SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Monofocal Posterior Chamber Accommodating Intraocular Lens (IOL)

Device Trade Name: crystalens™ Model AT-45 Accommodating Intraocular Lens

Applicant's Name and Address:

eyeonics inc. (formerly C&C Vision)
6 Journey, Suite 125
Aliso Viejo, CA 92656

Date(s) of Panel Recommendation: May 23, 2003

Premarket Approval Application (PMA) Number: P030002

Date of Notice of Approval to Applicant: November 14, 2003

II. INDICATIONS FOR USE

The crystalens™ Model AT-45 Accommodating IOL is intended for primary implantation in the capsular bag of the eye for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed and is intended to provide near, intermediate, and distance vision without spectacles. The crystalens™ IOL provides approximately one diopter of monocular accommodation.

III. CONTRAINDICATIONS

None known.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the crystalens™ IOL labeling.

V. DEVICE DESCRIPTION

The crystalens™ IOL is a modified plate haptic lens with polyimide loops and hinges across the plates adjacent to the optic. The overall length of the lens is 11.5 mm (loop tip to loop tip measurement), while the length as measured from the ends of the plate haptics is 10.5 m. The lens optic is biconvex, 4.5 mm in diameter, with an A-Constant of 119.24,

and is designed for placement into the capsular bag.

VI. ALTERNATIVE PRACTICES OR PROCEDURES

Multifocal IOLs are used for the visual correction of aphakia and may also provide near, intermediate and distance vision without spectacles.

VII. MARKETING HISTORY

The crystalens™ IOL has been marketed in over 10 countries, including Belgium, Brazil, Germany, Greece, Italy, Mexico, Portugal, Singapore, Spain, Switzerland, Saudi Arabia, and the United Kingdom. The crystalens™ has not been withdrawn from any market for reasons relating to safety and effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The adverse events experienced during the clinical trial of the crystalens™ IOL included persistent iritis (<1.0%), persistent cystoid macular edema (<1.0%), and cumulative cystoid macular edema (3.7%). The incidence of adverse events was comparable to or lower than the incidence reported in the historical control ("FDA grid") population (Table 1).

Table 1
Adverse Events Reported at 12 months

Adverse Event	Cumulative	FDA Grid	Persistent	FDA Grid
Endophthalmitis	1/324 (0.3%)	0.1%	----	----
Hyphema	1/324 (0.3%)	2.2%	----	----
Hypopyon	0/324	0.3%	----	----
IOL Dislocation	0/324	0.1%	----	----
Cystoid Macular Edema	12/324 (3.7%)	3.0%	2/304 (0.7%)	0.5%
Pupillary Block	0/324	0.1%	----	----
Retinal Detachment	0/324	0.3%	----	----
Secondary Surgical Reintervention	2/324 (0.6%)	0.8%	----	----
Corneal Edema	----		0/298	0.3%
Iritis	----		2/298 (0.7%)	0.3%
Raised IOP Requiring Treatment	----		0/304	0.4%

Potential adverse events which did not occur in this clinical trial, but which may accompany cataract or implant surgery include, but are not limited to, the following: corneal endothelial damage, non-pigment precipitates, infection, retinal detachment, vitreous wick syndrome, uveitis and pupillary membrane. No cases of hypopyon or acute corneal decompensation were reported during the clinical study.

Potential secondary surgical interventions that have been associated with intraocular lenses, but did not occur in this clinical trial include: lens removal due to corneal touch, lens removal due to inflammation, corneal transplant, vitreous aspiration for pupillary block, iridectomy for pupillary block.

IX. SUMMARY OF PRECLINICAL STUDIES

Preclinical studies on this device that are consistent with the FDA draft guidance document for testing intraocular lenses dated October 14, 1999 were performed. The applicant conducted a battery of in vivo and in vitro acute and chronic toxicity tests that establish the biocompatibility of the lens materials. These studies, combined with data from chemistry and engineering analyses, demonstrate the suitability of the material and overall device design for use in an intraocular lens. The adequacy of the manufacturing processes, including sterilization, was established through review of the manufacturing information in the PMA as well as through on-site inspections. Preclinical testing demonstrates the safety and effectiveness of this device from microbiology, toxicology, engineering, and manufacturing perspectives.

X. SUMMARY OF CLINICAL STUDIES

Objectives. The objectives of the clinical studies were to assess the safety and effectiveness of the crystalens™ IOL for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed and assess its ability to provide near, intermediate, and distance vision without spectacles.

Study Design

The crystalens™ IOL was evaluated in a prospective, nonrandomized study of 324 subjects followed for one year. The range of axial lengths studied in the clinical trial was 21.0 to 26.6 mm and the dioptric power range was 16.5 to 27.5 D. The clinical results were obtained using an 'A' Constant of 119.0, the SRK/T formula, immersion biometry or interferometry and manual keratometry. Inclusion criteria required visual potential to be 20/30 or better in the operative eye, 1.00 D or less of corneal astigmatism, an intact capsular bag and zonules after cataract extraction and before implantation of the lens.

The clinical effectiveness endpoint was visual performance at near, intermediate and distance.

Gender Bias

The population at risk for developing visually-disabling cataracts and needing cataract surgery is typically elderly; the elderly population has a slightly higher proportion of females to males. The average age of the 324 subjects (497 eyes) was 69.7 years at the time of surgery; 55.9% of the 324 subjects were female and 44.1% were male. The inclusion/exclusion criteria did not exclude patients on the basis of gender or gender-related pathology. The study population was more than 90% Caucasian; 1.2% African-American, 6.8% were Hispanic and less than 1% was Asian. All patients who met the inclusion criteria were included in the study.

Patient Assessments

Clinical evaluations included visual acuity, contrast sensitivity, subject survey and ophthalmic examinations to determine adverse event rates.

Uncorrected and distance corrected visual acuities were determined at near, intermediate and distance for all bilateral subjects. Distance corrected visual acuities were determined at near, intermediate and distance for all unilateral subjects. Uncorrected visual acuities were determined at near and distance for all unilateral subjects. A subset of the subjects was compared to subjects with standard monofocal IOLs for visual acuity at all distances.

A contrast sensitivity substudy was conducted to address concerns related to the 4.5 mm optic of the crystalens™ IOL. The substudy compared the crystalens™ IOL with a control group comprised of several models of standard monofocal IOLs of varying types (e.g., single piece, multipiece) and materials (e.g., silicone, acrylic). Contrast sensitivity was performed with a cohort of 126 crystalens™ IOL subjects and a matched control group of 64 eyes implanted with several models of standard IOLs. Testing was performed at the 3 to 6 month postoperative exam (Form 4) or later, under mesopic light conditions, in order to simulate vision in the presence of poor illumination and a large pupil. The luminance level employed was 3 cd/m^2 and the glare stimulus was 3 lux.

A subject survey substudy included one hundred and twenty-eight bilaterally implanted subjects who were asked at the one-year post-operative visit to assess their dependency on spectacles and to evaluate their night vision. Subjects were also asked to evaluate their daily lifestyle activities without spectacles.

Data Analysis and Results

The bilateral postoperative uncorrected visual acuity results for the crystalens™ IOL at near, intermediate and distance are shown in Table 2. Of the subjects implanted bilaterally, 93.5% achieve visual acuities of 20/32 or better uncorrected at near, distance or intermediate one year after surgery.

Table 2
Bilateral – Uncorrected Visual Acuity

	Near at 40 cm		Intermediate at 80 cm		Distance	
20/20 or better	39/124	31.5%	120/124	96.8%	98/123	79.7%
20/25 or better	90/124	72.6%	122/124	98.4%	113/123	91.9%
20/32 or better	116/124	93.5%	124/124	100%	120/123	97.6%
20/40 or better	122/124	98.4%	124/124	100%	121/123	98.4%
Worse than 20/40	2/124	1.6%	0/124	0%	2/123	1.6%

Table 3 shows the uncorrected visual acuity for a subset of the bilateral subjects in the study that were within ±0.5D of plano in each eye. Uncorrected visual acuities of 20/32 or better at near, distance or intermediate one year after surgery improved to 97.3% of the subjects when within 0.5D of plano in each eye.

Table 3
Bilateral – Uncorrected Visual Acuity for Patients within ±0.5D of Plano in Each Eye

	Near at 40 cm		Intermediate at 80 cm		Distance	
20/20 or better	17/74	23.0%	--	--	67/74	90.5%
20/25 or better	49/74	66.2%	74/74	100%	73/74	98.6%
20/32 or better	72/74	97.3%	74/74	100%	74/74	100%
20/40 or better	74/74	100%	74/74	100%	74/74	100%
Worse than 20/40	0/74	0%	0/74	0%	0/74	0%

Table 4 shows the unilateral results for subjects implanted with the crystalens™ IOL. Uncorrected visual acuities of 20/40 or better at near or distance one year after surgery were reported in more than 89% of the subjects.

Table 4
Unilateral – Uncorrected Visual Acuity (All Eyes)

	Near at 40 cm		Intermediate at 80 cm		Distance	
20/20 or better	52/368	14.1%	--	--	184/371	49.6%
20/25 or better	161/368	43.8%	--	--	269/371	72.5%
20/32 or better	256/368	69.6%	--	--	311/371	83.8%
20/40 or better	328/368	89.1%	--	--	339/371	91.4%
Worse than 20/40	40/368	10.9%	--	--	32/371	8.6%

Table 5 shows the unilateral results for the subset of subjects implanted with the crystalens™ IOL compared to the unilateral results for subjects with the standard monofocal IOL (these were the subjects in the contrast sensitivity substudy). Distance

corrected visual acuities of 20/40 or better at near, intermediate and distance 3-6 months or more after surgery were reported in 88.4% of the subjects with the crystalens™ IOL and 35.9% of the subjects implanted with the standard monofocal IOL.

Table 5
crystalens™ IOL vs. Standard IOL Distance Corrected Visual Acuity at All Distances (Distance, Near and Intermediate)

	crystalens™		Standard IOL	
20/20 or better	1/121	0.8%	0/64	0.0%
20/25 or better	29/121	24.0%	0/64	0.0%
20/32 or better	61/121	50.4%	3/64	4.7%
20/40 or better	107/121	88.4%	23/64	35.9%
Worse than 20/40	14/121	11.6%	41/64	64.1%

The stability of the visual acuity outcomes was demonstrated in a consistent cohort of patients across the Form 3 to Form 4 (1-2 months to 3-6 months) and Form 4 to Form 5 (3-6 months to 11-15- months) postoperative intervals. As shown in Table 6 below, a change of $\leq \pm 0.50$ D was reported for over 84% of implanted eyes, and a change of $\leq \pm 1.00$ D was reported for over 96% of implanted eyes. Consistent with good stability of the manifest refraction, 182 of 228 primary eyes (79.8%) had no change in DCNVA in the Form 3 to Form 4 postoperative interval as compared to 181 of 229 primary eyes (79.0%) in the Form 4 to Form 5 postoperative interval.

Table 6
Stability of Manifest Spherical Equivalent (MRSE) and Near Visual Acuity Through Distance Correction (DCNVA)
US Eyes - One-Year Consistent Cohort

Change in MRSE	Form 3 to Form 4 (N = 234) N (Missing) = 6		Form 4 to Form 5 (N = 234) N (Missing) = 5	
	N	%	N	%
$\leq \pm 0.50$ D	197	84.5	201	85.9
$\leq \pm 1.00$ D	225	96.6	226	96.6
Line Change in DCNVA				
Decrease $\geq$ 2 lines	18	7.9	11	4.8
Decrease/Increase within 1 line	182	79.8	181	79.0

Table 7 shows the results of the contrast sensitivity/ glare substudy. There were no statistically significant differences in contrast sensitivity measured under mesopic lighting, with a glare source, for eyes implanted with the crystalens™ IOL as compared to standard monofocal IOLs.

Table 7
Mean Contrast Sensitivity at 3-6 Months or Later
With Glare (3 cd/m^2 Illumination, 3 lux)
crystalens™ IOL Versus Standard Monofocal IOL

Contrast Sensitivity – Spatial Frequency	Crystalens N = 126 Mean (SD)	Standard IOL N = 64 Mean (SD)
Series A (1.5 cpd)	1.53 (0.22)	1.57 (0.23)
Series B (3 cpd)	1.77 (0.23)	1.70 (0.25)
Series C (6 cpd)	1.34 (0.35)	1.24 (0.31)
Series D (12 cpd)	1.06 (0.34)	0.95 (0.26)
Series E (18 cpd)	0.73 (0.35)	0.57 (0.24)

The results of the subject survey substudy are shown in Tables 8, 9, and 10.

Table 8 reports on the percentages of subjects that were able to perform various tasks without the use of spectacles. Of the 128 subjects that completed the survey, 120 (93.8%) reported performing most visual functions without spectacles.

Table 8
Bilateral Patient Survey
Activities Without Spectacles (US Bilateral Subjects)

Activity	Yes N/N (%)	No n/N (%)
Perform most visual functions	120/128 (93.8%)	8/128 (6.3%)
Read most things	100/129 (77.5%)	29/129 (22.5%)
Go shopping	116/124 (93.5%)	8/124 (6.5%)
Participate in sports	84/87 (96.6%)	3/87 (3.4%)
Attend social gatherings	120/126 (95.2%)	6/126 (4.8%)
Drive	111/121 (91.7%)	10/121 (8.3%)
Read a newspaper	73/128 (57.0%)	55/128 (43.0%)
Sew or do needlework	35/91 (38.5%)	56/91 (61.5%)
Work on a computer	75/93 (80.6%)	18/93 (19.4%)
Do handy work around the house	119/126 (94.4%)	7/126 (5.6%)
Walk	126/129 (97.7%)	3/129 (2.3%)
Shop	117/128 (91.4%)	11/128 (8.6%)
Watch television	120/130 (92.3%)	10/130 (7.7%)

Table 9 reports on the percentages of subjects that experienced difficulty with night activities.

Table 9
Bilateral Patient Survey
Difficulty With Night Activity (US Bilateral Subjects)

Symptoms	Absent N/N (%)	Mild N/N (%)	Moderate n/N (%)	Severe n/N (%)
Night-time glare/flare	74/130 (56.9%)	31/130 (23.8%)	18/130 (13.8%)	7/130 (5.4%)
Night vision (difficulty driving at night)	82/121 (67.8%)	21/121 (17.4%)	14/121 (11.6%)	4/121 (3.3%)
Halos (rings around lights)	80/130 (61.5%)	26/130 (20.0%)	16/130 (12.3%)	8/130 (6.2%)

Table 10 reports on the percentage of subjects wearing spectacles during waking hours and to see at night. Twenty-six percent of subjects reported that they no longer needed spectacles for any task. An additional 48 percent reduced their spectacle dependency by at least 75% and 16% of subjects by at least 50%. Eleven percent reported wearing glasses more than 50% of the time. In addition, 110/130 subjects (84.6%) reported needing no spectacles to see at night.

Table 10
Bilateral Patient Survey
Wearing Spectacles During Waking Hours And to See At Night
(US Bilateral Subjects)

Wearing Spectacles	n/N (%)
How often do you wear spectacles during waking hours?	
I do not wear spectacles	33/128 (25.8%)
I wear spectacles almost none of the time (10%-25%)	61/128 (47.7%)
I wear spectacles some of the time (26%-50%)	20/128 (15.6%)
I wear spectacles most of the time (51%-75%)	8/128 (6.3%)
I wear spectacles all the time or almost all the time (76%-100%)	6/128 (4.7%)
Do you wear spectacles to see at night?	
No	110/130 (84.6%)
Yes	20/130 (15.4%)

XI. CONCLUSIONS DRAWN FROM THE STUDIES

SAFETY

The rates of adverse events associated with the crystalens™ IOL are comparable to or lower than the rates associated with the historical control population of standard monofocal IOLs.

EFFECTIVENESS

The crystalens™ IOL provides improved visual acuity at near and intermediate distances compared to standard monofocal IOLs.

XII. PANEL RECOMMENDATION

At an advisory meeting held on May 23, 2003, the Ophthalmic Devices Panel recommended that eyeonics' PMA for the crystalens™ IOL be approved subject to submission to, and approval by, the Center for Devices and Radiological Health (CDRH) of modified physician and patient labeling that incorporated their recommendations.

XIII. CDRH DECISION

CDRH concurred with the Ophthalmic Devices Panel recommendation of May 23, 2003, and issued a letter to eyeonics, on June 27, 2003, advising that its PMA was approvable subject to eyeonics' modifications of the physician and patient labeling as recommended by the Panel and required by FDA. In an amendment received by FDA on October 27, 2003, eyeonics submitted the required modified labeling. FDA issued an approval order on November 14, 2003. The applicant's manufacturing facility was inspected on July 8-10 and 14, 2003 and was found to be in compliance with the Quality System Regulation (21 CFR 820).

The crystalens™ IOL was granted expedited review status on February 24, 2003, because the Model AT-45 accommodating IOL represents a clear, clinically meaningful advantage over existing technology.

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, precautions and Adverse Events in the labeling.

Postapproval Requirements and Restrictions: See approval order.