## SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

## I. GENERAL INFORMATION

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| **Device Generic Name:** | Excimer Laser |
| **Device Trade Name:** | MEL 80™ Excimer Laser System |
| **Applicant's Name and Address:** | Carl Zeiss Meditec Inc.<br>5160 Hacienda Drive<br>Dublin, California 94568 USA<br>(925) 557-4100 |
| **Date(s) of Panel Recommendation:** | None |
| **PMA Number:** | P060004/S1 |
| **Date of Notice of Approval to Applicant:** | March 28, 2011 |

The original PMA (P040006) was approved August 11, 2006 and is indicated for use in primary Laser Assisted *in situ* Keratomileusis (LASIK) treatments for the reduction or elimination of myopia of less than or equal to -7.0 diopter (D) with or without astigmatism of less than or equal to -3.0 D, with a maximum manifest refraction spherical equivalent (MRSE) of -7.00 D, in patients who are 21 years of age or older with documentation of stable manifest refraction over the past year as demonstrated by change in sphere and cylinder of ≤ 0.5 D. The SSED to support the indication is available on the CDRH website and is incorporated by reference here: **http://www.accessdata.fda.gov/cdrh_docs/pdf6/P060004b.pdf**. The current supplement was submitted to expand the indication for the MEL 80™ Excimer Laser System.

## II. INDICATIONS FOR USE

The MEL 80™ Excimer Laser is indicated for use in primary Laser Assisted *in situ* Keratomileusis (LASIK) treatments for the reduction or elimination of naturally-occurring hyperopia of less than or equal to +5.0 D with or without refractive astigmatism of > +0.5 D and ≤ +3.0 D, with a maximum MRSE of +5.0 D, in patients who are 21 years of age or older with documentation of stable manifest refraction over the past year as demonstrated by change in sphere and cylinder of ≤ 0.5 D.

## III. CONTRAINDICATIONS

The device should not be used under the conditions listed in this section, because the risk of use clearly outweighs any possible benefit.

- Patients with severe dry eye;
- Patients with active corneal infection or inflammation;
- Patients with glaucoma with marked optic nerve cupping, advanced visual field loss or visual acuity loss, because of the risk of further loss of visual function related to microkeratome-induced pressure spikes;
- Patients with projected residual corneal stromal bed thickness after ablation of less than 250 microns, because this may lead to ectasia;
- Patients with active connective tissue diseases or autoimmune diseases which have been associated with corneal melting such as rheumatoid arthritis, Wegener's granulomatosis, relapsing polychondritis, and polyarteritis nodosa;
- Pregnant or nursing women;
- Patients with signs of ectatic disorders such as keratoconus or pellucid marginal degeneration;
- Patients with active, uncontrolled diabetes mellitus or visually significant diabetic complications;
- Patients with recent herpes keratitis (simplex or zoster) or significant corneal damge (poor sensation, scarring, neovascularization) from prior herpes infection; and
- Patients with immunodeficiency diseases, such as AIDS.

## IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the MEL 80™ Excimer Laser labeling.

## V. DEVICE DESCRIPTION

The Carl Zeiss Meditec MEL 80™ Excimer Laser System is designed for refractive surgery based on the ablation of corneal tissue achieved with a short pulse excimer laser having a wavelength of 193 nanometers. The laser head emits 4 to 7 nanosecond pulses with a repetition rate of 250 Hertz (Hz). The MEL 80™ Excimer Laser is a spot-scanning laser that utilizes a Gaussian beam with a 0.7 millimeter (mm) spot diameter.

The MEL 80™ Excimer Laser System also contains an ablation debris removal system called the Cone for Controlled Atmosphere (CCA+). The CCA+ is a patented airflow system that ensures constant ablation debris removal from the beam path.

The MEL 80™ Excimer Laser System includes a 250 Hz eyetracker. The system determines the pupil center from an infrared (IR) image of the patient's eye, refreshed and processed at 250 Hz.

A green light-emitting diode (LED) (525 nm) light located inside the surgical microscope and centered on its optical axis serves as a fixation target for the patient. For ease of fixation, the LED is employed in a blinking mode at a frequency of 2 Hz. The fixation light blinks during the entire surgery.

User control of the MEL 80™ Excimer Laser is implemented by a software application called the Operation Assistant (OPASS), which runs on a familiar Windows PC (operating system Windows XP®) computer interface in order to provide the surgeon direct control over the preoperative data and an integrated application manual. The OPASS program allows the surgeon to input clinical data and monitor the progress of the operation on a visual control panel. The Windows PC transfers data to the central control unit of the excimer laser, which is fully independent and controls the operation of the excimer laser (note: the surgeon has no access to this central control unit).

For this PMA supplement for hyperopia with or without astigmatism, the MEL 80™ Laser specifications have changed to reflect a new range of ablation diameter and new software versions. Additionally, lockouts have been changed to reflect hyperopia treatments.

The MEL 80™ Excimer Laser System consists of the following major components:

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| **Laser Arm** | The Laser Arm contains the operating microscope, the debris removal system (called CCA+), the galvanometric scanners, the eye tracking camera, a portion of the optical system, the control panel and the laser arm interface. |
| **Laser Unit** | The excimer laser unit consists of the laser head with high voltage (HV) power supply, the trigger unit and the laser interface. The communication with the central control unit PC104 is done fiber-optically via the laser interface, which also optically controls the trigger unit. The laser head is provided with premix gas by the gas handling system. |
| **Optics** | The optics form the excimer raw beam and guide it to the treatment plane by means of a beam shaper, two lenses, and different mirrors, so that a well-defined beam of Gaussian shape emerges. A vacuum pump is used to evacuate air present in the beam path; this function is initiated automatically when the laser is started. |
| **PC104** | The central control unit PC104 with laser control software (called POLO) provides the control of the whole laser system. It performs the following tasks: execution of the treatment (i.e., triggering of the laser head), monitoring and setting of the scanner position, control of the blower and the plume suction (debris removal), communication with user interface software (called OPASS), execution of the gas management system functions, and energy control via high voltage setting and energy measuring. |
| **Control Panel** | The control panel provides control of the distance lasers (which are used for correct height adjustment of the patient's eye), the white light illumination, and the eyetracker parameters. The control panel displays messages in the event of a lost connection between OPASS and POLO via a mini display. |
| **Eyetracker** | A fast eyetracker unit ensures alignment of the laser beam to the eye of the patient. It is comprised of a 250 Hz infrared charge-coupled device (CCD) camera, an infrared LED illumination system (810 nm) and a separate control computer (EyePAC). |
| **Operating Microscope** | An operating stereomicroscope (OPMI) allows the surgeon to observe the patient's eye during the treatment. |
| **Illumination System** | An LED ring light consisting of 72 single visible light LEDs arranged in an annular pattern is mounted at the laser exit aperture for illumination of the operating area (maximum irradiance in treatment plane is 3.76 $mW/cm^2$). In addition, there is a satellite illumination system (two visible light LEDs) mounted on the CCA+ unit to allow grazing-angle illumination of the patient's eye (maximum irradiance in treatment plane is 0.55 $mW/cm^2$). |
| **Gas Handling System** | The gas handling system consists of a flushing gas (helium) and a laser gas (premix) bottle, pipes, valves, pressure sensors, vacuum pump, filters (halogen), and pressure reducers. The central control unit performs an automatic gas change on user request. The bottles are placed inside the device. |
| **CCA+ Debris Removal** | A blower and suction unit called CCA+ debris removal provides a controlled environment at the patient's eye by removing the debris. It is mounted on a swivel arm (the entire component is referred to as the CCA+ unit), and also carries the infrared illumination. The CCA+ unit can be moved away when not in use. |
| **Patient Bed** | A motor-driven patient bed is movable in all 3 dimensions (X-, Y- and Z-directions). In addition, the patient headrest can be moved in the Z-direction and can be tilted in a dorsal and ventral direction. The bed can be swung out manually for easy exit of the patient. |
| **Slit Lamp (optional)** | The slit lamp produces an evenly illuminated field approximately 8 cm in front of a reflecting prism, the geometry and color of which can be varied by the use of apertures and filters. The slit lamp has a 6 V (10 W) halogen bulb, a slit width of 0.15 mm to 0.75 mm, and a slit height and illumination field size of 2 mm to 12 mm (continuous). |

## A. MEL 80™ Laser Specifications

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| Laser Type | Argon Fluoride |
| Laser Wavelength | 193 nm |
| Laser Spot Size (FWHM diameter) | 0.7 mm ± 0.1 mm |
| Laser Pulse Duration | 4 to 7 nanoseconds (ns) |
| Laser Head Repetition Rate | 250 Hz |
| Fluence (at the treatment area) | > 150 mJ/cm$^2$ (peak) |
| Range of Ablation Diameter | For hyperopia, up to 10.0 mm (optic zone of 6.0 to 6.5 mm, with a transition zone of 2.0 to 4.0 mm. Note: the laser does not apply shots outside of the 10.0 mm diameter). |
| Eyetracker<br>- Tracking frequency | 250 Hz |
| Installation Requirements | Please refer to the Operator's Manual for restrictions, tolerances or other requirements established regarding room air circulation, clearance between the laser room walls, and distance between the laser and other electronic or radiation-producing medical equipment. |

The software versions in the laser system are as follows:

a. OPASS Software version 3.6
b. OPASS PC Operating System: Windows XP
c. POLO Software version 2.3
d. Eyetracker Firmware version 10.09

This laser is locked out for treatments exceeding +5.0 D sphere, cylinder ≤ +0.5 and > +3.0 D, and +5.0 D MRSE. Optical zones below 6.0 mm and above 6.5 mm are also locked out. If the refraction setting exceeds the permitted nomogram range, a plain text message will be displayed and the fluence test will be locked (treatment will not be permitted).

## B. Microkeratome

The LASIK procedure requires the use of a commercially available mechanical or laser microkeratome that has been cleared for marketing via premarket notification. The microkeratome is used to make a thin flap of tissue of pre-selected thickness and diameter on the cornea. This flap is then folded out of the way, and the excimer laser is used to reshape the front surface of the cornea below the flap. Three different keratomes were used in this study. Two devices were traditional microkeratomes that utilize a stainless steel blade to make the flap. The cornea is held in position by a suction ring, with a geared drive mechanism on the suction ring used as a track for the motorized microkeratome. The third device was a femtosecond ophthalmic surgical laser that creates a LASIK flap through precise individual microphotodisruptions of

tissue, created by tightly focused ultrashort pulses which are delivered through a disposable applanation lens while fixating the eye under very low vacuum.

## VI. ALTERNATIVE PRACTICES OR PROCEDURES

Alternative methods of correcting farsightedness (hyperopia) with and without astigmatism include: glasses, contact lenses, LASIK with another laser system, and photorefractive keratectomy (PRK).

## VII. MARKETING HISTORY

The Carl Zeiss Meditec MEL 80 Excimer Laser System has been marketed in the following countries: Australia, Austria, Belgium, Canada, Czech Republic, China, Croatia, Denmark, Egypt, Estonia, Finland, France, Germany, India, Iran, Italy, Japan, Kazakhstan, Kuwait, Latvia, Libya, Lithuania, Malaysia, Morocco, Mexico, Netherlands, Oman, Palestine, Portugal, Russia, South Africa, Slovenia, Spain, Switzerland, Thailand, Turkey, United Arab Emirates, United Kingdom, and the United States.

The Carl Zeiss Meditec MEL 80 Excimer Laser System has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

## VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse reactions associated with LASIK include: loss of best spectacle corrected visual acuity, overcorrection, increase in refractive cylinder, worsening of patient complaints such as double vision and glare, sensitivity to bright lights, increased difficulty with night vision, fluctuations in vision, increase in intraocular pressure, corneal haze, corneal infection/infiltrate/ulcer, corneal epithelial defect, corneal decompensation/edema, problems associated with the flap including a lost, misplaced or misaligned flap, retinal detachment, and retinal vascular accidents. The occurrence of many of these events may involve the necessity of secondary (additional) surgical intervention.

Please refer to the complete list of adverse events and complications observed during the clinical study, which are presented in the clinical study section X.

## IX. SUMMARY OF PRECLINICAL STUDIES

Refer to a summary of the preclinical section of the original SSED for P060004.

## X. SUMMARY OF PRIMARY CLINICAL STUDIES

### A. Objectives

The objective of this study was to evaluate the safety and effectiveness of the Carl Zeiss Meditec MEL 80™ Excimer Laser System for the reduction or elimination of hyperopia of less than or equal to +6.00 D, astigmatism ≥ +0.50 D and ≤ +3.50 D at the spectacle plane (hyperopia with or without astigmatism), and MRSE ≤ +6.50 D when used as part of the LASIK surgical procedure. An optic zone of 6.0 to 6.5 mm with a transition zone of 2.0 to 4.0 mm was used during the study.

### B. Study Design

Subjects were treated between August 2004 and October 2006. The database for this PMA reflected data collected through October 18, 2007. A total of 369 eyes were treated at six investigational sites.

This was a prospective multicenter clinical trial in which a total of 369 eyes of consecutive subjects at six (6) clinical sites were enrolled, treated with the MEL 80 Excimer Laser, and followed for a 24-month period from August 13, 2004 through August 25, 2008. The pre-treatment condition of the eye was considered the control state for most comparisons.

Subjects were screened for eligibility, and informed consent was obtained from those who met screening criteria and were interested in participating in the study. Eligible patients were examined preoperatively to obtain a medical history and to establish a baseline for ocular condition. Baseline and postoperative measurements included manifest refraction, cycloplegic refraction, distance visual acuity (best corrected and uncorrected), slit-lamp examination, fundus examination, and intraocular pressure (IOP).

Hyperopic eyes without astigmatism were treated with a spherical treatment only, and hyperopic eyes with ≥ +0.50 D and ≤ +3.50 D of astigmatism were treated with a combination of a single cylinder and spherical treatment.

Subjects were permitted to have second eyes (fellow eyes) treated simultaneously with the first eye surgery or sequentially. Monovision treatments and retreatments before 12 months postoperatively were not allowed during the study.

A total of 369 eyes were enrolled in this study. Based on interim data, the effectiveness of the device treatment algorithm was adjusted by adding +0.75 D to the sphere component after treatment of 57 subjects (110 eyes). The remaining 259 eyes (113 subjects) were treated with an algorithm adjustment of +0.75 D added to the sphere component. Since the algorithm adjustment was determined to be beneficial, only the eyes treated with the ablation algorithm adjustment (259 eyes) would be included in the effectiveness analysis. Through analysis of these 259 eyes, it was found that insufficient effectiveness data existed to approve the following range of treatment: sphere > +5.0 D, cylinder ≤ +0.50 D and

> +3.00 D, and MRSE > +5.0 D. Excluding the eyes treated outside of these parameters, the Effectiveness Cohort consists of 160 eyes, with 149 eyes available at the 9 month point of refractive stability. Safety data are provided for all 369 eyes enrolled in the study.

1. Inclusion and Exclusion Criteria

In order to be enrolled in the study, subjects needed to meet these conditions: have hyperopia less than or equal to +6.00 D, astigmatism ≥ +0.50 D and ≤ +3.50 D at the spectacle plane, and MRSE ≤ +6.50 D; have < 0.75 D of latent hyperopia as determined by the difference between the preoperative MRSE and cycloplegic refraction spherical equivalent (CRSE); have a stable refraction for the past year, as demonstrated by a change of ≤ 0.50 D; discontinue use of contact lenses at least 2 weeks for hard contacts and 1 week for soft lenses prior to the preoperative examination; hard contact lens wearers must have two central keratometry readings and two manifest refractions taken at least one week apart that did not differ by more than 0.50 D; have visual acuity correctable to at least 20/40 in both eyes; the operative eye must be targeted for emmetropia; be at least 21 years of age; be willing and able to return for scheduled follow-up examinations; and provide written informed consent.

Subjects not meeting the above inclusion criteria were excluded from the study. In addition, subjects who presented any of the following conditions were excluded: history of anterior segment pathology, including cataracts (in the operative eye); severe dry eye syndrome unresolved by treatment; residual, recurrent, active ocular or uncontrolled eyelid disease, corneal scars within the ablation zone or other corneal abnormality such as recurrent corneal erosion or severe basement membrane disease; ophthalmoscopic signs of progressive or unstable hyperopia or keratoconus (or keratoconus suspect); required ablation was deeper than 250 microns from the corneal endothelium; irregular or unstable (distorted/not clear) corneal mires on central keratometry readings; blind in the fellow eye; previous intraocular or corneal surgery; history of ocular herpes zoster or herpes simplex keratitis; history of steroid-responsive rise in intraocular pressure, glaucoma, or preoperative IOP > 21 mm Hg; diabetes, diagnosed autoimmune disease, connective tissue disease or clinically significant atopic syndrome; immunocompromised patients, or use of chronic systemic corticosteroid or other immunosuppressive therapy; pregnant, lactating, or child-bearing potential and not practicing a medically approved method of birth control; sensitivity to planned study medications; simultaneous participation in other ophthalmic drug or device clinical trial; at risk for angle closure or for developing strabismus postoperatively.

2. Follow-up Schedule and Assessments

All subjects were expected to return for follow-up examinations at 1 day, 1 week, 1 month, 3 months, 6 months, 9 months, 12 months, 18 months, and 24 months postoperatively. The allowed protocol time windows are listed below. Retreatments were allowed after the 12-month follow-up visit.

- Postop Day 1: Days 1 to 2
- Postop Week 1: Days 5 to 9
- Postop Month 1: Days 21 to 43 (Weeks 3 to 6)
- Postop Month 3: Days 60 to 120 (Weeks 10 to 17)
- Postop Month 6: Days 134 to 210 (Weeks 20 to 30)
- Postop Month 9: Days 245 to 301 (Weeks 35 to 43)
- Postop Month 12: Days 330 to 420 (Months 11 to 14)
- Postop Month 18: Days 480 to 600 (Months 16 to 20)
- Postop Month 24: Days 660 to 780 (Months 22 to 26)

Preoperatively, the subjects' medical and ocular histories were recorded. The objective parameters measured during the study included: uncorrected visual acuity (UCVA), best spectacle corrected visual acuity (BSCVA), manifest refraction, cycloplegic refraction, intraocular pressure, corneal pachymetry, slit lamp examination of the anterior segment, fundus examination, computerized corneal topography, central keratometry, and subjective self-evaluation questionnaire.

3. Clinical Endpoints

The primary effectiveness variables for the study are:

- Predictability: Decrease in manifest refraction spherical equivalent (MRSE) to within ± 1.00 D and ± 0.50 D of the intended refractive outcome at the point at which stability is first reached. A minimum of 75% of eyes should have an achieved refraction within ± 1.00 D of the intended outcome, and at least 50% of eyes should be within ± 0.50 D of the intended outcome.
- Improvement in UCVA following treatment: A minimum of 85% of eyes targeted for emmetropia should have an uncorrected visual acuity of 20/40 or better at the postoperative interval at which stability has been established.
- Stability of Manifest Refraction: A minimum of 95% of eyes should have a change of ≤ 1.00 D in manifest refraction spherical equivalent between 2 refractions performed at least 3 months apart, and the mean rate of MRSE change per month should be ≤ 0.04 D.
- Change in Manifest Refraction Astigmatism: 75% of eyes undergoing astigmatic treatment should be within ± 1.00 D of the attempted astigmatism correction by the point of stability.

- Subject Satisfaction: As measured by a subjective questionnaire, and will be considered as a secondary efficacy variable.

The primary safety variables for the study are:

- Preservation of Best-Spectacle Corrected Visual Acuity (BSCVA):
  - Distance BSCVA of worse than 20/40 at the postoperative interval at which stability has been established should occur in less than 1.0% of eyes that had a BSCVA of 20/20 or better before surgery.
  - Loss of more than 2 lines of BSCVA should occur in less than 5.0% of eyes.
- Induced manifest refractive astigmatism: Less than 5% of eyes treated for sphere only should have a magnitude of postoperative manifest refractive astigmatism that varies from baseline cylinder by greater than 2.00 D at the postoperative interval at which stability has been established.
- Incidence of Adverse Events
- Incidence of Complications: will be considered as secondary safety variables
- Patient Symptoms: will be considered as secondary safety variables.

## C. Study Population Demographics and Baseline (Preoperative) Parameters

### 1. Demographics

The demographics of this study are typical for a contemporary refractive surgery trial performed in the U.S. (see Table 1). The study cohort consists primarily of Caucasians.

**TABLE 1**
**DEMOGRAPHICS**
**ALL TREATED EYES**

| Demographics | Percentage | Number |
|---|---|---|
| **NUMBER OF EYES & SUBJECTS[1]** | 369 Eyes of 189 Enrolled Subjects | |
| **GENDER[2]** | | |
| Male | 54.5% | 103 |
| Female | 45.5% | 86 |
| **RACE[2]** | | |
| White | 94.7% | 179 |
| Black | 3.2% | 6 |
| Asian | 1.1% | 2 |
| Other | 1.1% | 2 |
| **SURGICAL EYE[2]** | | |
| Right | 50.1% | 185 |
| Left | 49.9% | 184 |
| **AGE (in years)[2]** | | |
| Mean (SD) | 46.6 (9.3) | |
| Minimum, Maximum | 22.0, 69.0 | |

1 Two eyes had aborted procedures and were not included in the effectiveness analyses.
2 Gender, Race, and Age were based on subjects, but Surgical Eye is based on eyes.

2. Preoperative Characteristics

The preoperative refraction parameters for eyes treated for spherical hyperopia only are shown in Table 2A, stratified by MRSE and cylinder components. Preoperative refraction parameters for eyes treated for astigmatic hyperopia are shown in Table 2B, similarly stratified by MRSE and cylinder components. Refractive parameters not in the approved range of treatment have been provided as part of the complete study population, but are shown with shading.

**TABLE 2A**
**PREOPERATIVE REFRACTION PARAMETERS**
**STRATIFIED BY MRSE AND CYLINDER COMPONENTS**
**EYES TREATED FOR SPHERICAL HYPEROPIA ONLY**

| MRSE | Manifest Cylinder | | | | Total | |
|---|---|---|---|---|---|---|
| | 0.00 D | | 0.25 D | | | |
| | % | n/N | % | n/N | % | n/N |
| **Without Algorithm Adjustment<br>MRSE: Mean: 2.468, SD: 1.270, Range: 1.25 to 5.88<br>MRCYL:Mean: 0.065, SD: 0.112, Range: 0.00 to 0.25** | | | | | | |
| 0.00 to 1.00 D | 0.0% | (0/27) | 0.0% | (0/27) | 0.0% | (0/27) |
| 1.01 to 2.00 D | 44.4% | (12/27) | 14.8% | (4/27) | 59.3% | (16/27) |
| 2.01 to 3.00 D | 11.1% | (3/27) | 0.0% | (0/27) | 11.1% | (3/27) |
| 3.01 to 4.00 D | 18.5% | (5/27) | 0.0% | (0/27) | 18.5% | (5/27) |
| 4.01 to 5.00 D | 0.0% | (0/27) | 3.7% | (1/27) | 3.7% | (1/27) |
| 5.01 to 6.00 D | 0.0% | (0/27) | 7.4% | (2/27) | 7.4% | (2/27) |
| Total | 74.1% | (20/27) | 25.9% | (7/27) | 100.0% | (27/27) |
| **With Algorithm Adjustment<br>MRSE: Mean: 2.468, SD: 1.115, Range: 1.00 to 5.25<br>MRCYL:Mean: 0.033, SD: 0.086, Range: 0.00 to 0.25** | | | | | | |
| 0.00 to 1.00 D | 3.3% | (2/60) | 0.0% | (0/60) | 3.3% | (2/60) |
| 1.01 to 2.00 D | 28.3% | (17/60) | 6.7% | (4/60) | 35.0% | (21/60) |
| 2.01 to 3.00 D | 31.7% | (19/60) | 3.3% | (2/60) | 35.0% | (21/60) |
| 3.01 to 4.00 D | 8.3% | (5/60) | 1.7% | (1/60) | 10.0% | (6/60) |
| 4.01 to 5.00 D | 11.7% | (7/60) | 1.7% | (1/60) | 13.3% | (8/60) |
| 5.01 to 6.00 D | 3.3% | (2/60) | 0.0% | (0/60) | 3.3% | (2/60) |
| Total | 86.7% | (52/60) | 13.3% | (8/60) | 100.0% | (60/60) |

The shaded cells were not included in the effectiveness cohort.

## TABLE 2B
## PREOPERATIVE REFRACTION PARAMETERS
## STRATIFIED BY MRSE AND CYLINDER COMPONENTS
## EYES TREATED FOR ASTIGMATIC HYPEROPIA

| MRSE | Manifest Cylinder | | | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0.25 to 0.50 D | | 0.51 to 1.00 D | | 1.01 to 2.00 D | | 2.01 to 3.00 D | | | |
| | % | n/N | % | n/N | % | n/N | % | n/N | % | n/N |
| **Without Algorithm Adjustment<br>MRSE: Mean: 2.965, SD: 1.253, Range: 1.00 to 6.38<br>MRCYL:Mean: 0.943, SD: 0.583, Range: 0.25 to 2.75** | | | | | | | | | | |
| 0.00 to 1.00 D | 1.2% | (1/83) | 1.2% | (1/83) | 0.0% | (0/83) | 0.0% | (0/83) | 2.4% | (2/83) |
| 1.01 to 2.00 D | 13.3% | (11/83) | 9.6% | (8/83) | 3.6% | (3/83) | 2.4% | (2/83) | 28.9% | (24/83) |
| 2.01 to 3.00 D | 6.0% | (5/83) | 4.8% | (4/83) | 3.6% | (3/83) | 1.2% | (1/83) | 15.7% | (13/83) |
| 3.01 to 4.00 D | 7.2% | (6/83) | 16.9% | (14/83) | 8.4% | (7/83) | 0.0% | (0/83) | 32.5% | (27/83) |
| 4.01 to 5.00 D | 6.0% | (5/83) | 3.6% | (3/83) | 3.6% | (3/83) | 1.2% | (1/83) | 14.5% | (12/83) |
| 5.01 to 6.00 D | 2.4% | (2/83) | 1.2% | (1/83) | 1.2% | (1/83) | 0.0% | (0/83) | 4.8% | (4/83) |
| 6.01 to 7.00 D | 0.0% | (0/83) | 0.0% | (0/83) | 1.2% | (1/83) | 0.0% | (0/83) | 1.2% | (1/83) |
| Total | 36.1% | (30/83) | 37.3% | (31/83) | 21.7% | (18/83) | 4.8% | (4/83) | 100.0% | (83/83) |
| **With Algorithm Adjustment<br>MRSE: Mean: 2.965, SD: 1.222, Range: 0.88 to 6.38<br>MRCYL:Mean: 0.970, SD: 0.609, Range: 0.50 to 3.00** | | | | | | | | | | |
| 0.00 to 1.00 D | 2.5% | (5/199) | 0.0% | (0/199) | 1.5% | (3/199) | 0.0% | (0/199) | 4.0% | (8/199) |
| 1.01 to 2.00 D | 10.6% | (21/199) | 7.5% | (15/199) | 4.0% | (8/199) | 2.0% | (4/199) | 24.1% | (48/199) |
| 2.01 to 3.00 D | 14.1% | (28/199) | 8.5% | (17/199) | 6.0% | (12/199) | 0.5% | (1/199) | 29.1% | (58/199) |
| 3.01 to 4.00 D | 11.6% | (23/199) | 5.5% | (11/199) | 4.5% | (9/199) | 3.5% | (7/199) | 25.1% | (50/199) |
| 4.01 to 5.00 D | 5.0% | (10/199) | 2.0% | (4/199) | 5.5% | (11/199) | 0.5% | (1/199) | 13.1% | (26/199) |
| 5.01 to 6.00 D | 1.5% | (3/199) | 1.0% | (2/199) | 1.0% | (2/199) | 0.0% | (0/199) | 3.5% | (7/199) |
| 6.01 to 7.00 D | 0.0% | (0/199) | 0.0% | (0/199) | 1.0% | (2/199) | 0.0% | (0/199) | 1.0% | (2/199) |
| Total | 45.2% | (90/199) | 24.6% | (49/199) | 23.6% | (47/199) | 6.5% | (13/199) | 100.0% | (199/199) |

Two eyes (with refraction of 3.50+1.00x176, 3.00+1.25x20) were reported with an aborted procedure and were not treated later. These eyes were excluded from the effectiveness analyses.

The shaded cells were not included in the effectiveness cohort. Additionally, 1 eye in the non-shaded cells was not included in the effectiveness cohort due to an aborted procedure.

## D. Accountability of PMA Cohort

At the time of database lock, of the 369 eyes enrolled in the PMA study, 94.6% (349/369) were available for analysis at the 12-month visit. Accountability at 9 months was very high with only 8 eyes lost to follow-up. A total of 16 eyes missed the 9-month visit, and 2 eyes were discontinued due to aborted treatment (because of problems with the microkeratome). Accountability for all treated eyes through 12 months is presented in Table 3A.

**TABLE 3A**
**ACCOUNTABILITY**
**ALL TREATED EYES**

| Total Subjects (N) = 369 | | Day 1 | Day 7 | 1 Month | 3 Months | 6 Months | 9 Months | 12 Months |
|---|---|---|---|---|---|---|---|---|
| Available for Analysis | %, n/N | 99.7%<br>368/369 | 99.7%<br>368/369 | 99.7%<br>368/369 | 97.8%<br>361/369 | 97.3%<br>359/369 | 93.0%<br>343/369 | 94.6%<br>349/369 |
| Discontinued* | %, n/N | 0.3%<br>1/369 | 0.3%<br>1/369 | 0.3%<br>1/369 | 0.5%<br>2/369 | 0.5%<br>2/369 | 0.5%<br>2/369 | 0.5%<br>2/369 |
| Deceased | %, n/N | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 |
| Retreatment | %, n/N | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 |
| Aborted | %, n/N | 0.3%<br>1/369 | 0.3%<br>1/369 | 0.3%<br>1/369 | 0.5%<br>2/369 | 0.5%<br>2/369 | 0.5%<br>2/369 | 0.5%<br>2/369 |
| Active (Not yet eligible for the interval) | %, n/N | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 |
| Lost to Follow-up† | %, n/N | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 1.1%<br>4/369 | 2.2%<br>8/369 | 2.2%<br>8/369 |
| Missed Visit‡ | %, n/N | 0.0%<br>0/369 | 0.0%<br>0/369 | 0.0%<br>0/369 | 1.6%<br>6/369 | 1.1%<br>4/369 | 4.3%<br>16/369 | 2.7%<br>10/369 |
| % Accountability = Available for Analysis ÷ (Enrolled - Discontinued - Not yet eligible) | | 100.0%<br>368/368 | 100.0%<br>368/368 | 100.0%<br>368/368 | 98.4%<br>361/367 | 97.8%<br>359/367 | 93.5%<br>343/367 | 95.1%<br>349/367 |

160 eyes were in the effectiveness cohort: treated with algorithm adjustment, treated for MRSE and MRSPH of 5.0 D or less, and treated for sphere or astigmatic eyes treated for MRCYL of > 0.50 D.

N = Total number of eyes enrolled.

* Discontinued = due to retreatment, aborted procedure, or death. The eyes with aborted procedures and without successful treatments later were not included in the effectiveness analyses.

† Lost to follow-up: Eyes were not examined at the 24-month visit, and were not considered active or discontinued.

‡ Missed visit: Eyes were not examined at the scheduled visit, however, were examined or may have been examined at a subsequent visit.

Accountability at 9 months for the effectiveness cohort eyes was very high, with only 4 eyes lost to follow-up. Seven (7) eyes missed the 9-month visit, and no eyes were discontinued. Accountability for the effectiveness cohort of eyes through 12 months is presented in Table 3B.

**TABLE 3B**
**ACCOUNTABILITY**
**EFFECTIVENESS COHORT EYES**

| Total Subjects (N) = 160 | | Day 1 | Day 7 | 1 Month | 3 Months | 6 Months | 9 Months | 12 Months |
|---|---|---|---|---|---|---|---|---|
| Available for Analysis | %, n/N | 100.0%<br>160/160 | 100.0%<br>160/160 | 100.0%<br>160/160 | 98.8%<br>158/160 | 100.0%<br>160/160 | 93.1%<br>149/160 | 95.6%<br>153/160 |
| Discontinued* | %, n/N | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 |
| Deceased | %, n/N | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 |
| Retreatment | %, n/N | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 |
| Aborted | %, n/N | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 |
| Active (Not yet eligible for the interval) | %, n/N | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 |
| Lost to Follow-up† | %, n/N | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 2.5%<br>4/160 | 2.5%<br>4/160 |
| Missed Visit‡ | %, n/N | 0.0%<br>0/160 | 0.0%<br>0/160 | 0.0%<br>0/160 | 1.3%<br>2/160 | 0.0%<br>0/160 | 4.4%<br>7/160 | 1.9%<br>3/160 |
| % Accountability = Available for Analysis ÷ (Enrolled - Discontinued - Not yet eligible) | | 100.0%<br>160/160 | 100.0%<br>160/160 | 100.0%<br>160/160 | 98.8%<br>158/160 | 100.0%<br>160/160 | 93.1%<br>149/160 | 95.6%<br>153/160 |

N = Total number of eyes enrolled.

* Discontinued = due to retreatment, aborted procedure, or death.

† Lost to follow-up: Eyes were not examined at the 24-month visit, and were not considered active or discontinued.

‡ Missed visit: Eyes were not examined at the scheduled visit, however, were examined or may have been examined at a subsequent visit.

## E. Safety and Effectiveness Results

### 1. Stability of Refractive Outcome

Table 4A shows the stability of MRSE for all study eyes. In a consistent cohort of eyes, the mean change in MRSE between 6 and 9 months was 0.071 D (SD 0.338 D), and between 9 and 12 months the mean change was 0.033 D (SD 0.294 D). Between 6 and 9 months and 9 and 12 months, the change in MRSE per month was 0.024 D and 0.011 D, respectively, well below the target value of 0.04 D. In addition, >99% of eyes had a change of MRSE of ≤ 1.00 D at both intervals. Thus, stability of MRSE was demonstrated at 9 months postoperatively.

**TABLE 4A**
**STABILITY OF MANIFEST REFRACTION SPHERICAL EQUIVALENT (MRSE)**
**ALL TREATED EYES**

| MRSE[1] | 1 and 3 Months | 3 and 6 Months | 6 and 9 Months | 9 and 12 Months |
|---|---|---|---|---|
| **Pairwise Sequential Visits*** | | | | |
| Eyes with ≤ 1.00 D change (%, n/N, [% CI])[2] | 97.0% (350/361) (94.6%, 98.5%) | 98.3% (351/357) (96.4%, 99.4%) | 99.1% (338/341) (97.5%, 99.8%) | 99.7% (336/337) (98.4%, 100.0%) |
| Mean change between visits<br>SD<br>95% CI | 0.137<br>0.426<br>(0.093, 0.181) | 0.064<br>0.349<br>(0.028, 0.100) | 0.072<br>0.336<br>(0.036, 0.108) | 0.032<br>0.294<br>(0.000, 0.063) |
| Mean change per month | 0.069 | 0.021 | 0.024 | 0.011 |
| Mean change per year (change per month × 12) | 0.823 | 0.256 | 0.289 | 0.126 |
| **Consistent Cohort*** | | | | |
| Eyes with ≤ 1.00 D change (%, n/N, [% CI])[2] | 96.7% (324/335) (94.2%, 98.3%) | 98.2% (329/335) (96.1%, 99.3%) | 99.1% (332/335) (97.4%, 99.8%) | 99.7% (334/335) (98.3%, 100.0%) |
| Mean change between visits<br>SD<br>95% CI | 0.134<br>0.433<br>(0.087, 0.180) | 0.065<br>0.351<br>(0.028, 0.103) | 0.071<br>0.338<br>(0.035, 0.108) | 0.033<br>0.294<br>(0.001, 0.064) |
| Mean change per month | 0.067 | 0.022 | 0.024 | 0.011 |
| Mean change per year (change per month × 12) | 0.801 | 0.261 | 0.285 | 0.131 |

* Pairwise Sequential Visits ≡ Eyes that had two consecutive exams, but not necessarily every follow-up exam. Consistent Cohort ≡ All eyes examined at 1, 3, 6, 9, and 12 months.

1 The difference between the postoperative MRSE.

2 The 95%CI ≡ 95% CI around the percentage of eyes meeting the criterion. It was calculated based on Clopper-Pearson exact method.

Table 4B shows the stability of MRSE for the effectiveness cohort of eyes. Stability of the MRSE for the effectiveness cohort of eyes was very similar to the stability of the MRSE for the population of all study eyes. In the consistent cohort of eyes, the mean change in MRSE between 6 and 9 months and 9 and 12 months was 0.071 D (SD 0.328 D) and 0.059 D (SD 0.287), respectively. Between 6 and 9 months and 9 and 12 months, the mean change in MRSE per month was 0.024 D and 0.020, respectively, well below the target value of 0.04 D. In addition, > 99% of eyes had a change in MRSE of ≤ 1.00 D at both intervals. Thus, stability was demonstrated at 9 months postoperatively.

**TABLE 4B**
**STABILITY OF MANIFEST REFRACTION SPHERICAL EQUIVALENT (MRSE)**
**EFFECTIVENESS COHORT**

| MRSE[1] | 1 and 3 Months | 3 and 6 Months | 6 and 9 Months | 9 and 12 Months |
|---|---|---|---|---|
| **Pairwise Sequential Visits*** | | | | |
| Eyes with ≤ 1.00 D change (%, n/N, [% CI])[2] | 96.8% (153/158) (92.8%, 99.0%) | 98.7% (156/158) (95.5%, 99.8%) | 99.3% (148/149) (96.3%, 100.0%) | 100.0% (148/148) (97.5%, 100.0%) |
| Mean change between visits<br>SD<br>95% CI | 0.122<br>0.421<br>(0.056, 0.188) | 0.063<br>0.303<br>(0.016, 0.111) | 0.073<br>0.328<br>(0.020, 0.126) | 0.059<br>0.287<br>(0.012, 0.106) |
| Mean change per month | 0.061 | 0.021 | 0.024 | 0.020 |
| Mean change per year (change per month × 12) | 0.731 | 0.253 | 0.292 | 0.236 |
| **Consistent Cohort*** | | | | |
| Eyes with ≤ 1.00 D change (%, n/N, [% CI])[2] | 96.6% (143/148) (92.3%, 98.9%) | 98.6% (146/148) (95.2%, 99.8%) | 99.3% (147/148) (96.3%, 100.0%) | 100.0% (148/148) (97.5%, 100.0%) |
| Mean change between visits<br>SD<br>95% CI | 0.127<br>0.426<br>(0.057, 0.196) | 0.058<br>0.307<br>(0.008, 0.108) | 0.071<br>0.328<br>(0.018, 0.124) | 0.059<br>0.287<br>(0.012, 0.106) |
| Mean change per month | 0.063 | 0.019 | 0.024 | 0.020 |
| Mean change per year (change per month × 12) | 0.760 | 0.233 | 0.284 | 0.236 |

**Effectiveness Cohort**: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and manifest refraction sphere (MRSPH) of 5.0 D or less.

* Pairwise Sequential Visits = Eyes that had two consecutive exams, but not necessarily every follow-up exam. Consistent Cohort = All eyes examined at 1, 3, 6, 9, and 12 months.

1 The difference between the postoperative MRSE.

2 The 95%CI = 95% CI around the percentage of eyes meeting the criterion. It was calculated based on Clopper-Pearson exact method.

Mean manifest spherical equivalent (MRSE) results for the effectiveness cohort of eyes through 12 months postoperatively is shown in Table 4C. From 9 to 12 months there was very little change in mean MRSE (-0.062 D and -0.023 D, respectively).

**TABLE 4C**
**MEAN OF MANIFEST REFRACTION SPHERICAL EQUIVALENT**
**EFFECTIVENESS COHORT**

| | Preop. | 1 Month | 3 Months | 6 Months | 9 Months | 12 Months |
|---|---|---|---|---|---|---|
| N | 160 | 160 | 158 | 160 | 149 | 153 |
| Mean | 2.699 | -0.336 | -0.210 | -0.148 | -0.062 | -0.023 |
| 95% Confidence Interval | 2.533, 2.866 | -0.418, -0.254 | -0.291, -0.130 | -0.230, -0.067 | -0.155, 0.031 | -0.109, 0.064 |
| Standard Deviation | 1.067 | 0.526 | 0.512 | 0.522 | 0.575 | 0.541 |

Refraction measurement was not required at Day-1 Visit.
**Effectiveness Cohort**: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of available CRFs received with non-missing values at each visit.

As shown in Table 4D for the consistent cohort of eyes, the mean change in manifest refraction cylinder (MRCYL) between 6 and 9 months and 9 and 12 months was -0.034 D (SD 0.389 D) and 0.009 D (SD 0.331), respectively, for eyes treated for astigmatic hyperopia with cylinder > 0.5 D. The mean change in MRCYL per month was -0.011 D and 0.003, respectively at these intervals, well below the target value of 0.04 D. In addition, > 97% of eyes had a change in MRCYL of ≤ 1.00 D at both intervals. Thus, stability was demonstrated at 9 months postoperatively.

**TABLE 4D**
**STABILITY OF MANIFEST REFRACTION CYLINDER (MRCYL)**
**EYES TREATED FOR ASTIGMATIC HYPEROPIA WITH CYLINDER OF > 0.50**

| MRCYL | 1 and 3 Months | 3 and 6 Months | 6 and 9 Months | 9 and 12 Months |
|---|---|---|---|---|
| **Pairwise Sequential Visits*** | | | | |
| Eyes with ≤ 1.00 D change (%, n/N, [% CI])[2] | 98.7% (155/157) (95.5%, 99.8%) | 98.7% (152/154) (95.4%, 99.8%) | 97.9% (141/144) (94.0%, 99.6%) | 99.3% (140/141) (96.1%, 100.0%) |
| Mean change between visits<br>SD<br>95% CI | 0.027<br>0.310<br>(-0.022, 0.076) | 0.054<br>0.339<br>(-0.000, 0.108) | -0.031<br>0.388<br>(-0.095, 0.033) | 0.009<br>0.331<br>(-0.046, 0.064) |
| Mean change per month | 0.014 | 0.018 | -0.010 | 0.003 |
| Mean change per year (change per month × 12) | 0.162 | 0.214 | -0.125 | 0.035 |
| **Consistent Cohort*** | | | | |
| Eyes with ≤ 1.00 D change (%, n/N, [% CI])[2] | 98.6% (139/141) (95.0%, 99.8%) | 98.6% (139/141) (95.0%, 99.8%) | 97.9% (138/141) (93.9%, 99.6%) | 99.3% (140/141) (96.1%, 100.0%) |
| Mean change between visits<br>SD<br>95% CI | 0.039<br>0.315<br>(-0.013, 0.091) | 0.060<br>0.346<br>(0.003, 0.118) | -0.034<br>0.389<br>(-0.098, 0.031) | 0.009<br>0.331<br>(-0.046, 0.064) |
| Mean change per month | 0.020 | 0.020 | -0.011 | 0.003 |
| Mean change per year (change per month × 12) | 0.234 | 0.241 | -0.135 | 0.035 |

* Pairwise Sequential Visits = Eyes that had two consecutive exams, but not necessarily every follow-up exam. Consistent Cohort = All eyes examined at 1, 3, 6, 9, and 12 months.

1 The difference between the postoperative MRCYL.

2 The 95%CI = 95% CI around the percentage of eyes meeting the criterion. It was calculated based on Clopper-Pearson exact method.

Table 4E shows the stability of MRCYL for the effectiveness cohort of eyes. Stability for the effectiveness cohort of eyes was similar to stability for the astigmatic hyperopia eyes with > 0.50 D of cylinder treatment. In the consistent cohort of eyes, the mean change in manifest refraction cylinder (MRCYL) between 6 and 9 months and 9 and 12 months was -0.071 D (SD 0.350 D) and 0.014 D (SD 0.342), respectively. Between 6 and 9 months and 9 and 12 months, the mean change in MRCYL per month was -0.024 D and 0.005 D, respectively, well below the target value of 0.04 D. In addition, > 97% of eyes had a change of MRCYL by ≤ 1.00 D at both intervals. Thus, stability was demonstrated at 9 months postoperatively.

**TABLE 4E**
**STABILITY OF MANIFEST REFRACTION CYLINDER (MRCYL)**
**EFFECTIVENESS COHORT TREATED FOR ASTIGMATIC HYPEROPIA WITH CYLINDER OF > 0.50 D AND WITH ALGORITHM ADJUSTMENT**

| MRCYL[1] | 1 and 3 Months | 3 and 6 Months | 6 and 9 Months | 9 and 12 Months |
|---|---|---|---|---|
| **Pairwise Sequential Visits*** | | | | |
| Eyes with ≤ 1.00 D change (%, n/N, [% CI])[2] | 99.0% (100/101) (94.6%, 100.0%) | 99.0% (100/101) (94.6%, 100.0%) | 97.8% (90/92) (92.4%, 99.7%) | 98.9% (90/91) (94.0%, 100.0%) |
| Mean change between visits<br>SD<br>95% CI | 0.037<br>0.305<br>(-0.023, 0.097) | 0.072<br>0.294<br>(0.014, 0.130) | -0.073<br>0.349<br>(-0.146, -0.001) | 0.014<br>0.342<br>(-0.058, 0.085) |
| Mean change per month | 0.019 | 0.024 | -0.024 | 0.005 |
| Mean change per year (change per month × 12) | 0.223 | 0.287 | -0.293 | 0.055 |
| **Consistent Cohort*** | | | | |
| Eyes with ≤ 1.00 D change (%, n/N, [% CI])[2] | 98.9% (90/91) (94.0%, 100.0%) | 98.9% (90/91) (94.0%, 100.0%) | 97.8% (89/91) (92.3%, 99.7%) | 98.9% (90/91) (94.0%, 100.0%) |
| Mean change between visits<br>SD<br>95% CI | 0.047<br>0.309<br>(-0.018, 0.111) | 0.077<br>0.297<br>(0.015, 0.139) | -0.071<br>0.350<br>(-0.144, 0.001) | 0.014<br>0.342<br>(-0.058, 0.085) |
| Mean change per month | 0.023 | 0.026 | -0.024 | 0.005 |
| Mean change per year (change per month × 12) | 0.280 | 0.308 | -0.286 | 0.055 |

**Effectiveness Cohort**: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.

* Pairwise Sequential Visits = Eyes that had two consecutive exams, but not necessarily every follow-up exam. Consistent Cohort = All eyes examined at 1, 3, 6, 9, and 12 months.

1 The difference between the postoperative MRCYL.

2 The 95%CI = 95% CI around the percentage of eyes meeting the criterion. It was calculated based on Clopper-Pearson exact method.

2. Safety Outcomes

Analysis of safety was based on the total PMA cohort of 369 eyes. The safety tables show all 369 eyes, but have shaded areas for eyes not included in the approved indication for use.

The key safety variables for all treated eyes stratified by algorithm and treatment are presented in Table 5. Only one eye lost ≥ 2 lines BSCVA at the last available visit.

All reported adverse events stratified by algorithm and treatment are summarized in Table 6. The cumulative adverse event rate for all reported events was quite low, with no category of event exceeding 0.5% on a cumulative basis, with the exception of diabetes at 1.1%. Overall, the device was deemed to be safe.

**TABLE 5**
**SUMMARY OF KEY SAFETY VARIABLES AT LAST AVAILABLE VISIT**
**ALL TREATED EYES STRATIFIED BY ALGORITHM AND TREATMENT**

| Key Safety Variables | Without Algorithm Adjustment | | | With Algorithm Adjustment | | | |
|---|---|---|---|---|---|---|---|
| | Sphere % (n/N) | Sphere + 0.5 D Cylinder % (n/N) | Sphere + >0.5 D Cylinder % (n/N) | Sphere % (n/N) | Sphere + 0.5 D Cylinder % (n/N) | Sphere + >0.5 D Cylinder % (n/N) | Total % (n/N) |
| Loss of ≥ 2 lines BSCVA | 0.0% (0/27) | 0.0% (0/30) | 1.9% (1/52) | 0.0% (0/60) | 0.0% (0/90) | 0.0% (0/108) | 0.3% (1/367) |
| Loss of > 2 lines BSCVA | 0.0% (0/27) | 0.0% (0/30) | 0.0% (0/52) | 0.0% (0/60) | 0.0% (0/90) | 0.0% (0/108) | 0.0% (0/367) |
| BSCVA worse than 20/40 | 0.0% (0/27) | 0.0% (0/30) | 0.0% (0/52) | 0.0% (0/60) | 0.0% (0/90) | 0.0% (0/108) | 0.0% (0/367) |
| BSCVA worse than 20/25 if 20/20 or better preoperatively | 0.0% (0/27) | 0.0% (0/28) | 0.0% (0/52) | 0.0% (0/59) | 0.0% (0/87) | 0.0% (0/98) | 0.0% (0/351) |
| Haze ≥ trace with loss of BSCVA > 2 lines | 0.0% (0/27) | 0.0% (0/30) | 0.0% (0/52) | 0.0% (0/60) | 0.0% (0/90) | 0.0% (0/108) | 0.0% (0/367) |
| Increased manifest refractive astigmatism > 2.0D* | 0.0% (0/27) | 3.3% (1/30) | 0.0% (0/52) | 0.0% (0/60) | 0.0% (0/90) | 0.0% (0/108) | 0.3% (1/367) |

Data collected through July 15, 2008. **2 eyes with aborted procedures were excluded.**
The shaded columns were not included in the effectiveness cohort. Additionally, 8 eyes in the non-shaded columns were not included in the effectiveness cohort due to MRSE or MRSPH > 5.0 D.
* For eyes treated with spherical hyperopia only.

## TABLE 6
## ADVERSE EVENTS REPORTED AT ANY POSTOPERATIVE VISITS
## ALL TREATED EYES STRATIFIED BY ALGORITHM AND TREATMENT

| Adverse Event | Without Algorithm Adjustment | | | With Algorithm Adjustment | | | Total |
|---|---|---|---|---|---|---|---|
| | Sphere % (n/N) | Sphere + 0.5 D Cylinder % (n/N) | Sphere + >0.5 D Cylinder % (n/N) | Sphere % (n/N) | Sphere + 0.5 D Cylinder % (n/N) | Sphere + >0.5 D Cylinder % (n/N) | % (n/N) |
| Corneal epithelial defect involving the keratectomy at one month or later | 0.0% (0/27) | 0.0% (0/30) | 1.9% (1/53) | 0.0% (0/60) | 0.0% (0/90) | 0.0% (0/109) | 0.3% (1/369) |
| Decrease in BSCVA ≥ 2 lines at the most recent evaluation | 0.0% (0/27) | 0.0% (0/30) | 1.9% (1/53) | 0.0% (0/60) | 0.0% (0/90) | 0.0% (0/109) | 0.3% (1/369) |
| Diabetes | 0.0% (0/27) | 3.3% (1/30) | 1.9% (1/53) | 0.0% (0/60) | 2.2% (2/90) | 0.0% (0/109) | 1.1% (4/369) |
| Melting of the flap | 0.0% (0/27) | 0.0% (0/30) | 1.9% (1/53) | 0.0% (0/60) | 0.0% (0/90) | 0.0% (0/109) | 0.3% (1/369) |
| Miscreated flap (lost, incomplete, too thin) | 0.0% (0/27) | 3.3% (1/30) | 1.9% (1/53) | 0.0% (0/60) | 0.0% (0/90) | 0.0% (0/109) | 0.5% (2/369) |
| Ocular migraine | 0.0% (0/27) | 0.0% (0/30) | 3.8% (2/53) | 0.0% (0/60) | 0.0% (0/90) | 0.0% (0/109) | 0.5% (2/369) |
| Vitreous floaters | 0.0% (0/27) | 0.0% (0/30) | 1.9% (1/53) | 0.0% (0/60) | 0.0% (0/90) | 0.0% (0/109) | 0.3% (1/369) |

N = number of treated eyes. n = number of eyes reported with the corresponding event. % = n ÷ N ×100%.
Data collected through July 15, 2008.
The shaded columns were not included in the effectiveness cohort. Additionally, 9 eyes in the non-shaded columns were not included in the effectiveness cohort due to MRSE or MRSPH > 5.0 D.

Change in BSCVA stratified by visit and by diopter of preoperative MRSE for all treated eyes is presented in Tables 7A and 7B. At the 9 month visit, 5 eyes lost more than 2 lines, and 11 eyes lost 2 lines of BSCVA. As shown in Table 7C, 5 eyes treated in the sphere + 0.5 D cylinder group lost > 2 lines of BSCVA at the 9 month visit and 4 eyes lost > 2 lines BSCVA at the 12 month visit. Also, at the 9 month visit, 4 eyes in the sphere only group, and 2 eyes in the sphere + 0.50 D cylinder, and 5 eyes in the sphere + >0.50 D cylinder group lost 2 lines of BSCVA. These subjects were asked to return for an additional examination, and at this visit, only one eye had a loss of 2 lines of BSCVA. No eyes lost > 2 lines BSCVA (Table 5).

**TABLE 7A**
**CHANGE IN BEST SPECTACLE-CORRECTED VISUAL ACUITY (BSCVA)**
**ALL TREATED EYES**

| Change in BSCVA from Preop | 1 Month % (n/N) | 3 Months % (n/N) | 6 Months % (n/N) | 9 Months % (n/N) | 12 Months % (n/N) |
|---|---|---|---|---|---|
| Decrease > 2 lines (Decrease >10 letters) | 1.4% (5/368) | 0.8% (3/361) | 1.9% (7/359) | 1.5% (5/341) | 1.1% (4/349) |
| Decrease 2 lines (Decrease 8 to 10 letters) | 2.7% (10/368) | 1.7% (6/361) | 2.5% (9/359) | 3.2% (11/341) | 2.3% (8/349) |
| Decrease 1 line (Decrease 3 to 7 letters) | 22.6% (83/368) | 18.3% (66/361) | 19.2% (69/359) | 16.4% (56/341) | 17.8% (62/349) |
| No change (Change within 2 letters) | 56.5% (208/368) | 58.2% (210/361) | 51.0% (183/359) | 54.0% (184/341) | 50.4% (176/349) |
| Increase 1 line (Increase 3 to 7 letters) | 15.5% (57/368) | 18.3% (66/361) | 22.6% (81/359) | 22.3% (76/341) | 24.4% (85/349) |
| Increase 2 lines (Increase 8 to 10 letters) | 1.4% (5/368) | 2.8% (10/361) | 2.8% (10/359) | 2.6% (9/341) | 4.0% (14/349) |
| Increase > 2 lines (Increase >10 letters) | 0.0% (0/368) | 0.0% (0/361) | 0.0% (0/359) | 0.0% (0/341) | 0.0% (0/349) |
| Not Data on CRFs* | 0 | 0 | 0 | 2 | 0 |
| Total CRFs† | 368 | 361 | 359 | 343 | 349 |
| Missed Visit‡ | 1 | 8 | 10 | 26 | 20 |

N = Number of available CRFs received with non-missing values at preop and each postoperative visit. BSCVA measurement was not required at Day-1 visit.

* Number of available CRFs received with missing values at preop or the corresponding postoperative visit.

† Number of available CRFs received at each visit.

‡ Number of eyes missed visit.

## TABLE 7B
## CHANGE IN BEST SPECTACLE-CORRECTED VISUAL ACUITY (BSCVA)
## STRATIFIED BY PREOPERATIVE MRSE
## ALL TREATED EYES

| Change in BSCVA from Preop | Preoperative MRSE | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|
| | 0.00 to 1.00 D % (n/N) | 1.01 to 2.00 D % (n/N) | 2.01 to 3.00 D % (n/N) | 3.01 to 4.00 D % (n/N) | 4.01 to 5.00 D % (n/N) | 5.01 to 6.00 D % (n/N) | 6.01 to 7.00 D % (n/N) | % (n/N) |
| **9 Months** | | | | | | | | |
| Decrease > 2 lines (Decrease >10 letters) | 0.0% (0/10) | 1.0% (1/97) | 0.0% (0/87) | 3.7% (3/82) | 0.0% (0/47) | 6.7% (1/15) | 0.0% (0/3) | 1.5% (5/341) |
| Decrease 2 lines (Decrease 8 to 10 letters) | 0.0% (0/10) | 2.1% (2/97) | 1.1% (1/87) | 6.1% (5/82) | 6.4% (3/47) | 0.0% (0/15) | 0.0% (0/3) | 3.2% (11/341) |
| Decrease 1 line (Decrease 3 to 7 letters) | 20.0% (2/10) | 11.3% (11/97) | 16.1% (14/87) | 15.9% (13/82) | 23.4% (11/47) | 26.7% (4/15) | 33.3% (1/3) | 16.4% (56/341) |
| No change (Change within 2 letters) | 40.0% (4/10) | 56.7% (55/97) | 52.9% (46/87) | 51.2% (42/82) | 57.4% (27/47) | 53.3% (8/15) | 66.7% (2/3) | 54.0% (184/341) |
| Increase 1 line (Increase 3 to 7 letters) | 40.0% (4/10) | 25.8% (25/97) | 24.1% (21/87) | 23.2% (19/82) | 10.6% (5/47) | 13.3% (2/15) | 0.0% (0/3) | 22.3% (76/341) |
| Increase 2 lines (Increase 8 to 10 letters) | 0.0% (0/10) | 3.1% (3/97) | 5.7% (5/87) | 0.0% (0/82) | 2.1% (1/47) | 0.0% (0/15) | 0.0% (0/3) | 2.6% (9/341) |
| Increase > 2 lines (Increase >10 letters) | 0.0% (0/10) | 0.0% (0/97) | 0.0% (0/87) | 0.0% (0/82) | 0.0% (0/47) | 0.0% (0/15) | 0.0% (0/3) | 0.0% (0/341) |
| Not Data on CRFs* | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 2 |
| Total CRFs† | 10 | 99 | 87 | 82 | 47 | 15 | 3 | 343 |
| Missed Visit‡ | 2 | 10 | 8 | 6 | NA | NA | NA | 26 |
| **12 Months** | | | | | | | | |
| Decrease > 2 lines (Decrease >10 letters) | 0.0% (0/12) | 1.0% (1/102) | 0.0% (0/92) | 3.8% (3/80) | 0.0% (0/46) | 0.0% (0/14) | 0.0% (0/3) | 1.1% (4/349) |
| Decrease 2 lines (Decrease 8 to 10 letters) | 0.0% (0/12) | 0.0% (0/102) | 1.1% (1/92) | 6.3% (5/80) | 4.3% (2/46) | 0.0% (0/14) | 0.0% (0/3) | 2.3% (8/349) |
| Decrease 1 line (Decrease 3 to 7 letters) | 8.3% (1/12) | 18.6% (19/102) | 9.8% (9/92) | 18.8% (15/80) | 34.8% (16/46) | 7.1% (1/14) | 33.3% (1/3) | 17.8% (62/349) |
| No change (Change within 2 letters) | 33.3% (4/12) | 53.9% (55/102) | 48.9% (45/92) | 45.0% (36/80) | 50.0% (23/46) | 85.7% (12/14) | 33.3% (1/3) | 50.4% (176/349) |
| Increase 1 line (Increase 3 to 7 letters) | 50.0% (6/12) | 22.5% (23/102) | 33.7% (31/92) | 25.0% (20/80) | 6.5% (3/46) | 7.1% (1/14) | 33.3% (1/3) | 24.4% (85/349) |
| Increase 2 lines (Increase 8 to 10 letters) | 8.3% (1/12) | 3.9% (4/102) | 6.5% (6/92) | 1.3% (1/80) | 4.3% (2/46) | 0.0% (0/14) | 0.0% (0/3) | 4.0% (14/349) |
| Increase > 2 lines (Increase >10 letters) | 0.0% (0/12) | 0.0% (0/102) | 0.0% (0/92) | 0.0% (0/80) | 0.0% (0/46) | 0.0% (0/14) | 0.0% (0/3) | 0.0% (0/349) |
| Not Data on CRFs* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total CRFs† | 12 | 102 | 92 | 80 | 46 | 14 | 3 | 349 |
| Missed Visit‡ | NA | 7 | 3 | 8 | 1 | 1 | NA | 20 |

Eyes in the shaded cells were not included in the effectiveness cohort. Some eyes in the non-shaded cells were not included in the effectiveness cohort due to no algorithm adjustment, MRSE or MRSPH treatment of > 5.0 D, or MRCYL treatment of 0.50 D.

N = Number of CRFs received with non-missing values for each subgroup.

* Number of available CRFs received with missing BSCVA at the corresponding visit.

† Number of available CRFs received at the corresponding visit.

‡ Number of eyes missed visit.

## TABLE 7C
## CHANGE IN BEST SPECTACLE-CORRECTED VISUAL ACUITY (BSCVA)
## STRATIFIED BY TREATMENT
## ALL TREATED EYES

| Change in BSCVA from Preop | Treatment | | | Total |
|---|---|---|---|---|
| | Sphere % (n/N) | Sphere + 0.5 D Cylinder % (n/N) | Sphere + >0.5 D Cylinder % (n/N) | % (n/N) |
| **9 Months** | | | | |
| Decrease > 2 lines (Decrease >10 letters) | 0.0% (0/85) | 4.5% (5/112) | 0.0% (0/144) | 1.5% (5/341) |
| Decrease 2 lines (Decrease 8 to 10 letters) | 4.7% (4/85) | 1.8% (2/112) | 3.5% (5/144) | 3.2% (11/341) |
| Decrease 1 line (Decrease 3 to 7 letters) | 14.1% (12/85) | 19.6% (22/112) | 15.3% (22/144) | 16.4% (56/341) |
| No change (Change within 2 letters) | 60.0% (51/85) | 47.3% (53/112) | 55.6% (80/144) | 54.0% (184/341) |
| Increase 1 line (Increase 3 to 7 letters) | 20.0% (17/85) | 23.2% (26/112) | 22.9% (33/144) | 22.3% (76/341) |
| Increase 2 lines (Increase 8 to 10 letters) | 1.2% (1/85) | 3.6% (4/112) | 2.8% (4/144) | 2.6% (9/341) |
| Increase > 2 lines (Increase >10 letters) | 0.0% (0/85) | 0.0% (0/112) | 0.0% (0/144) | 0.0% (0/341) |
| Not Data on CRFs* | 0 | 2 | 0 | 2 |
| Total CRFs† | 85 | 114 | 144 | 343 |
| Missed Visit‡ | 2 | 6 | 18 | 26 |
| **12 Months** | | | | |
| Decrease > 2 lines (Decrease >10 letters) | 0.0% (0/87) | 3.4% (4/116) | 0.0% (0/146) | 1.1% (4/349) |
| Decrease 2 lines (Decrease 8 to 10 letters) | 2.3% (2/87) | 2.6% (3/116) | 2.1% (3/146) | 2.3% (8/349) |
| Decrease 1 line (Decrease 3 to 7 letters) | 14.9% (13/87) | 18.1% (21/116) | 19.2% (28/146) | 17.8% (62/349) |
| No change (Change within 2 letters) | 55.2% (48/87) | 50.0% (58/116) | 47.9% (70/146) | 50.4% (176/349) |
| Increase 1 line (Increase 3 to 7 letters) | 24.1% (21/87) | 23.3% (27/116) | 25.3% (37/146) | 24.4% (85/349) |
| Increase 2 lines (Increase 8 to 10 letters) | 3.4% (3/87) | 2.6% (3/116) | 5.5% (8/146) | 4.0% (14/349) |
| Increase > 2 lines (Increase >10 letters) | 0.0% (0/87) | 0.0% (0/116) | 0.0% (0/146) | 0.0% (0/349) |
| Not Data on CRFs* | 0 | 0 | 0 | 0 |
| Total CRFs† | 87 | 116 | 146 | 349 |
| Missed Visit‡ | NA | 4 | 16 | 20 |

Eyes in the shaded cells were not included in the effectiveness cohort. Some eyes in the non-shaded cells were not included in the effectiveness cohort due to no algorithm adjustment, MRSE or MRSPH treatment of > 5.0 D, or MRCYL treatment of 0.50 D.

N = Number of CRFs received with non-missing values for each subgroup.

* Number of available CRFs received with missing BSCVA at the corresponding visit.

† Number of available CRFs received at the corresponding visit.

‡ Number of eyes missed visit.

Table 8 shows the postoperative UCVA compared to the preoperative BSCVA for the effectiveness cohort of eyes. At 9 and 12 months after surgery, 49.7% (74/149) and 51.0% (78/153) of the study eyes saw as well *without* glasses after surgery as *with* glasses before surgery, respectively.

**TABLE 8**
**POSTOPERATIVE UNCORRECTED VISUAL ACUITY (UCVA) COMPARED TO PREOPERATIVE BEST SPECTACLE CORRECTED VISUAL ACUITY (BSCVA) EFFECTIVENESS COHORT**

| Uncorrected Visual Acuity | 1 Month % (n/N) | 3 Months % (n/N) | 6 Months % (n/N) | 9 Months % (n/N) | 12 Months % (n/N) |
|---|---|---|---|---|---|
| UCVA >2 Lines Better than Preop BSCVA | 0.0% (0/160) | 0.0% (0/158) | 0.0% (0/160) | 0.0% (0/149) | 0.0% (0/153) |
| UCVA 2 Lines Better than Preop BSCVA | 0.6% (1/160) | 2.5% (4/158) | 1.9% (3/160) | 2.0% (3/149) | 5.2% (8/153) |
| UCVA 1 Line Better than Preop BSCVA | 7.5% (12/160) | 11.4% (18/158) | 11.9% (19/160) | 8.1% (12/149) | 11.8% (18/153) |
| UCVA Equal to Preop BSCVA | 22.5% (36/160) | 29.1% (46/158) | 31.9% (51/160) | 39.6% (59/149) | 34.0% (52/153) |
| UCVA 1 Line Worse than Preop BSCVA | 31.9% (51/160) | 29.1% (46/158) | 27.5% (44/160) | 26.8% (40/149) | 26.8% (41/153) |
| UCVA 2 Lines Worse than Preop BSCVA | 16.9% (27/160) | 12.0% (19/158) | 15.6% (25/160) | 11.4% (17/149) | 13.1% (20/153) |
| UCVA >2 Lines Worse than Preop BSCVA | 20.6% (33/160) | 15.8% (25/158) | 11.3% (18/160) | 12.1% (18/149) | 9.2% (14/153) |
| UCVA Better than or Equal to Preop BSCVA | 30.6% (49/160) | 43.0% (68/158) | 45.6% (73/160) | 49.7% (74/149) | 51.0% (78/153) |
| Not reported* | 0 | 0 | 0 | 0 | 0 |
| Total† | 160 | 158 | 160 | 149 | 153 |

**Effectiveness Cohort**: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of available CRFs received with non-missing values at each visit.
* Number of available CRFs received with missing values at each visit.
† Number of available CRFs received at each visit.

**Complications and Subject Symptoms**

Table 9 presents a summary of all complications reported for all treated eyes through the 12-month visit. At the 9-month visit, the following complications were reported: dry eye (0.3%), epithelium in the interface (0.3%), pain at 1 month or later (0.6%), punctal plug insertion (0.9%), superficial punctuate keratitis (SPK) (0.6%), and vitreous floaters (0.6%). Cumulative events reported through the course of the study at a frequency of >1% included conjunctivitis (1.1%), corneal edema between 1 week and < 1 month (1.1%), diffuse lamellar keratitis (4.6%), double/ghost images (2.4%), dry eye (4.1%), epithelium at flap edge (1.9%), epithelium in the interface (7.9%), foreign body sensation at 1 month or later (2.4%), punctal plug inserted (13.3%), superficial punctuate keratitis (SPK) (6.8%), steroid-induced IOP increase (2.2%), and transient light sensitivity syndrome (TLSS) (3.3%).

## TABLE 9
## COMPLICATIONS
## ALL TREATED EYES

| Complications | D 1 N=368 % (n) | D 7 N=368 % (n) | 1 M N=368 % (n) | 3 M N=361 % (n) | 6 M N=359 % (n) | 9 M N=343 % (n) | 12 M N=349 % (n) | Cum* N=369 % (n) |
|---|---|---|---|---|---|---|---|---|
| Allergic conjunctivitis | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.8% (3) |
| Blepharitis | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.5% (2) |
| Conjunctivitis | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.6% (2) | 0.0% (0) | 0.0% (0) | 1.1% (4) |
| Corneal abrasion | 0.3% (1) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.5% (2) |
| Corneal edema between 1 week to less than 1 month after the procedure | 0.0% (0) | 0.8% (3) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 1.1% (4) |
| Corneal haze | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) |
| Corneal scar | 0.0% (0) | 0.0% (0) | 0.3% (1) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) |
| Debris in the interface | 0.0% (0) | 0.3% (1) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) |
| Diffuse lamellar keratitis[1] | 3.8% (14) | 0.5% (2) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 4.6% (17) |
| Double/ghost images in the operative eye | 0.0% (0) | 0.3% (1) | 0.0% (0) | 1.4% (5) | 0.8% (3) | 0.0% (0) | 0.0% (0) | 2.4% (9) |
| Dry eye | 0.0% (0) | 0.8% (3) | 1.1% (4) | 0.6% (2) | 1.1% (4) | 0.3% (1) | 0.3% (1) | 4.1% (15) |
| Enhancement not done due to flap fibrosis | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) |
| Epithelium at flap edge | 0.0% (0) | 0.8% (3) | 1.1% (4) | 0.0% (0) | 0.3% (1) | 0.0% (0) | 0.0% (0) | 1.9% (7) |
| Epithelium in the interface | 0.3% (1) | 1.1% (4) | 3.0% (11) | 3.6% (13) | 1.7% (6) | 0.3% (1) | 0.3% (1) | 7.9% (29) |
| Foreign body sensation at 1 month or later | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) | 0.0% (0) | 1.4% (5) | 2.4% (9) |
| Iritis | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) |
| Loose epithelium | 0.0% (0) | 0.5% (2) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.5% (2) |
| Meibomian gland dysfunction | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.5% (2) |
| Mucus under edge of flap | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) | 0.0% (0) | 0.0% (0) | 0.3% (1) |
| Pain at 1 month or later | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.6% (2) | 0.6% (2) | 0.6% (2) | 0.5% (2) |
| Possible allergic reaction to plugs or eyedrops | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.5% (2) |
| Post-operative flap complications: (flap is not the size and shape initially intended, the microkeratome stopped in mid-cut, or the resultant flap is misaligned) | 0.3% (1) | 0.3% (1) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) |
| Punctal plug inserted | 0.0% (0) | 5.2% (19) | 5.2% (19) | 0.6% (2) | 0.8% (3) | 0.9% (3) | 0.0% (0) | 13.3% (49) |
| Punctal plug replaced | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) | 0.0% (0) | 0.0% (0) | 0.3% (1) |
| Rough epithelium | 0.3% (1) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) |
| SPK | 0.0% (0) | 2.4% (9) | 3.0% (11) | 0.0% (0) | 0.0% (0) | 0.6% (2) | 0.3% (1) | 6.8% (25) |
| Steroid induced IOP increase | 0.0% (0) | 0.5% (2) | 1.6% (6) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 2.2% (8) |
| Subconjunctival hemorrhage | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) |
| TLSS | 0.0% (0) | 0.0% (0) | 1.6% (6) | 0.6% (2) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 3.3% (12) |
| Trace Microstriae | 0.0% (0) | 0.3% (1) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.3% (1) |
| Trace corneal haze | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.6% (2) | 0.6% (2) | 0.0% (0) | 0.0% (0) | 0.5% (2) |
| Vitreous floaters | 0.0% (0) | 0.0% (0) | 0.0% (0) | 0.6% (2) | 0.6% (2) | 0.6% (2) | 0.6% (2) | 0.8% (3) |

N = number of eyes returned for the visits. n = number of eyes reported with the corresponding event. % = n ÷N ×100.

* Unsch = Unscheduled visits. Cumulative = during the course of the study. Eyes without any follow-up visits were excluded.

1 12 of 17 reports of diffuse lamellar keratitis (DLK) were associated with use of the Intralase Laser Keratome and 5 of 17 reports of DLK were associated with the Hansatome Microkeratome.

Subjects filled out a subject questionnaire at the preoperative visit and at each visit from the 3-month postoperative visit on. They graded their symptoms according to severity as either none, mild, moderate, marked, or severe (see Table 10). Table 11 presents the subject symptoms change from baseline to 9 months postoperatively. Any symptom for which there is at least a one grade increase from baseline is considered "worse" and at least a one grade decrease is considered "better."

Table 10 displays subject symptoms for all treated eyes both preoperatively and at 6, 9, and 12 months. Symptoms are grouped by severity level into absent, mild, moderate, marked, and severe. Symptoms in the mild category are not considered to be clinically significant. It can be seen that those symptoms reported at 9 and 12 months fall predominantly into the "mild" category. Symptoms (those rated moderate to severe) reported with an incidence of at least 5% at month 9 include light sensitivity (moderate, 7%), dryness (moderate, 8.5%), blurred vision (moderate, 7.9%), fluctuation of vision (moderate, 5.6%), and variation of vision in normal and dim light (moderate 5.6% and 7.0%, respectively). At 9 months, no symptom was reported as marked or severe with an incidence of 5% or greater.

## TABLE 10
## SUBJECT SYMPTOMS
## ALL TREATED EYES



| Symptom | Visit | N | Absent % (n) | Mild % (n) | Moderate % (n) | Marked % (n) | Severe % (n) |
|---|---|---|---|---|---|---|---|
| **Light sensitivity** | **Preop** | 361 | 74.8% (270) | 15.0% (54) | 9.1% (33) | 0.6% (2) | 0.6% (2) |
| | **6 Months** | 357 | 66.1% (236) | 26.1% (93) | 4.5% (16) | 3.4% (12) | 0.0% (0) |
| | **9 Months** | 341 | 70.4% (240) | 21.4% (73) | 7.0% (24) | 1.2% (4) | 0.0% (0) |
| | **12 Months** | 347 | 67.7% (235) | 27.7% (96) | 2.3% (8) | 2.3% (8) | 0.0% (0) |
| **Headaches** | **Preop** | 361 | 90.9% (328) | 6.6% (24) | 1.7% (6) | 0.8% (3) | 0.0% (0) |
| | **6 Months** | 357 | 89.6% (320) | 8.1% (29) | 2.2% (8) | 0.0% (0) | 0.0% (0) |
| | **9 Months** | 341 | 89.4% (305) | 8.2% (28) | 2.3% (8) | 0.0% (0) | 0.0% (0) |
| | **12 Months** | 347 | 92.5% (321) | 6.9% (24) | 0.6% (2) | 0.0% (0) | 0.0% (0) |
| **Pain/burning** | **Preop** | 361 | 94.7% (342) | 4.4% (16) | 0.6% (2) | 0.3% (1) | 0.0% (0) |
| | **6 Months** | 356 | 87.1% (310) | 10.4% (37) | 2.5% (9) | 0.0% (0) | 0.0% (0) |
| | **9 Months** | 341 | 90.9% (310) | 6.7% (23) | 2.3% (8) | 0.0% (0) | 0.0% (0) |
| | **12 Months** | 347 | 92.5% (321) | 7.2% (25) | 0.3% (1) | 0.0% (0) | 0.0% (0) |
| **Dryness** | **Preop** | 361 | 75.6% (273) | 19.1% (69) | 5.0% (18) | 0.3% (1) | 0.0% (0) |
| | **6 Months** | 357 | 52.9% (189) | 33.6% (120) | 9.8% (35) | 3.4% (12) | 0.3% (1) |
| | **9 Months** | 341 | 55.1% (188) | 33.4% (114) | 8.5% (29) | 2.3% (8) | 0.6% (2) |
| | **12 Months** | 346 | 54.0% (187) | 35.5% (123) | 7.8% (27) | 2.6% (9) | 0.0% (0) |
| **Excessive tearing** | **Preop** | 361 | 92.8% (335) | 4.2% (15) | 1.7% (6) | 0.8% (3) | 0.6% (2) |
| | **6 Months** | 357 | 96.9% (346) | 2.2% (8) | 0.8% (3) | 0.0% (0) | 0.0% (0) |
| | **9 Months** | 340 | 95.3% (324) | 4.7% (16) | 0.0% (0) | 0.0% (0) | 0.0% (0) |
| | **12 Months** | 347 | 93.4% (324) | 5.5% (19) | 0.9% (3) | 0.3% (1) | 0.0% (0) |
| **Gritty, scratchy** | **Preop** | 361 | 87.8% (317) | 11.1% (40) | 0.6% (2) | 0.3% (1) | 0.3% (1) |
| | **6 Months** | 357 | 80.7% (288) | 14.3% (51) | 4.2% (15) | 0.8% (3) | 0.0% (0) |
| | **9 Months** | 341 | 80.1% (273) | 15.0% (51) | 3.8% (13) | 1.2% (4) | 0.0% (0) |
| | **12 Months** | 347 | 78.7% (273) | 17.0% (59) | 3.5% (12) | 0.9% (3) | 0.0% (0) |
| **Glare** | **Preop** | 361 | 82.5% (298) | 12.2% (44) | 4.7% (17) | 0.0% (0) | 0.6% (2) |
| | **6 Months** | 357 | 72.0% (257) | 22.1% (79) | 3.6% (13) | 2.2% (8) | 0.0% (0) |
| | **9 Months** | 341 | 73.3% (250) | 22.9% (78) | 2.6% (9) | 1.2% (4) | 0.0% (0) |
| | **12 Months** | 346 | 75.7% (262) | 20.5% (71) | 3.2% (11) | 0.6% (2) | 0.0% (0) |
| **Halos** | **Preop** | 361 | 92.5% (334) | 5.3% (19) | 2.2% (8) | 0.0% (0) | 0.0% (0) |
| | **6 Months** | 357 | 79.0% (282) | 16.0% (57) | 2.8% (10) | 2.0% (7) | 0.3% (1) |
| | **9 Months** | 341 | 80.1% (273) | 16.4% (56) | 2.1% (7) | 1.5% (5) | 0.0% (0) |
| | **12 Months** | 347 | 83.3% (289) | 12.7% (44) | 3.5% (12) | 0.6% (2) | 0.0% (0) |

N = Number of Self-evaluation Forms received with non-missing response for the corresponding symptom at each visit.
% = n ÷ N × 100%.

## TABLE 10 *(CONTINUED)*
## SUBJECT SYMPTOMS
## ALL TREATED EYES



| Symptom | Visit | N | Absent % (n) | Mild % (n) | Moderate % (n) | Marked % (n) | Severe % (n) |
|---|---|---|---|---|---|---|---|
| **Blurred vision** | **Preop** | 361 | 85.3% (308) | 6.1% (22) | 4.7% (17) | 3.0% (11) | 0.8% (3) |
| | **6 Months** | 357 | 71.7% (256) | 18.2% (65) | 7.3% (26) | 2.0% (7) | 0.8% (3) |
| | **9 Months** | 341 | 71.6% (244) | 18.8% (64) | 7.9% (27) | 1.8% (6) | 0.0% (0) |
| | **12 Months** | 347 | 72.9% (253) | 16.7% (58) | 8.9% (31) | 1.4% (5) | 0.0% (0) |
| **Double vision** | **Preop** | 361 | 96.7% (349) | 2.8% (10) | 0.6% (2) | 0.0% (0) | 0.0% (0) |
| | **6 Months** | 357 | 87.4% (312) | 8.1% (29) | 3.4% (12) | 1.1% (4) | 0.0% (0) |
| | **9 Months** | 341 | 90.6% (309) | 6.7% (23) | 2.6% (9) | 0.0% (0) | 0.0% (0) |
| | **12 Months** | 346 | 91.3% (316) | 6.4% (22) | 2.3% (8) | 0.0% (0) | 0.0% (0) |
| **Fluctuation of vision** | **Preop** | 361 | 88.1% (318) | 6.9% (25) | 5.0% (18) | 0.0% (0) | 0.0% (0) |
| | **6 Months** | 357 | 65.3% (233) | 24.1% (86) | 7.0% (25) | 3.6% (13) | 0.0% (0) |
| | **9 Months** | 341 | 68.9% (235) | 23.2% (79) | 5.6% (19) | 1.8% (6) | 0.6% (2) |
| | **12 Months** | 347 | 70.6% (245) | 21.9% (76) | 5.5% (19) | 2.0% (7) | 0.0% (0) |
| **Variation - bright light** | **Preop** | 361 | 87.0% (314) | 7.5% (27) | 3.9% (14) | 1.1% (4) | 0.6% (2) |
| | **6 Months** | 357 | 73.9% (264) | 19.6% (70) | 5.3% (19) | 0.6% (2) | 0.6% (2) |
| | **9 Months** | 341 | 83.6% (285) | 13.2% (45) | 1.5% (5) | 1.8% (6) | 0.0% (0) |
| | **12 Months** | 347 | 80.7% (280) | 12.1% (42) | 4.3% (15) | 2.9% (10) | 0.0% (0) |
| **Variation - normal light** | **Preop** | 361 | 90.6% (327) | 8.3% (30) | 0.6% (2) | 0.6% (2) | 0.0% (0) |
| | **6 Months** | 356 | 80.6% (287) | 15.2% (54) | 3.7% (13) | 0.6% (2) | 0.0% (0) |
| | **9 Months** | 339 | 86.4% (293) | 7.7% (26) | 5.6% (19) | 0.3% (1) | 0.0% (0) |
| | **12 Months** | 347 | 86.5% (300) | 6.9% (24) | 6.1% (21) | 0.6% (2) | 0.0% (0) |
| **Variation - dim light** | **Preop** | 361 | 82.0% (296) | 11.1% (40) | 5.3% (19) | 1.7% (6) | 0.0% (0) |
| | **6 Months** | 357 | 62.7% (224) | 23.8% (85) | 10.6% (38) | 2.8% (10) | 0.0% (0) |
| | **9 Months** | 341 | 69.8% (238) | 18.8% (64) | 7.0% (24) | 4.4% (15) | 0.0% (0) |
| | **12 Months** | 347 | 68.6% (238) | 17.0% (59) | 11.5% (40) | 2.9% (10) | 0.0% (0) |
| **Night driving vision** | **Preop** | 361 | 70.9% (256) | 19.7% (71) | 6.6% (24) | 2.2% (8) | 0.6% (2) |
| | **6 Months** | 356 | 68.5% (244) | 19.1% (68) | 7.9% (28) | 3.4% (12) | 1.1% (4) |
| | **9 Months** | 341 | 70.1% (239) | 22.3% (76) | 4.7% (16) | 2.9% (10) | 0.0% (0) |
| | **12 Months** | 347 | 70.9% (246) | 19.6% (68) | 7.8% (27) | 1.7% (6) | 0.0% (0) |
| **Other** | **Preop** | 361 | 98.1% (354) | 0.6% (2) | 0.8% (3) | 0.0% (0) | 0.6% (2) |
| | **6 Months** | 356 | 96.6% (344) | 2.0% (7) | 1.1% (4) | 0.0% (0) | 0.3% (1) |
| | **9 Months** | 341 | 96.8% (330) | 1.2% (4) | 1.5% (5) | 0.6% (2) | 0.0% (0) |
| | **12 Months** | 347 | 95.1% (330) | 2.9% (10) | 1.2% (4) | 0.6% (2) | 0.3% (1) |

N = Number of Self-evaluation Forms received with non-missing response for the corresponding symptom at each visit.
% = n ÷ N × 100%.

Table 11 presents the change in patient symptoms from baseline to 9 months for all treated eyes. A greater proportion of subjects experienced a worsening rather than an improvement from baseline to 9 months in light sensitivity, dryness, glare, halos, blurred vision, double vision, fluctuation of vision, variation of vision in bright, normal, and dim light, and night driving vision.

**TABLE 11**
**SUBJECT SYMPTOMS CHANGE FROM BASELINE AT 9 MONTHS**
**ALL TREATED EYES**

| Symptom | N | Significantly Better % (n) | Better % (n) | No Change % (n) | Worse % (n) | Significantly Worse % (n) |
|---|---|---|---|---|---|---|
| Light sensitivity | 335 | 5.7% (19) | 7.5% (25) | 65.7% (220) | 17.9% (60) | 3.3% (11) |
| Headaches | 335 | 1.8% (6) | 6.0% (20) | 83.3% (279) | 7.5% (25) | 1.5% (5) |
| Pain/burning | 335 | 0.0% (0) | 5.1% (17) | 86.3% (289) | 6.9% (23) | 1.8% (6) |
| Dryness | 335 | 1.8% (6) | 9.6% (32) | 54.6% (183) | 26.0% (87) | 8.1% (27) |
| Excessive tearing | 334 | 3.3% (11) | 3.0% (10) | 90.7% (303) | 3.0% (10) | 0.0% (0) |
| Gritty, scratchy | 335 | 0.6% (2) | 6.9% (23) | 78.8% (264) | 9.0% (30) | 4.8% (16) |
| Glare | 335 | 2.7% (9) | 7.2% (24) | 69.6% (233) | 18.5% (62) | 2.1% (7) |
| Halos | 335 | 1.2% (4) | 2.7% (9) | 78.5% (263) | 14.6% (49) | 3.0% (10) |
| Blurred vision | 335 | 6.3% (21) | 4.2% (14) | 67.2% (225) | 15.2% (51) | 7.2% (24) |
| Double vision | 335 | 0.0% (0) | 0.9% (3) | 90.7% (304) | 6.3% (21) | 2.1% (7) |
| Fluctuation of vision | 335 | 2.7% (9) | 4.8% (16) | 67.5% (226) | 19.4% (65) | 5.7% (19) |
| Variation - bright light | 335 | 3.6% (12) | 4.5% (15) | 79.1% (265) | 11.6% (39) | 1.2% (4) |
| Variation - normal light | 333 | 0.6% (2) | 6.6% (22) | 81.1% (270) | 7.2% (24) | 4.5% (15) |
| Variation - dim light | 335 | 5.1% (17) | 4.8% (16) | 67.2% (225) | 13.1% (44) | 9.9% (33) |
| Night driving vision | 335 | 5.4% (18) | 13.1% (44) | 62.7% (210) | 14.6% (49) | 4.2% (14) |
| Other | 335 | 1.5% (5) | 0.6% (2) | 94.6% (317) | 1.2% (4) | 2.1% (7) |

N = Number of eyes with nonmissing preoperative and postoperative responses. % = n ÷ N × 100%.
Better (worse) is one grade better (worse). Significantly better (worse) is ≥ 2 grades better (worse).

Table 12 shows the clinically significant symptoms (those rated moderate to severe) with at least a 3% change from baseline to month 9. These include dryness (increased from 5% at baseline to 11%), excessive tearing (decreased from 3% at baseline to 0%), gritty/scratchy feeling (increased from 1% at baseline to 5%), fluctuation of vision (increased 5% to 8%), variation of vision in normal light (increased from 1% at baseline to 6%), and variation of vision in dim light (increased from 7% at baseline to 11%).

Clinically significant symptoms (those rated moderate to severe) with at least a 3% change from baseline to month 12 were light sensitivity (decreased from 10% at baseline to 5%), dryness (increased from 5% at baseline to 10%), gritty/scratchy feeling (increased from 1% at baseline to 4%), variation of vision in normal light (increased from 1% at baseline to 7%), and variation of vision in dim light (increased from 7% at baseline to 14%).

**TABLE 12**
**CLINICALLY SIGNIFICANT SUBJECT SYMPTOMS***
**ALL TREATED EYES**

| Symptom | Preop | | 6 Months | | 9 Months | | 12 Months | |
|---|---|---|---|---|---|---|---|---|
| | % | n/N | % | n/N | % | n/N | % | n/N |
| Light sensitivity | 10.2% | 37/361 | 7.8% | 28/357 | 8.2% | 28/341 | 4.6% | 16/347 |
| Headaches | 2.5% | 9/361 | 2.2% | 8/357 | 2.3% | 8/341 | 0.6% | 2/347 |
| Pain/burning | 0.8% | 3/361 | 2.5% | 9/356 | 2.3% | 8/341 | 0.3% | 1/347 |
| Dryness | 5.3% | 19/361 | 13.4% | 48/357 | 11.4% | 39/341 | 10.4% | 36/346 |
| Excessive tearing | 3.0% | 11/361 | 0.8% | 3/357 | 0.0% | 0/340 | 1.2% | 4/347 |
| Gritty, scratchy | 1.1% | 4/361 | 5.0% | 18/357 | 5.0% | 17/341 | 4.3% | 15/347 |
| Glare | 5.3% | 19/361 | 5.9% | 21/357 | 3.8% | 13/341 | 3.8% | 13/346 |
| Halos | 2.2% | 8/361 | 5.0% | 18/357 | 3.5% | 12/341 | 4.0% | 14/347 |
| Blurred vision | 8.6% | 31/361 | 10.1% | 36/357 | 9.7% | 33/341 | 10.4% | 36/347 |
| Double vision | 0.6% | 2/361 | 4.5% | 16/357 | 2.6% | 9/341 | 2.3% | 8/346 |
| Fluctuation of vision | 5.0% | 18/361 | 10.6% | 38/357 | 7.9% | 27/341 | 7.5% | 26/347 |
| Variation - bright light | 5.5% | 20/361 | 6.4% | 23/357 | 3.2% | 11/341 | 7.2% | 25/347 |
| Variation - normal light | 1.1% | 4/361 | 4.2% | 15/356 | 5.9% | 20/339 | 6.6% | 23/347 |
| Variation - dim light | 6.9% | 25/361 | 13.4% | 48/357 | 11.4% | 39/341 | 14.4% | 50/347 |
| Night driving vision | 9.4% | 34/361 | 12.4% | 44/356 | 7.6% | 26/341 | 9.5% | 33/347 |
| Other | 1.4% | 5/361 | 1.4% | 5/356 | 2.1% | 7/341 | 2.0% | 7/347 |

* A level of moderate, marked, or severe is clinically significant. N = Number of eyes with non-missing responses. % = n ÷ N × 100%.

3. Effectiveness Outcomes

Determination of effectiveness for marketing approval was based on an effectiveness cohort of 160 eyes treated with the adjusted algorithm and consistent with the approved refractive indications for use.

The following will explain how and why the entire study cohort of 369 eyes was reduced to the 160 eyes used for the effectiveness cohort. The first 110 eyes (Phase 1) were treated without an ablation algorithm adjustment. Analyses of the clinical trial data showed a systematic undercorrection, and therefore an ablation algorithm adjustment was made (addition) to the sphere component of +0.75 D. The remaining 259 eyes (Phase 2) were treated with an ablation algorithm adjustment of +0.75 D added to the sphere component. Eyes treated with the ablation algorithm adjustment had statistically significantly higher predictability of outcomes within ± 0.50 D of attempted versus achieved MRSE at 9 months (p= 0.0006), but no other key effectiveness endpoint was shown to be statistically significant with regards to the ablation algorithm adjustment (i.e., MRSE within ± 1.00 D and UCVA of 20/40 or better). The algorithm adjustment was determined to be beneficial and therefore only eyes treated with the ablation algorithm adjustment (259 eyes) are included. Through analysis of these 259 eyes, it was found that insufficient effectiveness data existed to approve the following parameters: sphere values > +5.0 D, cylinder values ≤ +0.50 D and > +3.00 D, and for MRSE values > +5.0 D. Excluding the eyes treated outside of these parameters, the Effectiveness Cohort consists of 160 eyes, with 149 eyes available at the 9 month point of refractive stability.

Presented in Tables 13A and 13B are the summaries of key effectiveness variables for the effectiveness cohort of eyes and for all eyes treated at 9 months (point of stability) stratified by ablation algorithm adjustment and treatment, respectively. Table 13B includes stratification by ablation algorithm adjustment and treatment. Eight (8) eyes had sphere > +5.0 D or MRSE > +5.0 D and were not therefore included in the effectiveness cohort. Two (2) eyes were sphere only treatments and had > +5.0 D sphere and > +5.0 D MRSE. Five (5) eyes were astigmatic treatments and had > +5.0 D sphere and > +5.0 D MRSE. One (1) eye was an astigmatic treatment and had > +5.0 D MRSE.

Key effectiveness outcomes at 9 months (point of stability) stratified by each diopter of preoperative MRSE are presented in Tables 14A, 14B, and 14C for the effectiveness cohort of eyes, the effectiveness cohort of eyes treated for spherical hyperopia only, and the effectiveness cohort of eyes treated for astigmatic hyperopia, respectively. Key effectiveness parameters at 9 months stratified by optical zone for the effectiveness cohort of eyes are presented in Table 14D.

Eyes with preoperative sphere of 5.01 D to 6.00 D and MRSE > +5.0 D did not meet the target values of 75% of eyes within ± 1.00 D and 50.0% of eyes within ± 0.50 D of the intended outcome. Since target values were not achieved and

also due in part to the small sample size, treatment of sphere > +5.0 D, and MRSE > +5.0 D, is locked out from the approved device.

Eyes treated for a preoperative cylinder of ≤ +0.50 D showed a higher tendency for overcorrection and larger axis deviations upon vector analysis. The study did not enroll any eyes with > +3.0 D of cylinder and therefore did not seek approval for this level of hyperopia. Since the treatment of ≤ +0.50 D was not shown to be effective and the study did not treat any eyes with > +3.0 D of cylinder, treatment of cylinder ≤ +0.50 D and > +3.0 D is locked out from the approved device.

During the course of the clinical study, a spherical adjustment of +0.75 D was added to the spherical component. After the first 110 eyes were treated, an analysis was performed to evaluate the data. The analysis revealed a systematic undercorrection and therefore a spherical adjustment of +0.75 D would be added to the spherical component. When comparing the groups with and without algorithm adjustment at 9 months, for eyes with the algorithm adjustment, the MRSE predictability for eyes within ± 0.50 D and ± 1.00 D (77.4% and 90.6%, respectively) and eyes without adjustment (58.6% and 82.8%, respectively) were greater than the target values of 50% and 75% consistent with FDA guidance. Although the targets were exceeded for eyes treated with and without an algorithm adjustment, the algorithm adjustment treated eyes were less undercorrected and had an increased predictability within ± 0.50 D and ± 1.00 D. Thus, the algorithm adjustment of +0.75 D will be included in the treatment software.

The effect of the optical zone on the efficacy parameters of uncorrected visual acuity and accuracy of the postoperative refraction is shown in Table 14D. The analyses revealed that the optical zone size selected did not play a significant role in efficacy outcomes with regard to the proportion of eyes with UCVA of 20/40 or better postoperatively.. However, eyes treated with a 6.5 mm optic zone had a greater predictability with more eyes within ± 0.50 D and within ± 1.00 D of attempted versus achieved MRSE at 9 months.

As shown in Table 13A, for the effectiveness cohort of eyes, the three primary effectiveness outcomes consisting of the percent of eyes with 20/40 or better uncorrected visual acuity and the percent of eyes within ± 0.50 D and within ± 1.00 D of attempted correction exceed target values established in the study protocol and consistent with FDA guidance. At 9 months, 66.4% of eyes had UCVA 20/20 or better, and 96.6% of eyes had UCVA 20/40 or better. At 12 months, 66.7% of eyes had UCVA 20/20 or better, and 96.7% of eyes had UCVA 20/40 or better.

Table 13B shows the key effectiveness outcomes at 9 months stratified by ablation algorithm adjustment and treatment. The treatments not included in the approved indication for use are shown in the shaded areas of Table 13B.

**TABLE 13A**
**SUMMARY OF KEY EFFECTIVENESS VARIABLES**
**EFFECTIVENESS COHORT**

| Key Effectiveness Variables | 1 Month % (n/N) 95% CI* | 3 Months % (n/N) 95% CI* | 6 Months % (n/N) 95% CI* | 9 Months % (n/N) 95% CI* | 12 Months % (n/N) 95% CI* |
|---|---|---|---|---|---|
| UCVA 20/20 or better | 46.3% (74/160) (38.3%, 54.3%) | 58.9% (93/158) (50.8%, 66.6%) | 61.9% (99/160) (53.9%, 69.4%) | 66.4% (99/149) (58.3%, 74.0%) | 66.7% (102/153) (58.6%, 74.1%) |
| UCVA 20/40 or better | 95.6% (153/160) (91.2%, 98.2%) | 96.8% (153/158) (92.8%, 99.0%) | 97.5% (156/160) (93.7%, 99.3%) | 96.6% (144/149) (92.3%, 98.9%) | 96.7% (148/153) (92.5%, 98.9%) |
| MRSE†, Attempted vs. Achieved, ±0.50D | 71.3% (114/160) (63.6%, 78.1%) | 76.6% (121/158) (69.2%, 82.9%) | 73.8% (118/160) (66.2%, 80.4%) | 74.5% (111/149) (66.7%, 81.3%) | 78.4% (120/153) (71.1%, 84.7%) |
| MRSE†, Attempted vs. Achieved, ±1.00D | 90.0% (144/160) (84.3%, 94.2%) | 94.9% (150/158) (90.3%, 97.8%) | 92.5% (148/160) (87.3%, 96.1%) | 90.6% (135/149) (84.7%, 94.8%) | 92.2% (141/153) (86.7%, 95.9%) |
| MRSE†, Attempted vs. Achieved, ±2.00D | 100.0% (160/160) (97.7%, 100.0%) | 100.0% (158/158) (97.7%, 100.0%) | 100.0% (160/160) (97.7%, 100.0%) | 100.0% (149/149) (97.6%, 100.0%) | 100.0% (153/153) (97.6%, 100.0%) |

**Effectiveness Cohort**: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of case report forms (CRFs) received with non-missing values at each visit.
* The exact confidence interval was calculated based on Clopper-Pearson exact method.
† MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

## TABLE 13B
## SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 9 MONTHS (POINT OF STABILITY) STRATIFIED BY ALGORITHM ADJUSTMENT AND TREATMENT
## ALL TREATED EYES

| Key Effectiveness Variables | Without Algorithm Adjustment | | | With Algorithm Adjustment | | |
|---|---|---|---|---|---|---|
| | Sphere | Sphere + 0.5 D Cylinder | Sphere + >0.5 D Cylinder | Sphere | Sphere + 0.5 D Cylinder | Sphere + ≥0.5 D Cylinder |
| | % (n/N) 95% CI* | % (n/N) 95% CI* | % (n/N) 95% CI* | % (n/N) 95% CI* | % (n/N) 95% CI* | % (n/N) 95% CI* |
| UCVA 20/20 or better | 88.5% (23/26) (69.8%, 97.6%) | 59.3% (16/27) (38.8%, 77.6%) | 63.0% (29/46) (47.5%, 76.8%) | 78.0% (46/59) (65.3%, 87.7%) | 68.2% (58/85) (57.2%, 77.9%) | 56.1% (55/98) (45.7%, 66.1%) |
| UCVA 20/40 or better | 100.0% (26/26) (86.8%, 100.0%) | 92.6% (25/27) (75.7%, 99.1%) | 100.0% (46/46) (92.3%, 100.0%) | 96.6% (57/59) (88.3%, 99.6%) | 95.3% (81/85) (88.4%, 98.7%) | 95.9% (94/98) (89.9%, 98.9%) |
| MRSE†, Attempted vs. Achieved, ±0.50D | 76.9% (20/26) (56.4%, 91.0%) | 48.1% (13/27) (28.7%, 68.1%) | 54.3% (25/46) (39.0%, 69.1%) | 78.0% (46/59) (65.3%, 87.7%) | 86.2% (75/87) (77.1%, 92.7%) | 69.4% (68/98) (59.3%, 78.3%) |
| MRSE†, Attempted vs. Achieved, ±1.00D | 88.5% (23/26) (69.8%, 97.6%) | 77.8% (21/27) (57.7%, 91.4%) | 82.6% (38/46) (68.6%, 92.2%) | 93.2% (55/59) (83.5%, 98.1%) | 95.4% (83/87) (88.6%, 98.7%) | 84.7% (83/98) (76.0%, 91.2%) |
| MRSE†, Attempted vs. Achieved, ±2.00D | 100.0% (26/26) (86.8%, 100.0%) | 96.3% (26/27) (81.0%, 99.9%) | 97.8% (45/46) (88.5%, 99.9%) | 100.0% (59/59) (93.9%, 100.0%) | 98.9% (86/87) (93.8%, 100.0%) | 100.0% (98/98) (96.3%, 100.0%) |

N = Number of CRFs received with non-missing values in each group.

The shaded columns were not included in the effectiveness cohort. Additionally, 8 eyes in the non-shaded columns were not included in the effectiveness cohort due to MRSE or MRSPH > 5.0 D.

* The exact confidence interval was calculated based on Clopper-Pearson exact method.

† MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

Key effectiveness outcomes at 9 months for the effectiveness cohort, stratified by preoperative MRSE, met the protocol target values and are consistent with FDA guidance.

**TABLE 14A**
**SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 9 MONTHS (POINT OF STABILITY) STRATIFIED BY PREOPERATIVE MRSE**
**EFFECTIVENESS COHORT**

| Key Effectiveness Variables | Preoperative MRSE | | | | | Total |
|---|---|---|---|---|---|---|
| | 0.00 to 1.00 D % (n/N) | 1.01 to 2.00 D % (n/N) | 2.01 to 3.00 D % (n/N) | 3.01 to 4.00 D % (n/N) | 4.01 to 5.00 D % (n/N) | % (n/N) |
| UCVA 20/20 or better | 66.7% (2/3) | 80.5% (33/41) | 57.1% (28/49) | 75.0% (24/32) | 50.0% (12/24) | 66.4% (99/149) |
| UCVA 20/40 or better | 100.0% (3/3) | 97.6% (40/41) | 91.8% (45/49) | 100.0% (32/32) | 100.0% (24/24) | 96.6% (144/149) |
| MRSE*, Attempted vs. Achieved, ± 0.50D | 66.7% (2/3) | 82.9% (34/41) | 69.4% (34/49) | 78.1% (25/32) | 66.7% (16/24) | 74.5% (111/149) |
| MRSE*, Attempted vs. Achieved, ± 1.00D | 100.0% (3/3) | 92.7% (38/41) | 85.7% (42/49) | 96.9% (31/32) | 87.5% (21/24) | 90.6% (135/149) |
| MRSE*, Attempted vs. Achieved, ± 2.00D | 100.0% (3/3) | 100.0% (41/41) | 100.0% (49/49) | 100.0% (32/32) | 100.0% (24/24) | 100.0% (149/149) |

**Effectiveness Cohort**: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of CRFs received with non-missing values for each subgroup.
* MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

Similarly, efficacy data at 9 months for the effectiveness cohort treated for spherical hyperopia only stratified in one diopter increments of preoperative MRSE met the target values consistent with FDA guidance (Table 14B). All baseline MRSE groups for the effectiveness cohort of eyes treated for astigmatic hyperopia also met the target values consistent with FDA guidance (Table 14C).

**TABLE 14B**
**SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 9 MONTHS (POINT OF STABILITY) STRATIFIED BY PREOPERATIVE MRSE**
**EFFECTIVENESS COHORT TREATED FOR SPHERICAL HYPEROPIA ONLY AND WITH ALGORITHM ADJUSTMENT**

| Key Effectiveness Variables | Preoperative MRSE | | | | | Total |
|---|---|---|---|---|---|---|
| | 0.00 to 1.00 D % (n/N) | 1.01 to 2.00 D % (n/N) | 2.01 to 3.00 D % (n/N) | 3.01 to 4.00 D % (n/N) | 4.01 to 5.00 D % (n/N) | % (n/N) |
| UCVA 20/20 or better | 100.0% (2/2) | 90.0% (18/20) | 57.1% (12/21) | 83.3% (5/6) | 87.5% (7/8) | 77.2% (44/57) |
| UCVA 20/40 or better | 100.0% (2/2) | 100.0% (20/20) | 90.5% (19/21) | 100.0% (6/6) | 100.0% (8/8) | 96.5% (55/57) |
| MRSE*, Attempted vs. Achieved, ± 0.50D | 100.0% (2/2) | 85.0% (17/20) | 66.7% (14/21) | 66.7% (4/6) | 87.5% (7/8) | 77.2% (44/57) |
| MRSE*, Attempted vs. Achieved, ± 1.00D | 100.0% (2/2) | 100.0% (20/20) | 81.0% (17/21) | 100.0% (6/6) | 100.0% (8/8) | 93.0% (53/57) |
| MRSE*, Attempted vs. Achieved, ± 2.00D | 100.0% (2/2) | 100.0% (20/20) | 100.0% (21/21) | 100.0% (6/6) | 100.0% (8/8) | 100.0% (57/57) |

**Effectiveness Cohort**: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of CRFs received with non-missing values for each subgroup.
* MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

## TABLE 14C
## SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 9 MONTHS (POINT OF STABILITY) STRATIFIED BY PREOPERATIVE MRSE
## EFFECTIVENESS COHORT TREATED FOR ASTIGMATIC HYPEROPIA WITH CYLINDER OF > 0.50 D AND WITH ALGORITHM ADJUSTMENT

| Key Effectiveness Variables | Preoperative MRSE | | | | | Total |
|---|---|---|---|---|---|---|
| | 0.00 to 1.00 D % (n/N) | 1.01 to 2.00 D % (n/N) | 2.01 to 3.00 D % (n/N) | 3.01 to 4.00 D % (n/N) | 4.01 to 5.00 D % (n/N) | % (n/N) |
| UCVA 20/20 or better | 0.0% (0/1) | 71.4% (15/21) | 57.1% (16/28) | 73.1% (19/26) | 31.3% (5/16) | 59.8% (55/92) |
| UCVA 20/40 or better | 100.0% (1/1) | 95.2% (20/21) | 92.9% (26/28) | 100.0% (26/26) | 100.0% (16/16) | 96.7% (89/92) |
| MRSE*, Attempted vs. Achieved, ± 0.50D | 0.0% (0/1) | 81.0% (17/21) | 71.4% (20/28) | 80.8% (21/26) | 56.3% (9/16) | 72.8% (67/92) |
| MRSE*, Attempted vs. Achieved, ± 1.00D | 100.0% (1/1) | 85.7% (18/21) | 89.3% (25/28) | 96.2% (25/26) | 81.3% (13/16) | 89.1% (82/92) |
| MRSE*, Attempted vs. Achieved, ± 2.00D | 100.0% (1/1) | 100.0% (21/21) | 100.0% (28/28) | 100.0% (26/26) | 100.0% (16/16) | 100.0% (92/92) |

**Effectiveness Cohort**: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of CRFs received with non-missing values for each subgroup.
* MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

Effectiveness data at 9 months for the effectiveness cohort stratified by optical zone is shown in Table 14D. Both optical zones used in the study met target values consistent with FDA guidance except for the MRSE within ± 1.00 D for the 6.0 mm optical zone (66.7%). This result may also be influenced by the small number of eyes in this group (6 eyes).

**TABLE 14D**
**SUMMARY OF KEY EFFECTIVENESS VARIABLES AT 9 MONTHS (POINT OF STABILITY) STRATIFIED BY OPTICAL ZONE**
**SPHERICAL EYES AND ASTIGMATIC EYES WITH CYLINDER OF > 0.50 D WITH ALGORITHM ADJUSTMENT**

| Key Effectiveness Variables | Optical Zone | | Total |
|---|---|---|---|
| | 6.0 mm | 6.5 mm | |
| | % (n/N) | % (n/N) | % (n/N) |
| UCVA 20/20 or better | 50.0% (3/6) | 67.1% (96/143) | 66.4% (99/149) |
| UCVA 20/40 or better | 100.0% (6/6) | 96.5% (138/143) | 96.6% (144/149) |
| MRSE*, Attempted vs. Achieved, ± 0.50D | 50.0% (3/6) | 75.5% (108/143) | 74.5% (111/149) |
| MRSE*, Attempted vs. Achieved, ± 1.00D | 66.7% (4/6) | 91.6% (131/143) | 90.6% (135/149) |
| MRSE*, Attempted vs. Achieved, ± 2.00D | 100.0% (6/6) | 100.0% (143/143) | 100.0% (149/149) |

**Effectiveness Cohort**: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of CRFs received with non-missing values for each subgroup.
* MRSE = Manifest Spherical Equivalent = Manifest Sphere + 0.5 × Manifest Cylinder.

**Correction of Cylindrical Component**

Table 15A presents the vector magnitude analysis of the cylinder correction at 6, 9, and 12 months for the effectiveness cohort treated for astigmatic hyperopia. The achieved versus intended vector magnitude ratio, or Correction Ratio CR surgically induced refractive correction/intended refractive correction (SIRC/IRC), at 9 months was 0.95, which is slightly less than the target value of 1.0, indicating undercorrection.

A vector analysis summary is presented in Table 15B for the effectiveness cohort of eyes at 9 months postoperatively. The mean CR for the effectiveness cohort is 0.951. When eyes treated for the cylinder range of 0.25 to 0.50 D are removed (as seen in Table 15B), the CR is closer to the desired target of 1.

Eyes with a preoperative cylinder of $\leq +0.50$ D had a higher tendency for overcorrection and larger axis deviations upon vector analysis. Since the treatment of $\leq +0.50$ D showed a decrease in effectiveness when compared to other cylinder ranges and eyes with $> +3.0$ D of cylinder were not treated in this study, treatment of cylinder $\leq +0.50$ D and $> +3.0$ D are locked out from the approved device.

## TABLE 15A
## VECTOR MAGNITUDE ANALYSIS SUMMARY
## EFFECTIVENESS COHORT TREATED FOR ASTIGMATIC HYPEROPIA AND WITH COMPLETE PREOPERATIVE AND POSTOPERATIVE REFRACTION WITH ALGORITHM ADJUSTMENT

| Statistics | Preoperative[1] | Postoperative[1] | IRC[2] | SIRC[2] | CR[2] |
|---|---|---|---|---|---|
| **6 Months** | | | | | |
| N | 102 | 102 | 102 | 102 | 102 |
| Mean | 1.355 | 0.426 | 1.458 | 1.403 | 0.99 |
| Standard Deviation | 0.599 | 0.511 | 0.651 | 0.651 | 0.30 |
| Minimum | 0.750 | 0.000 | 0.772 | 0.131 | 0.09 |
| Maximum | 3.000 | 2.500 | 3.282 | 3.183 | 2.24 |
| **9 Months** | | | | | |
| N | 92 | 92 | 92 | 92 | 92 |
| Mean | 1.356 | 0.364 | 1.465 | 1.348 | 0.95 |
| Standard Deviation | 0.616 | 0.466 | 0.672 | 0.626 | 0.31 |
| Minimum | 0.750 | 0.000 | 0.776 | 0.056 | 0.07 |
| Maximum | 3.000 | 1.750 | 3.282 | 2.940 | 2.19 |
| **12 Months** | | | | | |
| N | 95 | 95 | 95 | 95 | 95 |
| Mean | 1.350 | 0.376 | 1.456 | 1.388 | 0.97 |
| Standard Deviation | 0.612 | 0.522 | 0.667 | 0.654 | 0.28 |
| Minimum | 0.750 | 0.000 | 0.776 | 0.027 | 0.03 |
| Maximum | 3.000 | 2.000 | 3.282 | 3.055 | 1.81 |

**Effectiveness Cohort**: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.

N = Number of available CRFs received with non-missing values at each visit.

1 Manifest refraction on spectacle plane.

2 Refraction was converted from the spectacle to the corneal plane and cylinder axis of left eye was flipped around the vertical axis. Then IRC, SIRC and CR were calculated. CR = |SIRC|/|IRC|.

## TABLE 15B
## VECTOR ANALYSIS SUMMARY AT 9 MONTHS (POINT OF STABILITY)
## EFFECTIVENESS COHORT TREATED FOR ASTIGMATIC HYPEROPIA WITH ALGORITHM ADJUSTMENT

| Preoperative Cylinder | n | IRC Mean ± SD | SIRC Mean ± SD | EV[1] Mean ± SD | CR[2] Mean ± SD | ER[3] Mean ± SD |
|---|---|---|---|---|---|---|
| **9 Months** | | | | | | |
| All | 92 | 1.465 ± 0.672 | 1.348 ± 0.626 | 0.420 ± 0.460 | 0.951 ± 0.306 | 0.303 ± 0.355 |
| 0.51 to 1.00 D | 44 | 0.925 ± 0.136 | 0.974 ± 0.422 | 0.317 ± 0.422 | 1.038 ± 0.361 | 0.335 ± 0.439 |
| 1.01 to 2.00 D | 35 | 1.664 ± 0.301 | 1.432 ± 0.429 | 0.507 ± 0.467 | 0.869 ± 0.242 | 0.309 ± 0.278 |
| 2.01 to 3.00 D | 13 | 2.755 ± 0.326 | 2.384 ± 0.332 | 0.532 ± 0.525 | 0.877 ± 0.155 | 0.181 ± 0.169 |

**Effectiveness Cohort**: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.

Refraction was converted from the spectacle to the corneal plane and cylinder axis of left eye was flipped around the vertical axis. Then IRC, SIRC, CR and Error Ratio (ER) were calculated.

1 Error Vector (EV) = IRC - SIRC.

2 CR = |SIRC|/|IRC|.

3 ER = |EV|/|IRC|.

## F. Retreatment

A total of 8 eyes were retreated with the study laser for undercorrection. All of these eyes were initially treated without the algorithm adjustment (Phase 1). At the last available examination after re-treatment, the MRSE outcomes were within 0.25 D of the intended target (i.e., plano) for all but 2 eyes. All eyes but one had UCVA of 20/20 or better, 1 eye had UCVA of 20/63 due to a MRSE of -1.5 D. All eyes had BSCVA of 20/16 or better. The refractive target for all re-treatments was plano, and the laser settings were based on a manifest refraction taken prior to the re-treatment procedure. No complications or adverse events were reported following the re-treatment procedure.

## G. Factors Associated with Outcomes

Gender, preoperative refraction, age, baseline MRSE, primary vs. fellow eye, study site, and use of an ablation algorithm adjustment were evaluated as statistically significant predictors of the UCVA and refractive outcome for the LASIK procedure. These analyses identified a site effect, an ablation algorithm adjustment effect, an effect of baseline MRSE, a small cylinder cyclorotational effect, and a keratome effect.

Statistical analysis of the study data by site revealed that the percentage of eyes reported with MRSE within ± 0.50 D of the attempted correction was significantly different among the six investigational sites at 9 months. At 9 months, 93% of eyes were within 0.50 D of intended MRSE at site #5, compared with 81%, 67%, 63%, 62%, and 65% at the other five study sites. There were no statistically significant differences observed between the study sites with respect to attempted versus achieved MRSE within ± 1.00 D of the intended correction at 9 months.

Statistical analysis of the study data by site revealed that the percentage of eyes reported with UCVA outcomes of 20/40 or better and 20/20 or better were not significantly different among the six investigational sites at 9 months. At 9 months, 100% of eyes had 20/32 or better UCVA at site #1 and #6, compared with 99%, 92%, 96%, and 86%, at the other four study sites. Similar findings were observed for UCVA outcomes of 20/25 or better, 20/16 or better, and 20/12.5 or better. The clinical significance, if any, of this difference is uncertain.

Analyses of the effect of the use of an ablation algorithm adjustment revealed that eyes treated with the ablation algorithm adjustment had significantly better predictability outcomes for the population of eyes within ± 0.50 D of attempted versus achieved MRSE at 9 months ($p = 0.0006$). No other key effectiveness endpoint was shown to be significantly better as a result of the algorithm adjustment.

Eyes with preoperative MRSE of +5.01 to +6.00 D and eyes with a preoperative MRSE > 5.0 D were significantly less likely to achieve refractive predictability within ± 0.50 D of the intended outcome at 9 months. In contrast, at 9 months, eyes

with baseline MRSE up to +5.00 D had significantly better MRSE accuracy outcome (>61% within ± 0.50 D of intended MRSE) than eyes with baseline MRSE greater than +5.00 D (ranging from 33% to 40% for both groups within 0.50 D of intended MRSE). Baseline MRSE did not have a significant association with UCVA outcomes of 20/40 or better at 9 months. However, a greater proportion of eyes with baseline MRSE ≤ +5.00 D achieved UCVA better than 20/40 (i.e., 20/16 to 20/25 at 9 months) than eyes with baseline MRSE higher than +5.00 D.

Analysis of the cylinder treatment revealed a small amount of cyclorotation. This may have been the result of cyclotorsional movement of the subject's eye from the sitting position to the position under the laser. It is recommended that a mark be made on the subject's corneal limbus using a sterile single use marker for alignment with the reticle of the laser surgical microscope to be certain that no cyclorotation is present. The marking should be made with the patient in the sitting position behind a slit lamp. Once the subject is lying down, if necessary, the subject's head can be repositioned to properly align the reticle with the mark(s) during the treatment to reduce or eliminate any rotational misalignment.

An analysis of the keratome used in the study procedures revealed a possible effect on UCVA outcomes and MRSE predictability. Site 5, which used the Moria keratome, showed better effectiveness outcomes with regard to the proportion of eyes with deviation from the intended correction within ± 0.50 D at 9 months postoperatively (92.9%, $p < 0.0001$). In addition, the IntraLase keratome and the Hansatome keratome were associated with a significantly lower proportion of eyes achieving UCVA of 20/20 or better (62.1% and 62.9%, respectively) as compared to the other keratomes. However, this analysis of outcomes by keratome type is confounded by other factors that may have contributed to this difference in outcomes, including site and introduction of the algorithm adjustment. Since the key effectiveness outcomes for the total cohort of eyes were not affected by the type of keratome used, the differences observed with different keratomes for the sphere only and the astigmatic hyperopia eyes in the study may reflect other, non-keratome factors.

In addition, the complications were reported with a significantly higher proportion of eyes for the IntraLase keratome as compared to the various mechanical microkeratomes. Complications included diffuse lamellar keratitis (8.3%), dry eye (8.3%), epithelium at flap edge (4.9%), epithelium in the interface (13.9%), foreign body sensation (5.6%), punctal plug insertion (30.6%), superficial punctate keratitis (16.0%), steroid induced IOP increase (5.6%), and transient light sensitivity syndrome (8.3%).

## H. Subject Satisfaction

Responses provided by the study subjects at 6, 9, and 12 months to three questions regarding their experiences with the laser surgery are provided in Table 16A for all treated subjects and in Table 16B for the effectiveness cohort of eyes. These three questions related to: 1) the perceived overall quality of vision following surgery; 2) the subject's willingness to have the surgery again if he/she could make the choice over; and 3) the subject's overall satisfaction with the results of the surgical procedure.

In Table 16A, at 9 months, the overall quality of vision was rated highly, with 98.9% of patients indicating that there was an improvement, while only 1.1% indicated that there was no improvement; 90.9% would elect to have the surgery again; 94.3% reported being satisfied, while 2.9% were neutral and 2.9% were dissatisfied.

**TABLE 16A**
**SUBJECT EVALUATION OF SATISFACTION AND VISION QUALITY IMPROVEMENT**
**ALL TREATED SUBJECTS (SUBJECT BASIS)**

| Response | 6 Months % (n/N) | 9 Months % (n/N) | 12 Months % (n/N) |
|---|---|---|---|
| **Overall Vision Quality** | | | |
| Extreme Improvement | 50.8% (93/183) | 53.1% (93/175) | 57.9% (103/178) |
| Marked Improvement | 33.9% (62/183) | 29.1% (51/175) | 26.4% (47/178) |
| Moderate Improvement | 9.3% (17/183) | 10.9% (19/175) | 9.0% (16/178) |
| Slight Improvement | 4.9% (9/183) | 5.7% (10/175) | 6.2% (11/178) |
| No Improvement | 1.1% (2/183) | 1.1% (2/175) | 0.6% (1/178) |
| Not reported* | 0 | 0 | 0 |
| Total† | 183 | 175 | 178 |
| **Select Refractive Surgery Again** | | | |
| Yes | 90.2% (165/183) | 90.9% (159/175) | 91.6% (163/178) |
| No | 2.2% (4/183) | 3.4% (6/175) | 1.7% (3/178) |
| Unsure | 7.7% (14/183) | 5.7% (10/175) | 6.7% (12/178) |
| Not reported* | 0 | 0 | 0 |
| Total† | 183 | 175 | 178 |
| **Satisfaction** | | | |
| Very Satisfied | 73.8% (135/183) | 75.4% (132/175) | 75.8% (135/178) |
| Moderately Satisfied | 20.2% (37/183) | 18.9% (33/175) | 18.0% (32/178) |
| Neutral | 4.4% (8/183) | 2.9% (5/175) | 3.9% (7/178) |
| Dissatisfied | 1.1% (2/183) | 2.9% (5/175) | 2.2% (4/178) |
| Very Dissatisfied | 0.5% (1/183) | 0.0% (0/175) | 0.0% (0/178) |
| Not reported* | 0 | 0 | 0 |
| Total† | 183 | 175 | 178 |

N = Number of available eyes with non-missing values at each visit. % = n ÷ N × 100%.

* Number of available eyes with missing values at the visit.

† Number of available eyes at the visit.

In Table 16B, at 9 months, the overall quality of vision was rated highly, with 97.9% of subjects indicating that there was an improvement, while only 2.1% indicated that there was no improvement; 88.5% would elect to have the surgery again; 95.8% reported being satisfied, while 3.1% were neutral and 1.0% were dissatisfied.

**TABLE 16B**
**SUBJECT EVALUATION OF SATISFACTION AND VISION QUALITY IMPROVEMENT EFFECTIVENESS COHORT SUBJECTS (SUBJECT BASIS)**

| Response | 6 Months % (n/N) | 9 Months % (n/N) | 12 Months % (n/N) |
|---|---|---|---|
| **Overall Vision Quality** | | | |
| Extreme Improvement | 52.5% (53/101) | 51.0% (49/96) | 60.8% (59/97) |
| Marked Improvement | 29.7% (30/101) | 35.4% (34/96) | 23.7% (23/97) |
| Moderate Improvement | 10.9% (11/101) | 6.3% (6/96) | 8.2% (8/97) |
| Slight Improvement | 5.9% (6/101) | 5.2% (5/96) | 6.2% (6/97) |
| No Improvement | 1.0% (1/101) | 2.1% (2/96) | 1.0% (1/97) |
| Not reported* | 0 | 0 | 0 |
| Total† | 101 | 96 | 97 |
| **Select Refractive Surgery Again** | | | |
| Yes | 85.1% (86/101) | 88.5% (85/96) | 89.7% (87/97) |
| No | 4.0% (4/101) | 5.2% (5/96) | 3.1% (3/97) |
| Unsure | 10.9% (11/101) | 6.3% (6/96) | 7.2% (7/97) |
| Not reported* | 0 | 0 | 0 |
| Total† | 101 | 96 | 97 |
| **Satisfaction** | | | |
| Very Satisfied | 71.3% (72/101) | 76.0% (73/96) | 75.3% (73/97) |
| Moderately Satisfied | 19.8% (20/101) | 19.8% (19/96) | 17.5% (17/97) |
| Neutral | 6.9% (7/101) | 3.1% (3/96) | 4.1% (4/97) |
| Dissatisfied | 1.0% (1/101) | 1.0% (1/96) | 3.1% (3/97) |
| Very Dissatisfied | 1.0% (1/101) | 0.0% (0/96) | 0.0% (0/97) |
| Not reported* | 0 | 0 | 0 |
| Total† | 101 | 96 | 97 |

**Effectiveness Cohort**: spherical eyes and astigmatic eyes with MRCYL of > 0.50 D with algorithm adjustment, and treated for MRSE and MRSPH of 5.0 D or less.
N = Number of available eyes with non-missing values at each visit. % = n ÷ N × 100%.
* Number of available eyes with missing values at the visit.
† Number of available eyes at the visit.

### I. Device Failures and Replacements

There were no laser failures/malfunctions and there were no device replacements during the course of the study.

## XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

## XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

### A. Safety Conclusions

The adverse effects of the device are based on data collected in a clinical study conducted to support PMA approval as described above. Analysis of safety was based on the total PMA cohort of 369 eyes. The primary safety variables for the study included preservation of best-spectacle corrected visual acuity (BSCVA), induced manifest refractive astigmatism and incidence of adverse events. All endpoint target values were met. One eye lost $\geq 2$ lines BSCVA and one eye had an increase in manifest refractive astigmatism >2 diopters (D) at the last available visit; neither occurred in the cohort treated with the approved adjusted algorithm. The cumulative adverse event rate was quite low, with no category of event exceeding 0.5% on a cumulative basis, with the exception of diabetes at 1.1%. Outcomes for the secondary safety variables, Incidence of Complications and Patient Symptoms, also support reasonable assurance of device safety. Postoperative uncorrected visual acuity (UCVA) was compared to the preoperative BSCVA for the effectiveness cohort at 9 months, for which 49.7% (74/149) of the study eyes saw as well without glasses after surgery as with glasses before surgery. Clinically significant symptoms (i.e., those rated moderate to severe) with at least a 3% change from baseline to month 9 include dryness (increased from 5% at baseline to 11%), excessive tearing (decreased from 3% at baseline to 0%), gritty/scratchy feeling (increased from 1% at baseline to 5%), fluctuation of vision (increased 5% to 8%), variation of vision in normal light (increased from 1% at baseline to 6%), and variation of vision in dim light (increased from 7% at baseline to 11%).

### B. Effectiveness Conclusions

The effectiveness of the device is based on data collected in a clinical study conducted to support PMA approval as described above. Determination of effectiveness for marketing approval was based on an effectiveness cohort of 160 eyes treated with the adjusted algorithm and consistent with the approved refractive indications for use. The primary effectiveness variables for the study included predictability of manifest refraction spherical equivalent (MRSE) to the intended

refractive outcome, improvement in UCVA uncorrected visual acuity, stability of manifest refraction, and predictability of manifest refraction astigmatism to the attempted astigmatism correction. All endpoint target values were met for the effectiveness cohort. In the clinical study, stability was demonstrated 9 months after LASIK treatment. At 9 months, 66.4% of eyes had UCVA 20/20 or better, 96.6% of eyes had UCVA 20/40 or better, 74.5% of eyes had MRSE within 0.5 diopters of intended, and 90.6% had MRSE within 1.0 D of intended. Subject Satisfaction was measured by a subjective questionnaire as a secondary effectiveness variable. For the effectiveness cohort (subject basis) at 9 months, the overall quality of vision was rated by 97.9% of subjects indicating that there was an improvement and by 2.1% indicating no improvement; 88.5% would elect to have the surgery again; 95.8% reported being satisfied while 3.1% were neutral and 1.0% were dissatisfied.

### C. Overall Conclusions

The data provided in this application provide reasonable assurance of the safety and effectiveness of this device when used in accordance with the indications and directions for use. Safety and effectiveness endpoint outcomes met target criteria for the cohort that was treated consistent with the indication for use. The overall clinical risk is reasonable when compared to the anticipated clinical benefit as demonstrated in the clinical study. The refractive range in the approved Indications for Use is more limited than the range studied in the clinical study, excluding refractive range where outcomes did not support reasonable assurance of safety and effectiveness. Also, the device to be marketed is approved only for the adjusted treatment algorithm.

## XIII. CDRH DECISION

CDRH issued an approval order on March 28, 2011.

The applicant's manufacturing facility was inspected and was found to be in compliance with the Quality System Regulation (21 CFR 820).

## XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.