviously play a role.
18 And as I've said, any knee which is -- any knee
19 surgery which is well performed will do well. Any
20 badly performed knee surgery is likely to fail. And
21 this is equally important, be they fixed or mobile
22 bearings.

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1 And at the end of the day, it's the
2 surgeon's technical skill and expertise, and
3 particularly his feel for the operation and his
4 experience, that will be the indicator of success. No
5 instrumentation can compensate for poor surgical
6 technique.

7 The earlier instrumentation involved
8 tensing devices to try and balance the ligament on the
9 line of the Freeman knee. But subsequently
10 instrumentation has been simplified to what I can only
11 describe as a lollipop. This is a spacer that is
12 inserted into the knee in both flexion and extension
13 to ensure that the ligaments are balanced in both
14 flexion and extension, as this is vitally important.

15 If the cuts are not correct -- and, in my
16 experience, they almost always are correct -- then, if
17 they are not correct, then further adjustment to the
18 bone cuts at this stage is essential. Unless people
19 are overly enthusiastic at resecting one or other of
20 the bone surfaces, either the proximal tibia or the
21 distal femur, then the bone cuts usually come out
22 right.

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1 But it is vitally important to check the
2 gaps after the cuts have been made. And as I've said,
3 if the cuts are not correct, then it is important to
4 correct them at this stage. And this really does not
5 need to be different between the fixed and mobile
6 bearing knees, as I keep emphasizing.

7 So the take-home points basically are
8 insert dislocations are not a clinical issue, and
9 gross dislocations are not happening at a significant
10 rate -- less than one percent. And this is contrary
11 to some of the evidence that has been produced.

12 There is no difference in the operative
13 technique unless it is imposed upon or desired by the
14 surgeon. In other words, a fixed bearing and a mobile
15 bearing knee require the same level of surgical skill,
16 and, in the case of the Corin, exactly the same
17 instrumentation are used.

18 And whether fixed or mobile bearings, the
19 final arbiter to a good fit is the surgeon's tactile
20 field during the trial reduction.

21 Thank you very much.

22 CHAIRPERSON YASZEMSKI: Thank you very

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1 much, Dr. Ruddlesdin.

2 Is there anyone else who would like to
3 address the panel at this time? If so, please
4 identify yourself, be recognized, and come forward.
5 Sir?

6 DR. FERRING: My name is Tom Ferring. I'm
7 an orthopedic surgeon, Charlotte, North Carolina. I'm
8 adjunct professor of mechanical engineering at
9 University of North Carolina-Charlotte. And I'm a
10 consultant for DePuy, who paid my way here.

11 I have a special interest in osteolysis.
12 I've been published on this subject. And I'm
13 concerned about the potential for a significant
14 difference in wear debris with the new designs of
15 mobile bearings. I am also concerned about the long-
16 term effects that small changes in knee design will
17 have.

18 One only has to look at the effects of
19 moving a posterior stabilized post a few millimeters
20 in a fixed bearing knee, which led to instability of
21 certain designs that have been marketed or the
22 addition of a posterior stabilized post in the LCSPS,

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1 which is a mobile bearing knee that led to early
2 failure.

3 Therefore, it is counterintuitive to me to
4 conclude that a variety of new mobile bearings with
5 back side stops and different pivot points are
6 equivalent to proven designs. As one of the speakers
7 earlier said, in orthopedics we rarely see failures
8 before five years. I would urge you to recommend that
9 new mobile bearing implants be placed through standard
10 scientific methods to prove their efficacy and safety
11 for our patients.

12 Thank you.

13 CHAIRPERSON YASZEMSKI: Thanks very much,
14 Dr. Ferring.

15 Would other people like to speak? Sir?

16 DR. SORRELS: Good morning.

17 CHAIRPERSON YASZEMSKI: Good morning.

18 DR. SORRELS: I am Barry Sorrels from
19 Little Rock, Arkansas. I thank DePuy for inviting me
20 to this meeting.

21 I had the pleasure of serving as one of
22 the original clinical investigators with the LCS in

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1 the beginning of 1980. In 1980, there were over 300
2 knee designs on the market, and this was the first and
3 only knee to undergo an FDA evaluation.

4 The reason for that is it's more
5 complicated and it's fraught with potential
6 complications for the patient. My interest in this --
7 I have never been funded by the company nor paid for
8 the investigation. But my interest is on the part of
9 the patient.

10 Our patients were served very well with
11 the IDE. There were 15 of us. We collaborated
12 frequently, we met, we discussed complications,
13 discussed instrumentation, and ultimately I think the
14 patient was much better served as a result of going
15 through this process.

16 When I look back on my clinical results of
17 over 3,000 cases, I realize that 50 percent of my
18 complications were technical error committed by me,
19 and half of those were in the first three years of
20 this procedure.

21 There's a steep learning curve with these
22 mobile bearing knees, and I think if we can

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1 collaborate, if we can meet together, if we can
2 exchange our problems and our ideas, I think
3 ultimately the patient is much better served. And I
4 think that there's a real purpose served for the
5 patient by this process.

6 Thank you.

7 CHAIRPERSON YASZEMSKI: Thanks very much,
8 Dr. Sorrels.

9 Would someone else like to speak? Sir?

10 DR. FITZPATRICK: Good morning. My name
11 is David Fitzpatrick. I'm a bioengineer. I'm a
12 faculty member at the Department of Mechanical
13 Engineering in University College-Dublin. I have
14 research interests in knee joint kinematics modeling
15 and in vitro analysis of implant design.

16 DePuy has financially supported my costs
17 associated with attending this meeting, and I would
18 just like to concentrate on the issue of special
19 controls relating to these mobile bearing knee joint
20 designs.

21 It is clear that total knee operations are
22 very dependent on the management of the soft tissues,

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1 and the level of success is directly related to the
2 operative technique and surgeon experience. And when
3 compared with fixed bearing knee designs, the reduced
4 level of constraint within mobile bearing knees places
5 a higher level of demand on the surgeon and the
6 operative technique.

7 Post-operative joint stability is a
8 critical factor in clinical success, and the
9 sensitivity of various mobile knee designs to
10 operative technique is highly variable. The clinical
11 history of mobile bearing knees has shown that device
12 redesign or revised clinical indications is a common
13 outcome following initial clinical experience.

14 I would propose that the existing
15 preclinical tools, such as those proposed within the
16 special controls in the petition, do not have
17 sufficient capabilities to assess the kinematic
18 performance or the ability to predict the clinical
19 performance of mobile bearing knees in use.

20 Thank you.

21 CHAIRPERSON YASZEMSKI: Thanks very much,
22 Dr. Fitzpatrick.

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1 Would someone else like to make a
2 statement?

3 Seeing no other speakers, I'd like to
4 suggest that we proceed now to the OSMA presentation.
5 The OSMA representatives will now present on their
6 proposed reclassification position for the total and
7 the unicompartmental mobile bearing knee joint
8 prostheses.

9 I'd like to remind public attendees now
10 that the meeting is still open for public observation,
11 but public attendees may not participate except at the
12 specific request of the panel.

13 The first OSMA presenter is Dr. Toni
14 Kingsley. Dr. Kingsley?

15 DR. KINGSLEY: Good morning. I am Toni
16 Kingsley, and I am representing OSMA, the Orthopedic
17 Surgical Manufacturers Association. OSMA is an
18 organization of manufacturers of both medical devices
19 and biological products used in the treatment of
20 orthopedic pathologies.

21 OSMA has sponsored a number of
22 reclassification petitions in recent years for the

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1 purpose of bringing safe and effective medical devices
2 to the public through the least burdensome regulatory
3 path possible. We are here this morning as the
4 sponsor of the petition to request the
5 reclassification of mobile bearing knees -- MBKs --
6 from Class III to Class II.

7 The petition requests reclassification of
8 mobile bearing total knees and unicompartmental knees,
9 both cemented and uncemented. Included within these
10 general categories are a number of subcategories
11 listed on this slide. Any given mobile bearing knee
12 on the market today will exemplify several of these
13 characteristics.

14 At FDA's request, OSMA considered each of
15 these subcategories in evaluating the risks and
16 special controls specific to mobile bearing knees.

17 MBKs have been on the market for nearly 25
18 years. The first mobile bearing knee approved in the
19 United States was J&J DePuy's rotating platform LCS
20 knee approved in 1985. Since that time, there has
21 been considerable technical progress leading to
22 development of second and third generation devices.

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1 A review of the devices on the market
2 today reveals that approximately 46 mobile bearing
3 knee designs are available around the world. In the
4 United States, there are six designs currently
5 approved by the FDA, including five marketed by J&J
6 DePuy and one recently approved meniscal bearing
7 unicompartmental device marketed by Biomed.

8 It should be noted that FDA previously, in
9 January 1998, considered the reclassification of
10 mobile bearing knees as part of the petition to
11 reclassify uncemented porous knees. At that time, the
12 panel recommended reclassification only of those MBKs
13 that were tricompartmental, cemented, and had a
14 rotating or translating base.

15 However, FDA subsequently chose to
16 recommend submission of a new reclassification
17 petition for the entire class of mobile bearing knees
18 rather than reclassify specific subcategories.

19 In the six years since these decisions,
20 considerable additional information on mobile bearing
21 knees has become available. OSMA will present today
22 summaries of clinical data, including seven ongoing or

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1 completed IDE studies, two international clinical
2 outcome studies, and published data on approximately
3 14 knee designs, most with two-year or longer
4 followup.

5 OSMA will also present information on
6 risks specific to mobile bearing knees, with a focus
7 on the issues of wear, including back side wear, and
8 the potential for bearing dislocation. We will
9 discuss special controls, including existing FDA
10 guidance and standard test protocols. Where no
11 standard test protocol exists, we will present
12 suggestions to be developed further for inclusion in
13 an FDA guidance document.

14 We believe these special controls will be
15 adequate to enable the FDA to regulate mobile bearing
16 knees as Class II devices. OSMA will also present a
17 summary of two meta-analyses on published data that
18 support the claim that the clinical performance of
19 mobile bearing knees is not different from fixed
20 bearing knees, and that survivorship of the various
21 subcategories of mobile bearing knees are similar to
22 one another.

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1 OSMA believes that the information
2 presented will establish that mobile bearing knees of
3 all the subcategories included in the petition -- for
4 all of these there is well documented, successful
5 clinical history, design requirements are well
6 understood, associated risks are well defined, and
7 special controls either already exist or can be
8 developed for inclusion in FDA guidelines.

9 Because of these factors, OSMA believes
10 that mobile bearing knees should be reclassified to
11 Class II, since the special controls either currently
12 available or to be developed are sufficient to provide
13 the required reasonable assurance of safety and
14 effectiveness.

15 Presenting for OSMA today will be Dr.
16 James B. Stiehl, clinical associate professor of
17 orthopedic surgery, Medical College of Wisconsin, who
18 will discuss the clinical data. Dr. Peter S. Walker,
19 director of minimally-invasive surgery, laboratory,
20 and professor of orthopedic surgery, at the New York
21 University Medical Center, will discuss risks and
22 special controls. And the meta-analyses will be

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1 discussed by Greg Maislin, principal biostatistician
2 of Biomedical Statistical Consulting.

3 In addition, there are a number of
4 representatives of contributing OSMA companies present
5 together with expert surgeons who are expert in the
6 specific knee designs manufactured by those companies.

7 Dr. Stiehl?

8 CHAIRPERSON YASZEMSKI: Tanks very much,
9 Dr. Kingsley.

10 Dr. Stiehl, welcome.

11 DR. STIEHL: Thanks.

12 Dr. Jim Stiehl. I'm from Milwaukee,
13 Wisconsin. I am a private surgeon in orthopedic
14 practice. I have worked for a number of years in the
15 area of orthopedic biomechanics. I have over 10
16 years' experience with mobile bearing total knee
17 arthroplasty, specifically the LCS. And I continue to
18 have a very active practice with that particular
19 device.

20 My financial interest -- I am a consultant
21 for Zimmer, not specifically with mobile bearing total
22 knee arthroplasty. I currently do not have any vested

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1 interest in any mobile bearing knee implant.

2 The information that will be presented in
3 this petition is extensive. There is a comprehensive
4 literature review and summary, both of unpublished and
5 published clinical studies, and I would point out that
6 the unpublished studies currently come from the OSMA
7 companies that are supporting this petition.

8 They include IDE clinical trials that are
9 under current process of investigation and two
10 important international clinical outcome studies that
11 have been compiled and are currently ongoing. We do
12 a comprehensive literature review from 1977 until
13 2002, which includes clinical outcome scores and
14 complications.

15 This slide summarizes the current IDE
16 studies that are ongoing. There are seven different
17 series of studies. The Oxford Meniscal Bearing Uni is
18 currently approved through the PMA process, and that
19 IDE study is completed. The remaining devices, as you
20 can see -- the Genesis, Profix, and Scorpio MBK and
21 NexGen -- are mobile bearing devices.

22 And I would state that the -- there are a

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1 couple of devices in this group -- the Genesis,
2 Profix, and Scorpio -- that are fixed bearing devices
3 that have been adapted for mobile bearing application.

4 The revision rate is being looked very
5 carefully at for these devices. As you can see, the
6 Oxford, which is a completed study, had a 6.8 percent
7 revision rate. After approximately four years'
8 followup, the numbers towards the bottom of the other
9 devices have relatively short followup to date. But
10 as you can see, the clinical outcome has been very
11 successful to date with nil or very few revisions.

12 There are two international outcome
13 studies that are currently being collected by Zimmer.
14 These specific studies are with mobile bearing
15 devices. The European and Asian and other groups
16 around the world do not necessarily require the
17 control that the U.S. FDA requires, so it's able --
18 we're able to get these studies done. These are open
19 enrollment studies, open surgeon participation. They
20 literally come from around the world.

21 We believe these studies to be very
22 important, because their results are generalizable,

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1 and they really measure the performance in the hands
2 of general orthopedic surgeons who have new experience
3 with a new device.

4 The MBK is the first study that we would
5 cite. There are 1,254 cases collected at the point of
6 data collection from 22 surgeons from seven countries.
7 To date there have been eight revisions. The overall
8 revision rate with this particular device has been
9 .6 percent through an average of two-year followup.

10 The NexGen LPS flex mobile knee, again,
11 has a similar study that's ongoing, and at the point
12 of data collection there were 390 cases from 19
13 international surgeons from 17 centers around the
14 world. In this particular study, there were two
15 revisions, one for infection and one for instability.
16 The overall revision rate, again, was .5 percent
17 through two years of followup.

18 We have also collected data of the
19 outcomes, and I think this is an important issue
20 because most clinical series have global knee rating
21 scores that are evaluated, and they will be discussed
22 in the statistics section where we look at the good to

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1 excellent results. And as you can see for those of
2 these, the devices at two years -- that ranges from 85
3 to 100 percent. There have been no red flags with
4 either of these devices.

5 We then look at the literature that is
6 collected from 1977 until 2002. There are 274
7 articles available that talk about mobile bearing
8 devices in some form or another. We specifically look
9 at the papers that have clinical results. There were
10 57 such articles; 48 summarized clinical outcome with
11 data. And this included the broad spectrum of devices
12 available -- multi-directional rotating platform,
13 meniscal bearing, and unicondylar. And there are nine
14 review articles.

15 Summarizing this data, the multi-
16 directional platform devices -- and, basically, this
17 is a polyethylene bearing that allows both rotation
18 and anterior motion in the transverse plane. The
19 number that I highlight is 91.7 percent with 5.6-year
20 followup, and that excludes the results of the Johnson
21 Accord.

22 The Johnson Accord was an early device.

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1 It comes from the '70s. It was abandoned, really,
2 quite a number of years ago because of significant
3 design problems, and really doesn't meet current
4 criteria and from the knowledge that we have. So I
5 think it was appropriate to remove that device from
6 this conclusion.

7 The rotating platform, which really is the
8 hallmark of certainly the LCS experience, has been a
9 very, very durable implant. And as you can see, of
10 the four clinical trials that we cite, 96.5 percent
11 survivorship at 9.3 years. The meniscal bearing is a
12 rotating bearing that has two bearings that slide in
13 tracks. This implant has a long experience from the
14 LCS, really nearly 25 plus years of experience. In
15 the eight clinical trials that we cite, 97.4 percent
16 survivorship at 8.2-year followup.

17 And then we have a large group of
18 unicondylar knees that are reported from 21 series
19 that offer 92.1 percent survivorship at 8.8 years.

20 One of the articles in our review is from
21 Dr. Callahan, and in that article they cite a number
22 of series. The one series from Murray quotes 144

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1 Oxford medial unis with 98 percent survival at 10
2 years. He was a designer involved with that series.

3 But we also have the experience of Price,
4 et al. This study was done in Sweden by private
5 practitioners -- 378 Oxford medial unis with 95
6 percent survivorship at 10 years. We have the
7 experience of Dr. Jordan, et all, with 473 LCS
8 meniscal bearing -- again, a private surgeon, non-
9 designer, 94.6 percent survival at eight years.

10 And we have the extensive experience of
11 Dr. Sorrels, who you just heard from a moment ago. He
12 reported 665 LCS rotating platform, cemented version,
13 with 95 percent survivorship at 11 years; and 119 LCS
14 rotating platform, uncemented, with 100 percent
15 survival at 12 years.

16 There is a very large study that comes
17 from the Norwegian Arthroplasty Registry. This had
18 7,174 total knees, of which 982 were the LCS with a
19 small addition of interacts 23 cases. This group
20 showed slightly better results with the mobile bearing
21 as opposed to the general fixed bearing group -- 97.2
22 percent survivorship after five years.

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1 However, they concluded that there was no
2 statistical differences between mobile and fixed
3 bearing designs pertaining to either survivorship or
4 complications.

5 I have published a number of studies on
6 mobile bearings, and I have one review article where
7 I review the literature on this subject. From all of
8 the studies that I have looked at, the mobile bearing
9 revision rate approximates one percent per year. This
10 is analogous to the fixed bearing rates of failure
11 that are described virtually across the literature.

12 The surgical technique is similar to fixed
13 bearing knees. And despite the unique elements of the
14 LCS technique that we all learned and developed years
15 ago, most current mobile bearing knees are falling
16 along surgical technique which is similar to other
17 fixed bearing knees. Bearing-related complications
18 with the LCS are .5 percent overall for rotating
19 platforms, and 2.5 percent for meniscal bearings.

20 Most of us believe that the LCS rotating
21 platform is a very safe design. And our technique, as
22 Dr. Sorrels mentioned, relates specifically to this

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1 outcome.

2 I think the most important issue of mobile
3 bearings -- and this is the reason why we are here
4 today, this is the reason why I believe these devices
5 should be available in general for our patients -- is
6 that the current experience looking at osteolysis and
7 the complications with these devices are minimal. It
8 really is an advance in orthopedic surgery to remove
9 osteolysis, because this is the primary cause, in my
10 view, of late failure of total knees.

11 Vertullo has outlined the potential
12 advantage of mobile bearings, and I think this really
13 carefully gives us some idea of what this is all
14 about. Axial rotation decreases loosening due to
15 axial torque. This was certainly one of the early
16 design parameters that we felt important. It has been
17 improved over the years.

18 Actual rotation may account for self-
19 correction of some of the tibial component
20 malrotation. Tibial component malrotation is a
21 significant issue in current technique of any total
22 knee. And if you've got a device that gives you some

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1 freedom with that particular issue, it is a help --
2 and we believe that these devices reduce contact
3 stresses, which is important to wear.

4 I don't think you have to have all three
5 of these design advantages in a specific mobile
6 bearing knee to make it optimal. I think you can have
7 a mobile bearing that gives one or two of these and
8 certainly makes it worth the trouble. But these are
9 the advantage of a mobile bearing design, and I
10 believe that's why these devices are so important.

11 This author concludes by stating
12 hypothetically longer term followup of mobile bearing
13 knee arthroplasty results may reveal a significant
14 difference from fixed bearing total knee as a fatigue
15 failure threshold of incongruent polyethylene is
16 exceeded. Really, this is the subject. This is why
17 we believe these devices are so good.

18 In summary, the literature suggests that
19 mobile bearing knee devices performed similarly to
20 well designed fixed bearing knees in terms of
21 survivorship and clinical function. Current IDE and
22 international outcome studies suggest that other

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1 mobile bearing knee designs are clinically successful
2 and comparable to fixed bearing designs.

3 The potential benefit of this technology
4 is improved long-term clinical performance and
5 longevity for our patients.

6 Thank you.

7 CHAIRPERSON YASZEMSKI: Thanks very much,
8 Dr. Stiehl.

9 The next presenter will be Dr. Walker.

10 DR. WALKER: Good morning, panel members.
11 I am pleased to address this issue on behalf of OSMA,
12 and they are paying my expenses. And I ought to
13 declare that as a knee designer for many years I do
14 receive financial benefit from two companies for knee
15 designs, notably Stryker and Zimmer.

16 I'm a biomechanical engineer. I've worked
17 on the biomechanics of the knee and knee design and
18 knee testing methods since 1966. I've worked at
19 notable institutions in the UK and in the USA.

20 I'm addressing risks and special controls.
21 In other words, the purpose of tests is to ensure a
22 device is safe and effective, so I will talk about

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1 what kinds of tests are appropriate for mobile bearing
2 knees. And I will also reference fixed bearing knees,
3 which are already approved devices.

4 The risks are divided into known and
5 potential. Now, known mobile bearing design risks
6 have been elucidated in the previous talks, but also
7 in the medical device registry, which reports
8 significant problems, and there have been reports.
9 But of tens of thousands of knees, they have received
10 385 reports, of which a small number are to do with
11 the mobile bearing metal-poly separation and
12 loosening.

13 Now, further known risks with mobile
14 bearing knees include dislocation and subluxation
15 because the bearing is mobile and not fixed. And
16 also, another known potential risk is, of course, wear
17 because of the extra bearing surface in the design.

18 Other potential mobile bearing risks with
19 the different kinds of designs have been studied by
20 OSMA by looking at all of the available 46 designs,
21 looking at them and grouping them, as was shown in the
22 very first talk, and then identifying potential risks

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1 and mechanical problems with these different designs.

2 So let me just summarize these different
3 risks. The first group of risks has to do with fixed
4 and mobile bearing knees in common. In other words,
5 these are risks which are well known and fixed
6 designs, as well as mobile bearing designs. The
7 second group includes risks and special controls that
8 have specific considerations when applied to mobile
9 bearing knees. And I will focus my talk on those.

10 But, however, I will just mention the
11 first group. These are risks and special controls
12 common to fixed and mobile bearing knees. So any new
13 fixed bearing design has to satisfy the FDA on these
14 different aspects.

15 Just looking down the left-hand column if
16 you will, the risk, and the special control means the
17 accepted tests which have to be provided to the FDA
18 for approval. So we have sterility, biocompatibility,
19 metal compatibility, metal corrosion, delamination of
20 porous coating.

21 Now let's look at the second group. These
22 are risks and special controls that have specific

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1 considerations when applied to mobile bearing knees.
2 We are not saying that all mobile bearing knees are
3 alike. Clearly, they are not alike.

4 What we are saying, however, is that the
5 following risks have been evaluated and identified,
6 and tests have also been identified which will
7 evaluate these particular risks for any new design
8 that is submitted to the FDA. These tests are not
9 intended to be rubber stamps. They're intended to be
10 tough standards, tough tests, which any new design has
11 to pass before being accepted.

12 So, first of all, tibial tray fracture --
13 this, of course, applies to fixed bearing designs.
14 But in mobile bearing designs we could, for example,
15 have features such as tracks, stops, and other things
16 that could increase the stress on the tibial tray.
17 There's a very well accepted standard -- ASTM and ISO
18 standard, as well as articles in the literature, which
19 can reliably test this aspect, and also stress
20 analysis using computer technology.

21 The other very important issue is wear of
22 the articulating surfaces. Of course, it is probably

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1 the case that a multi-directional mobile bearing knee
2 may wear more than a unidirectional mobile bearing
3 knee. It is quite possible. However, the bottom
4 line, in fact, is wear testing. That's what the tests
5 are supposed to do. They find out whether a
6 particular design has more wear than is acceptable.

7 Now, there are two tests -- the ASTM and
8 ISO tests -- and there are well developed simulating
9 machines which have been developed here and in Europe
10 for testing the wear of any kind of knee. The total
11 wear is measured, and the extra test, if you like,
12 that can be applied to mobile bearing knees is to make
13 sure any mobile bearing knee is compared to a well-
14 known fixed bearing knee design with a long clinical
15 history. All wear testing should have a standard like
16 that to make it credible.

17 Now, back side wear -- if one wanted to
18 look at the back side wear as well, because this may
19 be a concern -- certainly in testing little marks or
20 engravings can be put on the back side of the plastic.
21 And at the end of the wear test one can look at the
22 wear associated with just the back side as well as the

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1 top side. Obviously, the simulator measures the total
2 wear, and we can now measure the wear on both sides of
3 the bearing.

4 The wear particles is a concern. We've
5 heard earlier that the particles may resemble hip
6 particles. The point of this is that hip particles
7 tend to be submicron and are more reactive to tissues.
8 Knee replacements generally have larger particles, and
9 they are probably less reactive to tissue. And there
10 is also less wear associated with knees anyway.

11 However, again, that's what the tests are
12 for. A particular mobile bearing knee design would be
13 tested. The particle distribution, the particle size,
14 would be measured by these well accepted test methods
15 looking at fibrils, flakes, and granules, and looking
16 at the size distribution of these different particles.

17 Now, spinout of the insert -- you've heard
18 about this, and I think the panel members have seen
19 this implant being passed about -- it is possible to
20 lift the insert right off the tray, but also it's
21 possible that the femoral component could roll off the
22 plastic. This has been recorded, particularly with

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1 the Oxford meniscal knee where the meniscus is a
2 freely-floating anterior/posterior piece of plastic.

3 This is definitely an issue with mobile
4 bearing knees. However, the incidence, as you have
5 heard, is very, very small, for example, with the LCS
6 knee. It's a very, very small incidence indeed. In
7 order to test for this, the constraint testing, as you
8 see here -- spinout of the insert -- constraint
9 testing, where you put the thing -- the device in a
10 machine, apply A/P, internal/external, medial/lateral,
11 and various analogous forces, and look at the
12 stability of the femoral component on the plastic
13 insert -- now, again, the additional tests that should
14 be done with mobile bearing knees is not only to do
15 that but to measure the actual jump height of the
16 femoral on the plastic. This can be added by the FDA
17 in their new guidance document.

18 So, in other words, the lift -- the amount
19 of lift that the femoral component has to go to
20 dislocate from the plastic can be measured at all
21 different angles of flexion -- extension and high
22 flexion.

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1 Insert/tray disassociation -- again, this
2 device that was passed around -- you can actually lift
3 the device off. This is an issue with fixed bearing
4 designs as well. The plastic is snapped into a metal
5 tray. Occasionally, a plastic insert, if it's thick,
6 for example, can flip out of the metal tray. It's a
7 very rare, but occasional, risk.

8 This risk also exists with mobile bearing
9 knees. Now, there are tests -- the FDA guidance
10 document component interlock strength section -- if
11 you look at the underlined piece, component interlock
12 strength section, encourages tests where we load the
13 front and the back of the insert at the extremes of
14 loading as if a patient was getting up from a very low
15 position or extending very violently.

16 So these instances have been identified,
17 and tests have also been identified by the industry --
18 and are well-known tests -- to test for plastic coming
19 loose from the metal tray.

20 Insert defamation or fracture -- nobody
21 mentioned so far the rotating platform, of course,
22 because it's rotating, the plastic can overhang from

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1 the edge of the metal. You could say, "Well, this
2 might increase the stresses on the plastic bearing and
3 be dangerous."

4 Now, again, in modern designs, this is not
5 an issue. This is no failure that I'm aware of,
6 certainly, that the literature has identified, since
7 the very early meniscal bearing knees, fracture of
8 inserts. It's a very rare occurrence. However, it
9 needs to be tested.

10 And, again, the FDA guidance document on
11 contact area and stresses for mobile bearing knees,
12 the new guidance document for mobile bearing knees,
13 should include a section on measuring the contact
14 areas and stresses in a mobile bearing knee at all the
15 degrees of rotation of the insert on the metal tray to
16 ensure safety and avoidance of excessive stresses.

17 Soft issue impingement or joint not
18 balance -- you've heard from several surgeons that in
19 their opinion the surgical technique is very similar.
20 Balancing the knee, making the ligaments just the
21 right tightness in extension and in flexion, indeed at
22 all angles of flexion, is a prerequisite for any

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1 design. And that applies equally to mobile bearing
2 knees as well as to fixed bearing designs.

3 This is primarily the job of the surgeon
4 community itself -- in training, in lecturing. And,
5 of course, surgical technique by the experts who
6 develop these devices, and also training courses which
7 are appropriately put on by different companies.

8 One more thing -- damage to the insert of
9 the rotational stop. We've heard about this. Some
10 devices, including the one that was passed around, has
11 stops to stop it rotating. Again, the standard wear
12 testing can be used to evaluate this. This will stop
13 the form of the plastic and prevent the bearing from
14 functioning correctly.

15 What I'm trying to get over in these
16 discussions is the tests that already exist -- well
17 established or else they're in the literature and can
18 relatively easily be devised by the FDA where
19 necessary to augment the tests for mobile bearing
20 knees.

21 Patella wear -- I won't dwell on that. If
22 a mobile bearing patella was submitted to the FDA --

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1 and to my knowledge there is only one -- similar kinds
2 of tests can be applied to patellas.

3 So, in summary, I believe the mobile
4 bearing knee risks are well understood and are similar
5 for the most part to fixed bearing designs. However,
6 special controls for the risks associated with mobile
7 bearing knees are either commonly used in industry,
8 exist as ASTM and ISO standards, or can be adapted for
9 any unique characteristic of a specific mobile bearing
10 knee design.

11 Every mobile bearing knee design must pass
12 a range of tests appropriate for that design. So I
13 believe that a new special controls -- if you'll look
14 at this here. A new special controls guidance
15 document we believe is needed from the FDA to
16 recognize these extra risks, or extra nuances if you'd
17 like, of mobile bearing knees, that just describe very
18 clearly each test and each test parameter that is
19 required for mobile bearing knees.

20 And I believe that the literature, current
21 practice, experts abound in order to come up with
22 suitable tests for mobile bearing knees. And there is

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1 enough knowledge, I believe, today to be assured that
2 the tests are reasonable.

3 OSMA, which I represent, believe that
4 special controls, when combined with the general
5 controls, will be sufficient to provide reasonable
6 assurance of the safety and effectiveness of mobile
7 bearing knees.

8 Thank you very much for your attention.
9 Thank you.

10 CHAIRPERSON YASZEMSKI: Thanks very much,
11 Dr. Walker.

12 Mr. Maislin, you're going to speak next.

13 MR. MAISLIN: Good morning to the panel.
14 My name is Greg Maislin, and I am the principal
15 biostatistician of Biomedical Statistical Consulting.
16 We're a contract research organization that
17 specializes in randomized clinical trials for
18 regulatory support. I'm also an adjunct faculty
19 member at the University of Pennsylvania School of
20 Medicine, where I serve as the director of the
21 Biostatistics and Patient Recruiting Corps at the
22 Center for Sleep and Respiratory Neurobiology.

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1 I have the privilege today of having OSMA
2 support my appearance here to summarize their work in
3 summarizing the current literature. And I also should
4 say that Biomedical Statistical Consulting has or has
5 had several of the petitioning sponsors as clients.

6 It's important to have a feel for what the
7 current literature looks like when we try to extract
8 literature to compare the mobile bearing and fixed
9 bearing clinical outcomes. Randomized clinical trials
10 comparing mobile bearing implants to fixed bearing
11 implants are largely unavailable in the literature.

12 Therefore, methods of meta-analysis that
13 are appropriate for observational studies were
14 utilized as opposed to those that might be appropriate
15 for randomized clinical trials where two treatments
16 are compared head to head.

17 The authors of the study utilized methods
18 that were in the literature to produce their
19 literature summary meta-analysis, particularly a
20 summary from Callahan that was published in JAMA in
21 1994, which included a meta-analysis of fixed bearing
22 implants.

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1 There were two separate meta-analyses that
2 were performed. One of them will give rise to an
3 estimate of what the clinical outcomes look like,
4 comparing fixed bearing to mobile bearing. And the
5 other specifically addressed what does the profile of
6 implant survival look like.

7 And I'm going to jump in a sense to a last
8 slide. I'll come back during the next few moments and
9 try to justify this. But essentially, at the end of
10 the day, what the outcome of the first meta-analysis
11 said was that the proportion of knees that are
12 expected to have good to excellent clinical results
13 are very similar in this particular set of studies
14 that were summarized.

15 Moreover, that the cumulative survival was
16 also very similar. There will be claim that the
17 survival is better for mobile bearing compared to
18 fixed in this set of studies, even though it was 93
19 percent survival versus 91 percent survival. But what
20 we will claim is that there is good evidence that the
21 survival is similar between mobile bearing and fixed
22 bearing, at least in the current set of studies that

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1 were revised.

2 An important additional aspect that I'll
3 bring out in implant survival is that the variability
4 in implant survival in the set of studies that were
5 summarized was very similar to the variability in
6 revision rates in the set of fixed studies that were
7 summarized.

8 So it didn't appear that the several
9 different designs that were summarized for mobile
10 bearing had any impact on variability in revision
11 rates. Moreover, an earlier speaker indicated that
12 the wear characteristics of mobile bearing devices
13 cannot be predicted from fixed bearing devices.

14 But to the extent that the most important
15 consequence of wear is increased revision rates, the
16 literature doesn't support that contention. It seems
17 to support the contention that in terms of the wear
18 effect on revision, the revision rates of mobile
19 bearing knees can be predicted from the fixed bearing
20 counterparts.

21 I'm going to briefly just summarize how
22 those few numbers came to be. It was an English

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1 language articles summary. There was an
2 identification of 22 cohorts from 21 studies that --
3 that met the criteria and contained the mobile bearing
4 devices. The reference group for the first comparison
5 of clinical outcomes was extracted from the Callahan
6 meta-analysis of fixed bearing.

7 A separate set of criteria, which I'll
8 detail in just a second, summarize the experience from
9 mobile bearing devices, and compared it to another set
10 of studies that produce 30 fixed bearing survival
11 estimates. These were obtained in 16 articles.

12 In general, for both studies, the mobile
13 bearing knee designs that were contained in this
14 literature summary meta-analysis included both
15 cemented and uncemented designs, unicompartmental,
16 bicompartamental, tricompartmental replacements, multi-
17 directional platforms, rotating platforms, meniscal
18 bearing articulations, both PCL sacrificing and PCL
19 sparing. All mobile bearing articles were included
20 without regard to the cement technique, number of
21 components replaced, or mobile bearing type and PCL
22 treatment.

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1 This is the same approach that Callahan
2 used to construct their fixed bearing meta-analysis,
3 and that was used as the control group for the first
4 comparison.

5 So, in summary, in order to include a
6 sufficient number of mobile bearing knee articles for
7 the meta-analysis, the bearing type and number of
8 compartments replaced was not used to exclude studies.
9 All were included.

10 Specifically, for the first meta-analysis,
11 the only criteria was that every study had to have at
12 least 10 or more patients. They had to report post-
13 operative clinical results, and specifically they had
14 to report post-operative clinical results in terms of
15 a 100-point rating score, so that those could be
16 summarized.

17 In total, the population had about 3,000
18 knees, about 2,500 patients. It was a typical
19 population. There were almost two-thirds female, 82
20 percent osteoarthritis, and 13 percent of the knees
21 were in bilateral patients. So this is the mobile
22 bearing cohort that was constructed on the basis of

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1 those criteria.

2 Two outcomes were compared from that
3 cohort to the Callahan cohort. There was a mean
4 percent improvement in the -- in a post-operative
5 global rating, and, in particular, I typically used
6 percent of cases with good to excellent post-operative
7 results.

8 Also, following the Callahan technique,
9 the studies were weighted in terms of the contribution
10 to the overall success by the number of knees, by the
11 size of the study.

12 This is a summary of the primary results,
13 and I'll call your attention to this row here. This
14 is the numbers that I quoted at the beginning on the
15 first -- on average among those studies weighted by
16 the number of knees per study. The success rate was
17 90.3 percent, comparable to 89.3 percent.

18 In several places I will call attention to
19 two devices which are obsolete and no longer used in
20 current implantation. It's the Oxford Phase I and the
21 Accord. If you were to remove these outliers -- and
22 they look like outliers along a number of dimensions

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1 -- the success rate goes up. But to be conservative
2 we could just note that these success rates between
3 the mobile bearing and fixed bearing are virtually
4 identical.

5 I'll note that the -- that in this first
6 meta-analysis the weighted mean followup was six
7 years. It was four years in the Callahan. The
8 revisions are going to be more formally analyzed in a
9 second, but I'll just note that if the revision rate
10 is six percent in the mobile and four percent in the
11 fixed, and if the revision rate is about one percent
12 per year, which Dr. Stiehl noted in his review it is
13 for mobile, and also it has been -- that approximates
14 what we know about fixed, then this two percent
15 increase in the revision rate would be explained by
16 the two-year increase in mean followup. And we'll see
17 a reverse relationship shortly.

18 The other meta-analysis focused on
19 survival. For the mobile bearing, 10 patients were
20 required. They had to report an estimate of implant
21 survival. For the fixed bearing -- this is important
22 to note -- that a criteria that was used was that

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1 there had to be at least one cohort in the study that
2 had at least 10 years of followup, and that the study
3 had to be cited at least twice in peer reviewed
4 journals as having high durability and clinical
5 success. In other words, the attempt was to create a
6 fixed bearing control group of high quality.

7 The details were that there were 37
8 articles that met these criteria -- 16 and 21. There
9 were 111 survival estimates. There were multiple
10 estimates in each of the studies, because of various
11 definitions. For studies that reported multiple
12 estimates, the estimate that was most consistent --
13 that had a most consistent definition of revision --
14 for example, revision for any reason -- and the
15 longest followup was retained. This was a consistent
16 rule used, and it was a priori specified.

17 What it culminated in was 30 estimates of
18 fixed bearing implant survival and 26 estimates of
19 mobile bearing survival. And these were the studies
20 that were compared.

21 Among those studies, I'll note that the
22 mean followup was about six in the mobile bearing. It

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1 was about eight in the fixed bearing as a consequence
2 of requiring at least 10 years in any one cohort in
3 the studies. And what we end up seeing is this
4 picture -- I don't want to dwell on this picture,
5 except to note the following characteristic.

6 First of all, these confidence intervals
7 here are only reported in the mobile for primarily
8 compared with fixed, because these studies were later,
9 and statisticians finally had their way and induced
10 authors to report confidence intervals.

11 These are the confidence intervals that
12 are reported in the articles themselves. The earlier
13 studies didn't report confidence internals.

14 Besides that editorial, I just want to
15 comment on these blue dots. These are the revision
16 estimates. The main finding is that if you look at
17 the weighted average, the centerline here, these are
18 about the same in the fixed cohort studies that met
19 the inclusion criteria compared to the mobile studies
20 that met the inclusion criteria.

21 And, moreover, if you look at the
22 variability around the centerline, and you look at the

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1 variability around the centerline, generally speaking
2 they look very, very close. Even though there was a
3 number of different design features, those design
4 features didn't translate into increased variability
5 in revision rates.

6 The variability in revision rates seems
7 comparable to fixed. So both the average is the same
8 and the variability around the average is the same.
9 Those two red dots are highlighted, because those are
10 the two outliers that I mentioned earlier as being
11 obsolete and no longer used designed.

12 So the bottom line is that the -- that in
13 this cohort of studies that met the criteria that was
14 put out by the authors of the study, there was 93
15 percent survival in the mobile bearing and 91 percent
16 survival in the fixed. But note again that there's
17 about a two-year difference in average followup, but
18 this time the mobile bearing had less, and that
19 translated into about a two percent increase in
20 survival.

21 In conclusion, that the -- I'll point out
22 very quickly that this is the statistical techniques

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1 that were used to take all those numbers and reduce
2 them down to those two numbers -- weighted least
3 squares, weighting by nears, resampling for robust
4 confidence interval estimation.

5 The model assumptions were tested and
6 verified from the analysis of variance that was used,
7 and heterogeneity and survival was estimated with
8 formal testing with chi square statistics, and there
9 was no heterogeneity in either group.

10 I'll summarize and say that the meta-
11 analysis results found that the mobile and fixed
12 bearing implants are similar in both effectiveness and
13 survival. The clinical outcome was about 90 percent
14 success in both mobile and fixed. The implant
15 survival was about the same -- about 90, 91 to 93
16 percent cumulative survival in both the mobile and the
17 fixed.

18 The mobile characteristics -- cemented
19 versus uncemented, rotating platform versus meniscal
20 bearing, etcetera -- did not demonstrate significant
21 differences in clinical outcomes, and the results
22 appeared to favor the downclassification of mobile

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1 bearing from Class III to Class II, given the
2 similarity in clinical outcomes and homogeneity among
3 device survivals.

4 Thank you.

5 CHAIRPERSON YASZEMSKI: Thanks very much,
6 Mr. Maislin.

7 What I'd like to do now is ask Mr. Allen
8 to come up and give the FDA presentation. We'll have
9 an opportunity for panel questions of both OSMA and
10 FDA.

11 MR. ALLEN: Good morning. My name is
12 Peter Allen. I'm a biomedical engineer in the
13 Orthopedics Branch in the Office of Device Evaluation
14 at FDA. I would like to thank OSMA for their
15 presentation and for their efforts in preparing this
16 reclassification petition.

17 Today I will present a summary of FDA's
18 review of this petition, along with some questions we
19 would like our panel members to discuss and answer.

20 Before we get to that, I'd like to provide
21 a bit of an overview on the current regulatory status
22 and marketing history of mobile bearing knees. First,

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1 I'll cover some general background in the medical
2 device classification process. Then I'll briefly
3 discuss the mobile bearing knees that have been
4 approved for use and are currently on the market in
5 the United States.

6 After that I'll discuss the information
7 provided in the petition and how it fits in with the
8 requirements for reclassification. And then I'll
9 identify the questions we'd like our panel to discuss.

10 The 1976 amendments to the Food, Drug, and
11 Cosmetic Act provided regulations for the
12 classification and regulation of medical devices. The
13 Act established three classes of medical devices
14 dependent on the regulatory controls needed to provide
15 a reasonable assurance of safety and effectiveness.

16 To provide a reasonable assurance of
17 safety and effectiveness for Class I devices, general
18 controls are considered adequate. This slide
19 identifies some examples of general controls.

20 When general controls alone are
21 insufficient, a device may be classified into
22 Class II. Class II devices require additional special

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1 controls. Special controls include guidance
2 documents, performance or consensus standards,
3 labeling, and possibly even clinical data. The
4 special controls issue will be the focus of much of
5 our later discussion, and we will have a few of our
6 panel questions directed to this issue.

7 Devices classified into Class III -- pre-
8 market approval -- when it cannot be classified into
9 Class I or Class II, because general and special
10 controls are insufficient to provide reasonable
11 assurance of safety and effectiveness. In addition,
12 any new device type first introduced into commerce
13 after the 1976 amendments to the Act, commonly
14 referred to as post-amendments devices, are by statute
15 automatically classified into Class III.

16 Class III devices are regulated using the
17 validated scientific evidence that is presented to FDA
18 in a pre-market approval application, or PMA, to
19 establish the safety and effectiveness of the device.
20 Typically, this requires the submission of clinical
21 data.

22 Just like classification, FDA will

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1 reclassify a device into Class I, II, or III,
2 depending on the level of regulatory control needed to
3 provide reasonable assurance of safety and
4 effectiveness. FDA may initiate the reclassification,
5 or any person, manufacturer, or importer may submit a
6 petition for reclassification.

7 A Class III device may be reclassified in
8 Class II when FDA can identify the risks associated
9 with the device and the manner in which these risks
10 can be controlled by general and special controls.

11 A special controls guidance document is
12 one way in which risks can be controlled. This is a
13 document created by FDA that provides acceptable
14 methods for controlling the risks identified for a
15 given device type. It is intended to provide guidance
16 by conveying FDA's current thinking about a specific
17 device type. And it provides recommendations on how
18 to address the issues presented in the guidance, such
19 as the use of performance and consensus standards, the
20 use of labeling for those instances when clinical data
21 may be deemed necessary.

22 A company need only demonstrate that their

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1 Class II device meets the recommendations of the
2 special controls guidance document to receive FDA
3 clearance for marketing.

4 So there's a quick overview of the
5 reclassification process. Now let's turn our
6 attention to the devices being considered in this
7 reclassification petition -- the mobile bearing knees.

8 I'll discuss the current classification
9 status of these devices and look at their marketing
10 history here in the U.S., as well as the indications
11 for use for which they were originally approved.

12 Mobile bearing knees were first introduced
13 for commercial distribution in the U.S. after the 1976
14 amendments to the Act. Therefore, by regulation, they
15 are Class III post-amendments devices and require an
16 approved PMA prior to marketing.

17 To date, FDA has approved three mobile
18 bearing knee PMAs. The first PMA for the DePuy LCS
19 total knee system was approved in 1985. The original
20 approval included two design versions -- a rotating
21 platform design, which was crucial at sacrificing, and
22 a meniscal bearing design was crucial at retaining.

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1 In addition to the knees approved in the
2 original PMA, over the years numerous design
3 modifications and variations have been approved
4 through supplements to that PMA. So there are
5 actually multiple mobile bearing knee designs on the
6 market resulting from this one PMA, but they are all
7 offshoots from the same device system.

8 The second PMA was for the LCS
9 unicompartmental knee, which was approved in 1992.
10 And the third PMA was for the Oxford unicompartmental
11 knee from Biomed, which was just approved this past
12 April, although older versions of the device have been
13 on the market in Europe for over 25 years.

14 All three of these systems are well
15 described in the published literature. Each of these
16 three devices have their own approved indications for
17 us. Indications approved for the original rotating
18 platform and meniscal bearing versions of the LCS are
19 listed here -- the only difference between the two
20 being that the rotating platform version was approved
21 for use in revision procedures, while the meniscal
22 bearing was not.

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1 The additional design variations, since
2 added to the system over the years, may have slightly
3 different implications from those approved with these
4 original designs.

5 Here are the indications for use approved
6 for the LCS and the Oxford unicompartmental knee
7 systems -- the main differences between the two
8 systems being that the LCS was indicated for
9 uncemented use on either condyle in older patients,
10 and the Oxford was indicated for cemented use only on
11 the medial condyle with no limitations in patient age.

12 Now I'll move on to the current petition
13 in which OSMA has provided a proposal to reclassify
14 the mobile bearing knees from Class III to Class II.
15 I have already reviewed for you what's required to
16 reclassify a device from Class III to Class II. That
17 is, you must identify the risks and the manner in
18 which these risks can be controlled by general and
19 special controls.

20 So I will now review the following items
21 included in the petition -- most important being the
22 risks identified for mobile bearing knees and the

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1 special controls proposed to address these risks.

2 The petition is split into two groups of
3 mobile bearing knee designs. The first consists of a
4 total knee design, which contains patella, femoral,
5 and tibial components, and is intended to replace the
6 entire knee joint. The second consists of a
7 unicompartmental design and contains only femoral and
8 tibial components intended to replace either the
9 medial or lateral compartment of the knee.

10 The proposed classification descriptions
11 for both designs are listed here. Further description
12 of the classification definitions are included with
13 the panel questions in the presentation packet you
14 received this morning. I note this simply because the
15 adequacy of these classification definitions is
16 included as one of the panel questions.

17 Both device type are available in many
18 design variations, depending, for example, on the
19 directional mobility of the bearings, the type of
20 constraint, levels of congruence, management of the
21 patella, and management of the posterior crucial
22 ligament.

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1 Each group of colors here represents a
2 different design variable, such as the bearing type,
3 method of constraint, amount of constraint, etcetera.
4 As you can see, there are a large combination of
5 variables that can affect the design of a mobile
6 bearing total knee. Reclassification of the currently
7 approved devices, which by regulation is what we are
8 actually doing, would potentially provide for the
9 reclassification of these design variables, many of
10 which are incorporated in the approved devices.

11 Again, please note that questions
12 regarding the adequacy of the data in the petition
13 supports these multiple design types. That is, the
14 identification of the risks and the appropriate
15 special controls are included in the list of panel
16 questions.

17 Although much fewer in number, there are
18 also various combinations of design variables that go
19 into the development of a unicompartamental knee, as
20 you can see here.

21 Turning now to the indications for use --
22 the proposed indications for the mobile bearing total

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1 knee are listed here. These devices are also
2 indicated for use with or without bone cement. The
3 proposed indications for use for the mobile bearing
4 unicompartmental knees are listed here as well.
5 Again, these devices are indicated for use with or
6 without the use of bone cement.

7 The sponsor has provided over 230
8 published references in support of the preclinical and
9 clinical issues in this petition. Some of the
10 preclinical issues addressed include evaluation of
11 device kinematics, wear of the mobile bearings, and
12 device biomechanics. With regards to the clinical
13 data, the sponsor summarized a series of 48 studies
14 which evaluated the various types of bearings listed
15 here.

16 Data presented for each study included
17 study design, demographics, safety, effectiveness, and
18 survivorship. The majority of these studies focused
19 on those devices already approved for use in the
20 United States -- that is, the LCS and the Oxford
21 mobile bearing devices.

22 In addition, there are also nine published

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1 review articles on mobile bearing knees, information
2 from seven ongoing FDA approved clinical trials, two
3 international clinical outcome studies, two meta-
4 analyses, one comparing clinical outcomes of mobile
5 bearing knees of different types, and the second
6 comparing survivorship of mobile bearing knees versus
7 fixed bearing knees.

8 These clinical experiences underscore the
9 strong influence of the technical performance of the
10 operation on the long-term success of a new device.
11 Properly aligned knee replacements that have restored
12 ligament balance appear to have survival rates of 10
13 years or greater, irrespective of bearing mobility.
14 These data indicate that when provided with
15 medial/lateral stabilization, mobile bearing knees
16 provide equivalent results to fixed bearing knees.

17 The sponsor has also provided information
18 on adverse events. This includes data gathered from
19 searches of FDA's medical device reporting program, or
20 MDRs, reports from the published literature, and data
21 from manufacturers on their FDA approved clinical
22 trials.

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1 Again, the vast majority of this
2 information relates to the DePuy LCS devices and the
3 Oxford unicompartmental device from Biomed. The MDRs,
4 in particular, relate specifically to the LCS devices.

5 Here I have listed the most commonly cited
6 adverse events that were associated with revision,
7 although they're not listed in any particular order.
8 It is noted that the three most common adverse events
9 cited in the MDR database for the LCS knees were pain
10 accompanied with swelling, fractured bearings, and
11 loosening, respectively.

12 As you can see, the patient-related
13 adverse events are fairly typical of the type of
14 events you might see with any total joint replacement
15 procedure. And the device-related adverse events are
16 consistent with those types of complications often
17 seen with fixed bearing knees, although there does
18 appear to be a tendency to see a greater number of
19 bearing dislocations, subluxations, and impingement
20 with the mobile bearing knee designs. And the way in
21 which these events occur may be somewhat different
22 from the mobile bearing knee versus the fixed bearing

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1 knee.

2 The sponsors proposed methods to control
3 for these potential device-related risks. Again, I
4 alert the panel that there will be some questions
5 forthcoming regarding these risks and the adequacy of
6 proposed special controls. High wear rates of
7 polyethylene bearings can lead to particle-induced
8 osteolysis, which can in turn lead to loosening of
9 device components.

10 To address the risk of wear, which
11 includes all of the different modes of wear envisioned
12 with the mobile wearing knees -- that is, designs with
13 tibial posts, rotational stops, grooved tracks, multi-
14 directional platforms, patella bearings, etcetera --
15 the petitions have suggested the following two
16 standards: ASTM F1715 and/or ISO 14243-1.

17 The ASTM standard is a general guideline
18 for establishing test conditions and obtaining wear
19 measurements for wear simulation of the femoral/tibial
20 components of knee joint prostheses. As such, it does
21 not provide any specifics on wear testing of the
22 patellar/femoral compartment of the knee joint.

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1 The ISO standard is an international
2 standard for wear testing of total knee joint
3 prostheses, which includes loading, displacement, and
4 environmental testing parameters. Of concern to FDA
5 is whether such tests can provide results that
6 reproduce clinical wear behavior of the many mobile
7 bearing knee designs.

8 One way to determine this is through
9 analysis of the wear surfaces and wear particles. To
10 evaluate the wear of the bearing surfaces, the sponsor
11 has suggested two additional methods of analysis,
12 including the use of coordinate measuring machines to
13 quantify the volume of wear on the articulating
14 surface, and the measurement of changes and engraved
15 markings on the back side of the bearing.

16 Back side wear measured by this method on
17 bearings tested in knee joint simulators has been
18 shown to correlate well with wear measured and
19 clinically retrieved specimens according to the
20 sponsor.

21 The sponsor has also proposed a means to
22 evaluate wear particles. For analysis of the wear

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1 particles, they recommend ASTM F2025 and/or ISO
2 14243-2. The ASTM standard uses a weight loss method
3 of wear determination for polymeric components used in
4 human joint prostheses.

5 The ISO standard also employs gravimetric
6 methods for measurement of wear in total knee joint
7 prostheses, as well as dimensional methods using a
8 coordinate measuring machine to determine biometric
9 wear rate.

10 To evaluate or mitigate the risk of tibial
11 insert or patellar bearing deformation or fracture,
12 which may result from overhang with respect to the
13 metal tibial base plate, the sponsor has proposed
14 utilizing the wear test just previously mentioned.

15 However, the wide variety of mobile
16 bearing knee designs proposed -- however, with the
17 wide variety of mobile bearing knees proposed, it is
18 not clear if such wear tests can provide results that
19 reproduce the bearing deformation and/or fracture that
20 is seen clinically.

21 Contact area changes and stress changes on
22 the insert can change dramatically as the insert moves

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1 throughout its available range of motion. To evaluate
2 the effect of this, the sponsor again proposes using
3 wear simulator testing standards to address the
4 potential risk that damage due to the changing load
5 profile might impart on the components.

6 In addition, they also propose using
7 existing recommendations for contact area stress
8 evaluation and the current FDA guidance documents for
9 fixed bearing knees. These include evaluations of the
10 tibial/femoral and patella/femoral interfaces, several
11 different angles of flexion, using relevant
12 physiologic loads.

13 A copy of the fixed bearing knee guidance
14 document was provided in the panel presentation
15 package you received this morning.

16 Separation of the tibial bearing from the
17 metal base plate is an inherent risk associated with
18 the design of most mobile bearing knees. This may
19 lead to dislocation, subluxation, instability, or
20 impingement. Due to their requirement for mobility,
21 tibial bearings cannot be held rigidly in place, and,
22 therefore, are susceptible to separation as a result

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1 of the shear and torque forces experienced in the
2 knee.

3 To address this risk, the sponsor has
4 proposed a characterization of the component interlock
5 strengths as recommended in the current fixed bearing
6 knee guidance. This includes anterior/posterior and
7 medial/lateral shear testing and/or static tensile
8 pulloff testing of the tibial bearing.

9 But as a number of mobile bearing designs
10 have no means or limited means of fixation between
11 components, the value of such testing appears of
12 questionable use for some of the designs.

13 Tipping of the tibial insert is a risk
14 that has been identified for the rotating platform
15 design with the Cohen and Cohen configuration. Edge
16 loading of the insert can lead to the tipping of the
17 insert and partial dislocation or subluxation of the
18 component. Repeated tipping of the insert may lead to
19 deformation, wear, or fracture of the component.

20 The sponsor recommends characterization of
21 the component interlock strengths as recommended in
22 the current fixed bearing knee guidance. However,

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