

1 DR. MATHERS: I am also interested in who
2 gets induced cylinder. I wondered if you looked at
3 this in terms of the number of spots or age or their
4 pre-op cylinder to give us some indication as to who
5 you could predict would get cylinder.

6 DR. GORDON-MEYER: Surprisingly, there was
7 no relationship between number of spots and induced
8 cylinder, but I don't think I know or recall whether
9 there was a relationship between preoperative cylinder
10 and induced cylinder.

11 There was not in the hyperopia population,
12 and there was less cylinder induced here, So I can
13 find out, but other factors did not have any effect.

14 DR. MATHERS: Thank you.

15 CHAIRMAN WEISS: Dr. Schein.

16 DR. SCHEIN: Thank you. First, my
17 compliments to the sponsor for a very clear
18 presentation. I have a question that relates to a
19 difference between temporary and reversible,
20 reversibility.

21 So imagine if monovision is successful in
22 the contact lens trials in the 60 or 70 percent range,

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1 and everyone gets a contact lens trial. If they fail
2 it, they don't get this procedure. It's not going to
3 be 100 percent, that everyone is going to be happy
4 with the more permanent monovision, and you have just
5 divulged to the patient that it's not temporary, but
6 what information do you think is appropriate for
7 indicating potential reversibility of the procedure?

8 It may be a good thing that it is
9 temporary for some patients.

10 DR. DURRIE: One thing that was
11 interesting is when you get the chance to really look
12 at this data, what was interesting is in this study we
13 didn't have anybody in the study who was intolerant of
14 their monovision and had any -- We had no requests for
15 reversal. We didn't have anybody who wanted to go
16 back. We had undercorrections.

17 So I thought that was an interesting fact,
18 because the screening that we did, which we are
19 suggesting in the label and the same that was done
20 with the monovision trial within future labeling, did
21 a good job; because we didn't have that happen.

22 I think that reversibility of the

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1 procedure goes back to what I said before about re-
2 treatment. You certainly wouldn't add more CK spots,
3 but doing a laser treatment is an option, and I have
4 done that, not in this procedure but I have done that
5 procedure with overcorrected LTKs way in the past,
6 which should have some similarity, where somebody is
7 very overcorrected, that I did do a PRK procedure for
8 myopia, and it worked fine with no haze or problems.
9 But certainly, we have to label that we don't know
10 anything about that, but it is one of those things
11 where, theoretically, correcting a little bit of
12 myopia shouldn't be that hard.

13 DR. SCHEIN: Right. The other question I
14 had has to do with: Did you measure uncorrected
15 distance acuity in the treated eye?

16 DR. GORDON-MEYER: We haven't looked at
17 that data, and we did not do that consistently,
18 because it was not making a lot of sense.

19 DR. SCHEIN: The concern I have as an
20 emmetropic presbyope is that, if I am only correctable
21 distance now with the spectacle that I didn't have to
22 wear before or there is some induction of irregular

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1 astigmatism which is potentially correctable, that
2 would be a downside for an emmetrope.

3 CHAIRMAN WEISS: Thank you. Dr. Macsai.

4 DR. SCHEIN: No response

5 DR. BULLIMORE: We have a response.

6 CHAIRMAN WEISS: A short one, I
7 anticipate.

8 DR. BULLIMORE: It should be handled in
9 the labeling, and it is not unusual for a monovision
10 contact lens patient to have a pair of occasional
11 distance glasses that they put on, say, if they were
12 driving home in bad weather conditions.

13 Just to point out that the combined
14 binocular distance acuity was excellent in these
15 patients. They did have the benefit of two eyes, were
16 not blurred in one eye and not allowing them to use
17 the other eye.

18 DR. SCHEIN: Somehow in the survey the
19 distance vision improved dramatically in your survey.

20 DR. GORDON-MEYER: I think that had to do
21 with the correction, that we are actually very
22 successful in the 38 hyperopic eyes.

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1 DR. SCHEIN: Oh, hyperopic eye?

2 DR. GORDON-MEYER: Right. So they had an
3 average planned refractive change of about two
4 diopters.

5 CHAIRMAN WEISS: Dr. Macsai?

6 DR. MACSAI: Can you give us some
7 information on the patients that are on slide 75 and
8 76 who preoperatively seem to have J5 or better?
9 There's even some patients who are J2 or J1 or better,
10 J3 or better.

11 I am curious on a number of issues. One,
12 why did they have this done? Two, what happened to
13 them? Three, what was their specific regression rate?
14 That's question number one.

15 Question number two is: If we are saying
16 that this is not stable and it is temporary, and we
17 are treating an average of 55-year-olds -- I guess
18 maybe this question goes to Dr. Durrie -- how do you
19 do IOL calcs in these patients, should they develop
20 cataracts within five years after their treatment or
21 how do you predict your PRK treatment, if they are not
22 stable?

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1 DR. DURRIE: Well, in general, the "not
2 stable" is something that we are agreeing with in the
3 label, but these patients are quite stable, because
4 when we looked at the data, all of the patients who
5 were J3 or better at six months -- all of them in the
6 cohort were still J3 or better at 12 months.

7 I just think that I like the fact that we
8 are saying temporary, but I don't want to
9 overemphasize. It's not like these people go up and
10 down all over the place. You know, they have a
11 tendency to maybe drift slightly over a long period of
12 time.

13 I IOL calculation, I think, is a very
14 important issue, because these patients are older. So
15 we have been looking at this with the technology of a
16 topography refraction, K readings. I have yet to have
17 a patient who has had cataract surgery, but I've been
18 looking at it, and it doesn't appear that there is a
19 difficulty like we see in the myopic flattening that
20 really throws our tests off with the hyperopic
21 steepening.

22 I have had hyperopic LASIK steepened

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1 corneas that have gone on to cataract surgery and have
2 not had any difficulty at all choosing the IOLs in
3 those patients compared to myopes. So I am not as
4 worried about the steepening as our past history is,
5 but again we are going to have to label for that one,
6 too, because we don't know.

7 DR. MACSAI: Can you get the data from the
8 first question?

9 DR. DURRIE: Yes. The first question, I
10 think we will have to dig for the data a little bit,
11 but why would somebody who is J3 preoperatively have
12 this procedure?

13 This was a very defined entrance criteria
14 into the study. They had to be of this age and have
15 this problem and everything else, and there were
16 people that fit. They were candidates, and they fit
17 within the criteria. So we did do them.

18 The interesting thing is they did
19 extremely well. Matter of fact, those patients who
20 had a little bit more near vision did even better than
21 the patients who didn't. I think it gets back to
22 Woody's comment a little, or somebody's comment about

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1 -- I think it was Tim's -- about when can you do this.

2 I don't really know, but I think that my
3 feeling is some of the patients that do it younger,
4 earlier in the future, that have still more residual
5 accommodation may do even better. But I think that's
6 wait to be seen.

7 CHAIRMAN WEISS: If Mr. McCarley or Ms.
8 Such has any brief questions -- If they are just
9 comments, I would respectfully --

10 MR. MCCARLEY: This is Rick McCarley, the
11 industry rep. Sorry I have a cold. I hope you can
12 hear me okay. Just one question.

13 I don't have access to the clinical data.
14 So I'll ask a more general question. Since this
15 procedure can be done with available equipment on the
16 market now, what percent or number of patients do you
17 think out of the 25,000 procedures that have been done
18 -- do you think people have actually done this outside
19 your study? In other words, is it a common thing,
20 once it became available, that people just started
21 recognizing that it was something that was a
22 potential?

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1 DR. DURRIE: I would say that from the
2 doctors I have talked to, greater than 50 percent of
3 them that do CK on a regular basis use it for
4 monovision in one eye.

5 CHAIRMAN WEISS: Ms. Such, did you have
6 any questions?

7 MS. SUCH: Let's see if I can do this and
8 bend at the same time.

9 Given that -- I was going to mention a
10 computer screen, since I am a technology person.
11 Given that computer screens, the -- as we call them,
12 the font sizes, as you call them the J factors --
13 range from J1 to J4, depending on the size of the
14 screen, the contrast and resolution, I'm wondering:
15 When you talk about that patients were asked about do
16 they have problems with the computer screen, whether
17 they were done in center and, at the same time, on
18 their patient reporting form were they asked that same
19 question while they were in front of the same computer
20 screen?

21 Your difference between the laptop and an
22 18 inch monitor could be the difference between J1 and

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1 J3 to J4.

2 DR. DURRIE: I think that it is a great
3 point, and no, we did not ask them whether they --
4 When we asked the subjective question, can you read
5 the computer, we did not control for can you read the
6 same computer you could read before surgery. I think
7 it is a very important point.

8 These questionnaires really need to look
9 at these issues in the future, because near vision
10 tasks can certainly change with the type of print that
11 you are looking at. But we did not control for that.

12 CHAIRMAN WEISS: Okay. We have about
13 three more minutes. We have three more questions. So
14 what I would ask the sponsor is, if you could answer
15 these questions in two sentences, not paragraphs, I
16 would really appreciate that; and if the people asking
17 the questions could ask them in one sentence, not
18 paragraphs.

19 So with that introduction of mine, Dr.
20 Bandeen-Roche.

21 DR. BANDEEN-ROCHE: This is just a follow-
22 up to the data that I requested. I regret if I was

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1 unclear. What I'd like is a cross-tabulation, six
2 months to 12 months of the overall do you wear glasses
3 or spectacles question, please. I would be happy to
4 receive that during the break. I can read it into the
5 record.

6 CHAIRMAN WEISS: Thank you so much.

7 DR. GORDON-MEYER: That is what we
8 provided.

9 CHAIRMAN WEISS: Okay, you'll provide it.
10 That's a good sentence.

11 DR. GORDON-MEYER: That is what I just
12 provided.

13 DR. BANDEEN-ROCHE: No, it's not quite,
14 because you gave for all tasks, not the overall
15 question. You gave "do you have difficulty" -- "do
16 you wear glasses for all tasks, 13, 14, 15 percent?"
17 I also want a cross-tabulation, not just the
18 consistent cohort, six to 12 months. Thank you.

19 CHAIRMAN WEISS: Okay. That's elucidated.
20 Dr. Grimmett had two questions which I think were
21 important. I'll read, and these actually probably
22 could be done in a sentence or two.

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1 I think, Dr. Durrie, you had mentioned 90
2 percent retention at what year. Dr. Grimmatt and I
3 also would like to know retention of what? Are you
4 talking about retention of uncorrected vision? Okay,
5 you got out of that one. What was that?

6 DR. GORDON-MEYER: It was a calculation
7 that was requested by FDA for initially labeling for
8 the hyperopia PMA and now for this. So the
9 calculation is of the refractive effect.

10 CHAIRMAN WEISS: So 90 percent -- So if
11 you intended to correct a +2.00, at 12 months down the
12 line you would have 90 percent of that 2.00 corrected?

13 DR. GORDON-MEYER: I am looking here to my
14 colleagues from Refractec just to confirm.

15 DR. GRIMMETT: Does that take into account
16 the original overshoot? You're talking about what
17 your target was.

18 DR. GORDON-MEYER: No. From six to 12
19 months.

20 DR. GRIMMETT: That's from six to 12
21 months? You only lose 10 percent more from six to 12
22 months?

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1 DR. GORDON-MEYER: Correct.

2 DR. GRIMMETT: What do you lose overall
3 from the start?

4 CHAIRMAN WEISS: From zero to 12 months?

5 DR. GRIMMETT: Do you lose a third?

6 DR. GORDON-MEYER: I don't have the answer
7 to that. We can get it. Mark has the answer.

8 DR. BULLIMORE: It's tough, because
9 there's initial overshoot. There is initial
10 overcorrection. So it would be like hindsight, you
11 know, what is the change initially to whatever. So
12 it's difficult. I think it is more prudent to think
13 about what goes on from three to six, six to 12, 12 to
14 twenty-four.

15 CHAIRMAN WEISS: What would you lose from
16 three to six?

17 DR. BULLIMORE: Three to six -- The change
18 in effects, which are presented in the tables for you,
19 is about actually all the way from three months out to
20 12 months is about .03 to .04 diopters per month.
21 Those are the numbers that are in the tables.

22 CHAIRMAN WEISS: We'll calculate out.

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1 DR. GRIMMETT: If at some point later
2 somewhere after lunch you could tell me, of the total
3 surgical effect you get, how much you actually lose at
4 the longest time period that you have. I did the
5 original review of the PMA a couple of years ago, and
6 I would like to know if you have longer data or give
7 me a sense of what you are losing.

8 DR. DURRIE: We would be happy to provide
9 you with what you want.

10 CHAIRMAN WEISS: And I thank you for
11 staying on track. So with that, I am going to thank
12 the sponsor, and they can move back from the table,
13 and we will now go on to the FDA presentation.

14 We digress. My apologies.

15 MS. CALLAWAY: Dr. Beers was going to
16 defer in the interest of time.

17 Good morning. I am Jan Callaway, the FDA
18 Team Leader for this application. Since the company
19 has already introduced the device, I have just a few
20 brief comments.

21 First, I want to thank the Panel for
22 reviewing and discussing this application today, as

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1 well as the primary reviewers, Dr. Andrew Huang and
2 Dr. Timothy McMahon, for their expertise.

3 I want to commend the sponsor for being so
4 responsive to all FDA and Panel review questions and
5 concerns.

6 The FDA team responsible for Supplement 5
7 included Dr. Sheryl Berman, medical officer and
8 clinician; Mr. T.C. Lu, statistician; Ms. Carol
9 Clayton for review of patient labeling; and Ms. Pam
10 Reynolds for bioresearch monitoring. I would like to
11 thank them for their diligent work, and I would like
12 to introduce Dr. Sherri Berman who will present the
13 areas for which your input is being requested today.

14 DR. BERMAN: Good morning. Today the
15 Panel members are being asked for their clinical
16 judgment as to whether the PMA study outcomes provide
17 reasonable assurance of safety and effectiveness for
18 the indication that is being requested.

19 In my presentation this morning, I would
20 like to highlight a few issues which I think warrant
21 Panel discussion to make their determination.

22 Refractec is currently requesting approval

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1 for the following indication: Temporary induction of
2 myopia, -1.00 to -2.00 diopters, to improve near
3 vision in the non-dominant eye of presbyopic hyperopes
4 or presbyopic emmetropes, via spherical hyperopic
5 treatment of up to 3.00 diopters in patients 40 years
6 of age or greater with a documented stability of
7 refraction for the prior 12 months as demonstrated by
8 a change of less than a half diopter in spherical and
9 cylindrical components of the manifest refraction, and
10 with less than or equal to .75 diopters of cycloplegic
11 refractive cylinder and with a successful preoperative
12 trial of monovision or history of monovision wear --
13 that is, the dominant eye corrected for distance
14 vision and the non-dominant eye corrected for near
15 vision.

16 In April of 2002, Refractec received FDA
17 approval for conductive keratoplasty for .75 to 3.00
18 diopters of spherical hyperopia. The approved
19 surgical procedure, treatment patterns, and magnitude
20 of refractive correction are the same in the requested
21 indication today. However, the patient population and
22 refractive target differ.

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1 The proposed treatment is for presbyopic
2 emmetropes and hyperopes targeted to myopia rather
3 than spherical hyperopes targeted to emmetropia, as in
4 the original PMA.

5 The creation of monovision is a widely
6 accepted method for the management of presbyopia.
7 This PMA supplement is the first time a monovision
8 indication has been requested for an ophthalmic
9 surgical device.

10 Accountability is summarized in these
11 tables, and is identical to the accountability that
12 was acceptable in the original PMA for the treatment
13 of hyperopia. For the record, I'd just like to
14 indicate that the sponsor has updated the original PMA
15 labeling with 24 month study outcomes and has
16 indicated their willingness to do so for this PMA
17 supplement for monovision.

18 I have also provided the distribution of
19 eyes for the various spot patterns as performed in
20 this PMA study. Only four eyes were treated with the
21 8-spot pattern, and a relatively similar number for
22 the other three spot patterns. Just keep the small

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1 number for the 8-spot pattern in mind when you are
2 looking at the rest of the data tables.

3 For the PMA cohort, given the relatively
4 small magnitude of the intended correction, accuracy
5 of MRSE is less than ideal. As you can see from the
6 first table, at six months 24 percent of subjects were
7 undercorrected by more than 1.00 diopter. This was 16
8 percent at 12 months.

9 A significant proportion of
10 undercorrection can be attributed to the 32-spot
11 treatment pattern, as indicated on the second table
12 where 59 percent of those eyes treated with 32 spots
13 were undercorrected by more than a diopter at six
14 months, and 63 percent at 12 months. The numbers for
15 the other three spot patterns are significantly lower.

16 The sponsor, I just want to indicate, in a
17 very recent submission reanalyzed the data, excluding
18 those eyes treated with 32 spots, and the reanalysis
19 indicates a significant reduction in the proportion
20 undercorrected.

21 Whereas, 24 percent were undercorrected by
22 more than a diopter at six months for the overall

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1 cohort, this dropped to eight percent when you exclude
2 eyes with the 32-spot treatment. It drops to nine
3 percent at nine months and six percent at 12 months.
4 Similarly, zero percent of eyes were undercorrected by
5 more than 2.00 diopters with the exclusion of the 32-
6 spot treatment.

7 Protocol predetermined target endpoints
8 that were set by the sponsor were met or approximated
9 for the overall cohort for accuracy. However,
10 Refractec performed statistical modeling to address
11 the impact of age, baseline refractive status of
12 emmetropia or hyperopia and spot pattern on their
13 effectiveness outcomes.

14 While age was not found to be predictive
15 of outcome, the 32-spot pattern was associated with
16 lower accuracy. This was most clearly manifested in
17 older patients and in hyperopic ones. The effective
18 of age was concluded to be confounded by spot pattern,
19 in that older subjects would require larger near add,
20 and these had the largest relative proportion treated
21 with 32 spots.

22 As you can see in the second table, there

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1 is a significant dropoff in accuracy observed for the
2 32-spot treatment group.

3 Again, the sponsor recently submitted data
4 excluding those eyes treated with 32 spots and, as
5 predicted, there was a significant improvement in the
6 study outcome for accuracy. They have provided all
7 those slides in their presentation. So I won't repeat
8 them here, but I will just point out some of the
9 differences.

10 At six months this 49 percent increased to
11 64 percent within a half diopter, and at 12 months the
12 improvement was not as significant, 61 percent
13 improved to 66 percent.

14 Within 1,00 diopter the 76 percent at six
15 months improved to 92 percent, right here, and the 84
16 percent at 12 months improved to 94 percent within
17 1.00 diopter, excluding the eyes treated with 32
18 spots.

19 I did a similar analysis here, just
20 pointing out the differences when you stratify by age.

21 Relatively similar number of patients in the three
22 bins, and you can see that there is a significant

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1 dropoff in the accuracy in the older patients, again
2 attributed to the proportion that required the 32-spot
3 treatment.

4 I do want to point out that, of the 45
5 subjects treated in that age group, 41 of them did
6 receive full correction for near.

7 The sponsor indicates their believe that
8 near uncorrected acuity that is achieved in the study
9 is reasonable. However, I do want to point out that
10 22 percent of subjects had final uncorrected vision of
11 J5 or worse, both at 12 months and at six months.

12 Of note, I also want to point out that
13 there appears to be a trend of decreasing proportion
14 of eyes with an outcome of J1 over time, 45 percent at
15 six months, 34 percent at 12 months.

16 Also here, you can see a significant
17 dropoff in the uncorrected acuity for the 32-spot
18 treatment pattern, 59 percent for the 24 spot and 32
19 percent for the 32 spot treatment, J1 or better.

20 Since the 32-spot monovision can currently
21 be done as an off-label procedure, and the sponsor
22 indicates that that is very commonly done at this

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1 time, the sponsor has indicated their wish to provide
2 labeling information to patients and physicians.

3 Again, in their most recent submission
4 they reanalyzed data excluding eyes treated with 32
5 spots, and the results indicate a moderate improvement
6 in near uncorrected acuity outcomes, not as
7 significant as the improvement in the accuracy
8 outcomes.

9 The number of eyes J1 or better improved
10 at six months from 45 percent to 51 percent, and at 12
11 months from 34 percent to 39 percent. The J3 or
12 better outcome improved from 78 percent at six months
13 to 82 percent, and improved from 78 percent at 12
14 months to 81 percent.

15 Again, I provided a similar table here
16 stratifying the outcome by age. Again you can see a
17 dropoff in the uncorrected near outcome with the older
18 age group.

19 The sponsor indicates their belief that,
20 despite its limited effectiveness, the 32-spot
21 treatment, quote, "still provides adequate levels of
22 J3 or better." Here you can see that that level is 66

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1 percent at month six.

2 FDA also looked at a comparison of
3 effectiveness for the hyperopes and emmetropes, since
4 this is the first time that this procedure would be
5 used to treat emmetropic patients. This
6 stratification reveals that effectiveness endpoints
7 are clearly dissimilar between the two cohorts.

8 The sponsor attributes this difference to
9 the disproportionate number of eyes in the hyperopic
10 cohort that received a 32-spot treatment. I indicated
11 down here that 65 percent of hyperopes received 32
12 spots versus only eight percent of emmetropes, and
13 that the remainder of the hyperopes all received 24-
14 spot treatment.

15 As you can see, there is a significantly
16 lower accuracy for the hyperopes as compared to the
17 emmetropes, and a somewhat lower J3 uncorrected near
18 outcome, though not as significantly lower than the
19 accuracy outcome.

20 Regarding the need for spectacle use after
21 the procedure, a large proportion of subjects who
22 underwent the procedure are unable to read without

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1 glasses. The study initial questionnaire that was
2 given to all patients treated indicates, when asked
3 the question "Do you wear spectacles of contact lenses
4 for near in the treated eye for reading?" 40 percent
5 of patients indicated yes at month six and 55 percent
6 did so at month 12.

7 The sponsor -- I just want to clarify --
8 also partway through the study, as they have
9 indicated, initiated a second questionnaire to more
10 clearly elucidate the near tasks that patients
11 required spectacles for.

12 FDA noted several issues that raised
13 question about the validity of drawing conclusions
14 from this questionnaire. Firstly, the small number of
15 patients: There were only 22 patients at month six
16 and 16 at month 12. Secondly, it is unclear. One of
17 the questions asked patients about whether they could
18 see fine print, and it is not defined what fine print
19 is, how this is different from a magazine print or a
20 newspaper print.

21 Also, it asks patients what can you see
22 without glasses. Again, "see" is not defined, and it

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1 is unclear to me whether this means see clearly, see
2 blurry or what. I think the potential for different
3 interpretations is there.

4 Finally, there were several concerns about
5 recall bias, since the patients were not given the
6 questionnaire preoperatively and had to recall what
7 they were able to see before they had the procedure.
8 So I'll ask you to take those concerns into your
9 deliberations regarding labeling.

10 In their most recent response, again the
11 sponsor stated that the goal of monovision is to
12 improve functional near uncorrected vision at a
13 patient's habitual near point demand, and that
14 complete independence from spectacles is not a goal of
15 this procedure and is unrealistic.

16 It is important to note that excluding the
17 32 eye treatment cohort, the outcomes for this
18 questionnaire did not change in a clinically
19 significant fashion; whereas, 40 percent indicated
20 that they wore spectacles for reading at six months
21 and 55 percent at 12 months, excluding the eyes
22 treated for 32 spots, 38 percent indicated that they

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1 wore spectacles for reading at month six and,
2 similarly, 55 percent indicated that they wore
3 spectacles for reading at month 12.

4 I'll provide some brief information for
5 cylinder outcomes, just for your information. Induced
6 cylinder at least 1.00 diopter, 11 percent at month
7 six and nine percent at month 12. Whereas, none of
8 the eyes had an absolute magnitude of cylinder more
9 than .75 diopter at baseline, 29 percent did so at
10 month six, and 21 percent did have this level of
11 cylinder at month 12.

12 The sponsor was asked to perform
13 comparative analyses to assess the clinical impact of
14 induced cylinder, and these analyses appear to
15 demonstrate no clinically significant compromise in
16 near uncorrected acuity.

17 I'll summarize here the FDA questions for
18 the Panel deliberation today. The first question is:
19 Is the length of follow-up sufficient to demonstrate
20 reasonable assurance of safety and effectiveness for
21 the proposed indication?

22 Number two: Is the magnitude of induced

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1 cylinder and the associated effect on uncorrected
2 acuity clinically acceptable for the proposed
3 indication?

4 Number three: Is the rate of
5 undercorrection more, more than a diopter, clinically
6 acceptable? Are there any subgroups of the PMA cohort
7 for which this outcome is not acceptable.

8 Number four: Are the reduced accuracy to
9 target refraction and poorer near uncorrected acuity
10 outcomes, both monocular and binocular, reasonable to
11 justify the risk of elective surgery with "temporary"
12 results; and is the near uncorrected correction
13 achieved clinically useful in the following groups:

14 (a) Eyes treated with 32 spots?

15 (b) Subjects greater than 55 years of age?

16 (c) Hyperopic patients?

17 (d) Any other populations or any other
18 magnitude of refractive correction?

19 If the answer to any of these is no, how
20 do you suggest the indication and/or labeling be
21 modified?

22 Number five: Do the spectacle dependence

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1 rates for near activities support approval for the
2 requested indication in a presbyopic population?

3 Number six: Do the safety and
4 effectiveness data support approval for the requested
5 indication? If not, what indication does the data
6 support?

7 Finally, I'd like to say that adequate
8 physician and patient labeling are critically
9 important to prevent unrealistic expectations. Do you
10 have any additional labeling recommendations, either
11 descriptive text or data? Should additional data
12 tables be added to the physician and/or patient
13 labeling?

14 Finally, I just wish to point out three
15 other short points regarding things that came up in
16 the sponsor's presentation.

17 The first is that reduced stereopsis is
18 known to be an effect of monovision correction. The
19 sponsor claims from their study data that depth
20 perception is unchanged from baseline.

21 I just want you to note that this
22 determination is based on a comparison to preoperative

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1 depth perception with contact lens monovision wear,
2 not with non-monovision spectacles.

3 The second comment I would like to make is
4 that the sponsor was asked to perform a calculation to
5 indicate in the labeling what percent of eyes retained
6 their initial correction at one year.

7 They performed it similarly to how they
8 calculated it for their initial original PMA, and they
9 concluded 90 percent retention at one year. I just
10 want to clarify that this calculation was defined as
11 maintaining effect by comparing the six month's
12 outcome to the 12 month outcome and calling any eye
13 that retained within .50 diopter of the six-month
14 outcome as maintaining initial effect.

15 Finally -- sorry for this long winded
16 presentation here -- I just want to indicate regarding
17 subjective questionnaire that there were many
18 subjective symptoms reported as, quote, "none" pre-op
19 that significantly increased in the percentage of
20 "none" post-op. I hope I made that clear.

21 A few of them were transient, such as
22 gritty feeling, but many of them had long term changes

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1 in the reports of "none." I will just briefly run
2 through them.

3 Light sensitivity, 81 percent of people
4 reported no light sensitivity pre-op, whereas only 75
5 percent did at month 12.

6 Dryness: 85 percent to 76 percent.

7 Glare: 93 percent to 71 percent.

8 Halos: 95 percent to 75 percent.

9 Blurred vision: 79 to 68 percent.

10 Double vision: 97 percent had none pre-
11 op, whereas only 80 percent had none at month 12.

12 Fluctuation in vision: 93 percent none
13 pre-op, 68 percent none at month 12.

14 Several different iterations of variation
15 in vision, all with similar decreases and,
16 interestingly, night vision driving problems, 84
17 percent had none pre-op, 81 percent had none at month
18 twelve.

19 That concludes my presentation.

20 CHAIRMAN WEISS: Thank you very much. If
21 that concludes the FDA presentation, what we will do
22 is break for lunch for exactly one hour. Please be

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seated so we can be ready to begin at that moment.

(Whereupon, the foregoing matter went off
the record at 12:07 p.m.)

- - -

1 effectivity of this treatment is, especially in view
2 of the fact that, talking about plus and minus one is
3 fairly irrelevant when you are treating a +1.00.

4 Some of us might even have an effective
5 treatment while we are sitting here, because we are
6 within ± 1.00 , although we actually don't even have to
7 have the treatment done.

8 So in any case, would you be able to
9 address that?

10 DR. BERMAN: I'll try. Basically, as I
11 had pointed out in my short presentation, you know,
12 based on the limited magnitude of treatment, FDA felt
13 that the accuracy of the correction was less than
14 idea.

15 One of the deficiencies that was
16 communicated to the sponsor was a request to perform
17 an analysis to indicate in the labeling or to provide
18 in the labeling a patient information about how much
19 correction can be anticipated at the one-year time
20 point, since that is the extent to which this PMA has
21 data submitted at this time.

22 Only about a week or two ago, we received

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1 a response. If the Panel feels the response is
2 adequate as I presented at the very end of my
3 presentation when I described how they did the six-
4 month to the 12-month comparison with the definition
5 of maintaining effect being plus or minus a half-
6 diopter -- If you feel that is acceptable, then there
7 is nothing more to say. However, if the Panel -- and,
8 you know, FDA will have their own issues that we will
9 take up with the sponsor as well afterwards, but today
10 we are here to hear the Panel's clinical judgment.

11 So if the Panel decides that that is not
12 acceptable and they want additional description or an
13 additional analysis or type of calculation to be
14 performed, that can be made a condition of approval or
15 a labeling recommendation or however you would like to
16 word that.

17 CHAIRMAN WEISS: They had submitted two-
18 year data as well, 24-month data. I don't recall
19 seeing that? Did I see that?

20 DR. BERMAN: They don't have 24-month
21 data.

22 DR. BEERS: The 24-month data -- Wasn't it

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1 referring to the original PMA that they recently
2 submitted?

3 DR. BERMAN: Correct. Right. The
4 original PMA. The only reason I brought that up was
5 to indicate that they have indicated to us their
6 willingness -- Although they only have six and 12
7 month data, that they have indicated their willingness
8 to update this labeling with 24-month data when it
9 becomes available, just as they did for the original
10 PMA. And they did do that.

11 DR. GRIMMETT: I am strongly in favor of
12 that, because that is a relevant issue, even though it
13 comes from a different PMA. I would be specifically
14 interested in the graph of, on the X axis, time and,
15 on the Y axis, MRSE and diopters at every time point.

16 That way, the reader can interpret what he wants to
17 know, not only six months to 12, but you can analyze
18 anything you want, Day One to three months. You can
19 see how it levels off and see how it asymptotes.

20 DR. BERMAN: And would you want just one
21 line or -- You might want to discuss this, whether you
22 would want it differentiated between emmetropes and

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1 hyperopes or different cohorts or what have you.

2 CHAIRMAN WEISS: Any other -- Are you
3 satisfied? Any other questions from Panel to FDA?
4 Thank you.

5 We will then move on to the primary panel
6 reviewers. Dr. Huang is first, followed by Dr.
7 McMahon.

8 DR. HUANG: Good afternoon. Dr. Weiss and
9 fellow Panel members, I would like to present my
10 review regarding this PMA P010018/Supplement 5.

11 First, I would like to thank my fellow
12 reviewers, Dr. Berman and Dr. McMahon, for their
13 detailed review. That made my job much easier.

14 As we all know that this device has
15 previously received approval for hyperopic indications
16 in April 2002. However, the off-label use of the
17 conductive keratoplasty for astigmatism as well as the
18 monovision has been prevalent. Yet prior to
19 submission, the efficacy and safety of this device for
20 monovision remains unclear.

21 I would like to commend sponsor for their
22 willingness to subject their data for our scrutiny.

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1 First, I would like to present the safety
2 issue. As we heard this morning, a cohort of 150
3 patients with 188 eyes were presented, of which 150
4 eyes were treated for near and 38 eyes previously had
5 been treated for distance.

6 The safety profile is similar to the
7 hyperopic study and raised no additional concern.
8 However, the patients were treated with 24 or less
9 spots. Greater than 90 percent of them were within
10 1.00 diopter. Conversely, when the patient was
11 treated with 32 spots, only 45 percent or less than 45
12 percent of the patients -- they were only within 1.00
13 diopter.

14 In this group of grossly undercorrected
15 patients, there is a lack of information regarding
16 future re-treatment or management options for
17 undercorrection. Of note, 34 percent of the patients
18 with loss of one line best spectacle corrected visual
19 acuity at distance at one month -- This is an alarming
20 portion of the patients that with initial post-
21 operative visual compromise.

22 The question related to their depth

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1 perception and quality of life remain unanswered in
2 this submission.

3 There is a significant number of protocol
4 deviations, and some of it will be addressed. Dr.
5 Mathers' question earlier today might be able to get
6 some insight from here.

7 One site had 16 patients with additional
8 intraoperative spots to decrease the CK-induced
9 astigmatism, of which 11 were used for near vision.
10 As shown in this stratification, one patients in the
11 24-spot treatment group out of 51 had additional
12 enhancement or treatment to reduce astigmatism. Ten
13 of these patients in the -- In 52 of the patients
14 treated with 32 spots had to use this -- ten patients
15 had intraoperative spots to decrease the astigmatism.

16 It is very perplexing to this reviewer
17 that ten of these patients were originally excluded in
18 the initial analysis. However, in their amendment
19 submitted in January, they were included in the
20 efficacy study. Furthermore, there were only four
21 patients treated with eight spots.

22 When we look at the safety issue, we also

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1 like to look at the clinical efficacy. First, there
2 are two parameters for this reviewer to rely upon.
3 One is the accuracy to the refractive targets.

4 As we all know, FDA has provided
5 predictability guidance for myopic refractive lasers
6 in which 75 percent of the patients is expected to be
7 within 1 diopter of target. Fifty percent of the
8 patients is expected to be within .5 diopter of
9 target, and I think this is used by the reviewer, used
10 by the sponsor.

11 Second, uncorrected near visual acuity
12 should be our gold standard, since this is the
13 treatment for monovision. Unfortunately, there is no
14 established FDA guidance for this parameter. However,
15 the sponsor willingly submitted a criterion.

16 They indicated 75 percent of the patients
17 with uncorrected visual acuity at distance should be
18 J3 or better. As a reviewer, as a potential consumer,
19 I would like to propose that 75 percent of the
20 patients need to have a near uncorrected visual acuity
21 of J3 or better.

22 I also would like to -- This is for their

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1 functional vision. I will also like to propose 50
2 percent of the patients ideally should have an
3 uncorrected visual acuity at near at J1 or better --
4 that is a 20/25 equivalent -- for their reading.

5 Upon stratification of their initial
6 submitted data, there were 24 percent of the patients
7 was grossly undercorrected by greater than 1 diopter
8 at six months. Sixteen percent of them were
9 undercorrected by 12 months.

10 When we stratified them by spot sites, the
11 amount of treatment, 59 percent of the patients
12 probably was grossly undercorrected at six months in
13 the 32-spot treatment group, and this incidence
14 increased to 63 percent in 12 months.

15 Looking at those ten patients excluded and
16 then later included in the study, potentially those
17 were the patients -- they had a higher amount of
18 induced astigmatism and, therefore, that they were
19 excluded from the study. So if we were including
20 those patients to review the entire aspect of the
21 treatment parameters, the 32-spot certainly has a
22 significant amount of induced astigmatism as well as

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1 reduced efficacy.

2 Again, you know, if we stratify this data
3 by the sponsor as well as by Dr. Berman, we can see
4 that patients, when treated with 24 spots or less at
5 any given point, that they had less than -- within 5
6 diopters -- half a diopter of target is about 66
7 percent, and the patients within 1 diopter of
8 treatment target is about 90 percent in the 24 spots
9 or less. Both of these findings met FDA guidance.
10 However, if you look at the 32-spot treatment, only
11 about 25 percent of the patients are within 1 diopter
12 of treatment at six months, nine months and 12 month
13 spots.

14 The incidence further decreased to 45
15 percent of the patients that were only within 1
16 diopter of target, and that incidence further
17 decreased toward 12 months.

18 So if we would look at the -- stratified
19 within 1 diopter of target at six months by the age
20 group, you can see the patients with 16 and 24 spot
21 treatment, that regardless of the age group, they were
22 always in FDA guidelines. Greater than 75 percent of

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1 the patients met the criteria. However, 32-spot
2 treatment is not the case.

3 Thirty percent to 50 percent of the
4 patients actually is only within 1 diopter. So the
5 majority of the patients, greater than half of the
6 patients, were outside the 1 diopter range with 32
7 spots. So this did not meet the FDA criteria.

8 So if we -- Finally, using the near vision
9 as our gold standard for the treatment, if the patient
10 can see J3 or better vision, 80 to 85 percent of the
11 patients with 24 spots or less treatment can achieve
12 that goal, which meets the FDA guidance. However, if
13 you use the 32 spots -- I'm sorry, which meets the
14 sponsor's guidance. If you use the 32-spot treatment,
15 none of it exceeds 70 percent. So it did not even
16 meet the sponsor's criterion.

17 For the consumer or for the reviewer's
18 criteria, only 24 spots at six months reached 51
19 percent. So that is the only treatment, to me, that
20 is satisfactory.

21 In summary, I think the reviewer's data
22 has met FDA guidance regarding the safety, with no

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1 patient loss of best spectacle corrected visual acuity
2 greater than two lines. The efficacy, however, is
3 only temporary, and this monovision is not reversible.

4 The data has indicated that 40 percent of
5 the patients resume full time reading aids at six
6 months, and 55 percent of the patients resume full
7 time reading aids at 12 months, and the 32-spot
8 treatment failed to meet FDA guidance and sponsor's
9 goal.

10 I took a look at the risk/benefit ratio.
11 As a consumer, as a reviewer, I certainly would like
12 to look at cost versus benefit ratio. For emmetropic
13 hyperope -- I'm sorry, for emmetropic presbyope, I
14 would like to think that I can use the over-the-
15 counter readers which cost about \$15 per pair.

16 If I have to buy three pairs a year, it is
17 going to cost me about \$45, and that would probably
18 last me for a year, because my presbyopic change may
19 shift. However, with the monovision by conductive
20 keratoplasty, no spectacle correction for one year --
21 that will cost me at least \$1500.

22 For me, the best analogy for this kind of

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1 expanded indication is probably to eyeliner versus
2 eyelid tattooing.

3 This reviewer also has a great reservation
4 and concern regarding the premature advertisement of
5 yet unapproved indications that I just received in my
6 office, that there is a training course for people to
7 sign up since January 17 to this kind of procedure for
8 their patients.

9 Granted, this has been indicated -- The
10 procedure has been used for off-label, but I think it
11 is somewhat disrespectful to the FDA to have this
12 premature advertisement.

13 So the recommendation by this reviewer,
14 based upon the limited efficacy and the safety, I
15 would like to urge the Panel members to consider
16 restriction of this indication to induction of
17 monovision via spherical hyperopic treatment up to
18 2.25 diopters using 24 spot sites. This is in
19 contrast to the previous approved indication, up to
20 3.00 diopters and 32 spots in the non-dominant eye.

21 Also, sufficient labels should be provided
22 regarding a warning against 8-spot treatment. Thank

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1 you very much for your attention.

2 CHAIRMAN WEISS: Thank you very much, Dr.
3 Huang. I guess I'll stick to my eyeliner.

4 Dr. McMahon.

5 DR. McMAHON: Thank you. I am going to
6 sound like a broken record from the previous
7 presentation.

8 First of all, I would like to thank the
9 sponsor for presenting a nice, clean study presented
10 in clear, understandable and organized format. IT
11 makes it so much easier to review and get to the heart
12 of the issue in terms of safety and efficacy when
13 these PMAs are presented in this format, and I want to
14 thank them personally for that, and particularly since
15 it was over the holidays that we had to read this.
16 The fact that I didn't have to agonize over the PMA
17 like the folks from yesterday, I had an easier job.

18 A few comments: Accountability was
19 excellent. This has been commented on. One issue is
20 enrollment was highly skewed toward one site. Even
21 though GEE modeling indicate this is not statistically
22 biasing, the numbers at the other sites were low

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1 enough that I have some questionable faith in that
2 statistical modeling.

3 As you know, there are lies and lies and
4 bigger lies where there are statistics. So I am
5 wondering if this might be an issue. However, I have
6 no evidence to go beyond that.

7 The subjects were almost exclusively
8 white. This is a trend in refractive surgery, and
9 mostly female. These numbers are almost identical to
10 other studies.

11 The protocol deviations were minor and
12 small in number, and of not great importance to me.

13 From a safety perspective, let's deal with
14 this first. The key issue has to do with induced
15 cylinder. As you will recall, the target amount of
16 induced cylinder is less than or equal to five percent
17 of the cohort, would be 2.00 diopters or greater, and
18 none of the cases in this particular PMA demonstrated
19 that.

20 Of some concern is the fact that there
21 are, at months one, six, and 12 months, 28 percent, 11
22 percent and 9 percent had greater than 1 diopter of

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1 induced astigmatism. However, the mean cylinder at
2 baseline was a third of a diopter.

3 It increased a little bit to a little over
4 half-diopter at six months, and dropped another small
5 percentage at 12 months, but this is relatively small
6 compared to the mean baseline cylinder. Collectively,
7 this does not appear to be overly worrisome, to me.
8 However, for those with greater than 1 diopter of
9 induced cylinder, 12 to 14 percent of those lost one
10 line of best corrected spectacle acuity at six months
11 and 12 months respectively.

12 The number of absolute patients who had
13 this type of loss is relatively small, but I do
14 believe this is worth putting in the labeling, and the
15 sponsor agrees to this.

16 Best corrected acuity or distance acuity:

17 The target was less than one percent of the cohort
18 having acuity worse than 20/40, and no eyes exceeded
19 this criteria. Very few eyes had a loss of greater or
20 equal to 2 diopters of best corrected acuity at either
21 far or near, indicating that this, from an acuity
22 perspective, is a safe procedure.

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1 No eyes had greater than 25 millimeters of
2 mercury of increase in IOP. Corneal haze and adverse
3 events were not impressive. Complication rate at
4 eight percent seems high, but the type of
5 complications that they had actually were quite small
6 and, in fact, if you take out the viral
7 conjunctivitis, the number almost drops in half.

8 Therefore, from a safety perspective, I
9 believe that CK for the inducement of near correction
10 appears to be reasonably safe. Two-year follow-up
11 data on induced cylinder and its effect on best
12 corrected acuity seems warranted and, as I understand
13 it, the sponsor is willing to provide that.

14 Efficacy is a little different story, as
15 you have been hearing thus far. You will recall, the
16 FDA guidance for refractive surgery procedures in
17 October of 1996 specified the target rates for end
18 results, since this is for distance correction of the
19 design, 75 percent within plus or minus one diopter
20 and half of those cases being within plus or minus a
21 half.

22 Sponsor and FDA agree that this should be

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1 employed toward intended corrections. An important
2 review in intended corrections is the total amount of
3 correction; whereas, the sponsor's indication is
4 toward achieving between up to one to two diopters of
5 resultant myopia.

6 So patients who are hyperopic by one
7 diopter who you want to achieve a two diopter
8 presbyopic correction needs three diopters of intended
9 correction.

10 For treated eyes for near, for all eyes
11 treated completely for near, the number of patients
12 within plus or minus one diopters can be displayed on
13 the screen as a function of the number of the spots
14 applied. The bold areas stipulate those individuals
15 that don't meet this criteria.

16 As has been mentioned, the criteria for
17 plus or minus one diopter for a total intended
18 correction of three diopters is wide enough to drive a
19 truck through, and in this circumstance with the 32-
20 spot circumstance the treatment does not meet that for
21 any time course.

22 For those to have a tighter criteria,

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1 which I think is a much more reasonable benchmark to
2 look at a plus or minus a half-diopter -- For those
3 between .75 diopters of correction and 2.25, all those
4 eyes met that except for the very low correction
5 numbers at nine and 12 months, and all of the 32-spot
6 corrections. It is important to realize, though, that
7 there were less than a handful of individuals who had
8 eight spots.

9 Plotted otherwise, if you put both of
10 these guys for emmetropic eyes and exclude the
11 hyperopic eyes, all of the individuals in this cohort
12 met the benchmark of plus and minus 1 for all time
13 periods, as did all those for plus and minus 1/2 for
14 emmetropic eyes.

15 It is important to realize, however,
16 though, that the number of spots that are applied is
17 directly related to the native emmetropic or hyperopic
18 correction. In fact, the vast majority of the
19 patients who were emmetropes were treated with 16 and
20 24 spots.

21 If you moved up to the 32-spot character,
22 6, 4 and emmetrope, you had actually only a third of

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1 individuals within plus or minus 1, again a very wide
2 benchmark to shoot for.

3 If you look at the half-diopter, plus or
4 minus 1/2 intended correction, again you have
5 individuals between 8 spots and 24 spots, all meeting
6 this benchmark, but again only a third of those
7 individuals who were treated with 32 spots, but again
8 the number here is quite small.

9 The story is a little different for
10 hyperopic eyes. If you look at the plus and minus 1/2
11 and plus and minus 1, virtually none of these eyes met
12 either one of these benchmarks, if you are a hyperope
13 to start with.

14 All the hyperopic eyes were treated with
15 either 24 spots or 32 spots, and the reason that the
16 hyperopes don't make it is because the 32 spots have a
17 very poor outcome. For those individuals who were
18 hyperopic who had 24 spots, 94 percent were within the
19 plus or minus 1 characteristic, and 67 percent within
20 the plus or minus 1/2. Again, the 32 spot group
21 performed poorly in terms of accuracy.

22 The near visual acuity is an important

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1 adjunct and is sort of the baseline of the benchmark
2 that we are eventually going to have to come to deal
3 with here, because this is what the procedure is for.

4 Sponsor and FDA converged on 75 percent seeing J3 or
5 better at near, and with all eyes included you can see
6 that individuals met this characteristic as an
7 aggregate, though the number of those individuals as
8 you move to smaller font sizes drops off relatively
9 remarkably.

10 Now if you take out the 32 spot group,
11 that number improves about nine percentage points. So
12 that now you get into the upper 80s and low 90s for
13 individuals seeing J3 or better if you take out the
14 32-spot group, and even at the J1 level improve
15 significantly except at the 12 month interval.

16 It is quite evident that there is a decay
17 in response as you deal with finer and finer vision,
18 and that is most likely because at the J1 level you
19 are much closer to threshold. So you are failing off
20 a threshold; whereas, when you are dealing with a
21 patient who has J3 or better who might have a post-
22 operative best acuity of J2, you've got a little slot

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1 to be able to withstand decay in treatment.

2 So actually looking at the finer vision
3 acuity measures, I think, is a better indicator of
4 what is actually happening relative to stability of
5 effect.

6 A few comments: There are very few eyes
7 treated with 8 spots, and sponsor acknowledges this
8 and it is actually small enough that you can't analyze
9 this in any meaningful manner. Therefore, it raises
10 the question of should the application of 8 spots then
11 be removed from the indication for treatment.

12 The intended treatment range, as I
13 mentioned, is between .75 and 3.00 diopters, but the
14 target ranges were virtually almost as large as the
15 treatment range itself. Is this a reasonable target
16 range for this or procedures similar in the future
17 seeking relatively small corrections? I submit to you
18 that it is not.

19 CK for near is not very effective, in my
20 view, when 32-spot treatment regimen is used. The
21 near vision procedure is more effective, therefore, in
22 emmetropes, because the intended correction range is

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1 more suitable for emmetropes than hyperopes, and at no
2 interval did hyperopics meet the plus and minus 75
3 target criteria that was agreed upon.

4 Patient satisfaction: The frequency of
5 change in symptoms -- and I am going to look at those
6 for the worst rather than those for the better,
7 because from our point of view of safety and efficacy,
8 we are looking for the worst side rather than the
9 better side.

10 Symptoms do appear to persist and, in some
11 cases, increase over time. I reference you to my page
12 6 of my report toward that side. However, patients
13 have asked about the terms in terms of quality of
14 improvement, not given the opportunity to say that
15 things are worse, by the way -- it's basically same to
16 better. Thirty-seven percent demonstrated extreme
17 improvement down to moderate improvement of 16
18 percent.

19 If you exclude the 32-spot group,
20 actually, these numbers change very little, which I
21 found quite remarkable. Seventy-nine to 84 percent,
22 depending on the time interval, report being satisfied

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1 or very satisfied, and this actually happens to trend
2 very nicely with those percentage of patients who see
3 J3 or better. Whether that is a statistically
4 significant correlation, I can't say, but it visually
5 is.

6 The sponsor in their latest comments and
7 review -- which, by the way, thank you very much for
8 providing data relative to those with 8, 16 and 24
9 spots, because I think that is where the real story is
10 for this procedure. But the sponsor commented in
11 their response of January indicating that hyperopes
12 and, to a lesser extent, I'll posit, presbyopes will
13 appreciate virtually any improvement in their
14 uncorrected vision.

15 I think that this is important to
16 recognize, in that the more desperate the group, the
17 more likely it is to satisfy them, and I don't think
18 we should overweight the patient satisfaction results
19 because of that. So in that circumstance you could
20 have a procedure that has a relatively modest
21 treatment effect, and you could generate a fairly high
22 satisfaction rate.

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1 Spectacle dependence: Now this is the one
2 that diverges the greatest, and I have not been able
3 to come to resolution on this. Keep in mind, these
4 are individuals that passed a trial of monovision for
5 suitability and tolerance, and that the number of
6 individuals who use spectacles, whether they have all
7 treatment spots included or those excluded where the
8 32-spot treatment is excluded, are virtually
9 identical, and virtually half the patients end up
10 using glasses for reading. I don't have an answer as
11 to why that would be the case.

12 One comment that I think is important for
13 all of us to realize is that threshold acuities near
14 the target size that you want to look at is a very
15 poor benchmark to use to measure near vision
16 performance. We don't read at threshold.

17 You need to have the target that you are
18 looking at to read comfortably and for long periods of
19 time at least two steps larger than your threshold
20 levels. That is well understood in the clinical
21 domain.

22 Now just like you don't want to use all of

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1 your accommodation to be able to read comfortably, you
2 don't want to be operating at a threshold level. So
3 we need to be very careful about establishing what is
4 a reasonable level for near vision for reading
5 performance, and Dr. Huang's notion of adapting some
6 of the distance correction things to multiple steps, I
7 think, actually is a very valid one. The notion of
8 having 50 percent of the group at J2 or better, I
9 think, is actually a very good idea.

10 Conclusions: CK for near appears to be
11 reasonably safe, though I think longer term follow-up
12 concerning loss of best corrected spectral acuity from
13 induced cylinders and the symptoms that have been
14 demonstrated to increase over time seems warranted. I
15 understand that the sponsor is willing to do this.

16 CK as a procedure for near is modestly
17 effective at best. In my view, the 32-spot treatment
18 is not effective and should be excluded from approval
19 for the near indication.

20 The treatment has not been shown to be
21 effective for less than 1.00 diopter of intended
22 effect or 8 spots either, because there is not enough

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1 data here to make that judgment. Therefore, the
2 effective range that potentially could be considered,
3 in my view, is between 2.00 diopter and 2.25 diopter
4 of intended effect.

5 This will have the result of basically
6 eliminating many myopes from the group -- or my
7 hyperopes, excuse me, from the applicable pool of
8 subjects.

9 There also is no data that supports
10 efficacy for re-treatment or intraoperative placement
11 of additional spots, and the sponsor acknowledges
12 that. That is important to make sure that is clearly
13 labeled in patient labeling -- in physician labeling.

14 One additional comment, and Dr. Huang has
15 addressed this to some degree. It doesn't apply to
16 this particular sponsor, but I think for future
17 applications -- there are more of these near things
18 coming. For future device applications, I would
19 suggest that FDA should consider dropping the plus or
20 minus 1.00 target for accuracy procedures in those
21 that are seeking less than 4.00 to 5.00 diopters of
22 treatment effect, and increase the target rate for

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1 plus and minus .50 to .70 percent of intended
2 treatments, and potentially adding numbers similar to
3 the ones that Dr. Huang specified.

4 Thank you for your attention.

5 CHAIRMAN WEISS: Thank you very much. I
6 want to thank both of the Panel reviewers. I would
7 like the sponsor perhaps, if they have the
8 information, to answer the questions that Dr. Mathers
9 and Dr. Bandeen-Roche had posed in the morning, if
10 they could just come forward.

11 I will let the Panel know that this is not
12 the time for any other questions. This is just to
13 answer the two that we had to get further data on
14 before we go to discussion of the FDA questions to the
15 Panel.

16 DR. GORDON-MEYER: Yes. Just briefly, we
17 have provided the cross-tabulation or a cross-
18 tabulation to Dr. Bandeen-Roche. I was not sure if
19 that is what she is looking for but, if not, we can
20 revise.

21 We also looked at uncorrected visual
22 acuity over time for the eyes that had pre-operative

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1 J5 and J3. This was in response to Dr. Macsai's
2 question, the question being how did they do, and did
3 they experience improvement.

4 At three months, six months, nine months
5 and 12 months, they were generally 90, 95 percent, 91
6 percent, J2 or J1. So there was improvement to a
7 higher level of visual acuity than they started with.

8 In fact, all of them did have that level of
9 improvement. So we hadn't looked at that before.

10 That was a good question.

11 I'm thinking what else. Was there another
12 question?

13 CHAIRMAN WEISS: I think those were the
14 only two. Your set, Dr. Smith. Dr. Mathers, are you
15 set as well?

16 DR. GORDON-MEYER: Dr. Mathers, I think,
17 we had responded to before, that we didn't see. And I
18 think Dr. McMahon spoke to no difference or no effect
19 of 32 spots on some of the other parameters.

20 CHAIRMAN WEISS: Great. Thank you so
21 much.

22 DR. GORDON-MEYER: Thank you.

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1 CHAIRMAN WEISS: I would ask the FDA to be
2 so kind as to show us their individual questions to
3 allow us to begin the Panel discussion.

4 The first question that I am going to pose
5 to the Panel is: Is the length of follow-up
6 sufficient to demonstrate reasonable assurance of
7 safety and efficacy for the requested indication?

8 Why don't we go around, and you can tell
9 us yes or no or if you have anything else you want to
10 say that is applicable and brief. Dr. Macsai:
11 Question Number 1: Is the length of follow-up
12 sufficient to demonstrate reasonable assurance of
13 safety and efficacy for the requested indication?

14 We are specifically talking about the
15 length of follow-up, not necessarily how you might
16 want to change the indication. Am I correct on that,
17 because otherwise we could get involved in -- and I am
18 just posing this to the agency.

19 The first question, you just want us to
20 talk about the length of follow-up as opposed to if we
21 wanted to change how the requested indication was
22 phrased? Yes. So number 1 is only talking about the

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1 length of follow-up?

2 DR. BERMAN: Yes, but if you have anything
3 you want to add, that's great. I just wanted
4 basically the -- get a sense that the panel was
5 satisfied with the length of follow-up.

6 CHAIRMAN WEISS: We are just going to talk
7 about length of follow-up, because Sally has pointed
8 out to me question number 6 talks about the indication
9 and, if you don't agree with the indication, what
10 indication would you prefer. So we are just going to
11 talk about length of follow-up. Are you satisfied
12 with the length of follow-up? Yes or no, or what
13 would you like?

14 DR. MACSAI: It appears safe, but I can't
15 tell if it is effective yet.

16 CHAIRMAN WEISS: Fine. So but the length
17 of follow-up is not an issue for you? That's a good
18 enough answer for me.

19 DR. MACSAI: No. I don't know.

20 DR. McMAHON: Could I ask a pointed
21 question?

22 CHAIRMAN WEISS: I don't know is an answer

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1 as well. We'll increase it to three: Yes, no or I
2 don't know.

3 DR. McMAHON: Jayne, question about your
4 question.

5 CHAIRMAN WEISS: Yes?

6 DR. McMAHON: Length of follow-up with the
7 current data or the willingness to provide two-year
8 data?

9 CHAIRMAN WEISS: You can ask for the
10 willingness. I think what this question is really
11 trying to address: Do you want two-year data? Do you
12 want three-year data? Are you happy with one-year
13 data to make any assessments that you want to make?

14 Of course, you can always, when we get to
15 question 6, voice the opinion that you want a
16 different indication. So I'd like to sort of stay
17 focused on a time period for this question.

18 Dr. Schein?

19 DR. SCHEIN: Yes.

20 CHAIRMAN WEISS: Yes. Thank you. Dr.
21 Mathers?

22 DR. MATHERS: Safety is fine. We can't

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1 tell about longer duration. So I would like to know
2 more about longer duration, but I think there are ways
3 we can do it.

4 CHAIRMAN WEISS: So that sounds like a
5 maybe.

6 DR. MATHERS: Maybe.

7 CHAIRMAN WEISS: Maybe. Dr. Casey.

8 DR. CASEY: I don't know.

9 CHAIRMAN WEISS: I don't know. Dr.
10 Grimmett.

11 DR. GRIMMETT: Dr. Grimmett. The sponsor,
12 I believe, has agreed to provide 24-month data on the
13 original PMA in the treatment of hyperopes. That
14 would factor into my decision about how much
15 regression actually takes place, and my probable
16 answer is yes, there is sufficient follow-up. But it
17 sounds like the sponsor is willing to provide longer
18 term data to help us as well.

19 CHAIRMAN WEISS: So, basically, if you
20 want two-year data, you can get it from one of the
21 other PMAs rather than this one, and that would
22 provide you with more information and perhaps enough

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1 information.

2 DR. GRIMMETT: Yes. And even though it is
3 a different PMA, I believe it is relevant.

4 CHAIRMAN WEISS: Thank you. Dr. Bradley.

5 DR. BRADLEY: Simple answer, yes.
6 Basically, since the indication is for temporary
7 treatment, I think one-year data is sufficient. I
8 think it is in the sponsor's interest to provide
9 longer term data rather than rely on anecdotal reports
10 of the surgeons regarding the stability and longevity
11 of the treatment.

12 CHAIRMAN WEISS: Dr. Van Meter.

13 DR. VAN METER: Yes.

14 CHAIRMAN WEISS: Dr. Coleman.

15 DR. COLEMAN: Yes.

16 CHAIRMAN WEISS: Dr. McMahon.

17 DR. McMAHON: I echo Dr. Bradley's
18 comment.

19 CHAIRMAN WEISS: Dr. >Smith.

20 DR. SMITH: Yes.

21 CHAIRMAN WEISS: Dr. Bandeen-Roche.

22 DR. BANDEEN-ROCHE: I echo Dr. Grimmatt's

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1 comment, I guess, with the qualifier that I would
2 really sort of like to see the complete one-year data
3 to feed into the labeling.

4 CHAIRMAN WEISS: The complete one-year
5 data is data that the sponsor has that they have not
6 given to FDA or more data?

7 DR. BANDEEN-ROCHE: Well, my understanding
8 is it doesn't yet exist. I mean that it is still
9 accruing. Correct me if I am wrong.

10 CHAIRMAN WEISS: Dr. Huang.

11 DR. HUANG: There is a very limited number
12 of the patients at 12 months. So I would like to --
13 The answer to your question is yes, but I would like
14 to see post-market surveillance for up to another
15 year.

16 CHAIRMAN WEISS: Dr. Rosenthal.

17 DR. ROSENTHAL: Just a comment, that the
18 sponsor is obliged every three months, I think, to
19 update the PMA with data that comes in. I mean, I
20 don't know how much of the one-year data will be
21 available over the next few months. I'm not sure when
22 they --

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1 DR. GORDON-MEYER: Can I speak to that?

2 DR. ROSENTHAL: Yes.

3 CHAIRMAN WEISS: Yes.

4 DR. GORDON-MEYER: Okay. Because of the
5 relatively short time we have to respond between
6 getting questions and the Panel, we focused on that,
7 and we will provide a 90-day update with considerably
8 additional 12-month data.

9 We also are organizing, and we will show
10 you as we close, the very high level of consistency.
11 We have an n of 320 from the original PMA hyperopia
12 population where there is still excellent
13 accountability at 24 months.

14 That data is in the public domain in the
15 physician labeling for hyperopia, and the stability to
16 date in the current population is exactly the same as
17 the stability in that population. But we, of course,
18 don't have the 12 to 24, but the pattern is extremely
19 consistent between the populations, as you would
20 expect with the same procedure.

21 We will provide ongoing data. The study
22 is a 24-month study. It will be completed, and the

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1 information submitted to FDA over time.

2 CHAIRMAN WEISS: So from what I hear from
3 members of the Panel on question number 1, you will be
4 able to address perhaps all of the concerns in that
5 there will be further data coming from this PMA, that
6 there will be two-year data coming from a prior PMA,
7 if desired, and rather than doing a post-market, there
8 will two years data coming from this PMA.

9 So I would think -- and if anyone
10 disagrees, please interrupt me, but that would address
11 all the concerns from question 1. Dr. Bradley?

12 DR. BRADLEY: Yes. I think the sponsor
13 wishes to argue equivalence with the earlier PMA data
14 for stability and longevity of the effect. A general
15 equivalence analysis should be done and provided to
16 the FDA to substantiate those comparisons.

17 DR. GORDON-MEYER: We would be glad to do
18 that. To date, the data look similar.

19 CHAIRMAN WEISS: And at this point, I
20 would prefer not to have any dialogue, ongoing
21 dialogue. I appreciate your answering those
22 questions, though. Thank you.

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1 Question number 2: Is the magnitude of
2 induced cylinder and axis shift, and the associated
3 effect on uncorrected visual acuity, clinically
4 acceptable for the requested indication?

5 Well, I guess, we will be doing this
6 verbally as opposed to slide-wise, but -- Okay.

7 Question 2 -- We just did question 1.
8 Question 2. Okay. So we are talking about the
9 cylinder and basically, are you concerned about this
10 issue? Dr. Macsai?

11 DR. MACSAI: I'm confused why it doesn't
12 interfere with the vision more, but the answer is yes.

13 CHAIRMAN WEISS: Dr. Schein.

14 DR. SCHEIN: Yes.

15 CHAIRMAN WEISS: Dr. Mathers.

16 DR. MATHERS: Yes.

17 CHAIRMAN WEISS: Dr. Casey.

18 DR. CASEY: Yes.

19 DR. GRIMMETT: Yes.

20 CHAIRMAN WEISS: Dr. Grimmatt. That was
21 Dr. Grimmatt. Dr. Bradley.

22 DR. BRADLEY: Since my read of the table

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1 showed that the presence of uncorrected astigmatism
2 improved near acuity, I would have to say yes.

3 CHAIRMAN WEISS: So then you should ask
4 your doctor for some of that. Dr. Van Meter.

5 DR. VAN METER: Yes. I think the
6 induction of irregular astigmatism is probably due to
7 centration on the cornea, and this is a physician
8 issue that we can discuss in labeling.

9 CHAIRMAN WEISS: Okay. Dr. Coleman.

10 DR. COLEMAN: Yes.

11 CHAIRMAN WEISS: Dr. McMahon.

12 DR. McMAHON: Since two-year data is going
13 to be provided, yes.

14 CHAIRMAN WEISS: Dr. Smith?

15 DR. SMITH: Yes.

16 CHAIRMAN WEISS: Dr. Bandeen-Roche.

17 DR. BANDEEN-ROCHE: I defer to my clinical
18 colleagues.

19 CHAIRMAN WEISS: Dr. Huang.

20 DR. HUANG: Yes.

21 CHAIRMAN WEISS: So agency, there do not
22 appear to be any concerns about the magnitude of

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1 induced cylinder and axis shift.

2 Question 3: Is the rate of
3 undercorrection, greater than 1 diopter, clinically
4 acceptable? Why don't we just answer that one.

5 Dr. Huang, is the rate of undercorrection
6 of greater than a diopter clinically acceptable?

7 DR. HUANG: No.

8 CHAIRMAN WEISS: No? Dr. Bandeen-Roche?

9 DR. BANDEEN-ROCHE: Same. Defer to my
10 clinical colleagues.

11 CHAIRMAN WEISS: Dr. Smith.

12 DR. SMITH: No.

13 CHAIRMAN WEISS: Dr. McMahon.

14 DR. McMAHON: No.

15 CHAIRMAN WEISS: Dr. Coleman.

16 DR. COLEMAN: No.

17 CHAIRMAN WEISS: Dr. Van Meter.

18 DR. VAN METER: No.

19 CHAIRMAN WEISS: Dr. Bradley.

20 DR. BRADLEY: No.

21 CHAIRMAN WEISS: Dr. Grimmett.

22 DR. GRIMMETT: No.

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1 CHAIRMAN WEISS: Dr. Casey.

2 DR. CASEY: No.

3 CHAIRMAN WEISS: Dr. Mathers.

4 DR. MATHERS: Yes, I think it is.

5 CHAIRMAN WEISS: It is? Okay. Dr.

6 Schein.

7 DR. SCHEIN: Yes.

8 CHAIRMAN WEISS: Dr. Macsai.

9 DR. MACSAI: No.

10 CHAIRMAN WEISS: So as a poll, the
11 majority feel that it is clinically --

12 DR. BRADLEY: I would like to change my
13 poll to yes.

14 CHAIRMAN WEISS: So the majority feel that
15 it is not acceptable. Most feel that it is not
16 acceptable. So we will go on to question, Part B.

17 Are there subgroups of the PMA cohort for
18 which this outcome is not acceptable?

19 So in other words, if we are talking about
20 the 8, the 16, the 32, etcetera, are there some
21 subgroups that are not acceptable, making the rest of
22 the subgroups acceptable? Dr. Macsai?

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1 DR. MACSAI: Thirty-two spots hyperopes.

2 CHAIRMAN WEISS: Is unacceptable?

3 DR. MACSAI: Right. Correct.

4 CHAIRMAN WEISS: Dr. Mathers. Dr. Schein

5 DR. SCHEIN: No.

6 CHAIRMAN WEISS: So you feel that all of
7 the subgroups are clinically acceptable?

8 DR. SCHEIN: Yes.

9 CHAIRMAN WEISS: Dr. Mathers.

10 DR. MATHERS: Yes, they are all
11 acceptable, including the 32.

12 CHAIRMAN WEISS: Dr. Casey.

13 DR. CASEY: I feel that the 32 is not
14 acceptable.

15 CHAIRMAN WEISS: Dr. Grimmett.

16 DR. GRIMMETT: I feel that 32-spot is not
17 acceptable.

18 CHAIRMAN WEISS: Dr. Bradley.

19 DR. BRADLEY: I also agree that 32-spot is
20 not acceptable.

21 CHAIRMAN WEISS: For someone who is name
22 challenged, this is really taxing. Dr. Van Meter.

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1 DR. VAN METER: Thirty-two spots is not
2 acceptable.

3 CHAIRMAN WEISS: Dr. Coleman.

4 DR. COLEMAN: The same.

5 CHAIRMAN WEISS: And Dr. McMahon.

6 DR. McMAHON: Thirty-two spot is not
7 acceptable. Eight spot, but not enough data to
8 analyze.

9 CHAIRMAN WEISS: Dr. Smith.

10 DR. SMITH: I agree with Dr. McMahon.

11 CHAIRMAN WEISS: Dr. Bandeen-Roche.

12 DR. BANDEEN-ROCHE: Also agree with Dr.
13 McMahon.

14 CHAIRMAN WEISS: Dr. Huang.

15 DR. HUANG: I agree with Dr. McMahon.

16 CHAIRMAN WEISS: So the consensus that I
17 hear is the majority do not feel the efficacy for the
18 32-spot is acceptable, and would like more data in
19 order to make a determination about the 8-spot, but
20 the other two spot sizes are clinically acceptable.

21 Okay, moving on to Number 4: Are the
22 reduced accuracy to target refraction and poorer near

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1 uncorrected visual acuity outcomes, monocular and
2 binocular, reasonable to justify the risk of elective
3 surgery with "temporary" results?

4 Should we break this up, FDA, into two
5 questions?

6 DR. MATHERS: There are four questions.

7 CHAIRMAN WEISS: Well, no, but the preface
8 is -- We will keep it how you have that.

9 And is the near uncorrected visual acuity
10 correction achieved clinically useful in the following
11 groups?

12 DR. GRIMMETT: I don't understand the
13 question.

14 CHAIRMAN WEISS: Can you clarify for the
15 simple minded among us?

16 DR. BERMAN: Yes, I will clarify. I'm not
17 looking for answers to every bullet there. I am
18 looking for your overall clinical judgment as to the
19 approvability for each of these cohorts, basically,
20 and I am bringing up some of the things that you may
21 want to take into consideration in making your
22 decision about A, B, C and D.

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1 CHAIRMAN WEISS: Well, I think the Panel
2 has already answered that in the majority, they do not
3 think that it is justifiable because of clinical
4 efficacy for the 32-spot pattern. I think that is
5 what I just heard.

6 I think what I just heard, at least for a
7 good proportion -- and I don't know if it is the
8 majority, and that could be coming up in a labeling
9 unless, Ralph, you feel we should go around and poll -
10 - for 8 spots, there is data that is requested by a
11 significant minority of, if not majority, of the
12 Panel.

13 For subjects greater than 55 years of age
14 and for hyperopic patients, I believe you have already
15 showed us that that has less clinical efficacy, but
16 that is associated with the fact that they had more
17 people with 32-spot pattern. So I'm not sure that we
18 need to discuss that unless there is anyone on Panel
19 who wants to comment on the age or the fact that
20 people had hyperopia.

21 Dr. Bandeen-Roche and then Dr. Bradley.

22 DR. BANDEEN-ROCHE: I would just say that,

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1 with respect to age, there is very little power to
2 distinguish there not being an age effect. So I would
3 just be careful about saying that, while we have shown
4 that there is, you know, not really an effect with
5 respect to age, we don't know this.

6 CHAIRMAN WEISS: We don't know about age,
7 and hyperopia, would you say -- What would you say
8 about hyperopia?

9 DR. BANDEEN-ROCHE: Hyperopia -- I mean,
10 to me, I felt less confident about the 32 versus -- I
11 feel less confident commenting about that.

12 CHAIRMAN WEISS: Dr. Bradley, and then Dr.
13 McMahan.

14 DR. BRADLEY: Of course, the 32-spot
15 pattern, the subject age, the initial subject
16 refraction all interact, and it would be -- Rather
17 than making a decision based upon our clinical
18 judgment, seems to me, this is an opportunity to
19 employ multivariate statistics and find out which of
20 these really is the key problem.

21 DR. BANDEEN-ROCHE: It's not enough data.
22 I mean, there is a -- If you look at the data, it

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1 sure looks like there is an interaction, but there is
2 not nearly enough statistical power to document it. I
3 agree, it would be nice to, as maybe more -- Well, I
4 guess there isn't going to be fuller data accruing.
5 Maybe we should think about future data.

6 CHAIRMAN WEISS: Okay. Dr. McMahon and
7 then Dr. Mathers, and then Dr. Schein.

8 DR. McMAHON: The age of the patient in
9 the pre-operative distance ametropia and the resultant
10 near acuity are unalienably intertwined here, and the
11 issue is, does the intended effect meet the pre-
12 operative requirements.

13 Age and bifocal power add are linearly
14 aligned. So age is going to be related to how much
15 add effect you are going to have. So this is an issue
16 not specifically of age but of intended correction
17 amount that you want to achieve.

18 CHAIRMAN WEISS: Dr. Mathers.

19 DR. MATHERS: I think that there are two
20 properties here. There is the objective measurement
21 of accuracy as acuity J3 or whatever, and there is the
22 quality of vision satisfaction issue.

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1 Quality of vision and satisfaction issue
2 does fine for the whole group. In fact, for 32-spot
3 it is at least as good as the less than 32, and same
4 with satisfaction. But it doesn't achieve a
5 measurable improvement.

6 That may be a good thing, because these
7 patients may not actually tolerate three diopters of
8 anisometropia, but in terms of efficacy, if we are
9 talking about patients being happy, they're happy, and
10 they are satisfied.

11 CHAIRMAN WEISS: Dr. Schein.

12 DR. SCHEIN: I plan to magnify on that.
13 It is my understanding, the indications for this
14 device is to reduce spectacle dependence for near
15 activities in emmetropes and hyperopes, and that
16 reduction in dependence and the patient outcomes are
17 equivalent for the hyperopes in the lower, and I see
18 no justification to parse an approval based on a
19 refractive outcome.

20 CHAIRMAN WEISS: Dr. McMahon.

21 DR. McMAHON: Just a point, and that is,
22 even with Dr. Mathers' comment, for those who are

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1 hyperopic to start with, the majority of those
2 patients had their other eye treated for distance. So
3 their anisometropic correction at the end was very
4 similar to that of the emmetropes. So you're dealing
5 with really two diopters of anisometropia rather than
6 three.

7 CHAIRMAN WEISS: Is the FDA satisfied with
8 that discussion on that particular issue?

9 DR. VAN METER: Dr. Weiss, can I make one
10 comment?

11 CHAIRMAN WEISS: Dr. Van Meter.

12 DR. VAN METER: One issue that was raised
13 earlier is the older hyperopes that had the 32-spot
14 size would still get some improvement from the 24-spot
15 size. We just don't know how much improvement they
16 would get. There is some reason to think that in an
17 older cornea, you might get more effect from the same
18 treatment. We learned that from the old RK data.

19 So this is not to say that an older
20 patient that got 24 spots would not necessarily be
21 unhappy.

22 CHAIRMAN WEISS: Dr. McMahon.

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1 DR. McMAHON: Along those lines, and I
2 brought this up before, there actually may be no
3 different in effect between 24 spots and 32 spots, and
4 actually that would be something the sponsor would
5 want to look at.

6 CHAIRMAN WEISS: I think, really, what I
7 would like to see is for each of the spot sizes how
8 much hyperopia was treated at different time points,
9 so you know what a 24 and what a 32 and what an 8 on
10 the average treats and how it degenerates with time.
11 That would, I think, answer the question that you are
12 asking, is does it do any different than the 24-spot.

13 DR. McMAHON: You would have to decouple
14 it from the binning that they are using down
15 individual data, and it might be there under those
16 circumstances.

17 CHAIRMAN WEISS: So on those particular
18 issues, does the FDA -- We will go on in a moment to
19 other subgroups or the last section of Question 4, but
20 on the sections that we just covered, are you
21 satisfied? Okay.

22 So the last section is: "Are the reduced

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1 accuracy to target refraction and poorer," etcetera.
2 "How do you suggest the indication and/or labeling be
3 modified for any other subgroups or refractive
4 correction?"

5 So aside from what we have already
6 discussed, are there any other stipulations that you
7 would want, aside from talking about the actual spot
8 patterns, because that is the only thing that I have
9 heard that people sort of want to have either more
10 information on or maybe say some of them don't show
11 any efficacy. Anything besides what we have
12 mentioned? Dr. Macsai?

13 DR. MACSAI: Dr. Weiss, is this for any
14 labeling or only in regard to these things?

15 CHAIRMAN WEISS: Only in regard to these
16 things. Question 7 will address labeling
17 recommendations, additional ones. Dr. Bradley?

18 DR. BRADLEY: I don't want us to get too
19 focused on the number of dots. I mean, with this
20 procedure the number of dots is correlated with the
21 intended refractive change, and it may be more
22 sensible to analyze the data.

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1 If we are concerned about a particular
2 dataset, it may be better to describe it as we are not
3 satisfied with data when the intended correction
4 exceeds 2.25 diopters as opposed to 32 dots, because
5 they are one and the same, and in the end that may be
6 the better way to define the limited range of this
7 procedure, not in terms of number of dots, because
8 again, as Dr. McMahon has explained, we are not quite
9 sure if it is a dot problem, and it may just be a
10 limit to the procedure. You can't do more than two-
11 plus diopters.

12 CHAIRMAN WEISS: Dr. McMahon.

13 DR. McMAHON: Actually, I would argue just
14 the opposite, in that because they are related, it may
15 be that the spots is the key issue, not the intended
16 correction, within certain bounds.

17 CHAIRMAN WEISS: Well, I would assume that
18 the agency could request to look at it both ways in
19 terms of what is the maximal correction that you can
20 get from this procedure, and in addition, is there any
21 difference in terms of the average correction -- and
22 those statisticians at the table can phrase this much

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1 better than I can, but between a 32 versus a 24, how
2 much additional correction are you going to get from
3 that, if you are going to get any additional
4 correction.

5 I see a nod. So that is comforting, from
6 Dr. Bandeen-Roche. So we are going to go on to
7 question number 5. I'm told she was drifting off.
8 Thank you.

9 DR. BANDEEN-ROCHE: False advertising.

10 CHAIRMAN WEISS: Okay. Question 5 : Do
11 the spectacle dependence rates for near activities
12 support approval for the requested indication in a
13 presbyopic population?

14 So I think what FDA is referring to is
15 there's a lot of folks here who have to wear reading
16 glasses. But given that, does this show reasonable
17 efficacy? Dr. Huang.

18 DR. HUANG: I don't know.

19 CHAIRMAN WEISS: Dr. Bandeen-Roche.

20 DR. BANDEEN-ROCHE: My concern would be
21 that people very clearly understand what the rates
22 are, what their chances are.

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1 CHAIRMAN WEISS: So you can address this.
2 I would assume your answer is yes, as long as you
3 address it in labeling?

4 DR. BANDEEN-ROCHE: Yes.

5 CHAIRMAN WEISS: Dr. Smith.

6 DR. SMITH: I agree with Dr. Bandeen-
7 Roche.

8 CHAIRMAN WEISS: Dr. McMahon.

9 DR. McMAHON: I agree, same.

10 CHAIRMAN WEISS: Dr. Coleman.

11 DR. COLEMAN: I agree.

12 CHAIRMAN WEISS: Dr. Van Meter.

13 DR. VAN METER: I don't know, because I
14 think spectacle dependence rates are so nebulous, to
15 start with, that I have no idea how to answer this.

16 CHAIRMAN WEISS: Dr. Bradley.

17 DR. BRADLEY: I also don't really know.
18 It seems to me they did two surveys. One survey
19 biased the data to say, yes, I need spectacles. The
20 second survey biased the data to say, well, I can do
21 without them. In the end, I'm not really sure what
22 was going on with the patients.

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1 CHAIRMAN WEISS: How many "I don't knows"
2 do we have at this point?

3 DR. McMAHON: A lot of them. Everyone so
4 far.

5 CHAIRMAN WEISS: We can't even know how
6 many "I don't knows" we have. Okay. Dr. Grimmett.

7 DR. GRIMMETT: Yes, with proper informed
8 consent.

9 CHAIRMAN WEISS: Dr. Casey.

10 DR. CASEY: I agree with Dr. Van Meter. I
11 don't know.

12 CHAIRMAN WEISS: Dr. Mathers.

13 DR. MATHERS: Yes, with informed consent
14 or addressed in labeling.

15 CHAIRMAN WEISS: Dr. Schein.

16 DR. SCHEIN: Yes.

17 CHAIRMAN WEISS: Dr. Macsai.

18 DR. MACSAI: Yes, with a disclaimer.

19 CHAIRMAN WEISS: For labeling.

20 DR. MACSAI: Labeling.

21 CHAIRMAN WEISS: Dr. McMahon.

22 DR. McMAHON: I want to make it clear that

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1 I was voting I don't know, but it could be addressed
2 in the labeling.

3 CHAIRMAN WEISS: Dr. Bandeen-Roche.

4 DR. BANDEEN-ROCHE: Yes. I mean,
5 certainly the concern about the quality of this
6 questionnaire measurement is very valid. I mean,
7 maybe this is a good time to just very briefly cite
8 something off of this table, and I will cite more of
9 it later.

10 Going no to yes, 33 percent, 34 percent
11 from six month to 12 month -- I guess that would be
12 incidence of using glasses, but there was 15 percent
13 remission of using glasses. So I don't know what that
14 means, whether it speaks to the quality of measurement
15 or what.

16 CHAIRMAN WEISS: So from the agency's
17 standpoint, there may be a slight majority on one side
18 or another, but basically it's either it does support
19 it or there's uncertainty whether it supports it.

20 DR. VAN METER: Dr. Van Meter. I believe
21 all the "I don't knows" would agree that labeling can
22 solve the issue.

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1 DR. McMAHON: I concur.

2 CHAIRMAN WEISS: Dr. Bandeen-Roche?
3 Agency satisfied?

4 Question Number 6: Do the safety and
5 efficacy data support approval for the requested
6 indication? If not, what indication does the data
7 support?

8 So this was the question that I promised
9 you we would get to. I think we have answered some of
10 it, but perhaps not enough. Dr. Macsai?

11 DR. MACSAI: I thought we answered it with
12 the 32 spots.

13 CHAIRMAN WEISS: So that you feel that the
14 safety and efficacy data support the indication for
15 treatment for all the spot sizes except for the 32-
16 spot?

17 DR. MACSAI: Yes, with the disclaimer that
18 we don't have enough patients on the 8, and we have no
19 idea how long the temporary lasts for.

20 CHAIRMAN WEISS: Dr. Schein.

21 DR. SCHEIN: The answer is yes to the
22 question.

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1 CHAIRMAN WEISS: Dr. Mathers.

2 DR. MATHERS: Yes.

3 CHAIRMAN WEISS: Dr. Casey.

4 DR. CASEY: I agree with Dr. Macsai.

5 CHAIRMAN WEISS: Okay. Dr. Grimmett.

6 DR. GRIMMETT: Yes. And I would like to
7 offer an explanation. I look at it differently in
8 terms of whether the product is already in the
9 marketplace versus whether it is not. If this
10 procedure were not in the marketplace, I would do as
11 Dr. Macsai suggested, that the 32-spot size be
12 eliminated due to effectiveness issues. However, this
13 is a procedure that is in the marketplace.

14 It is my believe that physicians will use
15 it off-label anyway, because the 32-spot indication is
16 already out there, and I would rather have as much
17 information available to physicians and patients as
18 possible so that in that circumstance they have
19 something to rely upon.

20 I also would want FDA to have access to
21 wordsmith it. So I answer the question yes.

22 CHAIRMAN WEISS: You probably, though,

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1 could change the indication but still put the data in
2 the labeling.

3 DR. GRIMMETT: As long as the data is in
4 the labeling, I'm happy, no matter what happens.

5 CHAIRMAN WEISS: Okay. So we have a two
6 and a half on one side and a two and a half on the
7 other. Dr. Bradley.

8 DR. BRADLEY: Safety, yes. Regarding
9 efficacy, somehow we need to either put it in
10 labeling. I'm thinking that the procedure is
11 efficacious for creating a near reading add for
12 emmetropes. It is efficacious for correcting distance
13 vision for the hyperopes, but it is going to produce
14 only a limited aid for reading in the hyperopes.

15 So it is efficacious for reading add for
16 the emmetropes, but for the hyperopes it has limited
17 efficacy, because of the limited range of the
18 procedure.

19 CHAIRMAN WEISS: So what would your
20 indications be? So this is safe and effective for --
21 fill in the blank.

22 DR. BRADLEY: Safe and effective for

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1 emmetropes. For the hyperopes, it has limited
2 efficacy.

3 CHAIRMAN WEISS: Safe and effective for
4 increasing near vision --

5 DR. BRADLEY: Yes. Providing a reading
6 add.

7 CHAIRMAN WEISS: For emmetropes. Up to?

8 DR. BRADLEY: Just emmetropes.

9 CHAIRMAN WEISS: Oh, just emmetropes.

10 DR. BRADLEY: Yes. As soon as we get into
11 hyperopia, we run into the limit of the procedure. It
12 produces less than desirable effects. That is what
13 we have been talking about.

14 CHAIRMAN WEISS: Dr. Grimmett.

15 DR. GRIMMETT: Dr. Rosenthal, I have a
16 question. Is it possible to limit the range of
17 approval, exclude the 32-spot, yet still include all
18 that data in the labeling?

19 DR. ROSENTHAL: Absolutely.

20 DR. GRIMMETT: Fabulous. That would be my
21 vote.

22 CHAIRMAN WEISS: We're not voting now. We

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1 are voicing opinions.

2 DR. ROSENTHAL: We do it with the excimer
3 lasers all the time.

4 DR. BRADLEY: We are all agreeing. It's
5 just a matter of how that gets presented. As the FDA
6 gets a sense of what our concerns are, and I think
7 that the concerns are very self-evident in the data.
8 Sponsor is aware of them. Sponsor raises the
9 concerns, too, in their analysis. It's just a matter
10 of how that gets packaged in the final product, it
11 seems to me, whether it's an issue of restricting it
12 for hyperopes or number of dots or whatever.

13 CHAIRMAN WEISS: Dr. Berman.

14 DR. BERMAN: I just want to remind you
15 that my first slide had the proposed indication as the
16 sponsor currently has it proposed, and in there in the
17 second line they are proposing presbyopic hyperopes or
18 presbyopic emmetropes.

19 So I just wanted to clarify. Are all of
20 you in agreement that you are recommending that you
21 would delete the words "presbyopic hyperopes" from the
22 indication?

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1 CHAIRMAN WEISS: I think we have to go
2 around again, because that, I think, was really just
3 brought up this moment. So why don't we -- The
4 requested indication, of course, doesn't distinguish
5 between presbyopic hyperopes and presbyopic
6 emmetropes.

7 Dr. Bradley has proposed that presbyopic
8 emmetropes be the only ones included in the efficacy
9 and in the indication.

10 DR. BRADLEY: No, that's not what I said.

11 I said it has limited efficacy for the hyperopes. IT
12 does provide them with some extra add power. They end
13 up being slightly myopic, but not as much myopia in
14 that eye as the emmetropes can achieve, and maybe not
15 quite enough for the reading that they may request.
16 But it does give them some add power. So it is going
17 to help them a little bit.

18 CHAIRMAN WEISS: So is that something that
19 we can put an indications, that it is indicated to
20 improve near vision in one group but is limited -- I
21 mean, help me on this.

22 DR. ROSENTHAL: No, I don't think --

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1 DR. BERMAN; I think you would indicate
2 who it is indicated for, and then in the labeling you
3 would provide the various outcomes.

4 CHAIRMAN WEISS: Dr. McMahon has a
5 comment.

6 DR. McMAHON: Let me suggest some
7 wordsmithing, and it comes actually from my
8 recommendation in the presentation, that this is a
9 safe and efficacious procedure for intended near
10 corrections of 1.00 to 2.25 diopters of effect.

11 DR. MACSAI: Temporary.

12 DR. McMAHON: Right. Temporary. The
13 issue then is you have a range of 1.00 to 2.25 worth
14 of effect, and it's what is your end goal. So if your
15 end goal is to have a 1.00 diopter worth of effect,
16 you can actually do 1.00 diopter of hyperopia, too.

17 So this has been proven to be reasonably
18 efficacious, in my view, for that particular region,
19 and I think that's enough.

20 CHAIRMAN WEISS: Would you be in agreement
21 with that, Dr. Bradley?

22 DR. BRADLEY: Yes.

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1 CHAIRMAN WEISS: And then you could always
2 address your concerns about any of the subgroups in
3 labeling, if you wanted to.

4 DR. BRADLEY: Yes. I think it may be need
5 some labeling because, given the fact that we have
6 struggled with this issue, it would be worth laying it
7 out in clear language for both the physician and the
8 patient.

9 CHAIRMAN WEISS: So, actually, can you
10 refresh my memory? What is the present -- Dr. McMahon
11 suggests saying specifically 1.00 to 2.25 of effect.
12 What is it presently listed as, the present
13 indication?

14 DR. BERMAN: The current one says
15 temporary induction of myopia to improve near vision
16 in the non-dominant eye presbyopic hyperopes or
17 presbyopic emmetropes, blah, blah, blah.

18 It currently says up to 3 diopters but, of
19 course, FDA has indicated to the sponsor in previous
20 communication that it would be not up to, but it would
21 be .75 -- you know, it would be the amount treated in
22 the PMA, which didn't include zero to 1 or zero to

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1 .75.

2 CHAIRMAN WEISS: So if we basically let
3 you do whatever you wanted but gave you the guidance
4 that -- with some of these words here, because it is
5 fairly lengthy -- but gave you the guidance that --
6 and after we get consensus, if we get consensus on
7 this proposal, 1.00 to 2.25 effect -- that would
8 answer your question?

9 Okay. So Dr. McMahon has proposed using
10 that. I would like to sort of have the rest of the
11 Panel members address that, and then we are just going
12 to go back over that for those who haven't addressed
13 that. Dr. Van Meter.

14 DR. VAN METER; I agree with Dr. McMahon.

15 CHAIRMAN WEISS: Dr. Coleman.

16 DR. COLEMAN: I do, too.

17 CHAIRMAN WEISS: Dr. McMahon, I assume you
18 agree with yourself on most days.

19 DR. McMAHON: Fairly likely.

20 CHAIRMAN WEISS: Okay. Good. Dr. Smith.

21 DR. SMITH: That's fine.

22 CHAIRMAN WEISS: Dr. Bandeen-Roche.

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1 DR. BANDEEN-ROCHE: Ditto, plus I second
2 Dr. Grimmett's comments about the data.

3 CHAIRMAN WEISS: Dr. Huang.

4 DR. HUANG: I agree with Dr. McMahon.

5 CHAIRMAN WEISS: And starting it back
6 again, Dr. Macsai, would you be in agreement with
7 that?

8 DR. MACSAI: Yes.

9 CHAIRMAN WEISS: Dr. Schein.

10 DR. SCHEIN: Yes.

11 CHAIRMAN WEISS: Dr. Mathers.

12 DR. MATHERS: Yes.

13 CHAIRMAN WEISS: Dr. Casey.

14 DR. CASEY: Yes.

15 CHAIRMAN WEISS: Dr. Grimmett.

16 DR. GRIMMETT: Yes.

17 CHAIRMAN WEISS: Okay. I have not meant
18 to exclude industry and consumer reps here. If you
19 have any comments on any of these things, including
20 this one in particular, please let us know. You
21 would? Then give us your comment.

22 MR. MCCARLEY: I would let you know.

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1 CHAIRMAN WEISS: Oh, you would let me
2 know. Okay. Question Number 7: Do you have
3 additional labeling recommendations, explanatory text
4 or data? Are there data tables that should be added
5 to the labeling for physicians and/or patients?

6 So why don't we start with the primary
7 reviewers, and then we can go on from there. Dr.
8 McMahan.

9 DR. McMAHON: Do you want me to read out
10 the number of labeling suggestions I put in my report
11 or can we --

12 CHAIRMAN WEISS: Yes, if you can just --
13 You don't have to belabor them, but if you can just
14 state them, and then I can give you this so you don't
15 have to write it out, and we can just check them off.

16 This is the review from Dr. McMahan.

17 DR. McMAHON: It starts on page 11. The
18 first one, which had to do with blended vision -- The
19 sponsor has already acknowledged that they will drop
20 that. So it is not an issue.

21 On page 11 of 31 of the patient
22 information booklet, the first bullet, I suggest that

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1 adding "keloids" in parentheses. Since they talk
2 about scars, the real issue is keloid formers, I
3 believe.

4 Page 11 of 13, the sixth bullet: I have
5 some concerns about concluding nystagmus as a
6 precaution. This is done under topical anesthesia,
7 and I can't understand why it is not a
8 contraindication unless surgeons are good enough to
9 move their hands at the same rate as the nystagmus.

10 Page 14 of 31, the first bullet address
11 re-treatment, and I would remove this item, as the
12 effectiveness and safety of re-treatments have not
13 been determined.

14 On page 13 and 14 of 31, when they go over
15 about important things for consideration, there is
16 really no mention about the monovision trial. It is
17 later on, on page 19. I think it should be up here,
18 because this is an important part for the patient to
19 understand, and the sponsor, I believe, agrees that a
20 monovision trial is needed.

21 Page 12 of 31 -- Am I going too fast,
22 Michael? The last two paragraphs of the first days

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1 seems to better fit in the first paragraph of the
2 weeks after surgery. That is sort of wordsmithing.

3 On page 23 of 31, Table 8, if there is any
4 data relative to response to worse -- you know,
5 because it is same -- you know, little improvement,
6 marked improvement. If there is any data relative to
7 worse, that should be added. If there was none
8 available -- in other words, it wasn't questioned
9 which I think is the case -- then ignore that.

10 Page 24 of 31 in the section of questions
11 to ask your doctor, omit the first bullet pertaining
12 to nystagmus, if we are going to make it
13 contraindicated.

14 Add a table to finding the frequency of
15 induced cylinder and effect this has on near and
16 distance visual acuity in the trial.

17 A cautionary statement should be added
18 after Table 1, which is on page 8 of 31, indicating
19 that equivalent outcomes in non-Caucasians have not
20 been determined. This is an issue, I think, for
21 Asians in particular, since their corneal architecture
22 is a bit different than others. This may pertain to

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1 other ethnic groups as well.

2 Under physician labeling, remove nystagmus
3 from warning and place it into contraindications.

4 In the section on how long contact lenses
5 should be removed prior to the procedure, I have a
6 little bugaboo about this in refractive surgery in
7 general, and I don't have real solid wording, but in
8 particular with rigid lens wears the notion of some
9 fixed time period, to me, is not realistic.

10 It needs to be that there's corneal
11 stability in terms of its shape or the equivalent
12 refractive error before this is done rather than some
13 fixed time frame. I know that that is an awkward
14 situation for refractive surgeons, but it is reality.

15 Add a statement: "The effectiveness of
16 this procedure device has not been determined for
17 patients with less than 20/25 best spectacle corrected
18 visual acuity pre-operatively," as all these patients
19 had normal acuity.

20 That's all I have at the moment.

21 CHAIRMAN WEISS: Dr. Huang.

22 DR. GRIMMETT: There is a re-treatment

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1 comment in there that has not been determined?

2 DR. McMAHON: Yes, I mentioned that.

3 DR. GRIMMETT: It's in there?

4 DR. McMAHON: Re-treatment and as well as
5 the effectiveness of intraoperative spots beyond the
6 standardized treatment has not -- The effectiveness of
7 that has not been determined as well.

8 DR. GRIMMETT: Thank you.

9 CHAIRMAN WEISS: Dr. Huang.

10 DR. HUANG: I would suggest to add
11 additional data tables to the physician labeling, if
12 there is any information regarding the re-treatment,
13 as well as those ten excluded patients that had
14 additional intraoperative additional spots to reduce
15 the CK induced astigmatism, if those data were
16 available; because this device has been already
17 approved for hyperopic indications.

18 So the physician may not read the label
19 carefully. I think, you know, they can treat with the
20 32 spots easily, and then there is induced increase
21 amount of astigmatism induced. So I think the warning
22 or label should adequately reflect these kind of

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1 precautions.

2 CHAIRMAN WEISS: Just to clarify, I think
3 they have tables already in the physician's and
4 perhaps the patient labeling as well.

5 DR. HUANG: Not the ten excluded patients.
6 There are additional ten patients in the 32 spots
7 treated with additional intraoperative spots, in
8 addition to the 32 spots. They have additional spots.
9 They treat additional spots in the area of the
10 cylinder induced.

11 CHAIRMAN WEISS: I see. Well, that's
12 totally off-label.

13 DR. HUANG: Yes, that is totally off-
14 label. Yes, but you know, given this device is likely
15 to be used off-label anyway, so I think they should
16 warn the physician, if you want to treat with 32
17 spots, be prepared, you may have to deal with
18 astigmatism.

19 CHAIRMAN WEISS: There was more induced
20 astigmatism in the 32-spot?

21 DR. HUANG: Well, the data is not
22 submitted for analysis.

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1 DR. MACSAI: It is the 11 patients that
2 were excluded, right? Ten of them had 32 spots, and
3 they got treated with more spots for induced
4 astigmatism?

5 DR. HUANG: Yes.

6 DR. MACSAI: They are the ten out of 52.

7 DR. HUANG: Yes, exactly.

8 DR. MACSAI: Those ten need to be in the
9 warning to doctors.

10 DR. HUANG: Yes.

11 CHAIRMAN WEISS: What do you want to say
12 about them? Well, what do you say about these people.

13 DR. McMAHON: They just need to present
14 the data.

15 DR. HUANG: Yes, just show additional
16 physician warning table, say, well, ten patients in
17 the 32 spots were treated with additional
18 intraoperative spots, and these were the outcomes;
19 because there was no data that I could find.

20 CHAIRMAN WEISS: I see. So, basically,
21 you would like data in the physician's booklet on the
22 10 excluded patients?

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1 DR. HUANG: Exactly.

2 CHAIRMAN WEISS: Okay.

3 DR. HUANG: Because that is the question:
4 Should additional data table be added?

5 CHAIRMAN WEISS: We understand that.
6 Thank you. Any other comments, Dr. Huang?

7 Dr. Van Meter.

8 DR. VAN METER: If you are going in order
9 about labeling, that's fine.

10 CHAIRMAN WEISS: We are just going to go
11 to those who have relevant comments. Dr. Van Meter?

12 DR. VAN METER: I have two questions in
13 the patient labeling under "Be Sure to Talk to Your
14 Doctor If," and I will go with Dr. McMahon's
15 pagination, because I think mine is different.

16 It says "Be sure to talk to your doctor if
17 you have a cornea that is too thick for the procedure
18 to be completed safely." That is beyond the scope of
19 most patients, I think. That probably ought to go in
20 physician labeling.

21 Also, I would like in physician labeling
22 the importance of accurate centration on a properly

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1 identified visual axis of the cornea.

2 CHAIRMAN WEISS: And basically along the
3 same line, it indicates that if you have keratoconus
4 as a contraindication. I think it should say
5 keratoconus and ectatic -- other ectatic conditions
6 such as if you have pellucida, that is obviously also-
7 -

8 DR. SCHEIN: A history of RK.

9 CHAIRMAN WEISS: You are right, prior
10 refractive surgery -- Now is that an absolute?

11 DR. SCHEIN: RK, I said, rather than
12 refractive surgery.

13 CHAIRMAN WEISS: Incisional keratotomy.
14 So we could add that.

15 DR. MACSAI: We don't have data on the
16 other refractive surgeries. That has to be put in
17 there.

18 CHAIRMAN WEISS: Yes, I think you have to
19 -- and I don't know if it's in there already -- say
20 that prior refractive surgery may be a
21 contraindication. There is no data on the results of
22 this after prior refractive surgery. Then that will

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1 include everything.

2 DR. GRIMMETT: But I'd like to add
3 something. Mike Grimmett. I think with incisional
4 keratotomy, in particular, there is reason to believe
5 that shrinking the cornea may put additional stress on
6 wounds that may not be totally healed and may cause
7 additional irregular astigmatism. I believe
8 Marguerite McDonald made a comment agreeing with that
9 fact or alluding to that.

10 CHAIRMAN WEISS: She is nodding her head.

11 DR. GRIMMETT: So I think incisional
12 keratotomy probably warrants a special line, and the
13 other ones just say there is no data.

14 CHAIRMAN WEISS: So separate that out.
15 Okay, we'll separate that out. Likewise --

16 DR. McMAHON: You are going to put that in
17 contraindications?

18 CHAIRMAN WEISS: Radial keratotomy?
19 Incisional keratotomy will be in contraindications,
20 yes, or can be. Likewise, it may already be in the
21 labeling, the effective of other refractive procedures
22 after CK is not known. I don't know. If that is not

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1 in the labeling, that should be in both of them. Dr.
2 Coleman.

3 DR. COLEMAN: Yes. Under physician
4 precautions on page 12, I would add steroid-responsive
5 intraocular pressure or pressure greater than 21
6 millimeters of mercury to patients with history of
7 glaucoma as a precaution.

8 CHAIRMAN WEISS: I'm going to ask you to
9 scribe these again. Thank you so much. You are
10 anticipating.

11 DR. COLEMAN: Those individuals weren't
12 allowed to participate in the study. Then for the
13 patient precautions, you should also add the same
14 thing, instead of just putting -- You know, it says if
15 you have a history of glaucoma, but also if you had a
16 history of elevated intraocular pressures.

17 CHAIRMAN WEISS: The other thing in
18 patient labeling, it had that there is no effect on --
19 There could be an effect on stereovision, and I think
20 it indicated that there wasn't. But the way the study
21 was done, one wouldn't know. So this is on page 27 of
22 -- This is actually the physician's reference guide.

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1 I would change it also in the patient reference guide,
2 if it is listed.

3 It says this just near correction did not
4 have an adverse impact on binocular uncorrected
5 distance acuity. This is on page 27 of the
6 physician's reference guide draft, and I think we
7 don't know.

8 Okay. Dr. Bandeen-Roche, then Dr. Schein
9 and then Dr. Grimmatt, Mr. McCarley. Ms. Such if you
10 have any comments as well, I'll ask you to chime in.
11 Dr. Bandeen-Roche.

12 DR. BANDEEN-ROCHE: Yes. Just two points.
13 The first goes to the definition of temporary. I
14 hope that it will be stressed even more than it is in
15 the patient information guidebook the fact that it is
16 temporary, that we do not know beyond two years how
17 long the correction lasts and that sort of thing.

18 I would urge FDA to look into some of the
19 analyses we talked about yesterday, for instance, that
20 Dr. Gray presented maybe with manifest refraction
21 going to percentages who lose a certain amount, and
22 not only with the mean manifest refraction loss is.

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1 Then the second point would just be
2 concerns about the consistent cohort. Honestly, the
3 data that I requested, you know, certainly were
4 consistent with the comments that we have heard, that
5 the six and 12 month cohorts don't look dramatically
6 different. But there is the potential to mislead on a
7 table, any one of these tables, where you have only
8 half the people at 12 months that you do at six
9 months. I would just urge FDA to make sure that there
10 isn't a misleading comparison by virtue of there not
11 being a consistent cohort.

12 CHAIRMAN WEISS: Dr. Schein.

13 DR. SCHEIN: For label, I'm concerned
14 about an overemphasis on this word temporary, because
15 I think it may be irreversible for many people and, if
16 you really emphasize the temporary, you give the
17 impression that something is reversible.

18 So I -- apologies to the sponsor -- see
19 this a bit like offering a facelift to a patient. It
20 is not reversible, but it may only be temporary. I
21 think it is not a play on words. It really gives the
22 impression of reversibility when something in the

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1 label has to say it is presumed not to be reversible,
2 although it may be temporary.

3 DR. SMITH: Actually, it already says --
4 In the patient information part it says it is not
5 reversible on page 48 of 33.

6 DR. SCHEIN: Okay. I missed that, but
7 that's a difficult concept.

8 DR. SMITH: I agree, it should be
9 emphasized. It actually is not in the physician
10 section, but it is in the patient section.

11 CHAIRMAN WEISS: Maybe just for FDA, there
12 is a way to indicate that this -- that additional data
13 has been requested for the two-year. So maybe you
14 will have some curve to show how much this wears off
15 over what period of time. But if that is not clear,
16 then you will have to put in there, we don't know what
17 an individual -- how much effect they will lose over
18 what period of time, and put that next to, I guess,
19 the fact that this is not reversible, but some of the
20 effect will be lost, and how much over what period of
21 time we don't know. Dr. Bandeen-Roche, is that okay?

22 DR. BANDEEN-ROCHE: That's good. Thank

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1 you.

2 CHAIRMAN WEISS: That's good. Dr. Schein.

3 DR. SCHEIN: The other labeling comment I
4 have was a mention that this has not been studied in
5 pseudophakic patients. My concern here would be with
6 unknown effect of spots near a corneal incision.

7 CHAIRMAN WEISS: Then you will have to --
8 Then if you are going to say this has not been studied
9 in pseudophakic, it hasn't been studied in corneal
10 transplants. It hasn't been studied in a lot of other
11 things. So do you have a wish list of things you want
12 to indicate it wasn't studied in?

13 DR. SCHEIN: Well, this is distinctive
14 because of the age and prevalence. I can think of
15 lots of rare things, but --

16 DR. GRIMMETT: Would you rather than just
17 say that there are unknown effects near corneal
18 incisions, because that is what you are worried about,
19 rather than the type of surgery?

20 CHAIRMAN WEISS: Or when someone who has
21 had prior ocular surgery.

22 DR. SCHEIN: Right. The other thing, you

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1 know, a pseudophakic patient has absolutely zero
2 accommodative reserve, and the efficacy may be
3 completely different in that group as well.

4 CHAIRMAN WEISS: Well, I'm going to leave
5 that one up to the agency in terms of having another
6 warning to patients that, if it got used -- and I
7 don't recall if that was a contraindication if you are
8 pseudophakic, but if get used in off-label ways, maybe
9 we can make it a little bit broad, not just if you've
10 had prior refractive surgery but if you have had
11 corneal incisions, if you are pseudophakic, if you had
12 -- and maybe you have a laundry list of things. Dr.
13 Grimmett.

14 DR. GRIMMETT: Dr. Grimmett. Earlier
15 there was raised an issue about intraocular lens
16 calculation formulae with the alteration in corneal
17 curvature from this device. Dr. Durrie indicated that
18 he hasn't seen a problem in hyperopes, but I'm not
19 aware that there is a body of data that we actually
20 know the answer.

21 I would be in favor in an older population
22 that may be undergoing cataract surgery to make some

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1 affirmative statement that outcomes of IOL power
2 formulae are unknown after this procedure, and the
3 implications of changing a corneal curvature on all of
4 our regression formulas for lenses.

5 CHAIRMAN WEISS: Were there any other
6 tables or charts that were mentioned in the discussion
7 that we have not mentioned in labeling? Dr. Macsai.

8 DR. MACSAI: Well, in the patient
9 information booklet, page 25, there's Table 11 and 12.

10 We talked about the fact that these are not great
11 surveys and not validated, and they are not
12 standardized, and they could be misleading to the
13 consumer when you look at these.

14 So there should be some warning about
15 that, about the interpretation of these two tables.
16 It is the table of spectacle dependence for near
17 vision -- That's the title, Table 11 and 12, and they
18 talk about wearing spectacles at six and 12 months for
19 working on a computer, reading, all near activities,
20 night driving, watching TV, etcetera.

21 There's got to be some sort of disclaimer
22 that these are nonvalidated questionnaires, and not

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1 standardized. As Ms. Such brought up, you know,
2 computers come in thousands of forms nowadays.

3 CHAIRMAN WEISS: We could put a little
4 disclaimer there. Any other -- Ms. Such?

5 MS. SUCH: Actually, speaking to that,
6 talking about computers, I actually would like to see
7 the computer component taken out of this, because of
8 the amount of variables that were never taken into
9 consideration at all in this study.

10 There's just too many of them, and by
11 admission from the sponsor that they were not
12 considered, I'd like to see the words "for computer"
13 removed from this entire study, from physicians as
14 well, because it's not been actually proven. There's
15 just too many things, distance, size, contrast,
16 everything that you can imagine.

17 The other thing I would like to mention,
18 not on this topic, is I'd like to see -- I'm sorry to
19 say to my colleague -- that I would like to have put
20 back in the patient "What You Should Ask Your Doctor"
21 the issue about nystagmus.

22 Even though it is going to be brought up

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1 in contraindications, if you look at what you are
2 asking your doctor, most of these things are
3 redundant. Most of the things that you see in there
4 are brought up over and over and over again. It's
5 just once again bringing it up so somebody thinks
6 about it.

7 So if we were to take apart things that
8 are mentioned in contraindications, precautions or
9 warnings, we would be left probably with nothing left
10 on the list. So I think that we need to really think
11 about putting that back in.

12 The only one that I think that really
13 bothers me in that list is one that feels a bit
14 insulting, and that is the one about being able to
15 follow your doctor's instructions about leaving your
16 contact lens out, like as if you wouldn't be able to
17 follow instructions.

18 CHAIRMAN WEISS: Oh, I would really want
19 that in, because many patients don't, and I'm a
20 patient as well. So this is not meant as an insult to
21 patients. At some point, we all become patients, but
22 some patients take it very cavalierly, and it's

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1 terribly important to the result of your procedure,
2 and many contact lens wearers do not want to give up
3 their contact lens wear even for a moment.

4 So this is not to insult people. This is
5 to ensure a better result by underscoring it is very
6 important that they do this.

7 MS. SUCH: So perhaps we could wordsmith
8 that better to say to understand the importance that
9 you need to leave in.

10 CHAIRMAN WEISS: That's fine. We can tell
11 the agency to make it less insulting, if that is how
12 it comes across.

13 MS. SUCH: Yes, I'd like to see that a
14 little bit better. That's all from my end.

15 CHAIRMAN WEISS: In terms of whoever
16 wanted that item to be -- nystagmus to be taken out, I
17 would assume they are in agreement. It can get put
18 back in. Dr. McMahon?

19 DR. McMAHON: Sure, if it's a question.

20 CHAIRMAN WEISS: Fine. So it's back.

21 DR. GRIMMETT: Nystagmus under topical
22 anesthesia. That was your intent, right? We are not

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1 talking about blocking or putting people under general
2 anesthesia here. Right?

3 DR. McMAHON: Correct. And I don't --
4 It's not inappropriate. The question is asked about
5 what the fact that I have nystagmus, which I think is
6 what Glenda is getting to.

7 CHAIRMAN WEISS: Any other labeling
8 issues? So the agency is clear what extra charts in
9 terms of two-year data from the prior PMA and the
10 change with time over the year of the various
11 treatments that the Panel wanted, if that is the case,
12 if agency doesn't have any other -- Does agency have
13 any other requests or questions? No.

14 So we have now ended the Panel discussion.
15 We are going to go to the Open Public Hearing
16 session. Is there anyone who wanted to address during
17 the open public hearing session? Seeing no one, we
18 will close the open public hearing session.

19 Does the FDA have any closing comments?
20 No closing comments from the FDA.

21 The sponsor has five minutes for closing
22 comments, if they desire.

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1 DR. GORDON-MEYER: I'll be very brief. We
2 appreciate all of the good input from the Panel, and
3 we look forward to providing the additional analyses,
4 including equivalence of the stability, and we welcome
5 and appreciate this good review. Thank you all very
6 much.

7 CHAIRMAN WEISS: And I want to thank the
8 sponsor for a very clear review and a very excellent
9 presentation.

10 DR. GORDON-MEYER: Thank you.

11 CHAIRMAN WEISS: So now we will have Sally
12 Thornton read the voting options.

13 MS. THORNTON: The medical device
14 amendments to the Federal Food, Drug and Cosmetic Act,
15 as amended by the Safe Medical Devices Act of 1990,
16 allows the Food and Drug Administration to obtain a
17 recommendation from an expert advisory panel on
18 designated medical device pre-market approval
19 applications or PMAs that are filed with the agency.

20 The PMA must stand on its own merits, and
21 your recommendation must be supported by safety and
22 effectiveness data in the application or by applicable

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1 publicly available information.

2 Safety is defined in the Act as reasonable
3 assurance based on valid scientific evidence that the
4 probable benefits to health under conditions of
5 intended use outweigh any probable risk.

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

11 Your recommendation option for the vote
12 are as follows: Approval, if there are no conditions
13 attached; approvable with conditions, the Panel may
14 recommend that the PMA be found approval subject to
15 specified conditions such as physician or patient
16 education, labeling changes or a further analysis of
17 existing data. Prior to voting, all of the conditions
18 should be addressed by the Panel -- discussed by the
19 Panel, sorry.

20 Not approval: The Panel may recommend
21 that the PMA is not approvable if the data do not
22 provide a reasonable assurance that the device is safe

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

5 Following the voting, the Chair will ask
6 each Panel member to present a brief statement
7 outlining the reasons for their vote. Thank you.

8 CHAIRMAN WEISS: Thank you, Sally. Does
9 anyone want to propose a main motion? Dr. Van Meter?

10 DR. VAN METER: I would like to move that
11 the PMA be approvable with the conditions that we have
12 discussed. Now we have to list the conditions again.

13 Is that correct?

14 CHAIRMAN WEISS: Yes. The first motion
15 being approvable with conditions. Does anyone second
16 that?

17 DR. MATHERS: Second.

18 CHAIRMAN WEISS: Dr. Mathers seconds that.

19 So now we will go on to discussion of that and, if
20 there is no discussion, then we can just go on to each
21 of the conditions that anyone wants to propose.

22 I think we should start with Dr. Grimmett,

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1 who has been scribing for us. If you could introduce
2 the conditions, and I would ask perhaps introduce the
3 indication condition first.

4 DR. GRIMMETT: Condition Number 1: Change
5 the indication statement to the intended range of
6 effect; that is, 1.00 diopter to 2.25 diopters of
7 effect, as suggested by Dr. McMahon.

8 CHAIRMAN WEISS: Anyone second that?

9 DR. MACSAI: Second.

10 CHAIRMAN WEISS: Dr. Macsai seconds. All
11 of those in favor -- As we typically do, we will vote
12 on each of the individual conditions before voting on
13 the main motion. So for this particular condition of
14 the indications, all of those in favor, please signify
15 by raising your hand.

16 MS. THORNTON: Voting for the condition,
17 Dr. Huang, Bandeen-Roche, Smith, McMahon, Coleman, Van
18 Meter, Bradley, Grimmett, Casey, Mathers, Schein,
19 Macsai. That is unanimous.

20 CHAIRMAN WEISS: This passes unanimously.
21 Then I believe Dr. Grimmett will read the labeling
22 conditions, as it appears that most of the other

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1 condition items are labeling and, if they are not,
2 then we will just pick them out and subsequently do
3 them.

4 So these will be a list of all the
5 labeling issues. This will be voted on as one
6 condition. If you can propose the condition, and then
7 someone will second it.

8 DR. McMAHON: So move.

9 CHAIRMAN WEISS: I don't think the
10 condition was proposed yet.

11 MS. THORNTON: Would you state that,
12 please, Dr. McMahon?

13 DR. McMAHON: That is actually standard
14 Robert's Rules. You just gave it, and I just --

15 CHAIRMAN WEISS: Well, I didn't want to
16 give it, but okay. That's fine. Second.

17 DR. GRIMMETT: This is Dr. Grimmatt. I
18 believe most of them are labeling. If one of them is
19 not, we will decide it as I go through sequentially.

20 There was a comment that there was a claim
21 that the depth perception is unchanged, but the
22 comparison was not fair, if you will. It compared

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1 pre-op contact lens monovision and not spectacles.
2 That needs to be better defined in the labeling of
3 what was being compared, and it saying that there is
4 no change in depth perception is probably not really
5 correct. Do we vote on that?

6 CHAIRMAN WEISS: No. We are going to list
7 all the labeling -- The condition is that of labeling,
8 and all the labeling things will be listed as one.

9 DR. GRIMMETT: List them as you go. If
10 anyone disagrees with any of these, just speak right
11 up.

12 CHAIRMAN WEISS: Yes.

13 DR. GRIMMETT: In the labeling, include a
14 graph of treatment effect that is regression with
15 time, both for the overall cohort, the emmetropes, the
16 hyperopes, this PMA and the prior PMA.

17 In the labeling, include information on
18 the spot pattern efficacy as well as the efficacy with
19 intended correction. Include it both ways.

20 Include in the labeling information
21 regarding spectacle dependence issues, with Dr.
22 Macsai, I believe, making a provision on that, that

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1 the data are from nonvalidated questionnaires.

2 Dr. McMahon submitted 13 suggested items
3 that he read on his typewritten page 11 and 12. Would
4 you like me to reread all 13 or can I include those as
5 "the McMahon 13"?

6 CHAIRMAN WEISS: I would love to hear them
7 again.

8 DR. GRIMMETT: Okay. McMahon Subgroup I:
9 As the sponsor has already agreed to remove the term
10 "blended vision" as a euphemism -- that was his first
11 suggestion -- use the word monovision.

12 Number 2: On page 11 of 31, add the term
13 "keloid" in parentheses after "scars."

14 On page 11 of 31, include nystagmus as a
15 contraindication under topical anesthesia.

16 Number 4: On page 14 of 31, state that
17 the effectiveness and safety of re-treatments have
18 not been determined in this trial.

19 Number 5: Page 13 and 14 of 31, mention
20 in this section regarding the need for a monovision
21 trial, as it was part of the entry criteria for this
22 protocol.

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1 Number 6: Page 12 of 31, a housekeeping
2 item regarding moving a couple of paragraphs of first
3 days after paragraphs of the weeks.

4 Number 7: page 23 of 31, in Table 8,
5 wanted a row added regarding "worse" data.

6 Number 8: Page 24 of 31, regarding
7 questions to ask your doctor. Recommending omitting
8 the first bullet, if nystagmus is ultimately
9 contraindicated.

10 Number 9: Adding a table defining the
11 frequency of induced cylinder and the effect this had
12 on near and distance vision in the trial.

13 Number 10: Adding a cautionary statement
14 after Table 1, page 8 of 31, indicating that the
15 equivalent outcomes in non-Caucasians have not been
16 determined.

17 I'm back to the reading glasses here. My
18 accommodation ran out.

19 Number 11: The recommendation was to
20 remove nystagmus from the warning, but Glenda Such
21 recommended that it be left in, in several sections,
22 including in contraindications as well as in other

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1 sections. I agree with that. You okay with the
2 amendment to your original suggestion?

3 DR. McMAHON; Yes. That was in the "Ask
4 the Doctor" part.

5 DR. GRIMMETT: Yes. Thank you.

6 Number 12: Recommendation regarding
7 adding the statement that a stable refraction should
8 be determined if at any visit the pre-operative
9 corneal topography is abnormal, especially with rigid
10 gas perm lenses.

11 Number 13: Add a statement: The
12 effectiveness of this procedure or device has not been
13 determined for patients with less than 20/25 best
14 spectacle corrected visual acuity pre-operatively.

15 That concludes the McMahon 13.

16 Dr. Huang wanted included the data table
17 on excluded eyes.

18 CHAIRMAN WEISS: Are we also including the
19 data table on the 32 spots?

20 DR. GRIMMETT: That is one and the same?
21 Isn't that correct? That's one and the same?

22 CHAIRMAN WEISS: That's one and the same.

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1 DR. GRIMMETT: Okay.

2 CHAIRMAN WEISS: So all the 32-spot eyes,
3 not just the excluded ones.

4 DR. MACSAI: Correct.

5 DR. GRIMMETT: The more, the better.

6 Dr. Van Meter suggested in the physician
7 labeling to emphasize the importance of proper
8 centration on the visual axis for a multitude of
9 reasons, including irregular astigmatism induced
10 cylinder, so on and so forth.

11 Someone made a statement regarding a
12 contraindication or a consideration for keratoconus
13 and other ectatic diseases. I believe that was the
14 phrase that needed to be added. Is that correct?

15 CHAIRMAN WEISS: Yes.

16 DR. GRIMMETT: Add a statement, from Dr.
17 Schein, that prior incisional keratotomy is a
18 contraindication. The next statement: There are no
19 data on eyes with prior refractive surgery.

20 Dr. Coleman had --

21 DR. MACSAI: I thought it was prior --

22 DR. SCHEIN: Cataract surgery, aphakic.

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1 DR. MACSAI: Or prior surgery, prior
2 ophthalmic surgery.

3 DR. GRIMMETT: Okay. No data regarding
4 prior refractive surgery or other ophthalmic surgery.

5 CHAIRMAN WEISS: Just I'm wondering, with
6 keratotomy, if you have a limbal relaxing incision,
7 that is a keratotomy, but the CK is not going to be in
8 that area. Well, is it a contraindication or is it I
9 don't know?

10 DR. GRIMMETT: Well, there is just a
11 statement being made that there is no data.

12 CHAIRMAN WEISS: I think the one -- The
13 complication of which I am aware was a radial
14 keratotomy.

15 CHAIRMAN WEISS: Do you want to specify,
16 instead of incisional keratotomy, to just radial
17 keratotomy or astigmatic keratotomy? Are we leaving
18 out limbal relaxing incision?

19 CHAIRMAN WEISS: Well, an LRI is an "I
20 don't know" as opposed to a contraindication.

21 DR. SMITH: The current language is in the
22 precaution section for the physicians, and it says

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1 corneal or intraocular surgery.

2 CHAIRMAN WEISS: Fine. Let's leave it as
3 that, so we don't even have to -- Dr. Beers and then
4 Dr. McMahon.

5 DR. BEERS: Yes. We can certainly put for
6 ophthalmic surgery "such as," and make some examples.
7 However, the importance of this in the patient
8 labeling is, for anything, is that they should speak
9 with their doctor if they have had this, not -- You
10 know, we don't want to define it too closely. It's
11 just, if you had something, talk to your doctor about
12 it. Let him know, and you all discuss it.

13 CHAIRMAN WEISS: Okay. So you have the
14 sentiment of it. You don't need anymore particulars,
15 it sounds like. Yes?

16 DR. GRIMMETT: Dr. Coleman's suggestions
17 in the physician precautions, page 12 of 57, regarding
18 steroid response pressure rise or IOP greater than 21
19 -- That's a contraindication, Anne?

20 CHAIRMAN WEISS: Dr. Coleman.

21 DR. COLEMAN: Just as a precaution.

22 DR. GRIMMETT: A precaution?

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1 DR. COLEMAN: Add it to the precaution
2 section.

3 DR. GRIMMETT: Okay. Precaution section
4 regarding steroid response, glaucoma or pressure
5 greater than 21, patients with ocular hypertension and
6 patients with a history of glaucoma. You want it
7 added just to the physician and patient precaution
8 section? Is that the intent?

9 DR. COLEMAN: Correct. Yes, because there
10 is a place where it says patients with a history of
11 glaucoma, but to also add that to that precaution.

12 DR. GRIMMETT: All right. Dr. Weiss'
13 statement, add a statement specifically stating that
14 monovision may affect depth perception. That is
15 probably already in there, I'll bet.

16 Dr. Bandeen-Roche emphasizing the
17 importance of the temporary effect of the data, some
18 way emphasizing that or showing that information, as
19 well as my previous recommendation showing the mean
20 manifest refraction loss data. I think I already
21 recommended that.

22 Dr. Schein recommended some type of

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1 wordsmithing trying to discuss the differentiation
2 between temporary and reversible.

3 CHAIRMAN WEISS: I think it was listed in
4 there already that it is irreversible.

5 DR. GRIMMETT: Okay. Add a statement
6 regarding the information that effects of the change
7 in corneal curvature have unknown effects on current
8 lens power calculation formulae and cataract surgery.

9 Glenda Such recommending delete the
10 reference altogether to the patient's functioning with
11 computers, given the data was not sufficiently
12 studied.

13 Then the suggestion to re-wordsmith the
14 following instructions regarding taking out your
15 contact lens to eliminate any condescending or
16 insulting type of inference.

17 CHAIRMAN WEISS: Well, no, we are going to
18 keep that in there, I think.

19 DR. GRIMMETT: Keep it in, but re-
20 wordsmith to get rid of the inference.

21 CHAIRMAN WEISS: Yes, to make it sound
22 better.

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1 DR. GRIMMETT: And I believe that is all I
2 have on labeling.

3 CHAIRMAN WEISS: Mr. McCarley.

4 MR. McCARLEY: Just one comment. I think
5 the reversibility issue should be there is no
6 evidence. You should not put it that it is not
7 reversible, because you don't know whether it is or
8 not.

9 CHAIRMAN WEISS: It's 100 percent not
10 reversible. You can't stick a needle in the eye and
11 then --

12 MR. McCARLEY: The effects are what you
13 were talking about, though, weren't they? The effects
14 are --

15 CHAIRMAN WEISS: -- not reversible. They
16 actually had it in the labeling that it is
17 irreversible. So it's really not an issue.

18 MR. McCARLEY: So we are talking about the
19 effects of the surgery. I understood from Dr. Durrie
20 that, in fact, he had reversed the effects. He had
21 re-treated a patient with -- So he changed the effect
22 is what I'm saying.

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1 CHAIRMAN WEISS: Well, he needed to do a
2 re-treatment, but he didn't reverse the effect.

3 DR. SMITH: Can I suggest one sentence?

4 CHAIRMAN WEISS: Sure. Dr. Smith.

5 DR. SMITH: "Although the effect of CK on
6 near vision is temporary, the overall effect of CK on
7 the cornea is not reversible."

8 CHAIRMAN WEISS: It's more than that. It
9 is not only the effect on the cornea. It is also the
10 refractive effect. Maybe you will get a temporary
11 effect, but you will get half as much eventually as
12 what you wanted. So it's not just the cuts into the
13 cornea, but it's also the refractive.

14 DR. SMITH: The temporary aspect is really
15 the effect on near vision.

16 CHAIRMAN WEISS: I would defer to agency.
17 I think you probably get -- We would like to convey
18 to the patient as well as the physician as well as
19 possible that, one, there is no eraser on the edge of
20 this probe and, two, that unless you can edify us
21 further with the addition of the two-year data, we
22 can't guaranty someone where they are exactly going to

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1 end up when they spin the wheel.

2 DR. GRIMMETT: Those are all the labeling
3 conditions I have.

4 CHAIRMAN WEISS: Dr. Bandeen-Roche.

5 DR. BANDEEN-ROCHE: Yes. Just to update
6 the labeling packet with the most complete one-year
7 data available as it is ready to go.

8 CHAIRMAN WEISS: Good suggestion. So we
9 will add that.

10 If there is no other additions to the
11 laundry list, then I would like to have a vote on the
12 labeling. All of those who agree with the labeling as
13 listed, can you please raise your hand in the
14 affirmative.

15 MS. THORNTON: In the affirmative, Dr.
16 Huang, Dr. Bandeen-Roche, Smith, McMahon, Coleman, Van
17 Meter, Bradley, Grimmett, Casey, Mathers, Schein,
18 Macsai. That is unanimous, 12.

19 CHAIRMAN WEISS: So the condition of
20 labeling is unanimously accepted. Are there any other
21 conditions that you have listed, Dr. Grimmett?

22 DR. GRIMMETT: There are no others that I

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1 have listed.

2 CHAIRMAN WEISS: Are there any other
3 conditions that anyone on the Panel -- Dr. Grimmett?

4 DR. GRIMMETT: I think it was implicit,
5 but even though the indication we read limiting up to
6 2.25, I would feel strongly that the data that they
7 have higher than that should be included in the
8 current labeling, because the procedure is already out
9 in the marketplace.

10 CHAIRMAN WEISS: So we had said in the
11 labeling with Dr. Huang's exclusionary 11 eyes of the
12 32, that at the same time we would include that chart
13 on the 32.

14 DR. GRIMMETT: I want not only just -- I
15 want all 32 spot or greater than 2.25 diopter data
16 included regarding the effectiveness outcomes,
17 irrespective of the fact we have limited the procedure
18 to 2.25.

19 DR. BEERS: We will do that, because the
20 fact is we can't lock it out at that point.

21 DR. GRIMMETT: Excellent. So that doesn't
22 even need to be a condition. It sounds like you are

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1 going to do it anyway.

2 DR. BEERS: Yes.

3 CHAIRMAN WEISS: The other thing is I
4 could use someone to refresh my memory. There were
5 some members of the Panel that proposed that the
6 effectiveness in the 8-spot has not been determined,
7 because there weren't enough patients. I don't know
8 if that was addressed in any of these motions or if
9 that was not.

10 If that was not addressed, does anyone
11 want to propose that as a motion or as a condition,
12 which basically would mean that you need -- the FDA
13 would have to look at further data or put it in the
14 labeling.

15 DR. McMAHON: Well, I had proposed that
16 the indication would be as it is, and then there would
17 be a statement that there is insufficient data to
18 validate the use of 8 spots in the treatment.

19 CHAIRMAN WEISS: You want to say 8 spots
20 or the refractive error that you would be using the 8
21 spots for, because a patient wouldn't know what 8
22 spots mean?

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1 DR. MACSAI: Leave it to the agency.

2 DR. McMAHON: That is a wordsmithing
3 thing. The agency can deal with it, but I got around
4 that by doing the 1.00 to 2.25, which eliminates 8 and
5 32. So I think you just leave it that way.

6 CHAIRMAN WEISS: So you are basically
7 giving an indication. You are getting rid of the low
8 end, and you are getting rid of the high end, as far
9 as efficacious. Then would you like to put in there
10 then -- As long as you are putting in the data for the
11 32, do you want to put in the data for the 8?

12 DR. McMAHON: More data is better.

13 DR. GRIMMETT: It sounds like the agency
14 would do that anyway.

15 CHAIRMAN WEISS: The agency is putting in
16 the data for the 8, in any case? So the way it is
17 presently listed, you would not need anything else
18 from us?

19 DR. BEERS: I just wanted to clarify the
20 indication, because when you started asking again
21 about 8-spot, I thought, as Dr. McMahon said, that
22 from 1.00 to 2.25 is eliminating 8, the low end and

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1 the high end, just to make sure this is what you all
2 were saying.

3 CHAIRMAN WEISS: So the Panel has agreed
4 to eliminate the low end and the high end, but put all
5 the data in there, if a physician intends to treat
6 off-label. We have that as an indication. So the
7 indication is for +1.00 to +2.25.

8 We are listing it as a refractive
9 indication, but basically the 8-spot was less than 1
10 diopter of attempted treatment, and the 32-spot was
11 more than 2.25 diopter of attempted treatment. So,
12 effectively, those two were eliminated by that
13 indication. Dr. Macsai.

14 DR. MACSAI: We had also requested the 24-
15 month data with the establishment of substantial
16 equivalence included.

17 CHAIRMAN WEISS: Was that listed in your--

18 DR. GRIMMETT: I intended to include that.
19 If it's not clear, but I did intend to include that
20 when I asked for the 24-month data on the old PMA.
21 Yes.

22 DR. MACSAI: Okay.

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1 CHAIRMAN WEISS: So I don't think we need
2 to vote on that again, because the Panel agreed to
3 that. Just so the agency knows that, if that wasn't
4 included in the transcript, substantial equivalency
5 between the two groups was also requested, between the
6 previous PMA group and this group.

7 Any other conditions? Okay, so if there
8 are no other conditions, then we will have a vote on
9 the main motion, the motion being approvable with
10 conditions for PMA PO10018/S005.

11 Those of you who are in agreement to
12 approve this PMA with conditions, can you raise your
13 hand, if you are voting in the affirmative?

14 MS. THORNTON: Voting in the affirmative,
15 Dr. Huang, Bandeen-Roche, Smith, McMahon, Coleman, Van
16 Meter, Bradley, Grimmett, Casey, Mathers, Schein, and
17 Macsai. It is unanimous, 12 votes.

18 CHAIRMAN WEISS: So the PMA has passed
19 unanimously. I am going to now poll the members of
20 the Panel as to why you voted the way you did. Dr.
21 Macsai?

22 DR. MACSAI: I voted in the affirmative.

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1 The device is already on the market. Safety has been
2 established. The effect is temporary.

3 CHAIRMAN WEISS: Dr. Schein.

4 DR. SCHEIN: The excellent safety profile
5 excuses moderate effectiveness.

6 CHAIRMAN WEISS: Dr. Mathers.

7 DR. MATHERS: I believe it offers
8 considerable patient satisfaction and has excellent
9 safety.

10 CHAIRMAN WEISS: Dr. Casey.

11 DR. CASEY: The procedure seems to be
12 safe, and patients are satisfied. It seems to be
13 effective in the limited range that we have discussed.

14 CHAIRMAN WEISS: Dr. Grimmitt.

15 DR. GRIMMETT: I am in favor of the
16 proposal, because even though the treatment range is
17 limited, the data available to both patients and
18 physicians will now be available for a previous
19 practice that was off-label.

20 CHAIRMAN WEISS: Dr. Bradley.

21 DR. BRADLEY: The device is clearly safe
22 and sufficiently effective.

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1 CHAIRMAN WEISS: Dr. Van Meter.

2 DR. VAN METER: I agree with Dr. Grimmett.

3 CHAIRMAN WEISS: Dr. Coleman.

4 DR. COLEMAN: I voted approvable with
5 conditions, because I had reasonable assurance of
6 safety and effectiveness.

7 CHAIRMAN WEISS: Dr. McMahon.

8 DR. McMAHON: I voted for approvable with
9 conditions on the basis that the procedure appears to
10 be safe and effective within the limits that we have
11 defined.

12 CHAIRMAN WEISS: Dr. Smith.

13 DR. SMITH: I agree with Dr. McMahon.

14 CHAIRMAN WEISS: Dr. Bandeen-Roche.

15 DR. BANDEEN-ROCHE: I also agree with Dr.
16 McMahon.

17 CHAIRMAN WEISS: Dr. Huang.

18 DR. HUANG: I voted for approvable with
19 conditions based on the limited efficacy and good
20 safety. In addition, I also feel approval will
21 provide a guideline to the general public that this is
22 a viable alternative for us. Some of the patients may

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1 be benefiting from this procedure.

2 CHAIRMAN WEISS: Mr. McCarley, do you have
3 any comments?

4 MR. MCCARLEY: The only comment is I am
5 glad the Panel saw this, taking the opportunity to
6 take a device that is already being used on the market
7 and allowing the company to reasonably provide
8 additional information to doctors and to patients.
9 Otherwise, they would have continued to use this
10 without it. So I think it was the right decision.

11 CHAIRMAN WEISS: Ms. Such?

12 MS. SUCH: I would like to thank the Panel
13 for the time that they spent in considering the
14 patients' concerns and for also including them in the
15 passage of this particular device.

16 CHAIRMAN WEISS: I wanted to thank members
17 of the Panel and the primary reviewers for their
18 excellent reviews, and the FDA for their usual
19 thorough job, and the sponsor for making it so easy to
20 evaluate their study and for their hard work.

21 Sally, do you have any closing comments?

22 MS. THORNTON: I just wanted to thank the

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1 Panel for bearing with us all and for two days of very
2 good work, and also for the staff putting their heart
3 behind this.

4 I also want to announce to everyone that
5 there is going to be another Panel meeting March 5th,
6 and it is going to be a general issues discussion
7 surrounding the use of intraocular lenses with clear
8 lens extraction. So we will see you then.

9 CHAIRMAN WEISS: The Open Meeting is
10 adjourned.

11 (Whereupon, the foregoing matter went off
12 the record at 3:09 p.m.)
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