Please comment on the following: (1) Whether there is the need for a post-approval study in the U.S. patient population; (2) If a post-approval study is recommended, please discuss the following: the objectives; clinical endpoints, including the need to assess the risk of severe acute inflammatory reaction; study size; comparison group; duration of follow-up of study subjects; and other specific issues that you may like to be addressed in PAS.

DR. MABREY: So I'll remind the Panel that this is not a vote for approval or disapproval and the mere fact that we're considering a post-approval study does not mean that approval is a forgone conclusion. However, having sat on this Panel for several years now, this process has evolved to this point and we found that it makes it -- it's a lot more efficient, a little bit cleaner, if we consider these factors ahead of the final vote.

So Dr. Skinner, I'll go with you. And remember that we're really answering two questions: Number 1, do you think a post-approval study would be necessary if the device were approved, and if so, what would you want included in the study?

DR. SKINNER: Well, I've sat on these

panels for a number of years myself, and I've seen wild, extravagant requests for post-approval studies at various times. And in general, I think that many of these things, while well intended, are not particular useful. So I would not recommend anything in the way of a post-approval study. Having said that, the company may be interested in finding out how this particular material works in Hispanics, blacks and people with high BMIs.

DR. MABREY: Thank you. Dr. Blumenstein?

DR. BLUMENSTEIN: I concur.

DR. MABREY: Okay. Ms. Rue?

MS. RUE: I agree.

MS. GEORGE: I agree.

DR. MABREY: You guys are too easy. Dr. Evans?

DR. EVANS: I guess, me being a researcher, I'd like to see such studies. I guess, given some of the conversations that took place today, I'm particularly concerned about the BMI issue. I also wonder -- perhaps this doesn't apply, but I wonder if supportive care is different enough here that it could influence outcome differently than what happens in Europe. And if so, then they may want to consider those issues, looking at, you know, people with

higher BMI and in U.S. settings.

And also, given some of the earlier comments from Dr. Blumenstein about sort of comparing how does this sort of single-injection strategy work, say, versus the three-injection strategy and maybe even a direct comparison might be worth thinking about, to get some idea about if there's any differences between them.

DR. MABREY: Thank you. Dr. Goodman?

DR. GOODMAN: I concur with Dr. Skinner's comments.

DR. MABREY: Thank you. And Dr. Olsen?

DR. OLSEN: I would think that given the, in some aspects, the -- of data, that more data would be better, and so I would lean towards saying that there should be a post-approval study in the U.S. patient population, again remembering that all these kinds of trials still study kind of a selected group of individuals who qualify for trials, not necessarily everybody out there, but that such a trial should aim to try to reflect the epidemiology of osteoarthritis in this country, in terms of racial, size -- racial composition, body size, and some of those other aspects.

And I don't know about study size, but it

would be nice because of some of these other questions we've asked, if it were big enough to do some subset analyses in terms of -- maybe BMI doesn't even matter and that could be dispensed with forever, for example. Subset analyses for Hispanics, which is a growing population where we really don't have much information about whether any of these things work, and it would help us target the agent to the person most likely to benefit, and it might help the Sponsor know exactly how to apply this drug in the future. So I would be in favor of that.

DR. MABREY: Mr. Melkerson, the Panel believes that if a post-approval study were necessary, that they would want it to address certain issues, such as effect of ethnicity and body mass index on the overall effectiveness of the device, and that perhaps the sample size be large enough to allow for subset analysis of that data. Is that appropriate for the FDA?

MR. MELKERSON: Yes, thank you.

DR. MABREY: Thank you. And I'll just add the influence of supportive care as well. Dr. Evans brought that up. I think that's a very good point. Okay. And I'd like to thank the Panel for taking us through this process efficiently.

We will now proceed with the Second Open Public Hearing of this meeting. Is Mr. Don Boller in the room? Don Boller? Boller? Okay. If so, please come forward to the podium.

(No response.)

DR. MABREY: Not seeing any hands, Dr. Leadbetter, are you present? Great. Would you like to approach the podium and address the Panel?

DR. LEADBETTER: Thank you, Mr. Chairman and members of the Panel. My name is Wayne B. Leadbetter. I'm a practicing orthopedic surgeon, and I've been practicing for 32 years. I am presently on the full-time faculty at the Rubin Institute for Advanced Orthopedics in Sinai Hospital, Baltimore, where I work in the Center for Joint Preservation and Replacement.

I've had a specialty that has concentrated on total joint replacement as well as joint salvage, for the last 15 or 20 years. I have published and edited in the area of joint inflammation as well as tendinopathy and edited two books, one on sports-inducted inflammation, with the Academy of Orthopedic Surgeons, and one on tendinopathy.

I come to you today both as a patient as well as a practitioner on the front lines, if you

will, very much, I suspect, like Dr. Goldman -- Goodman, rather. As patient and a member of the public, my first emotion here today is to thank the Panel and all that participated in this presentation and proceedings for the diligence which I witnessed today in trying to come to the best truth and evidence-based decision. It's very assuring to me, as a patient, that this process really does seem to work. I can also say that my wife has enjoyed the benefits of viscosupplementation, and she has been afflicted with arthritis of her knees at a young age, in her 50s and, as such, has delayed surgical intervention successfully with that approach. So I speak with some familiarity with viscosupplementation on a personal basis.

As a clinician, I would like to come here to represent, again, my patients and what I think is the best care for them, that we keep open the multi-modal, if you will, approach to nonoperative management of osteoarthritis, recognizing that it's not a curable condition as has been mentioned in presentations today.

And the fact that while I agree with Dr. Goodman, as a surgeon, I certainly agree that surgical solutions have effectiveness and are

encouraging. I'm not particular fond of total joint as the first solution. I'm definitely in favor of joint preservation and partial replacement, arthroplasty, and conservation of the joint. But I can say that total joint, while it works very well and has the highest statistical efficacy, it certainly has the highest risk profile, and when it doesn't work, it has the greatest adverse outcomes. And I can tell you that, in our referral center at Sinai where we see a very, very large population of tertiary problems from total joint replacement, that the costs are incredible, both human as well as financial, that the opportunity for patients to reach that goal of treatment and have an outcome which is satisfactory is slipping away because reimbursement's being reduced in this country, for those of us who do this kind of work, and we've become essentially a referral center for everybody else's problems, and we have not shirked that responsibility, but on the other hand, I would not encourage a wave of total joint replacement in this country without countermeasures to try to reduce those indications when possible.

In that respect, I would reflect on the statistics that Dr. Waddell, an orthopedic surgeon of

repute in this country, has published and presented to the American Academy of Orthopedic Surgeons, and in the literature showing, in his large population of patients, that there was a significant diminution in the rate of conversion to total knee replacement in patients that were selected based on, again, matched criteria, with osteoarthritis that was advanced and yet they were able to delay -- a significant number of those patients were able to delay the choice of total joint replacement. That's particularly important in patients who are in the middle-age group where the younger you are -- and we have patients in this series, in this trial for the Synvisc-One that were 40 years and older, and so we're talking about a total joint solution in a population which would almost surely require revision prostheses in their lifetime, and that would carry with it, again, even more morbidity and lesser predictability of outcome.

So I think it's very important that we promote these kinds of solutions which frankly are a lot more physiologic than the corticosteroid and lidocaine injection which we've used as a standard of care for some 50 years or more. And now we have coming into the literature -- we've always had a great deal of literature on the catabolic effects of

corticosteroids and repeated injection.

But now we have caveats regarding the lidocaines and Marcaines and their cytotoxic effects on articular cartilage. And there's been a number of articles in the last year or two, especially in our sports medicine literature, warning us that this is not to be done with impunity. So I think the viscosupplementation, for me as a clinician and for my patients, will become more prominent as a more physiologic option. I've not heard today reflected much about the number of physiologic effects which actually are promotional and beneficial with viscosupplementation and hyaluronic augmentation, but there are well-documented literature, including T-cell depression of activated T-cell activity, and the promotional activity that may come with cartilage regeneration in the face of an augmented hyaluronic environment.

So it's kind of interesting that we're in an age in orthopedics where we're getting away from the hammer and tong a little bit, and we certainly need a cradle-to-grave treatment spectrum for the patient, and this represents that type of treatment. In my patient population, I do see a lot of Afro-American patients. I work in Baltimore, Maryland.

We have one of the highest, if not the highest, concentrations of Afro-American population in a city demographic. I see a lot of obesity, and I see a lot of diabetes coincident with that group, and I can tell you that I've noticed no difference, in my 10 years of using this modality, in that population versus the population at one time where I treated them in Montgomery County, and it was more of a broader demographic. So I can tell you that it would be interesting to stratify the results and look at future study, but I have a feeling that we'll still see efficacy in a group that seems to need this type of alternative because they don't represent a tract of total joint candidates because of their risk factors, such as diabetes and obesity, which make them a higher risk for adverse effects with total joint replacement.

That said, I would also comment on Dr. Wang's observation, from the FDA presentation, that there was a high risk or there was -- there were very increased serious side effects with the viscosupplementation. He quoted Dr. Goldberg's work in 2004. And I'll only point out that not only was that not reflected in this statistical data, that occurrence, but also that there's been no change in

protocol or utilization in this country, that I'm aware of, predicated on Dr. Goldberg's statistics or discussion in 2004, and so I think that the impact of that may not be entirely relevant.

We heard about safety margins here being quite safe, and I would concur with that as a clinician. I've had only one or two synovitic reactions, and I would say that, again, as was pointed out by the Panel, technique is important, and in the Canadian study that was done at the inception of its use in Canada, Synvisc in Canada, with a three-shot regimen, it was published then that the portal of entry for the injection is highly related to the rate of adverse reactions, and that proper technique generally almost eliminates that. And we've seen that in Dr. Jackson's articles, as alluded to. Dr. Mott, in my practice, also has published, this past year, on efficacy of anterolateral portal injection.

So I'd like to conclude by just again emphasizing that I would reinforce the comments of Dr. Spitzer this morning. I've been here all day. I felt it was a day well spent. It happens to be my birthday, and I'm not regretting it one bit. My wife said, what were you doing coming down here? And I

said, well, it's an important role that you play. You don't get a chance to step up to the plate every time. I do have a disclosure.

I am on the speaker panel for Genzyme, but as I said, I am also very, very engaged and have been way before any relationship with Genzyme with this modality, and I think it does help us with a number of difficult, otherwise, clinical management problems. I want to thank the Panel for the opportunity to participate in these proceedings. Thank you.

DR. MABREY: Thank you very much. From this morning, we still have two speakers that did not have a chance to speak, Mary Lou Gundersen and Diane White. Are Mary Lou Gundersen or Diane White in the room?

(No response.)

DR. MABREY: Seeing no raised hands, it's now 2:15. Oh, does anyone else want to address the Panel before I put us off on break?

(No response.)

DR. MABREY: Again, seeing no raised hands, it's 2:15. I'll be generous and have you all back here at 2:30. That'll be a nice round number to remember. So we'll resume deliberations at 2:30.

(Off the record at 2:15 p.m.)

(On the record at 2:30 p.m.)

DR. MABREY: It is now 2:30. If we could close the outside doors, we'll resume the meeting. Is there any further comment or clarification from FDA? Dr. Lee? Mr. Melkerson?

(No response.)

DR. MABREY: And is there any further comment or clarification from the Sponsor?

MS. LAWTON: Good afternoon, my name is Alison Lawton. I'm Senior Vice President for Regulatory Affairs and Corporate Quality Systems at Genzyme, and I'd like to just start by thanking all of the Panel members for what I think has been a very helpful discussion for us at Genzyme this afternoon. I'd like to just take a few minutes just to maybe offer some thoughts and perspectives before you consider your vote that you're going to be asked to make by the FDA.

So to start with, I think we've all talked today, and I probably don't need to spend very long at all talking about the fact that osteoarthritis, of course, is a very painful and debilitating disease. And again, we've heard from Dr. Polisson, and many of the discussions that have taken place, about the

limited number of options that are available for patients, and in particular, those options actually have been reduced over the last few years because of some of the safety issues relating to systemic use of some of these therapies.

And so, obviously, we believe that this local application offers potential advantages for patients. And you've also heard that Synvisc-One, of course, is the same material as Synvisc, which has been approved for a number of years. Yes, it's packaged differently, in a single administration of six mL, but it's the same material. And we do have significant experience with Synvisc in more than four and a half million patients, and I think that there's no disagreement here between Genzyme and the Sponsor as far as the clinical studies that were conducted didn't show any evidence of any new safety signals for Synvisc-One.

So obviously clinical effectiveness, you have discussed this, and I don't think I need to, again, spend a lot of time on the fact that I think there was agreement around the statistical significance of the primary endpoint. And with regard to the secondary endpoints, again, we've also discussed the fact that Genzyme believes we did the

appropriate analyses. They were pre-specified

And of course the discussion about the multiplicity took place, and we were very thankful for the discussion and the recommendation from the Advisory Committee regarding the fact that we did not need to do that adjustment of the multiplicity, although, obviously, you need to take into account the number of secondary endpoints that were looked at.

So I think really I want to concentrate some of my comments around the clinical meaningfulness. And again, I know that you have discussed this and I think that you've all talked about the fact that the totality of the evidence is really what's a critical piece here. And I'd like to actually just put up this slide that Dr. Dworkin presented as an expert in these pain trials, and he listed these multiple factors that need to be considered in determining the clinical meaningfulness. And as I look through this slide, I realize that, in fact, we have data from the Synvisc-One clinical study that actually addresses every single one of these 11 or more points that Dr. Dworkin put up, as far as multiple factors required to show clinical meaningfulness.

So what I'd like to specifically talk about is some of the secondary endpoints. Again, I'm not going to spend a lot of time because I recognize that you've discussed these at some length. And it's not to say -- to make claims about any one of these individuals, but again to show the consistency across all of the secondary endpoints, as far as clinical benefit for patients.

And of course, we saw the 36-percent improvement from baseline for patients on the WOMAC A scale. And importantly, we saw the effect size increase from .23 to .44 when we looked at patients with only one knee involvement in this clinical study as well. And then, for the WOMAC A1, I think you heard that WOMAC A1 is particularly important. This is walking on a flat surface, for the mild to moderate patients, which is the target patient population for Synvisc-One, and we saw a significant effect size in that group, of .36. And particularly, also, when we looked at the responder analysis, we saw a statistically significant difference in favor of Synvisc on that WOMAC A1 responder analysis. And then, finally, of course the patient and the physician global assessments. Again, this is very important because the patients were scoring

themselves, and they were twice as likely to score themselves as feeling better based on having received Synvisc versus control.

So all of those are very important pieces that lead into the clinical meaningfulness of Synvisc-One. In particular, again, many members of the Panel have made mention to the fact that Dr. Simon talked about comparable effect size for other osteoarthritis products, and I would remind you that many of those other osteoarthritis products are for systemic products with some of those safety issues, and Synvisc was absolutely in the range, as far as the effect size, compared to those other products.

And then the last point is really talking about Dr. Dworkin again, also provided some very useful information with regards to benchmarking for how individual patients thought about their response, as far as chronic pain. And if we look at our results, we actually see that, for overall effect, we see patients would score themselves as moderately improved or substantially improved in this analysis. And if you take the patients, again, just with a single knee involvement, you actually come very close to the patient saying that they had a substantial

improvement. So could I go back one slide, please?

Before I come to my last slide, there's obviously been a lot of discussion here about post-approval studies, and I'd like to just take a few minutes just to maybe comment on that. If I understood correctly, as I heard it go round the Panel, I believe I heard that many of you, if not the majority of you, suggested that there was no need for a post-approval study. But I think there was some very important issues that came up that would be things that maybe we need to understand more.

And so we've managed to pull just a few pieces of information. I don't have a slide, so this is very last minute, during the 15-minute break, and I just thought it might be interesting for you to consider some of these points. So with regards to the BMI, obviously this is one of the issues that had been proposed and maybe we want to understand more about. I would like to just point out that, with regards to the BMI in the Synvisc-One study, more than 50 percent of the patients had a BMI over 29 and we actually had, at the upper end of the range for Synvisc, a BMI of 46, and for 52 in the control group, so it did go up to a considerable BMI number.

Also, of course, I think you heard earlier

from Dr. Simon, that he believes, from the publications and the analyses that have been done, that no differences have been seen with viscosupplementations across these different BMIs. And then, finally, as far as the -- we've done the analyses ourselves, and we see consistency of the treatment effect across both lower and higher BMIs. So secondly, I'd like to just take a minute to talk about the ethnicity and the race aspect. And we recognize that the population that we do have, a very small percentage compared to the general U.S. population, with regards to non-Caucasian patients.

And so what we took a look at it is just to get a feel, given remembering that Synvisc-One is the same material as Synvisc and we've used Synvisc, again, in over four and a half million patients around the world. So it doesn't give us efficacy data, but I thought at least it might be interesting from a safety perspective. We have just managed to pull together some data to look at the number of kits sold in the last six years in the different regions, looking specifically, for example, at Latin America and Asia-Pacific and we've sold 192,000 kits, for example, in Latin America and 20,000 kits in Asia-Pacific. And when we look at the adverse event

reporting in those regions -- and I recognize that's spontaneous adverse event reporting, so that has its limitations.

Nevertheless, I think it might be important for you to know that the overall adverse event rate for Synvisc-One is .43 percent. In Latin America and Asia-Pacific, it's very similar, if not lower, with it being a rate of .14 for Latin America and .22 for Asia-Pacific. So it gives us, I think, at least a sense that, from a safety perspective, there are no concerns there from the considerable experience that we've had at least with Synvisc in use in these different patients.

I think the one other comment I might make also is that I certainly understand, with drugs that may be used for osteoarthritis, the issue of ethnicity and potential metabolism of drugs obviously is a very key piece. But I think there's less likely to be such an impact with the ethnic differences, in a product like Synvisc-One, where it's given locally. So that may be worth considering as well. I think the final comment I would like to say is that I think, as Genzyme, we certainly believe and look forward to understanding and gathering a lot more information in those patient populations where we do

have limited information or limited experience at the moment. And, of course, we will absolutely plan to do that in the post-approval setting. But I think that we would agree with the majority of the Panel that that's probably not necessary as part of the condition for approval.

So with that, I'd like to finish on my last slide, which really is just to say that we believe that Synvisc-One offers clinical meaningfulness and I think, very importantly for both the patients and the physicians, a convenient treatment option, remembering it's the same material as Synvisc that's been out there for many, many years and that this product should be made available as an option for both patients and for treaters in the use of this painful and debilitating disease. And that ends my comments. Thank you very much.

DR. MABREY: Thank you, Ms. Lawton. Before we proceed to the vote, I would like to ask Ms. Karen Rue, our Consumer Representative, and Ms. Elisabeth George, our Industry Representative, if they have any additional comments. Ms. Rue?

MS. RUE: Only to say, as I mentioned earlier, I think that, obviously, that the safety and the efficacy is of utmost importance, but we also

need to think about the social impacts of this for the consumer as far as access to care and how it affects their life, and I think that's a significant issue.

DR. MABREY: Thank you. Ms. George?

MS. GEORGE: I think the only comment I'd like to make is, is just to say that I think that the Panel did a good job of reviewing all the data and the questions and trying to focus on the fact that the Sponsor did meet the endpoints, the primary endpoint, and the fact that it is safe and that it's really -- the product is a packaging difference, and hopefully, with the focus on the patient, that it will have easier access for them with the single visit. And so I guess wish you guys luck in the voting.

DR. MABREY: Thank you. We're now ready to vote on the Panel's recommendation to FDA for this PMA. Panel members, please refer to the voting options flow chart in your folders. Dr. Jean will now read the Panel recommendation options for premarket approval applications. Dr. Jean?

DR. JEAN: The Medical Devices Amendments to the Federal Food, Drug and Cosmetic Act, as amended by the Safe Medical Devices Act of 1990,

allows the Food and Drug Administration to obtain a recommendation from an expert advisory panel on designated medical device premarket approval applications that are filed with the Agency. The PMA must stand on its own merits, and your recommendation must be supported by safety and effectiveness data in the application or by applicable publicly available information.

The definitions of safety, effectiveness and valid scientific evidence are as follows: Safety, as defined under 21 C.F.R. Section 860.7(d)(1). There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks.

Effectiveness, as defined in 21 C.F.R. Section 960.7(e)(1). There is reasonable assurance that a device is effect when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use

and warnings against unsafe use, will provide clinically significant results.

Valid scientific evidence, as defined in 21 C.F.R. Section 860.7(c)(2). Valid scientific evidence is evidence from well-controlled investigations, partially controlled studies, studies in objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of uses.

Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness.

Your recommendation options for the vote are as follows:

Approval - if there are no conditions attached;

Approvable with conditions - the Panel may recommend that the PMA be found approvable, subject

to specified conditions, such as physician or patient education, labeling changes, or a further analysis of existing data. Prior to voting, all of the conditions should be discussed by the Panel.

Not approvable - the Panel may recommend that the PMA is not approvable if the data do not provide a reasonable assurance that the device is safe or the data do not provide a reasonable assurance that a device is effective under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

Following the voting, the Chair will ask each Panel member to present a brief statement outlining the reason for his or her vote.

DR. MABREY: Are there any questions from anyone on the Panel about these voting options before I ask for a main motion on the approvability of this PMA? Any questions about the voting options?

(No response.)

DR. MABREY: Okay. Is there a motion for either approval, approvable with conditions, or not approvable from the Panel? Dr. Skinner?

DR. SKINNER: I move approvable with no conditions.

DR. MABREY: That's approvable.

DR. SKINNER: Yes.

DR. MABREY: Okay.

DR. BLUMENSTEIN: I second.

DR. MABREY: Okay. Okay, since there's been a motion and second for approval, is there any discussion on the motion?

(No response.)

DR. MABREY: Okay. So it's been moved and seconded that Supplement 12 of PMA P940015, for Genzyme Synvisc-One be approved. With a show of hands, please indicate if you concur with the recommendation that Genzyme Synvisc-One be found approved. So those members -- oh, I can't vote.

Okay, the voting members who are raising their hands are indicating that they concur with the recommendation that the above-stated PMA is approved, and they are Dr. Blumenstein, Dr. Skinner, Dr. Olsen, Dr. Goodman and Dr. Evans. And there were no nay votes, so I don't have to ask if you oppose.

Okay. I will now -- okay, the motion -- okay. It is the recommendation of this Panel, then, to the FDA that Supplement 12 of PMA 940015 for Genzyme Synvisc-One be approved. The motion carried five to zero. There were no abstentions.

I will now ask each Panel member to state

the reason for his or her vote, starting with Dr. Blumenstein.

DR. BLUMENSTEIN: I voted yes because I saw no safety issues and the primary analysis met statistical criteria and stood up to numerous sensitivity analyses.

DR. MABREY: Thank you. Dr. Skinner?

DR. SKINNER: I agree with what Dr. Blumenstein said, and I also feel that we have modest clinical improvement also, efficacy or whatever the appropriate term is.

DR. MABREY: Okay. Dr. Olsen?

DR. OLSEN: I saw this as really not a major change over an agent that's already been out there and approved, and this would expand. I like the idea that it's going to expand the availability to more patients.

DR. MABREY: Dr. Goodman?

DR. GOODMAN: I would agree with the previous comments. I'm pleased that patients don't have to suffer through three injections. They can get it all hopefully with one. I would strongly encourage Genzyme to continue to do clinical studies in the United States of America.

DR. MABREY: Dr. Evans?

DR. EVANS: I voted for approval because of the consistency of the effect size and significance of the primary endpoint under varying models and under sensitivity analyses and due to the minimal safety issues.

DR. MABREY: Thank you. And as the Chairman of the Panel, I would like to thank both the FDA and the Sponsor for excellent presentations. I myself found this to be an interesting learning experience today, especially, Dr. Dworkin, I thought that was an excellent presentation on patient response versus group response. And I think the Panel members have reflected the overall gist of understanding regarding Synvisc-One. So the December 9 --

Oh, I'm sorry. Mr. Melkerson, anything to say?

MR. MELKERSON: Just that I'd like to thank the Panel for your time and effort, as well as the Sponsor and the FDA staff, for their presentations and their efforts.

DR. MABREY: Okay. And does the Sponsor have anything to say?

MR. HALPIN: I'd just like to thank the Advisory Panel and the FDA for the time today. Thank

you.

DR. MABREY: The December 9, 2008 meeting of the Orthopedic and Rehabilitation Devices Panel is now adjourned.

(Whereupon, at 2:53 p.m., the meeting was concluded.)

C E R T I F I C A T E

This is to certify that the attached proceedings in the matter of:

ORTHOPEDIC AND REHABILITATION DEVICES PANEL

December 9, 2008

Gaithersburg, Maryland

were held as herein appears, and that this is the original transcription thereof for the files of the Food and Drug Administration, Center for Devices and Radiological Health, Medical Devices Advisory Committee.

_____

DOMINICO QUATTROCIOCCHI

Official Reporter