

**SUMMARY MINUTES**

**OF THE**

**OPHTHALMIC DEVICES PANEL MEETING**

**OPEN SESSION**

**May 23, 2003**

**Gaithersburg Marriott  
Gaithersburg, MD**

## OPHTHALMIC DEVICES PANEL ROSTER

May 23, 2003

Jayne S. Weiss, M.D.	Chair
Arthur Bradley, Ph.D.	Voting Member
Anne L. Coleman, M.D., Ph.D.	Voting Member
Michael R. Grimmett, M.D.	Voting Member
Allen C. Ho, M.D.	Voting Member
Alice Y. Matoba, M.D.	Voting Member
Timothy T. McMahon, O.D., F.A.A.O.	Voting Member
Terri L. Young, M.D.	Consultant, deputized to vote
Glenda V. Such, M.Ed.	Consumer Representative
Ronald E. McCarley	Industry Representative

## FOOD AND DRUG ADMINISTRATION PARTICIPANTS

Sara M. Thornton	Panel Executive Secretary
A. Ralph Rosenthal, M.D.	Director, Division of Ophthalmic Devices
Jan C. Callaway	Acting Chief, Diagnostic and Surgical Devices Branch
Bernard L. Lepri, O.D., M.S., M.Ed.	Optometrist, Vitreoretinal and Extraocular Devices Branch; Clinical Reviewer
Donna R. Lochner	Chief, Intraocular and Corneal Implants Branch
James F. Saviola, O.D.	Chief, Vitreoretinal and Extraocular Devices Branch

## **CALL TO ORDER**

**Panel Chair Jayne Weiss, M.D.**, called the meeting to order at 8:34 a.m. **Panel Executive Secretary Sara Thornton** extended a special welcome to new panel consultant Terry L. Young, M.D., and asked the panel members to introduce themselves. She then read the conflict of interest statement. A full waiver had been granted to Dr. Weiss for her consulting with a competitor's unrelated product. The agency took into consideration certain matters regarding Drs. Weiss and Young as well as Anne L. Coleman, M.D., Ph.D., Allen C. Ho, M.D., and Michael R. Grimmett, M.D., who reported current or past interests in firms at issue but in matters not related to the day's agenda; they could therefore participate fully in the panel's deliberations. Ms. Thornton noted that industry representative Ronald E. McCarley is president of a firm at issue. She then read the appointment to temporary voting status, which stated that panel consultant Dr. Young had been given temporary voting status for the meeting.

## **OPEN PUBLIC HEARING**

No comments were made.

## **OPEN COMMITTEE SESSION**

### **Division Update**

**A. Ralph Rosenthal, M.D., director, Division of Ophthalmic Devices**, said that the division has been given leave to make new hires. He noted that Congress has introduced a bill to amend the Food, Drug, and Cosmetics Safety Act to recognize both corrective and noncorrective contact lenses as medical devices, regardless of intended use.

## **Branch Updates**

**James F. Saviola, O.D., chief, Vitreoretinal and Extraocular Devices Branch,** provided information on FDA's regulation of decorative contact lenses. Decorative contact lenses are cosmetics, provided that they are not marketed with claims that they change the eye. In October 2002, FDA issued an Import Alert for decorative lenses; the alert does not cover contact lenses that are intended for vision correction or for prosthetic or other medical use.

Some lenses currently on the market under cleared 510(k)s include contact lenses intended for both vision correction and for solely decorative purposes. The sponsors in those cases voluntarily included a plano lens in the range of corrective powers described in the 510(k) submissions. These products are regulated by FDA as medical devices under the Act. Such control is not available for decorative contact lenses because they are cosmetics under section 201(i) of the Act. Until legislation is passed, that is how the lenses are regulated.

FDA is taking a strong position that eye care providers are needed to fit decorative contact lenses. FDA has sent a notice to eye care professionals about the risks of decorative lenses and is encouraging all eye care professionals to document cases of injury. CDRH also issued a Public Health Web Notification directed to health care professions that noted the significant risk of blindness and other eye injuries if noncorrective decorative or cosmetic lenses are distributed without an eye care professional's involvement. The FDA's MedWatch database has subsequently recorded more than 10 reports of decorative or colored contact lens events.

**Jan C. Callaway, acting chief, Diagnostic and Surgical Devices Branch,** said that three devices have been approved since the August 2002 panel meeting. On October 18, 2002, FDA approved P970043 for the Alcon LADARVision 4000 CustomCornea, for wavefront-guided LASIK for the reduction or elimination of myopia up to -7.00 diopters (D) with less than

-0.50 D of astigmatism at the spectacle plane. On February 25, 2003, FDA approved P990027 for the Bausch and Lomb TECHNOLAS 217A Excimer Laser System for LASIK treatments for the reduction or elimination of low-to-moderate, naturally occurring hyperopia of +1.00 to +4.00 D with or without refractive astigmatism up to +2.00 D.

Since August 2002, the agency has cleared about 30 510(k) applications. In addition, the agency recently sent a form letter to all IDE sponsors suggesting that even if they had prior approval, they should meet with FDA to review the data needs for their PMA to avoid deficiencies.

Note: Ms. Thornton announced later in the day, that the FDA had just approved P930016 for the VISX Star S4 WaveScan excimer laser for wavefront-guided laser in situ keratomileusis (LASIK) for the reduction or elimination of myopic astigmatism up to -6.00 D mean refractive spherical equivalent (MRSE) with cylinder between 0.00 D and -3.00 D at the spectacle plane.

**Donna R. Lochner, chief, Intraocular and Corneal Implants Branch**, updated the panel on the status of P010059, the Morcher GmbH endocapsular tension ring for capsular bag stabilization in patients with pseudoexfoliation syndrome or other situations of compromised zonules. In January 2002, the panel recommended that the PMA was approvable and requested what amounted to a complete reanalysis of the clinical data to resolve discrepancies in the PMA. The PMA has not been approved; the Agency is working with the sponsor to resolve the remaining issues.

## **SPONSOR PRESENTATION**

**Paul Kramsky, vice president, Regulatory and Quality Systems, C&C Vision**, introduced the sponsor presenters. CrystaLens is a posterior chamber accommodating intraocular lens that is

indicated for primary implantation for the visual correction of aphakia in adult patients with cataracts to provide improved near, intermediate, and distance vision without spectacles.

**Michael Breen, OD, director, Clinical Outcomes, C&C Vision,** presented the technical overview. He defined *accommodation* as “the ability of the eye to change focus and provide a clear image over a range of distances.” Conventional intraocular lenses focus light at a fixed distance, providing vision at a single focal point; after cataract surgery, patients require correction for intermediate and near vision. Some treatment approaches include reading glasses; progressive lenses; monovision, multifocal, and bifocal intraocular lenses (IOLs); and development of accommodating IOLs.

Dr. Breen summarized the rationale for accommodating IOLs and described supporting studies. He then described technical aspects of the CrystaLens device and the proposed mechanism of action. Ciliary muscle contraction and relaxation results in the redistribution of muscle mass, which results in an increase in pressure of the vitreous cavity and a decrease in anterior chamber pressure. Because the optic locates against the vitreous face, the pressure changes move the optic forward and backward. Hinges facilitate movement of the optic by minimizing resistance.

Preclinical testing was conducted according to FDA guidance and ISO standards. Testing encompassed biocompatibility; YAG laser effect in vitro; hydrolytic stability, photostability, and exhaustive extraction; and optical and mechanical testing, including dynamic fatigue testing. All testing was successfully completed and was submitted as part of the IDE application and as part of this submission.

**Stephen Slade, M.D., medical monitor and study investigator,** presented the design and results of the prospective multicenter trial, which was conducted under FDA-approved

guidance. Patients had to be at least 50 years old, scheduled for cataract surgery by phacoemulsification, have a potential for best corrected visual acuity of 20/32 or better in each eye, and have a corneal cylinder of 1.00 D or less. Measures of near, intermediate, and distance visual acuity were taken using the Stereo Optical Optec X1600 Vision Tester calibrated for a distance of 20 feet and MN Read Acuity at 16 and 32 inches. Patients were followed for 1 year. Study participants consisted of 324 subjects (497 eyes; 181 women; 143 men).

At 1 year, data on 246 primary eyes and 124 bilateral implanted subjects were available. Results indicated that 88.4 percent of primary eyes and 98.4 percent of bilateral subjects had uncorrected near visual acuity of 20/40 or better; 90.1 percent of primary eyes and 100 percent of bilateral subjects had corrected near visual acuity of 20/40 or better. Results were similar for intermediate and distance visual acuity. Outcomes were good regardless of the biometry method, patient age, and history of YAG capsulotomy. Near visual acuity and manifest refraction were stable at several follow-up points. All bilateral subjects and 89.6 percent of primary eyes achieved corrected distance visual acuity of 20/40 or better.

A survey of bilaterally implanted patients found that approximately three-fourths of patients did not wear spectacles or wore them rarely; 93.8 percent were able to perform most daily functions without spectacles. Of the 128 bilaterally implanted subjects, 64 percent rated their near vision as very good or excellent, 80.3 percent rated their intermediate vision as very good or excellent, and 82 percent rated their distance vision as very good or excellent.

**Michael Colvard, M.D., medical monitor and study investigator,** presented results of a substudy to evaluate performance under low light and poor light conditions. A total of 126 eyes receiving CrystaLens were compared with 64 eyes receiving standard IOLs. The eligibility criteria were identical to the clinical trial. Mesopic contrast sensitivity was measured with the

Stereo Optical Optec X1600 Vision Tester; patients were tested at 3 cd/m<sup>2</sup> following 10 minutes of dark adaptation, with and without glare source of 3 lux.. The device was calibrated for 20 feet. No significant difference was found between CrystaLens and standard IOLs. CrystaLens showed no effect of glare on contrast sensitivity, consistent with standard IOL outcomes.

Dr. Colvard then presented safety data. The cumulative adverse event rate for all eyes (*N* = 497) was low. The most common adverse event was cystoid macular edema (CME). Incidence of adverse events was slightly higher than the FDA grid of historical controls. All eyes with CME or iritis were 20/32 or better at 1 year. No serious or unanticipated lens-related adverse events were reported.

**Adrian Glassar, Ph.D., a consultant to C&C Vision,** presented information on accommodation mechanisms and assessment. After providing authoritative definitions of accommodation, he described the proposed mechanism of action of the device. Despite years of study, the mechanism of physiological accommodation is still not understood. Pseudophakic accommodation is a new concept, and its mechanism is not fully understood. In patients implanted with the CrystaLens, objective measurements of changes in anterior chamber depth show forward IOL movement. Near and intermediate visual acuity measured through the distance correction provides evidence of accommodation. Compared with subjects who received standard IOLs, CrystaLens subjects required 1.12 D less add to achieve best corrected near visual acuity.

Finally, Dr. Slade summarized the sponsor's data. He noted that the CrystaLens was designed to provide patients with the full range of clear vision without glasses. More than 89 percent of bilaterally implanted subjects have uncorrected near, intermediate, and distance acuity of 20/40 or better.

## **Panel Questions for Sponsor**

Panel members asked questions concerning the definition of accommodation, the study protocol, optic size and its relation to patient satisfaction outcomes, hinge fatigue, effects of YAG capsulotomy following implantation of the lens, contraindications, and why atropine was used postoperatively. Sponsor representatives provided clarification to the panel's satisfaction.

## **FDA PRESENTATION**

Ms. Lochner introduced the FDA presentation. She noted that a central issue for the panel review of the sponsor's extraordinary claims is whether the near visual acuity data and limited other outcomes support the claim of accommodation. The panel is being asked to focus on the clinical and technical merits of the claims, not on the exact wording for the labeling.

**Bernard P. Lepri, O.D., M.S., M.Ed.**, presented the FDA review. The achievement of near visual acuity through accommodation is germane to the fundamental indication of the device. The sponsor conducted additional testing in an effort to document the mechanism of action (i.e., accommodation through the forward and backward movement of the lens optic along the eye axis). The testing included dynamic retinoscopy, defocus, near point evaluation, near vision, power mapping, and anterior chamber depth. A wide spread in the dioptric results was measured (0.72 D to 3.14 D). The highest correlation among the findings is between the Tracey Aberrometer findings and the change in anterior chamber depth. The lowest correlation is that between dynamic retinoscopy and aberrometry. Dr. Lepri summarized the rest of the sponsor's data and reviewed the indications for use.

## COMMITTEE DELIBERATIONS

**Panel Reviewer Anne Coleman** stated that the effectiveness data appear to support a claim of accommodation for CrystaLens: Approximately 80 percent of primary eyes had uncorrected distance and near acuity of 20/40 or better. Because eyes within  $\pm 0.50$  D of plano were more likely to have distance and near acuity of 20/40 or better and because fellow eyes that were targeted for plano had a greater frequency of uncorrected distance and near acuity of 20/40 or better, the labeling on page 2 (first sentence) should be changed from “ $-0.50$  sphere” to “aiming for plano.” Ninety-six percent of eyes had a change in distance acuity of  $\pm 1.0$  D; the large range in the acuity difference between the postoperative visits is of concern. The data should be presented in the labeling as the proportion that had a change of  $\pm 0.50$  D. In addition, 10 years of accommodative ability by the CrystaLens may or may not be adequate; that information should be included in the labeling. The following other changes to the labeling are appropriate:

- ?? Add a warning or precaution that the effects of vitrectomy on accommodative performance of the CrystaLens are unknown.
- ?? Include information from the patient survey.
- ?? Mention the range of axial length and lens powers that were used in the study.
- ?? Mention that atropine sulfate 1 percent should be given immediately after operation and on the first day after the operation.
- ?? In the Adverse Events section, mention the possible increased rate of CME associated with sulcus-bag placement of haptics.

With the above additions and modifications to the labeling, the data provide reasonable assurance of safety and effectiveness.

**Panel Reviewer Arthur Bradley** noted that he focused his review on (1) the device’s effectiveness—whether it allows eye to accommodate, and by how much; (2) the mechanism of action; and (3) whether the device provides adequate quality near vision. With regard to effectiveness, he stated that the CrystaLens generates somewhere between 0.5 and 1.0 D of extra power (accommodative amplitude) during pharmacologically induced and natural

accommodative effort. It is unfortunate that the most compelling data sets were only carried out on 5 subjects and, rather than obtain the data while patients made accommodative effort, the data were obtained by measuring the difference between two states.

Regarding mechanism of action, the data show forward movement, but only in 10 eyes; anterior chamber depth was compared for each eye with cyclopentolate and pilocarpine. Both drugs affect ciliary muscle as well as iris, so measurements were made with unnatural pupil size—extreme dilation and contraction of the iris. Biometry measurements should have been made during work. The lens can move axially, but no evidence indicates that it does so during near work.

The extra power provided by the CrystaLens may not be sufficient, and patients may still require a reading add. The sponsor's patient survey indicates that about half could read a newspaper without spectacles. The CrystaLens may provide adequate near vision for about half of the patients who receive it.

Dr. Bradley also stated that the sponsor should have measured refraction objectively and dynamically, while patients viewed distance and near targets. This method could have generated unequivocal data to support the sponsor's claims of accommodation. The coupling of pupil size and accommodation is accentuated when using cyclopentolate and pilocarpine, and the impact of pupil size on visual acuity is magnified whenever the retinal image is defocused. Because of the reliance on visual acuity and the failure to control pupil size, the data are difficult to interpret. Refraction data also must be collected using controlled pupil size. Dr. Bradley recommended that the FDA require more compelling evidence of active accommodation, not near visual acuity, when evaluating IOLs that claim to provide active accommodation. He also noted the need for careful attention to the definition of accommodation.

Dr. Bradley then answered the four panel questions. Although it is unclear how the lens works, it clearly provided near visual acuity comparable to that provided by a standard IOL and therefore seems effective. The hinge is capable of more than 1 million movements and seems stable; however, it is unclear whether it moves in the eye while viewing distance changes because no in vivo data are available. The labeling should reflect that the sponsor has failed to provide conclusive evidence of mechanism of action. Evidence clearly shows that this lens will not eliminate the need for a reading add in about half of the eyes. The device seems safe.

## **PANEL DISCUSSION OF P030002**

### **1a. This is the first IOL that proposes accommodation as its mechanism of action. Do the effectiveness data support a claim of accommodation?**

Several panel members concurred that although the data are minimal, they basically support the claim. Other panel members said that the objective evidence shows a limited effect and other data are circumstantial. It is a revolutionary device, but a standard needs to be set. Clinical data should demonstrate that the accommodation process actually exists; this could be accomplished through a variety of psychophysical methods in a follow-up (but not postmarket) study.

Dr. Weiss observed that the panel was not in consensus and that several members were declining to comment. When asked to provide a show of hands, four panel members indicated that the data support a claim of accommodation, and three indicated that the data do not support the claim.

### **1b) What performance issues should be considered both generally and for product labeling?**

The panel concurred that the labeling should indicate that although the product improved near vision, certain tasks would require glasses in a percentage of patients. Several panel members suggested including a table that listed different activities patients could do without spectacles.

The panel suggested that the Agency work with the sponsor to correct misleading text in the labeling stating that “almost all patients could pass a driver’s test.”

**2. Do you believe that the sponsor has demonstrated the stability of the hinge, and therefore the stability of the accommodative refractive effect?**

The panel concurred that the labeling should state that the effects on visual acuity with an obliquely situated lens and that effects of more than 1 million extrusions have not been established. It is important to distinguish between the stability of the hinge and stability of the accommodative refractive effect. The Agency should require the sponsor to demonstrate that the lens moves back and forth before including the claim in the labeling.

**3. Does the panel recommend any other modifications to the proposed physician and patient labeling?**

The panel agreed that tables 10.3, 10.5, 10.7 from the PMA submission should be included in the patient and physician labeling. Panel members suggested that the labeling provide percentages in the text rather than just refer readers to a table, because patients will not always look at a table. The panel also concurred that neither the physician nor the patient labeling should state that the lens moves backward and forward. Both sets of labeling should state that effects of YAG capsulotomy at less than 12 weeks are not known and that the lens has only been used in patients older than age 50—results are not known in younger patients. Both the physician and the patient labeling should state that long-term stability of the hinge and accommodative refractive effect are not known and that patients may still need glasses for many tasks. Panel members agreed that information on power range should go in the physician labeling only.

The panel discussed the fact that the device has not been studied in patients younger than age 50 and that the pupil can become smaller as people age. However, pupil size varies enough in the population that setting an age limit could be inappropriate. Clinicians need to understand

that the size of the optic will create problems for patients with pupils larger than 4.5 mm. The panel did not reach consensus on whether the device should be recommended for patients below a certain age, but a majority (4-3) supported the idea. Panel members concurred that the labeling should mention the issue of pupil size and that the sponsor should provide data on patient satisfaction related to pupil size.

Donna Lochner noted that FDA already requires a warning for lenses with optics that are smaller than 5.5 mm.

**4. Do the data in PMA P030002 support the proposed indication statement?**

?? **Primary implantation for the visual correction of aphakia in adult patients with cataracts.**

?? **Provide improved near, intermediate, and distance vision without spectacles.**

The panel concurred that the data support the proposed indication.

**OPEN PUBLIC HEARING**

No comments were made.

**FDA CLOSING COMMENTS**

No comments were made.

**SPONSOR CLOSING COMMENTS**

Adrian Glasser clarified how the sponsor measured and demonstrated 1.00 D of actual accommodation or accommodative amplitude. He noted that objective measurements of changes in anterior chamber depth show forward IOL movement. Intermediate and near visual acuity provides evidence of accommodation. CrystaLens subjects required less add to achieve best corrected near acuity than subjects with standard IOLs.

**VOTE**

The panel voted unanimously that PMA P030002 was approvable with the following conditions:

1. Tables 10.3, 10.5, 10.7 from the sponsor's submission should be included in the physician and patient labeling; the text in the patient labeling should specify percentages when describing the data in the tables.
2. Both the physician and patient labeling should state that the effectiveness of accommodative ability after YAG capsulotomy prior to 12 weeks has not been established.
3. The information on lens movement should be removed from the patient labeling.
4. Both the physician and patient labeling should state that the visual results are not known if the CrystaLens is placed in one eye and the other eye is pseudophakic with another standard IOL.
5. Both the physician and patient labeling should state that data on patients younger than age 50 are not known.
6. Both the physician and patient labeling should state that long-term stability has not been established for the hinge or the accommodative refractive effect.
7. Both the physician and patient labeling should state that patients may require glasses, particularly for near work.
8. The physician labeling should state that the CrystaLens will provide approximately 1.0 D of accommodative amplitude.
9. In the precautions section, the physician labeling should mention that the axial length range of 21 to 26.6 millimeters and lens powers of 16.5 to 27.5 D were used in the study.
10. The physician labeling should mention that atropine sulfate should be given immediately postoperatively and again at postoperative day 1.
11. The physician labeling should state in the precautions section that the effect of vitrectomy on accommodative performance of the CrystaLens is unknown.
12. In the adverse events section, the physician labeling should mention the possibility of increased rate of cystoid macular edema (CME) associated with sulcus-bag placement of haptics.
13. The sponsor will provide the Agency with information on pupil size and will stratify the results of the patient satisfaction survey as related to pupil size data.
14. The labeling should include the table showing that subjects that had the primary implant were able to achieve about 80 percent uncorrected visual acuity of 20/40 or better, while subjects having bilateral implantation could achieve 97 percent uncorrected acuity..

When asked to explain the rationale for their votes, panel members indicated that they thought the sponsor had demonstrated reasonable assurance of safety and effectiveness. Several members expressed concern over the issue of accommodation; the data are not substantial enough to include the claim of an accommodative effect. Several panel members stated that the data demonstrate marginal effectiveness and were concerned about the true measurement of accommodation under nonpharmacologic circumstances.

### **ADJOURNMENT**

Dr. Weiss thanked the participants and adjourned the panel at 3:02 p.m. Ms. Thornton noted that the July panel meeting had been canceled. Information on the status of the meeting tentatively scheduled for September 11 and 12, 2003, will be available by the end of July.

I certify that I attended the meeting of the  
Ophthalmic Devices Panel on May 23, 2003,  
and that this summary accurately reflects  
what transpired.

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Sara M. Thornton  
Panel Executive Secretary

I approve the minutes of this meeting  
as recorded in this summary.

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Jayne S. Weiss, M.D.  
Panel Chair

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