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FOOD AND DRUG ADMINISTRATION

ORTHOPAEDICS AND
REHABILITATION DEVICES
ADVISORY PANEL MEETING

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CASET Associates, Ltd.
10201 Lee Highway, Suite 160
Fairfax, Virginia 22030
(703) 352-0091

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P R O C E E D I N G S (7:35 a.m.)

MS. NASHMAN: Good morning, everybody. We are ready to begin this meeting of the orthopedic and rehabilitation panel.

My name is Jodi Nashman. I am the executive secretary of this panel, also a biomedical engineer and reviewer in the orthopedic devices branch.

I would like to remind everyone that you are requested to sign in on the attendance sheets which are available at the tables by the door. When you entered, they might not have been available. I believe they are available now. You need not jump up at this moment and sign in, but if you could sign in during a break, it would be appreciated.

You may also pick up an agenda and information about today's meeting, including how to find out about future meeting dates through the advisory panel phone lines, and also how to obtain meeting minutes, transcripts and videos.

I am going to now read two statements that are required to be read into the record, the deputization of temporary voting members statement, and the conflict of

interest statement.

Appointment to temporary voting status. Pursuant to the authority granted under the medical devices advisory committee charter, dated October 27, 1990, as amended April 20, 1995, I appoint the following people as voting members of the orthopedic and rehabilitation devices panel for the January 13, 1998 session of the panel meeting:

Dr. Cato Laurencin, Dr. Michael Yaszemski, Dr. Albert Aboulafia, Dr. Marcus Besser, Dr. James Hill, Dr. David Nelson, Dr. Steven Stern, who will be limited to discussion only during the reclassification, Dr. Richard Friedman who recused himself from participation in the reclassification, and Dr. Harry Skinner, who will not participate in the classification of plaster of paris pellets.

For the record, these people are special government employees and are consultants to this panel under the medical devices advisory committee.

They have undergone the customary conflict of interest review. They have reviewed the material to be considered at this meeting.

Also, because the position of panel chairperson for the orthopedic and rehabilitation devices panel is currently vacant, I invite Barbara Boyan to act as temporary

chairperson when the panel addresses reclassification petitions during this session of the meeting, and David Nelson to act as temporary chairperson when the panel addresses the classification of plaster of paris pellets.

For the record, Dr. Boyan is a special government employee and is a voting member of the orthopedic and rehabilitation devices panel.

Dr. Boyan has undergone a customary conflict of interest review, and she has reviewed the material to be considered at this meeting.

Also, for the record, Dr. Nelson is a consultant to the panel. He has undergone the customary conflict of interest review, and he has additionally reviewed the material to be considered at this meeting.

This memorandum is signed D. Bruce Burlington, director, Center for Devices and Radiologic Health, and is dated January 8, 1998.

Additionally, pursuant to authority granted under the Medical Devices Advisory Committee charter of the Center for Devices and Radiologic Health, dated October 27, 1990 and as amended April 20, 1995, I appoint Philip T. Lavin, PhD, as a voting member of the orthopedic and rehabilitation devices panel for the duration of the meeting on January 12 and 13.

For the record, Dr. Lavin is a consultant to the Center for Drug Evaluation Research. He is a special government employee who has undergone the customary conflict of interest review and has reviewed the material to be considered at this meeting.

This memorandum is signed Michael A. Friedman, M.D., lead deputy commissioner, and is dated January 8, 1998.

The following announcement addresses conflict of interest issues associated with this meeting, and is made part of the record to preclude even the appearance of impropriety.

To determine if any conflict existed, the agency reviewed the submitted agenda and all financial interests reported by the committee participants.

The conflict of interest statutes prohibit special government employees from participating in matters that could affect their or their employers financial interests.

Due to this prohibition, Dr. Richard Friedman will not participate in matters related to knee reclassifications during today's session, and Drs. Boyan and Harry Skinner will not participate in matters related to plaster of paris pellet reclassification.

However, the agency has determined that the

participation of certain members and consultants, the need for whose services outweighs the potential conflict of interest involved, is in the best interests of the government.

Waivers have been granted for Drs. Laurencin, Nelson, Lavin, Yaszemski, Stern and Skinner, because of their interests in firms which could potentially be affected by the panel's decisions today.

The waivers granted for Drs. Laurencin and Nelson allow them to participate in all matters before the panel.

The waiver granted for Dr. Lavin permits him to participate in all reclassification matters.

The waiver granted for Dr. Yaszemski permits him to participate in all plaster of paris pellet classification matters.

The waiver granted to Dr. Skinner allows him to participate in all matters related to knee reclassification.

The waiver granted to Dr. Stern allows him to participate in deliberations, but not vote on knee reclassification matters.

Copies of these waivers may be obtained from the agency's freedom of information office, Room 12A-15 of this building.

We would also like to note for the record that the

agency took into consideration other matters regarding Drs. Philip Lavin and Barbara Boyan, who reported involvements with firms at issue, but on matters unrelated to the meeting's agenda.

Since the matters are not related to the specific issues of this meeting, the agency has determined that Dr. Lavin may participate fully in today's deliberations, and that Dr. Boyan may participate fully in matters related to knee reclassification.

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

With respect to all other participants, we ask in the interest of fairness, that all persons making statements or presentations disclose any current or previous involvement in firms whose products they may wish to comment upon.

Before turning the meeting over to Dr. Boyan, I would like to go through some panel introductions. Generally, I would read through a list of panel members' names.

In the interest of the public knowing who has what

expertise, I am going to ask the panel members to introduce themselves and give a very brief synopsis of their expertise. I will start with Dr. Boyan to my right and then we will proceed to Dr. Besser and around. Panel members, you need not wait for Dr. Boyan to call on you before introducing yourself.

DR. BOYAN: I am Dr. Barbara Boyan. I am a professor of orthopedics at the University of Texas Health Science Center at San Antonio, and director of orthopedic research there.

I am also the chairman of the board of a company, Osteobiologics, which is a tissue engineering company. Our research expertise is in the cell biology of bone and cartilage. I am also quite interested in new restorative methods for bone and cartilage repair.

DR. BESSER: My name is Marc Besser. I am assistant professor of physical therapy at Thomas Jefferson University in Philadelphia.

I am a biomechanist. My degree is in mechanical engineering. My main areas of work are in gait analysis, motion analysis and lower extremity biomechanics.

DR. SKINNER: My name is Harry Skinner. I am professor and chair of orthopedic surgery and professor of mechanical engineering at the University of California,

Irvine.

My research interests include joint mechanics, finite element analysis, gait analysis and biomaterials.

DR. ABOULAFIA: My name is Albert Aboulafia. I am a full-time member of the Department of Orthopedic Surgery at Emory University in Atlanta.

I am a practicing orthopedist with an area of interest and expertise in musculoskeletal oncology and traumatology.

DR. WITTEN: Celia Witten, division director of the Division of General And Restorative Devices in the Center for Devices and Radiologic Health.

DR. SILKAITIS: My name is Dr. Raymond Silkaitis. I have a PhD in pharmacology. I am also a pharmacist. I am the industry representative for the panel.

I am the vice president of medical and regulatory affairs at Gliatech, Incorporated, and have been in the medical device business for about 18 years, conducting clinical trials and regulatory affairs issues.

DR. HOLEMAN: My name is Doris holeman. I am coordinator of the graduate nursing program at Albany State University, Albany, Georgia.

I am the consumer rep, and I direct the nursing outreach screening clinic at Albany State.

DR. NELSON: I am David Nelson. I am an orthopedic hand surgeon in practice in San Francisco, California.

I have an expertise in distal radius fractures, tendon healing and respiratory mechanics.

DR. LAVIN: My name is Philip Lavin. I am a biostatistician with Boston Biostatistics, and I am also on the faculty of Harvard Medical School. I will be the biostatistics consultant today.

DR. YASZEMSKI: My name is Michael Yaszemski. I am an associate professor of orthopedic surgery and bioengineering at Mayo Clinic in Rochester, Minnesota.

My clinical practice is spine surgery and adult reconstructive surgery. My research interests are in biomaterials with reference to bone regeneration via tissue engineering.

DR. STERN: My name is Steven Stern. I am an associate professor of clinical orthopedics at Northwestern University in Chicago.

I do lower extremity orthopedics including knee and hip arthroplasty. My research interests are computer simulations of total joints.

DR. HILL: My name is Jim Hill. I am a professor of orthopedic surgery at Northwestern University. My main

interest is orthopedic athletic injuries to the shoulder and knee.

MS. NASHMAN: Thank you all very much. I appreciate your introductions. At this time, I would like to turn the meeting over to our chairperson for the morning, Dr. Barbara Boyan.

DR. BOYAN: Good morning. My name is Dr. Barbara Boyan. I am the acting chairperson for the remaining reclassification portion of this meeting.

Today we will be making recommendations to the Food and Drug Administration on two reclassification petitions and a classification proposal: first, the reclassification of the patellofemorotibial knee; second, the reclassification of the patellofemoral knees; and third, the classification of calcium sulfate preformed pellets.

I would like to take note for the record that the voting members present constitute a quorum as required by 21 CSF Part 14.

We will now proceed with the open public hearing of this meeting. I would like to ask at this time that all persons addressing the panel come forward and speak clearly into the microphone, as the transcriptionist is dependent on this means of providing an accurate record of this meeting.

We are requesting that all persons making

statements during the open public hearing of the meeting disclose whether they have financial interests in any medical device company.

Before making your presentation to panel, in addition to stating your name and affiliation, please state the nature of your financial interests, if any.

We will first hear statements from Dr. C.H. Rorabeck and Richard W. Parkinson read into the record by Ms. Jodi Nashman.

It is noted that their financial interests and associations have not been included within their statements.

Agenda Item: Open Public Hearing.

MS. NASHMAN: Good morning again. The first statement I have is from a Dr. C.H. Rorabeck, who is with the Division of Orthopedic Surgery, University of Western Ontario.

He addresses his correspondence to Dr. Boyan. He writes:

I understand that your panel is meeting to consider the reclassification of cementless total knee implants on January 13, 1998.

The meeting will consider the request to reclassify, as put forward in a petition, filed by July 25, 1997, by the Orthopedic Surgical Manufacturers Association.

As total knee implants with mobile bearing articular surfaces are also included in this petition, I would like to offer some comments for consideration by the panel, as unfortunately, because of a prior commitment, I will be unable to attend the meeting.

As one of the original users of the SAL mobile bearing device mentioned in the petition, I would like to point out to the panel that our clinical experience with this device has largely been with cemented use.

The device is not currently designed, nor is it intended for use, without cement.

Early usage of a cementless femoral component with the SAL was dropped, following an initial experience with femoral loosening.

There has never been a cementless tibial component with this device.

Dr. Bourne, my partner and co-developer of the SAL mobile bearing device, will be at the panel and will be able to expand on these points.

In addition, I would like to express concern with the inclusion of mobile bearing devices, and a petition being considered at the same time as cementless, as compared to cemented, use of total knee implants.

To my knowledge, and as demonstrated by our SAL

experience, there is no data on cementless use of any mobile bearing devices, with the exception of the LCS total knee system manufactured by DePuy.

I personally do not believe that the issues relevant to the cement porous coating distinction are necessarily the same for a fixed bearing as they are for mobile bearing devices.

As I understand it, currently both cemented and cementless mobile bearing devices are class III. I believe that the issue of reclassification of the cementless use of mobile bearing devices should not be considered in the same discussion as cementless use of fixed bearing total knees.

My fear is that the consideration of these two altogether different designs in the context of cement will result in the loss of attention to the issues which are unique to the mobile bearing needs.

Finally, I would like to express my firm support and commitment for graduated device introduction for mobile bearing knees that is consistent with class III handling.

I believe this is the approach which will be presented by Dr. Bourne. I would therefore support an approach for mobile bearing devices which would include small clinical studies followed by multi-center clinical studies once the appropriate preclinical and engineering

testing has been performed.

As you know, there is tremendous variability from one mobile bearing design to the next. I don't believe that one can necessarily infer that the results from one design will be similar to another.

Some complications, such as the ones that we observed on the femoral component of the SAL design may well be seen in some designs but not in others.

Again, this is not predictable from the design features alone.

In summary, therefore, I believe that the issues of cemented versus cementless should be considered separately for mobile bearing knees, and not in the same context as fixed bearing knees.

Yours very sincerely, signed, C.H. Rorabeck, M.D.

The second piece of correspondence I have to read is from a Dr. Richard W. Parkinson, consultant, orthopedic surgeon. He does not provide his affiliation.

Dear Dr. Boyan: I am a consultant orthopedic surgeon, working in a large district general hospital in the United Kingdom. The majority of my elective orthopedic practice is in knee surgery.

Until 1993, large numbers of the Accord Johnson LOM total knee replacements were implanted here by another

surgeon.

Reports in the literature suggest that the results of this implant were satisfactory. My experience here at Aeropark Hospital has shown this is definitely not the case.

In the last four years I have explanted nearly 100 Accord total knees. Eighty percent of the revision procedures have been due to aseptic loosening, meniscus dislocation and subluxation and patella maltracking.

I still see many patients who have had unacceptable results with the Accord TKR. This prosthesis is now obsolete, and rightly so.

I am concerned that if the market is flooded with other designs of mobile bearing TKR, that this unfortunate experience may be repeated.

Yours sincerely, signed Richard W. Parkinson.

Dr. Boyan?

DR. NELSON: Madam Chairman, may I ask a point of information?

DR. BOYAN: Sure.

DR. NELSON: Could someone define mobile bearing knee?

DR. STERN: There are basically two types of knee arthroplasties in this regard. There is a fixed bearing knee in which the articulating surface is fixed.

So, the femoral component is fixed to the femur and the tibial component is fixed to the tibia. The bearing surfaces do not move. That is now days called a fixed bearing knee.

In a mobile bearing knee, there is a mobile bearing, normally within the tibial component. The tibial polyethylene is not fixed to the tibial face plate; hence the term mobile bearing.

The bearing surface is moving back and forth in the tibia and that is as opposed to the fixed bearing knees that we are probably all a little more familiar with.

DR. BOYAN: Thank you. We will now hear from Dr. Jur Robos, Dr. Stephen Lewold and Dr. John Collier, who will have a total of 30 minutes between the three of them.

If they would come forward, please?

While they are coming forward, one of our panel members has just arrived, Dr. Cato Laurencin. I would like for him to tell for the record what his expertise is in the area of orthopedics.

DR. LAURENCIN: Thank you. I am an orthopedic surgeon with clinical work in total joint replacement, sports and shoulder, and also research in biomaterials in related areas.

DR. BOYAN: Thank you very much, Dr. Laurencin.

Okay.

DR. PEOPLES: Madam Chairperson, executive secretary, members of the advisory panel, my name is Dr. Steven Peoples. I am vice president of clinical and regulatory affairs at DePuy.

As with full disclosure, I must disclose to you and confess that I do have a financial interest as an employee of DePuy in the deliberations of this panel.

DePuy is presenting some information today, and I won't keep you in suspense, that there are a number of issues involved in the pending petition on reclassifying total knees, specifically that of the inclusion of mobile bearing concepts, that we feel are not in the best interests of public health and are not supported by the publicly available information and knowledge about these concepts.

I will keep my comments very brief and serve merely to introduce three speakers.

Unfortunately, Dr. John Collier from Thayer School of Engineering at Dartmouth is unable to attend today due to health. In place of him, we will have another speaker to address engineering concerns.

The three speakers you will hear from will be, first, Jur Strobos, who is a consultant to DePuy. He will discuss issues related to reclassification and the petition

that is in front of you, presented by OSMA.

Dr. Strobos currently is consulting in medical device law and related matters, previously served for four-and-a-half years as the director of policy research in the office of the commissioner of FDA under Dr. David Kessler.

Following Dr. Strobos will be Dr. Stephen Lewold, from the Lundt University Hospital in Sweden, who will share information related to mobile bearing knees data and clinical follow up in the Swedish implant registry.

Finally, speaking to engineering aspects related to these issues will be Dr. David Fitzpatrick, a design development engineer with DePuy International in Leeds, who has spent his design experience in the laboratories along with John O'Connor at Oxford.

I will now turn over to Dr. Strobos for his comments.

DR. STROBOS: Good morning. My name is Jur Strobos and I am the culprit behind the fairly lengthy document that you got, that talks a lot about mobile bearing knees and a little bit about cementless.

I was formerly with the FDA and I was heavily involved at the time with pedicle screws and reclassification. I have written and given speeches about reclassification.

I am going to try to sort of limit myself to just 10 minutes here, although it is one of my favorite subjects, and allow Dr. Lewold a little bit of time to talk about failures of mobile bearing knees and Dr. Fitzpatrick to talk about them.

There are three things I wanted to address today that really relate to what I think of as the public health issue, the public health impact of reclassification.

Then I wanted to talk a little bit about why does one reclassify. What is the whole purpose behind reclassification and why is it different for every joint in every sort of circumstance. Why is this different from pedicle screws.

The third thing I just wanted to point out is that when you are dealing with reclassification issues, you really want to deal with the future and what you anticipate being future devices, and less with what the products are on the market today, especially when you are dealing with products that are not all that successful.

The first thing on the public health issues, the petition talks about the fact that there are 250,000 total knee replacements in the United States.

There are basically four different data bases, the way you figure out population numbers. One is by looking at

discharge diagnoses, another is looking at Medicare data and extrapolating, a third is to look at population statistics like Ohmstead County, where Mayo Clinic is located, and the fourth is looking at sales data.

I went through the numbers on each of these and I get a whole lot more than 250,000 total knee implants in 1997, probably over 300,000.

I would say that, looking at the growth rates, that we are talking about 400,000 total knee replacements in the next few years, per year.

If you look at the sales data, the petition talks about the fact that cementless represents a significant portion of that.

That was true, you know, five or six years ago. That is not true any more. People are not using cementless that much.

The question is why does this matter. I think that one is that details count. When you are reading these petitions and reading this literature, I think you have to pay close attention to really what you are talking about.

The second thing is that we really shouldn't hide the mobile issues in the cement.

Cementless, my estimate is that we will probably see more mobile bearing knees than we will see cementless

knees.

So, to a certain extent, the discussion about cement and cementless fixation is less important from a public health standpoint, frankly, than the issues regarding mobile bearing knees.

The third thing is that to a certain the petition represents what I think of as a wolf in sheep's clothing in that regard.

In other words, it talks a lot about cement, biological fixation and so forth. In fact, the public health impact is going to be in the mobile bearing area.

We don't know a whole lot about the mobile bearing area, to tell you the truth.

I think the other thing that you need to recognize about cement is that cement doesn't seem to have been that much of a success in the knee.

I had the privilege of reading a lot of work by Dr. Insall in the last few weeks. Apparently his views are that cementless fixation, although not exactly a failure, did not prove as successful as was hoped.

I think that, again, focuses the fact on why should one reclassify. In other words, let's sort of ask ourselves what are the benefits of class II and what are the benefits of class III.

Let me just view class III, if it works. Now, it doesn't always works. But if class III works, you get very good science. You get rapid introduction. You get rapid review.

In fact, if you look at review times of PMAs, they are coming down. Review times of 510(k)s are going up.

You get a better product understanding and you get a better return on investment.

Now, why is that? The answer to that is, if you actually have -- it takes a lot of money and investment to develop good clinical data, to hire clinical investigators and to put patients in trials and stuff like that.

That information you develop becomes part of the product. It is part of the understanding of the product.

If you can't protect that information, then there is no reason to invest in it. You can't get companies to do good clinical data unless they have some way of protecting the information and associating that information with a product.

The only way you can do that is in class III. You can't do it in class II. So, a lot of people will dispute that you get rapid introduction with class III, and I would say that you do.

If class III works the way it is supposed to work,

you get very rapid science. You get people who are interested in developing a good product and running the clinical trials.

Then the question would be, why have I supported it in the past, reclassification, like reclassification of pedicle screws?

I think the answer is that there are really two fundamental reasons why you want to reclassify.

One is if you know so much about the device, so much about the design, that all the devices are clinically the same.

No matter how many little changes you make on the edge -- in other words, a lot of companies have to come up with ways to work around patents, so they have to make some changes in the device to avoid a patent.

If the basic concept of how a device works is understood and these little changes really aren't going to affect the safety and effectiveness, or the safety and effectiveness can be evaluated through a 510(k) type process that piggy backs on the existing data, then you have a device that is very suitable for reclassification.

The second thing I think you need to recognize, or another issue, is when you are looking at future devices, future modifications and improvements, if the future

modifications and improvements aren't really going to affect the basic performance of the device, then the example that I use over and over again is a pace maker and a defibrillator.

If you are selling someone a defibrillator and you have given them a pace maker, then the value of the pace makers, to a certain extent, hasn't changed.

That may be true for a lot of knee -- especially true for hip implants. No matter what little changes you make on the edges, the basic science and understanding of hip implants is pretty straightforward.

I think there is another reason that you reclassify. That is what I think of as the end around theory.

That is that there has somehow been widespread clinical and accepted use. This is an example with pedicle screws and cementless hips. You have widespread accepted use.

Then the question is, how do I go about getting the data. The answer to that is, it is very difficult. In the pedicle screw arena, I think a lot of people on the committee understand how difficult that was to do.

Then, reclassification may be a very useful way to sort of move forward.

I think, again, the issues in reclassification

are, are all the devices all clinically the same, you know, one design to another.

Think about the future. Where is the future going with these devices? Are we talking about adding biomaterials? What are the likely new changes that are going to be happening to these devices.

Again, I have just sort of gone over why I think that cementless hips and pedicle screws ought to be reclassified and were properly reclassified, and why I think that cementless knees and mobile bearing knees it is not really applicable to.

Let me just briefly review mobile bearing knees and then sit down here.

You basically have actual clinical materials with sort of five different types. Dr. Lewold is going to discuss in a little bit more detail the Oxford.

The LCS, as you know, is an approved EMA product. The Oxford is basically a failed device, you know, had tibial loosening, bearing failure, bearing dislocation.

The Minns actually tried to design around the failings of the Oxford, as Dr. Fitzpatrick discussed, and also had failures.

The SAL, you know, ended up with this femoral loosening, which is somewhat of a bizarre complication.

Yesterday one of the panel members pointed out that, you know, cementless femurs seemed to be a sort of easy thing to do. But I guess when you have mobile bearings they are not that easy.

I think, then, that we don't have a really good track record here. Polyzoides is in clinical trials. I had the pleasure of meeting Dr. Insall earlier today and my understanding today is that he is also in clinical trials with a new product.

The question really is, can we relate the design failures of the past and the design successes of the past to a new product. I think the answer is no.

There are a couple of issues that are coming up, I think, that a lot of people have talked about, polyethylene wear stems, osteolysis, the relationship between those.

There are issues of cruciate sparing and non-cruciate sparing. There is patellofemoral design. Patellofemoral design seems to be a particular problem with mobile bearing knees, if you look at the past clinical history.

I think one of the issues has to do with allografts, biomaterials, bone stock. We have really no experience with a lot of this kind of stuff and their interrelationships with mobile bearing knees, which have

very different dynamics.

There is a lot of discussion of sort of what I think of as a hot topic in mobile bearing knees now, is the femoral component curve.

As Dr. Nelson was asking about what mobile bearings are, in some ways, they seem somehow more anatomic. They have a little meniscus in there that moves around.

So, it seems somewhat more anatomic and the question is, do you have an anatomic femoral component where the curve, as you go into flexion, changes, the radius of the curvature changes, or do you have a fixed radius curve like you see more in fixed bearing knees.

The two significant failures in this area both had single radius of curvature components, femoral components. The LCS does not have a single radius of curvature.

Some of the newer products have single radius of curvatures. We don't know how that is going to work.

There are issues with proprietary polyethylene. One of the things that the OSMA petition points out is that there are polyethylene standards.

Mobile bearings have dual surface wear because the mobile bearing is moving. It is polyethylene. It moves both against the tibial component and against the femoral component. So, there is potentially more wear.

I can tell you that the LCS has a whole lot of proprietary standards with regard to polyethylene that are not duplicated by ISO and ASTM standards.

It seems that those standards have to be developed more or less device specific as well.

We will have some discussion about the curve of the bearing track and the fact that that is a total unknown with regard to mobile bearings as well.

The final issue, I think, has to do with this polyethylene, stems, screw holes, osteolysis. This is sort of a big issue, these days I understand, in knee implants.

If you go to a cementless version and if you are trying to get better tibial fixation with stems and screws, what does that say about cementless use, where you don't have a cement to protect you from wear debris.

The OSMA petition seems to indicate that one of their concerns is that mobile bearings may have dual surface wear and increased wear debris.

I think we need to look at that issue as well. There are a lot of unknowns.

With that, let me turn it over to Dr. Lewold, who has a little more experience with orthopedics.

DR. LEWOLD: Thank you. My name is Stephen Lewold. I am an orthopedic surgeon from Lundt University

Hospital in Sweden, where I am also one of the four doctors running the Swedish knee osteoplasty register. We have hospital has been doing so for eight, nine years now.

I don't have any financial interest in the industry, other than having DePuy to provide the means for me to be here and present our experience with the mobile bearing, from the Swedish knee arthroplasty register on mobile bearings.

In Sweden, being a rather conservative country with regard to choice of prosthesis, normally only one type of prosthesis pops up and is being used in sufficient numbers to make any statistical analysis of it.

With this case, this happened to be the Oxford meniscal bearing knee, which is mostly used for unicompartmental arthrosis, and in almost all cases, also used cemented.

First of all, I would like to briefly describe the register, which probably not everybody has heard about. It is a prospective nationwide study, which started already in 1975 by the Swedish Orthopedic Society.

It has today all units involved in the knee prosthetic surgery, and that is today 80 participating units.

The yearly number of arthroplasties in Sweden are

given from the registry. Here is 1975 and we go all the way up to today, the numbers being done for arthrosis and rheumatoid arthritis.

Those are the ones that have registered in this study. By comparing that with this line, which is the official patient administrative system for having all the data on inpatients, we can extrapolate that we cover about 80 percent of the tests that have been done in Sweden in this respect.

Here is the entry form, which is quite simple. It says the diagnosis, what kind of prosthesis, what type of prosthesis, whether or not the patella has been used, et cetera, et cetera.

What I would like to point out is that this for Sweden and for some of the other Scandinavian countries, is a unique civic number, which makes it possible to have prospective study running.

That is, if a person is being primarily operated on in Lundt and then moves to Stockholm and has his revision there, if the file and operating record is sent to us, that would be matched with the primary procedure.

In that respect, we can carry that study on, on a nationwide basis.

We define as the end point for our survival

analysis, revision. In this case it has been defined as either removal, open reduction, exchange, or addition or any prosthetic component.

Like I said, for mobile bearing knees, the Oxford was used in sufficient numbers to do this type of analysis.

We had, at the end of 1992, 699. They were mainly medial unicompartmental Oxford prosthesis. Those were analyzed and compared with, at that time, the gold standard of the Marmor knee or poly, which had been done in 2,364 cases.

Out of this, 50 Oxfords had been revised, compared to 87 from the Marmor group, giving a true revision rate of 7.2 percent for the Oxford and 3.7 percent for the Marmor.

Looking at the pattern of the failure or reason for revision, and also splitting it up into early and late revisions, you can see, for the Oxford, not surprisingly, dislocation of the meniscus stands for the majority of the instances of the revisions, followed by loosening.

For the Marmor, loosening and progressive arthrosis of the other compartment.

There is no difference in this pattern of whether it is early or late loosening.

For those 60 meniscus bearings that were dislocated, nine were exchanged, of which seven had further

revisions, mainly converted to a total knee.

We found a bit surprising, something we had not seen before with this type of device, other than perhaps with a PCA unicompartmental, that there were a lot of femoral component loosening.

There were six isolated femoral component loosening, four isolated tibial component loosening and four cases with both femoral and tibial component loosening, so 10 femoral component loosening.

The survival showed that already after one year there was a significant difference in favor of the Marmor. After five years, the cumulative revision rate of the Oxford was twice that of the Marmor.

There were 19 departments having used the Oxford. Of those 19, two departments had been doing more than 100 procedures each.

If we compared their results with the other 17 departments having done less than 100 procedures, there was no difference between these two groups, indicating that there is a design-related problem.

Also, the question of the improvement over time with a generalized Wilcoxon test for trend, it indicated for the Marmors, the results improved with a callendiara operation, whereas this was not possible to show for the

Oxford knee.

Our conclusion, then, was that the Oxford knee was not yet suitable for full-scale use. Therefore, we recommended its use on a limited basis only, in comparative studies with other unicompartmental knees with known failure rates and pattern. Thank you.

I may add, my friend here, while I was talking, has delivered -- there are actually six papers here. That is actually my thesis where this article which I have presented here is one of them.

I think the main subject of the thesis is design technique related problems to outcome in terms of survival. Thank you very much.

DR. BOYAN: Are there any questions that the panel would like to address to these speakers?

You have still one more speaker?

DR. PEOPLES: Yes.

DR. FITZPATRICK: My name is David Fitzpatrick. I am senior development manager for DePuy International based in Leeds, in the United Kingdom.

I would like to talk to you for a few moments about design considerations relating to the use of mobile bearing knee prostheses.

The modes of failure, as we have heard from Dr.

Lewold, traditionally are bearing subluxation, bearing dislocation, component loosening, and also there have been reports of bearing fracture and bearing wear.

Designs have evolved over time. Typically the evolution of the design has been based on an observation of the clinical problem.

For example, the observation that the natural bearing of the Oxford were dislocating when used as a total knee resulted in a proposed solution in the Minns knee, where the bearings were constrained to move in the AP tracks.

The outcome of that solution was that the device provided insufficient medial lateral stability and had femoral subluxation, requiring revision.

In addition, rotational constraints at the bearing tibia interface resulted in increased wear.

The final outcome of this was that the device was redesigned within five years for subluxation, dislocation and bearing fracture.

Within mobile bearing knees there are design trade offs. You need to determine what the acceptable levels of constraint are that can be tolerated by the system, and you need to determine what are the acceptable means of providing that constraint to the system.

You also need to consider what is the balance between the requirements of the tibia femoral joint and the patella femoral joint, and determine whether you want to use a polycentric or a single radius tibia femoral articulation.

This topic alone has a direct impact on the patella femoral joint requirement.

The outcome of these trade offs in the design is often unpredictable and unexpected.

If we look at the means by which we can validate these devices, we can use proposed tests such as the STM F1223, which is a simulated evaluation of the constraint between the tibia and the femur.

We can do direct mechanical simulation with knee simulators, for which there are ISO and ASTM draft proposals.

We can carry out analytical simulation using computer models, although there are no realistic models available at this present time.

We can carry out prospective clinical trials.

Evaluation of constraints using a model such as the STM 1223 has been found to provide a wide scatter in the data. It provides unreliable and unreproducible outcomes.

In addition, in my opinion, it provides no constructive or informative data. It is, in effect, a test

for testing's sake. This type of test is not a critical analysis tool.

The STM task force is currently reviewing the poll that it carried out, to determine the future, if any, of the proposal.

The chemical simulation using knee simulators provides no evaluation of patella femoral joint performance, which is a critical factor in mobile bearing knees.

There are no agreed standards and there is no consensus on the overall requirements for these knee simulators. Speedy resolution of these issues is very unlikely.

Analytical simulation is currently stymied by the fact that there are no reliable models available. Simplified models are available, but these are not sufficient for use as a predictive analytical tool.

These analytical tools really remain a long-term goal, probably up to five years or longer.

In conclusion, when considering mobile bearing knee design considerations, mobile bearing knee devices contain trade offs in significant areas of function and performance.

These design trade offs have no clean solutions. The developments that lead to new designs remain based on

clinical experience and observation.

There are no reliable predictive preclinical tools available for us to use at this time. In my opinion, prospective clinical validation is still required as the only reliable measure of performance. Thank you.

DR. BOYAN: Thank you. Well, you can't sit down yet. I have to ask everybody if they would like to ask you any questions. Yes, Dr. Nelson?

DR. NELSON: I could address this to either of you three speakers. Does DePuy have an FDA approved mobile bearing design?

DR. PEOPLES: Yes, we do. The LCS knee has undergone the PMA review process. That is the only mobile bearing knee undergoing the PMA process available.

DR. BOYAN: As you move the microphone down, what I would like for you each to do -- to remind you -- we practiced a lot yesterday, so we are very good at this. You have to state your name each time, no matter how ridiculous it is. Just say your last name and speak.

DR. STROBOS: I think, you know, I have been involved with FDA for a long time. The other thing I think you have to realize about an approved PMA, and that people sitting on the table probably realize this, is that when you have the data in a data base and you can play with it and

look at statistics and so forth, it is a different sort of order of magnitude of data than the sort of data that is in peer reviewed publications.

If you look at these other devices that we have discussed briefly -- the Oxford, the Minns -- there is some published data on it.

There are no published data, at least yet, on the SAL. I understand we are going to have some data presentation today.

There is no published data on the Polyzoides. That is also in clinical testing.

I think as you go forward with this and you realize some of the unknown design trade offs and some of the problems, you have to say to yourself whether you want future devices coming on the market without the same kind of quality data you have had to evaluate in the past on a product like the LCS.

DR. BOYAN: Any other questions? Dr. Stern?

DR. STERN: I wonder if anyone from DePuy can tell us how long the LCS has been on the market in the United States?

DR. PEOPLES: The original PMA was approved via panel review and FDA review in 1985 for the cemented versions of the knee.

DR. BOYAN: Any questions?

DR. STERN: You have talked about the results of a whole host of other mobile bearing knees. I wonder if someone from DePuy can comment on the results that have been achieved with the LCS mobile bearing knee.

DR. PEOPLES: We have continued to follow patients, 2,256 cases, that were in the cemented and cementless investigational device exemption clinical studies that led to premarket approval of the cemented and cementless versions of the LCS knee over time, both for our internal purposes as well as requirements as a condition of our PMA approval that we follow those patients for nine years.

We have followed them and, within the cementless version of the posterior cruciate retaining configuration of the device, that we have a survivorship at eight years of 97 percent.

DR. STROBOS: I think one of the other things that is important is that if you look at all of the four devices that we talked about plus some of the newer devices that are coming on the market, they all have very markedly different designs, in the way in which the curve of the bearing is made, the curve of the bearing track, the curve of the femoral component.

There are a lot of differences in these designs. Many of them are purposeful. I don't think we yet know whether or not they will achieve better results.

DR. BOYAN: Thank you. I think Dr. Silkaitis would like to make a comment.

DR. SILKAITIS: I would like to ask Dr. Peoples about the fact that this is a cemented knee, the LCS. Back in 1985 or earlier to that I believe cemented knees were a class II.

For some reason you had to do an IDE. That meant that it was different in its design or radically different, that you had to do an IDE.

DR. PEOPLES: The answer to that question is yes, because of the mobile bearing design concepts. Other so-called fixed bearing knees for use with cement were class II, handled under the premarket notification 510(k) route of substantial equivalency.

Because of the uniqueness and the design differences and considerations for mobile bearing knees, even for a cemented knee, the LCS was considered to be a class III product, even with cement fixation, having to undergo the premarket review necessary at a class III level.

DR. STROBOS: From a policy standpoint, I think that is an important question. We have had to deal with, as

a policy matter, a lot of off-label use, as it were, of products that have gone through the 510(k) system.

That is not an issue in the United States with regard to mobile bearing knees, because all mobile bearing knees have had to go through the class III process. There are no marketed mobile bearing knees that have gone through a 510(k).

DR. SKINNER: I am curious. Other than the registry that DePuy has maintained, are there published reports of mobile bearing knees that show the same results or are the results different if published by other investigators?

DR. STROBOS: I tried to go through the literature to find out whether there were other publications specifically relating to the LCS.

Most of the publications relating to the LCS in the published literature relate to the experience of Bequan Pappas, the developers of this product.

The data presented to this panel in 1985 and subsequently in cementless versions, I think, is a broader experience. That data was not published. It is part of the PMA.

Additionally, there is one unusual paper that I discovered from Hungary, in which they published results

from the LCS comparing it to the QCA and another knee.

They found, frankly, similarly surprisingly good results. That paper is in the packet. I don't have the tab number with me. I can track that down if you want, though.

DR. BOYAN: I think we all received copies of the packet. Seeing no further questions from the panel, I would like to thank you for your testimony. We will move on.

Is there anyone else in the audience that wishes to address the panel at this time. If so, please raise your hand.

Seeing no volunteers, then we will proceed with the reclassification petition for the patellofemoral tibial knee.

We are now going to begin the discussion of the first reclassification petition for the patellofemoral tibial knee. We will begin with the petitioner's presentation followed by the FDA presentation.

We will then have a general panel discussion of this topic, followed by a panel discussion aimed at answering FDA's question.

We will finish by going through the repaper classification work sheet and supplemental work sheet and voting upon our recommendation.

I would now like to remind public observers of

this meeting that, while this portion of the meeting is open to public observation, public attendees may not participate except at the specific request of the panel.

The first presentation will come from OSMA. They will present their petition. It will be followed by an FDA presentation by Peter Allen and then we will have the general panel discussion.

I see the OSMA group is gathering. Mr. Craig, will you be presenting?

While you get started, I remind you to state your name, the company with which you are affiliated, any financial relationship you may have other than getting a pay check.

Then, when you speak again, reminding everybody, state your name, but before you speak, because the transcriber has emotional difficulties when she reaches some of our speaking parts and we have not identified ourselves by name.

Agenda Item: Reclassification of Patellofemorotibial Knee. Petitioner Presentation.

MR. CRAIG: Good morning. My name is Tom Craig. I am with Smith and Nephew Orthopedics. I am here this morning representing the Orthopedic Surgical Manufacturers Association for the total knee reclassification petition.

To prepare this petition, OSMA consulted with FDA to determine what the petition should cover, conducted a comprehensive literature search and consulted with AAOS and ORS to determine which articles would be appropriate for inclusion.

After drafting, the petition was submitted to AAOS, AOA, ORS, ASTM and OSMA members for review and comment.

Where possible, these comments were incorporated in the petition, and they have been included in your copy of the petition.

The OSMA members are on the right. There is a significant omission in there. Sulzer Orthopedics has been prominent in this panel meeting, was omitted, and I am sorry for that.

The petition includes, one, cementless dry compartmental, two, cementless unicompartamental, and three, mobile bearings in both the cemented and cementless modes.

We believe that there is sufficient preclinical and clinical data to regulate these devices as class II and believe that the panel should concur.

There exist a number of controls and we ask that the panel review these and determine that the controls available under class II, most notably the extensive 510(k)

and quality system requirements we discussed yesterday, and determine that they are adequate to control these devices in class II.

Over a decade ago, this panel requested down classing arthroplastic components for biological fixation. A transcript of that request is in the blue booklet which was provided to you for this meeting.

Industry responded with the petition for down classing hips by two manufacturers that resulted in a reclassification in February 1992. The petition submitted this week furthered that effort.

As noted in the petition, uncemented use of these devices is already a widespread practice at large and small institutions alike.

We believe that the most significant effect of this petition will be to allow manufacturers to openly and legitimately support educational courses and literature to address the specific requirements of cementless fixation.

This can only serve to improve the success of this already successful procedure.

I don't want to take issue with Dr. Strobos, but this is simply a direct quote from Orthopedic Network News.

We also included in this petition mobile bearing knees. There is extensive and rapidly growing experience

with these designs outside the United States, as well as experience with one design within the United States.

We believe that this combined experience warrants reclassifying these devices to expand the use of this evolutionary design in the United States.

When we met with the FDA to determine the requirements for this petition, we were advised that the most important were to identify the risks to health and to show that class II regulatory controls can control these risks.

From the literature we reviewed, we identified these risks to health. I might mention we also reviewed NDRS. They did not add anything to what was also in the literature.

We then identified these class II regulatory controls for the identified risks. In the petition we identified which controls are currently available for each specific risk.

Perhaps the most extensive of these are the FDA's quality system requirements which requires, among many other things, design controls and adequate response to complaints, and 510(k) requirements.

FDA's track record for keeping unsafe devices off the market, while not perfect, is extremely good. That

combined with the corrective actions taken by responsible manufacturers makes the regulation of class II devices in the United States extremely robust.

In covering the less responsible manufacturers, there are NDR requirements that require reporting the device failures to the FDA.

I am extremely pleased to be able to introduce the following presenters. Their credentials and reputations need no introduction.

Nevertheless, their CVs are included in the blue booklet with the panel transcript. The expenses for these presenters to come to this meeting were paid by OSMA, or will be paid by OSMA.

No other financial remuneration has been given to them. Like many of you, they are away from more lucrative activities to be at this panel meeting, and we appreciate their efforts.

The first presenter will be Dr. Joshua Jacobs from Rush Medical College in Chicago. He will cover the cementless aspects of this petition.

The second presenter will be Dr. John Insall from the Insall Scott Kelly Institute in New York. He will address the mobile bearing aspects of the petition.

The third presenter will be Dr. Robert Bourne from

the London Health Sciences Center in London, Ontario, Canada. He will also address the mobile bearing knee aspects of the petition from the position of a mobile bearing knee designer and user from outside the United States.

DR. JACOBS: Thank you very much, Dr. Craig. I am Josh Jacobs from Rush Medical College in Chicago. My charge is to talk about issues related to fixation and total knee, in particular comparing fixation with cement to fixation without cement.

I need to disclose potential conflicts of interest. Myself and my collaborators at Rush in Chicago have been designers of knee systems in the past, and currently have received royalties from one manufacturer as well as research funding.

Having said that, I am going to break up this talk into essentially three segments. First, I am going to talk about the basic biology of bone ingrowth, briefly talk about the mechanics of the interfaces based on retrieval analysis, and then finally, talk about the clinical results, both at our institution and what is reported in the literature.

Why would an orthopedic surgeon want to use a device without cement in the first place?

There are some advantages, and those are

preservation of bone stock, particularly when one avoids the use of stems and one does not need to use cement, which can interdigitate with the upper end of the tibia and femur.

There is ease of revision because of the lack of bone cement, and also there is a potential for better durability of fixation because this is a natural or biological fixation process.

Bone ingrowth has been extensively studied in the late 1960s and early 1970s in animal models, and subsequently there have been a number of retrieval studies in humans, which I will discuss.

The phenomenon of bone ingrowth has been well described and is essentially a variation of intramembranous bone formation with the following steps that I will not go through in detail.

What has been learned through both animal and human studies is that there are certain prerequisites for bone ingrowth, including adequate material, having adequate interconnectivity -- pore size is listed between 100 and 400 microns -- minimizing gaps at the interface so that bone implant surface contact is maximizing, and minimizing relative displacement or micromotion.

It should be noted, in a variety of animal studies, a number of materials and types of porous surfaces

have been studied. All have been shown, with appropriate pore size, to be effective in promoting bone ingrowth.

These include plasma spray, beads, fiber mesh, et cetera.

Bone ingrowth is a time dependent phenomenon, as is seen here. This is from one of our human studies. From one of our canine studies we see, along with this time dependency of bone ingrowth, there is a time dependency of the strength of fixation. So, there is a direct correlation between bone ingrowth and strength of fixation.

Here are some histologic slides. These are from human retrievals. This happens to be a fiber mesh. Here are the fibers and here is the interstices.

This is an early phase, within two weeks, showing woven bones. Later on, at six weeks, you see more mature lamellar bone and, in some of the longer term retrievals, one can see mature osteonal bone and, in some cases, nearly completely filling the void space.

It has been shown in a number of animal models -- and here is one, this happens to be one, a bone chamber -- that micromotion and minimizing this is critical in achieving bone ingrowth.

In this particular study one can see that when there is no motion you get bone ingrowth in, in this case,

eight of nine.

However, with large motions of 500 microns, you see only one of eight getting bone ingrowth. However, if this motion is minimized at 250 microns, you see all three of these animals had bone ingrowth. So, there is a direct correlation between micromotion and bone ingrowth.

This has been addressed directly by a variety of design features on particularly the tibial component, where it has been shown that the incorporation of pegs or screws can substantially minimize the displacement at the bone/cement interface.

In this case, with four pegs or four screws, you can see that the micromotion is under 100 microns, which is within the so-called safe zone or safe window to achieve reliable bone ingrowth.

If one looks at the literature and looks at the literature with retrievals, one sees that there is a great variability in the amount of bone ingrowth that has been reported.

The earliest studies came out in the mid to late 1980s showing quite disappointing results with looking at retrieval components, particularly tibial components.

In this case, we can see ranges of the instance of bone ingrowth activity is from less than 10 percent to up to

100 percent. I think it is useful to look at the individual studies in a little bit more detail.

The study from Dartmouth was one of the first reports. These are 40 specimens that actually were the worst cases.

These were devices that had failed, some of them early, for a variety of reasons. While the femoral components were uniformly well ingrown and most of the patellar components were actually half and half, they identified a problem with tibial component ingrowth.

Similarly, in the study from Tulane, they identified a problem with lesser degrees of bone growth on the tibial components.

However, we and others have looked at this issue of tibial bone ingrowth. The way we measure it is to report two things.

One is the volume fraction which is actually the percent of void space occupied by bone. Another measure which we call extended bone ingrowth is actually a measure of the topographic distribution of bone ingrowth; in this case, the percent of one millimeter fields that are occupied by bone.

We use those two measures to report bone ingrowth on 13 first generation cementless tibial trays and primary

cases.

These 13 were removed for reasons unrelated to loosening or infection; typically for unexplained pain or for ligament instability.

All were well fixed at the time of removal with a mean age of 59, mean time in situ, 50 months.

In contrast to previous studies, all these cases had bone ingrowth, with the extent averaging slightly less than a third, with a large range, with the volume fractions about a third of that.

Note additionally that there seems to be a higher volume fraction in the vicinity of pegs.

There is one such case where you can map the bone ingrowth on the undersurface of the tibia. It seems to be more around the pegs and within the pegs. That was a reproducible finding.

The representative histology from this human retrieval is showing a high extent of bone ingrowth and, in this particular section, a high volume fraction.

If we looked at our other retrievals where they were removed for other reasons, such as loosening or if they were infected, we see a dramatic difference and much less bone ingrowth.

So, the reasons for removal is an important source

of variability in implant retrieval studies. This helps to explain some of the differences in the studies observed.

We also observed that there are some surgical technical factors that can affect the extent of bone ingrowth, including the inverse relationship between posterior and lateral resection depth and the amount of local bone ingrowth.

We believe this is due to the quality of the bone that the tibial component is supported on.

Actually, we believe that the best information to determine the amount of bone ingrowth comes from our autopsy retrieval studies.

These are representative of the great percentage of individuals that have had successful cementless total knees.

We have had the opportunity to look at seven cementless tibial components from five cadavers retrieved at a range from four to 89 months.

All had excellent hospital for special surgery needs scores prior to death.

We happened to be using the Miller-Galante design shown here. I will not bore you with the details of that design.

This is only to say that the quantitative

evaluations were similar to what we reported before. That is, we measured the extent of bone within the porous coating and also the bone tray interface.

We were reporting this as the extent -- that is, the extent of one millimeter fields -- that are occupied by bone.

Note in these autopsy retrievals, the extent of bone ingrowth was in excess of a third. The range is much less than what we see in our retrievals which were revisions for cause.

The extent of bone ingrowth was actually greater at the tray bone interface, nearly 40 percent. Other tissues are present as well, including fibrous tissue, and about 10 percent of the interface is taken up with what we determined was microgranuloma.

We also get considerable insight into the mechanics of the interface looking at these retrievals. This is a study that we presented at the ORS where we looked at four cementless and three cemented retrievals at autopsy. All were clinically successful.

We measured six degrees of freedom in motion using six LVDTs with a system accuracy of less than two microns, using a set-up as shown here.

I will not go into the details of this system,

only to show you on the left a loading regime and to indicate that we tested the cementless systems with and without screws.

Here is a summary of our results. We have plotted here a total average motion, which is the displacement of microns, versus the time of implantation.

One can see that with the exception of the earliest retrieval of the cementless device, that the cemented and cementless are all within the same range.

That is, three of four of the cementless were in the range of the cemented.

The effect of screws were interesting. Only in the shortest term -- and this is the four month case -- was there any effect with increased displacement when one removed the screws. At longer follow up, this really had no effect.

We conclude from these interface mechanical studies on these autopsy retrievals, that substantial stability can be obtained regardless of the type of interface, whether it is cement or cementless.

Furthermore, screws did not have any effect in the longer term cases.

These autopsy results can be supported by information available in the literature on clinical follow

up using a technique known as Renken stereophotogrammetry, which has been perfected and utilized mostly in Sweden.

In this study, what they showed was that cementless components fixed with screws had a stability equivalent to cement.

These are important studies in that they can show relative motion or tibial components of decidence with a resolution of about .2 millimeters, which is an order of magnitude greater than the current radiographs.

With this very sensitive radiographic tools, they also show that cementless and cemented components are equivalent in terms of their stability.

Finally, I would like to discuss the experience and the clinical results with these implants. I will spend a great deal of time talking about our experience at Rush using an identically designed component, but one with cement and one with cementless use. These are five to ten-year follow up data.

We have 134 knees. On the left will be the cemented and on the right will be direct comparison with cementless.

One hundred thirty four knees that are in the cemented group with five to ten-year follow up, average 80 months, versus 101 knees in the cementless group with

similar follow up, actually slightly longer.

I should emphasize that this is a prospective but it is not a randomized study. The patients in the cemented group are older. Their mean age is 72. The mean age in the cementless group are 58.

So, these patients in the cementless group are high risk patients. They have placed the greatest demands on their prosthesis. So, this needs to be kept in mind as we look at these results.

If we look at the clinical knee score, it is similar pre op and it is similar at the post operative follow up; really no difference between cement and cementless.

If we look at the breakdown of clinical results, we see similar percentages of good to excellent results. There were slightly more failures in the cementless group, and we will discuss these in some detail.

In terms of pain, we see similar results. However, in the cementless group, there were slightly more that had moderate pain.

Again, these were younger, more active individuals who placed more demands on their prosthesis.

In terms of limp, it was similar, with both methods of fixation. With support, actually, this would

favor somewhat the cementless group with 75 percent of them using no support.

We attribute this to the fact that because they are younger, they tend to be less debilitated and are less likely to have other joint involvement.

Range of motion was quite similar at five to ten year follow up between cemented and cementless, as was the achievement of active flexion.

In fact, slightly higher degrees of flexion were achieved in the cementless group; again, probably reflecting their younger age.

The reoperation rate was high in both groups. The predominant reason for this was due to problems with the extensor mechanism, as many of you are aware, primarily with problems with the patellar component.

In these first generation cementless designs there were significant difficulties with the patellofemoral component, and I will discuss those a little more as we go.

Now, these failures actually represent tibiofemoral failures. Whereas we have revised a number of patellar components and continue to do so, revision of the tibia and femur are much less common.

Note that for the cemented series there were no revisions for loosening, whereas in the cementless series,

to date we have had three loose tibial components, for a tibial loosening rate of three percent at 89 month follow up.

We also had revised four femurs because of articular wear, from unintended metal/metal articulation from failed patellar components.

If we look at the radiographic evaluation in comparing the two, we see that in the cemented group there are no complete tibial radiolucencies, whereas there are five in the cementless group.

Similarly, in the cemented series, we saw no osteolysis, whereas in the cementless series we saw an incidence of seven percent with screw lucencies in 12 percent.

Now, it should be noted that the seven percent incidence are lesions that are quite small. There have been no revisions for osteolysis in this series. Again, we believe this is due primarily to the fact that this is our high demand patient population.

Looking at the overall survivorship, at 10 years it is 96 percent for cemented, 92 percent for cementless.

So, what have we learned from our experience. In our hands, we believe that using cement and cementless techniques is essentially equivalent.

We believe that the differences that we see in the patient groups is because of the differences in demand. That is, the patients with cementless devices are younger, more active, and are our high demand patients.

We learned about the high rate of failure of metal backed patellar components. This has been addressed to a large extent in second generation designs, redesigning the patellofemoral component, the trochlear groove, improving the fixation of the pegs, the stem and, in particular, designing components with thicker polyethylene.

We have learned that those were critical factors in the failure of the first generation design.

We have also learned that femoral fixation is not an issue. In our series, and others as I will discuss, fixation failure of the femoral component are quite rare.

We have learned that the function is quite similar. With regard to the tibial side, we have found that while there are no loose in the cemented group, three were loose in the cementless group. Again, we believe this relates to the difference in the patient populations.

Now, what does the literature tell us? In the petition you will see an extensive review of the literature. I am going to go through some of what I consider the most important and salient studies very briefly.

Rorabeck and Bourne, who will talk to you later today, presented a series in 1988 in JBJS. This is an earlier series looking at comparison of cemented -- these are kinematics versus cementless PCA knees.

This study is similar to ours in that this is a selected patient population. The cementless knees are much younger and, presumably, more active and higher demand.

DR. BOYAN: Excuse me, Dr. Jacobs. I don't mean to cut you short. I do want us to be aware of the fact that it is now 9:00 o'clock and there are more speakers to come after.

DR. JACOBS: I can wrap up very briefly.

DR. BOYAN: That would be wonderful. Thanks.

DR. JACOBS: I apologize for going over. There have been some paired studies which have shown quite similar results.

I do want to show this study, which is an 11-year mean follow up study showing excellent long-term fixation, with a cementless total knee.

Likewise, long-term follow up studies from a number of studies using a variety of devices, showing excellent fixation on the tibial side.

The main problem and the contemporary issue that we are seeing in total knee replacement does not relate to

fixation in 1998. It relates to issues of where fixation can be achieved with both cement and cementless techniques.

Any innovations that we can encourage with regard to improving wear is something that is highly desirable to improve the current results that we are getting with cementless fixation as well as cemented fixation. Thank you for your attention.

I am going to turn the discussion now over to Dr. Insall of New York.

DR. INSALL: Good morning. My name is John Insall. I am a professor of orthopedics at Albert Einstein College of Medicine in New York.

I should reveal that I have a royalty agreement with a manufacturer for designing knee prostheses. This includes a mobile bearing knee.

I am going to make my presentation on a video. Unfortunately, we only have a small monitor. I think the panel, at least, will be able to see this well. Would you run it, please?

I am going to discuss the rationale and a little bit about design of mobile bearing knees. One might begin by asking why one would think of a mobile bearing knee, given that the fixed bearing knee has a very successful record, particularly with metal backed tibial components.

This is a minimum 10-year follow up from my own institution which I think is representative. Most 10-year follow ups indicate that 90 percent of cases are good or excellent and the survivorship of the prosthesis is 95 percent or better at 10 years.

Remember that these cases are mostly in an elderly population, and still there are problems of polyethylene wear, of osteolysis, and perhaps of kinematics.

The type of polyethylene wear that we are most familiar with is articular wear. This was a problem mainly in the flat-on-flat design of the 1980s, and this is an example.

The solution to this seems to be a round-on-round design, which gives you a better contact area and is more forgiving of technical error.

Designs like this have good conformity and extension; not complete, but good. The reason they are not completely conforming is because of the need for rotation.

By conformity I mean, the ratio of the tibial component with the femoral component, which is close in extension, but fixed bearing knees have a decreasing radius of the femoral component as the knee is flexed.

So, the contact area gets smaller as the knee goes into flexion in the sagittal plane. But in the frontal

plane, this does not happen. You have almost complete conformity and extension and this remains the same throughout the range of motion.

You might criticize the design of this kind on the kinematics that are present. You must realize that rotation and conformity are incompatible.

This may not matter in older patients, but it may in younger and more active people; for example, those who like to play golf.

The second type of polyethylene wear is related to modularity. Attention was drawn to this by Jerry Eng, who pointed out that all contemporary knee implants with metal backed tibias have some movement between the polyethylene and the base plate.

This is one of my own knees. You can see a considerable amount of motion occurring. There is abrasion and co-flow of the undersurface of the polyethylene.

In this case, it produced a large osteolytic lesion in the medial tibia, and I would point out that we never saw this type of problem with a monoblock metal backed tibial component. It is a problem of modularity.

So, how do you solve the problem of kinematics, geometry and modularity? The obvious solution that suggests itself is a mobile bearing knee.

Let's look at the contact area. This is the sort of contact area a good fixed bearing knee will have, something on the order of 200 square millimeters.

You can increase this between five and seven fold if you don't need rotation and you have a mobile bearing type of design.

So, you can increase the contact area from 200 to over 1,000 square millimeters, and the resulting polyethylene contact stress is reduced from dangerously high levels to under four megapascals with a mobile bearing design. It is a difference between a high heeled shoe and a boot.

So, you can address the issue of modularity because, in a mobile bearing knee, you have a highly polished, cobalt chrome base plate, upon which the meniscus, the mobile bearing, is placed.

So, you can get a high contact area and you can get free rotation in the same design, which is actually impossible with a fixed bearing knee.

One might discuss the design issues of mobile bearing. There are various possibilities. Let's look at the rotation axis.

The LCS rotates about a central pivot. This seems to function well, but it has the drawback that roll forward

on one side is produced by roll back on the other side. This is not physiological.

You can offset this by moving the axis medially to some degree. For anatomical reasons, you can't move the axis very far.

So, you can reduce the roll forward to a degree with this type of mechanism.

It is perhaps better to have a combination of rotation and glide. This is what the natural knee does. The mechanism that allows this is certainly the most physiological.

Should you have full conformity throughout the range of motion? By that, I mean that at least through a 90 degree arc with contact area between femur and tibia remains the same.

Possible criticism of this is the range of motion that is achievable. There may be a place for what one might call a hybrid design.

Probably this is best suited to a posterior stabilized type of knee, which conforms in extension but behaves as a fixed bearing knee as the knee is flexed.

You can improve the characteristics of a fixed bearing knee if you have a rotating platform. You can now have full conformity and extension, again because you don't

need rotation.

As the knee is flexed, in order to get good motion, the contact area will decrease in the sagittal plane.

In the frontal plane, again, in extension with another mechanism to get rotation, you can have full conformity.

You can maintain full conformity throughout the whole range of flexion, again, because rotation occurs, not at the articular surface, but elsewhere. So, you can have a better contact area than a comparable fixed bearing knee.

The question of anti-dislocation stop comes up and you may want to provide a post or a mushroom to restrict movement of the meniscus, and perhaps a stop, to prevent subluxation, and perhaps a snap-on mechanism that further prevents bearing dislocation.

What do we know about results of mobile bearing knees? Well, information is available on the Oxford knee, and polyethylene wear is negligible, from retrieval analysis. On the LCS, the clinical results are excellent.

Complications have been reported -- instability, bearing dislocation, and bearing breakage.

I can give you some short-term results on the MBK, which is a sliding, gliding knee. These were done in Italy,

and I was present at the surgery and at the follow up.

We have two series of cases studied in details. The demographics are typical of the population for knee arthroplasty, mainly osteoarthritis.

The Knee Society score went from 40 to 89 post-operatively. This is the proportion of excellent and good results.

There were two poor results. One was a knee that was left in varus for technical reasons. The other knee had pain, but the patient had an arthritic hip on the same side.

You will see on the left the knee that was left in varus. This was a technical error and automatically makes the result poor.

The average range of motion was 110 degrees. The problems we noticed were a lack of hyperextension in the MK I, and this was modified, and a tendency to translocate in the MKII. Another minor modification was required.

The knee then went to a multi-center evaluation in several different countries, and there are now about 500 cases.

The conclusion that we have is that these knees behave like a fixed bearing knee, except that some improvement has been shown in the gait lap.

So, that is what I have to say to you. Thank you

very much. I am going to pass this over to Bob Bourne.

DR. BOYAN: While we are stretching, I don't want you to stretch too much, though. What I am going to do at the end of your presentation is the FDA presentation.

Then right after -- Ms. Nashman and I have just been discussing the fact that we have started early and this is right about this time of the day.

So, what we will do, at the end of the OSMA presentation is, we will give everybody five minutes; five. I really mean five minutes, not 25. So, plan your brain. All you have to do is wait until the end of Dr. Bourne's presentation.

DR. BOURNE: I am Dr. Robert Bourne. I am a professor of orthopedic surgery at the University of Western Ontario.

I would like to admit that I have been a co-developer, with Dr. Cecil Rorabeck, of the SAL knee replacement over the last decade or so.

Our laboratory has received industry support from at least six different companies over that period, and I am obviously a consultant with regard to this particular knee replacement.

Basically, I am amazed at the similarity between the presentation and the observations that Dr. Insall and

our group have made.

Basically, the early knee replacements were primarily non-linked hinges, which were extremely congruent.

As clinicians found that they often had to sacrifice the posterior cruciate ligament just to get them to bend, they did have the advantages of very broad surface areas because of their congruency.

However, the congruency did limit some range of motion and led some investigators to look at other designs, namely, the round-on-flat articulations, thinking this would give more range of motion.

The theory was that you would preserve the posterior cruciate ligament and you would get roll back and, hence, increased range of motion. This worked in many instances but not always.

There were, unfortunately, some adverse complications to this -- and Dr. Insall had the same observations -- that the contact stresses were remarkably increased between the femoral and tibial components.

There often was uncontrolled sliding, posterior medial wear was quite common, and there were a number of cases of catastrophic failure.

This basically left the surgeon with a dilemma. The congruent articulations had good weight bearing areas

and low contact stresses, but had difficulties with range of motion.

The incongruent articulations might enhance range of motion, but they had the risk of wear.

This is just graphically showing the dilemma. The arrows go in opposite directions for these two types of implants. We often end up with catastrophic failures you see on your right.

It appeared to us, in the late 1970s and early 1980s, that a mobile bearing knee might be the best of both worlds.

I was a fellow of John Goodfellow and John O'Connor in 1976 and 1977, and was involved in the early development of the Oxford knee replacement, which you see on your left. This was put in in 1978 and still functions.

We presented the first publication in the mid-1980s of the five to seven year follow up of our experience, suggesting that in osteoarthritic knees, this was not a good solution, and we abandoned this particular prosthesis in 1979.

The implant you see on your right is the SAL, or self-aligning knee replacement, which we conceptualized in 1984 and have worked on since that time.

The advantages of a mobile bearing knee such as

you see on your right -- this is the original self-aligning knee or SAL knee replacement -- was that it had a congruent articulation.

This was from five degrees hyperextension to 90 degrees flexion. It had a very large weight-bearing area. It had reduced contact stresses well within the tolerances that we know for polyethylene.

It would allow rotation and translation, and it would be self-aligning. The idea that it is very simple or very easy for a surgeon to misalign the femoral or tibial component by five degrees, this can have an adverse effect on not only tibiofemoral motion but also patellofemoral function.

There have been a number of mobile knee replacements on the market. Several have been discussed. We have first-hand experience with the Oxford knee, and this is one of my patients on the right.

I think it is very wise to point out at this time that all mobile bearing knees are not the same.

There are meniscal designs, such as this, or one version of the LCS, and there are rotating platform designs.

We feel strongly, from our experience, that the rotating platform design is the way to go.

Some have argued that the mobile bearing knees are

more demanding and that there is a dislocation risk. This has not been our experience.

We are in a teaching environment. Residents do this as easily as they can do a fixed bearing knee replacement.

We have experienced occasionally with our design in patients with a flexion contraction of the hip, movement of the bearing with a hard end point, some sound, but no adverse clinical effect.

So, the advantages are decreased contact stresses. We have three patients where we had femoral component loosening, and I will discuss these in a moment.

This is a patient of mine that I revised at five-and-a-half years. You can see the excellent wear characteristics. There is some third body wear, but it seems to stand up. So, the rationale is decreased wear, basically.

We endeavored to have a study to look at the SAL knee. We introduced a stepwise introduction. After we had developed our implant, we did preclinical testing, including Fuji film analysis, simulator studies, and we are happy with our design.

Dr. Rorabeck and I then implanted our first 10 SAL knee replacements in 1988. We watched them for a little

over a year. We made certain enhancements.

We then did 100 consecutive knee replacements, and have continued to use the knee since that time. In 1993, a multi-center trial was introduced in Europe.

I am going to report on a series which included our first 234 SAL knee replacements. As is our tendency, we like to have a very clean population.

I am just going to restrict this discussion to patients with osteoarthritis, because the other groups were much smaller numbers.

This is a snapshot of the patients that we operated on. This is an SAL knee replacement on your right. This is a fixed bearing knee replacement on your left, which is showing early signs of wear.

One of the stimuluses to go to a mobile bearing knee, you can see the sex distribution. The age was 71 years of age, the height and the weight.

As is the case with most studies, the majority of these patients had a varus deformity. In terms of the Knee Society clinical ratings, our scores are almost identical to Dr. Insall, who used the Hospital for Special Surgeries scores.

This is a score out of 200, instead of 100 as Dr. Insalls. Pre-operatively the mean score was 81. Two

years, 160, and this has held out to five years. There is no reason, in those patients who are five to ten years, that we suspect that these are going to deteriorate.

In terms of range of motion, you can see the pre-operative range of motion, six to 110 degrees. This improved and basically beyond one year it is fairly constant. It is much like other knees. What you start with is what you end with.

It is our perception that these bend maybe four to five degrees more than fixed bearing knees that we have been used to.

We have had some problems and most of these were early. We had two infections, which I don't know if we could do anything about, but we did have some early problems with stiffness.

We had two vertical patellar fractures and we have had three loose femoral components.

I think we have learned lessons from each, particularly the seven where we had stiffness problems. I am perhaps being a little hard on myself calling this a reoperation, a manipulation under anesthesia, but I think it is fair for the purposes of this discussion. We have had two arthroscopic arthrolyses.

The lessons we have learned, or perhaps reinforced

to ourselves, is do not over-stuff the flexion space. The soft tissue balancing is extremely important in a design such as this, and we need at least five sizes of femoral component instead of the three that we started with.

This is when I said we did ten and then made some modifications. This is one of the modifications we made.

We also, in this series, were encouraged to go press fit on the femoral component. I stress that there was no coating on these femoral components.

Dr. Michael Friedman, this basically is identical to his component. He encouraged us that all we had to do was press fit these. That turned out to be a mistake.

Three of the 56 have had to be revised. Whether this is condemning cementless fixation, it really isn't. It is press fit fixation.

My lesson is do not press fit the femoral component. Our tendency is to cement the implant, but I can see no reason why we could not have a coated surface that would work just as well.

In conclusion, I think in 1998 that we should not only consider posterior cruciate ligament preserving and sacrificing implants, but I believe the time has come to consider the mobile bearing knee replacement as well in the treatment options available to patients with severe

arthritis.

I think we have a nine-year track record. The implant appears durable. The outcomes are just as good, if not better, than any fixed bearing knee replacement we have had.

We think the self aligning ability has reduced our patellofemoral problems.

The final point is that we think the range of motion is at least as good, if not slightly enhanced.

We think that the successful clinical results at five to nine years make it reasonable to consider releasing mobile bearing or rotating platform knee replacements such as the SAL knee replacement.

Finally, I think this whole concept -- this is the SAL-II knee replacement, with a femoral component which is not dissimilar to what Dr. Insall has described, with the rounding rather than it being a cylinder and a trough. It also has a medial lateral curvature.

We think it is extremely intellectually attractive. It has very promising clinical results. The concept that it is more demanding technically we have not found to be the case.

Its place, I think, will be primarily in expanding the indications for knee replacements. Particularly for

those patients who are less than 60 or 65 years of age, there is no other option.

I think this has a certain place. Whether it is necessary in people who are 70 and over remains to be seen. We really think this line of development should be encouraged. I thank you very much.

DR. CRAIG: In the interests of time, Dr. Boyan, I am going to forego my last couple of slides. I do want to note, however, that we realize that we have provided you with a lot of data, and we realize that we have provided you with a lot of different options by covering tricompartmental cementless, unicompartmental cementless and both cemented and cementless mobile bearing knees.

We have probably complicated your deliberations. We would encourage you to do like you did yesterday, divide it out as you see fit, and consider any separate issues that you consider significantly different from others.

On behalf of OSMA and the OSMA membership, I would like to thank you in advance for your time and deliberations.

DR. BOYAN: Thank you very much, Mr. Craig. At this point, before the FDA presentation, if we can have -- remember, five minutes, and we will start promptly in five.

(Brief recess.)

DR. BOYAN: We will resume with the FDA presentation. Mr. Allen?

Agenda Item: FDA Presentation.

MR. ALLEN: I am Peter Allen. I am a mechanical engineer and reviewer in the orthopedic devices branch of the Division of General and Restorative Devices, in the Office of Device Evaluation.

I will present to you today a brief summary of the FDA's review of the reclassification petition for uncemented porous coated patellofemorotibial knee prostheses submitted by OSMA.

I would like to thank OSMA for their presentation and for their efforts in preparing this reclassification petition.

This petition, as submitted, is actually broken into two groups of knee devices. The first consists of a total knee design which contains patellar, femoral and tibial components, and is intended to replace the entire knee joint.

The second consists of a unicompartamental or unicondylar design and contains only femoral or tibial components. It is intended for replacement of either the medial or lateral compartment of the knee.

As proposed, both groups are to include mobile

bearings. These mobile bearings are polyethylene tibial and/or patellar bearings that articulate with their metal base as well as with the femoral component.

The femoral components of these two generic knee designs are made of cobalt chrome alloy or surface hardened titanium alloy.

The tibial components consist of an ultrahigh molecular weight polyethylene bearing insert fixed to, or articulated with, a metal base of cobalt chrome or titanium alloy.

The patellar component of the total knee design also consists of a polyethylene bearing, affixed to, or articulated with, a metal base of cobalt chrome or titanium alloy.

A description of the porous coating for the metal components, specified in the device identification section on page four of the petition is the same as that currently used for the class II uncemented porous coated hip prostheses.

Both total and unicompartmental knee designs are intended for the following indications: degenerative arthritis or post-traumatic arthritis, rheumatoid arthritis, failed osteotomies and failed unicompartmental or total knee replacements.

These are the same indications for which cemented knee prostheses are intended.

It should be noted that the unicompartmental design is intended for use when only one compartment of the knee is affected by these conditions.

All of the knee devices covered by this reclassification petition are post-amendment class III devices.

That is, they require an approved premarket approval application, or PMA, before they may be legally marketed in the United States.

To date, four PMAs have been approved for uncemented use. Two of these PMAs involved only fixed bearing designs. One included both fixed and mobile bearing designs, and one included a unicompartmental mobile bearing design.

IN addition, one of the PMAs that included mobile bearing designs was also approved for cemented use.

The sponsor has provided a bibliography containing over 300 references in support of the preclinical and clinical issues in this petition.

These references include clinical studies reported in peer reviewed journals, case studies, testing and materials standards, industry technical reports, book

excerpts and open meeting transactions.

I will not describe any of these in detail. However, I would like to provide a very brief summary of the information addressed by these references.

Some of the preclinical issues addressed include mechanical properties such as device endurance, integrity of the porous coating and material biocompatibility.

With regard to clinical data, the sponsor provided a table which summarized a series of 48 studies. Available demographic, safety, effectiveness and survivorship data was provided for each study.

Four studies of fixed bearing, uncemented, porous coated unicompartmental knee devices were presented, along with 26 studies of fixed bearing, uncemented, porous coated, total knee devices.

Ten studies containing data on cemented mobile bearing knee devices were also summarized in the table. All 10 studies on the cemented mobile bearings were for total knee designs.

One of these studies also contained data on cemented, unicompartmental mobile bearings. However, this was limited to only seven patients.

With respect to uncemented porous coated mobile bearing knee devices, two studies included the

unicompartmental design and six included the total knee design.

The data provided indicates that cemented and uncemented knees are used for similar indications for a similar range of patients.

Both fixation methods, when used appropriately, achieve similar complication, pain, function and survivorship results, with the exception that the uncemented use requires a longer time to be pain free.

From the evaluation of these studies, the sponsor has identified the following risks to health for uncemented knee arthroplasty.

These include infection, which is not unique, in that it occurs equally between the cemented and uncemented devices, early loosening, which is unique to uncemented devices and which can occur due to inappropriate surgical technique, incomplete biological attachment, or poor bone quality, metal based patellar failure, a complication that is often associated with the earlier designs, wear.

Although polyethylene wear is not unique to uncemented devices, the mobile bearings appear to have a greater potential for dual surface wear, although this was not seen in the references cited in the petition.

Bead delamination is unique to porous coatings.

Disassembly and bioincompatibility occurs equally with the cemented devices. Dislocation and instability, although not unique to the uncemented designs, has been cited as an occasional complication in the mobile bearing designs.

There may also be other additional risks that have not been addressed in this petition.

Controls for consideration of reclassification include recognized standards, labeling requirements, guidance documents, quality systems regulations and design controls.

Other additional controls may exist or may need to be added to this list.

Information of pain from FDA's medical device reporting data base from 1994 to 1997 reveals 652 reports under the product code for total cemented knees, of which 532 contained information on device related problems.

However, no reports were found corresponding to product codes for total uncemented porous coated devices or unicompartmental uncemented porous coated devices.

It appears that the MDRs for these products have been lumped under other product codes. As a result, we do not have any meaningful data to report on these two specific device configurations.

This reveals some of the obvious limitations of

the MDR data base. These limitations include the failure to capture the reports under the correct product code categories, incomplete or inaccurate reporting, and the lack of a known denominator for the number of devices on the market.

Based on the data provided by the sponsor, FDA has four questions that we would like the panel to address in order to help us reach a decision on this reclassification decision.

We ask for your input on these questions after you have completed your discussion. Please refer to the questions included in the presentation packet provided to you this morning.

The questions are as follows:

Number one. Do the proposed classification definitions sufficiently describe the devices recommended for reclassification?

If not, what additional changes in the definitions do you recommend?

Number two. Are the risks to health, of the following device configurations proposed for reclassification, adequately described?

If not, what additional risks should be included?

A. Patellofemorotibial uncemented porous coated

total knee prosthesis.

B. Femorotibial -- unicompartmental -- uncemented porous coated knee prosthesis.

C. Mobile bearing knee prostheses -- uncemented and/or cemented -- within each of the above two device configurations.

Three. Have appropriate special controls been identified to adequately address the risks to health for each of the above referenced device configurations?

If not, what other special controls are necessary to address the risks presented by these devices?

In addition, please respond to the following questions regarding special controls:

A. Dissociation of metal-based patella components has been cited as a complication in early uncemented knee designs.

Have appropriate controls been identified to adequately address this risk? If not, what additional controls, if any, are necessary to address the risk?

B. Dislocation and subluxation of mobile bearing components have been cited as common complications in the literature.

Are appropriate controls identified to adequately address this risk? If not, what additional controls, if

any, are necessary to address the risk?

C. Labeling information typically includes such things as device description, material, indications for use, contraindications, adverse events, warnings, precautions, et cetera.

Is any additional labeling information necessary for the design configurations listed in question number two? If so, what would you recommend?

Lastly and most important, number four. Does the data presented in this petition support the reclassification of:

A. Patellofemorotibial uncemented porous coated total knee prostheses?

B. Femorotibial or unicompartmental uncemented porous coated knee prostheses?

C. Mobile bearing knee prostheses -- uncemented and/or cemented -- within each of the above two device configurations?

At this time, I would like to thank the panel for your time and attention. This concludes FDA's presentation. I will now turn the floor over to the chair for discussion.

DR. BOYAN: Thank you, Mr. Allan. Let's begin the discussion with -- we will begin with Dr. Stern and ask you to ask any of the members of the petition team or the FDA or

us or anyone else that you deem appropriate, your questions. Thank you.

Agenda Item: Questions and Voting.

DR. STERN: I guess I have a question for Dr. Insall, although I do think probably in the interests of full disclosure, at least in terms of the panel, you guys should know that I know Dr. Insall.

I was actually his fellow in 1989 and 1990. So, kind of in the interests of all disclosure.

I have two questions for Dr. Insall. One, for years you have been one of the strongest advocates of cemented total knee arthroplasties. I wonder if you have any comment about uncemented.

My second question has to do with both you and Dr. Bourne spoke in detail about the rationale in certain instances for the use of MBK knees.

The panel is not -- the actual rationale for the use is not probably as much an issue to us as the similarities or dissimilarities between mobile bearing knees and fixed knees.

I wonder if you could address kind of that issue, how similar these types of knees are or are not.

DR. INSALL: The first question, Steve, as you well know, I have no personal experience with uncemented

knee prostheses.

I have never seen fixation problems in the knee. So, I have never been tempted to solve a non-problem.

That doesn't mean that I disapprove of uncemented knees. I just have no experience.

The second question, I think it is worth pointing out, because neither Bob nor I went into design details of the devices that we have been involved in.

It seems -- which is something that I really learned last night -- that the two knees are remarkably similar in all important features.

I knew Bob was working with a mobile bearing knee, but I didn't truly understand how it worked until I came to this meeting.

Independently, we have arrived at designs that are remarkably similar. We both, I think, feel that from the surgeon's point of view, they can be inserted just as you would insert a fixed bearing knee.

The principles of the surgical technique are really identical, with the principles described 25 years ago for the total condylar knee, which was actually my first entry into designing knee prostheses.

There is nothing unique for the surgeon and there appears to be nothing unique about at least these two

devices in the follow up.

They look and behave, the problems are identical with those of fixed bearing knees. The only difference that I have been able to see so far is that the gait lag evaluation which was done in Bologne, Italy shows that in some respects the mobile bearing knees behave a little closer to normal knees.

DR. BOYAN: Any additional questions? Let's go the reverse now. Dr. Hill.

DR. HILL: My question has to do with going back to Dr. Rorabeck's letter, and it is kind of directed to Bob Bourne.

He was commenting on his experience with the mobile knee in the non-cemented arena. In all the presentations, I didn't get a clear demarcation of the difference, and what studies have been done on the cemented versus non-cemented.

DR. BOURNE: Thanks, Jim. Dr. Rorabeck's letter dealt specifically with those 56 patients where we press fit a femoral component.

I stress there was no coating, no beaded surfaces, no wire surface. It was just a press fit. It was based on a suggestion by Dr. Michael Friedman that he uses it this way.

As you saw from my presentation, we have had to revise three of those 56 patients because they had basically recurrent hemarthrosis and they had some pain. I think it was just from movement of the implant.

That is the only thing I can see where his aspect was based upon.

Dr. Rorabeck and I have a large experience with cementless knee replacements. We have performed well over 900 cementless knee replacements.

We have published in the journal, Bone and Joint Surgery, on the Miller-Galante-I knee replacement. Our data basically mirrors what Dr. Jacobs presented.

Included in that large group of patients, we actually randomized 100, 50 getting hybrid implants where the femoral components were uncemented and the tibial and patellar components were cemented, versus completely cementless. We have not found any difference in clinical results.

DR. BOYAN: I have a couple of questions, and I am coming at this from a non-surgeon point of view.

As I reviewed your petition and as I listened to the presentations -- all of them -- today, it has struck me that there are multiple designs here.

Even though they may all share in common that they

are replacing a knee, there are a lot of subtleties that are hard to sift through. So, I have a couple questions first for Dr. Jacobs.

If you were to state what you think are the absolute requirements for what would be considered so basic for a cementless design, what I gleaned from what you said is they would have to have a pore size within a certain range and it has to have motion less than a hundred micrometers. Is that the basic bottom line, Dr. Jacobs?

DR. JACOBS: Yes. To that, I would add that it has to be with an appropriate material. Both cobalt alloy and titanium alloy have been shown to promote bone ingrowth.

On the other side of the equation is the host. You would also need to have an individual with adequate bone stock. I would equate those with kind of the basic bottom line of requirements for cementless fixation.

DR. BOYAN: Since that was an easier question and I did Dr. Jacobs first, now what is the bottom line on this mobile bearing knee.

DR. JACOBS: Who are you asking?

DR. BOYAN: I am asking whoever has the courage to answer.

DR. BOURNE: I will start. I think the bottom line is that you have an extra articulating surface, the

tibial base plate.

I think it should be made of cobalt chrome. I think there is ample evidence that they are better bearing surfaces than a titanium alloy.

First I would start with a polished cobalt chrome tibial base plate.

The polyethylene, you perhaps could go a little thinner in thickness than with a fixed bearing knee because of the better contact area and reduced contact stresses.

Our analysis suggests you could get down to a minimum of six millimeters, much like they suggest in the hip. Our preference is to build in eight millimeters, just to have a little extra.

I think the other basis is, you have to have some inherent stability, in other words, a congruent articulation, to give you some stability both in an anterior posterior direction and a medial lateral direction in your fixed bearing.

If you made a mobile bearing which was round on flat, for instance, it would be very unstable. You have to have some inherent stability built into the tibiofemoral articulation.

I think we could debate amongst the various mobile bearing knee designers whether this has to be from five

degrees hyperextension to 90 degrees flexion like ours has, or if you would be all right to get away with maybe congruence up to maybe 55 to 60 degrees.

You have to remember that in the gait cycle, the range of motion is from 10 to 65 degrees. There are differences going up and down stairs and things like that. I pass it over to Dr. Insall.

DR. INSALL: I would agree with everything Bob has said. I would add that I think you need some way of preventing bearing dislocation, as that seemed to be a major criticism of mobile bearing knees.

Whether this be a rotating platform type of mechanism or through a tibial post that does the same kind of thing, I think those are both acceptable ways of preventing bearing dislocation.

DR. BOYAN: I have one last bottom line question. Do you believe that you can prove all of those things without doing a human study?

DR. INSALL: I think you need to do a clinical evaluation, which is, in fact, what both Bob and I have done. We just haven't done it in the United States.

DR. BOYAN: Dr. Skinner wants to comment on my comment.

DR. SKINNER: I think there may be a bit of

fuzziness in the understanding among the committee as to what we are actually talking about here.

I will ask either Tom Craig or Steve Peoples to address this.

I think, if my understanding is correct, when we are talking about the approved PMA product that DePuy has, we are talking about a mobile bearing knee. But we are talking about two different mobile bearing knees.

My understanding is that we have the thing that is fixed to a post on the tibia and we have the thing where there are two loose pieces that can go wherever they might want to go.

If that was clarified, I think that we would see that there is something that Dr. Bourne is talking about, Dr. Insall is talking about, and then there is an entirely different product that is involved here.

MR. CRAIG: There are different PMA designs. I would prefer not to go into the specifics of those designs and defer that to Dr. Peoples.

Yes, to some extent, what is being talked about by Dr. Insall and Dr. Bourne, and I think if you look at the data in the presentation we have Dr. Minns and others, from around the world, with a variety of designs, all have the common feature that the bearings are mobile.

What we are asking for in the petition is that the bearings that are mobile also have some degree of constraint, whether that be a post or a track or, like one of the LCS designs, a post on the tibia inside a hole in the tibia component, or basically asking for a degree of constraint that has been proposed here as a necessary component of a mobile bearing design.

DR. PEOPLES: In commenting, really responding, to what is involved in the LCS PMAs, I guess I can speak to that with some authority. I was involved in writing the original IDE that ever went in on the mobile bearings on the LCS.

For those of you who have never sat through a review of a PMA yet on this panel, the LCS PMA that has been submitted establishing the designs in that PMA as being safe and effective now stands at close to seven feet tall for one copy of 30,000 pages of data and analysis.

That is what we are talking about here, is the quality and the level of analysis necessary to evaluate these design concepts.

In answering Dr. Skinner's specific question, the LCS knee within the PMA has coverage under that premarket approval for two different design concepts.

One is a meniscal bearing design, in which the

posterior cruciate ligament is retained, which are separate medial and lateral polyethylene mobile bearings, as well as a rotating platform design in which, in those cases, when the posterior cruciate ligament is sacrificed or is not intact at surgery.

In regard to some information that was presented earlier relating to mobile bearing knee literature that was cited in the petition, I noticed that it was presented in the FDA presentation that there were six studies quoted in the petition on uncemented mobile bearing knees.

I believe that there were six studies quoted in there on uncemented, but they were all on the LCS knee, whereas several of the other mobile bearing literature articles that were quoted were only on cemented uses of those devices.

DR. INSALL: I just wanted to respond to Dr. Skinner's comment about the two separate menisci, if you like.

My perusal of the literature suggests that the dislocation problems have occurred with mobile bearings of that type, rather than a single piece design.

I believe it is true, for the LCS, which has both types approved, that the majority, the big majority today are done with the single piece rotating platform rather than

the two separate menisci.

DR. BOYAN: As I turn this over to Besser, I want to clarify what it is that I as chairman think that we are doing here today. If FDA wants to correct me, this is your opportunity here.

I think we are being asked to consider a classification of a group of products into class II, whether we think that is an adequate thing.

What I am trying to clarify in my brain is what is the class of products, or what is the group of characteristics that fits into class II, as we try to sift through all of this information.

If you can help me, as you start answering the questions, if you have an opportunity, to clarify so we get this into a neat, usable piece of information that we as a committee can view what is actually going to go into a consideration for a class II or possible recommendation for class II. Dr. Besser?

DR. BESSER: A couple of questions directed to anyone who would like to answer them. First, am I correct, the SAL knee is not approved in the United States?

DR. INSALL: That is right.

DR. BESSER: Someone presented some results that were from Italy on the MK-I and MK-II prosthesis, where the

phrase you made was, a small modification was made based on, I believe it was a wear problem on one of them. Can you tell me what a small modification is?

DR. INSALL: Yes. The first modification -- they were both modifications made of the intercondylar eminence rather than the main concept of the geometry of the prosthesis.

The first modification was that we had not provided in the MK-I any hyperextension. We found that we needed it. This was simply to allow 10 degrees of hyperextension in the design.

The second problem was not a clinical problem, but we noticed that there didn't seem to be enough intercondylar stability during the surgery itself.

This didn't show up as a clinical problem in the patient, but we enlarged the intercondylar eminence to give more side-to-side stability.

I would have to say that that is a problem -- if it is a problem -- that is shared by many fixed bearing knees. It is not a unique problem to mobile bearing. The fixed bearing knees can also translocate side to side unless the eminence is big enough.

DR. BOYAN: Are you still on, Dr. Besser? I didn't want to stop you from asking questions.

Members of the audience, we can't have you speak unless specifically requested by panel. Dr. Besser, this is your call.

DR. BESSER: I did say anyone could respond.

DR. BOYAN: If you come forward to speak, please identify yourself, your relationship to any company involved in this proceeding in any way, and financial interests that you might have with those companies.

DR. FITZPATRICK: DePuy International. I would just like to clarify Dr. Insall's comments there, and ask him whether it is true that they also made some design changes to the tibial components and the position of the stops that existed on that tibial component when they were evolving the design following their clinical experience.

DR. INSALL: We took off a stop that was present in MK-I. We had a posterior stop. We decided we didn't need it. We took it away.

DR. BESSER: Thank you. My second question relates, I guess, to one of the FDA questions. For the dissociation of the metal backed patella, I know that the thickness of the polyethylene on the patella has been increased.

Can you address, I guess, the problems with the metal backed patella, and whether you feel that those

problems have been solved. If so, how? Those at the table only, please.

DR. JACOBS: I discussed this to some extent in my presentation, and we had a lot of experience with failed metal backed patellas.

The failures were in two regimes. One was a delamination at the peg/metal backing interfacing. The second was a delamination and/or wear through at the interface between the polyethylene and the metal backing.

A lot of that was surgeon dependent and technique dependent. Those surgeons that paid less attention to soft tissue balance had a higher rate of patella problems.

It has been extensively addressed in the newer designs of cementless knees. First of all, the junction between the pegs and the plate has been addressed and the delamination failures are much less likely.

Porous coating has been removed from some of those pegs. So, you obviate the situation where you have an ingrown peg and a non-ingrown tray, then sheer loading at that interface. In addition to that, the polyethylene has been thickened.

Also, there has been a tremendous evolution in the design of the patellofemoral geometry in terms of the trochlear groove, how the patella engages in flexion.

Furthermore, I think surgeons are much more attuned to appropriate surgical technique, in particular ligament releases and particularly the rotation of the tibial and femoral components.

So, whereas initially reports of metal backed patella failures were quite common in the first generation of the devices, they are quite rare in the second generation.

DR. SKINNER: I would like to ask the people at the table if they feel -- if anybody at that table feels -- that there is a difference between cemented and uncemented knees, whether it is a mobile or non-mobile bearing situation.

I know we have already gotten response from Dr. Insall, Dr. Eng, Dr. Bourne. Maybe some data, if Tom Craig has some data and if not, then possibly Jerry Eng might be willing to address that.

MR. CRAIG: Certainly, there are differences between cemented and cementless knees. I think it is largely a difference of philosophy by different surgeons.

As Dr. Jacobs mentioned earlier, they tend to put their cementless knees into younger, more active patients. They tend to use cement in older, less active patients.

In cases where you do dual use of cemented,

cementless, I think that tends to be the case. It is largely a matter of individual surgeon selection.

What we are trying to do with this petition is to allow that individual surgeon selection occur, and not have that artificially affected by regulation of the product.

DR. SKINNER: I guess what I am driving at is that, as a panel member, I am trying to -- I have my own opinion, but I am trying to see if there is a difference between cemented and uncemented in any of these knees.

In other words, why should we consider an uncemented or cemented mobile bearing knee to be different from a non-mobile bearing knee? Is there a reason why we would do that?

DR. INSALL: My opinion is that there isn't a difference.

DR. BOURNE: I would agree with Dr. Insall. I think a couple of other factors are important. I think our data and those of many other people have suggested that the results are equivalent.

You have a fact that one in five American surgeons insert total knees with at least one cementless right now. It seems incongruous that they are doing something so-called illegal or against regulations. It seems that they do accept this practice.

I suppose the only negative things that you may say with cementless implants are that they cost more, which is a factor in our health care environment.

You could say that there may be a little bit more bleeding immediately post-op from the bony surfaces that aren't plugged with cement, but that doesn't seem to be a detrimental factor in the long run.

All this business about screw osteolysis, I am not sure you can blame the cementless devices.

I agree entirely with Dr. Jacobs. It basically had to do with fixation of the plastic. Basically you had movement of the plastic on the base plate, and you often had some co-flow of the polyethylene into the screw holes. It was just a perfect mechanism for producing debris and causing screw osteolysis. Other than that, I think they are equivalent.

DR. ENG: I am Jerry Eng.

DR. BOYAN: Dr. Eng, make a total disclosure of your life for us, please.

DR. ENG: I do receive royalties from DePuy. I did want to make a comment in response to Dr. Skinner's question.

Cementless fixation, which I have a great deal of experience with, demands that the interface be highly

incongruent.

All the designs that you have heard talked about today are highly incongruent. The MG-1 mobile bearing designs, they put very little stress on the fixation interface, and that is why they work.

When you start going to a more congruent design, you stress the fixation interface more. I had experience with that with a DePuy knee called the Cenatomic knee, that had high rates of osteolysis.

A mobile bearing knee works very well cementless, as long as the mobile bearings move. As has been shown, they don't always move. In a study by Doug Dennis, roughly 50 percent of them don't move.

Then you have a very highly congruent design and you have to question the issue, will cementless fixation work if the bearing doesn't move. Thank you.

DR. STERN: Could I ask Dr. Eng a question?

DR. BOYAN: Yes, but while you are doing that, is that directly following from what he just said?

DR. STERN: Absolutely.

DR. BOYAN: Okay.

DR. STERN: I just wanted to ask him, on that same situation with cemented fixation, would a mobile bearing knee be okay?

If I follow what you just said, you said cementless fixation was a question. What about cemented fixation?

DR. ENG: If the bearing doesn't move, I don't have any direct experience with that.

DR. BOYAN: Thank you. Dr. Bourne, one last comment, and then we will go to the next questioner.

DR. BOURNE: With the rotating platform from a mobile bearing, I think there is ample evidence that they do move.

I don't know if you noticed in our radiographs, there were three tantalum beads in the polyethylene, and on the three posts off the tibial component there were points.

We have a radiographic technique, from lateral radiographs of people walking up inclines or stairs, that you can triangulate these various factors and they move. They rotate.

Also, the five retrievals that we have had in our entire series for infections or the loose femoral components, they all show some evidence of third body wear on the undersurface, where you can see the actual rotation and translation.

It has not been our experience, at least with the design that I am familiar with, that they do not rotate.

They do rotate.

DR. BOYAN: Dr. Skinner, do you feel that your question has been addressed adequately?

DR. SKINNER: Yes. I would like to ask one more. From my viewpoint, it looks to me that the kinematic skin that Helmetica makes is actually a mobile bearing knee, very similar to the designs that are talked about here, except it has a hinge attached on one side.

Would any of you disagree with that? Are you familiar with that design? It causes rotation along the axial aspect.

DR. BOURNE: Yes. It is a revision knee, of course. The only difference is that on the tibial articulation it is not flat. It is dished from front to back.

So, there is some inherent restraint for rotation of that particular device. So, it is a little different but it has been utilized for at least 10 to 14 years.

DR. BOYAN: Thank you. Dr. Laurencin.

DR. LAURENCIN: It seems to me that we are talking about a number of different types of implants. We are talking about unicompartmental implants, mobile bearing implants and the more traditional protocondylar implants.

First, in terms of the unicompartmental implants,

is there a significant amount of data that we have about uncemented unicompartmental implants, especially those that may be very constrained in terms of their safety and efficacy in terms of the long term? Can anyone comment on that in terms of the long term unicompartmental uncemented?

DR. JACOBS: I have no experience with cementless unicompartmentals. In your petition there is reference to four to six studies on cementless unicompartmentals. There is some support in some of the studies for good results in intermediate to long-term fixation in some of the implant systems.

The data on these cementless unicompartmentals, however, are far less extensive than the data on the cementless tricompartmentals.

DR. BOURNE: Unicompartmental knee replacements are used with varying frequency. I think Dr. Insall uses none. There are other people that use it 50 percent of the time. We personally use it about six percent of the time.

Our experience has been entirely with cement, and we have been influenced by a few studies, namely that of Brian with the PCA uncemented unicompartmental, where they didn't have as good results as when they used cement. So, we continue to use cement.

DR. INSALL: It is true that I don't any longer do

unicompartmental replacements. But I think a comment is in order about the menisci, separate menisci, which can be used either for one compartment or two compartments.

I think I would emphasize that if you look at the literature, the problems with mobile bearings, cemented or uncemented, are with the separate menisci.

I think perhaps they should be separated off from the other kind that is a one piece meniscus.

I think the types that jam up, as Jerry said, I believe I am correct in saying that those are the two piece, or the one piece in the case of a unicompartmental, that they tend to jam up in the track.

DR. BOURNE: If I may make one other comment to support what Dr. Insall says, as I said, in 1978-79, we did the Oxford knee, which was the freely mobile meniscal knee.

The problem with that is that it was very difficult to get perfect balance. The medial and lateral sides were each receiving load.

If you had all the load just on one bearing, you could see tremendous stresses, and you could also see the potential for dislocation of the opposite bearing which wasn't unloaded.

Indeed, most of the cases which we talked about this morning, it was the lateral bearing that dislocated,

because most of the knees that we do are varus knees. You are overloading the medial side and underloading the lateral side and it made it an unstable situation.

I think it is really very, very important to differentiate the ones where the menisci move versus the rotating platform.

DR. BOYAN: Dr. Laurencin, I am just going to give you all a time check. It is 10:25. What I would like to see us do, if we can, so that everybody has a chance to ask questions, I am sure that some of the same questions will be asked by our colleagues over here. If not, if we miss them, we will come back around and ask what we miss. Are you through?

DR. LAURENCIN: I have one more question.

DR. BOYAN: Then we will go to Dr. Aboulafia. I don't need to call on you. As soon as the questioner is finished, go to the next questioner, state your name, and we will try to go quickly so we cover all the people.

DR. LAURENCIN: Outside of the LCS, which has shown very good results in terms of cemented and has shown some good results in terms of uncemented, is there other literature on uncemented systems using mobile bearing knees in an uncemented form with long-term studies that have shown efficacy at all, mobile bearing?

DR. BOURNE: Not that I am aware of.

DR. INSALL: Not that I am aware of.

MR. CRAIG: We looked very hard to try to pull up all the literature that we could find on mobile bearing knees. What is in the petition is absolutely everything we could get our hands on.

Basically, we put in uncemented mobile bearing knees in both the tricompartmental and unicompartmental mode.

We felt that the issue of cemented/cementless is not a very significant mobile bearing issue. We think the issues are two different issues.

DR. JACOBS: I wanted to address that with regard to mobile bearings and also with unicompartmentals. What we know about the basic biology of bone ingrowth is that if you can achieve a situation where you have an adequate material, adequate pore size, minimized micromotion and have adequate host/bone contact, you will get bone ingrowth, whether it is a unicompartmental, a mobile bearing or a fixed bearing.

DR. ABOULAFIA: I have a couple of very brief questions that I think can be answered quickly as well. In the petition it returns to cementless exclusively. Is that for us to decide to include press fit and porous coated or is that asking specifically in every one of the cases porous

coated and not press fit.

MR. CRAIG: The intention of the petition was porous coated, not press fit without a porous coating.

DR. ABOULAFIA: But we would have to specify that if that was our intention as well?

MR. CRAIG: Yes.

DR. ABOULAFIA: The second question is, it has been said in various forms that not all mobile knees are alike. Yet the petition, because of the general nature of it, requires all mobile bearing knees to be alike.

Are there any recommendations sort of to speak to the same question that Dr. Boyan asked? Are there certain things that members of the panel would say are requirements to classify something into a class II that was a mobile bearing knee?

For instance, we do have experience with the rotating kinematic hinged knee. So, that might be a design that is very acceptable, whereas the Oxford design probably is less acceptable.

Are there other limitations or design features that you would want written into a proposal that would be acceptable to use?

MR. CRAIG: From the petition itself, we included in things like the rotating hinges and noted that that is

actually class II, where you have an across-the-joint linkage in a revision-type prosthesis.

There are others like that, like the lacy knee, that go back historically. So, we are not really addressing those particular designs in this petition, because they are already class II.

Beyond that, as far as requirements, we specifically eliminated in our request the Oxford knee and knees where there is no limitation to movement medial lateral or AP.

Beyond that, we didn't get specific on what that limitation should be or what the design features would have to be.

DR. BOYAN: Dr. Insall, before you do comment, I have taken careful notes on what both Dr. Bourne and Dr. Insall thought were bottom line requirements for a mobile bearing knee, if that is adequate for you, Dr. Aboulafia.

DR. ABOULAFIA: Yes. Last question. Some of these things -- and we have talked about as groups before, I am sure -- are industry drive versus knee driven.

Dr. Insall, starting with you, is there a need for a porous ingrowth patella?

DR. INSALL: No.

DR. ABOULAFIA: Anyone else support a need for a porous ingrowth patella component?

DR. INSALL: I would agree that there really isn't an overriding need.

DR. JACOBS: For those surgeons that use exclusively cementless devices -- and there are many that exist -- yes, there is a need for a porous surface patella.

DR. ABOULAFIA: A follow up question. Why can't you not cement two other components and go ahead and cement the patella?

DR. JACOBS: You can do that. That is certainly an acceptable option which a number of us do. For that surgeon that his skills and techniques are such that he prefers to use cementless patellas, he needs that.

DR. BOYAN: I think that is into surgical technique and that is away from the device. Mr. Craig, do you have something really --

MR. CRAIG: I would just like to point out that the PMAs that were approved where they did look at the porous coated uncemented devices, they typically had a porous coated patella that was approved along with the tibia and the femur.

So, for the people that do use cementless, that is part of what to consider something they need.

DR. SILKAITIS: I would like to ask a question of Mr. Allen. I am sorry, I may have been distracted at the time.

The approved uncemented use of the mobile bearing knee, is that the same one as the cemented one, or is it a different design?

MR. ALLEN: In the slide presentation that you had regarding device history and on the paper that I have here, it would be on the second page in the middle.

You say there are four PMAs approved for uncemented use, and the second item there is one fixed and mobile bearing. Is that the same design as the one below where it says one PMA submitted for approved use, mobile bearing, or are we talking about two different designs?

MR. ALLEN: There were four unicompartmental knees in the study. Wait, excuse me.

MR. MELKERSON: When you are describing the fixed and mobile bearing knees for cemented and uncemented, you are talking about the meniscal bearing and the rotating platform, both in cemented and uncemented modes.

DR. SILKAITIS: I guess, taking a look at the science of implants -- and we have learned a lot over time regarding the design requirements, and as a matter of fact, whether we take a look at -- at least this is my impression.

As we take a look at implants and as they evolve, they begin to look similar and there is a proliferation of implants that become available that kind of look all similar, indicating that there is a standardization of design characteristics.

The question that I have for Tom Craig, has the mobile design been somewhat codified, published somewhere that those are the requirements for that knee?

MR. CRAIG: No, it really hasn't, Dr. Silkaitis. The codification of knee designs and that sort of thing would typically occur in the auspices of ASTM and ISO.

Right now there is an effort ongoing in both places to write performance standards on what the requirements need to be for total knee replacements in general.

I don't think it is broken down yet, although it will clearly have to in the future, to what is specifically needed for mobile bearing versus fixed knees.

DR. SILKAITIS: Do they exist for uncemented and cemented knees?

MR. CRAIG: From a total knee design standpoint on the requirements, no, they do not at this point, although those are being worked on and prepared.

DR. SILKAITIS: So, it is an across-the-board kind

of issue?

MR. CRAIG: Yes, it is across the board.

DR. HOLEMAN: The questions which I will ask really fall into three categories, which has to do with the indication for use, labeling and effectiveness.

The data that you presented indicated that, for the most part, you were assuming that designs were used more or less for the older individual. With the uncemented, they were used in your younger patient.

The complication rate you reported was higher in the cementless knee, which indicates to me that you were doing more revision, which would impact the quality of life function of the patient over a longer period of time because of the revision.

The cement is more prevalent in older patients, although the outcome appeared to be that you have better results that are shorter duration of evaluation, which would indicate to me that it would also be effective in older patients. But that has not been evaluated clinically. I want someone to speak to that.

In addition, when you look at your indication that you have stated, it is very generally, but yet it is vague since we are talking about several designs.

When you are talking about, it is indicated for

degenerative arthritis, post-traumatic arthritis in older patients, yet we are talking about older and younger patients and I am not sure which design you are referring to. If you would comment on those, please?

DR. JACOBS: Dr. Holeman, I am not sure I got the gist of your entire question, but I will respond as best I can.

In terms of the series that I presented and also that Dr. Rorabeck has published with Dr. Bourne, when you try to do a head-to-head comparison between cemented and cementless, it can be confounded by the patient populations you start with.

The intent on the introduction of cementless technology was to address those patient populations that are not served as well by the use of cement.

There is a lot of literature, much of which Dr. Insall has contributed that would suggest that in the elderly patient cement fixation is successful for a long period of time.

Therefore, when these cementless devices were introduced in the mid-1980s, there was a concentration on using those that were at higher risk, i.e., the younger and more active.

Whether you treated those individuals with cement

or without cement, one would expect a higher revision rate, a higher complication rate. That could certainly impact on the quality of life.

So, the difference you observe is probably due to differences in activity and usage.

Our current indications for fixation and usage are those that tend to have longer life expectancy -- and that is a relative term depending on physiologic and chronologic age -- and also those that had adequate bone stock to support a cementless prosthesis.

DR. HOLEMAN: Getting back to your indication for use that you have published, would it make a difference, then -- I am looking on page 6 of your presentation where you have indication for use.

Is there a necessity to clarify that there may be some differences as far as the use of the design that you are indicating there?

DR. JACOBS: I think that these are indications in general for any knee arthroplasty. Maybe Tom Craig would also like to respond to this.

These are the indications that you would see for any knee arthroplasty. It is up to the surgeon, really, to determine in a particular patient what he thinks would be the best device, based on bone stock, activity level, the

surgeon's experience, the ability of the hospital to have the equipment he needs, et cetera.

So, it is a complex, multi-factorial decision by the surgeon. But these indications listed are the general indications for total knee arthroplasty.

DR. NELSON: This is partly in response to Dr. Boyan's earlier question and partly a statement. I think in order to properly discharge our duty -- that is, to protect the patients and be fair to industry -- it is good to recognize we have got a lot of apples and oranges here, some of which are obvious, and some are not.

Obviously, we are comparing fixed bearing and mobile bearing. Obviously we are comparing unicompartmental and total.

We are throwing around the term cementless, but that can be both porous coated and press fit and we are only talking about the porous.

There is also the use of a total knee implant as a hybrid; that is, you would cement the tibial side and not cement the femoral side or vice versa, although I believe it is mostly that way that it is done.

I think we need to, as we formulate how we want to fill out our work sheets, we are going to have to stratify it in that way, if anyone in the group feels that there is

good evidence, say, for a cementless tibia versus femoral, et cetera.

I just wanted to ask the FDA, would you think that is a correct summation of how this is stratifying out, at least in your view, from what we have been given to do?

We are not looking at press fit. We are not looking at cementless. But all these others are parameters that we have to address.

Just judging from nodding heads on the panel, you are agreeing that maybe this is the stratification we are going to do? It is going to drive us crazy filling out the sheets, possibly. You have got it under control?

MR. MELKERSON: Basically, what you are describing is what we saw as being the complexity of this petition. There were so many different stratifications.

In terms of looking at the petition itself, my understanding is the petition itself asked for uncemented, porous knees.

The other issues that you are bringing up are issues that would help us in a recommendation for potentially reclassification.

Hybrid is a question and that is a use that physicians have been doing and reporting in the literature.

DR. NELSON: I would just like to echo a comment

that was made, I believe it was by Dr. Aboulafia.

On the mobile bearing, there were actually multiple designs. That is, there are rotational designs, translational designs, and one or two piece designs.

We have one representative of each and limited data on each, as opposed to lots of experience with multiple design additions of each concept.

DR. BOYAN: I think for both Dr. Nelson and Dr. Aboulafia, as the non-surgeon, non-engineer here, I listen to it slightly differently with less commitment to any one particular position.

I have sifted out from all the presentations what sounded to me like the consensus position which, when we get to that place, I will read it, and see if it does meet everybody's needs. If it doesn't, then we can put it up there.

I think we have been developing a pretty solid consensus position here, though. Without taking any brand name, any specific design, there are some things that everybody seems to be in agreement on that would be acceptable and probably fairly well scientifically accepted as being okay.

DR. LAVIN: No further questions, just one observation. This is one place where, with such a large

amount of data, it would be good to have meta analyses to help straighten out these kinds of differences that we are being asked to judge upon.

A number of permutations and combinations could submit to a more rigorous analysis than just looking at it paper by paper. You don't need to respond to that.

DR. YASZEMSKI: Just very briefly --

DR. BOYAN: Wait, Dr. Yaszemski, I think Mr. Craig wants to make a comment.

MR. CRAIG: Just very brief, Dr. Yaszemski, this is actually the third petition that OSMA has tried to prepare on total knees.

The first two versions did include statistical analyses. When we got down to the time for preparation of this petition, the rules of the game had changed a little bit.

Statistical analysis was not part of the requirements at this point. That is why you don't see it.

To go back very briefly to the porous coating issues, if you look in the device description, there is a description about beads and so forth. So, it is clearly a porous coating versus press fit.

DR. BOYAN: Okay, Dr. Yaszemski.

DR. YASZEMSKI: As we have come around the table,

almost all of my questions have been checked off and answered by somebody else. I would like to just have two and they will speak to the questions that the FDA is going to ask us.

First, Dr. Jacobs, the question 3A that the FDA is going to ask us talks about dissociation of metal backed patella components.

You have talked about needing a cementless fixation patella. What do you think that will be if it comes to be?

Will it have metal backing all the time or will there be a complete polyethylene, some type of growth into a poly only component.

I think you have mentioned it before, but I will just ask you to emphasize that there is something new about the new metal backed patella that would obviate the problem that had happened before?

DR. JACOBS: I will let Dr. Bourne speak to all cementless polyethylene cementless patellas because I know he has some experience.

I envision it being metal backed. The changes that have been made by the manufacturer include beefing up - - as I mentioned before -- beefing up the junctions between the pegs and the metal base plate, in some cases eliminating

the porous coating from the pegs, and also designing so that at the corners of the metal backing you don't have this very thin polyethylene. That was the problem that we were getting into. That has really been designed around.

In addition, there have also been changes in the patellofemoral mechanism with the deep trochlear groove, et cetera.

DR. BOURNE: I guess just a comment. If I were ever to make a metal backed cementless patella component, I would want to inset it.

I think most literature suggests that an inset rather than an on-lay metal backed patella is appropriate.

With regard to the use of completely cementless patella components with the so-called magic pegs which I know have been used in some cementless devices in the United States, I think Michael Friedman was the originator of this particular device.

I know in Europe there are 30,000 plus of these that have been inserted. The results have been quite good, including reports from investigators in the United States and Salt Lake City and elsewhere.

In our particular experience, we have approximately 150 of our entire expanded group of SAL knees where we have used these, and several hundred of cemented

patella components.

They seem equivalent at five-plus years. But you would like it 10 or more years.

DR. BOYAN: Let me bring us back to task here. We are not designing future instruments or future devices. We are taking a look at what is on the market now, and feeling comfortable about what we think would make a class II designation, if we feel that at all.

A device that came in with a set of characteristics, do we feel comfortable with calling that a class II device, and we are going to make a recommendation.

So, we can't plan for what might come in for the future. We have to take a look at what exists now, and whether or not we are comfortable with it being a class II.

DR. YASZEMSKI: Thank you. I think actually Dr. Bourne's answer spoke to that. Right now there could be a cementless all poly or metal backed. Thank you, that was very useful to me.

Dr. Bourne, I am going to ask my second and last question to you, too, and that goes to question 3B that we are going to be asked to talk about, and that is the dislocation.

I think you spoke to this and perhaps I just don't remember it. In your Canadian SAL series, what was your

dislocation rate? Remind me again if this is a cruciate retaining or cruciate sacrificing prosthesis.

DR. BOURNE: It originally was designed to be a posterior cruciate retaining device, but we have used it both ways. The results seem comparable.

Our dislocation rate has been zero and in the multi-center trial this has been zero, but this is a rotating platform.

With the meniscal design, independent menisci, we did have approximately a five percent dislocation rate.

DR. YASZEMSKI: Thank you.

DR. BOYAN: We are back to you. So, panel, you have both had a chance. It has taken us a long way to get around and I think we have addressed most of the issues.

If there is any remaining issue that a panel member felt was not addressed, please identify yourself and let's get it out on the table. Yes, Dr. Laurencin?

DR. LAURENCIN: Just in terms of the DePuy people regarding the LCS, you have a paper that is a review from Jack Burt about dislocation subluxation of using it with the LCS knee, in which they reported almost a 10 percent incidence of subluxation and dislocation of the implant.

Which design was this paper reporting on? Do you have an idea?

MR. PEOPLES: What I am familiar with in the Burt article was in relationship to bearing dislocations in which the tibial platforms had been put in with too much posterior slope.

Additionally, I know there has been a lot of talk about the dual mobile bearings being potentially the sole or unique type of design that is related to dislocations.

We do have reports also in a rotating platform, all polyethylene with a post that rotates. A bearing spin-out and dislocation relates to that.

So, any of these subluxation or bearing problems are not totally unique to the separate menisci at all that are involved there.

Sort of one other type of comment, I have heard an awful lot of information on preliminary small series with shorter follow up on various mobile bearing knee concepts put around here, in the literature and not published, that is proposing that that information is adequate to gain a prediction in a generic class of device to assure safety and effectiveness at a class II level.

If the data is that robust and that strong and that available, my rhetorical question is, why have we seen no submitted PMAs based on that data to this point?

We would not be having a lot of these discussions

about this if three or four different designs had gone through the full PMA review process, that could cover a more generic class of device.

As we sit today, only one design concept has undergone the PMA process. Actually, being quite honest, that is pretty much where DePuy's position has come in on this.

It is very much like any of you who have spent 10 years in training, turn around and find out that someone has changed the bar on you after you have gone through that and said, after one year you can come out and be board certified and put total knees in. Thank you.

DR. BOYAN: Thank you. Is it a question, Dr. Nelson?

DR. NELSON: Yes, this is a question. Just relating to what we are going to have to do in just a moment, 4B, I would ask either you or possibly Mr. Craig, because we have seen a lot of stuff and I am just confused and I want to hear it again.

What is the evidence for purely the unicompartmental uncemented knees? What have we seen on that?

MR. CRAIG: I think if you turn to the table, it is in section 4. Starting on page 9, section 5, you see the

Lewold article there that was mentioned in the presentation by DePuy this morning.

On page 10, you see three additional, and they are listing both the cemented and the cementless applications. Then again, on page 11, you have a couple more with unicompartmental, and includes both cemented and cementless applications.

DR. NELSON: Thank you.

DR. BOYAN: Now, let's go through the panel questions and I think a lot of this is going to come to clarification as we go through this.

Just getting down to the specific issues here, we have the proposed device description. Why don't you put that up there first.

This is the device description that is in the petition. It is fairly complete. I would like to read to you what I have gleaned, is the device description that really defines what was discussed as opposed to an all-encompassing version that is here.

What it seems that we have agreed upon that we are discussing -- this will be in relative American English as opposed to engineering, but you can translate this later -- that we are agreeing to cemented and cementless, but not press fit devices, unless the press fit device is porous

coated.

We are discussing the not-mobile knee, I forget the exact precise term for that one, and no one is arguing about that.

When we get down to the mobile bearing knee, we have these following characteristics that it seems that we can agree upon:

It has a polished cobalt chrome tibial base plate. It has a meniscus of a single design that has a thickness between six millimeters and eight millimeters.

There should be in the design inherent stability in the anterior, posterior and medial lateral directions for the tibial, femoral articulation.

There should be a mechanism for preventing bearing dislocation, and that the design be an incongruent one, in that there is low stress on the interface.

Then when we talk about the cementless designs, what we are saying is that the surfaces of these devices, the metal surfaces, have a pore size -- whatever mechanism is used to achieve this -- that there be a pore size and up here it says one to two micrometers, but in Dr. Jacobs' presentation, he was much more limiting in what was the optimal pore size. I wrote down 150 to 200 microns, but I will let Dr. Jacobs clarify that.

The amount of motion that that design allowed be limited to less than 100 micrometers, that it be made of an appropriate material, either a titanium or cobalt chrome, and that there be an adequate bone stock, which I think is a surgeon decision and one that we can only recommend.

Did I cover over what it is pretty thoroughly?
Did I miss something?

DR. STERN: I don't know how detailed you want to be, but for instance, you said thickness of six to eight millimeters. I think that should be a minimum thickness of six to eight millimeters. You can go for more than that.

DR. NELSON: I am not sure how detailed we want to go into a description of a class. If we approve something to go to class II, we leave that in terms of a special controlled definition.

DR. BOYAN: That is exactly where I was trying to go. We say you have to have these things to make it into class II, is kind of where we are going, if we go there. We haven't gotten there yet.

DR. LAURENCIN: By this definition, then we are excluding in terms of movement, possible movement from class III to class II, those implants that are HA coated?

DR. BOYAN: I don't know that we have done that, actually.

DR. LAURENCIN: In other words, this wording states nothing about hydroxyapatite coated. Are we saying that companies that make these same sorts of implants that use hydroxyapatite coating, specifically for cementless applications, now their implants are going to be class III, whereas those that are not are class II.

DR. BOYAN: Let's do it this way. Let's do Stern, then Jacobs, then Besser, who want to comment on that. Jacobs can't comment? We are past Jacobs? I asked Jacobs for clarification on the pore size, though.

DR. JACOBS: I think I would put the upper limit more in the region of 400 to 500 microns, based on my understanding of the literature.

DR. BOYAN: Let's just do one thing at a time here. We are on to HA and Mr. Melkerson?

MR. MELKERSON: The petition itself is just for uncemented porous. It would not exclude a future action on HA coatings, which are currently class III for knees and other prostheses, but they have been cleared for cemented as well as mechanical or press fit in the hip.

DR. BOYAN: Let me repeat what I think you just said. We are not going to include or not exclude. We are just going to state some basic general characteristics that we think something in class II ought to have.

One of those is a porous surface of a certain pore size that would permit motion less than 100 microns.

DR. MELKERSON: That is correct.

DR. STERN: We almost did the exact same thing yesterday on the shoulder, if you remember, and we didn't get into any of this, as opposed to deciding how big the microns were, with FDA guidelines yesterday.

DR. BOYAN: Precisely. Dr. Besser?

DR. BESSER: A couple of things. You mentioned something about the congruence. I believe what was said is that if you don't have a mobile bearing, then you can't have high congruence. But with a mobile bearing, a higher congruence was possible.

I am not sure, what did you say about congruence?

DR. BOYAN: I was trying to take everybody into consideration, and I did hear some dissention from the audience which suggested that this kind of mobile bearing knee design was possible if the design was an incongruent design.

I admit that I am not an engineer. So, I can take that comment out completely. It can become history. It is history. Okay.

DR. BESSER: The other thing is gone. Never mind.

DR. BOYAN: So, what we are on is our device

description. I just want to clarify --

DR. BESSER: I remember what the second item is. It related to the pore size. The pore size given in the definition presented is between 100 and 1000 microns.

DR. BOYAN: Correct.

DR. BESSER: Are we changing that?

DR. BOYAN: We don't have to change anything. We are getting ready to make a recommendation. They have a petition and we are going to make some recommendations to FDA.

So, go to question number one. Question number one is, do the proposed classification definitions sufficiently describe the devices recommended for reclassification?

If not, what changes in the definitions do you recommend?

What I would put forward is a definition that we might recommend is the one that I just read.

I would like to go around the table and give all of you a chance to agree or disagree and make comments.

Let's start with Dr. Hill.

DR. HILL: I agree.

DR. BOYAN: Dr. Stern?

DR. STERN: I agree.

DR. YASZEMSKI: I agree.

DR. LAVIN: Agree.

DR. NELSON: Can you tell me what we are agreeing with? I apologize. You don't have to read the whole thing; just briefly summarize.

DR. BOYAN: Cemented and cementless but not press fit unless it is coated, mobile bearing knees that have the tibial base plate, a minimum of six to eight millimeter disk meniscus of a single design; that there be a mechanism for keeping this thing inherently stable and that it have a mechanism for preventing bearing dislocation. There are some comments on what kind of cementless surface it should have.

DR. NELSON: I just wonder if we should stratify uncemented femoral and tibial. There seems to be, in all the papers that were presented to us, very few of the femoral uncemented were revised, but a large number of the tibial uncemented were revised.

I would be willing to hear an opinion from Dr. Skinner. He is shaking his head.

DR. SKINNER: I think that is a matter of surgical technique. I don't think that has anything to do with classification.

DR. NELSON: I would accept that, then.

DR. BOYAN: We have -- we also have to decide whether we are going to include the unicompartmental design in this definition.

There are two different issues? I am missing the comment. Just a moment. We have two different definitions. So, we have to deal with them separately. Are we combining them or keeping them separate?

I was trying to put them together. I was trying to move quickly through it. Let's deal with the definition for the first and then determine whether or not this other one fits into that definition and we have to separate it out.

So, we are right now at Lavin has just agreed with the new revised definition. Nelson, you asked for clarification and you have it.

DR. NELSON: Agree.

DR. HOLEMAN: Agree.

DR. SILKAITIS: Nothing to add.

DR. ABOULAFIA: Agree with one stipulation or one comment. That is, I am not sure that I entirely agree with lumping all mobile bearing knees into one category.

I think we have some data on one particular design of mobile bearing knees, and not a lot of good data on the others.

DR. BOYAN: So, what I was trying to do was not lump them all, actually. I was trying to define, if you could make these criteria, you could get into this category. If you could not make these criteria, you would not be in this category.

DR. STERN: I thought that was just we just did. My understanding of what I just agreed to was a definition that included what we are calling a rotating hinge design, and not agreed to what is called a meniscal bearing design.

That is what I thought I just agreed to, that distinction.

DR. ABOULAFIA: I agree with Stern. I am not sure I agree with you, but if he agrees with you, then I agree with you.

DR. BOYAN: This is going to be one of these horror stories.

MS. NASHMAN: Before we go any further, just for the record, Dr. Stern is recused from voting on this petition and the one that will follow.

He is allowed to discuss the material. The point at which I have broken this is out is that Dr. Stern will be able to participate in this discussion, going through the FDA questions.

When we start working on the work sheet and the

supplemental data sheet, Dr. Stern will recuse himself. In case there is any question by the public, that is the way we are working it.

DR. STERN: I just want to make that I am all clear on this. I was okay at least through question two. I thought at question three I was going to stop.

DR. BOYAN: Let me just get a clarification. Aboulafia and Stern have accepted this definition as it relates to a mobile hinge design.

I guess I need clarification on, on the mobile bearing knee design you also accept it because we have put in a criteria for a mechanism for preventing bearing dislocating and inherent instability; is that correct? So, we are all right.

So, we are up to you, Aboulafia. Do you just want to make the statement to clarify that we make it very clear to FDA that we don't want all mobile bearing knees into this class II.

DR. ABOULAFIA: Agreed.

DR. LAURENCIN: Nothing to add.

DR. SKINNER: I agree with Stern. I am concerned about the meniscal bearing thing.

DR. BESSER: Nothing to add.

DR. BOYAN: Yes, Mark?

DR. MELKERSON: Point of clarification. You described a rotating hinge? Are we confusing this with other devices?

DR. BOYAN: Yes.

DR. MELKERSON: Please clarify.

DR. STERN: I apologize. I think a better term would be rotating platform. I apologize, rotating platform, not rotating hinge.

DR. BOYAN: Okay, this is a -- all right got it.

The next issue is the unicompartmental device. Do we want to include it in this group or do we want to consider it separately?

Let's take the hypothesis that we are going to include it. If you want it to be separated out, identify yourself and explain why.

DR. NELSON: I would like to hear maybe some discussion among the rest of the panel, but I think the quantity of the data on it is not quite the same type as the data on the total knees for uncemented.

DR. BOYAN: Are there any other comments?
Dr. Laurencin?

DR. LAURENCIN: I think it should be separated out because, number one, the quantity of data is not great, and two, I think the data that is there is actually conflicting.

Even the data that we had presented here, some don't show great results. I think it should be separate.

DR. BOYAN: I think we are going to have to go around and just get a statement here. The question, I will phrase it this way:

The unicompartmental device should be considered separately. An answer of yes would mean you mean it to be separate and an answer of no means you mean it to be separate. We will start again with Dr. Hill.

DR. HILL: I just need some clarification. Are we separating out the unicompartmental cemented and non-cemented as a group or as separate entities as a group.

DR. BOYAN: Uncemented only. Unicompartmental uncemented would be a separate thing. All this means it that we do a separate sheet for them.

DR. HILL: Meaning that we can accept unicompartmental that are accepted.

DR. BOYAN: It is already accepted. It is already done.

DR. HILL: I just wanted to clarify you are talking about the one thing.

DR. BOYAN: Unicompartmented, uncemented, yes or no. Yes to separate, no to keep together.

DR. HILL: Yes to separate.

DR. YASZEMSKI: Yes.

DR. LAVIN: Yes.

DR. NELSON: Yes.

DR. HOLEMAN: Yes.

DR. SILKAITIS: Yes.

DR. ABOULAFIA: Yes.

DR. LAURENCIN: It is my motion; yes.

DR. SKINNER: I don't see any reason to separate it. So, I guess, no.

DR. BESSER: No.

DR. BOYAN: As the chairman, I can't vote, but I couldn't see the reason to separate it either. But we voted to separate it. So, it will be separate.

Let's just deal. Let's work our way through it the best we can. So, FDA, have we answered question number one to your satisfaction?

DR. WITTEN: I think I am still a little bit confused about mobile bearing knees as they relate to the unicompartmental definition, whether you have answered that question.

DR. BESSER: I don't think there is a unicompartmental mobile bearing knee that would meet the criteria of having a mechanism to prevent bearing dislocation.

Therefore, I think if someone came up with one that did have such a mechanism, then it would fit into this class.

As the definition that we have created has that stipulation to have a means of preventing bearing dislocation, then that would probably preclude at least the current uniaxial mobile bearing knee.

DR. LAURENCIN: Would it be possible to have a written summary of the changes that were made on that, where we --

DR. BOYAN: If someone will get me an overhead, I will write it really fast onto an overhead and then we can all look at it.

DR. YASZEMSKI: While you are doing that, Dr. Boyan, I voted yes to specifically preclude that thing from being included in class II.

If the statement that Dr. Besser made is agreed by everybody, that the statement as written would preclude that, then I would agree with Dr. Skinner and Dr. Besser, and vote to combine them again.

DR. BOYAN: Did everybody understand that in our definition, the working definition right now that we feel would justify a device going into class II includes a mechanism for preventing bearing dislocation.

Given that definition, Dr. Yaszemski has pointed out that we would then eliminate one of the problems that he identified with the unicompartmental uncemented device. Would that change the votes of any of the other people who voted to separate?

If so, please raise your hand and let me just get a general view of whether or not we should do another vote. No. So, it stands that it is separated.

I am going to ask Ms. Nashman to copy my prose here onto this overhead while we go on to question number two.

We will do first our revised definition and then we will do the uncemented unicompartmental device. So, for the first one, are the risks to the health of the following device configurations proposed for reclassifications adequately described? If not, what additional risks should be included.

We will do first for our revised definition. Then, secondly, for the others. So, for the revised, we can accept the risks as defined in the petition.

Is there anybody that feels that there was some risk that was not defined in the petition? Please identify yourself.

Okay, hearing none, we will assume that the risks

as defined in the petition were adequate. What about for the unicompartmental device. If anybody has a risk that was not identified, please say your name. No.

So, hearing none, we feel that the risks were adequately described.

Okay, let's go down to -- FDA, do you want us to separate these out by type? I think that we have covered this question pretty adequately, but if not, please let us know.

Dr. Witten, mobile bearing knees, cemented, or uncemented?

DR. WITTEN: I guess I would like some clarification of the description of the patellofemorotibial uncemented porous coated total knee prosthesis. Does that definition you read include the mobile knee prosthesis and the mobile platform prosthesis also? Are we including those both in that definition?

DR. BOYAN: It has the rotating platform, is the one that we have actually described. I guess it would include the total knee in its present sort of non-mobile bearing sort of version.

DR. WITTEN: I think that was my question. Was it meant to include that.

DR. BOYAN: Yes, it is meant to include everything

but mobile bearing knees that don't fit into this characteristic.

We have included everything except for mobile bearing knees which don't fit into this description.

DR. NELSON: I think we need to stratify out fixed knee from mobile bearing. If you want to stratify mobile bearing as different kinds, I think that is okay, but I think we need to -- my feeling is that since we have three different design categories, one which has been shown to be a failure and two other design categories, there is only one entry in each, I, myself, don't feel that there is a long enough history to say that as a whole class they can be approved. I think that needs to be stratified out.

DR. BOYAN: Let's handle it this way, then.

DR. NELSON: Well, Dr. Boyan, see if anybody else agrees with me. If they don't agree with me, then we don't have to stratify it out.

DR. BOYAN: Let's not deal with the stratification at that level. Let's do question number two and worry about the stratification when we get to the work sheet.

Right now the questions are, are there risks to health involved in each of these different categories. Let's just go around the table. If there is a risk to health that needs to be stated or you feel needs to be

stated, tell me which category and what the risk is, and then we will get that information down in that format.

For this, let's begin -- we haven't started anything with Dr. Aboulafia. We are on panel question two. You will notice that they give A, B and C, patellofemorotibial uncemented porous coated total knee prostheses, femorotibial unicompartmental uncemented, and the mobile bearing knees.

Are there any risks to health that you think need to be defined that were not defined in the petition?

DR. ABOULAFIA: No additional risks to health that need to be defined that weren't clearly defined in the petition.

DR. LAURENCIN: No risks. The only question I have is, again, in terms of the risk of dislocation and subluxation, even with the platform type designs.

I am looking again at the one article I have, the Jack Burt article, almost a 10 percent incidence of dislocation and subluxation.

I guess it was stated that this was due to the fact that, in terms of the surgeon's positioning of the prosthesis, but I am not sure that I see that in the discussion of that as being the specific cause.

I am still not sure whether that design guarantees

that -- we are making an assumption that that design will guarantee no dislocation and subluxation events. I am not sure whether that has absolutely been proven.

DR. BOYAN: Is there anybody on the panel that can address that? Dr. Stern, can you address that question, whether it has been absolutely proven that, with our definition, we would eliminate the risk of dislocation and subluxation.

DR. STERN: I don't think there is any design that could absolutely guarantee anything, Cato. If you can reask your question?

DR. BOYAN: I think he is expressing still some concern that this may not be a perfect enough design category to justify a movement to class II.

DR. LAURENCIN: In other words, we have changed the design category to talk about a mobile platform, rotating platform type design.

The reason we are saying that is that we are saying that that minimizes subluxation events. However, is there data that says that design -- certainly it minimizes it over the other design -- but does that minimize the design.

The only article I have in front of me talks about that event occurring with, I assume, a platform type design.

That was attributed to surgeon's error by the people who came up and spoke, but in the discussion of their paper, they don't talk about that as being the reason. That is why I have a question about that.

DR. STERN: I think you are getting close with that question to what the panel has to decide. So, I am going to recuse myself from answering that. That is getting close, I think, to what the panel is being asked to decide.

DR. BOYAN: Right, thank you, Dr. Stern. That is exactly where we are. So, we have got that in mind from Dr. Laurencin, and let's go to panel question number three.

As soon as panel question number three goes up there, it is going to go back down and our definition is going to go back up.

Have appropriate special controls been identified to adequately address the risks to health for each of the above-referenced device configurations.

If not, what other special controls are necessary, and respond to these questions that are listed for us: one, dissociation of the metal backed patella components; one is dislocation and subluxation of the mobile bearing components; and the last one is the labeling information, typically whether or not there is sufficient labeling information, is there additional labeling information that

we need to do.

Let's start with sufficient controls for the dissociation of the metal backed patella.

DR. NELSON: I don't think that is the first question. The first questions are way back up in the main paragraph. Then, in addition, we have to do all the others. So, there is really three, then 3A, 3B and 3C.

DR. BOYAN: You are right. Let's do question number three. The special controls for the device configurations. What other special controls do we need to add in. Dr. Nelson, let's start with you.

DR. NELSON: I don't think we have identified any special controls. I think we have to identify some and I can't do that for you.

DR. HOLEMAN: I feel comfortable with the controls that were identified, but I will have to pass on whether they are adequate.

DR. SILKAITIS: If FDA has the controls, I am not sure what they are right now. But there are controls for the design of cemented knees. If those are applicable to cementless knees, then certainly they are in place, then.

DR. BOYAN: Thank you. Dr. Aboulafia?

DR. ABOULAFIA: I think it does stratify a little bit. There are special controls that I would want for some

of the things we are classifying and not for the others.

DR. LAURENCIN: I think I agree with Dr. Aboulafia. For instance, for the uncemented fixed bearing total knees, I think we have a good number of controls.

At the other end, I think that for uncemented unicompartamentals, we don't have enough controls.

DR. SKINNER: I think we have enough controls.

DR. BESSER: I think controls are sufficient.

DR. BOYAN: Dr. Besser said he thought the controls were sufficient. Dr. Hill?

DR. HILL: I do, too. I agree.

DR. BOYAN: Dr. Stern, are you out of this now? Okay, Dr. Yaszemski?

DR. YASZEMSKI: I think the controls are sufficient, in that from the list that will go over on the work sheet, I may not suggest that we apply all the boxes that we can check to every one of these configurations.

From among the boxes we can check, I think we can choose combinations that will satisfy each of the combinations of prostheses we are being asked to consider.

DR. BOYAN: Okay, Dr. Lavin?

DR. LAVIN: Sufficient at the time.

DR. BOYAN: Mr. Allen, would you like to make a

comment?

MR. ALLEN: Yes, Pete Allen, FDA. I would just like to point out that up on the screen, these are the controls that were proposed by the sponsor. You have those there for you to look over.

DR. BOYAN: Let's go to the specific questions and, as we discuss those, perhaps something additional will come out.

Let's focus in on the metal backed patella. Dr. Yaszemski, since this is one that you have thought about in depth, could you begin us with this one?

Are the appropriate controls present, and if not, what additional controls need to be added?

DR. YASZEMSKI: I think they are present and my concerns have been answered by the representatives of the petitioner.

DR. LAVIN: I am satisfied.

DR. NELSON: No comment.

DR. HOLEMAN: No additional information.

DR. SILKAITIS: No additional comments.

DR. ABOULAFIA: I am not sure to be in the dissenting opinion. For metal backed patellas, I am not sure that we do have a lot of information.

Can we just say that we would like post-marketing

data on that group of patients? If that is the same thing as Dr. Yaszemski is saying, then I am certain I agree and we can move along.

DR. BOYAN: I am not sure that it is. You can phrase it that way, but I think what we are asking for here is, you have stated that you don't think there is enough information, which is a suitable statement.

What additional information would you like to have?

DR. ABOULAFIA: Just follow up on patients that do have the implant, post-marketing surveillance, is the term I am trying to remember.

DR. BOYAN: All right, Dr. Laurencin?

DR. LAURENCIN: I agree with Dr. Aboulafia.

DR. SKINNER: While agreeing with Dr. Bourne and Dr. Insall, I also agree with Dr. Yaszemski. I would never put one of those things in.

DR. BOYAN: Dr. Besser, the question is, the metal backed patella, do you think there are enough controls in place?

DR. BESSER: Yes, adequate controls are in place.

DR. HILL: I think there should be some post-market surveillance. It sounds like a design in transition. It didn't sound like at this point in time that they had

answered all the questions as far as it being an adequate design. I think it needs to have some special controls.

DR. BOYAN: We are now down to the next question, number two. Dislocation and subluxation of mobile bearing components has been cited as a complication. Are appropriate controls identified to adequately assess this risk? If not, what additional controls?

We have a system going here. Yaszemski first.

DR. YASZEMSKI: I am going to answer the same as I did before. My concerns have been answered and I think that with a control such as post-market surveillance, I would be happy.

DR. LAVIN: I agree.

DR. NELSON: Without tipping my hand how I am going to vote in the future, I don't think special controls are going to be sufficient.

DR. HOLEMAN: I pass on that.

DR. SILKAITIS: No additional comments.

DR. ABOULAFIA: Agree with Yaszemski.

DR. LAURENCIN: I am not sure whether appropriate controls have been identified in the literature. I think that even in the best system that we are seeing with the LCS system, I think things occur that may take more constraint in terms of the system which may translate to -- in an

uncemented system, they may translate to failure there. I think that more appropriate controls need to be done.

DR. BOYAN: You don't have any specific ones that you would like to recommend?

DR. LAURENCIN: I don't.

DR. BOYAN: Okay, Dr. Skinner?

DR. SKINNER: I think the track record on the movable platform type prosthesis has shown that, in good hands, the risk of dislocation is small.

I think the problem comes in the meniscal type of prosthesis where there seems to be a fair bit of risk that, without the precise surgical techniques, there can be problems.

I think that for the platform there are adequate controls. I think that for the meniscus type of thing, I think that -- we eliminated that?

DR. BOYAN: No.

DR. SKINNER: It says mobile bearing components. It doesn't say what kind of mobile bearing components. Anyway, that is where I stand.

DR. BOYAN: Okay. Dr. Besser?

DR. BESSER: I am sorry, I was thinking. I didn't think that necessarily lacking a means of preventing varying dislocation would be included in this question. Therefore,

I wouldn't have any problem with the controls presently in place.

DR. BOYAN: Dr. Hill?

DR. HILL: I agree, as long, as Dr. Besser pointed out, you are eliminating the meniscus type mobile implant.

DR. BOYAN: My own comment, again, is going to be related to wear considerations, that this data base on wear is inadequate to make decisions for the future.

As new information becomes available, it needs to be taken into consideration.

Next issue, labeling information -- oh, we should ask, did we address that question okay for you, FDA?

DR. WITTEN: Yes.

DR. BOYAN: Labeling information typically includes device description, material indications for use, contraindication and so forth. Do we think there is any additional labeling information necessary for design configurations listed? If so, what do we recommend.

Labeling is Dr. Holeman's expertise. Let's start with Dr. Holeman.

DR. HOLEMAN: I think in the question and answer period I did make a comment that I didn't feel comfortable with the information that is indicated for indication for use.

I do feel that it should be clarified in the sense that we are talking about a variation of design which might have an impact on how it is used.

DR. BOYAN: Thank you. Dr. Silkaitis?

DR. SILKAITIS: I don't have an additional comment right now.

DR. ABOULAFIA: No additional comment.

DR. BOYAN: Dr. Laurencin, you are addressing the labeling question? I will pass you by, and Dr. Skinner, as being out of order with private conversations, and go to Dr. Besser.

DR. BESSER: No additional labeling requirements.

DR. HILL: I don't see any additional labeling requirements necessary.

DR. YASZEMSKI: No additional requirements necessary.

DR. LAVIN: I am not familiar with the specific labeling information for specific things that have been approved so far.

DR. NELSON: I don't think additional labeling is going to change anything.

DR. BOYAN: Now, Dr. Laurencin.

DR. LAURENCIN: Madam chairman, I want to apologize.

DR. BOYAN: I accept your apology.

DR. LAURENCIN: No additional labeling information is needed.

DR. BOYAN: Okay. Dr. Skinner?

DR. SKINNER: I agree with Dr. Nelson. No one is going to read it anyway.

DR. BOYAN: We have had this discussion before with you, Dr. Skinner. Now, are there any additional comments? FDA, have we addressed that question adequately?

DR. WITTEN: Yes, thank you.

DR. BOYAN: Question number four, does the data presented in this petition support -- now, here we go, and let's just take them one at a time. Can we have our definition back up, please?

Let's just go right around the table. Let's start off with -- we are not going to -- we are going to address this panel question, bearing in mind that we have this definition waiting in the wings.

We are just going to take exactly what is in the petition and say, does it support these various aspects.

Starting with the patellofemorotibial uncemented porous coated total knee prosthesis, does the data presented support reclassification.

Now, we are going to start with Dr. Hill. We are

going to go right around the table. You say yes or no. At this point, I also would appreciate, if you do say no, that you explain what you think is missing.

DR. BESSER: Before we vote, I would like to point out that choice C is going to be mobile bearing knees within each of the above two device types. I believe that the first time we go around the table we are voting on fixed bearing knees.

MS. NASHMAN: Just a point of information, we are not voting right now. We are discussing. We are answering questions.

DR. BOYAN: Good point, Ms. Nashman. Your point is, Dr. Besser; could you repeat that?

DR. BESSER: As we are going around the table, I would like to hear, the first time around I guess, when we comment on 4A and 4B, comments on fixed bearing knees, not mobile bearing knees.

DR. BOYAN: I think we are holding mobile bearing knees for the coup de grace here. Okay, let's just do A and then B and then we will do mobile bearing knees.

So, Dr. Besser's comments are A and B are both fixed. Then C and D, which C is theirs and D is ours, is going to be the mobile. Let's do A and B as a group together. Dr. Hill?

DR. HILL: A and B as a group together?

DR. BOYAN: Just say yes/yes, no/no, yes/no, no/yes, whatever.

DR. HILL: I think my answer would be yes/no, yes for the fixed and no on the non-cemented unicompartmental.

DR. BOYAN: For the reasons that you have given earlier today?

DR. HILL: For lack of literature to support the uncemented unicompartmental.

DR. BOYAN: Okay, Dr. Yaszemski.

DR. YASZEMSKI: Dr. Hill has made my answer easy by giving it precedence. My answer is, in addition, yes/no.

DR. LAVIN: Same answer.

DR. NELSON: Yes/no. In explaining the no, this doesn't mean -- I am saying no because I don't think there is sufficiently clear data that makes down classification appropriate.

I recognize that probably means a PMA. I want to point out that that PMA need not be prospective, which is quite expensive, but can be lesser.

DR. BOYAN: That is FDA's problem on that one, if we get that far.

DR. HOLEMAN: I would have to go with the yes/no, because of the lack of literature review.

DR. SILKAITIS: I will say yes to the first part. The second part, some data was presented, but I have to pass on the second answer.

DR. ABOULAFIA: Yes/no.

DR. LAURENCIN: Yes/no. There is some data that is there. Again, the question is, is there enough that brings you to say, yes, let's make it easier for new applications to get through.

DR. SKINNER: Yes/yes. I think that there is not enough reason not to approve it. It is a straightforward thing, from my viewpoint.

Again, I don't put in uncemented unicompartments, but I think there is no reason to expect them not to grow in.

DR. WITTEN: Excuse me. We are not approving or not approving devices. I just want to mention that again. We are talking about classification or reclassification of devices.

DR. BOYAN: Exactly, thank you, Dr. Witten. I really have to say as chairman that the way this whole thing is structured, we are looking at devices. I think that has been a confusion to the entire panel.

The way it is structured, it almost sounds as if we are approving devices that we have never seen before.

I think we need to state that we are not approving any of these devices or disapproving or recommending or anything.

We are talking about classification of devices that fit into a certain category that we are recommending. Is that correct, Mr. Dillard?

MR. DILLARD: I would like to maybe just, for 20 seconds, give a couple of clarifying statements. The first statement I believe Dr. Witten just made.

The second is that these are not classification recommendations. They are reclassification recommendations.

These devices have all been classified, either pre-amendments, as pre-amendment classified devices or post-amendments, by either a PMA approval decision or a not-substantially-equivalent decision through the 510(k) process. They become automatically post-amendments class III devices.

Really, what we are asking you to do with this question, and I think with a lot of questions today -- and I think yesterday you had it right on target -- was that the data, the generalized data in the literature, the data that is presented in this petition, should be sufficient enough that really, what it clarifies for you is that you get a sense that you can identify risks and the appropriate risks

for the kinds of devices.

Then there are also special controls to adequately control for those risks, associated with the kind of device that you have under discussion.

That is really a very important point that the literature brings you, that there is, in your mind, sufficient or insufficient information to be able to clarify what those risks are and what are the circumstances.

I think that is a key point that you should consider during your deliberations. Thank you.

DR. BOYAN: I think that is very well stated. Thank you. Dr. Skinner?

DR. SKINNER: Dr. Boyan, after hearing those remarks, I would like to ask that we go around the panel one more time.

I think that there is adequate information out there to consider this to be a class II device, this unicompartmental knee.

DR. YASZEMSKI: I will second that.

DR. BOYAN: We will do that. Let's just hear from Dr. Besser before we start that process.

DR. BESSER: Yes/yes.

DR. BOYAN: Okay, so, let's phrase this. Right now at this point we are not discussing any more the

patellofemorotibial uncemented porous coated total knee prosthesis.

The general tenor of the panel is that the data presented in this petition does support the reclassification of that device.

Now we are focusing in on the femorotibial unicompartmental uncemented porous coated knee. What we are trying to make a statement here is, do we think that there was sufficient data presented in the petition that would support reclassification of this device?

We will start again -- do we start with you, Dr. Hill?

DR. HILL: I guess I still don't see a reason to change my answer. I still don't think there is sufficient literature.

DR. YASZEMSKI: I seconded it. Clearly, I am going to change my answer. The reason I am going to is with Mr. Dillard's description.

I think what I had neglected to consider last time was that I think the controls that are available to us are adequate to control the risks that, to me, are still not clearly -- the outcome from those risks are not clearly delineated in the literature, but the controls are present, in my opinion, now, to allow us to evaluate them.

DR. LAVIN: I remain no.

DR. NELSON: No.

DR. HOLEMAN: I am going to stay with no. I thought that the question read, if the data presented, not just necessarily to support in all categories, but the data warrant reclassification. I don't think it does.

DR. SILKAITIS: I do change my answer to yes, for the reasons of the clarification that Mr. Dillard provided, also the fact that there is data and we do have the special controls in place that can help define what is required for the assurances.

DR. ABOULAFIA: I agree and thank Mr. Dillard. I would say change my answer to yes.

DR. LAURENCIN: Remain no.

DR. SKINNER: Yes.

DR. BESSER: Yes.

DR. BOYAN: Actually, it is very interesting. It is exactly a tie.

MS. NASHMAN: At this point, again, please note we are not voting. We are just discussing. Everyone can make notations and look into the future and see what happens in a little while, but currently we are not voting.

DR. BOYAN: Correct. So, what we are going to state to the FDA is that there was no clear consensus on

whether or not there was sufficient information presented in the petition to support the reclassification of the femorotibial unicompartamental, uncemented porous coated knee.

Now, let's deal with what they have written and then we can make a recommendation. Okay, what is written here is, specifically, do the data presented in this petition support the reclassification of mobile bearing knees, uncemented and/or cemented, within each of the above two device configurations?

I have listened to a whole lot and I have not heard that the data support that. So, if there is someone here who feels that the data do support that, please identify yourself. Dr. Skinner.

DR. SKINNER: You are saying that you don't think the committee feels that there is adequate data to justify the reclassification of the platform rotating --

DR. BOYAN: No, as presented in the petition. We are going to have an opportunity to make some recommendations now. So, I want us to deal with what is written here.

Do the data presented in this petition support the reclassification of mobile bearing knees, uncemented and/or cemented within each of the two devised configurations.

I would say that I have heard nothing today to say that the total category of mobile bearing knees was sufficiently well justified to include in a reclassification agreement.

I heard that we did feel that there were certain characteristics of mobile bearing knees that could include them in a reclassification.

Is there anybody that does not agree that we did not hear some characteristics that could qualify a knee of this type into a reclassification? No.

So, I would like for the definition that we have reconstructed, of what we think might qualify such a knee, this might be our recommendation to the FDA; that if they were to look at -- the petition is inadequate in defining this category of down classification.

We would like to offer some help to the FDA that this kind of a definition would be more appropriate for a downward classification.

DR. NELSON: I would like you to clarify, when you say rotating, you are referring to rotating, not translating. I think that is a big difference.

DR. BOYAN: I need some help with that. I realize, Dr. Stern, that you are not voting. Could you offer some clarification?

DR. STERN: My understanding of this definition is an attempt to also exclude the meniscal bearing type of knees.

I am thinking here of a rotating platform in which the polyethylene can rotate back and forth, or translate anterior posteriorly with one bearing surface, I guess.

Dr. Skinner, might that be a better way to put it, one bearing surface as opposed to two?

DR. BESSER: I think that at least what I was thinking of, we wanted to exclude those moving bearing systems that did not have a means, a constraint, against dislocation, be it a pin around which it rotated or along which it translated or something like that.

DR. LAURENCIN: Would it be easier -- I hate to do a lot of division -- to divide this? I get the sense from the panel that uncemented, fixed bearing knees are something that people would support being reclassified from III to II.

Mobile bearings, there is a question and the unicompartmental is a question.

Can we just look at the uncemented fixed bearing knees and then vote on -- total knees, and then vote on those and make the modifications from there?

DR. BOYAN: We are not voting, Dr. Laurencin. When we do the sheets, what we have already done is separate

out these two categories.

So, we already have fixed separated from mobile right now. Dr. Aboulafia has been trying really hard to get in something.

DR. ABOULAFIA: Just very quick, a procedural question. Is it our role to separate things out of the petition, or are we supposed to look at the evidence presented to us in the present form of the petition and say these are our recommendations?

If people who have attended this meeting have an idea that there might be some mobile bearing knees that we would recommend reclassification, but not other mobile bearing knees, would they come back to us with a petition that separates those out? That is more of a procedural question, I guess.

DR. BOYAN: Let's get some clarification from Mr. Dillard.

DR. WITTEN: I think what we are looking for is an answer for the matters in the petition. We would certainly be interested in other input as you describe.

I think if you had a clear recommendation as a group about something you thought we should do, we would take that recommendation as well.

Otherwise, what we want, I think, is an answer to

the questions that are in the petition.

DR. BOYAN: I think where we are on the question in the petition is that mobile bearing knees as defined in the petition was not adequately -- the data were not adequately presented to justify at this point for us a reclassification of class II.

Is that a fair statement? We will go around and give everybody a chance to say yes or no. I won't make you just stare at me. Yes, Dr. Nelson?

DR. NELSON: I think we still have to change that. Unless I am mistaken, there is only one device out with a rotating platform.

The intention was really either a rotating or translating platform or any platform that includes both condyles. Am I correct in saying that was what the real intention was?

DR. YASZEMSKI: Dr. Boyan, I suggest just to include rotation and translation, change the word rotating to mobile.

DR. BOYAN: Okay. We need to make that change. All right, let's go around the table now and address the question as written with the understanding that we are going to offer some advice back to FDA. Okay, Dr. Hill?

DR. HILL: I think I have the gist of what the

question is. I am still a little confused, but if you are asking me, do I accept the definition --

DR. BOYAN: No, no, I am asking you really specifically, do the data in the petition support the reclassification of mobile bearing knees within each of the above two device configurations. The answer to that is either a yes or a no.

Then, are you comfortable with this advice that we would offer back. In the event that you think there was not enough information provided in the petition, is this suitable advice to offer back to FDA.

DR. HILL: Yes.

DR. YASZEMSKI: My answer is no and the advice is suitable.

DR. LAVIN: No, and the advice is fine.

DR. NELSON: No.

DR. HOLEMAN: I would say no, and I would agree with the advice.

DR. SILKAITIS: I hate to ask, but could you repeat that? I got lost.

DR. BOYAN: There is a real specific question. They are just asking us, was there enough information in the petition that we felt, after listening to all of the evidence presented today, and after reading all the

information they sent to us, do we feel there was enough information to support the reclassification of mobile bearing knees, either cemented or uncemented, in the two categories described in A and B, which was the patellofemorotibial device, and the femorotibial unicompartmental device.

DR. SILKAITIS: What I thought I heard the panel say earlier it was, was that there was sufficient evidence at least to have specific controls. It looks like that was a partial yes.

DR. BOYAN: We already did the specific controls part. So, I see what you are trying to say. Phrase it another way, could you?

DR. SILKAITIS: In other words, information was provided in the petition regarding a specific design characteristic of a mobile knee to answer, I suppose, A. But B, there wasn't sufficient information provided.

DR. BOYAN: Did everybody understand what Dr. Silkaitis is trying to state to us, is that our definition really addresses A but not B.

DR. SILKAITIS: Right. I am asking the other panel members that voted no, I was wondering why they were changing their thoughts on that.

DR. HILL: I didn't think I was changing my

thought when I voted. I think that she asked me to accept both first, and that was a no, and yes was with our revisions.

DR. SILKAITIS: So, they are both combined.

DR. BOYAN: The way the question is phrased, they are asking us both combined. I think your answer actually clarifies what we really should be doing. A is addressed by our definition and B is not.

DR. SILKAITIS: Right.

DR. ABOULAFIA: So, if I am reading the question correctly, does the data presented in this petition support the reclassification from mobile bearing knees with each of the above two device types, I would say no.

DR. BOYAN: Are you comfortable with the definition? Is it addressing the design A adequately for you?

DR. ABOULAFIA: Design A is patellofemorotibial uncemented, porous coated total knee?

DR. BOYAN: Yes.

DR. ABOULAFIA: No. It is a mobile bearing knee -
- do you want to clarify what you mean?

DR. BOYAN: I think that this is the problem with the petition. I think the answer is probably justified with a no.

DR. HILL: That is where I am confused. When I was saying yes, I was saying yes assuming that we were talking about the definition that we are going to put in order.

If the answer is just based on the question, then if that also includes meniscal type moving components, then my answer was no/no.

DR. NELSON: I think, Madam Chairman, I think maybe if you stratify 4C into tricompartmental or unicompartamental and then just say, you know, I want a yes/yes or no/no or whatever variation, that would answer the question succinctly.

DR. BESSER: I think since this isn't a vote and we are just going around the table and presenting what we like, if I may, is there anybody who prefers the definition as in the petition presented by the petitioner over the one up on the wall?

DR. NELSON: I do, but only just because I am going to vote no/no. I think a lot of other people want to stratify it and I think we have to use the definition on the board.

DR. BOYAN: So, basically, the answer right now is -- let's address the petition question. Let's go right to the petition. Let's ignore anything -- take the definition

off right now. The definition is history.

Now, let's go really specifically to what is in the petition. I do want to state to you that this is going to be one of those situations where none of us are that clear on what is in the petition.

DR. NELSON: Do you have an overhead for the petition?

DR. SILKAITIS: Dr. Boyan, I would like to maybe ask FDA if there is any difference between having a definition that is all encompassing or a definition that is A, B, C or three different definitions.

I think that is what we are struggling with here. I don't know if there is a regulatory difference on having an evaluation of three different --

DR. BOYAN: Mr. Dillard?

MR. DILLARD: These were not intended to confuse or to cause this much difficulty, I am sure. I think the questions were intended to try to give you a sense or at least, Madam Chairman, a sense once we get to the work sheets, since these same issues come in the work sheet, to try to address the issues beforehand, so that they were clear before you get to the work sheet.

Perhaps this has been counterproductive in this case, and perhaps then I think -- what I keep hearing, I

believe -- let me offer one suggestion, that there seems to be some clear areas where you do have some consensus, Madam Chairman.

Then perhaps those are the very obvious kinds of work sheets to work through. Then there are some others where there is no clear consensus.

Perhaps it is time to look at Ted, maybe you could put up the questions that we have got, that breaks out -- I believe it is question number four -- that has got A, B and C to it.

I believe you answered A and you got through B. Now perhaps C is a little unclear because we are talking about mobile bearing knees, uncemented and cemented. So, under C, we have got four potential categories.

Maybe we could take each one, one by one, just real quickly just to get you through it and then move forward.

DR. BOYAN: I agree with you totally. We have done. We have done B. Now we will do C.1 and C.2, and then we will go to the sheets and we will do four sheets. That seems to be the only way to get through this.

We will go now to C.1. It will be the tricompartmental mobile bearing knee, cemented and uncemented.

All I want you to tell me is, do you think there is sufficient data in this petition to support reclassification.

We will start again. We will start here with Dr. Hill and we will limit our thinking to the tricompartmental mobile bearing knees, uncemented and/or cemented.

DR. HILL: I guess my answer to the question -- and I must admit that I am still a little bit confused on the way the question is structured -- is that I have no problem with the mobile being the platform with some restraints on it. I do have a problem with the meniscus type lesion.

If you are lumping those together, I would have to say no. If you separate them, I have no problem with the platform. That is why I have a problem with the question.

DR. BESSER: Can we separate them, just to get this around the table?

DR. BOYAN: We can. So, we have C.1.1. Let's define those two now. You have got the mobile bearing with the --

DR. ABOULAFIA: Can I suggest mobile bearing, tricompartmental knee, cemented, is C.1-A. Tricompartmental, mobile bearing knee, uncemented, is C.1-B.

Of those two, both of those would be a rotating -- what is the term we used -- platform. Then the next group would be C.1, tricompartmental mobile bearing knee, cemented, and that would be C.1-C. The next one would be mobile bearing knee, uncemented, which would be a C.1-D.

Of the final two varieties, C.1-C and C.1-D, both of those would be any design. In other words, it would be as written in the petition.

DR. BOYAN: Okay, we have got it now. Then we will do C.2, which is the unicompartmental and uncemented.

DR. NELSON: Madam Chairman, I think we ought to just put it on the overhead or we won't be able to know what we are talking about.

DR. BOYAN: Okay, it is coming. While we are getting the overhead, let's do what we can do simply. Let's start on a work sheet for the patellofemoral uncemented porous coated total knee prosthesis.

This one is going to be the patellofemorotibial uncemented porous coated total knee prosthesis.

MS. NASHMAN: (Housekeeping matters discussed.)

We are going to work our way through this one. This is the patellofemorotibial uncemented porous coated total knee.

When we did our original move around the table, we

felt that this had enough information presented in the petition to support reclassification.

I am going to say that, yes, the classification recommendation is II.

Is the device life sustaining or life supporting? The answer is no.

Is it of use to humans? The answer is yes.

Does it present an unreasonable risk of illness or injury? The answer is no.

Now we jump down to question number seven. Is there sufficient information to establish special controls to provide reasonable assurance of safety and effectiveness? If yes, check the special controls needed.

We felt, when we discussed this, that we need performance standards only. We did not have post-market surveillance for that one.

DR. NELSON: Madam Chairman, am I correct that these testing guidelines they are the biomechanical sorts of things?

DR. BOYAN: Yes.

DR. NELSON: So, we want that as well.

DR. BOYAN: Those are the standards.

DR. NELSON: In a 510(k) you want engineering data to say yes, it is adequately strong. So, we want both

performance standards and testing guidelines.

DR. BOYAN: Okay. So, we do not need -- we go to 11. Let's finish this first. Can there otherwise be reasonable assurance of its safety and effectiveness without restrictions on sale, distribution or use because of any potentially harmful effect of collateral measures necessary for device's use. The answer is no.

We have been answering these needed restrictions. All right. The needed restrictions is that it should have at least an oral authorization by a practitioner. That sheet is done.

That supplemental data sheet while we are on it, indications, it is a device, yes.

Indications for use prescribed, recommended or suggested in the device's labeling that were considered by the advisory panel on labeling? Were there any labeling issues that needed to be addressed? No.

DR. NELSON: Madam Chairman, I don't want to slow you down, but Dr. Holeman had just said she wanted to address some of the issues, I thought, like for bone stock or something like that. Let me defer to you. Did you want to add something here or not?

DR. HOLEMAN: I had indicated there was a labeling issue but that the panel didn't feel that it was necessary.

I will go with the panel.

DR. BOYAN: Okay. All right, identification of any risk to health presented by the device. It was, as in petition.

Any specific hazards to health? No.

Any characteristics or features of device associated with hazard? No.

Recommendation. We recommend class II.

If the device is an implant, or is life sustaining or life supporting and has been classified -- we don't have to do that one. Oh, wait, why did we down classify it? Because of the petition.

DR. NELSON: Madam Chairman, I am not sure that is it. We were just going to say there was adequate data to support it.

DR. BOYAN: Yes. Summary of information including clinical experience or judgement upon which classification recommendation is based.

Again, we felt that the petition explained things adequately.

Do we have any restrictions that we want to put onto the use of the device? Okay. So, turning the page.

Question 11. Existing standards applicable to the device, device subassemblies and device materials. We felt

yes, as in petition. We are done. Now, we need to vote.
So, I need a motion.

DR. NELSON: I make a motion that we accept the
petition as just outlined by Dr. Boyan.

DR. BOYAN: I need a second.

DR. HOLEMAN: I second.

DR. BOYAN: We will just go quickly around the
room and vote. State your name and vote, starting with
Dr. Hill.

DR. NELSON: Pardon me, Madam Chairman, we need
another second. We had a non-voting member.

DR. ABOULAFIA: Second.

DR. NELSON: Let's go with the vote.

DR. BOYAN: Okay, vote.

DR. HILL: My vote is yes.

DR. YASZEMSKI: Yes.

DR. LAVIN: Yes.

DR. NELSON: Yes.

DR. ABOULAFIA: Yes.

DR. LAURENCIN: Yes.

DR. SKINNER: Yes.

DR. BESSER: Yes.

DR. BOYAN: Okay, motion carries. Excellent work.
Okay, one down. Do you want to do the other one, the other

easy one, before we go to the part that is not so easy?

DR. ABOULAFIA: Motion.

DR. BOYAN: So give me another sheet. This one is, does the data presented in this petition support the reclassification of the femorotibial unicompartmental uncemented porous coated knees.

We were -- oh, this is not an easy one. We came to no real sense of commitment one way or another. We got to a tie where there half of us who thought yes, it did, half of us thought no, it didn't.

It came up to me and I will say yes just for the sake of discussion and break that tie. So, we are going to go with a yes, because we are going to have to fill this out either way.

DR. NELSON: Dr. Boyan, I think what you have to do is formulate something that we can vote either yes or no on. So, you have to do it as the yes.

DR. BOYAN: So, let's go. This one now is the femorotibial unicompartmental uncemented fixed bearing. Classification at the current time is to a II, and we will see how we do.

Is this life sustaining? No.

Is it of value to humans? Yes.

Does the device present a potential risk that is

horrible? No.

Did you answer yes to any of the above questions?

Yes.

Is there sufficient information to determine that the controls are sufficient to provide reasonable assurance of safety and effectiveness? This is where the discussion starts.

Fifty percent of us felt that there was not sufficient information, fifty percent felt there was.

DR. NELSON: Madam Chairman, I think in order to get this to something we can vote yes or no on, what you have to do is presume the yes answer, and then we can vote on it.

DR. ABOULAFIA: Not necessarily. I think there are people who supported the fact that there were restrictions that needed to be imposed.

DR. BOYAN: Yes, because we had to fill them in. So, the answer to this is no.

DR. NELSON: I am sorry, what is that question?

DR. BOYAN: The question is, is there sufficient information to determine that general controls are sufficient --

DR. NELSON: We are on number seven, special controls.

DR. BOYAN: We need to give a yes or a no to that. What do we give is.

DR. NELSON: We don't do five.

DR. BOYAN: Wonderful news. Wonderful news. Number seven. Is there sufficient information to establish special controls. Now we start to say yes to this, and what special controls would we add.

We added post market surveillance, we have performance standards. We want to have testing guidelines. Is there anything else?

DR. SILKAITIS: Dr. Boyan, could the panel members help out in defining the post-market surveillance? Are we talking about an open study of 15 knees?

DR. BOYAN: Dr. Aboulafia, that was your idea. What would you like?

DR. ABOULAFIA: I think this speaks -- I know we are not supposed to reference, but similar to what went on yesterday.

I think preapproved, small center, three or four or five surgeons, who do a total of maybe 30 with two-year follow up, or with even two-year follow up.

I would be willing to look at a proposal but I am not talking about 200 patients with a minimum two-year follow up, just so everyone understands what I am talking

about.

MR. MELKERSON: Just a point of clarification, both on the previous recommendation and this recommendation, when you are describing performance standards, you are actually talking consensus or voluntary standards and not those according to 514.

DR. ABOULAFIA: When we talk about performance status, or post-market surveillance, can we say we would like the implant to be used in a controlled clinical setting, for example, five surgeons at five centers?

DR. BOYAN: I think that that needs to come -- I don't think we need to get on that level of detail. We are stating that we want more information, we think that more information would be of value for FDA to make a decision, and the FDA can request a protocol from the petitioner, and review that protocol. I think we should leave that up to FDA.

DR. NELSON: Dr. Boyan, are you not then talking about class III? How is that different from class III?

DR. BOYAN: This is a post-marketing study.

DR. NELSON: I know.

DR. LAURENCIN: I agree with Dr. Nelson. If you are talking about saying that this should be looked at by five centers with maybe 30 patients, prospectively, two-year

follow-up, you are talking about a PMA.

You are talking about saying that the controls that are needed are the controls that are defined under the class III.

It is almost like we are saying, we will downgrade to class II, but it needs the controls that one has in class III to be able to downgrade it to class II.

DR. BOYAN: Let's get through this sheet. Then we will have a motion to accept the sheet as written or not. If we don't accept the sheet, we can make the classification recommendation be a III. We don't have to have it be a II.

MR. DILLARD: Dr. Boyan, if I could make two quick points, two things since you are on special controls that I think need to be clarified here, just real quickly.

The one Mark Melkerson started, which is performance standards, the kind of performance standards, again, for clarity, are you talking about 514 device specific performance standards for FDA to develop, or are you talking about typical consensus based ASTM, ANSI, ISO standards, for materials compatibility, for orthopedic implants; if you can make that very clear between the two of them, when you are talking about that area of special controls.

Then the other, about post-market surveillance

versus a post-approval study, for example, and premarket and postmarket.

I am not the expert in the area, but I think some of the way we interpret it, about the difference between surveillance and post-approval study, surveillance tends to be a lesser degree of what we are asking for on a study or what a manufacturer is doing in a study.

It is not that you have full data sets that you would consider in a premarketing kind of study. It is more of a surveillance, checking to look for adverse event rates, looking for maybe small parameters of effectiveness, not the magnitude that you are talking about when you talk about a preapproval study.

There can be issues that can come up during the investigation of a product where there might be a specific issue that gets highlighted.

Many times, panels have recommended to us, then, to do a post-approval study to target specific issues also.

Now, all three of those are options. Just to again clarify, even in a premarket situation, from a 150(k) standpoint, the FDA does have the regulatory discretion to ask for preclearance studies through a 510(k).

We do have that authority. We also have the authority to talk with the manufacturer about discretionary

post-market surveillance also.

Those are all options that we use as controls during a regular review process of products. I think to that extent, that you might be able to give us guidance about the kinds of information you would want to see.

That would help also clarify the kind of study or the kind of information that we might use perhaps a little bit more discretionary from your recommendation.

DR. BOYAN: Okay, based on that, what I am going to ask -- Dr. Skinner, would you like to start? Then I am going to ask Dr. Nelson to state clearly, in a format, all the things that he thinks needs to be tested on this device.

Okay, Dr. Skinner.

DR. SKINNER: I think what the consensus of the panel -- maybe I am speaking out of turn here, but I think the consensus of the panel is that we are talking about performance standards as defined by the ASTM, the American Society for Testing of Materials, consensus standards.

When it comes to this unicompartmental knee, the unicompartmental knee looks identical from the bone interface into the joint, as any other unicompartmental knee that is cemented into place.

The only thing that is of concern here is the fixation method. I think that is the only thing that we

would have to be concerned about in any post-marketing surveillance.

From my viewpoint, again, I go back to this being a porous coated material with a track record in total knees that is very good.

I think that if there are differences, it is probably surgical, and I think it would take a large number of patients to demonstrate big differences in loosening or failure of fixation.

I am not sure what we gain by going into a post-marketing surveillance. I think this is a relatively low-risk type of thing.

I would sort of try to urge the panel to move in that direction, not having a post-market surveillance that could add significantly to the cost of the prosthesis.

DR. NELSON: Madam Chairman, if I could defer on your request -- I don't think I am the one that could do that well.

I would just like to attempt to repeat what Mr. Dillard said in my own words. This is a question that I asked him yesterday in training twice. What is the difference between class III and class II with post-market surveillance, because they are both clinical studies.

What he has told me, both in public and private

discussions again is, it is basically a gestalt. If you think that this class needs clinical data before the things are approved, that is a PMA.

If you think this whole class doesn't need big clinical data, but you might need a little bit of stuff to tidy up something, then it is class II.

I think the question we have to ask ourselves is, as a whole class of mobile knees, either translational and rotational or separate things, is there enough clinical data out there from the multiple devices which don't exist being used of this design that say the whole class can be approved.

So, it is a question, do you get the gestalt, is this really something where it is class III and you want lots of data, or there is lots of data out there and you just need a little bit of clinical data in addition, and this is class II.

DR. SILKAITIS: You mentioned mobile knees. I think we are talking about unicondylar.

DR. NELSON: It doesn't make any difference what you are talking about. That is the differentiation.

DR. BOYAN: I am going to take the chairman's prerogative here. I see you there, Mr. Dillard. I think we have had a lot of discussion about this and I am not overly

concerned. I think I get the point.

We are being asked by the petitioner to address a change in classification and if we as a group are so stressed out about this, then I think we are sending a very clear message to FDA and they are getting that message.

Let's just work through these sheets. Let's not have any more philosophical discussion. Let's just answer the questions and the facts will get straightforward.

If we can't agree on answers, I think the message is very clear. If we agree, that message will also be very clear. Is that fair, Mr. Dillard?

MR. DILLARD: Yes, that is fair. I would just like to make one comment for the public record, that I would have a few other comments to Dr. Nelson's last discussion about clinical data and the difference between a class III and class II discussion. I will preserve those in case anybody wants to hear them and I will move on.

DR. BOYAN: I think that is very fair, Mr. Dillard, and I would certainly not want on the record that overall, that that would be the distinction between the two.

The bottom line is that there is a sense that class II designation conveys to the public that that device is safe and effective, and that there is enough experience

with it that it is reasonable to assume that it will be safe and effective if it fits into that classification.

Based on that, we are not even discussing that any more. We are discussing what information is necessary to assure that a device in this group would be safe and effective.

Right now, we have on the table, that we all agree that performance standards are necessary. We also realize, I think, that Dr. Skinner is correct, that those are the ASTM type studies.

Then we are also suggesting that preclinical studies be done according to the testing guidelines.

Right now, the real issue on the table is post-market surveillance. We had a recommendation for it. The argument at this point is not whether, if there is post-market surveillance, it makes it a class I or class II.

It is, is there a need felt by this panel, based on the information in the petition, that that additional study would enhance our feeling that these devices are safe and effective.

So, I don't know where are.

DR. ABOULAFIA: Yes.

DR. BOYAN: Okay, yes, what, yes, post-market surveillance?

DR. ABOULAFIA: Yes, post-marketing surveillance.

DR. BOYAN: Limited study as per the request of definition by Dr. Silkaitis. That would be a limited small study.

DR. LAURENCIN: Just to clarify, that is not post-market surveillance. That is premarket --

DR. BOYAN: No, no, no, that is up to FDA to figure out. This is a post-market study as pointed out by Dr. Skinner. Is the stuff fixed? Does it work.

Mr. Dillard, did I make a mistake? Did I make a mistake?

MR. DILLARD: Yes, I need to make one more comment. There is a difference in many people's minds in some of the terminology you are using, post-market study versus post-market surveillance.

I think this is what Dr. Silkaitis is curious about, which is, they are used interchangeably. Are we asking for surveillance because what you are feeling is that there isn't quite enough data to make a definitive kind of comment on non-clinically related special controls; that what you are asking for is some other information that ensures that the other kinds of controls that you are recommending are providing reasonable assurance of safety and effectiveness.

It is a little bit additional information to help clarify where you feel like the data does give you an indication, but is a little thin in terms of making a definitive decision.

That is the kind of situation in which surveillance information is very helpful for FDA.

Are you saying that, while there is some information, there are also some issues that have come up with the data, that we feel comfortable with, but you need to do a study, even though it is a post-market situation, a study that targets some parameters, targets some clinical end points, to give you the definitive information.

That is not completely the distinction between the two, but it might be a working way to think about the two of them for today.

DR. ABOULAFIA: Post-market surveillance, yes.

DR. BOYAN: Okay, now Dr. Laurencin.

DR. LAURENCIN: I disagree. I think there should be a post-market study if it is going to be utilized.

DR. SKINNER: I think that there shouldn't be any study. If there is going to be a study, I think it should be a study and not a surveillance, recognizing that this is going to have to happen for each prosthesis.

DR. BESSER: That was the clarification I wanted.

If we put this down here, that means each sponsor bringing a prosthesis to the committee will have to do this study or surveillance or whatever for their specific prosthesis; is that correct?

DR. BOYAN: We are not forcing anything. We are just recommending and FDA will consider each device as it comes across, independently.

DR. BESSER: I think we are classifying a class of devices.

DR. BOYAN: No, we are not. We are not.

MR. DILLARD: Would you like me to attempt that, Madam Chairman? I don't want to impose on your meeting.

DR. BOYAN: Yes, you get one last chance to clarify it.

MR. DILLARD: One last chance. You are making a recommendation that if this goes through, and post-market surveillance shows up here, you are making a recommendation to us that, because you are saying that it could be class II under these circumstances, that if these products were so classified as a class, somebody who would be submitting a premarket notification to us, to get clearance of the product as a 510(k), would need to meet those as special controls, the ones that you are recommending. That is your recommendation.

So, they would need to meet the standards that would be identified, that are appropriate for the product.

They would need to -- I am sorry, I can't see that far. I know post-market surveillance is on there. What is the other one that you identified?

DR. NELSON: Testing guidelines.

MR. DILLARD: Testing guidelines, you are recommending to us that a testing guideline be developed, probably an FDA testing guideline, and that post-market surveillance of the products, there would need to be some discussion with FDA and agreement about post-market surveillance of those individual product types.

They would not come back before the panel. It would be a clearance process that FDA would be taking on.

If we would enter into those negotiations and come to an agreement, we could clear those products. That would be your recommendation.

Those would be the controls that we would need to use to ensure each one of those products would be reasonably safe and effective for marketing.

DR. BOYAN: Okay, that is as good as we are going to do. If we don't have it by now, we aren't going to get it before lunch. Okay.

DR. BESSER: Yes.

DR. BOYAN: Yes, on this post-marketing surveillance phenomenon.

DR. BESSER: Yes on the post-marketing surveillance phenomenon, recognizing the fact that eventually, when enough of these things get out there to be boring, that post-marketing surveillance can probably be dropped for this class of devices.

DR. BOYAN: Okay. Dr. Hill?

DR. HILL: I agree.

DR. YASZEMSKI: Yes.

DR. LAVIN: Yes. I want to just add one thing further. First, I think the FDA should put a major effort to get their medical device report system in place, to take a lot of the burden off these post-marketing surveillance studies that we are about to proliferate.

DR. NELSON: No, I don't think special controls or anything else will do it.

DR. HOLEMAN: I pass.

DR. BOYAN: Dr. Silkaitis, we have already had --

DR. SILKAITIS: Yes, I agree with Dr. Aboulafia.

DR. BOYAN: Okay, so we are now down to number 8. We don't have to do 8, 9. We are to 11. Okay, can there otherwise be -- we don't have to do that. 11B, we want them to have for sure oral authorization.

We are now to the supplemental data sheet. Indications for use. It is a device? Yes. Indications for use, prescribed, recommended or suggested in the device's labeling that were considered by the advisory panel. Is there anything that we want to do in addition to the petition?

Identification of any risks in addition to what was in the petition?

Any specific hazards to health other than those identified in the petition?

Any characteristics of features of the device that are associated with this particular hazard?

So, we are recommending at this point, II, and we might not do that.

If device is an implant or life sustaining, why would we be down-regulating it? Therein lies the problem. Okay.

DR. BESSER: I believe that what we want to put in that slot is that sufficient data has been shown to allow us to down-class the item, and then we will vote on that later.

DR. BOYAN: Okay, and that we felt this information was in the petition and we are basing our judgement on that.

Any restrictions on the use of the device that we

noticed, that we would like to include?

We have to use the prescription.

DR. ABOULAFIA: I would say, I would restrict it to physicians who are going to participate in the post-market surveillance with a prospective control.

DR. BOYAN: Dr. Aboulafia, that is going to be the same as getting clinical data. I think when we deal with this, when we vote, I think we are going to handle that.

If device is class I -- we don't do that.

Existing standards applicable to the device, subassemblies or device materials as in petition?

Now, here comes this moment. The petition as it stands -- we should be painfully familiar with this.

This is for the femorotibial unicompartmental, all those other things. Okay, we are voting on a petition to classify as class II devices that are defined as being femorotibial unicompartmental uncemented porous coated knees.

Do I have a motion to accept the classification as a class II?

DR. YASZEMSKI: Amendment; fixed bearing.

MS. NASHMAN: When we are voting, we need to be clear. I know it is almost lunch time, that you guys want to go home. We are not reading the whole thing through.

Some things just need to be straight for the record. I apologize.

DR. BOYAN: Okay, do I have a motion?

DR. YASZEMSKI: Motion made.

DR. BOYAN: Second?

DR. SKINNER: Second.

DR. BOYAN: Now there is a motion on the floor to reclassify this petition as a class II, to accept this work sheet.

We are only voting to accept the work sheet. On the work sheet it states that we are recommending a reclassification to class II.

Let's start the vote and we always start with Dr. Hill lately, so let's start with Dr. Nelson.

DR. NELSON: No.

DR. ABOULAFIA: Accept the work sheet with the stipulations outlined.

DR. LAURENCIN: No. Do you need reasons now or afterwards?

DR. BOYAN: No, let's just get the vote and then we will decide.

DR. SKINNER: Yes.

DR. BESSER: Yes.

DR. HILL: Yes, and I am changing my prior vote

based on the post-marketing survey.

DR. YASZEMSKI: Yes.

DR. LAVIN: No.

DR. BOYAN: How is our vote, five yes? So, the work sheet, amazingly enough, has passed. We are recommending now to the FDA to accept the reclassification of the femorotibial unicompartmental uncemented porous coated knee as a class II, with the stipulations provided in the work sheet, to include the post-market surveillance.

Now with that training, here is what we can do. It is now 12:30. I am going to recommend that we work our way through. Remember, we have divided C into four different things.

We are going to have our components up there and we are going to march our way through them very, very quickly.

Then we will go down and -- oh, now we have to explain the no votes? Oh, people who voted against the work sheet, would you please give us a few statements as to why? Dr. Nelson.

DR. NELSON: I think we have described it before and I don't think we need to take too much time on it. I just don't think there was enough evidence to say that it was clear that further clinical data of a fairly general

nature would be needed.

DR. LAURENCIN: I want to reiterate what Dr. Nelson said. I think there is not enough clear data.

Also, I think just with unicompartmental knee replacements -- and I have written papers in the past actually supporting unicompartmental knee replacements, but particularly with unicompartmentals there is an issue of, number one, the average orthopedic surgeon does not do a lot of unicompartmental knee replacements.

We have studies from major centers that shows conflicting data, that shows negative data, knowing that these are actually going to be implanted.

The average orthopedic surgeon may implant maybe one a year or maybe two a year. In terms of the learning curve, in terms of putting them in, the data, the success of that orthopedic surgeon may not even be as good as the negative studies that are produced by large centers who have had a large experience with it.

Going from cemented to non-cemented is more than just a fixation. It is also a technique. That technique has to be more precise. It is less forgiving, I believe, in terms of doing a press fit unicompartmental versus a cemented.

I believe for those reasons that we may see

problems that may actually not show up very well with post-market surveillance even, because of the fact that they may be done at such sporadic levels by many people before we find real problems.

DR. NELSON: I wish you had made that speech before.

DR. BOYAN: We had one other no vote. Dr. Lavin?

DR. LAVIN: I share those sentiments. I am really concerned that the studies have to have the data to support them to go out to that level of detail.

We really are setting a precedent and lowering a hurdle. I feel sensitive to the safety end of things.

DR. BOYAN: I think those comments should be underlined and directed clearly to the FDA. Thank you very much.

We now need to make a decision. I need to know whether or not -- obviously, we can have food in this room because we have been eating doughnuts.

We could go get our lunch and bring it back, but we do need a break. So, we are going to finish this out and have a 30-minute lunch break. Do you think they need longer than 30 minutes?

MS. NASHMAN: Let's work through this, and keep going and we will decide after we are done.

DR. BOYAN: So, now we have got four categories. We are just going to go right through them.

DR. ABOULAFIA: If I may, may I have your permission to just outline what they are, and when we go to the other ones, we can make changes.

C.1-A is a tricompartmental mobile knee that is cemented. B is the same thing uncemented. The asterisk here shows that those two things, A and B, are referring to a rotating base.

C.1-C and D are both tricompartmental mobile knees, just like all the others. One is cemented. One is uncemented, following the same order as the group above. There are two asterisks here which indicate that these refer to all mobile bearing knees which is as presented in the petition. Is that straightforward?

DR. BOYAN: Now, let's start off right at the very top with the device is the tricompartmental mobile bearing knee cemented.

We are going to start with the philosophy that this is going to be a class II and then we can deal with it at the end.

The device is not life sustaining. It is of use to humans. It has no unreasonable risk of illness or injury.

So, we answered yes to any of the above-three questions. So, we jump down to seven. Now, here is where we decide what kind of information we want for this device.

We for sure said that we want performance standards of the ASTM kind. We want testing guidelines as in guidance documents.

Is there anything else that we want to add? Would someone like to make a recommendation for any additional information that we might need?

Seeing none, then those are the two special controls that we are suggesting. We go to number 11. On 11, we definitely are going to want a prescription. So, we check yes, and we want an oral or written prescription, and we are through with that sheet.

Now we go to the supplemental data sheet.

DR. YASZEMSKI: Madam Chairman, you checked no and went to 11-B.

DR. BOYAN: We are fixing that. You are right. Okay, indications for use prescribed, recommended or suggested in the device's labeling.

Dr. Holeman, I think this is where you wanted to add some labeling information? No.

Anybody else want to add any labeling information other than what was identified in the petition? Okay.

Anybody want to identify a health risk other than what was in the petition?

Any specific hazards to health? Any characteristics or features of the device associated with the hazard?

I, in all of these, so that I don't have to write it each time, FDA, would you please be aware that I do want the question of wear always taken into consideration and any new biological information that may come forward.

Classification then right now is in the category of II. Is the device an implant? Yes.

Why are we feeling that this is supportable for a reclassification as a II is the reason stated in the petition. Anything that we want to add? No.

Summary of information including clinical experience or judgement on which we based this? We thought the petition was sufficient.

We want to restrict this to prescription use.

Any other restrictions that we feel need to be taken into consideration?

All right, we don't have to do 10. 11, the standards, subassemblies or device materials, anything other than what is in the petition? Okay, we are ready to vote.

I need a recommendation or a motion to accept the

work sheets as --

DR. YASZEMSKI: Motion to accept.

DR. ABOULAFIA: Second.

DR. BOYAN: We will start around the table. Oh, discussion.

DR. SKINNER: One quick question. When you say rotating base, we are talking about the rotating, translating base that we have been discussing right along.

DR. BOYAN: Yes, it is the rotating, translating base and we need to add that word, translating. Yes, Nelson?

DR. NELSON: If we are having discussion, I don't want to drag anything out, but we are saying that this is based on two device examples, one of each of the two kinds. We are saying that is sufficient clinical data for down classification.

DR. BOYAN: If we vote for the work sheet, that is what we are saying. Seeing no further discussion, I call the question and we will start with Aboulafia.

The vote is whether or not to accept the work sheet in its current format, a vote yes to accept, no to not accept.

DR. ABOULAFIA: Yes, to accept.

DR. BOYAN: Just keep going right around.

Laurencin is next.

DR. LAURENCIN: No.

DR. SKINNER: Yes for accepting.

DR. BESSER: Yes.

DR. HILL: Yes.

DR. YASZEMSKI: Yes.

DR. LAVIN: No.

DR. NELSON: No.

DR. BOYAN: We need to explain the nos.

Laurencin, would you explain your reason for no?

DR. LAURENCIN: My concern is, first, that again on the one hand we have got data basically from one system, the LCS system. We are stating that after one system has worked, that other systems that are just like it can be a class II device.

I am not sure, but from my being on the committees, that may set a very different sort of precedent than what has gone on in the past in terms of new devices coming to the fore.

The second is that there is a supposition that by having a rotating platform base, that one will decrease or make to a very low significant level subluxation of the prosthesis.

I am not sure if that is true. Clearly, as we

increase the constraint of the prosthesis, I think we decrease subluxation.

The question then is if you are moving to a non-cemented form by increasing your constraints of your prosthesis, are you having more problems in terms of the interface with the prosthesis.

On that basis, it is not clear whether those results will stand out or not. So, my feeling is that for those reasons, I voted no.

DR. BOYAN: Thank you.

DR. BESSER: This was cemented that we just voted for.

DR. LAURENCIN: That is the same reason for cemented and uncemented, that I wouldn't for both.

DR. NELSON: I agree with Dr. Laurencin. I think there are three products out there with single studies done by their designers. This is not broad enough data to support a down classification.

I also agree that this is a dangerous precedent, to say that with limited clinical data we will just down class everything and say they can just 510(k) it.

DR. BOYAN: We had one other no vote. Dr. Lavin?

DR. LAVIN: For those same reasons, and I really do strongly believe that you need more companies and more

products out there to be able to feel more confident. I just don't have that confidence yet.

DR. BOYAN: Thank you very much for your comments. The motion carried to recommend to the FDA that the tricompartmental mobile bearing knee, cemented, with a rotating translating platform be classified as a class II device.

Now we are going to consider the tricompartmental mobile bearing knee, uncemented, rotating translating platform. We are on C.1-B, the uncemented.

DR. LAVIN: Madam Chairman, can we just say that the work sheets would be essentially the same and just ask for what changes you would like on the work sheets and just move to the vote?

DR. BOYAN: We certainly can. I think the fastest thing. It is not going to be any faster than just walking my way through it. Let me handle some stuff that I have got to do before I lose track of what I am doing.

MS. NASHMAN: Just in support of Dr. Boyan, we need to fill out the work sheet. We need it to be on the record.

When you start writing, just as before, when you are reading through the transcript, it becomes very difficult.

I know right now that may seem unimportant. If you were to want to read through this, say, in another year, you will be glad that we did it this way.

DR. BOYAN: Tricompartmental mobile bearing knee, uncemented, rotating, translating platform. Class II.

It is not life supporting. It is a value to humans. It is not going to have any horrible risk. We answered yes to three, so we go down to seven.

We are recommending performance standards. We are recommending testing guidelines. Do we want to recommend anything else?

Seeing none, we go over to question 11. The answer here is no, and we want there to be a prescription and we are through with that page.

Supplemental data sheet. It is a device.

Indications -- if you are going to change what I am saying, speak up and identify your name and what you are saying.

It is going to be as in petition for the indications for use.

Identification of any risk to health presented by device? As in petition.

Specific hazards to health? We haven't identified any.

Characteristics of features of the device associated with the hazard? We haven't identified any.

We are recommending class II.

If this device is an implant and has been down classified, we did it because of the information in the petition. Any other information that we need to add?

Okay, our information was as in petition, what we based our opinion on.

Any restrictions on the device are prescription and, I think here, in deference to Dr. Holeman, we should say sufficient bone stock. This is uncemented.

Existing standards applicable to the device or device assemblies or materials. That is as in petition. But I would like to put here the requirements identified by Dr. Jacobs, that we make some comment as to the characteristics of the uncemented surface be porous coated, and limiting motion to less than 100 microns.

That is done. Anything I missed? Okay, I need a motion.

DR. NELSON: Motion to move the question.

DR. BOYAN: Second?

DR. BESSER: Second.

DR. BOYAN: Now, any discussion on this particular one?

DR. ABOULAFIA: I think cemented and uncemented are different, yes.

DR. SKINNER: Dr. Boyan, I think there might have been a Roberts Rule of Order problem. He called the question. I don't think he moved to approve the motion.

DR. BOYAN: I heard that. He meant to say --

DR. SKINNER: He didn't, because he is going to vote against it, you see.

DR. NELSON: Dr. Skinner is correct.

DR. BOYAN: I was looking for a motion.

DR. NELSON: Dr. Skinner, move the motion.

DR. SKINNER: No, I won't move the motion. I will move that we accept the class II classification.

DR. BOYAN: The work sheet.

DR. SKINNER: The work sheet.

DR. BOYAN: Okay, and Aboulafia has seconded accepting the work sheet.

DR. ABOULAFIA: No, I do not. Besser seconded, but he seconded the wrong thing, but he will second this also.

DR. BOYAN: He will second the Skinner motion. We now have a motion to accept the work sheet that recommends a class II designation for the tricompartmental mobile bearing knee, uncemented, rotating, translating platform.

The motion that we have made is very similar to the previous one, but there are two differences.

One is that we are adding the restriction that there be sufficient bone stock. Secondly, we are making specific statements as to the characteristics of the uncemented stem, the surfaces of the uncemented stem.

Are there any other things that we need to do?

DR. SKINNER: Discussion.

DR. BOYAN: We have discussion. Discussion is now happening.

DR. SKINNER: I think that what we are looking at here is something that is essentially transparent when you look at it compared to what we have already gone through.

In other words, this is the same as the patellofemorotibial uncemented porous coated total knee prosthesis.

The difference between this and what we are considering in this motion is simply stuff inside the joint.

The interface is identical to the other. I don't see any difference between this interface, whether it has a mobile bearing or this interface when it has no mobile bearing.

DR. BOYAN: Any other discussion?

DR. NELSON: I am just asking what data we have

looked at? Am I correct in saying that the only study we had that was uncemented that said if they don't keep sliding, they loosen and it was a bad idea?

Was there a study saying that this worked?

DR. SKINNER: You are talking about one exception, which is the situation where the mobile bearing stops moving.

I think that referred to the meniscal type bearing, not the rotating tibial plateau, which Dr. Bourne referred to as all his continued to move.

DR. NELSON: My question again would just be, is there a study that looked on that particular thing that we are voting on now.

DR. BOYAN: Dr. Lavin, would you want to make a comment? You would not want to make a comment.

DR. SKINNER: The LCS tibial plateau is essentially this thing here. There are all sorts of data from Fred Bugle and Pappas on this.

DR. NELSON: So, you are saying there was a single device with multiple studies? Thank you.

DR. BOYAN: Did Dr. Skinner nod in acquiescence?

DR. SKINNER: I think there is more than one study. We just had data presented by Dr. Insall, we had data presented by Dr. Bourne. There is data in the packet

that refers to the LCS knee.

DR. NELSON: Dr. Insall was presenting uncemented?

DR. SKINNER: I have already said that the situation is, in my viewpoint, the interfaces is the difference between these. What is inside the joint doesn't make any difference.

DR. NELSON: I recognize this. I am just saying, are we down classifying this based on no data or are we down classifying this based on a single prosthesis with a couple of studies?

DR. SKINNER: I think there are all sorts of studies on uncemented total knees that demonstrate that the interface is fine.

If you have a mobile bearing knee where the bearing isn't mobile, then you have a fixed bearing knee, which is exactly like what we have with all the other studies. I don't see the differentiation.

DR. LAURENCIN: I tried to allude to this earlier, and I have to respectfully disagree with Dr. Skinner. What is inside the joint does reflect on what the stresses on the interfaces are going to be.

In fact, that is what I tried to allude to earlier. Even the type of conformation and the articulation between the tibia and the femur will reflect on stresses

that are going to be at the interface.

The type of implant that we are talking about makes a difference in terms of how that interface is going to respond.

Again, we have studies, I think with one company's type of device. To extrapolate and state that now any company that has something that is similar to that can come through, I think, it may be warranted, but the question is, is it warranted to make it easier for that to happen and not require that that group not go through doing studies.

I think that it may be that it may be that it is perfectly fine. The question is, what level of comfort should one have in terms of the types of studies that should be done.

Would a two-year even retrospective study be warranted on the device? I think that it would be.

DR. BOYAN: Let me just remind the panel that we have a situation whereby we have already felt that there were sufficiently -- we have already given advice to the FDA that there were sufficient special controls in place as to provide enough information as to whether or not this device was -- I am going to need help with the terminology, but essentially stable.

With those kinds of studies, the preclinical

studies, both engineering type studies and animal studies, that FDA might be able to make a determination as to whether or not the interface and the stability of this device could be reasonably predicted.

In the event that they don't feel that, they don't have to classify something as class II. They can write a letter back to the manufacturer and state, you didn't make the criteria.

We did feel that the kinds of studies that were in the petition were sufficiently well established for FDA to be able to use them to make a determination. At least, that is how I read our previous discussion.

We have lost one of our panel members and we cannot vote until he returns.

DR. BESSER: Can everybody vote but him?

DR. BOYAN: We can start around the table and hope we can get to him when he returns. I am sure he won't be gone long. We can start with you, Dr. Nelson, and go around to Aboulafia.

DR. NELSON: No.

DR. ABOULAFIA: No.

DR. LAURENCIN: No.

DR. SKINNER: Yes.

DR. BESSER: Yes.

DR. HILL: Yes.

DR. YASZEMSKI: No.

DR. BOYAN: We are just waiting on Lavin. We are ready for your vote, Dr. Lavin.

DR. LAVIN: No.

DR. BOYAN: So, we did not accept the classification questionnaire as we originally designed it, recommending a classification of II.

If I change this classification to III -- we have to explain the no votes if the no carried?

SPEAKER: Yes.

DR. BOYAN: Yes, we do. So, let's start back over with our first no vote which was you, Dr. Nelson. Do you want to give us a little rendition on the no?

DR. NELSON: I totally agree with what Dr. Laurencin said before. I think he summed it up fine. I don't need to say anything further.

DR. ABOULAFIA: Same as above.

DR. LAURENCIN: I summed it up earlier.

DR. YASZEMSKI: Since I voted yes before, I will explain what turned my vote. I agree with everything that Dr. Laurencin said.

In addition, I think that regardless of whether the mobile bearing moves or doesn't move in the non-cemented

case, we are asking for a biologic response different from the cemented case. We are asking for that to happen.

I think in Dr. Bourne's presentation before, he mentioned that there had been, in some of the early non-cemented designs with screws, there had been some osteolysis with screw loosening.

I am concerned, in this particular case, that by adding the dual bearing surface, and perhaps having a non-cemented tibia, with the dual surface having the potential for particulate debris getting onto the biologic interface that we are going to ask to grow in solid, that I would like to see some more information before I vote yes to that.

DR. BOYAN: Okay, thank you very much. Dr. Lavin, is there something that you might want to add?

DR. LAVIN: No.

DR. BOYAN: So, this particular work sheet did not pass. Now we are waiting for some statement from our leaders as to whether or not we have to do another work sheet. Say no, please, Mr. Dillard.

Mr. Dillard, if you want to remain in any shape -- you think we do?

MR. DILLARD: Could I make an overall suggestion? You voted no to this. Remind me, because I have gotten a little lost myself.

Did we vote on the original C, which was the combination of the mobile bearing cemented, uncemented, as the petition laid it out?

DR. NELSON: No, we said, we can't answer that. We are going to answer these. So, what we did to the first line up there we said yes, the second line there, we said no.

DR. DILLARD: As a point of clarification, I think you broke it out because if that question were taken as a whole, you would have to answer it one way that you all didn't feel comfortable with. Now you are breaking it out.

I think my recommendation would be to go through, complete what you have there. Please do the cemented, uncemented, the C.1-C and C.1-D, and see how that comes out.

I think we also need an overall motion on what the petition proposes, with an entire vote through the checklist, just after you get a clear sense of what you get from here, so that we can respond directly to the petitioner with what is proposed.

This is your proposal based on your uncomfortableness the way the petition is. I think we are going to get a lot of clear direction, but I think we have got to go through the sheet the way the petition stands, once you have gone through this.

I would say no, you don't have to go through what you just did. I think we have got your clear direction. C.1-B, you voted that motion down as a class II.

DR. BOYAN: But you still have made us do five sheets. Okay, we are on to the next one. We understand you. We are on to C.1-C.

This is the tricompartmental mobile bearing knee.

DR. ABOULAFIA: Which includes all mobile bearing knees, C.1-C cemented, C.1-D, uncemented.

DR. BOYAN: So, this is everything. This is the petition.

DR. ABOULAFIA: Right, in two forms, cemented and uncemented, C and D, respectively, C.1-C and C.1-D respectively.

DR. LAURENCIN: C and D doesn't include unicompartmentals.

DR. ABOULAFIA: We did that already.

DR. BOYAN: We have already done unicompartmentals.

DR. NELSON: I think Dr. Witten, who spoke without benefit of the microphone, is correct. We did unicompartmental but it was not for the mobile bearing.

DR. LAURENCIN: We did not do unicompartmental mobile bearing.

DR. BOYAN: This is tricompartmental and unicompartmental.

DR. NELSON: Negative. The motion as it is, C.1-C, is tricompartmental, all mobile bearing knees, cemented.

DR. BOYAN: You are right. We still have to do unicompartmental. We are going to be here forever.

DR. ABOULAFIA: Do you think, if we combined tricompartmental and unicompartmental, that we would answer the questions the same way?

DR. YASZEMSKI: I am going to agree with Dr. Aboulafia. I think that now that we have separated out C.1-A and C.1-B, I think we can make one more sheet and answer the questions. One sheet that incorporates everything we haven't done yet would be my suggestion.

DR. ABOULAFIA: Correct me if I am wrong. Can I say tricompartmental and unicompartmental mobile bearing knee cemented -- C.1-C is a tricompartmental and unicompartmental mobile bearing knee cemented.

C.1-D is a tricompartmental or unicompartmental mobile bearing knee uncemented. Both C.1-C and C.1-D refer to all mobile bearing knees as presented in the original proposal.

DR. HILL: Do we have to do two sheets? Can't we combine cemented and uncemented?

DR. YASZEMSKI: Agreed.

DR. BOYAN: We are. We are going to have one big giant thing here. Tricompartmental and unicompartamental mobile bearing knees --

DR. ABOULAFIA: I guess we are going to combine C.1-C and C.1-D. I was going to call it the mother of all Cs. I guess that would be sexist. I could we could just call it C.1-C. There would be no C.1-D.

It would include tricompartmental and unicompartamental mobile bearing knees, both cemented and uncemented as presented in the original proposal.

DR. NELSON: That is correct. That is what we are asking for.

DR. BOYAN: We already know that we are going to have a hard time passing this as a class II. We are going to have to write a whole other sheet if this one fails.

DR. BESSER: I would suggest that when we get down there, we answer that question no, and then we vote on it as class III.

DR. BOYAN: That is what I am proposing. Thank you, Dr. Besser. Do you want to make that as a motion?

DR. BESSER: No, it is not a motion. We are just filling out the sheet. Then later we will vote on it.

DR. BOYAN: So, let's just leave that right now.

Is the device life sustaining or life supporting? No.

Is it important? Yes.

Is it going to cause pain and injury? No.

Did you answer yes? Yes, we did. Down to 7.

We are saying that there have to be performance standards as in ASTM.

DR. ABOULAFIA: I would say answer seven, no.

DR. NELSON: Is there sufficient information to establish special controls. The recommendation by Dr. Aboulafia was no, and I agree with that.

DR. BOYAN: All right.

DR. ABOULAFIA: In the margin to the right, it says, if no, classify in class III.

DR. BOYAN: Now we get to answer 10. Low priority, medium priority or high priority, and we would probably say high.

DR. NELSON: We agreed before that we have no idea what that means.

DR. BOYAN: It just means what it means.

DR. WITTEN: We are not classifying it and we are not -- do we answer this?

DR. ABOULAFIA: I am not sure we answer it because we did not classify or reclassify.

DR. NELSON: Nonetheless, doesn't the FDA want us

to tell them, if we say this is not a II and it should be a III and therefore it should go to PMA, what the priority of that PMA is. I will defer that to Mr. Dillard.

MR. DILLARD: The question is for number 10; is that correct? I believe you can have a recommendation of not applicable.

DR. NELSON: I will withdraw my complaint that we have no idea what the terms mean. Let's vote on it.

DR. BOYAN: Give me a recommendation for a priority level.

DR. ABOULAFIA: If we are making a recommendation for a priority level, I would say it is low. There is not a demand for this because there isn't something else out there that will work reasonably well for the problem being addressed.

DR. BOYAN: Is there any problem with this? Okay.

11-A, do we answer that one now? Yes. It has to be used -- no, and then it has to be used by prescription. Okay, the other sheet.

Indications for use prescribed, recommended or suggested in the device's labeling that were considered by the advisory. These were as in petition, and as described in companion data sheets. We are just going to address them to our other data sheets that go with this.

Identifications, see petition and data sheets.

Number six, the classification here is III.

Seven, we have petition and our data sheets.

Eight is petition and data sheets.

Number nine is prescription and then data sheets.

Next page is, we don't do number 10. Number 11 we had what was in the petition and then we have our supplemental data sheets. They become subtended to this because they are our overriding event.

Right now we have, for the overall event, of all of the tricompartmental and unicompartmental mobile bearing knees, cemented and uncemented, we have recommended a class III designation. We are ready to go.

DR. YASZEMSKI: Motion to accept the recommendation.

DR. NELSON: Second.

DR. BOYAN: Okay.

DR. ABOULAFIA: Yes.

DR. LAURENCIN: What was it, I am sorry?

DR. BOYAN: Dr. Laurencin, I have worked with you and I have worked with you.

SPEAKER: Class III.

DR. LAURENCIN: Yes.

DR. SKINNER: Yes.

DR. BESSER: Yes.

DR. HILL: Yes.

DR. YASZEMSKI: Yes.

DR. LAVIN: Yes.

DR. NELSON: Yes.

DR. BOYAN: So, our overall recommendation to the FDA is that the tricompartmental and unicompartmental mobile bearing knees, cemented and uncemented be classified as class III.

We have provided them with specific information in supplemental data sheets with reference to the tricompartmental mobile bearing cemented rotating platform, and the mobile bearing tricompartmental uncemented device with a rotating, translating platform.

With that, I think that we are at a stopping point.

MR. ABOULAFIA: I think Mr. Dillard said that we have to vote also on the proposal as a whole, and I don't think we need to do the data sheets because we have already filled out the data sheets on all possibilities. We simply have to vote on do we recommend accepting the proposal as submitted.

MR. DILLARD: Madam Chairman, I would like to amend that based on Dr. Aboulafia's amendment and

modification to how you just handled the rest of this.

I believe what you just did is included everything mobile bearing, that you just gave us a recommendation -- this is where I would like a little clarification -- gave us a recommendation that you do not believe that as a whole group they can be reclassified.

Your recommendation would be that they remain in class III.

One point I would also like to just have you make, if you don't mind, Madam Chairman, ask everybody to give a very quick reason why they believe it should not and cannot be reclassified at this point in time, and should remain a class III device.

Just by way of remembrance, these are post-amendments class III devices as they currently stand.

Then I believe your recommendation would then be also that you could break out a subset, however, because you did just vote on the overall proposal.

You could break out a subset. You gave us a recommendation that C.1-A, the tricompartmental MBK cemented, only with a five-to-three vote, I believe.

You recommended that that one subset could be reclassified with the identified special controls on the work sheet.

I just want to make sure that everybody -- it appears to be where we came.

DR. BOYAN: Let me see if I can repeat what you just said. Our overall recommendation to you, then, is, that the petition as presented, that we believe that overall the mobile bearing knees, whether they are cemented or uncemented, should be classified as class III devices.

DR. ABOULAFIA: With the exception of a tricompartmental mobile bearing knee which is cemented and has a rotating translating base.

DR. BOYAN: The amendment is corrected. We would also like to bring to your attention that based on a vote of five to three, there is potential that the mobile bearing tricompartmental knee, uncemented, also may be reclassified as a class II, with the provisos as described by us in the supplemental data sheet.

DR. ABOULAFIA: You said uncemented, and I believe you meant cemented.

DR. BOYAN: I meant cemented. You are absolutely right. I meant cemented. So, that is our recommendation to you. Now I need a motion to accept that recommendation.

DR. NELSON: I make a motion to accept the recommendation as Dr. Boyan has just phrased, again, saying this is cemented.

DR. BOYAN: Then, do I have a second to that motion?

DR. BESSER: Second.

DR. BOYAN: Now we are going to go around one more time. You would vote to accept our overall recommendation for or against, and state your reasons for taking the position that you take. We will begin with Dr. Aboulafia.

DR. ABOULAFIA: Yes, accept the proposal as you presented it. Should I summarize it?

DR. BOYAN: No, it is just what -- you are comfortable with --

DR. ABOULAFIA: As written.

DR. BOYAN: Dr. Laurencin?

DR. LAURENCIN: No, I am not comfortable with the cemented mobile bearing portion.

DR. BOYAN: Dr. Skinner?

DR. SKINNER: Please read the motion to me again.

DR. ABOULAFIA: Do you want me to do it?

DR. BOYAN: Yes, please.

DR. ABOULAFIA: The proposal is to take all tricompartmental mobile knees and unicompartmental mobile knees and keep them in class III with the exception of a tricompartmental mobile bearing knee which is cemented, has a rotating translating base, and would require post-market

surveillance.

DR. SKINNER: Yes.

DR. BESSER: Yes.

DR. HILL: Yes.

DR. YASZEMSKI: Yes.

DR. LAVIN: No.

DR. NELSON: No.

DR. BOYAN: Dr. Lavin and Dr. Nelson, do you want to make any comments as to why no, other than things you have already said today?

DR. NELSON: No.

DR. LAVIN: No.

DR. BOYAN: There it is. It has passed, the recommendation, a vote of five to three. Yes?

MR. DILLARD: May I ask, again, for one point of clarification. I hate to do this and I know we can get through this. So, bear with me for one more second.

The motion that Dr. Aboulafia just made did not contain what your recommendation in the work sheet went through and contained.

DR. ABOULAFIA: Let me go through and rephrase it then, again. I see the obvious mistake.

The proposal is to maintain the classification of class III for all tricompartmental and unicompartmental

mobile bearing knees, with the exception of making the recommendation to reclassify tricompartmental mobile bearing knee which is cemented, has a rotating translating base, and will require post-market surveillance.

Mr. DILLARD: And reclassifying that one to class II.

DR. ABOULAFIA: And reclassifying that one to class II.

DR. BOYAN: That it be pointed out to FDA that there is the potential to also reclassify the femorotibial unicompartmental -- I did it wrong again.

There is a potential to reclassify the mobile bearing tricompartmental knee, uncemented, because the vote was five to three, and there were issues that were raised in the --

MR. DILLARD: Could I ask, there may be a simpler way.

DR. BOYAN: Okay, what is the simpler way?

MR. DILLARD: That would be the beginning of Dr. Aboulafia's proposal, which is that everything ought to be class III except the supplemental data work sheet that you filled out on C.1-A, the tricompartmental MBK cemented.

DR. ABOULAFIA: With a rotating translating case by a vote of five to three.

MR. DILLARD: That is all that is in the supplemental data sheet. I am trying to streamline that to just say, all of it you would recommend to us to remain in class III, except the one class II recommendation you went to on the tri-MBK cemented.

DR. BOYAN: That is exactly right. You, Mr. Dillard, and the FDA can take our supplemental data sheets and use them as you think appropriate.

MR. DILLARD: Thank you, Madam Chairman.

DR. BOYAN: I, as your chairperson, would entertain a motion to adjourn for the 30-minute lunch and calling of the traveling agent moment.

DR. BESSER: So move.

DR. NELSON: I make a motion to skip lunch and keep going.

DR. LAURENCIN: I would like to take a minimum bathroom break, phone, and maybe come back in 15 minutes and get going.

DR. NELSON: I second that.

DR. BOYAN: Our transcriptionist, I think, needs a bigger break than that. She is very important to the proceedings. Do you think you can do it in 15 minutes? Okay, 15 minutes.

That really amounts to a very brief break.

(Whereupon, at 1:15 p.m., the meeting was recessed, to reconvene at 1:30 p.m., that same day.)

DR. BOYAN: I would like, while we are on the record, to make a special statement, because we may not have time at the end of this, to thank Jodi Nashman, who has been our Executive Secretary my entire tenure as Acting Chairperson. And Jodi Nashperson has been an excellent Executive Secretary and we are going to miss her.

This is her last event today, and I am not going to be here at the very end when it all is done, because I will be recused, but I just want you to know, Jodi, that I - - this is a great way to learn how to be on the FDA Panel, because you were an absolutely incredibly good Executive Secretary. [Applause]

PANELIST: You may make a one-sentence speech.

DR. BOYAN: The other thing that I guess is that Hany Demian, this is going to be his last presentation as a non-executive secretary, so if we are going to get even with Hany for anything, we need to do it now.

Okay, are we ready? Yes, I think we are here. Okay. We will now begin the discussion of the second reclassification petition for the patellofemoral knee. We will begin with the petitioner's presentation, followed by the FDA presentation.

We will then have a general panel discussion of this topic, which will consist of one major question --

burning issue -- for each panel member, and then we will continue any necessary general discussion as we discuss the questions put before the panel by the FDA.

Then we will answer the FDA's questions and then we will finish by going through the reclassification worksheet and supplemental worksheet, and voting upon our recommendation.

I would like to remind the public observers at this meeting that, while this portion of the meeting is open to public observation, public attendees may not participate except at the special request of panel.

Now, I felt it very important earlier today, because of the complexity of that issue, to give as much latitude to discussion as was necessary. I think that a lot of our issues have been addressed, but we have to remember that each individual thing brought before the panel has to be considered in its own right. So, we have to be careful that we do not cross and think that we have handled something in one location that we may have handled in another, nor do we want to bias any decisions here by any decisions we made earlier.

Our first presentation is going to be from the petitioner, which is OSMA, and then Hany Demian will make the presentation from the FDA. Remember to identify

yourself by name, company, any relationship -- financially -
- you might have with any company that is involved in any
way with any of these devices.

**Agenda Item: Open Session -- Reclassification of
Patellofemoral Knee**

Petitioner Presentation

MR. DHORITY: Good afternoon. My name is Mitchell
Dhority and I am with Sulzer Orthopedics. I have no
financial interest in these devices I am about to speak on,
other than being an employee of Sulzer Orthopedics.

Today I would like to present the Reclassification
Petition for Patellofemoral Joint Prostheses, which was
filed by the Orthopedic Surgical Manufacturers Association.

Also with me today is Dr. Robert Bourne, who will
present some of the clinical history with patellofemoral
devices.

Patellofemoral joint arthroplasty is a procedure
in which the diseased or damaged articulating surfaces of
the patella and femoral soccus(?) are replaced with
prosthetic components.

The procedure was first performed by McKeever, who
in the mid-1950s, used a metallic cap-like prosthesis to
resurface the articulating surface of the patella.

The device articulated directly with the natural

femoral soccus. As will be shown later in this presentation, several authors report good long term results with the use of this device.

Later questions regarding the possibility of trochlear degeneration due to metal on cartilage wear led to the development of designs which incorporate a metallic femoral groove replacement, and a polyethylene patellar component.

These components, or slight variations of these components, represent the current offering of at least three orthopedic device companies.

These are some representative photos of those devices. On the left you will see the McKeever at the top and the Worrell, which were both used basically for resurfacing the patella. At the bottom, you see the Lubinus, and on the right the Bechtol and natural-knee components, which incorporate the metallic femoral soccus component as well as the polyethylene patellar component.

The other thing I am going to do at this time is pass around some sample devices. Basically, what I have done is, I have brought in a total knee femoral component -- I do not know if everyday can see this -- but, the purpose of this device -- the patellofemoral device -- is to take the anterior part of this -- which is this small device that

I will pass around with it -- articulate it with a polyethylene-type patella.

Patellofemoral joint devices were proposed for class III in 1982, and have been formally regulated as preamendment class III devices since publication of the final rule in September of 1987; 21 CFR 888.3540 classifies these devices as a polymer/metal semi-constrained cemented prosthesis, to be implanted to replace part of the knee joint in the treatment of primary patellofemoral arthritis or chondromalacia.

The classification further describes these devices as having a patellar component made of polyethylene, and an anterior distal femoral component made of metal.

In the early 1980s when FDA began placing medical devices into classes, relatively little information existed on patellofemoral devices. The two reasons for this were:

Many of the newer designs were introduced in the mid- to late 1970s, only a few short years before formal device classification began, thus limiting any potential for meaningful follow-up.

The population for which this device may be used is very focused, and therefore, the results are very limited. As such, this petition represents probably the only method by which these devices may continue to be made

available to surgeons, since time and cost of performing an IDE or a PMA would be restrictive.

Although the body of literature on the use of these devices is still very small, data does now exist with follow-up out as far as 18 years.

As the CFR classification depicts, the potential benefit of this procedure is to address that limited patient set in which alternative treatments, or total knee replacement, may not be fully warranted.

Additionally, with the more current designs, there is a significant amount of design similarity with total knee replacement devices. The geometry, articulating interface, and the fixation surfaces are typically very similar to total knee components, as you will see in the devices -- the sample devices -- that are coming around. As I will discuss later, it is our position that many of the risks may therefore be controlled, similar to those of total knees.

As will be shown in tabular format momentarily, existing clinical results are somewhat limited in comparison to the body of literature which is available on total knee replacements.

As has already been stated, much of this is the result of the very focused indications and limited population for which the device is used; however, eight of

the nine supporting published articles which do exist, indicate good to excellent results for between 71 to 87.5 percent of the patients.

The lone exception, which I will show in a minute, which cites only 52 percent satisfactory results, does cite that when only patients diagnosed and treated for localized diseases of the patella -- similar to that that is included in the CFR classification -- are considered, 86 percent had a satisfactory result.

In general, the literature reflects that the device does provide restoration of a range of motion, maintenance of quadriceps strength, and pain relief without the necessity of performing a total knee replacement.

Many authors cite this as encouraging in lieu of the results encountered with alternative forms of treatment, such as patellectomy, which has been shown to have the consequence of quadriceps weakness.

I apologize for the size of this; it is a little jumbled up, a little small, but these are the results of the McKeever prosthesis, the articles supported by that. The McKeever device only contains one of the two components of the current CFR classification, that being the patellar resurfacing component; however, the indications and mode of treatment are identical with the exception of the lack of

the femoral soccus component. You should have copies of these slides in your chairs, if you cannot see what is on the slide there.

The second slide shows the results of the more current type devices, and as you can see there, the results are relatively good. I am not going to dwell on these, because Dr. Bourne is going to speak a little while later on these results in a little more detail.

The complications reported in the published literature are also similar to those encountered in total knee replacement, and may therefore be similarly controlled, as will be discussed shortly. These include sepsis, stiffness, pain, patellar tracking and misalignment problems, device revision, and tibial compartment involvement.

Again, there is a limited set of complications that have been published there, due to the small patient population, but again, you can see that the complications are really no different than you would have in a total knee replacement.

The one comment that I would make is with regard to the Blazina article. Blazina notes that the revisionary procedures performed on his set of patients may be corrected by some minor design modifications. He suggests making a

patellar component that is more anatomic and button-shaped, and making a femoral component that is more rounded around the periphery.

He further states that patients for isolated patellofemoral joint replacement should be carefully selected. At the present time, the primary indications are distortion or severe degeneration of the femoral groove.

The other thing I would point out -- if I can go back to that one -- even with the high incidence of complications there, he reported a relatively high success rate, so --

The Orthopedic Panel originally identified three risks to health when the proposed rule was published in 1982. The first, loss of reduction -- loss or reduction of joint function due to improper design, or inadequate mechanical properties of the device, may now be addressed via special controls such as the 510(k) requirements, quality systems regulations, and labeling requirements.

Premarket notifications include review of similar designs in order to establish substantial equivalence; conformance to material standards such as ASTM and ISO; and preclinical testing.

The FDA Guidance Document for total knee devices outlines various tests which would all be applicable to this

type of device. These include patellar subluxation, patellar contact area, range of motion, and separation strength of metal-backed patellar components, if any.

The recently released quality systems regulations place emphasis on establishing design criteria early in development; consideration of these criteria during each stage of the development; ensuring that these are not -- ensuring that these are met prior to product release.

Loss of reduction is also identified in the labelings of possible complication. The accompanying surgical techniques and product brochures provide information to assist the surgeon in making proper patient selection and placing the device correctly.

Although not listed on the slide, the MDR regulations will also serve to ensure the continued safety of medical devices. MDRs for these devices will be discussed later in the presentation which will be made by FDA.

Adverse tissue reactions have not been shown to be a major problem with these devices; nonetheless, the chance for tissue reaction does exist, and should be no greater than that of total knee replacements that use similar materials. As such, the special controls which would minimize the risk, include the 510(k) requirements, the

quality systems regulations, and labeling regulations.

The 510(k) requirements would serve to ensure that the materials used meet acceptable standards. Additionally, modified surfaces for fixation of these devices -- such as porous coatings -- must be fully characterized and include testing data on metallurgical, chemical, physical, and mechanical properties of the surface that would address biocompatibility, strength, and wear concerns.

Once again, the QSR regulations would also serve to ensure that proper design criteria are identified, implemented, and incorporated into the final device.

The possibility of adverse tissue reactions, presence of wear particles, and other similar reactions are also addressed in the physician's labeling, which is included with these products.

Finally, infection was identified as a risk. Again, the same special controls may be used to minimize this risk. The 510(k) guidance for total knee prostheses includes a section pertinent to sterilization of medical devices.

Manufacturers must provide information regarding their method of sterilization, which includes the sterilization validation parameters. Various standards, such as AMY provide guidelines for sterilization.

Sterility requirements are typically identified as part of the design input and output for new designs. As such, they may be controlled via the QSR regulations.

Sterility may also be influenced at the time of surgery by such things as the technique that is used. As such, the physician's labeling and surgical technique brochures provide information relative to minimizing this risk to the patient.

As has been shown in the published literature, good results can be achieved with this type of device when patient selection is carried out carefully; the current CFR classification for these devices, which serve to control the risks of use in patients with other disease conditions. As has been discussed, regulations regarding the product labeling would also serve to regulate the use of these devices.

Promotional literature and product labeling, such as the physician's inserts, currently carry indications for use, contraindications, and instructions for use. Additionally, manufacturers provide a detailed surgical technique outlining the procedure for implantation.

With this information available to surgeons and others, there is no reason to believe that the importance of the surgical technique in patient selection could not be

adequately conveyed.

Design-related risks associated with PFJ surgery may be controlled via the same mechanisms used to control total knee replacement components. With the recent change in quality systems regulations, and the advent of the design history files for components, manufacturers are taking an even more focused look at design criteria, risk analyses, and design output, prior to release of new systems. In so doing, many potential problems may be averted.

Current FDA guidelines for premarket notifications on total knee replacement devices include testing parameters for items such as patellar subluxation, contact area, and constraint.

Since PFJ components share many similarities with total knee components, it is reasonable to believe that these same items would be addressed in the same manner.

In summary, based on the published literature available, these devices have been shown to have good clinical results with complications similar to those seen in total knee replacement, which are currently regulated as class II for cemented use.

You also recommended a little bit earlier that total condylar knees be given a class II classification for cementless fixation, with porous coating. As such, the

associated risk may be reasonably addressed via special controls such as the 510(k) requirements, quality systems regulations, and labeling regulations, in the same manner as total knee replacements.

Patellofemoral joint replacement devices are not the treatment option for all patients. They should be limited to that specific set of patients suffering from chondromalacia, arthritis limited to the patellofemoral joint, history of patellar dislocation or fracture, and those patients with failed previous surgery, where pain, deformity or dysfunction persist.

This patient population is so limited that imposition of an IDE or a PMA for these devices would likely never be undertaken, thus removing this treatment option from surgeons. Based on this information, it is our recommendation that patellofemoral joint devices be reclassified into class II.

I am now going to turn the presentation over to Dr. Bourne, who is going to present some of the clinical results with these devices.

DR. BOYAN: Dr. Bourne, you need to go through the whole rendition of your name, who you are, who you get money from, who you give money to --

DR. BOURNE: Well, thank you very much. I am Dr.

Robert Bourne. I am a Professor of Orthopedic Surgery at the University of Western Ontario. I am not a designer of this type of implant. I have no vested financial gain; I have just simply been asked, as I am here, to perhaps present the patellofemoral joint from a clinician's standpoint.

We have had -- as I mentioned this morning -- financial contributions to our orthopedic research laboratory from at least six orthopedic companies over the years -- the 20 years -- that I have been involved.

I have been asked to briefly discuss the rationale and results of patellofemoral joint arthroplasty. And basically, the problem is a patient with patellofemoral arthritis alone. And I must admit, in our unit, over the 20 years I have been there, we have performed between -- anywhere from 200 to 500 knee replacements a year; I could only find five patellofemoral arthroplasties, so it is very rare.

It has usually been used as a salvage procedure -- and you will see what I am talking about in a few minutes -- but it does have a very, very small window, I think, of usage.

In our particular center, if we had a patient over 60 with severe patellofemoral arthritis, we would do a total

knee replacement. There is some controversy in that regard; however, as you will see, there are some individuals -- primarily in Europe -- who would use a patellofemoral replacement, and they have had reasonable success.

The rationale is that perhaps a patellofemoral replacement is more conservative than a knee replacement that you see on your right. A knee replacement, as you know, sacrifices the articular surfaces of the tibiofemoral joint, and it is a bigger operation. So, in other words, you are leaving more of the normal joint in these people.

The history is fairly longstanding. In 1955, McKeever developed a metallic cap that would fit over the patella and was held by a screw, and to do right and left sides, you just simply flipped the implant over, and the results were reasonable with this, but people quickly realized that there are two sides to the patellofemoral joint, so you had not to only address the patella, but also the femoral aspect of the patellofemoral groove.

In 1974, Bechtol reported on his early results in which a polyethylene button -- an anatomic-type polyethylene button -- was placed on the patella, and a metallic runner placed on the femoral aspect of the groove.

Shortly thereafter, Lubinus of Germany presented his data, and more recently, Cartier from France -- and we

will get into some of this data in a moment.

You can see that many surgeons -- this is a patient that I revised -- but, surgeons in North America trying to deal with this difficult patellofemoral problem, tried various things. They simply took the polyethylene button from a knee replacement and tried just to resurface the patella, but this usually fails.

As you are aware, basically, it is just replacing the femoral aspect of the patellofemoral joint -- and you have seen an example, I think it is being passed around -- and placing a polyethylene button behind the kneecap, much like -- it is like a unicompartmental patellofemoral replacement, basically.

Now, the indications have been patellofemoral arthritis, chronic patellar dislocation, old patellar fractures, failed patellofemoral surgery, and we like to consider it a knee replacement, and use it primarily in people over the age of 60.

This particular slide -- but, it just shows a patient who I think has had six or seven patellar operations. You can see the deficiencies of some of the earlier designs. There were not enough sizes; it overhangs anteriorly. But this patient actually had a reasonable result in alleviating patellofemoral pain and was I really

think at the age of this patient, really in the late 40s, the only other thing you might have considered was knee replacement or arthrodesis.

The one good thing about this, if you do a patellofemoral replacement, provided there isn't sepsis involved, it is fairly easy to salvage it to a total knee replacement, and you will see this in some of the series that I allude to.

Now, when you critically try to analyze the data - - and I think you have had the same data that I have had presented to me, as well as some others -- you will quickly note that it is limited and infrequent in most parts of the world. As I mentioned, in 20 years, I could find five in our center. So, we do not use it very often.

The series are small, and the follow-up is anywhere from five months to 18 years. I am really surprised that the five-month data even made it to the literature.

There has been fairly consistent finding of pain relief, restoration of function, and at least restoration of the range of motion. And of all the series that I could find, there were 246 patients, and it seemed that 80 to 85 percent of the patients were deemed to have a satisfactory outcome. So, if you compare this to the total knee

replacement literature, you will be talking about tens of thousands that have been reported in the literature.

Just to go through a few of the series, to give you a flavor. This is the series of Philippe Cartier. Now, Dr. Cartier is a zealot for whatever he does. He described 65 Richards Type -- it should be I and II -- implants. He had only a mean of four-year follow-up, anywhere from two to twelve.

He felt that 85 percent were good or excellent, but he did allude to 13 complications, and 13 out of 65 is a fairly large number. Of those, he felt that six were implant-related, and on your right, you can see he had problems with lateral subluxation in two; one with persistent patellar pain -- or three with persistent patellar pain -- and one with patellar catching. And that is perhaps not surprising, because I suspect he had the same problems that I showed in that x-ray in ours, where the implant did not quite fit the femoral groove. But I think one of the problems is that this is such a niche product, that perhaps not enough sizes are made and that is something that might want to be considered.

Arciero reported in the Clinical Orthopedics and Related Research in 1998 on 25 implants; 14 were from Richards, and 11 from Wright. He had a three- to nine-year

follow-up, of which the mean was five years, and once again, he reported reasonable results, but found a marked difference between females and males. This is the only series that really has brought this out, but I am not quite sure what it means, but it is an interesting observation.

Argenson from France reported on a larger series in 1995 -- this time in the Journal of Bone and Joint Surgery -- of 79 implants. The majority were female; 13 were lost to follow-up and this certainly weakens this particular series. The mean follow-up was six years, but once again, 84 percent were considered satisfactory.

A special note is that 13 were converted to a total knee replacement, and according to the paper, at least, without really undue difficulties.

This particular group divided the clinical scores and they thought there was a slightly better result with patients with patellar dislocation; in other words, a person who had longstanding difficulties with their knee, the patellar never really tracked properly, and they had secondary arthritis, but the rest of the joint was quite good.

Patients with post-traumatic arthritis, such as you might see after a patellar fracture, do not fare quite as well, and these scores are out of 100 -- for those of you

that are not familiar with the Hospital for Special Surgery Score -- and those patients with primary patellofemoral arthritis had a score of 87 out of 100.

I guess to us, patellofemoral arthroplasty has limited, infrequent indications. My personal experience is based on three. I said there were five done in our center, so it is not common. And of those three, two have been for patients who had patellectomies, and they still had pain in the femoral groove, and it was an attempt to try to preserve the joint, but just put a metallic track for it to -- and I must admit, it had moderate success. And these were in younger patients, which -- now, I guess you could call it a knee replacement -- but, I could not think of much else to do, other than arthrodesing the knee.

According to the literature, at least, on -- I think it was 246 patients -- combined, they suggest that 80 to 85 percent have a satisfactory result at about the five-year follow-up. So it is not long term follow-up, but at least in the short term, they seem to do reasonably well.

I think you could argue that patellofemoral arthroplasty is a more conservative treatment option than patellectomy, fusion, or knee replacement in selective patellofemoral arthritis. And then finally, perhaps most importantly, is that there is a possibility of salvaging

such a device through a knee replacement. Thank you very much.

MR. DHORITY: Dr. Boyan?

DR. BOYAN: Yes.

MR. DHORITY: This is Mitchell Dhority.

DR. BOYAN: Yes. Right.

MR. DHORITY: Before we move on to the FDA portion of this, I have one clarification I think I probably need to do in watching some of the people look at the components, and I think it is probably just an education thing, that I may not have done an adequate enough job on.

DR. BOYAN: Did you watch me do that?

MR. DHORITY: These two do not articulate together

--

DR. BOYAN: I tried to, though.

MR. DHORITY: It is either this or this. Either of them articulate with a polyethylene patella.

DR. BOYAN: I finally -- thank you, Mr. Dhority. I finally figured that out, but --

MR. DHORITY: I will pass them back around with the patella so you can --

DR. BOYAN: I know who it was that you caught trying to articulate the two together. Okay, Mr. Demian?

Agenda Item: FDA Presentation

MR. DEMIAN: Thank you. Good afternoon, ladies and gentlemen. Madame Chair, distinguished panel, and members of the audience, I am Hany Demian, a scientific reviewer in the Orthopedics Devices Branch.

The device type under consideration for reclassification is the patellofemoral prosthesis. I would like to thank Mitchell Dhority and Dr. Robert Bourne from OSMA for a thorough presentation.

Today my presentation will be brief. I will discuss with you the current proposed CFR classification; the proposed indication for use; the proposed device description; supporting information; premarket history; medical device reports; risks to health, special controls, and then I will present the panel questions.

Currently, the patellofemoral prosthesis is classified under 21 CFR 888.3540, as a preamendments class III polymer/metal semi-constrained cemented prosthesis, to be implanted to replace part of the knee joint, in the treatment of primary patellofemoral arthritis, or chondromalacia. The uncemented patellofemoral prosthesis is considered a postamendments class III device.

The proposed reclassification definition would include cemented or uncemented press-fit patellofemoral prosthesis, used in the treatment of primary patellofemoral

arthritis, or chondromalacia.

This is the proposed indication for use. The applicant proposes to include osteoarthritis and remove patellofemoral arthritis and chondromalacia in this proposed indication for use.

The device consists of a metal femoral component, and ultra high mellegalate(?) polyethylene patellar component.

The femoral component resurfaces the inner condylar groove on the anterior aspect of the distal femur. The patellar component resurfaces the patella and articulates with the femoral component.

The patella has an optional metal backing. Both femoral and patellar components are either cemented or uncemented. Noncemented press-fit design utilizes a porous coating.

The applicant has provided five clinical articles regarding the use of the patellofemoral prosthesis. I am not going to go into any detail regarding these articles, because OSMA has provided an adequate summary.

Since 1976, there has been one 510(k) cleared for the cemented use, no PMAs or IDEs approved for the cemented or uncemented patellofemoral prosthesis. Currently, there are three companies listed as marketing the device in the

United States.

Since 1985, FDA has received 22 MDRs regarding the use of the patellofemoral prosthesis, and these include 17 separations of the metal backing; three breakages or fractured; one improper patella tracking; and one material reaction.

Limitations of the MDRs include incomplete reporting; events going unreported; and not knowing the denominator for the number of devices implanted.

The petitioner has identified the same risk to health as in the 1982 proposed rule regarding the patellofemoral knee. The risks to health are as follows. Loss or reduction of joint function; adverse tissue reaction; and infection. There may be other risks which you may identify during your discussion that should be considered.

In considering the reclassification from class III to class II, special controls must be used to adequately control for the risks to health. These include guidance documents, standards such as ASTM and ISO, device labeling, postmarket surveillance. Again, there may be other special controls which you may identify during your discussion that should also be considered.

I will now present the panel questions which the

agency is seeking recommendation for this reclassification petition.

Does the proposed classification description sufficiently describe the uncemented and cemented patellofemoral prosthesis?

Have the risks to health for the uncemented and cemented patellofemoral prosthesis been adequately identified? If not, what are the additional risks that should be described?

For patellofemoral prostheses, MDRs have identified dislocation of the metal backing from the polymeric patellar component. This is considered an additional risk -- no, excuse me -- Is this considered an additional risk beyond those for other metal-backed patellas of total knee prostheses? If so, what special controls can adequately address this risk?

When should clinical data be used as a special control for uncemented or cemented patellofemoral prostheses?

Have appropriate special controls been identified to adequately address the risks to health specific to the patellofemoral prosthesis? If not, what additional special controls are necessary to reclassify the cemented as well as uncemented patellofemoral prosthesis?

Lastly. Do the cemented patellofemoral prosthesis data presented in the petition support the reclassification of the uncemented porous coated patellofemoral prosthesis, and the cemented patellofemoral prosthesis?

Thank you. Now I will turn this back over to the Chair, Dr. Boyan.

Agenda Item: Questions and Voting

DR. BOYAN: Thank you very much. For the general discussion, just to remind you, we are going to -- we will start with Hill and go around the room.

If you have a question that needs clarification from either the FDA or the representatives of the petitioner -- from OSMA -- then feel free to ask that question, or a question of any member of the panel or the appropriate person in the audience, if you need clarification from that person.

Please address your question to the person that you would like to have answer it. If you do not feel like you need clarification on anything, just pass to the next person. So, Dr. Hill, would you like to begin the questions?

DR. HILL: I will begin it by saying I do not have any questions.

DR. BOYAN: Dr. Stern, Dr. Yaszemski?

DR. YASZEMSKI: No questions.

DR. BOYAN: Dr. Lavin?

DR. LAVIN: I will break a trend. What is the denominator of the number of subjects that have had these devices placed over its 20-year history?

DR. BOURNE: Well, in our center it would be -- it would be somewhere between 7,000 and 10,000 patients. So, it is very, very infrequent. It is just a very specified salvage procedure.

DR. NELSON: Can you tell me what percent of the patients that you are presenting here as part of the series were uncemented?

MR. DHORITY: In looking at the literature, most of the devices that were represented in the literature were cemented. A couple of them did not specify, but in looking at some of the photographs and other things that are usually included with the articles, you can see some cement in most of them, so I would venture to guess most of them were cemented.

DR. NELSON: Are you telling me you do not know -- you are applying in your petition for permission for uncemented use, but you do not know how many cases have ever been done?

MR. DHORITY: I can tell you that the device that

was passed around, the sample, does have a porous coated version, which is marketed -- which was marketed for use with cement, even though it is porous coated. And I can tell you I feel fairly certain that those that were purchased that were porous coated were more than likely put in cementless. Press-fit. It being at the doctor's discretion.

DR. NELSON: You are saying you do not know.

MR. DHORITY: No. That is correct.

DR. BOYAN: Dr. Holeman.

DR. HOLEMAN: No questions.

DR. SILKAITIS: I do not have any questions, but I think that the technology regarding porous ingrowth has been demonstrated, so I think from a concept point of view, you have to take that into account.

DR. ABOULAFIA: No questions.

DR. LAURENCIN: Just to get the idea, you are basing your petition to include uncemented, based upon cemented alone, with no data on uncemented.

MR. DHORITY: Basically, that is correct. That and the literature on the total knee replacement devices, which you just recently recommended you down-class to class II for the porous press-fit. Because again, if you look at the devices and the technology that is there, it is

extremely similar.

DR. BOYAN: As just a clarification, Mr. Dhority. If you -- in your review of the MDRs, were any of the MDRs reporting any problem with any porous coating, the interface being an issue?

MR. DHORITY: None that I could tell.

DR. SKINNER: Just a comment, and maybe you would care to comment on it. The prosthesis is already made in an uncemented porous coated version, and is labeled for cemented use. And if the panel here recommends a class II situation for this device, it will probably continue to be marketed in that same manner, whether it is labeled cemented or uncemented. Why be hypocritical about it? Why not just admit that the uncemented technology is valid, and go with it?

DR. BOYAN: That was a comment. Okay. I think it is to you, Besser.

DR. BESSER: The patellar component of this, is that in any way different than the patellar component for a total knee?

MR. DHORITY: For this particular device that was displayed today, no, it is not. It is identical to the total knee patellar component. The Bechtol component. The patellar component is a little bit different. It has a real

deep, almost triangular-type groove. Dr. Bourne may be able to speak a little more to that, having used it, but again, it has the same basic geometry. It is in a groove. It is a very deep groove --

DR. BESSER: I am specifically interested in the attachment of the polymer to the metal base.

MR. DHORITY: Again, the device that was passed around is identical to what is used in total knees.

DR. BOURNE: Our experience and those that I reported were all cemented devices, completely all polyethylene patellar buttons, and the other differentiating feature is that they were anatomic patellar buttons. That is one of the problems that I think some people have had, because if you do not get it perfectly orientated, then the patella has difficulties tracking down that groove. So, if you do not position both components perfectly.

I think one of the problems is, a lot of people just do not have the experience to get used to it, and particularly, if you have a deficient patellofemoral groove, which sometimes occurs, it is very, very difficult to find the proper siting of it. So, this is why I think maybe the results of very experienced people may be better than those who just use it infrequently.

DR. BESSER: Thank you.

DR. BOYAN: Thank you. Are there any other questions that need to be addressed to either the FDA or the panel before we start addressing the panel questions?

Seeing none, let's go to the panel question number One. The first question is, Does the proposed classification description sufficiently describe the uncemented and cemented patellofemoral prosthesis? And the second part of that question, Have the risks to health for the uncemented and cemented patellofemoral prosthesis been adequately identified? If not, what are the additional risks that should be described? And we are doing really well with the Hill access, so we will do Hill and just head back around like we have been doing.

DR. HILL: As far as the proposed classification description, I think the answer to that question is yes, that it has been adequately described.

As far as the risks to health, if I remember back, and looking at the copy of the slides, they only talk about the loss or reduction of joint function, adverse tissue reaction, infections, and other. And I think they ought to be a little bit more descriptive as far as talking about loosening; wear; metal back failure; dislocation; and instability.

DR. BOYAN: Okay. Dr. Stern, are you only

available -- are you part of us for this part of the discussion?

MS. NASHMAN: It was my understanding that you were welcome to participate through the questions.

DR. STERN: Now?

MS. NASHMAN: Yes, I think you are alright right now.

DR. STERN: I do not have much to add. I agree with Dr. Hill in number one, and I would concur with his suggestions for number two.

DR. YASZEMSKI: I am going to answer that both one and two are adequate. I think that -- as Dr. Bourne has pointed out -- this is something that is used very infrequently for a person whose other option at that time is a much larger operation. And with that much larger operation as a salvage, I would be happy with these as written, because I think this would be a good help to this class of patients, the cemented or noncemented.

DR. LAVIN: It is fine with me.

DR. NELSON: I do not want to prolong the discussion. I think one is quite good. I am not sure if we do not have any data for uncemented prostheses, we have understood the risks. I understand that it is similar to the, you know, porous coating on other joints, but I think

one needs to have data on each particular site, because the bone is quite different.

I appreciate Dr. Skinner's comment that it is going to be used anyway. That is not our point. Our point is, do we see data that supports it? I do not think.

DR. HOLEMAN: I would say, based on the use, the data is sufficient -- the data are sufficient.

DR. SILKAITIS: This is Dr. Silkaitis and I agree Dr. Yaszemski's comments.

DR. ABOULAFIA: I agree with Nelson. The first part of the question, yes. The second part of the question, even though I agree with him, I think the risks have been identified with the addition of Dr. Hill's comment.

DR. LAURENCIN: I agree with Dr. Nelson's comments.

DR. SKINNER: I agree with Dr. Hill.

DR. BESSER: I agree with Dr. Hill.

DR. BOYAN: And I also would like to state that I support Dr. Hill's comments on the risks to health, including a statement about loosening and the fact that there is a potential revision, because the patient should know that.

Okay. Panel question number two. For patellofemoral prostheses, medical device reports have

identified dislocation of the metal backing from the polymeric patellar component. Is this considered an additional risk beyond those used for other metal-backed patellas of total knee prostheses? If so, what controls can adequately address this risk? And start with you, again, Dr. Hill.

DR. HILL: I do not know if it is an additional risk, I think it is the same. The question is, does it occur more frequently in that circumstance, and I do not think there is any data available as yet, so -- there is some thought that maybe when we go over the sheet to look into it as far as control mechanism.

DR. STERN: To the extent that we are now talking special controls, and that is what the FDA uses to -- that is their buzzword, I think, between class II and class III, I am going to recuse myself.

DR. BOYAN: Okay.

DR. YASZEMSKI: I do not think it is an additional risk and pursuant to Dr. Jacobs' earlier comments about the specific design changes that have happened in the metal-backed patellas, I would consider this okay as is.

DR. LAVIN: Nothing to add.

DR. NELSON: Nothing to add.

DR. HOLEMAN: Nothing to add.

DR. SILKAITIS: Nothing to add.

DR. ABOULAFIA: Nothing to add.

DR. LAURENCIN: Nothing to add.

DR. SKINNER: I agree with Dr. Yaszemski.

DR. BESSER: Nothing to add.

DR. BOYAN: Okay. Thank you. Next panel question. I am trying to see if we can handle these together. When should clinical data be used as a special control for uncemented or cemented patellofemoral prostheses? And, Have appropriate special controls been identified to adequately address the risk to health? If not, what additional special controls are necessary? Dr. Hill.

DR. HILL: This prosthesis has been used in such a limited number of cases, that I think you could do some studies clinically to follow it, but I do not think any more special controls are needed.

DR. YASZEMSKI: I do not think any more special controls are needed. I am not sure anybody could do a clinical study, perhaps just a compilation of anybody who does it, reporting it, and perhaps Dr. Lavin can comment on whether any useful data can be gathered from multiple different surgeons and putting it in, otherwise I do not think clinical data need be used.

DR. LAVIN: I think that it is a real challenge to try to make something out of this, given that it is such a rare, you know, situation. So, I guess I would not recommend any postmarketing surveillance studies.

DR. NELSON: I do not think we need any further clinical data -- or special controls -- for the cemented. We do not see any data for uncemented. I do not think special controls can answer that, I think we need clinical data.

DR. HOLEMAN: I would say that special controls have been appropriately identified.

DR. SILKAITIS: I think the controls that exist are adequate. Thank you.

DR. ABOULAFIA: I agree with Dr. Nelson.

DR. LAURENCIN: I agree with Dr. Nelson.

DR. SKINNER: The -- I -- in philosophy, I agree with Dr. Nelson. Unfortunately, eliminating porous coating or bone ingrowth as a means of fixation for this prosthesis means that it will never be approved as a class III device. And I think that that may be a disservice to the orthopedic profession.

I think that we do not need that data. We have porous data -- porous ingrowth data -- on a variety of other prostheses in similar locations, including the anterior of

the femur growing into regular total knees.

I just do not think that data is necessary. I think we would could go with porous coated materials as a means of fixation for this prosthesis. What -- no difference from Dr. Yaszemski.

DR. BOYAN: Okay.

DR. BESSER: I agree with Dr. Skinner.

DR. BOYAN: Thank you very much. I have one -- I do not want to muddy the waters, but I just need this for my own information. Since at least for one device it is identical to two-thirds of the total knee, is there any reason to suspect that loosening would occur any more quickly with less surgical intervention in the knee than would occur more -- yes, Dr. Aboulafia?

DR. ABOULAFIA: Yes, I think there is a basic philosophical difference between what Dr. Laurencin and I and Dr. Nelson believe, and what Dr. Skinner believes; that you cannot extrapolate data from one joint to another, and -
-

DR. BOYAN: But this is the same joint, so that is my question.

DR. ABOULAFIA: But the mechanical forces across what you are actually doing are dramatically different.

DR. BOYAN: And you -- okay. And you are just

saying that you cannot extrapolate and I am saying, intuitively, it would seem that there would be less loosening. And you do not know.

DR. NELSON: May I also respond?

DR. BOYAN: Yes.

DR. NELSON: When we evaluated uncemented total knees, we really did not look at that component. The patella is a sesamoid, it is not a real bone the way the long bones are, it is a different bone.

DR. BOYAN: Thank you.

DR. ABOULAFIA: And -- can I ask a question? Are we in the discussion phase or no?

DR. BOYAN: We can have a brief one here, yes. Sure.

DR. ABOULAFIA: I will pass. Never mind.

DR. BOYAN: Okay. Did you have something to say, Dr. Yaszemski?

DR. YASZEMSKI: I was going to say, I agree that we cannot extrapolate, but I think from a practical perspective, given the rarity of it, I would like to personally see a result that allows surgeons to use their discretion, and pursuant to Dr. Skinner's comment, if we do not allow an uncemented one, that will remove that decision from the surgeon's purview.

DR. ABOULAFIA: Can I ask a question to that? What is the need for this device? An uncemented uni- -- I mean, patellofemoral joint. Can you envision a single case of a patient that would ever not be adequately treated with a device that has some support in the literature to support its existence, versus a device for which I am not sure anyone can offer a theoretical advantage, other than, having a surgeon try something new and different.

DR. YASZEMSKI: No, I cannot. On the other hand, I will restate that. Given the rarity of it, I personally might not use it, but I would like other surgeons to have the ability to use it, should they so desire. Given the rarity of the need for it.

DR. BOYAN: I think that we have addressed this issue back and forth. I think that we are pretty clear and this will simply become a philosophical discussion, for which there is no resolution today.

Last panel question. Do the cemented patellofemoral prosthesis data presented in the petition support the reclassification of the uncemented porous coated patellofemoral prosthesis; and the cemented patellofemoral prosthesis?

We will take these as -- uncemented first, cemented second. Yes or no. And we will start with Dr.

Hill.

DR. HILL: The answer in my mind is yes.

DR. BOYAN: Yes and yes?

DR. HILL: Yes and yes.

DR. BOYAN: Okay.

DR. YASZEMSKI: Dr. Yaszemski. I agree. Yes and
yes.

DR. LAVIN: Dr. Lavin. No.

DR. BOYAN: That is no and no, huh?

DR. NELSON: Dr. Nelson. No and yes.

DR. BOYAN: Wait, wait, wait. Dr. Lavin, was that
no and no?

DR. LAVIN: No. No and yes.

DR. BOYAN: Wait -- give me a second here.

DR. LAVIN: No for the uncemented and yes for the
cemented.

DR. BOYAN: Okay.

DR. HOLEMAN: Dr. Holeman. I pass.

DR. BOYAN: Okay, Dr. Holeman. And I have to go
back to Dr. Nelson, do your vote again.

DR. NELSON: No and yes.

DR. BOYAN: Okay. Dr. Holeman, you passed. Dr.
Silkaitis.

DR. SILKAITIS: I defer to the judgment of Dr.

Hill, which is yes and yes, I believe.

DR. ABOULAFIA: Aboulafia. No for uncemented, yes for cemented.

DR. LAURENCIN: Dr. Laurencin. No for uncemented, yes for cemented.

DR. SKINNER: Skinner. Yes. Yes.

DR. BOYAN: No, I do not have to vote.

DR. BESSER: Besser. Yes. Yes.

DR. BOYAN: Okay. So. Where we stand going into the worksheet is that it is the general feeling of the group right now that there is sufficient prosthesis data to support a reclassification as a class II device for both the uncemented and the cemented. And the not vote --

DR. STERN: I do not agree on that. What was -- how do you -- what do you -- how do you base that --

DR. BOYAN: It is not, it is five and four. Wait, how did we get five? I counted them carefully. Give me the yeses. One -- raise your hand if it was a yes. It was four-four.

PANELIST: For which one?

DR. BOYAN: For the uncemented. So it is a tie, so I get to vote, and I vote yes, so it is five-four. That is how that other vote got on there.

Okay. I was with the system, but I was not --

okay, now, realize, this is not a vote. This is just a discussion at this point. Now we go to the real thing. Okay.

DR. NELSON: Madam Chair, I would just like to go to something you said before. You do not need to vote because -- I mean, you do not need to break a tie because it is not a tie, it is not a vote.

DR. BOYAN: Correct. Right. But, I did have to make a statement about the general feeling of the group, because we have to put a number down.

DR. LAURENCIN: I think the group is actually split. The group is actually split, is really sort of the consensus about what is going on.

MS. NASHMAN: Correct. The group is split, so the Chairman votes and breaks the tie. That is all she was trying to figure out, how to write the worksheet so that we can vote upon it.

DR. BOYAN: That is correct. I am just trying to get to the little number at the top of the worksheet. Alright, now, I gather from this that we have to decide, based on the petition, if the petition is asking us to deal with these together or separately. And I need to go back to the original petition.

We can decide -- and actually, the way the

petition is stated, the device description actually does separate them, so we can -- I think that we probably should separate them as well. So, let's take --

MS. NASHMAN: Hold on a moment. I do not believe that the petition separates the two. That is just the way he broke it.

MR. DEMIAN. Demian. The petition is for both the uncemented as well as the cemented.

DR. BOYAN: Alright. So. We are now dealing with the reclassification petition for the patellofemorotibial --

MS. NASHMAN: No.

DR. BOYAN: Which one are we on?

PANELIST: The tibial.

PANELIST: Not tibial.

PANELIST: Patellofemoral.

DR. HOLEMAN(?): We did that this morning.

DR. BOYAN: -- device. Prosthesis. Alright. We will go quickly through this. We are right now in the class II mode, and this is uncemented and cemented in the same event. Okay. Now, think positively about this, everybody. Okay.

Is the device life-sustaining or life-supporting?

No.

Is it important? Yes.

Does it present a potential or unreasonable risk of illness or injury? No.

We answered yes to question two, so we go down to number seven.

In number seven, for sure, we want performance standards as in ASTM-type stuff, and we definitely want testing guidelines as in guidance documents.

Now, is there any other kind of anything that we want? We have realized that postmarket surveillance would not occur with any efficiency over the next -- over our lifetimes, so --

DR. YASZEMSKI: I would say that, since this is done so infrequently, device tracking may perhaps be appropriate here. Maybe we could follow all of them that go in. I do not know what that involves from an industry perspective. Dr. Silkaitis, can you comment?

DR. SILKAITIS: Yes. First of all, I would like to have FDA define device tracking as their perspective. As I understand it, it is tracing the lot numbers of where the product goes, as opposed to --

DR. BOYAN: Wait, is this going to add to the -- is this going to add in some way to the assurance of safety and effectiveness?

DR. SILKAITIS: I think it is more for recall

purposes. Is that right, Jim?

DR. BOYAN: But in this instance, Mr. Dillard --

MR. DILLARD: Yes, Madam Chair, would you like me to try to address that?

DR. BOYAN: -- [simultaneous discussion] -- describe what device tracking is.

MR. DILLARD: I was waiting for you to --

DR. BOYAN: I was going to try to forestall it, because to me it seems --

MR. DILLARD: Okay, okay.

DR. BOYAN: -- as if it is not the feeling of Dr. Yaszemski that to track this device would add to the safety and effectiveness to users of the device --

DR. YASZEMSKI: I withdraw.

DR. BOYAN: Okay.

MR. DILLARD: If you ask me back up, I will try not to extend anything, I promise.

DR. BOYAN: Okay. We are over on the next page and the answer is no, and the prescription business. And we are on now the supplemental data sheet.

It is a device. Are the indications for use prescribed, recommended, or suggested in the device's labeling that were considered by the advisory panel? Did we discuss labeling adequately, is the labeling adequate? I

think we felt that there should be some additions, based on Dr. Hill's recommendation and that was that there be an inclusion of potential revision.

DR. HILL: Loosening, wear, dislocation and instability, and also, metal back failure.

DR. BOYAN: Identification of any risks to health presented by device, and I think we have just shown that, potential for revision.

Okay, now, we are recommending class II at this point. If the device is an implant or is life-sustaining or life-supporting -- okay, why did we recommend a lower classification? Based on the petition.

What is the summary of the information, including clinical experience? It was found in the petition.

Identification of any needed restrictions on the use of the device, is the prescription. Are there any other restrictions that we want to state at this time?

Number 11. Existing standards applicable to the device, device subassemblies or device materials. They were adequately described in the petition.

Alright. Ready to vote.

At this time, we are recommending classification of a class II for the patellofemoral prosthesis, uncemented and cemented, and we are basing this on the information that

is in the petition as well as in the supplemental data sheet, as defined by Dr. Hill.

I need a motion.

DR. YASZEMSKI: Motion.

DR. BOYAN: I need a second. Dr. Skinner?

[The motion was duly seconded.]

Now, we can have brief discussion if we need to discuss before we vote.

PANELIST: Discussion.

DR. BOYAN: I heard the word, discussion, but Dr. Skinner had his hand up, so Dr. -- yes.

DR. SKINNER: I would like to make one additional suggestion to this -- to the labeling issue. The way this typically happens is that someone decides that someone needs a patellofemoral replacement, and they call up the manufacturer and the manufacturer brings out a product brochure that explains how to do the procedure.

Then the surgeon reads that, hopefully, the day before the surgery -- or whenever -- and then goes and does the procedure.

Then the patient is on the operating table, they open up the prosthesis, and that is where the package insert is. And the patient is scrubbed and it is in small print and he does not read it.

I would suggest that that brochure have the package insert labeling in it.

DR. BOYAN: Okay. Does anybody have a problem with that?

DR. NELSON: No, we -- this is Nelson. We discussed this at a previous one, and it is a wonderful idea for the surgeons.

DR. BOYAN: Okay. Is there -- Dr. Laurencin?

DR. LAURENCIN: I just want to voice my concern about the uncemented application. This is clearly something that has had 40 years of experience, but overall the cemented application has -- even the cemented case does not have a whole lot of data. And so, we are down-classifying it almost sort of on an sort of an orphan device type of deal, where we believe it is used as a salvage procedure, and so it sort of pushes and begs the question, even down-classifying it on that basis.

But then to state that we will down-classify an application of this -- in using this prosthesis -- in which the manufacturer cannot say how many have actually been put in this way, and there is no follow-up study that has been done over the last 40 years, using the uncemented -- using that type of component in that sort of way. But, that it is similar to other uncemented cases, really, I think, begs the

question.

Clearly, one could design a noncemented femoral component that could fail easily with that sort of femoral - - that sort of trochlear groove, but continuing on with other designs -- with another design -- that could fail.

I mean, I think that the statement that, because that groove area is similar to other total knee replacements, and extrapolating that data to saying that it should be approved, I think really begs the question. And so I have a real voice of caution in terms of the uncemented case.

I think also the fact that other people will use it anyway, should never be -- in my mind, should not be a reason to approve something or make it easier to be used, if one believes that adequate data is not there, because I think what we are saying is, if we have adequate safety and effectiveness that has been shown in terms of being able to loosen the controls in terms of being able to have it approved.

DR. BOYAN: Dr. Skinner.

DR. SKINNER: I basically agree with Dr. Laurencin. I think it is good to take the high road and be pure about how to go about this, but I look at it from a slightly different viewpoint.

I see a patient who is -- like the one that Dr. Bourne mentioned -- 40 years old, who is now going to have a patellofemoral replacement, and if I was 40 years old, I would like to have an uncemented one, I think, because I am young person, if I am 40.

If you look in the literature, there are patients who are in their 30s and 20s who are having these replacements done. Hopefully, not very many of them, but there are patients who are having those done.

Given that, I would rather have a prosthesis that is designed to be uncemented, and approved to be uncemented, than to have one that is designed to be cemented and happens to have porous coating on it and is used anyway.

DR. BOYAN: Dr. Nelson and then Dr. Silkaitis.

DR. NELSON: I will try to be brief. I would like to be fair to the manufacturer. I have asked them and they do not have any data, and I just went through and looked at all of the 16 studies they have, and none of them are talking about uncemented use.

I think most of the orthopedic surgeons would agree that even in a total hip, the amount of ingrowth you get on the acetabulum is not the same as on the femur, and on a knee it is not on the femur and the tibia.

Since this is a different bone, I think we need to

have some data. I would like to address the concern of those who would like to at least have it available; that, in the current situation, if we approve it for cemented use, if a physician in his surgical judgment wants to use it as uncemented, and they have it porous coated, they can. This is not going to remove that, if someone chooses to do that.

Also, just a point of information, Dr. Skinner, are you really 40?

DR. BOYAN: Let me just make one statement before we go any further. We are not going to approve anything. We are going to make this information available to the FDA, and I think that both Dr. Laurencin and you and Dr. Aboulafia -- and even Dr. Skinner and Dr. Yaszemski, and Hill and the whole collection of you -- have made it very clear to the FDA how you feel about going forward without data. And I think that that is now noted in the record, and Dr. Silkaitis, would you like to add anything else?

DR. SILKAITIS: I would like a clarification and I would like either Dr. Laurencin or Dr. Skinner to help me out on this. Is this device ever used as a press-fit? Or maybe, the manufacturer?

DR. BOYAN: Mr. Dhority?

MR. DHORITY: I am assuming when you say, press-fit, you are talking about non-porous coated.

DR. SILKAITIS: Right.

MR. DHORITY: As far as I know, the people who press it are going to be pressing a device that has porous coating on it.

DR. SILKAITIS: Okay, so we are talking about a porous device in this situation.

MR. DHORITY: Exactly.

DR. SILKAITIS: Okay. Thank you.

DR. BOYAN: Maybe we could make a note on the labeling, just for assurance that if a press-fit use is intended, that only the porous coated device be used. Would that satisfy that need? Can you add that, please, Ms. Nashman?

DR. ABOULAFIA: I think that is the way it appears throughout the text and through the petition.

DR. BOYAN: Okay. As in the petition. Alright. So, are you ready to vote? Alright. We are going to start back with Dr. Hill. And head around --

PANELIST: Do we need a motion for the vote?

DR. BOYAN: We have a motion, we had a second. The vote is to accept the -- I thought we had a motion, did we -- yes, we did. Okay. To accept the worksheet which recommends a class II classification for the patellofemoral prosthesis, uncemented and cemented. Dr. Hill.

DR. HILL: My answer is yes.

DR. YASZEMSKI: Yaszemski. Yes.

DR. LAVIN: Lavin. No.

DR. NELSON: Nelson. No.

DR. HOLEMAN(?): No.

DR. ABOULAFIA: Aboulafia. No.

DR. LAURENCIN: Laurencin. No.

DR. SKINNER: Skinner. Yes.

DR. BESSER: Besser. No.

DR. BOYAN: Oh, you did it to me. Okay. Now have
I got -- I think it went with the nos.

[The motion was not carried.]

PANELIST: Yes, it did.

PANELIST: Isn't it split?

DR. LAURENCIN: No, it --

DR. NELSON(?): We just made it class III.

DR. LAURENCIN: Class III.

DR. ABOULAFIA: That is right.

MS. NASHMAN: No, actually, you have not made
everything class III. Now you have the opportunity to split
it.

DR. NELSON: Madam Chairman, I would like to make
a motion that we reconsider the device for cemented use
only, using your same data worksheet, because I think we

have covered all the --

DR. ABOULAFIA: I second the motion.

DR. BOYAN: Okay, let me just get it -- wait, you cannot go that fast. I will fill this sheet in, but I at least have to get it down.

This is now going to be the patellofemoral prosthesis cemented. Everything the same as what we just did, except a two.

DR. NELSON: Madam Chairman. Yes, that is what I moved.

DR. BOYAN: Okay, and the second?

DR. NELSON: And has been seconded.

DR. ABOULAFIA: Aboulafia.

[The motion was duly seconded by Dr. Aboulafia.]

DR. BOYAN: Okay, discussion of this.

DR. YASZEMSKI: Call for a vote?

DR. BOYAN: Okay. Dr. Hill.

DR. HILL: Yes.

DR. YASZEMSKI: Yaszemski. Yes.

DR. LAVIN: Lavin. Yes.

DR. NELSON: Nelson. Yes.

DR. ABOULAFIA: Yes. Aboulafia.

DR. LAURENCIN: Laurencin. Yes.

DR. SKINNER: Skinner. Yes.

DR. BESSER: Besser. Yes.

DR. BOYAN: Okay. Besser, did you vote?

DR. BESSER: Yes.

[The motion was unanimously approved.]

DR. BOYAN: Okay. So the motion carried. So we are recommending to the FDA that the patellofemoral prosthesis cemented be classified as a class II device, with all of the labeling considerations as noted in the worksheet.

That is it. We have to explain no votes again, from the other one.

MR. DILLARD: A couple of things, if I might make a couple of points. Jim Dillard, FDA. I think it would be very beneficial for us if you would go through an uncemented worksheet that has the class III recommendation -- I mean, you can get to special controls that says no -- I am assuming that is the way it goes, since it carried the other motion that way -- and then go around and explain reasons. Because then I think we can have a full picture, and I think you can do that pretty rapidly.

DR. BOYAN: Okay. Another one, please.

MR. DILLARD: Thank you.

DR. BOYAN: That was fast. Okay, this is patellofemoral prosthesis, uncemented. Class III. It is

not life-sustaining.

It is of value.

It is not risky -- horribly.

Did you answer yes to any of these questions?

Yes.

Is there sufficient information to determine that the general controls are sufficient to provide -- and we said, no, there was not sufficient information. So, we go to question number six.

Is there sufficient information to establish special controls? And we did not think there were, or did we think there were?

DR. YASZEMSKI: Madam Chairperson. A point on the form. When you said yes to number four, you should go directly to number seven.

DR. BOYAN: You know, I have to read these instructions better. Okay. How do you ever get to do question five and six?

PANELIST: You do not. -- [simultaneous discussion]

PANELIST: You say no to the first three.

DR. BOYAN: Okay. Seven. Start telling me what it is that you want to do here. First of all, you want performance standards --

DR. YASZEMSKI: Say no to number seven and classify class III.

DR. BOYAN: So we do not even do that.

DR. ABOULAFIA: No.

DR. BOYAN: Eight.

PANELIST: No. Low priority -- [simultaneous discussion]

DR. ABOULAFIA: Eight, low priority --

DR. BOYAN: We have to do eight.

DR. ABOULAFIA: Low priority.

DR. NELSON: I would agree.

DR. BOYAN: Okay, we are over on 11. Okay, 11.
No. One, prescription. Supplemental page.

I have my back-up coach here in Ms. Rooney. Okay, we are on uncemented. Okay, indications for use prescribed, recommended, or suggested in the device's labeling that were considered by the advisory panel -- and we can put all those same things in from Dr. Hill. Anything else in addition to the loosening and so forth and so on that we had previously?
No.

Identification of any risks to health presented by the device? What were -- the potential for revision. Any other risks to health that we could identify?

Any specific hazards to health that we could

identify?

DR. ABOULAFIA: Would anyone agree that it may make revision surgery slightly more difficult? Is it worth including it, or no? Done.

DR. BOYAN: Any -- so we do not have -- the characteristics and features that might cause a hazard, we do not have to worry about.

We are recommending class III.

If the device is an implant -- which it is -- but it was not classified in any other class than III, so we do not have to do number seven.

Number eight. The information, including clinical experience and judgment upon which our classification was based, was lack of information on uncemented prostheses. Is that fair? Lack of published information.

Identification of any needed restrictions for use of this device. I am going to switch you back up to eight where it says, lack of published information on uncemented prosthesis for this use, because there is plenty of published data on the use of uncemented prostheses, but not for this particular use.

If the device -- we do not have to do number ten -
- number eleven. Existing standards applicable to the device, device assemblies, or device materials. Were there

any that we wanted to add, other than the ones that exist?

No.

Now, the new version for the patellofemoral prosthesis, uncemented, is a worksheet that recommends to the FDA that they classify this as a class III. With all of the things that I just said, I need a motion.

DR. YASZEMSKI: Motion to vote on the --

DR. NELSON: Second.

DR. BOYAN: Any discussion?

MS. NASHMAN: Dr. Yaszemski, you made the motion.

Does that presume you are voting for it?

DR. BOYAN: Okay, now, one thing I need to state here is, that some of the members of the panel felt that the class II is the correct classification, so you might remember that you felt that way as you get ready to vote for this one -- because now you are saying that you accept the worksheet that recommends a class III. Okay, so let's start with Dr. Hill.

DR. HILL: My answer is no.

DR. YASZEMSKI: Yaszemski. Yes.

DR. LAVIN: Lavin. Yes.

DR. NELSON: Nelson. Yes.

DR. ABOULAFIA: Aboulafia. Yes.

DR. LAURENCIN: Laurencin. Yes.

DR. SKINNER: Skinner, no.

DR. BESSER: Besser. Yes.

DR. BOYAN: Okay, so this particular worksheet -- the motion recommending this particular worksheet passes six to two.

[The motion carried by a vote of 6 to 2.]

Let's have some comments on the nos. Dr. Skinner, would you like to make a comment?

DR. SKINNER: I think my feelings are pretty well known. I think that what we have done here is kind of set a precedent that for every individual joint, every individual prosthesis, we are going to have to have clinical data to define the use of porous materials as a means of fixation. And I think that we have enough information and enough experience over, let's see, something like 15 years, to -- maybe 20 years, even -- to go beyond that.

I think we can draw conclusions from other joints. So, I think -- that is where my no comes from. I think we have enough data to classify this as a class II.

DR. BOYAN: Thank you. And Dr. Hill?

DR. HILL: I kind of echo Dr. Skinner's comments. You are talking about something that is similar to what is used in other areas, and I think it would be real difficult to come up with a study.

DR. BOYAN: Thank you. Any other comments to the FDA that we need to share with them? Have we satisfied the needs of the FDA, Mr. Dillard?

MR. DILLARD: Jim Dillard. I will not prolong this, but ten seconds more for each one of you. Here is the issue I am struggling with, with this recommendation. Which is, the recommendation is that, when I think about classification from FDA, you are saying that there is not enough data as a panel to make it --

DR. BOYAN: Wait -- one moment, please. I want to make sure that Dr. Nelson hears this.

MR. DILLARD: -- Nelson -- yes, yes. That there is not enough data in my mind -- because when I think about class II, I think that there is enough known about the risks associated with the type of device -- and we will use prosthesis here -- that some types of special controls can be utilized to adequately control for those risks. And so, are you saying -- which is what my thinking is -- is that, with no data, you cannot adequately identify all the risks, and that is what the lack of data gives us?

Or is it just that, it is the lack of data that makes you uncomfortable with granting approval for a product? Because -- and the only reason I say that is -- I throw that out -- is that, in the future -- and we will have

more classification and reclassification efforts to take before this panel -- we will continue to have that circumstance where, like this, there are no uncemented patellofemoral prostheses that are available for market in the United States, today.

There is one 510(k) cleared and it is a cemented version, and there may be some other preamendments products. One of the ways to handle a product like that would be to say, we do know enough about the risks associated with the product type. We can use the kinds of special controls that you all on the panel identified for other uncemented prostheses, but you believe, as the panel, that there is clinical information that needs to be known on each individual prosthesis.

That is a very appropriate approach in some cases -- I am not saying that it is here -- but, to have premarket clinical data in a 510(k), also, which could be utilized as a special control -- and I know this is conceptually difficult and you have struggled through it, and I think -- and you know, I would like -- you know, thank you for the last four reclassification efforts that you have been through, but to let you know that in the future, you know, sometimes these kinds of possibilities exist, too. So if you can comment --

Really, my question was, if you can comment at all about the need for data to adequately identify the risks versus clearance for the product, I would love some clarification.

DR. BOYAN: Since I did not get to vote on the last one, I would like to answer your question first, so that I can at least get some of my feelings stated into the record.

This data probably does exist, and in the future -- because I feel strongly that since -- since these devices that are porous coated are frequently used, clinically, in the absence of cement, and for biological reasons, in many instances for younger people, it is biologically advantageous to not use the cement, it bothers me that we -- as I have been a member of the panel now for two years -- it bothers me that we routinely have this discussion. And maybe you, as a representative of the FDA and your examiners as well, could encourage the companies to gather that data, which does exist.

Even though, technically, they are not marketing it for that purpose, they certainly know when a surgeon uses it without the cement, and perhaps some people will have the courage to come forward with the data that will prevent us from having what happened here today -- which I think is on

the unfortunate side. Dr. Hill.

DR. HILL: To go back to your question. I think, for me, the reason I answered yes is that, I think enough is known in other joints that -- I think it would be almost impossible to get that study performed.

DR. YASZEMSKI: I think I fall somewhere between the position -- as I understand it -- from Dr. Skinner and Dr. Laurencin. I think I would like the ability as a panel member to make a distinction between different types of joints.

I agree that much of the data on biologic fixation in other joints can be applied in a theoretical fashion to a new device.

I think the particular clinical situation is what made me make my situation here. This is not a case where every surgeon in every town is going to go out and start using this, if it is approved. This is a very infrequently used device, and I think for this particular one, individual surgeons with their preference for cemented or noncemented have enough biologic data to make that choice, and it is used so infrequently that to require the generation of clinical data is probably unreasonable.

DR. STERN: I think this is a general enough question that it is not really dealing with knees, so I

would like to say something, because to a certain extent, I would also fall in between, and I want to slightly take issue with something that Dr. Boyan just said.

The perception exists that porous coated implants are going to be better for younger patients, and hence, are better for younger patients. But whether or not that has actually been so well proved clinically for all joints, I think does remain open to some real question, and that probably is why panels continue to discuss with this, and it also may well be why there is not a lot of data that has ever been brought forth to the FDA. Because while it is clear that that was the theoretical basis for porous coated implants, whether that has actually been ever shown -- and I am talking all joints in general -- is I think open to enough question that people do fall in between.

DR. BOYAN: I accept your comments. Those are fair. I was more going for effect and you went for -- you were much better. Thank you.

DR. LAVIN: The one comment that I want to say -- I have been one of those people that have wanted more data.

The thing that just always concerns me is that if you have, say, 50 subjects were in a study, and you are looking for adverse events, and you see none in 50 subjects. All that means statistically is that you can rule out an

adverse event or a complication rate that is as high as 10 percent.

That, in this situation, may not be enough, and that may be a difference between one device and another device. And when you start looking at accumulating data, I think that, you know -- let me go on record that I think you will need to accumulate larger numbers than 50 subjects per device to be able to rule out complication rates that are lower than 10 percent. So, I think this is a matter where caution is advised, and that is the path that I have been following today.

DR. NELSON: Mr. Dillard. To answer your question. Despite the fact that I have been on one side of the fence throughout the whole time, I would like to take what I consider the middle position that some other people have said.

I do not think you need clinical data in every single circumstance. If you have a product or an application, or whatever, that -- when it is used in multiple sites, it has very similar and predictable results.

I disagree with some of my colleagues. I think that in the instance of porous ingrowth, it is variable, the data is variable. But I do not think you need data in every single circumstance.

I mean, if you told me, if you shoot yourself in the foot, it hurts, I do not need to get another study to find out if you are shooting yourself in the head, it is going to hurt. So, if there was a product that had uniform performance in other parts of the body, I would say we can expand the indications. I just feel, interpreting the porous ingrowth data, it is not uniform in the rest of the body and I think we need site by site data.

DR. ABOULAFIA: Very quickly. I think -- just to go on record as saying, you know, we saw that with other things, like Sylastic(?), that the performance in one joint was very, very, very -- radically different than performance in other joints. And if we had taken Sylastic off the market because of its performance in one joint, we would have done a tremendous disservice for patients with rheumatoid arthritis in the metacarpal pharyngeal joints. So, to extrapolate data from one joint to another, even within the hand, and moving up one joint, which is very close, I think one has to do with caution.

The other thing is, again, I am not sure our responsibility is to suggest that things are safe and effective, that are driven by industry rather than by need. We all agree this is an incredibly limited number of patients, and that if it is really a limited number of

patients, why do we need more than one prosthesis that may actually not have even a theoretical advantage to one that we do have some knowledge about.

DR. LAURENCIN: Just a short comment. I think the concept that biological implants around a joint are going to perform very differently, depending upon their location, really cannot be underscored more. And I think that we are going to see this -- especially when the biological implants, such as the carticell(?) procedures, or some of these new procedures that are being used for regenerating surfaces, that is sort of the ultimate biological sort of implant. And their indications are not -- for instance -- are not in the patellofemoral area, because of the sorts of biology that goes on in the patellofemoral area. Those are specifically for the medial femoral condyle, for different areas that are outside of the patellofemoral area.

A number of the other procedures that we do that have biological implants around the knee, in terms of biological osteochondral implants, actually specifically are not for the patellofemoral area. And so there are these differences that do occur, depending upon even location of an implant around the -- in a joint. And so, I think that is a very important consideration to make in terms of deciding on these implants.

DR. SKINNER: I also have one quick comment. Just to be a little bit funny here. Jim Dillard's Mama didn't raise no dummy, and the people from the FDA are not stupid. They are very good at this and they are very cautious. And I think that we should give them the lowest possible controls that we feel comfortable with, and let them raise those controls as necessary, because they will raise them, even if they have a floor that -- if they have a floor, if it is low enough.

They will look at a prosthesis and decide whether they think that it needs clinical trials, etcetera. And they will do a good job at that. They do not necessarily need us to put minimum standards in there. I think we probably made a mistake today in not going with the uncemented knee and the uncemented patellofemoral joint.

DR. BOYAN: Dr. Besser, and I do not want us to forget Dr. Silkaitis and Dr. Holeman.

DR. BESSER: I want to make sure that I understood what Mr. Dillard said correctly. As I understood what you said, essentially, we could have classified a device class II, and still required clinical trials?

MR. DILLARD: I actually did not want you to think about it that deeply for your discussions today. Just to say that there are a number of options, and one of the

things we are going to struggle with the most with your recommendation -- and that is really what I was trying to bring out -- is that, your recommendation to continue for the patellofemoral, to have it be in class III, not down-classified at class II, really I think what you are telling us -- based on lack of data -- at least, my take-home message is that, the lack of data is driving us to the regulatory point, which is the way I think, which is, because we do not have the data, we cannot identify all the potential risks that might be associated with an uncemented patellofemoral joint. And without that data, to be able to say, we understand the risks. We certainly cannot tell you or recommend to you -- FDA -- what sort of special controls might be able to be used to control for those risks.

I just wanted to make sure that -- I mean, is that the take-home point that you are giving us, or is it just the fact that, you know, we are uncomfortable with no data in that area, and we might be equally as comfortable if we had data on the individual devices, irrespective of what sort of process and what sort of class that it is in. And that is the differentiation and the delineation that I am asking you to comment for 20 seconds on.

DR. BESSER: I am not sure I understand what the difference is between those two statements, so --

DR. BOYAN: Well, I -- we got to --

PANELIST: Take a pass.

DR. BOYAN: Take a pass.

DR. BESSER: Yes. I will pass.

DR. SILKAITIS: Okay. In terms of the issues that we talked about today, and I know that the patient is the center of the focus. The surgeons here, the panel members, are certainly concerned about the issues of the implant in regards to the patient, and industry also wants to provide devices that are meaningful to the patient and provide a significant benefit to the patient.

The risks, as Jim was talking about before, and as we talked about yesterday, are there things that we can identify? We know the issues surrounding porous ingrowth, and what happens if it fails. What are the kind of things that occur to the patient when that device or porous interface does not happen?

I think we have enough experience in terms of knowing what those things are. So, in terms of the decision, from an industry point of view, putting it in class III means that the product has to come before the panel, because the risks are so unknown and so nebulous, that we need a panel of experts to tell us.

The alternate path, which is the class II path, we

can provide FDA with the judgment to evaluate whether that device passed a hurdle, whether we have that information today or not.

What I am referring to is the fact that we have porous ingrowth, and we know what it is supposed to achieve. There are guidance documents that FDA has that it is required for the 510(k) to get approved, that limited clinical studies be performed on 20 patients, or 50 patients -- I am not sure exactly which guidance documents. But the manufacturer must provide that data, and FDA will look at that data, and if that data does not satisfy the minimum hurdle that is required, then that 510(k) will not be approved.

I think the panel does have that option to say that in the class II we recognize what the risks are. They are very defined. And we are going to pass the judgement to FDA, because if they put this into the guidance document, then they can proceed and release that product to market. And I think that is what is the central issue of this whole thing.

DR. BOYAN: Dr. Holeman, did you have anything that you wanted to add?

DR. HOLEMAN: Nothing to add.

DR. BOYAN: Okay, and I guess we are going to let

you have the last word, Aboulafia --

DR. ABOULAFIA: No, I am not adding -- I was going to answer his question, only if you want us to.

DR. BOYAN: You have 20 seconds.

DR. ABOULAFIA: The answer is, I think the risks are known. I voted to class III because I thought it was a bad idea, and to summarize it, analogously, using a stupid analogy. I know the risks of playing with a gun; I think it is bad idea.

MR. DILLARD: I want to just thank the panel from the FDA perspective, and I appreciate the final few minutes to clarify that.

DR. BOYAN: Thanks.

MR. DILLARD: Thank you.

DR. BOYAN: Okay, now wait -- no, no -- you cannot move. You cannot move, I know you want to, but you cannot. We are going to get an actual real live break while we have the changing of the guard and Dr. Skinner and I take our conflicted bodies out of here. But our soon to be ex-Executive Secretary would like to make an announcement.

MS. NASHMAN: Just real quick, because I know I have you right now and I might not at the end of this meeting. You will have a whole bunch of information; none of it is classified. Anything that you would like to leave

here, please feel free to do so. If you could either leave at the end of the table, or underneath the table with information over there, it would be appreciated.

Also, in a Pavlovian sense, all of you have been given a certification sheet in your red folder. If you could just sign it and let me know what it is you have done with the material -- either leave it -- that you have left it here, or that you have left it at home and have destroyed it. I would appreciate it if you could return that to me.

I also want to take a moment and thank Drs. Skinner and Boyan for all their help, and I hope they enjoy their unconflicted ride home. This is a ten-minute break. We are reconvening at 3:30. We are only an hour behind schedule, and should make it out on time.

[Brief recess.]

Agenda Item: Classification of Plaster of Paris

[Dr. David L. Nelson was duly designated by Ms. Nashman, the Executive Secretary, as Acting Chairman of this panel. Dr. Nelson introduced Mr. Steve Reitzler, Vice President of Regulatory Affairs for Advanced Bioresearch Associates, or ABA, who proceeded with the first presentation on behalf of Wright Medical.]

Agenda Item: Wright Medical Presentation

MR. REITZLER: Good afternoon, ladies and

gentleman, Chairman Nelson, Secretary Nashman, and distinguished members of the panel. My name is Steve Reitzler, and I am Vice President of Regulatory Affairs for Advanced Bioresearch Associates, or ABA.

ABA is a paid consultant to Wright Medical Technology, and I am here today to assist Wright in presentation to the Advisory panel of information requested by the Food and Drug Administration to permit appropriate classification of calcium sulfate bone void filler. Wright currently markets such a device under the trademark name of Osteoset.

Before proceeding further, I would like to introduce the individuals who will assist with our presentation.

Dr. Jack Parr is Executive Vice President of Research and Development at Wright Medical Technology, where he is responsible for all research, product development, engineering, and clinical research activities. Dr. Parr has spent 20 years in the orthopedic device industry, and is a leading authority on the research, development, and characterization of biomaterials, including both organic and inorganic bone and fillers.

Dr. Parr is President Elect of the Society of Biomaterials, Adjunct Associate Professor of the Department

of Orthopedic Surgery at the University of Tennessee School of Medicine, and the Subcommittee Chairman of the ASTM Committee for Medical and Surgical Devices and Materials.

Dr. Parr has published dozens of articles on orthopedics and biomaterials, is the holder of numerous orthopedic device and biomaterial patents, and was the recipient of the FDA Center for Devices and Radiological Health's Director's Special Citation in 1997.

Dr. Parr will be presenting a brief overview and description of the sponsor's Osteoset calcium sulfate device.

Also joining me is Dr. George Rodeheaver, who is the Richard F. Edlich Professor of Biomedical Research and the Director of the Wound Healing Research Laboratory for the Department of Plastic Surgery at the University of Virginia Medical Center.

Dr. Rodeheaver has, for decades, specialized in the development of reproducible non-clinical models for the evaluation of tissue repair, and the evaluation of agents and biomaterials that influence this repair process.

He is the author of two textbooks, over 30 textbook chapters, and nearly 200 individual articles on the subject of tissue repair and wound healing. Dr. Rodeheaver will be summarizing non-clinical information regarding

calcium sulfate bone void filler.

Dr. Steven Gitelis is currently Professor of Orthopedic Surgery, and the Associate Chairman of the Department of Orthopedic Surgery at Rush Medical College. He is Director of the Section of Orthopedic Oncology at Rush-Presbyterian-St. Luke's Medical Center, a Lecturer in Orthopedics at the University of Illinois College of Medicine, and is cancer liaison physician for the American College of Surgeons.

Dr. Gitelis has contributed over 200 published articles, abstracts, textbook chapters, presentations, and visiting professorships in the areas of orthopedic surgery and orthopedic oncology, which serves to establish him as a knowledgeable authority in the field of orthopedic surgery and bone grafting.

Dr. Gitelis will be summarizing clinical experience with Osteoset and other calcium sulfate bone void fillers, and evidence of their safety and effectiveness.

I will be closing our presentation with a brief summary of issues associated with this classification proceeding. Following our prepared presentation, we will be happy to address any questions the panel members may have.

During the course of our presentation today we intend to establish that sufficient publicly available,

valid scientific evidence exists to demonstrate that calcium sulfate is reasonably safe and effective for its indicated use in filling bony voids and gaps which are not intrinsic to the stability of bony structure; that the risks to health potentially associated with use of the device are well known and can be controlled within class II; and that adequate information exists with which to establish special controls.

For these reasons, we believe that classification of Osteoset calcium sulfate bone void filler, and others of its generic type, into class II is appropriate, and will provide reasonable assurance of safety and effectiveness.

I would now like to introduce Dr. Parr.

DR. PARR: Thank you, Steve. Good afternoon. My name is Jack Parr, and I am the Executive Vice President of Research and Development at Wright Medical Technology, Incorporated.

I would like to provide you a brief overview of our Osteoset device, its characteristics, properties, and intended use, and the means by which we at Wright assure its consistent quality, safety, and effectiveness.

I will also indicate where I believe that the methods that we employ to characterize and control the device may serve as the basis for special controls in class II.

Osteoset bone void filler is offered in the form of very small pellets, each consisting of 98 percent of a highly purified form of medical grade calcium sulfate, also known as Plaster of Paris; up to 2 percent stearic acid may also be present as a tableting agent.

The calcium sulfate meets all specifications for both the U.S. Pharmacopeia and National Formulary official monograph, and the Food Chemicals Codex monograph for calcium sulfate. The stearic acid also meets USP official monograph requirements.

Our Osteoset product is currently cleared for market by the FDA. Osteoset pellets are radiopaque, biocompatible, biodegradable, and when used in accordance with labeling, will resorb naturally in the body in 30 to 60 days. The product is provided sterile in vials of 100 to 200 pellets.

Calcium sulfate occurs naturally in the dihydrate form, known as gypsum, wherein each molecule of calcium sulfate is associated with two molecules of water. Plaster of Paris is a hemihydrate form of calcium sulfate from which 75 percent of the water has been driven off by heating.

Two crystalline structures can occur in the hemihydrate form; an alpha-form and a beta-form. The alpha-form is very pure, and is highly uniform in its crystalline

structure. It is the alpha-form that we use to produce the Osteoset device, and to which the device owes its biocompatibility, its consistent and predictable rate of resorption.

The Osteoset device is indicated for use in filling bony voids or gaps, whether traumatically or surgically created, that are not intrinsic to the stability of the bony structure.

These indications include use in the extremities, spine, and pelvic. The device may be used alone, or in combination with other graft materials, such as autologous bone, allograft, or demineralized bone.

The chemical composition, purity, and physical properties of the Osteoset pellets are accurately determined and closely controlled using the available state-of-the-art analytical methods. Specific methodologies are delineated in published standards such as those issued by the U.S. Pharmacopeia and ASTM, among others.

USP monograph tests for the chemical composition of purity of calcium sulfate include: assays to identify and quantify calcium sulfate content; tests to determine water content; analyses to determine iron, fluorine, and heavy metals content; and then further elemental analyses to identify and quantify any other impurities.

In addition to these monograph tests, x-ray diffraction and thermogravimetric analysis are employed to verify that the calcium sulfate is, in fact, the desired alpha-hemihydrate form pH is also measured and controlled.

Standard methods that are used to assess and control the physical properties of the device are shown on the slide. Because the in vivo resorption rate is an important performance parameter, resorption rate determinations are also made using in vitro practices that are recommended by an FDA Guidance Document.

Recognized methods such as these can determine the significant characteristics of the Osteoset device to a fine degree, and thereby assure consistency of performance. Data from these tests may also be compared to published reference standards and guidelines.

These standard methods provide recognized, state-of-the-art means by which the safety and efficacy of the device may be controlled in class II, and from which special controls may be developed.

I would like to introduce Dr. Rodeheaver.

DR. RODEHEAVER: Thank you, Dr. Parr, Dr. Nelson, fellow panel members. I am Dr. George Rodeheaver. I am the Director of the Wound Healing Research Laboratory at the University of Virginia Medical Center. I have no financial

interest or equity position in Wright Medical Technology, except for receiving grants to conduct research studies.

My presentation will summarize the non-clinical experience with calcium sulfate, or Plaster of Paris, bone void filler.

Considerable experimental information has been cited in the literature regarding the safety and efficacy of Plaster of Paris in filling bony defects. The body of published work has demonstrated that, under appropriate conditions of use, calcium sulfate is a safe and effective resorbable material for filling bony defects created either surgically, or through trauma, or disease.

Furthermore, no increase in the incidence or severity of infection, wound complications, or other adverse effects have been attributed to the use of calcium sulfate by these researchers.

Published reports of non-clinical research using Plaster of Paris as a bone void filler span over 100 years. The material has been studied in numerous animal species, in a wide variety of anatomical locations, and employed numerous types of bone defect models.

In addition, Plaster of Paris has been evaluated experimentally in combination with such other materials as autologous bone, hydroxylapatite, and bone morphogenic

protein.

All told, 35 experimental studies of the use of calcium sulfate as a bone void filler were summarized in the background proposal presented to you.

The general consensus of this extensive research is that calcium sulfate is biocompatible, consistently resorbable, and results in replacement with histologically normal bone.

Dr. Peltier and his associates at the University of Kansas began experimentation with commercially-available Plaster of Paris in the 1950s, implanting the material in dogs in various sites and conditions over the next 40 years incurred.

From this substantial body of work, the following observations were drawn, all of which were largely consistent with previously published work.

Those observations were that the inflammatory response to Plaster of Paris is no greater than that normally seen at any site of bone repair; there is no observable inhibition of osteoblast growth or activity; new bone grown at the implant site is histologically normal; the material is completely absorbed in several weeks, ranging from five to ten weeks in various species; there is no evidence of an increase in the incidence or severity of

infection, wound complications, or other adverse effects associated with the use of this device.

My laboratory has also conducted animal evaluations of medical grade calcium sulfate. The model we employed was 3mm circular defects in the femurs of rats. These defects were filled either with calcium sulfate or allogeneic bone.

Resorption of bone void filler and healing was monitored over ten weeks, using quantitative radiological, mechanical, and histological techniques. Our results corroborated those of previous researchers. In specific, the resorption of calcium sulfate occurred in four to eight weeks, with replacement with normal bone. Resorption of the calcium sulfate occurred with no additional inflammatory reaction. And there were no adverse complications, including wound infection, in our studies.

Additional observations of Peltier and other researchers include the following. Plaster of Paris bone void filler provides no significant strength or support to the bone structure. When infection is present, the calcium sulfate can liquify and drain from the wound, thus not leaving a sequestrum. Local equilibrium pH is acidic; and a small transient elevation of serum calcium has been observed.

None of these observations represent significant risks, and as the experimental literature supports, there are virtually no adverse effects associated with the use of Plaster of Paris as a bone void filler. Nonetheless, certain of these observations warrant disclosure in labeling. Examples can be seen in the contraindications statement for Osteoset pellets, which advises against the use of the device for structural support, or in patients with hypercalcemia.

In unpublished work, the biocompatibility of Osteoset bone void filler has been determined in accordance with the recommendations of the International Standards Organization, or ISO, the standard being 10993, and entitled "Biological Evaluation of Medical Devices." This internationally recognized standard has been sanctioned by the FDA as the principle guidance for determining the biosafety of new medical device material.

Studies conducted by Wright Medical to evaluate the Osteoset device, in accordance with the recommendations of this standard are shown on the slide.

All testing was conducted in accordance with recognized, publicly available protocols promulgated by such organizations as the USP, and ASTM, and under the conditions of each of these tests, the Osteoset material proved quite

biocompatible.

In consideration of the data that I have summarized, and from my research experience, three conclusions can be drawn.

First, studies of safety and effectiveness in various animal species and bone models conducted over 100 years have demonstrated that, under appropriate conditions of use, calcium sulfate is a safe and effective bone void filler which is absorbed by the body and replaced by new bone growth without significant complications or adverse effects.

Second, in vivo and in vitro studies performed in accordance with internationally-recognized ISO biocompatibility standards, and conducted using current state-of-the-art methods, have established that the Osteoset device is biocompatible as an implant in bony tissue.

And lastly, it is apparent that state-of-the-art methods such as those recommended by the ISO standard, for determination of biocompatibility, can readily be applied to determine the biosafety of any calcium sulfate device to a fine degree, and provide the means by which the safety and efficacy of the device may be controlled in class II, and from which special controls may be developed.

I would now like to introduce Dr. Gitelis who will

present a summary of the clinical information.

DR. GITELIS: Thank you very much. Good afternoon. Thank you, Dr. Rodeheaver. My name is Dr. Steven Gitelis, and I am currently a Professor of Orthopedic Surgery and the Associate Chairman of the Department of Orthopedic Surgery of Rush Medical College in Chicago.

I am an orthopedic cancer surgeon and currently I am the President of the American Musculoskeletal Tumor Society. I am a consultant of Wright Medical Technology and serve as a clinical investigator in Wright's ongoing clinical study of Osteoset bone void filler. I have no equity position in the company, but as a co-inventor of calcium sulfate alpha-hemihydrate, I have a licensing agreement with Wright Medical.

I would like to take this opportunity to summarize for the panel the clinical experience gained with calcium sulfate bone void fillers, and with the Osteoset device in particular.

In this body of work there is ample evidence of the safety and effectiveness of calcium sulfate bone void filler, for a broad spectrum of applications, with remarkably few complications.

The earliest published reports of use of Plaster of Paris to fill bone voids actually predate the first

published accounts of experimental work, and date back more than 100 years. The first clinical use is ascribed to Dreesmann, who in 1892 used Plaster of Paris to fill bone defects.

Since Dreesmann's early experience, Plaster of Paris has been employed by numerous clinicians, and with generally successful results, to fill defects of traumatic, surgical, and disease origin. Calcium sulfate has been employed to treat defects in long bones, spine and pelvis; the hand and foot, and in maxillofacial and cranial bones as well. It has been shown effective in both sterile and infected sites.

In all this published work, relatively consistent results, favorable to its use as a bone void filler have been reported. In all, 25 published studies were summarized in the background package provided to you, representing use in over 500 patients, and with follow-up as long as 13 years in one case.

Owing to time limitations, I will not attempt to review each of the papers individually, but will summarize the collective observations of the authors in a more concise manner.

Peltier et al, Shaffer and George, and others have remarked that calcium sulfate bone void filler is well-

tolerated by the tissues of the implant site. They and others further note that it is readily resorbed over a period of some weeks.

Peltier and associates have observed that the material can be used safely in infected sites, and does not appear to aggravate the infection. It does not become sequestered in the site, but rather will liquify and drain from the wound. Bahn also observed drainage of the material from infected wounds.

Terry et al, and Peltier and associates, have observed that the material does not inhibit the normal growth or healing of the bone, while Alderman has reported that calcium sulfate acts as a scaffold for bone growth until the graft material is completely resorbed.

Peltier and others have suggested that Plaster of Paris can be used to extend or increase the ultimate volume of other graft materials, such as autologous, allograft, or demineralized bone.

Hauptli reported no deleterious effects associated with the use of Plaster of Paris to repair surgical defects, and Alderman reported comparable results. Others agree that generally low complication rates are associated with the use of calcium sulfate bone void fillers.

Notwithstanding the low rate of adverse events,

the published literature does cite such occurrences. The following complications have been reported associated with the use of calcium sulfate bone void filler, and they are shown here on the screen.

Many of these complications are clearly not unique to calcium sulfate, or even to bone grafting procedures generally, but rather, are commonly associated with virtually any surgical procedure. Risks such as these are readily managed in class II through labeling disclosures and warnings.

To provide clinicians with more contemporary knowledge, Wright Medical Technology is currently conducting a prospective study of Osteoset pellets in filling surgically-created, or traumatically-induced bone voids, or that are not intrinsic to the stability of the bony structure.

Patients will be evaluated by radiographic analysis of new bone growth, and percent resorption of the Osteoset pellets, and by the occurrence of complications.

The primary study endpoint is, percent fill of the bone void as determined by radiographic analysis. The secondary endpoint is the cumulative complication rate at six months postoperatively.

Inclusion criteria for the study include a

recommendation for cancellous bone grafting by the surgeon, a non-load bearing void in a long bone created surgically, or as the result of trauma, and a bone void in which the shape will contain the pellets.

Exclusion criteria include severe vascular or neurological disease, uncontrolled diabetes, severe degenerative bone disease, and hypercalcemia, among others.

As of December 4, 1997, a total of 65 patients were enrolled in this study. Patients' diagnoses include 19 bone lesions, 4 infected bone lesions, 34 traumatic lesions, and 8 others. The locations of the defects vary widely.

Osteoset pellets alone were used to treat 18 patients and a combination of Osteoset with other graft material, such as demineralized bone, was used to treat the other 47 patients.

Preliminary results are shown in this table. Depicted here for each postoperative evaluation interval are the percent of calcium sulfate resorption, and the percent bone growth, or defect fill.

As can be seen from these data, resorption of the Osteoset pellets proceeds at very nearly the same rate as that of new bone growth. This is an important feature of the device, as the resorption of the graft material is essentially complete between two and three months

postoperatively, by which time new bone growth is very nearly filling the entire defect.

There appears to be no correlation between the size of the defect, the amount of material used, and the results obtained.

It is also important to note that there have been no device-related complications reported in the study to date. The only two complications of any type were a plate fracture, and a graft site fracture 28 days post-op due to trauma.

It is also essential to note that Wright Medical is aware of no MDR-reportable events regarding use of the product since it was originally commercialized.

In summarizing the available information described in clinical experience with Osteoset pellets and other calcium sulfate bone void fillers, we can make the following general statements.

Reflective of the non-clinical data, they appear to be very biocompatible and do not elicit undue tissue reactions. They do not inhibit growth of new bone, and are resorbed over a period of some weeks at a rate which is roughly consistent with that of new bone growth.

In my experience, calcium sulfate actively participates in the bone repair process. They appear to

serve as a scaffold for new bone growth until resorption of the calcium sulfate is complete.

They can be used safely and effectively in infected as well as noninfected sites. They can be used equally effectively in conjunction with other bone graft materials, such as autologous, allograft, or demineralized bone.

They are associated with very low rates of complication and adverse events. The majority of the adverse events reported in the literature are common sequelae with any major grafting surgery, regardless of the material used, while some -- such as wound dehiscence, infection and drainage -- are risks associated with virtually any surgical procedure. Labeling disclosures and warnings are adequate to manage risks such as these in class II.

Given the information we have summarized here today, it is our belief that we have adequately established through valid scientific evidence, that calcium sulfate is reasonably safe and effective as a bone void filler when used as indicated, and further, that the risks to health are well-known and are not unreasonable.

I would now like to ask Steve Reitzler to complete our presentation.

MR. REITZLER: Thank you, Dr. Gitelis.

The fundamental basis for classification of a device is a determination of what level of regulatory control is necessary to provide reasonable assurance of its safety and effectiveness under its labeled conditions of use.

The level of regulatory control a device is subject to is determined by classification into class I, II, or III, and no device should be placed in a class higher than is necessary to provide such reasonable assurance.

We earnestly believe that the regulatory controls inherent in class II, including special controls, are more than adequate to provide reasonable assurance of the safety and effectiveness of Osteoset bone void filler, and any others of its generic type.

Devices in class I, II, and III are equally subject to the prodigious general controls authorized by the Law. Among the general controls as you have heard today are good manufacturing practice, or quality systems regulations, which govern all aspects of the manufacture of devices.

Devices in class II may also be subject to so-called special controls. Special controls can take the form of a performance standard, patient registries, postmarket surveillance, and device-specific guidance documents

promulgated by the agency.

Significantly, the agency's own interpretation of special controls, quote, reflects Congressional intent to provide considerable flexibility in establishing special controls, to avoid unnecessarily placing unclassified preamendment devices into class III.

Lastly, of course, class III premarket approval is reserved for devices whose safety and effectiveness cannot be reasonably assured through general controls or general controls in conjunction with special controls.

Perhaps a better comparison of the differences between device classes can be seen in this graphic. As you will note, the only difference in controls between class II and class III lies in whether special controls or premarket approval are imposed: class II being subject to special controls, while class III is subject to premarket approval.

In making your recommendation for classification of calcium sulfate bone void fillers, we ask you to consider the following.

First, is there sufficient, valid, scientific evidence to demonstrate the reasonable safety and effectiveness of the device for its labeled conditions of use?

It is our position that the information summarized

by Dr. Rodeheaver and Dr. Gitelis today, and which spans over 100 years of experimental and clinical use, is sufficient to do so.

Second, are the risks to health potentially associated with the device identified? Again, it is our position that the experimental and clinical information we provided adequately identifies all potential risks to health associated with use of the device.

Lastly, what level of regulatory control or device class is necessary to control these risks and provide reasonable assurance of the safety and effectiveness of the device? As we have said, it is our position that class II with special controls is adequate to do so.

In support of this position, we submit the following.

The generic type of device we have proposed adequately describes Osteoset and other calcium sulfate bone void fillers.

The device is neither life-supporting or life-sustaining, nor it is of substantial importance in preventing impairment of human health.

The safety and effectiveness of the device for all current indications for use have been supported through published and unpublished valid, scientific evidence.

The risks to health potentially associated with the device have been identified in the clinical information Dr. Gitelis has summarized. These risks are well-known to the clinical community, and are no different than those associated with any bone grafting material or surgical procedure.

Class II controls, including special controls, are adequate to manage these risks to health, and to provide reasonable assurance of the safety and effectiveness of the device.

Lastly, standards and recognized test methods exist with which to characterize and control device properties, characteristics, and performance in class II, and from which special controls could be developed.

These same methods can also be employed by the FDA as a basis upon which to determine the substantial equivalence of any future devices of this type.

Standards and recognized methods we have described today and from which special controls could be established include:

Conformance to official monograph requirements for composition and purity of the calcium sulfate material.

Use of USP, ASTM, and other internationally-recognized standard methods to further characterize and

control chemical and physical properties of the device.

Use of the internationally-recognized ISO biocompatibility standard to assure biosafety of all devices and device materials.

Reliance upon FDA guidance documents to evaluate other device properties and performance characteristics, including rate of resorption.

The use of prominent labeling disclosures, contraindications, and warnings to alert physicians to potential risks to health and the means to manage or avoid same.

Any, or all, of these potential special controls could be combined in an FDA-issued Guidance Document for this generic type of device.

Such documents are used increasingly by the agency to provide reasonable assurance of safety and effectiveness, and to facilitate a determination of substantial equivalence for new device types.

The fact that class II controls are adequate for such devices as the Osteoset bone void filler may be demonstrated by the fact that other, nearly identical devices are currently being managed effectively in class II.

Two examples include a bone filling device composed of calcium sulfate mixed with hydroxylapatite,

which was cleared by a 510(k) in 1991, and a similar bone filling device composed exclusively of calcium sulfate, cleared by 510(k) in 1995.

Both are indicated for fracture reduction, bone contour filling, and augmentation and reconstruction in maxillofacial and cranial surgery -- clearly, indications similar if not identical to those for which the subject device is indicated.

In summary, then, we believe that class II special controls, in conjunction with the general controls, are more than sufficient to provide reasonable assurance of the safety and effectiveness of Osteoset and other substantially equivalent calcium sulfate bone void fillers, and to control the risks to health associated therewith.

We further believe that class III premarket approval is unnecessary to provide such reasonable assurance, and it would be inappropriate for a device with over 100 years of safe and effective use to be so classified.

We respectfully ask the panel to concur with our position, and we thank you for your time and attention.

DR. NELSON: Thank you very much. We will next hear from Dr. Orlee Panitch, who is representing the FDA. It looks like we will have a substitution here.

Agenda Item: FDA Presentations

MS. SLOAN: Hi, good afternoon. My name is Nadine Sloan. I am a scientific reviewer in the Restorative Devices Branch, and I will be providing a very brief presentation of the regulatory history of the calcium sulfate bone void fillers, and I will also just be providing a brief overview of some of the issues which were fully described by the previous presenter.

Again, I will be providing FDA's proposed device description; device history of the preamendment and currently marketed calcium sulfate bone void fillers; some supporting information; the potential risks to health; and the proposed special controls.

This is a modified device description proposed by the FDA, compared to that provided in the classification proposal. This description removes the specific information regarding the minimum amount of calcium sulfate to be used, and a requirement of satisfying the USP monograph.

The reason for removing these references is, we think they can be more appropriately considered in the special controls proposed for the device.

Also, the statements regarding what substances can be added and what form the device should take have been removed, so you can read our final proposed device

description. I am not going to read it.

This overhead briefly summarizes the regulatory history of the preamendment device. Preamendment calcium sulfate was manufactured by Ethicon, Incorporated as Plaster of Paris, and the final material of this was medical grade calcium sulfate dihydrate with stearic acid, in pellet form.

The indications were for orthopedic bone void filling, which could include long bones, spine and pelvis.

To the best of our knowledge, it was last marketed over 20 years ago. And the device was never classified.

This is a summary of the currently marketed Wright Medical device, as previously described; 98 percent medical grade calcium sulfate dihydrate, mixed with 2 percent stearic acid, in pellet form.

The device was found substantially equivalent to Ethicon's preamendment calcium sulfate bone void filler; and it has been the only calcium sulfate bone void filler to be found substantially equivalent.

These are the current indications for use for the currently marketed device, and to summarize, the device is only to be used for bony voids or gaps that are not intrinsic to the stability of the bony structure, and can be packed into bony voids or gaps of the skeletal system, including the extremities, spine and pelvis. The defects

may be surgically created or created from traumatic injury to the bone; and the device may be used at an infected site.

These next few overheads provide more detailed information about the regulatory history of the currently marketed device.

The first submission was cleared on June 21, 1996, again, for medical grade calcium sulfate dihydrate and stearic acid in pellet form. And the indications are basically conveyed; it was for non-load bearing long bone voids, and it was found substantially equivalent to Ethicon.

There was a second 510(k) that was cleared March 24, 1997. It was for the same indications as previous, however it was for a kit version, which was calcium sulfate hemihydrate, stearic acid, and saline mixed and set in molds prior to implantation.

The third 510(k) was cleared May 7, 1997, and this 510(k) expanded the indications to include the spine, pelvis, and infected sites.

The indications were also modified to clarify the term, non-load bearing. The wording was changed to describe the situation in the current indications, in which the device is used to treat bony voids or gaps that are not intrinsic to the stability of the bony structure.

This brings us again to the current indications

for use, which you have seen previously.

The classification proposal includes several articles, including the clinical use of the preamendment device, and includes the results of a post-marketing clinical study using Wright Medical calcium sulfate pellets.

Dr. Orlee Panitch of the FDA will be presenting detailed information from the submission.

MDR information. There were no MDRs reported for preamendment or currently marketed device.

These are the potential risks to health which have been identified in the classification proposal; again, they include cyst; tumor recurrence; bone fracture; wound complication, as identified; transient hypercalcemia; fracture and/or extrusion of the implant; lack of or incomplete bone growth; and we have added, other, in case there are other risks that you would like to consider adding.

The last overhead just briefly discusses the proposed special controls, but actually, the previous presenter provided a more detailed discussion of those, so I am not going to go into those. They are also in your proposed classification petition.

At this time, I would like to introduce Orlee Panitch, who is going to provide the clinical discussion and

the FDA questions. Thank you very much.

DR. PANITCH: Thank you, and I would like to personally thank Dr. Gitelis for providing such a complete presentation; you have made my job very easy, and it should be rather brief. Again, I will be presenting the clinical data for Osteoset.

I would like to start off with a brief chemistry lesson. This is relevant, because Plaster of Paris, the true name is actually the hemihydrate of calcium sulfate. And this is important, because prior uses of the Plaster of Paris in the literature have used the hemihydrate form, and that, in conjunction with water, when implanted in the body, created an exothermic reaction. That may not be a problem, however, it is unclear how hydrous the form of calcium sulfate was at that point.

As discussed, the present form is gypsum, which is the implanted product, and that is the dihydrate form, and that is what has been provided by Peltier and the literature following.

Just briefly on the experience of Peltier, which really represents the most comprehensive literature on the subject. Most of what he has presented is really case studies of the use of calcium sulfate dihydrate in pellet form, and I have listed the 20 different patients that he

has discussed at length in most of his articles. And you can see the complications that he has had.

There is no specifications of the size of the lesions that he has used and how much calcium sulfate was implanted.

On to the study itself; you have seen all this information, so we will go through it very quickly, and here is the study design.

Again, the inclusion criteria and the exclusion criteria that are presented are identical to the sponsor.

Moving on just quickly, there are 65 patients enrolled, as presented by the sponsor and the brief demographics are presented above. SF-12 information for quality of life was collected on all of those patients; that information was not submitted in this petition.

Radiographic analysis was performed to look at new bone growth and resorption of the Osteoset. That technique was not provided in the petition.

This breaks down the 65 patients as they stood by diagnosis, where the majority are traumatic bone lesions and bone lesions otherwise not specified. Primarily, those were bone cysts.

Here, by location, we have 34 percent being femur and 43 percent being tibia.

If we look at the next slide, you will see pellet resorption and bone growth. I would just like to point out that at one month, the 30-day time point, we have 40 percent resorption here, and we see more complete resorption at the 60-day to 90-day mark.

I apologize for cutting off my Hs here. This is the information that was provided on bone infection. There were four patients, total.

As stated by the sponsor, Osteoset was used in 18 of the 65 patients, with 47 patients having another component mixed with the Osteoset, and they are all listed there, the majority of which being autograft, and demineralized bone. Other was not specified.

I think you have seen this, again, by the petitioner, the USP definition of calcium sulfate.

We can go on to the panel questions now.

Question number one. Have the risks to health for the calcium sulfate bone void filler been adequately characterized? And if not, what additional risks should be described?

Question number two. Does the proposed classification description sufficiently characterize the calcium sulfate bone void filler?

Number three. Have appropriate special controls

been identified to adequately address the risks to health specific to the calcium sulfate bone void filler? And if not, what additional special controls might be necessary?

Question number four. A long one. Most of the recent clinical data provided was based on the use of a combination of calcium sulfate bone void filler and other materials -- autograft, bone marrow, allograft, demineralized bone, and other.

Considering the data provided, what are the appropriate indications for use for this device?

The final question, number five -- Should the indications for use specify a maximum defect size and maximum amount of device to be used, based on the data presented?

I believe that concludes our presentation.

DR. NELSON: Thank you. We will next have a presentation from Dr. Yaszemski, the lead panel reviewer on this topic.

DR. YASZEMSKI: I think that the information presented does make sense from a preclinical and clinical standpoint. I do not think there are any compatibility issues, given the material's long history of use.

I personally have never used the device, but I think that in conjunction with other materials that we call

bone void fillers, it is a reasonable thing to have on the shelf.

The device's clinical and preclinical utility, I think perhaps as expander; that is, to -- an expander to autograft or another bone void filler, because as the study pointed out, it was used alone, only a little less than 30 percent of the time, and the other time was used in addition to another type of grafting device. And so, I think this would probably represent its utility as to expand the volume, when we are otherwise in short supply of the other device that we choose, or the other bone void filler that we choose.

Now, questions about the information. I think that I would like to separate them perhaps into a few areas, and I will just mention them all at once, and perhaps that will serve as a stimulus for discussion.

First with respect to the study. I make note that the study is not done and the endpoint was determined by the petitioners to be six months, and that will not occur until August of 1998.

Of the patients enrolled to date, 6 percent of the cases were infection cases, and none of them were in the spine. I do not think that is a problem; however, I think it bears to repeat that stability in -- I believe it is

somewhat of an oxymoron to call any bone a non-load bearing bone, but we all make decisions about stability when we take care of bone defects, and I think it would be perhaps appropriate to say that the stability -- at the discretion of the surgeon -- will be attained, or maintained, by something other than this device.

I will note that in the study to date, there are no complications and that the number of centers is ten.

I have a question with respect to volume, and I was actually -- the materials I had gotten pre-meeting did not have that question number five on them about, is there a maximum defect size, because with respect to a calcium overload -- it does mention that transient hypercalcemia is a potential concern, but that a maximum of 10 grams of the material would be okay. So, I would ask perhaps as a discussion, when we get to speaking with the petitioners, approximately what volume of a bone defect would 10 grams of the material fill, both alone, and perhaps in conjunction with autograft, and the percentages that it has been used in the study to date.

Secondly, the kit form, I noted, contained 25 grams, and if I said milligrams before, I was incorrect; I meant 10 grams is what I found in the materials presented to me. And so, it stated that a maximum of 10 grams was okay;

the kit contains 25 grams, and might that be okay, also, if the surgeon chooses the kit and makes a specific geometric shape and uses all of the kit and is there evidence to say that the entire 25 grams in one kit would be okay?

My first questions were about the study, the second concerned the volume. The third refers to the kit specifically, and that is, if the material is formulated into a specific geometric shape, what happens to its porosity? Is its porosity similar to that when it is loosely packed, as it is given in pellet forms, and is that porosity -- as it is for other bone void fillers -- perhaps an important concern with respect to the ingrowth of blood vessels and bone?

The fourth category of question refers to the statement that I have heard a few times of others of the generic type. If by others of the generic type, one means, other calcium sulfate dihydrate bone void fillers, then I agree that we should include all those in the discussion. I just was a little concerned that I did not hear that every time, and I want to be certain we do not discuss generic bone void fillers that have some sort of calcium in them, perhaps that are different than the formulation that is given to us here today.

Finally, I heard the word, scaffold, mentioned a

few times, and that there is a study that perhaps suggested that the device functioned as a scaffold, and I did not see any data to show me either laboratory cell culture data, or in vivo studies, how it functioned as a scaffold, and typically, from a tissue engineering perspective, scaffolds function either as a source of anchorage for the anchorage-dependent osteoblasts to express their phenotype. And I am wondering, how does this study --

Does this device serve as a scaffold? Is it osteo-conductive? Does it anchor osteoblasts? Does it serve primarily as a source of calcium when the adjunct -- that is, perhaps the autograft -- serves as the three-dimensional porous scaffold? Is it perhaps a guided tissue regeneration barrier and just performs dead space management until it goes away and blood vessels flow in?

Those are the comments I have, and I think that, though many of those extend beyond the regulatory issue we are being asked to discuss -- and I think with respect to the regulatory issue we are being asked to discuss, I would be comfortable suggesting that this be a class II device, because I think that the controls available are adequate to ensure patient safety at that level.

That is all I have.

MS. NASHMAN: Just a moment before proceeding.

This is Jodi Nashman. Because we have had people leave from the table and there will be various people voting and not voting, I want to just go through the list of who will be voting, who will not, and why.

Dr. Silkaitis and Dr. Holeman will not be voting because they are the industry rep. and consumer rep.

Dr. Lavin will be voting; Dr. Yaszemski will be voting; Dr. STERN and Dr. Hill will be voting. Dr. Nelson will be voting in the case of a tie. Dr. Aboulafia will be voting. Dr. Friedman will be voting and Dr. Besser will be voting.

A waiver has been granted for Dr. Laurencin to participate in all matters before the panel. He has chosen to limit his participation to just the discussion of this matter, and he has decided to recuse himself from the voting.

Agenda Item: Questions and Voting

DR. NELSON: Thank you, Jodi. We will now proceed with the general panel discussion. Does anyone have any comments? Then I will start with Dr. Hill. Do you have any particular comments that you would like to make?

DR. HILL: You mean, in general?

DR. NELSON: In general, yes, Sir.

DR. HILL: No, I do not.

DR. NELSON: Thank you. Dr. Stern, do you?

DR. STERN: Yes. Stern here. I guess I have a question for Dr. Gitelis, so maybe you can help with some of these questions that we are being asked, at least from the petitioner's point of view.

What is the maximum size that you have put in so far? Do you have any sense of what we should be thinking of? And two, a little bit in terms of indications, your study has that trauma was approximately half, and the tibia was also, I think half.

Was the tibia the trauma bone, and is that the situation where -- let me rephrase this, because I am just getting confusing.

Was the trauma cases where you were using adjunctive autograft to help union, more likely?

DR. GITELIS: Let me address the first question, which is the size of the defect. As a tumor surgeon, the defects that I most commonly treat with bone void filler are unicameral bone cysts, aneurysmal bone cysts. The maximum size that I have filled up with Osteoset pellets -- and I believe there were about four vials -- was a unicameral bone cyst of the upper end of humerus with dimensions of about 8 to 10 centimeters in length, and perhaps 4 centimeters in width. So, these are sizeable defects.

Interestingly, when I used them in the hands -- small tumors of the hand -- or large tumors of the humerus or the femur, I have not seen any difference in the repair process, both in terms of the rate of resorption, and in terms of bone repair. So, some of these defects are quite sizeable, and I have not observed a difference in the rate of repair or the effectiveness of repair. Your other question --

DR. STERN: Alright, let me try it another way. As a tumor surgeon, we know that you have used many of these in tumor cases. I am trying to just sort out, are the tumor cases more or less likely, or the same, as the trauma cases, for people to use things like autograft, also? Was the pellets more likely to be used alone with tumors?

DR. GITELIS: Eighteen of these 65 patients had Osteoset or calcium sulfate used alone, as mentioned, 30 percent of them, and the remainder had a mixture of autograft, demineralized bone powder, and other osteo-inductive materials.

I do not know if I can answer the question, how that stratifies between trauma and tumor. I can only explain my personal experience. When I started using this material, I felt compelled to add an osteo-inductive material to the scaffold, and I will address the scaffolding

effect in a moment. But later on, when I heard from my colleagues around the country, they are using -- many of them started using this alone and their results were very satisfactory.

In my most recent cases -- a dozen or so -- I have been using this alone. So I think currently what I believe is if you place this in a highly vascularized bed -- a bed where osteo-inductive materials are locally available, such as a cancellus area of the distal femur -- that you do not need really to add adjunctive materials.

If you put it in an area where the bone is sort of disvascular(?), like in revision hip surgery, a cystic area, there you might want to add an inductive material. But, I think what we are finding, it is sort of at the discretion of the surgeon.

It is a scaffold, and it is an anchorage for osteoblasts. I have been using this in the animal laboratory, doing dog experiments creating cavities in dogs and filling them with Osteoset, or calcium sulfate alone. And what I have found is this material resorbs. It creates microscopic residual. And we have beautiful histological sections which show that the osteoblasts lay themselves right along this microscopic residual; it actually anchors to it and sort of looks upon this microscopic residual as

part of itself. It is well-tolerated with no intervening fibrous membrane or inflammatory cells.

I think you are right; I think it acts as a microscopic anchor to osteoblasts.

DR. STERN: Thank you.

DR. LAVIN: I have a few questions. Could you estimate the number of patients in the country that are using this material, like say in 1997 or 1996?

DR. GITELIS: Dr. Parr is answering that. Over 5,000 patients have received this material.

DR. LAVIN: Another question. Is there ever any evidence of, say, elevated calcium levels in any of those patients, after they have had the material installed -- you know, placed?

DR. GITELIS: To my knowledge, there are no --

MS. NASHMAN: Excuse me. Excuse me. If you could state your name for the record each time you speak.

DR. GITELIS: I am sorry. Gitelis. To my knowledge, there is no clinical evidence of hypercalcemia that has been reported to us. In my personal use, again, at the initial -- when I started using this material, I actually measured serum calciums on a couple of days post-op and did not observe any spikes in the serum calcium levels. But I cannot speak for the other 5,000 patients.

DR. LAVIN: Would there ever be any reason to not have the product be used in a patient, say, who was on dialysis, sometimes their levels go out of control -- calcium.

MR. REITZLER: Steve Reitzler. I should mention at this point that the product is contraindicated in patients who are hypercalcemic.

DR. NELSON: Dr. Yaszemski. I did not mean to skip you. Did you have any specific questions you wanted to get answered right now?

DR. YASZEMSKI: Of the categories I was going to ask, Dr. Gitelis asked the one question I was going to speak, so it was a good segway into Dr. Lavin.

DR. NELSON: Good. Dr. Holeman, do you have any questions?

DR. HOLEMAN: No questions.

DR. SILKAITIS: No, no questions.

DR. NELSON: This is Dr. Nelson coming around the table. Dr. Aboulafia.

DR. ABOULAFIA: I do have a couple of quick questions for Dr. Gitelis. People have referred to a number of times -- and some of these have been touched on by Drs. Yaszemski and Lavin -- of small transient elevation in calcium. You said you did not see anything at three to four

or five days follow-up.

When is the small transient elevation in calcium? Who noticed it? Where was it observed? Was it with all patients who were checked within their first early -- in other words, I do not have an understanding of what small transient elevation entails here in this. And those are your words.

MR. REITZLER: True. Steve Reitzler. Alright, I will pass it down.

DR. PARR: Calcium spike post-implantation --

MS. NASHMAN: Excuse me. Excuse me --

DR. PARR: Jack Parr from Wright Medical. The calcium spike that was observed and reported in the literature was by Dr. Peltier in an animal study. He went back and studied his own clinical human patients, and did not find any. So, it was raised only as an observation, and, you know, a potential concern, not a real clinical concern at this point.

We have no further -- or no indication -- of it actually happening in clinical patients.

DR. ABOULAFIA: Although, has it been tested, because if you do not look for it, it does not -- you do not find it. It has been tested, is my question.

DR. PARR: Parr. Yes. It has been.

DR. ABOULAFIA: Okay. And in the tests that you have done, have you noticed that it is or is not related to volume; i.e., a serum calcium level might be transiently -- and small elevation in calcium may appear more likely in someone who has a large volume of Osteoset implanted versus a small volume of Osteoset implanted?

DR. PARR: The patients that were measured had a relatively high --

MS. NASHMAN: Excuse me --

DR. PARR: Parr from Wright Medical. The patients who were measured I think had a relatively -- what we would call, a large volume.

DR. ABOULAFIA: Dr. Gitelis, specifically for you. In any of the patients in whom you have implanted it, have you used any physical adjuvants? Obviously, I am referring to tumor cases. And if so, are there any relative contraindications in the setting of physical adjuvants?

DR. GITELIS: Since the vast majority of the tumors that I use this in include aneurysmal bone cysts and unicameral bone cysts, I do not routinely use physical adjuvants; i.e., liquid nitrogen or phenol, in those types of tumors. So, the answer to your question is, no, I have not used it in conjunction with cytotoxic physical adjuvants.

DR. ABOULAFIA: No further questions. Thank you.

DR. NELSON: Thank you. Dr. Laurencin.

DR. LAURENCIN: Yes. I have looked at the Osteoset material with great interest and I think it has great potential. The question I have is the histology of the material. It is interesting that there are over 100 studies, as you have mentioned, on the material, and about - - it is sort of unprecedented that over 90 percent of the studies, or 95 percent of the studies, are all implantation studies in humans, and they all talk about clinical results, whereas there are very few studies that have actually looked at histology of these materials.

Peltier's study that -- in dogs -- talks about putting an implant in and found that in half the cases, he decided there was no bone regeneration that occurred, and in one quarter of the cases, partial regeneration occurred.

Have there been any published studies looking -- examining the histology with maybe histomorphometry or anything of that sort? In other words, it mentioned here that there was histology done in different laboratories, like we have seen slides here. What is the histology like?

When I sort of looked at the literature and looked at, you know, why this material has been around for 100 years, but now it is sort of been rediscovered and

implanted. The question came up of what the quality of the bone formation that is present, and what the quality of the bone that is being produced, in terms of this material. And again, I think that all may reflect on the fact that in the literature there are very few papers that are actually -- that really have been, you know, very detailed analyses of the histology. Can anyone comment on that?

DR. GITELIS: Gitelis from Rush. I have been looking in the laboratory for ten years at calcium sulfate, and we have done numerous experiments with calcium sulfate, and looked at the histology. I wish I had the time. I was prepared to show histology here today.

What we see histologically with calcium sulfate is, we autopsy the animals at six weeks. By six weeks, what you see in the gap that we surgically created is simply a microscopic residual of calcium sulfate. And laying on this microscopic residual, is woven bone; healthy, osteoblastic bone formation, without adverse reactions such as foreign body, giant cells, fibrous membranes, inflammatory cells. So, we have studied it at quite length in the laboratory.

DR. LAURENCIN: What is the gap model that you used for this?

DR. GITELIS: The answer is, we use the dog humerus, and we create -- we surgically create a cylindrical

defect in the upper end of the humerus that measures 1.2 centimeters in diameter, and 5 centimeters in length, and then that cavity is filled up with these small calcium sulfate pellets.

DR. LAURENCIN: It is a unicortical --

DR. GITELIS: No, this is an intramedullary cancellus defect. It is in the metaphysis of the upper end of the humerus, where we drill a 1.2 by 5 centimeter hole in the humerus.

DR. LAURENCIN: Have any studies been taken to the point that you see mature bone being formed? You say you -- at six weeks, you find woven bone, but does that -- has it been taken out to the point where you can actually see mature remodeled bone?

DR. GITELIS: It is taken out to six weeks, so the type of bone repair that we are seeing at six weeks is what we would like to see, which is that the gap is filled from side to side and end to end, with a cellular bone formation.

We have not taken it to the point where we have seen remodeling of the bone due to stress transfer, if that is what you are asking. We have only studied these animals early on in the repair process.

DR. NELSON: Thank you. Dr. Friedman.

DR. FRIEDMAN: No questions.

DR. NELSON: Very good. Going on to Dr. Besser.

DR. BESSER: One question. I believe it was -- I am not sure who was speaking at the time. It was said that they had used up to four vials, and if I recall correctly, the vials were 25 grams each?

DR. YASZEMSKI: I will ask the petitioners to say, but I think the kit was 25 grams each, I am not sure of the vials, I --

DR. BESSER: How much is a vial, in grams?

DR. GITELIS: They are either 10 gram vials or 20 gram vials. I routinely use 10 gram vials. They are packaged differently.

DR. BESSER: So you use up to 40 grams?

DR. GITELIS: I have used up to 40 grams, yes.

DR. BESSER: Okay, then I will direct the question to Dr. Yaszemski. There was something you said that there was a limit of up to 10 grams was recommended?

DR. YASZEMSKI: In the materials that I reviewed, there was a statement that transient hypercalcemia could be a problem, and that 10 grams was safe; it did not state whether more grams were safe or whether there were problems shown after 10 grams. Okay, one of the --

DR. NELSON: Well, I would like to recognize Dr. Parr who wants to respond.

DR. PARR: At least one of the cases reported by Dr. Peltier reported using 1500 pellets in a defect in a patient. That was in a spinal pelvis lesion. And was successfully treated with that.

We have had -- and granted it is anecdotal -- what we are gathering is a lot of information from clinical cases as we get the information. There are many cases where large volumes -- up to 80 ccs -- have been treated in femurs, and proximal tibia, without adverse reaction, either hypercalcemia or any other reaction that has been -- and people had been looking for it.

That would be -- we are trying to do this relatively controlled without making claims that are unreasonable.

DR. BESSER: No one has done any maximum-tolerated dose kind of study to see how much of this you can implant before you end up with these transient problems, is that correct?

DR. PARR: No, there is not -- No, not that I am aware of. There has not been any sort of maximized dose put in. I am not exactly sure how you do it, but I would be willing to discuss that.

DR. NELSON: Dr. Besser, do you have any further questions?

DR. BESSER: No, no further questions.

DR. NELSON: I would like to ask two questions, and I will take any of our presenters. You had said that your products have been used with, quote, other bone graft materials and agents. That is rather unspecific and I noticed when the FDA did their indications, they did not include even an indication using it with bone graft.

I think we need to get this clarified, because we are going to have to do indications in a little while. Do you feel that there should be indications say, using it with anything else? Would you like to see the product with that as an indication?

DR. GITELIS: I would like that to be the surgeon's discretion. A surgeon is in the best position to judge the likelihood of bone healing by the defect that they are dealing with. And I would like the surgeon to look at a defect and say, oh, gee, this is a very sclerotic hole with a poor blood supply, not a lot of cancellus bone around it; oh, in that situation, I should use it as a scaffold, combined with some other form of osteo-inductive material. But on the other side, is a young child with a thick periosteum who all you need in that situation is a scaffold -- and I would like it to be at the surgeon's discretion, myself.

DR. NELSON: It will certainly be at the surgeon's discretion. I am simply saying, would you like to include on that any indications, or are you happy with the way the FDA has it phrased, currently? Because when you did your presentation, you had said, it should be used not only by itself, but with other bone graft materials, and other agents.

DR. GITELIS: Yes, I am happy with the way it is written.

DR. NELSON: Thank you. Do any of the other panel members have any questions? Dr. Friedman, you look like you wanted to ask a question. Very good.

I think we can proceed then to a panel discussion, directly aimed at the FDA questions. And question number one would be: Have the risks to health for the calcium sulfate bone void filler been adequately characterized? And if not, what additional risks should be described?

Actually, Dr. Yaszemski, can you start, please?

DR. YASZEMSKI: I think the risks have been adequately characterized.

DR. NELSON: Thank you. We are going to Dr. Lavin.

DR. LAVIN: I would agree.

DR. NELSON: Thank you, Dr. Lavin. Dr. Holeman.

DR. HOLEMAN: I would think that they have been identified, but I would have some reservation, based on some of the concerns that were raised around the table.

DR. NELSON: Thank you. Dr. Silkaitis.

DR. SILKAITIS: I agree that the risks have been identified.

DR. NELSON: Thank you. Coming around, Dr. Aboulafia.

DR. ABOULAFIA: I think there probably is not a substantial risk to transient elevation -- or to hypercalcemia, but it is something that has been introduced by the manufacturer, and it would be, I think, irresponsible for me to ignore it completely. Other than that, yes.

DR. NELSON: Thank you. Dr. Laurencin.

DR. LAURENCIN: Yes.

DR. NELSON: Thank you. Dr. Friedman.

DR. FRIEDMAN: Yes, the risks have been adequately characterized.

DR. NELSON: Dr. Besser.

DR. BESSER: Yes.

DR. NELSON: Thank you. We will go on. I like this -- oh, excuse me, Dr. Hill.

DR. HILL: Yes.

DR. NELSON: I apologize, Dr. Stern.

DR. STERN: Yes.

DR. NELSON: Thank you. I will try not to ignore you the next time. Panel question number two. Does the proposed classification description sufficiently characterize the calcium sulfate bone void filler? Dr. Hill, I will start with you to apologize for skipping you.

DR. BESSER: Can we have the proposed classification up on the wall instead of the question?

DR. STERN: This is the one thing I have a question on. I believe the description as in the petition has been changed by the FDA. So, we are voting now on the - - that is my question. We are voting on the FDA one, not the petition anymore? That is I guess a question to the FDA.

DR. NELSON: Thank you. This is Dr. Nelson and I am going to ask Mr. Dillard.

DR. WITTEN: This is Dr. Witten. This is what we proposed, but you can comment on it and modify it, and propose an appropriate classification description.

DR. NELSON: Again, I think what we are doing is, we are going to ask the question they have asked us. So, Dr. Stern, do you have a question? Well, are you happy with that?

DR. STERN: I am happy with that, yes. It is just

different than what the petition is.

DR. NELSON: I recognize that. Thank you. Dr. Yaszemski.

DR. YASZEMSKI: Yes.

DR. NELSON: Thank you. Dr. Lavin.

DR. LAVIN: Yes.

DR. HOLEMAN: Dr. Holeman. Yes.

DR. ABOULAFIA: Aboulafia. Yes.

DR. SILKAITIS: Could I have the manufacturer's petition's description?

DR. NELSON: Dr. Silkaitis, Dr. Stern can show you a copy.

DR. SILKAITIS: What is the difference?

DR. LAURENCIN(?): Steve, what is the difference?

DR. STERN: I think that the biggest difference is that the manufacturer's petition talks about at least 95 percent calcium sulfate, and that number has been removed, and actually, maybe we should ask someone from Wright Medical if they think that is an important thing that has been changed.

DR. NELSON: Thank you. I will entertain an answer from our commercial sponsors.

MR. REITZLER: What I believe the agency has done by, if you wish, simplifying the indications for -- are we

looking at indications for use? I am sorry, I have the wrong slide up -- the proposed classification was, by simplifying it, they are allowing their own review staff to use their expertise to make a determination of substantial equivalence if any new product does come before the review group.

I believe, as was mentioned in the agency's presentation, they are not ignoring conformance to USP monograph, and some of the other features of the description that we proposed, but rather are suggesting that they may be more appropriately referred to as special controls.

DR. NELSON: Thank you. Dr. Silkaitis.

DR. SILKAITIS: Yes, I agree.

DR. NELSON: Thank you. Coming across the table, Dr. Aboulafia, you have already voted, correct?

DR. ABOULAFIA: -- true.

DR. NELSON: Good. In the interest of time, I think you can immediately defer to the person next to you and we will go on up the table.

DR. LAURENCIN: Dr. Laurencin. Yes.

DR. FRIEDMAN: Dr. Friedman. Yes.

DR. BESSER: Dr. Besser. Yes.

DR. HILL: Dr. Hill. Yes.

DR. NELSON: Thank you. Going to panel question

three. Have appropriate special controls been identified to adequately address the risks to health specific to the calcium sulfate bone void filler? If not, what additional special controls might be necessary? I would like to start with Dr. Besser.

DR. BESSER: Sufficient -- appropriate special controls have been identified.

DR. NELSON: Thank you.

DR. FRIEDMAN: Yes.

DR. LAURENCIN: I suggest the possibility of -- and the question of whether calcium levels should be measured in patients who are placed on -- have Osteoset implanted, just as with different drugs that show increased LFTs, there is indication for monitoring the LFT levels.

DR. NELSON: Thank you. I think we can probably address that as a special control that could be at the -- well, we can deal with it at that time. One possibility, of course, is to let the FDA design exactly what special control they would like to fulfil to be able to answer that question.

To move on --

DR. ABOULAFIA: Agree with Dr. Laurencin.

DR. SILKAITIS: In terms of the elevated calcemia, could that be a package insert suggestion in handling it

that way, as a control, as an instruction to the surgeon that they may want to monitor this, if they --

DR. NELSON: If I could answer that. I think that that is more rigorous than we need, because we do not yet know that it needs to be done at all. So there might be as a special control, as a clinical follow-up.

I will come back to you, Dr. Friedman. Dr. Holeman.

DR. HOLEMAN: I will pass.

DR. LAVIN: Lavin. Yes.

DR. YASZEMSKI: Yaszemski. Yes.

DR. STERN: Stern. Yes and I think that the contraindications for hypercalcemia may well be enough.

DR. HILL: Hill. Yes.

DR. NELSON: Thank you. Dr. Friedman, then.

DR. FRIEDMAN: I just want to have the sponsors clarify something. In your study where you have completed any clinical cases to date, have you had a single case of hypercalcemia occur?

DR. GITELIS: In the patients that I have studied, no. In the other patients in the series, I frankly do not know.

DR. FRIEDMAN: To the best of the sponsor's knowledge, have you had a single case of hypercalcemia?

DR. GITELIS: I have been told -- here, I will let Dr. Parr --

DR. PARR: Jack Parr, Wright Medical. No.

DR. FRIEDMAN: Right. And in the study that you ran, though, you did look for it, is that correct?

DR. PARR: Yes.

DR. FRIEDMAN: Thank you.

DR. NELSON: Thank you very much. I think that is panel question four. Going to panel question number five. Should the -- excuse me. Now, we are going to start four, then.

Most of the recent clinical data provided was based on the use of a combination of calcium sulfate bone void filler and other materials, such as autograft, bone marrow, allograft, demineralized bone, and other.

Considering the data provided, what are the appropriate indications for the use of this device? I would like to start with Dr. Yaszemski.

DR. YASZEMSKI: I think the indications would be as a bone void filler to be used at the discretion of the surgeon with or without adjunct fillers, when -- it -- the Osteoset -- is not providing the structural stability to the part of the skeleton it is placed in.

DR. NELSON: Thank you. Dr. Stern.

DR. STERN: I agree. Nothing more to add.

DR. HILL(?): I have nothing more to add.

DR. BESSER: Nothing to add.

DR. FRIEDMAN: I think the statement is a little bit misleading, because 30 percent was used by itself, that is a small number, that is still one in four to one in three. And I agree with what has been said.

DR. LAURENCIN: Nothing to add.

DR. ABOULAFIA: I agree. Nothing to add.

DR. SILKAITIS: I agree with Dr. Yaszemski.

DR. HOLEMAN: Nothing to add.

DR. LAVIN: The only question I have is, of those 5,000 subjects who were treated in the past year, what proportion would you estimate were treated in combination with something else?

DR. PARR: Jack Parr, Wright. We do not know the answer to that, to be honest, we would probably have to speculate. But we know some have been doing it, using the product without other adjuncts, because they are the ones that communicated with Dr. Gitelis about their good results, that convinced him that he probably could switch.

DR. LAVIN: If you said that, say, at least 2,000 or 3,000 of them would, it probably would help our opinion.

DR. PARR: Only if I knew that there were 2,000 or

3,000.

DR. NELSON: Thank you. I would like to proceed then to panel question number five. Should the indications for use specify a maximum defect size and maximum amount of device to be used, based on the data presented?

I believe, Dr. Yaszemski, you had first raised that question. I would like you to answer that first, for the rest of us.

DR. YASZEMSKI: I do not think so, because I have heard anecdotally -- Dr. Gitelis said he has used perhaps 80 grams at once, and I think that, with the control in place to perhaps have hypocalcemia as a contraindication, and perhaps -- perhaps sometimes to check calcium levels. Perhaps if more than a certain amount is used, more than -- we have heard up to 80. We hear, typically, 10 to 40.

If there is some level that we would consider, gee, this is an outlier, maybe just saying, those patients, it might be nice to check their calcium level. And I am real soft on that. I am tending to think that is not even probably necessary.

DR. NELSON: I think you are going to have to follow that up, though, with a little something. You are either going to have to give us a threshold level of what you want to do that, or simply not add that --

DR. YASZEMSKI: With no data in mind, I would perhaps say, if someone put more than 100 grams in, we should check calcium levels.

DR. STERN: There is basically no data, so that there is nothing -- the indications for use should not -- based on the data presented, the answer would be no, although I think that there, we should leave the FDA some reasonable latitude to make appropriate distinctions.

DR. NELSON: Thank you. So, you are thinking that the FDA may have a -- clinical data that they request. From the sponsor.

DR. STERN: Yes.

DR. NELSON: Thank you. Dr. Hill.

DR. HILL: I do not think any -- I think it would be picked up by special controls, so I do not think there is anything that needs to be specified.

DR. NELSON: Thank you. Dr. Besser.

DR. BESSER: I never thought I would be saying this, but I think this should be left to the discretion of the surgeon. I do not think anyone is going to start shoveling this stuff in there with wild abandon, and there is no evidence that suggests there is a maximum amount of the device to be used after which it becomes dangerous, so, no.

DR. NELSON: Thank you. Dr. Friedman.

DR. FRIEDMAN: I would agree you should not specify a maximum size, you should not specify a maximum amount; leave that up to the surgeon. I, however, think if you want to put a statement in there saying that, with larger amounts, you should be concerned or just aware of the possibility, but I would not put an amount. Picking 100 or I could pick 80 or 40, there is no basis behind any of it.

If you wanted to say something, just keep it vague and that, if you are going to use large amounts, just keep that in mind.

DR. NELSON: Dr. Friedman, do you think then that if the FDA, after an approval on what was being used, did some patients where they checked some calcium levels and found that it never got elevated, then we would not have to do that?

DR. FRIEDMAN: I agree. I think that would be fine.

DR. NELSON: Thank you, to Dr. Laurencin.

DR. LAURENCIN: I agree with Dr. Friedman.

DR. ABOULAFIA: I agree with Friedman.

DR. SILKAITIS: I apologize, Dr. Yaszemski, that I mispronounced your name last time, but, yes, I do agree with you, but I do want to ask FDA to take into consideration

that there are other bone void fillers and that there be as uniform labeling as possible. And in consideration of volumes and other things like that.

DR. NELSON: Thank you. Dr. Holeman.

DR. HOLEMAN: I am going to leave that to medical advice.

DR. NELSON: Thank you. Dr. Lavin.

DR. LAVIN: I would agree with Ray.

DR. NELSON: Thank you. I think -- am I correct in summarizing, then, the feeling of the group, that we can not include a 100 gram amount --

DR. YASZEMSKI: I withdraw that, based on subsequent discussion.

DR. NELSON: Thank you very much. That will make it easier when we go to the supplemental data sheet.

The next panel question -- I have two more pages of panel questions, but -- they are thrown out. Very good.

I believe, then, we can start now on the worksheet. I have the general device classification questionnaire in front of me. The generic type. We have the classification recommendation. I am getting the feeling from the group that that they feel that a class II recommendation would be appropriate. If anyone disagrees with that, could they please speak up? Thank you. Hearing

nothing, question one.

Is the device life-sustaining or life-supporting? I believe it is no. I tell you what, I will move along here, and if someone objects, please speak up and I will be glad to recognize you.

Question two. Is the device for a use which is of substantial importance in preventing impairment of human health? Yes.

MS. NASHMAN: Okay, hold on just one second. For that one question, the sponsor answered that question as no. So, I would like the panel to decide if they either agree with the writer of the proposal, or if they would like to change that to yes.

DR. NELSON: We will go around the room. I believe that was -- when I heard it said, I recognized that, but I thought they did not quite intend what they were saying. So -- I am not going to poll everybody. We will just pause for a moment. Does anybody feel that this really should be answered no? That would be in distinction to what we have been doing previously.

PANELIST: What question was that, again?

MS. NASHMAN: This is question two on the classification questionnaire. Going either route, using either the petitioner's manner of working through the sheet,

which answers the first one is no; the second one is no; the third one then becomes no; the fourth one becomes no -- you can still end up with a class II, it is just the path that you choose to take. Basically, we are going to end up with class II as we vote, it is just up to you right now to look at the two paths that you can take to get to class II.

I do not think it is a very pressing point, but just please quickly decide.

DR. NELSON: So, we will go around the room. Dr. Hill, just saying that we have been previously been answering this yes. Would you like to -- on the previous devices. Would you like to do this as yes?

DR. HILL: And this is question number two.

DR. NELSON: Correct, Sir.

DR. HILL: I do not think -- in this instance I think I can put no.

DR. NELSON: Thank you. Dr. Stern?

DR. STERN: Let's do it the way the petitioner wants, so, no.

DR. YASZEMSKI: Agree with the petitioner.

DR. LAVIN: Agree.

DR. ABOULAFIA: Yes.

DR. NELSON: I believe it is Dr. Friedman.

DR. FRIEDMAN: No.

DR. NELSON: And Dr. Besser.

DR. BESSER: No.

DR. NELSON: Thank you. Question three. Does the device present a potential unreasonable risk of illness or injury? I have answered that no.

If you answer yes to any of the above. If no, go to item five.

Item five. Is there sufficient information to determine the general controls are sufficient to provide reasonable assurance of safety and effectiveness? Yes.

[Several responded in the negative.]

MS. NASHMAN: No, no, no, no.

PANELIST: General controls are safety --

DR. NELSON: Thank you very much. No. Now we are at question six. Is there sufficient information to establish special controls?

[Several responded in the affirmative.]

Thank you. Now we have to go to seven.

Is there sufficient information to establish special controls, etcetera? The only thing that I thought was -- in listening to people discuss, would be testing guidelines. Did anyone feel that we needed anything further? You need postmarket surveillance --

DR. BESSER: Clarification. Where does ASTM

standards and that sort of -- is that testing guidelines or is that performance standards?

DR. NELSON: Jodi Nashman is shaking her head, yes. Testing guidelines.

DR. BESSER: Yes, but behind you, she is shaking her head and saying, performance standards.

MS. ROONEY: The voluntary standards we have identified thus far have been under performance.

DR. NELSON: And the ASTM are the voluntary standards?

MS. ROONEY: Yes, performance.

DR. NELSON: Therefore, I think what we have to do, then, is answer yes to performance standards, based on that.

PANELIST: Dr. Witten, is that correct?

MR. REITZLER: Excuse me. Steve Reitzler. Performance standards, within the meaning of the law, are somewhat different. Those are mandatory, and they have to be established -- we are talking about voluntary standards to control the device performance.

Performance standards, capital P, is a whole different dish.

MS. ROONEY: Lisa Rooney, FDA. Under performance standards we have adopted both the mandatory, under Section

514, as well as voluntary, national and international type of standards.

DR. NELSON: Thank you. So, do we feel --

DR. PARR: Jack Parr, as a --

DR. NELSON: Tell you what, actually, I do not feel inclined to recognize you. I think we feel that we would like to have a performance standard. I am sorry, Jack.

There is testing guidelines we felt we wanted and a performance standard that we wanted. The question has been raised previously about the question of calcium levels. Did anyone feel that a postmarket surveillance of five cases, in looking at calcium levels for something like this, is what they wanted? If they wanted that, please speak affirmatively now.

DR. ABOULAFIA: I did, and I would be willing to accept it in an incredibly limited status, because it is not clear to me -- even though the question was answered -- that they did look at it; that they looked at it in any kind of a controlled way.

The only thing I understood was that Dr. Gitelis got it on some of his post-op patients, some who came back at three days, maybe some came back at five days. Even if it was one serum calcium within 24 hours -- I mean, I am not

asking for a lot, I promise. I really want a little. And I want the FDA to understand that.

DR. NELSON: I think you have made your point quite clear. Does anyone object to Dr. Aboulafia's suggestion? Hearing no objection, we will check off that box, and the FDA knows our intention.

DR. NELSON: Yes, Dr. Witten.

DR. WITTEN: Before you move on, I just want to make sure that I understand clearly when you recommend performance standards, or you are checking the box, are you referring to the voluntary performance standards, or mandatory FDA performance standards; as Lisa Rooney said, there were two. That could encompass either of those two options, and I guess we want to make sure we have a clear idea of what performance standards you are recommending as special controls.

DR. NELSON: Dr. Friedman, you would like to answer that.

DR. FRIEDMAN: May I make a suggestion? I think we are talking about the voluntary standards, and if right now we are not sure if that belongs in performance standard testing guidelines, why don't we just check other and put the voluntary down, and let the FDA make sure it is in the right column in terms of legal aspects.

We do not want to box them into something we did not mean to do.

DR. NELSON: I believe you are also referring to that, in the petition, they mentioned a bunch of standards that they felt they could use to identify their substance, and you are not asking for anything beyond that. Am I correct, Dr. Friedman?

DR. FRIEDMAN: That is correct.

DR. NELSON: Thank you very much. Going to number six. Excuse me -- I cannot read.

PANELIST: So we are at like 11.

DR. NELSON: We skipped 8, we are on 11, and we are on a roll. Is there otherwise -- or can there otherwise be a reasonable assurance of its safety and effectiveness without restricting on its sale distribution or use because of potential -- etcetera -- in the past we have answered that, yes.

PANELIST: You have answered it no in --
[simultaneous discussion]

PANELIST: That is a no.

DR. NELSON: No, then prescriptions. Thank you, Nashperson. And that was 11b.

We are now going to the supplemental data sheet. Is it an implant? Yes.

Indications. As in petition.

DR. BESSER: I think we voted for the FDA in the -
- no, I am sorry -- indications, I believe we accepted.

DR. NELSON: Thank you. The difference between
the two was that the petitioner had some figures at 95 and
98 percent with -- [simultaneous discussion]

DR. STERN: That has nothing to do with
indications. That was a description. That was not
indications. That was the description --

DR. NELSON: Okay. Dr. Stern, I will recognize
you. Do you want to recommend an answer to four, then? The
indications for use.

DR. STERN: I would -- I think we did discuss
that, basically accepting the petitioner's request. It
says, void filler in a non-weight-bearing status.

DR. ABOULAFIA: The question, in infected and
uninfected sites?

DR. NELSON: I got the feeling from discussions
that no one had any problem with that indication, so I will
take that as a yes.

I first answered number for as in the petition, we
agree with that. We are going to number five.
Identification of any risks to health presented by the
device. And I put down here, as in petition. Is there any

objection to that?

Jodi Nashman is saying this is a proposal not a petition. Thank you.

Specific hazards to health were none.

Characteristics or features associated with hazard were none.

Number six. Advisory classification.

Classification II.

Number seven. If device is an implant, etcetera, explain fully the reasons for lowering classification -- actually, we are not lowering, we are classifying it -- and I think our answer could be, we felt it was safe and effective as in petition.

Number eight. Summary of information including clinical experience upon which recommendation is based. I think easily we can answer to number eight, not only is this preamendment, but it is pre-century.

Identification of any needed restrictions on the use of the device, I think as in petition. It would seem that we did not develop a consensus saying we wanted to limit the size of the defects, or the grams.

DR. ABOULAFIA: I have one question. Could we change that to impaired calcium metabolism instead of hypercalcemia, which would encompass someone who was normal

calcemic today, who has renal failure, for example.

DR. NELSON: I think I would like --

DR. ABOULAFIA: -- or not necessary.

DR. NELSON: I would like to defer, I think, that nuance of hypercalcemia, or abnormal calcium, to the FDA when they are doing the limited clinical study that you want. Dr. Friedman.

DR. FRIEDMAN: Just to clarify. Is it already a contraindication, hypercalcemia? Then that is already in there. We do not have to deal with it.

DR. NELSON: Thank you. Am I correct saying we are on 11? Are existing standards applicable to the device, etcetera? And I believe the answer was yes.

We have then filled out both the classification and the supplemental data sheets, and I believe we are ready to move to a vote to accept this petition --

DR. ABOULAFIA: I will make a motion to accept the proposal.

DR. NELSON: Do I hear a second?

DR. YASZEMSKI: Second.

DR. NELSON: Thank you very much. Therefore, I am not going to read the entire thing because I think we have a strong consensus on this document. Is there any discussion before we vote? Seeing no discussion, I would like to start

with Dr. Hill.

DR. HILL: Dr. Hill. My vote is yes.

DR. STERN: Dr. Stern. Yes.

DR. YASZEMSKI: Yaszemski. Yes.

DR. LAVIN: Lavin. Yes.

DR. ABOULAFIA: Aboulafia. Yes.

DR. FRIEDMAN: Friedman. Yes.

DR. BESSER: Besser. Yes.

DR. NELSON: Thank you. There is no need for me to break a tie. I think that is it. Do you have anything that you need to tidy up with, Ms. Nashperson?

MS. NASHMAN: I know you are all on your way out. I just wanted to take a quick opportunity to thank you all. Leave your material here and we will have it taken care of. Thanks again.

DR. WITTEN: I would like to add my thanks and those of the division for your work today.

DR. NELSON: Thank you very much. We have made it in time for everyone to make their planes. I appreciate all the time you have done. Thank you to the sponsors for coming. And also, just recognizing this is Jodi Nashman's last one, I think the panel members might want to just give her a round of applause.

[Applause]

[Whereupon, at 5:10 p.m., the meeting was
concluded.]