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DR. MAGUIRE: Mr. Chairman, just to clarify that you are setting it so that it is spherical equivalent at 6.00.

DR. McCULLEY: Correct. So, presumably, it would be up to 5.00 diopters sphere, 4.00 diopters cylinder, not to exceed the spherical equivalent of 6.00. I didn't pick up anything else as I was writing down everyone's questions and concerns that I appreciated as being unaddressed. Are there any of the issues that anyone would like to address further or any new issues?

MS. MORRIS: I very much appreciated Dr. Maguire's comments, in particular about the post-surgery issues. I always get a little nervous. It seems like when we look at different PMAs, we lean more on labeling in some. So, when we start leaning a lot on labeling, I get nervous.

So I have just some general questions that you brought up that I hope would be addressed. Just, in general, I think that draft patient information is better at this time than I have seen in the past. I think there are some clear benefits and warnings and so on.

But, to me, there still seem to be some unanswered questions. When you talk about risks, in the information, it says that there may need to be additional surgeries. Those questions still seem very unanswered. Do patients really understand the statistics or have a gauge to judge

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if, in fact, they will need to have additional surgeries?

What does it mean in the long term if they continue to have those surgeries? That is not clear to me.

Also, in the information, post-surgery, there are general things, like statements about, "You will be sensitive to bright lights." What does that mean? I don't want to infringe on the practice issue. I understand the professional practice issue. But it seems like if we are going to put so much emphasis on labeling that some of that information really should be more clear.

Again, FDA staff said earlier that the labeling will reflect outcomes. How will we do that? How will we make those suggestions so that patients really better understand that?

The effects of the surgery on visual performance, again, under poor lighting, they talk about in the precautions. I think it is still very much a question. Can patients really--do they have a gauge to make those decisions?

DR. McCULLEY: A couple of those, the functioning under dim illumination and the sensitivity to bright lights, in the labeling, that should be some descriptors of what is apt to happen rather than just say, "You are going to be sensitive to bright lights to the degree that you are bothered on a very sunny day," or, "to the point that you

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have to stay in the house."

MS. MORRIS: Or when Dr. Maguire talked about the statistics. Can we propose some kind of gauge so that patients really can understand, when they make the decision to have treatments, what that means. I didn't realize, even all the materials that I have read, that there was that much pain associated with it. You certainly don't get that in the advertising.

DR. McCULLEY: There is a difference between hyperopic and myopic correction. That is one of the things that sponsor presented and presented their statistics of how many--

MS. MORRIS: But how do the statistics that the sponsor presents relate through patient materials to have the patient understand that? It can't just be a practice issue.

DR. McCULLEY: No, no; that is not a practice issue. It is an informed-consent issue. I think Leo brought that out in his labeling suggestions. Probably, in addition to giving the numbers, the statistics and the data, that it should be stressed to what degree the pain can incapacitate or not incapacitate.

I think, again, those are all labeling issues that I think are important. I think you are making a very good point that we don't just present--you have a 20 percent

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chance of having severe pain on day 3 but you have a 20 percent chance of having severe pain on day 3 that will be somewhat incapacitating or incompatible with normal activity.

MS. MORRIS: Certainly more than, "Pain and discomfort may last for up to three days after surgery."

DR. McCULLEY: No; that is not adequate. I agree.

MS. MORRIS: That doesn't say anything.

DR. McCULLEY: I agree. So there needs to be more lay language to describe what may happen with the statistical event being presented.

MS. MORRIS: There has to be materials that a patient can use as a gauge.

DR. McCULLEY: Right.

MS. MORRIS: I don't see any of that in here.

DR. McCULLEY: I agree with you, and I think everyone else would, that we would need that. I think a lot of what we have to do with labeling, and having something available to the doctor and to the public, there are simple terms. It is caveat venditor. The doctor has to know what he is selling. And caveat emptor, the patient has to know what they are buying. Both have to have adequate information to be able to deal with those issues.

That really comes into appropriate informed consent so that the doctor and the patient can make an

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informed decision as to whether the potential benefit outweighs significantly the potential risk. They have to be able to understand that.

MS. MORRIS: I agree with that, but I want to go one step further because I think, in this particular issue, there are still unanswered questions. The effect of retreatments in the long run--

DR. McCULLEY: We don't know that.

MS. MORRIS: That is a very big question that is unanswered.

DR. McCULLEY: We would have to put in there that that is an unanswered question. We do not have data to assess that and that would have to be in the labeling.

MS. MORRIS: I think that is really a significant thing for patients to understand.

DR. McCULLEY: Yes; I agree. You said that there were several. That one I already have done. That one, clearly, has to be addressed, that we do not have data to assess retreatment. What other things did you have?

MS. MORRIS: The other one is, "The effects on visual performance under poor lighting have not been determined."

DR. McCULLEY: I got that one. And I got the sensitivity to bright lights, what limitations that results in.

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MS. MORRIS: It is still very unclear that the level of pain--I am very sensitive to pain.

DR. McCULLEY: I have that one down, too.

MS. MORRIS: That is very unclear in the materials, the level of pain after surgery.

DR. McCULLEY: Okay. I have all of those down, that they would need to be clarified further along the lines you are suggesting in the labeling. Did you have anything else in labeling that you would be concerned about or that you felt like was not--

MS. MORRIS: Not really, at the moment.

DR. McCULLEY: If you find anything else, let me know.

DR. JURKUS: One of the other things, and I don't know if this would go in the labeling or not, would be what percentage of people would be using some sort of glasses after the surgery.

DR. McCULLEY: I got that; spectacle wear post-op that Dr. Maguire brought up.

The question that Dr. Maguire--I heard to my left, was does sponsor have that data. Sponsor will have a chance to respond to everything we have brought up again in a moment. If they don't have that to provide to us, we are going to be recommending to the FDA that that be obtained for labeling purposes.

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DR. ROSENTHAL: Ms. Morris has always made the most cogent argument on the part of the patient. This is just a general statement, that we have hampered at the agency by not having a standardized quality-of-life questionnaire that could be given about refractive surgery.

Every sponsor has used different ones and looked at things different ways. It is very difficult, until we have some sort of standardized--what is the word that you do with focus groups and then study it and go through the whole thing.

I am hoping that that will ultimately be available. It seems, though, it may be available long after all the refractive surgical approvals are done. But the National Eye Institute is moving in that direction to develop this type of questionnaire and then, hopefully, the sponsors will elect to use it and people will also begin study it on the outside in a more standardized way.

DR. MATOBA: I have two comments. The first is, going back to the pain question, if this booklet is going to combine PRK and LASIK, I think it is misleading. But, the way this is written, this labeling--

DR. McCULLEY: There is no labeling for--

DR. MATOBA: What I am looking at is this thing that the sponsor has provided, "What you need to know about PRK and LASIK." They talk about the two together.

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DR. McCULLEY: Because they are pulling everything together from everything into this.

DR. MATOBA: This is the patient information booklet.

DR. McCULLEY: For clarification, I guess what the sponsor is proposing to do is to have one patient information booklet that covers all approved indications.

DR. MATOBA: I don't think that that is fair, especially on the pain issue when it is so different for the two procedures.

DR. McCULLEY: They would have to address the difference in pain with hyperopic PRK.

DR. MATOBA: But, is that the plan, to have just one booklet for both?

DR. McCULLEY: We will have to--I see heads nodding in the audience from people that should know.

DR. MATOBA: That is why there is some confusion, then.

DR. McCULLEY: I think you are right.

DR. MATOBA: That has to be addressed. The second thing is that I don't see anything in here about the possibility of progression of refractive error so that, over time, they may, again, need to wear glasses for distance even if the procedure works well.

DR. McCULLEY: We have got that in the regression,

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in the shift toward hyperopia.

DR. MATOBA: Not simply regression of the procedure but just the patient's natural progression.

DR. McCULLEY: Progression; yes. And we don't know how much of what we are seeing in this "regression or shift toward hyperopia" is natural and how much is the result of loss of effect in the procedure.

DR. MATOBA: Hyperopia may not be that important, but if this is one booklet for PRK and LASIK, for both, it is near-sighted patients and far-sighted patients.

DR. McCULLEY: But it is for all approved indications for the laser, as I understand it, which would not include hyperopic LASIK. But we have to make it clear that the hyperopes have different--there are different labeling issues for the hyperopes that have to be made absolutely clear in the patient-information booklet. And that becomes even more important if they putting it all together into one.

DR. MAGUIRE: Dr. Rosenthal, is it standard practice for FDA to allow sponsor to put all things into one when the clinical course varies quite dramatically between some indications and others, or is it possible for panel to request that sponsor have a separate book for hyperopia, following up on Dr. Matoba's question?

DR. ROSENTHAL: The panel could make a

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recommendation.

DR. MAGUIRE: And that's it? Okay.

DR. BULLIMORE: I am just following up on Dr. Rosenthal's comment. I have been suggesting for years that the FDA encourage sponsors. I think the FDA needs to go a little bit further. I would like to see, particularly with new technologies now, that--to my knowledge, things like the RSVP and the RECQ have been available for some time to assess quality-of-life symptoms, vision function and whatever after refractive surgery.

I would like to see the FDA mandate that all new sponsors use standardized questionnaires.

DR. McCULLEY: The FDA, I trust, so notes.

DR. ROSENTHAL: Thank you, Dr. Bullimore, but, to the best of my knowledge, there is no standardized tested refractive surgical questionnaire. There are RVQ or whatever they are called about quality of vision. Most are related, I think, to cataract and macular degeneration. Maybe Dr. Maguire has--

DR. MAGUIRE: Dr. Rosenthal, there is one that is very good and it has been tested in both English and French by Brunet's group in Montreal. It is being published in Ophthalmology in the next couple of months. It is a very good metric.

DR. ROSENTHAL: Great.

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DR. McCULLEY: So I would suggest the FDA evaluate it.

DR. ROSENTHAL: Thank you. With regard to us mandating, that is difficult to do, Dr. Bullimore. We can discuss it with the sponsors and impress upon them how important it is, but we are not allowed to mandate what they use to evaluate their quality-of-life issues.

DR. McCULLEY: I think we are getting a little bit off.

DR. BULLIMORE: That is what I am here for.

DR. McCULLEY: To get us off?

DR. YAROSS: I was just going to add that, clearly, sponsors are interested in using good validated tools and appreciate recommendations, but we need to be able to bring any valid scientific evidence in front of the FDA and the panel.

DR. McCULLEY: We are getting into an operational, philosophical discussion that I think is not to our benefit or what our charge is.

Are there other questions or comments about this PMA, specifically about primary reviewers' comments?

DR. BULLIMORE: Mr. Chairman, I am still a little uncomfortable with the range. I can live with 6.00 equivalent sphere but I would draw the panel's attention to Table 2A and 2B in the supplemental information. If you

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look at the data stratified by per-op sphere, in table 2A and 2B, in particular, the 4.00 diopter to 5.00 diopter group, the outcomes seem to fall a little short of the guidance. Dr. Rosenthal's comments not withstanding, I think there is a suggestion in the table here that warrants some discussion and that discussion may be, "You are wrong, Dr. Bullimore," but I would like to hear it anyway.

DR. McCULLEY: What specifically in the table are you referring to? I don't have it in front of me. I don't know that everyone else does.

DR. BULLIMORE: I am trying to avoid the temptation to throw numbers out but if you look at table 2B, which is in volume 2, tag 4 or whatever, the stuff that was sent out.

DR. McCULLEY: You are talking about within 0.05 diopter, within 1.00 diopter data?

DR. BULLIMORE: Yes. Of the 24 patients that were seen at twelve months in the 4.00 to 5.00 diopter group, 46 percent are within 0.50 diopter and 58 within 1.00 diopter. That causes me at least a moment of quiet introspection.

Just to follow up on something Dr. Maguire said, the issue of outliers is a little pertinent here. In the higher refractive ranges, the outcomes seem to be less predictable. Maybe we should handle that through the

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labeling and not restrict the range, but I would like to see it in there.

DR. McCULLEY: What you just said is where we came to with Joel's suggestion. My only comment about this is the remarkable thing is that there are 46 percent within a half. Again, it is a guidance document for other things, but there are 46 percent with 0.50 diopter. The guidance for low myopia is 50 percent. So it is remarkably close.

The surprising thing, though, is the 58, 60 percent for 1.00 diopter. I noticed on their tables before that they had a more favorable percent within 0.50 diopter relative to guidance than they did 1.00 diopter which is not exactly what I would have thought or predicted.

DR. BULLIMORE: I just went through their twelve-month data, the data listings that we were provided with. There are actually 30 eyes out of the total cohort of 276 that are at least 2.00 diopters from emmetropia, 30 out of 276. If you just include the patients seen at twelve months, it is 30 out of about 230.

So, depending on which denominator you use, it is either 11 percent or 13 percent or eyes that are at least 2.00 diopters from emmetropia. To me, that is a lot of unhappy patients. The physicians using this device should be alerted to that and the patient's attention should be drawn to that.

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DR. McCULLEY: I agree. Whether the patient is happy or not probably depends on where they started and how unhappy they are. But you are saying the same thing that I think the consensus was before, was to be more inclusive and to deal with it with warnings.

DR. WEISS: This just reiterates Dr. Sugar's comment before. If you look at that group with the higher amounts of patients who do not fall in the 1.00 diopter, 100 percent are still 20/40 or better. That is what the patient is evaluating. So I would go back to discussion we had before and suggest it be put in the labeling but still be allowed to be approved for that higher amount.

DR. MAGUIRE: My cursory view through the beginning of the line-item data, though, shows that there are people who had marked overcorrections into the minus range that did not necessarily have follow up at nine and twelve months. There are some people that just drop out after six months.

Again, that is why I am saying that there are two issues here that I don't want people to confuse. One has to do with the drop-off of MRSE and sphere accuracy as the sphere increases. The data shows that. There is a separate issue that only partially overlaps and that is outliers.

There are some people in here who are +150.00 +150.00 who end up -5.25 and things like that, one month

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post-op, and shift around. So both of those issues have to be addressed and a more careful analysis has to go on of the line data for dropouts and to see how those--if all those that actually have farther data, would we be coming to the same conclusions as now.

Sponsor can't help the fact that the people don't show up. I respect the difficulty of getting complete follow up. But, at the same time, the line-item things have to be looked at in more detail.

DR. McCULLEY: I have down here the concern and the need to identify, in some way, the outliers so that that can be included in the labeling. But, on the other hand, their overall accountability was quite good.

Are there other questions or comments? Seeing none, I would like to open the floor for public hearing.

Open Public Hearing

DR. McCULLEY: Anyone in the audience who wishes to come forward and make comment is welcome to do so. No one?

DR. McCULLEY: I would like to ask the FDA to make your closing comments. You have none? Would someone identify themselves and say "no?" We need it for the record, please.

DR. ROSENTHAL: We have no further comments. But you will consider the questions.

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DR. McCULLEY: Do you want us to consider the questions now before going to your closing comments? Okay.

Questions for the Committee

DR. McCULLEY: Would you like to project your questions for us one at a time? I can read it. Has adequate refractive stability been demonstrated at nine months. Dr. Bullimore?

DR. BULLIMORE: No.

DR. McCULLEY: Could you expand upon your "no?"

DR. BULLIMORE: Dr. Sugar has encouraged me to say "no." My problem really sort of stems from the word "adequate." Adequate refractive stability in a group of patients that, on average, has been corrected for about 2.50 diopters, one would like to think that, at nine months, twelve months, they are changing on average by very little.

But the data suggest that, between six and twelve, they are changing by a third of a diopter and there is no guarantee that that is going to stabilize. I also have residual concerns that stability is poorer in the higher refractive ranges.

DR. McCULLEY: Is it possible for us to deal with refractive stability with labeling information?

DR. BULLIMORE: I am happy to deal with it. Just because I have answered "no" to that question doesn't mean that I am going to vote not-approvable.

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DR. McCULLEY: What I am trying to get at is what is our recommendation--okay; let me phrase the question this way. What is the panel's recommendation relative to the issue of refractive stability? Would you like to respond the that one?

DR. BULLIMORE: I think, at a minimum, it needs to be addressed in the labeling. I don't know about the inclusion of words such as "temporary" in the indication for use, but there needs to be some acknowledgement that, as presented here, the data do not show adequate stability in all refractive groups by nine months.

DR. McCULLEY: Do you think the issues can be dealt with in labeling?

DR. BULLIMORE: I think they can be dealt with in terms of the labeling and in terms of the range of approval.

DR. ROSENTHAL: Could I ask the panel if they feel that they need the updated twelve-month data with respect to stability which the company has and which we could not allow to be presented to you because they did not have it until a couple of days ago. That might clarify a lot of the issue regarding stability by twelve months.

DR. McCULLEY: Can we deal with that as a labeling recommendation that would be finalized based on FDA's analysis of the final stability data that you have not yet had a chance to assess.

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DR. ROSENTHAL: That they would have to present twelve-month--a more extensive--whatever.

DR. McCULLEY: Okay. Dr. Grimmett, does that satisfy you?

DR. GRIMMETT: I will just drive that home. I was going to say that, certainly, without the updated data, it would be impossible to answer adequately regarding refractive stability. But, in the usual fashion by Dr. Eydelman and others, I would want the tables that they have presented, like 2A and 2B for all time points, one, three, six, nine and twelve with the undercorrection and overcorrection so that we can track things with time, as you usually do.

That, in addition to the difference between visits will give an overall picture of stability. So I think that is the information that we need that is currently missing.

DR. McCULLEY: So, to put it in other terms, we would state that we cannot answer No. 1 adequately at this time, that a condition that we might want to see in a few minutes would be analysis of the twelve-month data, to then allow the FDA to include appropriate wording based on that information in labeling.

DR. ROSENTHAL: If the FDA felt that, in fact, it had reached stability--I mean reached a level of acceptable level, or has it reached an acceptable level.

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DR. McCULLEY: My sense of what the panel has been saying is that we think that the level that has been reached is acceptable with appropriate labeling.

DR. ROSENTHAL: Okay.

DR. McCULLEY: What the exact wording of that would be would depend on analysis of additional data but that our sense, I believe, and we can formalize this more, is that they are at a minimal threshold.

DR. BULLIMORE: The data we have been given for the 200-plus eyes, the updated cohort, and it is included in Dr. Chiacchierini's report is very similar to the data that was presented for the N of 134 in the summary of effectiveness and stability. It is a 0.30 diopter change between six and twelve months compared to 0.29. I am sure we need to go away and look at more data.

I think the data is here. It may not have been put through the mill by the FDA but if it is, as we believe, reasonable then we have, I think, everything we need here to make a decision.

DR. McCULLEY: So acceptable but not ideal. Needs definitely to be stressed in labeling. I suppose unless the additional analysis would drop it below the threshold that has already been achieved.

DR. BULLIMORE: The means are sitting here in table 4 on page 9 of the supplementary data that was

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presented. The change hasn't altered from what was originally presented.

DR. McCULLEY: Second question; do the safety and effectiveness outcomes stratified by diopter of preoperative MRSE support approval for the full range of requested refractive indications of 0.50 to +5.00 diopters sphere with cylinder from 0.50 to +4.00 diopters. I think we felt that, but with the added limit of total correction not exceeding a spherical equivalent of 6.00 diopters.

Are there any specific labeling recommendations? The answer to that is, clearly, yes. Is this where we should start our list of those recommendations? I sense a yes. Are you ready to scribe?

Sally says we are now just answering the question, are there specific labeling recommendations. This can alter before or during our recommendation discussion. There was a labeling issue--I scribed this--that the declining percentage of patients within 1.00 diopter of intended over time and that that decline varied with the initial attempted correction and that there was a greater variance in patients who had previously work contact lenses.

DR. MAGUIRE: It is not just contact lenses. It is also gender with men doing less well. There are age-related ones also so there are a multiple group--and, also, site differences. Five of eight of the sites fell below

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MRSE plus-or-minus 1.00 in their cohorts.

DR. McCULLEY: Leo, we have dealt with these, as Ralph said before, as large groups.

DR. MAGUIRE: Okay. The men--

DR. McCULLEY: No, no; I am not saying the men. I am talking about the site differential. I'm sorry. So males doing less well than females, the results being less good with increasing age. We have not dealt with the site and I really don't think we would want to.

DR. MAGUIRE: Because we group instead of split?

DR. McCULLEY: Yes.

DR. MAGUIRE: There is such a dramatic difference between one site and the rest that I have concerns about that.

DR. McCULLEY: I don't think we can deal with that with the labeling. I think what we could do would be to ask FDA to look further into that to be sure that there is not some confounding issue which I am told that the FDA does. So I think that is not for us to address.

But I think sex and age at it relates to this PMA should be addressed.

DR. GRIMMETT: I would have to go back and look at the page but, if my memory serves me correctly, were those changes with regard to gender and age statistically significant or not? If my memory serves me correctly, I

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think the numbers were too small to prove statistical significance, weren't they? I would have to turn back. It has been a few weeks.

DR. McCULLEY: But the changes relative to fall-off with increasing attempt at treatment and with prior contact-lens wear were real, presumed real.

DR. GRIMMETT: Those were statistically significant--

DR. McCULLEY: Statistically significantly different?

DR. GRIMMETT: Were they?

DR. McCULLEY: I don't know.

DR. GRIMMETT: I think they were not. Do you recall?

DR. YAROSS: What I was just going to suggest is that we recommend that you stratify the effectiveness data by attempted correction and significant demographic parameters. That way, if there is a significant difference, it can go in the labeling. If it is not, it doesn't need to.

DR. McCULLEY: That statement could relate to--outcome parameters is what you said? What was the word you used?

DR. YAROSS: I said stratify the effectiveness data which is how close they come to attempted--

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DR. McCULLEY: There are multiple things that go under effectiveness data. So why don't you enumerate those; such as--

DR. YAROSS: Such as the predictability of stability by attempted correction and any significant demographic predictors.

DR. McCULLEY: I think that is very well stated. It covers a lot of the issues that we have to deal with, quite honestly, not just with the -1.00 diopter but the stability, in quotes, and with specific wording in that regard that there appears to be a greater shift toward hyperopia in the treated group than one would expect in the normal population, and that that shift is greater with greater attempted correction, and that, within the label, the data be presented and stratified.

We had wanted another point in the labeling. Are we there? Are we together? You are not writing our brilliance down?

DR. EYDELMAN: I am not projecting anything. These are my own--

DR. McCULLEY: Do you have the ability to project so that we can see what we are recommending?

DR. EYDELMAN: I believe I was instructed not to do that until you have completed voting. So you need to do voting and then we can project.

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DR. McCULLEY: You are going to get to read some of this back to us. Is there agreement with Marcia suggested and I expanded on? There appears to be.

DR. MAGUIRE: Marcia, why don't you just use your phrase again.

DR. McCULLEY: Did you get it? She has it. Thank you, Leo. I am not sure how to word this but we need something in the labeling that relates to the identification of or inability to identify outliers, that there is a pool of shifting outliers. I don't know that those shift, but that there is a pool of outliers. I think Leo had suggested that there be some examples of what those outliers might be.

DR. MAGUIRE: There needs to be wording that says--in the labeling that we talked about earlier, we gave the aphorism, the thing that is generally true. The next paragraph or the next section says, while this gives a general trend, it is important to note that there are outliers that trend differently. We need to show representative examples of those, or every one.

Fortunately, it is a minority. It wouldn't be impossible to show them all. So I think we should do that. So FDA and some panel members, somehow, should agree upon clinically significant outliers and they should be listed, at least on the surgeon side of it. The patient information should say something to the effect that there are people who

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develop unpredictable and unstable results, that don't follow the trend and that these are still found at the nine to twelve-month window.

DR. WEISS: Just as a small addition to what Dr. Maguire said. Once there is a determination of what you need to be called an outlier for the patient packet, I think it would be helpful to say that 5 percent of patients at this month, X, just so a patient understands what is the chance of them falling into that unpredictable--

DR. MAGUIRE: I agree wholeheartedly.

DR. McCULLEY: So best description of the outlier group and the risk of one being in that group. When you are ready, we have got another long list of things. So let me know.

MS. CALLAWAY: Are you still answering Malvina's questions?

DR. McCULLEY: Yes; and we are hoping that you were writing these things down.

MS. CALLAWAY: We weren't prepared to do that until voting. But we are taking our own notes; yes.

DR. McCULLEY: I hope you are. I understand.

There are other labeling issues, then, we have discussed relative to having appropriate labeling not only with the entity and the statistics, the likelihood of them occurring, but with lay terms that the patient can clearly

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understand relative to pain, epithelial healing, visual-acuity recovery, function in dim illumination, sensitivity to bright lights, photophobia; that we do not have data on retreatment, on effect of pupil diameter or the efficacy relative to monovision and we would hope that there would be data to be included in the labeling relative to the need for near and distance spectacle wear post-op.

Are there any other labeling issues?

DR. MAGUIRE: Mr. Chairman, I think, while the laser delivers the beam and everything the same way, there is, obviously, a dramatic difference in immediately and relatively moderate longer postoperative course between this and PRK for myopia. I think one thing we should consider a separate book for hyperopic PRK. That should be something FDA should go under consideration.

DR. McCULLEY: I think now would be an appropriate time for us to address whether we should recommend to the FDA one patient-information book for all approved procedures or a separate patient-information book for hyperopia.

Your recommendation, Leo?

DR. MAGUIRE: My recommendation is there should be a separate book for hyperopic PRK and hyperopic PRK for astigmatism because of the pain, visual recovery, different instability. The outliers that are found here seem to me to be qualitatively, quantitatively different, than that seen

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in PRK as practiced in the Year 2000--PRK for myopia practiced in the Year 2000.

DR. McCULLEY: Is there concurrence with that opinion? Is there an opposing opinion? There seems to be none. I don't know that you need anything more from us in that regard. We would suggest a separate hyperopia patient-information book from the myopia book, or brochure.

DR. BULLIMORE: At the risk of being off-point, I would like to see the brochure mention the "p" word, presbyopia.

DR. McCULLEY: Okay. It would probably fit into the area of the need for spectacle wear for near or distance postoperatively. So I guess we would want to see presbyopia addressed thoroughly.

We are still on the FDA questions. Are there any other specific labeling recommendations? That, then, answers the FDA's three questions that were posed to us. Does FDA have any other questions for us?

DR. EYDELMAN: No; we do not.

DR. McCULLEY: I got out of order in terms of sequence, so I would now like, once again, to open the floor for public hearing.

Open Public Hearing

DR. McCULLEY: If anyone at this point would like to come forward and make comment, please approach the

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podium. No one? Thank you.

FDA Closing Comments

DR. McCULLEY: I would like to ask if the FDA has any closing comments. You have five minutes.

MS. CALLAWAY: There are no closing comments from the FDA.

Sponsor Closing Comments

DR. McCULLEY: I would like to invite sponsor to make up to five minutes of closing comments, if you so wish.

DR. ODRICH: The sponsor thanks the panel and the FDA for their considered review and has no further comments.

DR. McCULLEY: Thank you.

Panel Recommendations

DR. McCULLEY: I would like to turn the floor to Ms. Thornton to give us our instructions relative to voting and voting options.

MS. THORNTON: The Medical Device 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 outside expert advisory panel on designed medical-device premarket approval applications, or PMAs, that are filed with the agency.

The PMA must stand on its own merits and the panel's recommendation must be supported by safety and

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effectiveness data in the application or by applicable publicly available information. Safety is defined in the Act as reasonable assurance based on valid scientific evidence that the probable benefits to health under conditions of intended use outweigh any probable risks.

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

The panel's recommendation options for the vote are as follows: one, approvable; there are no conditions attached: two, 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 further analysis of existing data. Prior to voting, all the conditions are discussed by the panel and listed by the panel chair. Three, not approvable. The panel may recommend that the PMA is not approvable if the data do not provide reasonable assurance that the device is safe or if a reasonable assurance has not been given that the device is effective under the conditions of use prescribed, recommended or suggested in the proposed labeling.

DR. McCULLEY: I would ask that each of you get in front of you our little flow chart. We go box at a time. I

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would now entertain a motion relative to this PMA. Dr. Bullimore?

DR. BULLIMORE: I move that the PMA be approvable with conditions.

DR. McCULLEY: Is there a second to that motion?

DR. MAGUIRE: I will second that.

DR. McCULLEY: Is there any discussion relative to the motion and the second? I see none. We now will take conditions on the recommendation one at a time. Each condition must be put forward, seconded, discussed, voted on. Then, once we have our collection of conditions, we will vote on the entire motion with all of the conditions that we have agreed upon.

So, at this point, I will entertain recommendations for conditions. Are we able, now, to see what we were hoping you were writing before?

DR. EYDELMAN: Yes, except I just to clarify, these are my own notes and I am going to be correcting them as you are restating.

DR. McCULLEY: We will do that. I just didn't want to have to try to recreate from scratch.

DR. BULLIMORE: Mr. Chairman, would you like me to scribe these or are you happy with the FDA staff?

DR. McCULLEY: I think we can trust them now to--I think what we should do is have FDA scribe.

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DR. BULLIMORE: Second.

DR. McCULLEY: And we will approved the "scribed." The first condition relates to the indication, of the range.

DR. BULLIMORE: I move that the range of approval be up to +5.00 sphere with up to +4.00 cylinder but not to exceed a maximum mean spherical equivalent of +6.00 diopters.

DR. GRIMMETT: I second that.

DR. McCULLEY: Is there further discussion? I am told I want you to write that correctly, now.

All in favor of this first condition, signify by raising your right hand.

[Show of hands.]

DR. McCULLEY: Eight to nothing, so unanimous.

DR. McCULLEY: The second condition relates to stability. I actually should not be making a motion, so someone else is going to have to--Joel, would you try to deal with this one?

DR. SUGAR: I am not exactly sure what you want to say,

DR. McCULLEY: I think our consensus before was that stability be dealt with in the labeling with the exact wording being dependent upon the FDA's analysis of the updated cohort, with the understanding that we feel that the data submitted to us meets a minimal threshold for

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acceptability.

DR. BULLIMORE: Mr. Chairman, I would like to make a motion but it is not the one you want.

DR. McCULLEY: I don't care.

DR. BULLIMORE: You don't care that it is not the one you want, or you just--

DR. McCULLEY: No; I don't care that it is not the one I want. Make your motion.

DR. BULLIMORE: I move that the labeling include data on the long-term stability, complete data through twelve months. I would like a warning to be in there--actually, I should not use the word "warning." I would like the labeling to include an indication that stability has not been obtained and the possibility of long-term hyperopic changes of up to 0.50 diopter per year.

DR. McCULLEY: Is there a second to that motion?

DR. SUGAR: I think so. Yes.

DR. McCULLEY: Is there discussion on the motion?

DR. WEISS: I think it would be reasonable to get all the twelve-month data and have the FDA review that to see if our supposition that has been reached by Dr. Bullimore still holds. If it still holds, I would second it. If it does not hold, then I think the labeling should reflect the inclusion of the most recent data.

DR. BULLIMORE: I don't accept the friendly

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amendment.

DR. McCULLEY: You do not? Okay. Can you read the condition back to us or let us see the wording?

MS. CALLAWAY: The labeling should include complete long-term stability with the precaution that long-term hyperopic change up to 0.50 diopters per year. Is that the one you were talking about?

DR. McCULLEY: I am still looking for it. Where is it?

MS. CALLAWAY: It is hard to keep up typing.

DR. McCULLEY: Can you please put it up there for us? It is No. 2. It would be after stability, other than what we have up there.

MS. CALLAWAY: You haven't voted on it yet, though; right?

DR. McCULLEY: Dr. Bullimore, do you want to strike what is up there now and substitute your suggestion, or do you want to add your suggestion to what is there?

DR. BULLIMORE: My motion did not include the statement about formulate labeling language pending FDA analysis of outcomes.

DR. McCULLEY: Don't take that down yet until we have voted on--yes; we are open for--we had a second for that so it is open for discussion.

DR. JURKUS: In looking at what is typed up there

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under the labeling issues, it appears to me that the motion that Dr. Bullimore made is actually a combination of A and B as listed, where it is talking about the effectiveness data showing the difference in correction, and present all statistically significant findings--

DR. McCULLEY: No; we are at No. 2.

DR. JURKUS: But No. 2 was question No. 2. I thought we were talking about labeling issues now for conditions.

DR. McCULLEY: This is a separate condition.

DR. ROSENTHAL: Dr. McCulley, may I just clarify. I think you should take the labeling and put it under the labeling, and take the stability and put it under stability. Do you all believe they should update their tables with complete cohort information on twelve-month data.

[Many "yesses."]

DR. ROSENTHAL: Well, thank you. If I may suggest someone might want to consider to make that a motion, since I am not allowed to.

DR. McCULLEY: I can't make a motion.

DR. ROSENTHAL: I can't either

DR. WEISS: I will make that as a motion.

DR. GRIMMETT: But there is a motion on the table.

DR. McCULLEY: There is a motion on the table that most likely--what the motion on the table addresses will be

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moved to labeling as it has come out, unless you want to withdraw and let's start over.

DR. MATOBA: I would like to amend the motion on the table so it is what Dr. Rosenthal said.

DR. McCULLEY: Can't do that.

DR. MATOBA: That is that we, at this point, only consider the stability, that we recommend that the stability data up to twelve months be looked at.

DR. McCULLEY: We can't do that because Dr. Bullimore has the broader motion on the table that has been seconded and discussed. The only way we can do that is to defeat his motion and go back, unless he withdraws his motion.

DR. BULLIMORE: I withdraw my motion.

DR. McCULLEY: Thank you. We have listed what we said about stability before as a non-label issue. Would anyone like to make a motion to address that issue, and we will deal with the issue further under labeling.

DR. WEISS: I will make a motion to have the sponsor submit the twelve-month data and have that analyzed by the FDA to determine stability.

DR. McCULLEY: We did have, before, an additional statement in that we felt that the data, as presented, had met threshold.

[Several "no's"]

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DR. McCULLEY: There was a consensus to that effect. Do you want to include that in your motion, and it can be shot up or down.

DR. WEISS: I personally would prefer not to include that in my motion.

DR. McCULLEY: All right.

Is there a second to the motion?

DR. GRIMMETT: Second.

DR. McCULLEY: Dr. Sugar seconds the motion.

DR. SUGAR: No.

DR. McCULLEY: You did or didn't? Who did?

DR. GRIMMETT: I did.

DR. McCULLEY: Oh; okay. Further discussion on the motion? All in favor of the motion signify by raising your right hand.

[Show of hands.]

DR. McCULLEY: Eight. Unanimous.

Is there a group opinion that we now deal with all of the other issues as a condition under labeling conditions?

DR. MAGUIRE: Mr. Chairman, may I just ask a question. The evaluation of clinically significant outliers, is that covered under No. 2 as up here?

DR. McCULLEY: No; that was a separate labeling--or was it? We wanted the clinically significant outliers

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defined dealt with in the labeling. So, yes; it was a labeling issue as we did it before.

DR. MAGUIRE: So, if we put in labeling, we are assuming that FDA is going to hook up with panel members, or somebody's clinical expertise to identify the ones that we consider outliers, or are we saying that we are going to accept sponsor's definition of outliers?

DR. McCULLEY: We are saying that the FDA will determine that. We are leaving that to FDA and they will then seek whatever advice they feel they need.

DR. ROSENTHAL: May I comment, Mr. Chairman?

DR. McCULLEY: Please. Dr. Rosenthal.

DR. ROSENTHAL: If you make that as a condition, then the sponsor has to provide the information and our team has to review it.

DR. MAGUIRE: So that would be separate from No. 2?

DR. ROSENTHAL: It would be under labeling issues.

DR. McCULLEY: We had intended it to be separate from No. 2.

DR. ROSENTHAL: Yes; separate.

DR. McCULLEY: Who would like to address and state the motion relative to conditions of labeling?

DR. ROSENTHAL: Excuse me. If you want to include an analysis of outliers to be presented by the sponsor, that

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should be your third--I think a third one and then consider the labeling issues relating to that analysis I think might be the best way.

DR. McCULLEY: I think that is probably a good suggestion. Would anyone like to make a motion in that regard, clearly stated?

DR. MAGUIRE: That sponsor and FDA separately evaluate line-item data for clinically significant outliers.

DR. ROSENTHAL: With the greatest respect, what we do is we ask the sponsor to submit their analysis and then we review it.

DR. MAGUIRE: I think reasonable people can disagree about certain line items. I think there should be some--

DR. ROSENTHAL: Inherent in that would be our review of the line items.

DR. MAGUIRE: Okay.

DR. McCULLEY: Would you restate that?

DR. MAGUIRE: Okay; that FDA request sponsor to submit what they consider to be analysis of outliers.

DR. McCULLEY: That is your motion. Is there a second to that motion?

DR. WEISS: Second.

DR. McCULLEY: Is there discussion on the motion?

DR. SUGAR: Could you explain what the means, Leo?

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DR. MAGUIRE: Sponsor stated, and my line-item review confirms, that there are people whose postoperative clinical course varies from the aphorisms that we find are going to be included in the label. Those people have to be identified. For example, if you are a +1.50 +1.50 and, a month post-op, you end up as a -5.25 +1.00 and you are still a -3.25 +2.00 or something, you need to know it.

That is not a specific example from here, but there are a number of examples in the line-item analysis that don't fit with the general trend and sponsor has stated that they don't fall into any discernable causative pattern.

So they need to be identified and discussed.

DR. SUGAR: I am still playing sort of devil's advocate but they can take all those lines and pull them out from the 274, or whatever, patients and then do what with them?

DR. MAGUIRE: They should be displayed--at a minimum, they should be displayed in the information book that goes to the surgeon because if I am naive and I read the group data and I see that we get these nice trends and then, in my fifteenth case, a +1.50 +1.50 is -5.50 +1.00 when they epithelialize, I am going to wonder, is this something that happens or not?

What you need to do is you need to see the variation. That is important both for the patient and for

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the treating physician.

DR. SUGAR: I would just like to suggest that, if the data is presented in both the physician and patient booklet that includes not just standard deviations but also ranges, that information would be, I think, easier to assimilate as a physician looking at that and probably easier for a patient to assimilate rather than giving what are, in effect, anecdotal multiple case reports which I think are hard to fit into the bigger picture.

DR. MAGUIRE: The only problem is that they are part of the bigger picture and they don't follow any particular pattern. They are not individual case reports. They are part of the overall study that vary from the trends.

I think it is something that physicians would be interested in having at a minimum so that they could understand unusual results that occur post-op.

DR. McCULLEY: I think we have all agreed that there are unusual occurrences that have been reported in this PMA and that we would want the information passed on to both the ophthalmologist and to the patient that warns them that these can occur.

As I am hearing it, there are two opinions as to how that can be best dealt one. One is a separate analysis and presentation of this outlier group with some examples.

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The other is Dr. Sugar's, that the ranges be included with some verbal explanation relative to the range that goes beyond the standard deviation, indications of outliers there.

We need to decide which way we are going to go. There is a motion on the floor and seconded along the lines that Dr. Maguire has suggested.

DR. BULLIMORE: Call for the question.

DR. McCULLEY: Is the further discussion? All in favor of the condition as stated and seconded, raise your right hand.

[Show of hands.]

DR. McCULLEY: Four. All opposed?

[Show of hands.]

DR. McCULLEY: Three. Someone abstained. Let's vote again. All in favor?

[Show of hands.]

DR. McCULLEY: Five. The motion passes five to three with the condition.

Now we will go to labeling issues. Why don't we take each labeling issue in turn and vote on it rather than lumping them together unless there is a consensus that we should do them lumped. What is the panel's--

DR. BULLIMORE: One at a time.

DR. McCULLEY: One at a time; okay. Who would

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like to make a motion relative to the first labeling requirement?

DR. BULLIMORE: I move that the labeling include a stratification of the effectiveness data--that is, the predictability and the stability by attempted correction and present all statistically significant findings excluding--

DR. McCULLEY: No; including. Example; eg.

DR. BULLIMORE: All right; sorry. I need to get my prescription updated. For example, contact lenses and gender.

DR. McCULLEY: I don't know that it was--whatever pans out as being significant. Is there a second to that motion?

DR. SUGAR: Second.

DR. McCULLEY: Discussion?

DR. WEISS: I would just query the panel should we be making mention that there is no data in terms of--or there is very little data in terms of non-Caucasians?

DR. McCULLEY: I don't know how the FDA has dealt with that in the past. This is a pretty typical situation for us to be in in these studies. I think the FDA knows how to deal with that, so I don't think we need to make specific comment.

DR. MAGUIRE: Mr. Chairman, as a condition in our last PMA review, we specifically mention race in labeling.

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DR. McCULLEY: Like I said, the FDA deals with this frequently and I am sure they will deal with it effectively as they have in the past.

Is there discussion on this recommendation? All in favor, raise your right hand.

[Show of hands.]

DR. McCULLEY: Unanimous yes.

Next? Dr. Bullimore?

DR. BULLIMORE: I move that the labeling include an indication of the greater--let me restate this one again.

DR. McCULLEY: This is really our stability.

DR. BULLIMORE: Yes; I am going to move down to C but include B, so just bear with me a minute. I move that updated stability data be included in the labeling with a note describing the failure to reach complete stability within the study period, the likelihood of long-term hyperopic shifts and that these shifts are likely to be greater in higher attempted corrections.

DR. McCULLEY: We will give you a minute. Do you need for him to--where would you like for him to start restating it?

DR. EYDELMAN: If you would be kind enough to look at what I have up there and tell me what to correct.

DR. BULLIMORE: I would move the bit about long-term hyperopic shifts. I would make that the second item

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before the greater shift towards hyperopia with an increased attempted correction.

DR. MAGUIRE: Dr. Bullimore, you are basically saying that refractive stability is not reached--

DR. BULLIMORE: Yes; I am going to write a bit about that. If you can move the bit about the outlier, that bit in parenthesis about the outlier group for the moment. So, from where we are now, stability is the first word, stability data be included. That is good enough for me--with a note that complete stability has not been attained within the twelve-month period.

Mr. Chairman, that is an adequate reflection of my motion.

DR. McCULLEY: With what; with everything else that is that is up there. Long-term hyperopic change up to 0.50 diopter per year, greater shift toward hyperopia with increased attempted correction, data presented and stratified. So the entirety of it--would you read--

DR. BULLIMORE: To restate my motion, I move that the stability data be included with a note that complete stability has not been attained within the twelve-month study period. Long-term hyperopic changes up to half a diopter per year may be anticipated. And greater shifts toward hyperopia may occur with increased attempted correction. And--

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DR. McCULLEY: Don't do anything yet. Let them get that. We have heard your motion and we are getting it typed in. Is there a second to the motion?

DR. SUGAR: Second.

DR. McCULLEY: There is a second to the motion. Is there further discussion?

DR. WEISS: This seems to be somewhat of a repetition of the issue with No. 2 in that until we get the twelve-month data and the FDA analyzed it, I don't think we in a position to make the statement that stability has not been attained. I was under the impression that we had agreed that we needed to get that data before we made a final determination.

DR. McCULLEY: My impression is that we felt that it probably had been acceptably but not ideally reached and that labeling needed to reflect that, and that we wanted them to analyze the twelve-month data to be certain that that opinion still held. But we have gone a different route with this with the formal motion.

DR. EYDELMAN: I believe we understand what the panel's consensus is and we will try to reflect it.

DR. McCULLEY: But we still have to make a formal motion that has specifics in it. Is there further discussion? I don't disagree with your statement, but we have to vote on this motion as it is stated. Is there

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further discussion on this motion? All in favor of the motion, raise your right hand.

[Show of hands.]

DR. McCULLEY: All opposed?

[One hand raised.]

DR. McCULLEY: Seven to one in favor of the motion.

The next item?

DR. EYDELMAN: May I ask if Dr. Bullimore or Dr. Maguire wanted the outlier group in the physician labeling as a next--

DR. MAGUIRE: I think the outlier group follows after the stability, that there are exceptions to the stability trends. The condition is that since there are--

DR. McCULLEY: Let me ask, would an appropriate motion to--I think the answer is yes. Would an appropriate motion be to ask the FDA to include in the labeling appropriate definition and description of the outlier group, since we don't have the data there to be too terrible specific?

DR. EYDELMAN: Yes.

DR. McCULLEY: Would someone like to make such a motion?

DR. BULLIMORE: Mr. Chairman, I move that the patient and physician labeling include wording about the

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potential for instability during the postoperative period and that some indication of the proportion of patients that fall under the category of outliers be included.

DR. McCULLEY: Is there a second to that motion?

DR. GRIMMETT: Second.

DR. McCULLEY: Discussion? All in favor of the motion raise your right hand.

[Show of hands.]

DR. McCULLEY: All opposed?

[One hand raised.]

DR. McCULLEY: Seven to one.

Next? I think we probably should have this divided. We have things that we want clear labeling about and we want, in the labeling, as another category, things about which we do not have adequate data such as retreatments, monovision, pupil size.

DR. MAGUIRE: Mr. Chairman, I think that the initial labeling for this next area would deal with labeling regarding the early postoperative period, things involved in that, pain, foreign-body sensation--

DR. McCULLEY: Some are early. Some are not. We can split them. I mean, visual function under dim illumination, we have included in this. Photophobia, we have included in this. Need for spectacle wear. If they feel the need to divide them up into short- and longer-term,

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or more chronic, that is fine. But let's try to take all of these together.

They fall into two categories, those that are caveats for the patient relative to things that may happen and those that are caveats for doctor and patient about which we have no data.

The ones that we want to warn the patient about with full explanation are pain, epithelial healing, visual recovery, function under dim illumination, sensitivity to bright lights, need for spectacle wear at near and distance, with Dr. Bullimore's "p" word stressed. I think most of it is there.

We can do them one at a time from the list that I had before and then we can see if there is agreement. Pain. Epithelial healing, Visual recovery. Function under dim illumination. Sensitivity to light, photophobia, however you want to put that. Need for spectacle wear, near and distance. Stressing presbyopia. And then we do not have data on retreatment, pupil size, monovision.

DR. MAGUIRE: Mr. Chairman, how about anisometropia?

DR. McCULLEY: How about it?

DR. MAGUIRE: We don't have data on that either?

DR. McCULLEY: Yeah; we know about anisometropia.

DR. MAGUIRE: In these people who have had

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bilateral surgery?

DR. McCULLEY: Leo, we can't rewrite the ophthalmic textbook. We know that people don't tolerate, you know--I suppose that, in monovision--there is a limit to which we can take these things reasonably here. Sure; I suppose if you want to put in there we don't know about monovision but we do know about anisometropia. If you create monovision that goes beyond acceptable anisometropia, we are going to have problems.

But I don't think we need to do that.

DR. GRIMMETT: Dr. McCulley, I would like to see the Caucasian cohort up there, race limitations or however we want to say it up there in the labeling as well.

MS. CALLAWAY: It is already up there.

DR. GRIMMETT: It is already in there?

DR. McCULLEY: We have dealt with that before. The FDA deals with that in a standard way.

DR. BULLIMORE: I second Dr. Grimmett's motion.

DR. GRIMMETT: As long as it is in there, I'm happy.

DR. McCULLEY: You want it in there.

DR. GRIMMETT: As long as they can deal with it.

DR. McCULLEY: We want to be sure that you guys deal with, just as we recommend that you deal with the patient brochure as being two separate ones, we want to be

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certain that you deal effectively with the race representation in the cohort. The FDA does that standardly. I don't think we need to tell them to do what they do as normal operating procedure.

DR. BULLIMORE: Mr. Chairman, with respect, I think you do need to respect the wishes of your panel members when they put forward something.

DR. McCULLEY: Okay. We want to remind the FDA to do that.

MS. CALLAWAY: It's up there.

DR. McCULLEY: We have these additional conditions that we had enumerated before. Is there a motion? Does anyone wish to make a motion relative to the inclusion of these as conditions in labeling?

DR. WEISS: I make a motion to include all of the conditions under No. D in the labeling booklet.

DR. McCULLEY: Is there a second?

DR. GRIMMETT: Second.

DR. McCULLEY: Discussion? Seeing none, all in favor, raise your right hand.

[Show of hands.]

DR. McCULLEY: Unanimous.

Are there other conditions to be considered for the approvable with conditions?

DR. EYDELMAN: There was just the one labeling

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that you didn't have a motion for which was separate labeling booklet for hyperopia.

DR. McCULLEY: Okay. Is there a motion to that effect? We need something other than a head nod.

DR. MAGUIRE: I move that there be a separate booklet for the correction of hyperopia and astigmatism.

DR. McCULLEY: Is there a second?

DR. GRIMMETT: I second Dr. Maguire's motion.

DR. McCULLEY: Is there discussion? All in favor?

[Show of hands.]

DR. McCULLEY: Okay. Unanimous. Since we really wanted, and Dr. Bullimore insists, that we have the--I think it is appropriate that we have the racial--

MS. CALLAWAY: It is in there.

DR. EYDELMAN: I included it in No. 1.

DR. McCULLEY: Okay. Are there other conditions? Seeing none, we have a motion on the table for approvable with conditions, with conditions having been individually voted on and approved. I would now call a vote for the total approval--

MS. CALLAWAY: Excuse me. Would you clarify E. Is that hyperopia or hyperopia with astigmatism separately?

DR. McCULLEY: It was all. It was hyperopia, hyperopia with astigmatism, all hyperopes. So there is a motion with conditions on the floor. Is there any further

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discussion before the vote? All in favor of the motion, raise your right hand.

[Show of hands.]

DR. McCULLEY: Eight. Unanimous recommendation.

We now would like to ask each panel member to indicate why you voted as you did. We also are going to ask the consumer and industry representative for comments on the motion and its vote.

Let's start with Dr. Weiss.

DR. WEISS: Jayne Weiss. I voted for approval with conditions because of the excellent presentation documenting that the data would support that this would be of benefit to the public.

DR. GRIMMETT: Michael Grimmett. I voted approvable with conditions due to reasonable safety parameters as presented today as well as reasonable efficacy with the expected normal decline in effectiveness with higher hyperopic ranges.

DR. MATOBA: Alice Matoba. I voted for approval for approval with conditions because, as Dr. Grimmett said, the sponsors have presented data showing reasonable efficacy and safety.

DR. SUGAR: I voted likewise for approval with conditions because of reasonable safety and efficacy and the conditions that we stated enhanced the likelihood that the

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consumer will be better informed.

DR. BULLIMORE: Dr. Bullimore. I voted approvable with conditions. I believe that the sponsor has demonstrated reasonable safety and effectiveness. Of course, like many other members of the panel, I probably have the expectation that the device is going to be used for LASIK rather than for straight PRK by the community at large.

DR. MAGUIRE: Leo Maguire. Approvable with conditions. The safety information is very good and the accountability is excellent. It is with conditions because the postoperative recovery varies considerably from person to person and is long. Therefore, it is not quite as effective as it is safe, but it passes minimum FDA requirements.

DR. JURKUS: Jan Jurkus. I voted approvable with conditions since the data shows that this device is safe and could benefit a significant number of patients.

DR. COLEMAN: Anne Coleman. I voted approvable with conditions because I believe that reasonable safety and effectiveness were demonstrated.

DR. McCULLEY: Ms. Morris, our consumer representative?

MS. MORRIS: Well, since I don't have a vote, I certainly trust that the excellent expertise of the

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technical members on the panel that you have made a good decision on the clinical safety and efficacy.

There are a couple of things, at the risk of being redundant, still trouble me. That is the three areas that there is not enough--there is no data. I think those are still unknowns to the patient. Although we have addressed those issues in labeling, it still concerns me that patients are put in a position that they don't have that information.

And then the last thing is I just wanted to state that I hope that the labeling of all of the things that you have identified is done in a way that patients can have it as an effective tool to use as a gauge in their decisions.

DR. McCULLEY: Dr. Yaross, the industry representative?

DR. YAROSS: My only comment would be to congratulate the sponsor on presented data in a way that the panel could deal with it quickly and effectively.

DR. McCULLEY: Thank you. Further comment? Let me remind everyone that we start in the morning at 8:30 in this room. With that, the panel deliberations are adjourned.

[Whereupon, at 3:09 p.m., the meeting was recessed, to be continued at 8:30 a.m., Friday, May 12, 2000.]

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CERTIFICATE

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

Alice Toigo

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