**SUMMARY OF SAFETY AND EFFECTIVENESS DATA**
FOR A SUPPLEMENTAL PREMARKET APPROVAL APPLICATION

## I. GENERAL INFORMATION

| | |
|---|---|
| Device Generic Name: | Ophthalmic Excimer Laser System |
| Device Trade Name: | LADARVision® 4000 Excimer Laser System |
| Applicant's Name and Address: | Alcon<br>2501 Discovery Drive, Suite 500<br>Orlando, FL 32826 |
| Date of Panel Recommendation: | August 1, 2002 |
| Pre-market Approval (PMA) Application Number: | P970043/S10 |
| Date of Notice of Approval to Applicant: | October 18, 2002 |

The LADARVision® 4000 Excimer Laser System was approved on November 2, 1998 for the indication of photorefractive keratectomy (PRK) for the reduction or elimination of mild to moderate myopia of between -1.00 and -10.00D sphere and less than or equal to -4.00D astigmatism at the spectacle plane, the combination of which must result in an attempted correction of between -0.50 and -10.00D spherical equivalent at the spectacle plane where the sphere or cylinder is at least 1.00 D (P970043). On May 9, 2000, the device was also approved for the indication of laser assisted in-situ keratomileusis (LASIK) treatments for the reduction or elimination of myopia of less than -9.00 D sphere and -0.50 to less than -3.00 D of astigmatism at the spectacle plane (P970043/S5). On September 22, 2000, the device was approved for the indication of LASIK treatments for the reduction or elimination of refractive error of less than or equal to +6.00 D of sphere and -6.00 D of cylinder at the spectacle plane (hyperopia with or without astigmatism and mixed astigmatism) (P970043/S7).

The sponsor submitted this supplement to further expand the clinical indications. The updated pre-clinical and clinical work to support this expanded indication is provided in this summary. For more information on the data that supported the approved indications, the summaries of safety and effectiveness data (SSED) for the original PMA or supplement should be referenced. Written requests for copies of the SSED can be obtained from the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20857 under Docket #00M-1592 (P930046), Docket # 00M-1593 (S5), and Docket # 00M-1612 (S7) or you may download the files from the internet site http://www.fda.gov/cdrh/pdf/p970043.pdf.

## II. INDICATIONS FOR USE

The LADARVision® 4000 Excimer Laser System is indicated for wavefront-guided Laser Assisted In-Situ Keratomileusis (LASIK):

- for the reduction or elimination of myopia up to –7.00D sphere with less than –0.50D of astigmatism at the spectacle plane;
- in patients who are 21 years of age or older; and
- in patients with documented stability of refraction for the prior 12 months, as demonstrated by a change of less than or equal to 0.50D

## III. CONTRAINDICATIONS

CustomCornea® LASIK is contraindicated in:

- pregnant or nursing women.
- patients with signs of keratoconus.
- patients who are taking one or both of the following medications: isotretinoin (Accutane) or amiodarone hydrochloride (Cordarone).
- patients with an autoimmune, collagen vascular, or immunodeficiency disease.

## IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the device labeling.

## V. DEVICE DESCRIPTION

### A. Wavefront Measurement Device (WMD)

The first step in performing CustomCornea® LASIK surgery is to perform a wavefront examination on the patient using a wavefront measurement device (WMD) compatible with the LADARVision® 4000 Excimer Laser System. At the present time, the only compatible WMD is the Alcon LADARWave™ CustomCornea® Wavefront System. There were two versions of the WMD used in the clinical trial, the CustomCornea® Measurement Device (Alcon) and the LADARWave™ CustomCornea® Wavefront System (Alcon). Both versions are accurately characterized by the description provided below. Essential features of the compatible WMD are as follows:

1. Patient Fixation and Fogging

   The WMD includes a fixation optical subsystem that provides the patient with an unambiguous fixation point. In addition, the fixation subsystem

includes adjustable optics to compensate for the patient's inherent refractive error. The optics are used to "fog" the eye, first clarifying the fixation target and then it optically adjusts beyond the patient's far point to minimize accommodation.

2. Centration

   Prior to dilation, the WMD is used to record the geometric relation between the natural daytime pupil center and the limbus of the eye. This information is then used to center the wavefront measurement and subsequent ablative treatment on the natural line of sight.

3. Wavefront Measurement

   The WMD measures the wavefront profile of the eye with a high degree of accuracy, and characterizes the profile using Zernike polynomials up to the $4^{th}$ order.

4. Registration

   The WMD uses synchronized video imagery and on-screen software reticules to record the relationship of the wavefront data to the limbus of the eye and to ink marks applied to the sclera just before the wavefront exam. This registration information is used to position the excimer ablation profile at the right corneal location and cyclotorsional angle.

5. Data Export

   The WMD has the ability to export the wavefront examination data as an electronic file to floppy disk for transfer to the LADARVision® 4000 system. The electronic file is structured in a specific format, and contains essential patient information, centration/registration information, and the detailed aberration data. In addition, the electronic file is encrypted in a manner that can only be deciphered by the LADARVision® 4000 system.

B. Microkeratome

The LASIK procedure requires the use of a commercially available microkeratome that has been cleared for marketing via premarket notification. The device used in this study consists of a head, plates, ring, handle, wrenches, shaft, motor, hand-piece, disposable blades, and power supply with footswitches and power cords. The system is completed with the applanation lens set, tonometer, corneal storage jar, optical zone marker, spatula, stop attachment, and digital thickness gauge.

C. LADARVision®4000 Excimer Laser System

The LADARVision®4000 system uses a small diameter pulsed ultraviolet laser beam to reshape the cornea. Refractive correction is achieved by delivering hundreds to thousands of ablative laser pulses to the eye in a predetermined spatial pattern. The LADARVision®4000 system also incorporates an infrared eye tracking system to maximize accuracy of the corneal reshaping. The eye tracking system compensates for patient eye motion during procedures so that each excimer laser pulse is delivered to the appropriate corneal location.

Rather than the refractive correction being manually entered by the physician based on phoropter refraction for Conventional treatment, the CustomCornea® treatment requires that the preoperative aberrations in the eye be measured with a WMD. The treatment is based on Zernike data derived from a WMD, including treatment of lower-order sphere and astigmatism components and higher-order components, such as spherical aberration and coma. The electronic file that the LADARVision®4000 system receives from the WMD includes the following information:

- Patient information, including name, identification number, and clinical prescription.
- Eye information, including OD/OS and the geometric relationship of the wavefront data to the limbus and to the pupil center.
- Wavefront information, including a Zernike polynomial representation of the wavefront and the physical radius of that description.

The excimer laser beam characteristics (i.e., pulse energy, firing rate, fluence distribution at the treatment plane) are the same for Conventional and CustomCornea® treatment modalities. In addition, the same LADARVision®4000 eye tracking hardware and software are used to track Conventional and CustomCornea® LASIK eyes. The Conventional LADARVision®4000 treatment utilizes sphere, cylinder and axis components entered manually by the operator to generate the ablation profile. The CustomCornea® ablative shaping algorithm utilizes aberration information unique to a given eye that is obtained from the WMD to guide the ablation of the cornea. The wavefront information is registered to the anatomical geometry of the eye using the WMD. The operator of the LADARVision®4000 system uses the geometry information to accurately position the custom ablation profile on the eye.

CustomCornea® ablations use an optical zone of 6.5mm, a blend zone of 1.25mm for a total ablation zone of 9mm, and are locked out above -7.0 D as measured by manifest refraction. The software used in the clinical trial was Inverness version 4.06. The final commercial release version for CustomCornea®, incorporating the changes made during PMA supplement review, is Jupiter version 5.10.

## VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are currently several other alternatives for the correction of myopia:

Automated lamellar keratoplasty (ALK)
Contact Lenses
Conventional Laser in-situ keratomileusis (LASIK - based on phoropter refraction)
Conventional Photorefractive Keratectomy (PRK - based on phoropter refraction)
Radial Keratotomy (RK)
Spectacles

Each alternative has its own advantages and disadvantages. A prospective patient should fully discuss with his/her care provider these alternatives in order to select the correction method that best meets his/her expectation and lifestyle.

## VII. MARKETING HISTORY

The device has been marketed in the following countries: Argentina, Australia, Brazil, Canada, France, Greece, Hong Kong, Italy, Korea, Mexico, Netherlands, Norway, Philippines, Spain, Switzerland, Taiwan, Thailand, United Kingdom, and the United States. The LADARVision® 4000 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 effects associated with LASIK include: loss of best spectacle corrected visual acuity (BSCVA); worsening of patient complaints such as double vision, sensitivity to bright lights, increased difficulty with night vision, fluctuations in vision; increase in intraocular pressure; corneal haze; secondary surgical intervention; corneal infiltrate or ulcer; corneal epithelial defect; corneal edema; problems associated with the flap including a lost, misplaced or misaligned flap; retinal detachment; and retinal vascular accidents.

Please refer to the complete listing of adverse events and complications observed during the clinical study which are presented on pages 19-20 of the clinical study section.

## IX. SUMMARY OF PRECLINICAL STUDIES

A series of pre-clinical tests were conducted on the LADARVision® 4000 system when it was first developed for Conventional treatments and before it entered human clinical trials for the first time. Those tests involved algorithm simulations and ablation profiles using plastic blocks, as well as animal testing. A series of pre-clinical tests were conducted on the new CustomCornea® algorithms prior to

entering human clinical trials. These tests included algorithm validation, which tested the ablation shot pattern in both an ablation simulation program and actual PMMA substrate (surrogate) ablation experiments.

## X. SUMMARY OF CLINICAL STUDIES

The sponsor performed a clinical study of wavefront-guided CustomCornea® LASIK correction with the LADARVision® 4000 Excimer Laser System in the U.S. under an investigational device exemption application (IDE G950213). In addition, one foreign site collected data under an investigational device application in Canada using a protocol that was the same as the U.S. protocol in terms of the study procedures, patient measurements, and the treatment applied to the eye. Therefore, data from the U.S. and Canadian centers were pooled for the analysis of safety and effectiveness. A summary of the clinical trial is presented below.

### A. Study Objective

The objective of the multi-center clinical investigation of the LADARVision® 4000 Excimer Laser System for wavefront-guided CustomCornea® LASIK correction was to establish safety and effectiveness. Safety was assessed for the treatment of up to -7.00D of myopia with up to -4.00D of astigmatism. Effectiveness was assessed for up to -7.00D of myopia with less than –0.50D of astigmatism.

### B. Study Design

The study in the U.S. began as a prospective, randomized, unmasked, and multi-center trial, where one eye of the subject received CustomCornea® correction using data from a wavefront measurement system and the fellow eye received a conventional treatment based on phoropter manifest refraction.

Upon providing data to support expansion of the number of subjects for enrollment, the study design was changed to a prospective, non-randomized, unmasked, and multi-center trial with bilateral wavefront-guided CustomCornea® correction. In this case, the primary control was the preoperative state of the treated eye (i.e., comparison of pre-treatment and post-treatment visual parameters in the same eye). The Canadian protocol also allowed for bilateral CustomCornea® correction.

### C. Inclusion and Exclusion Criteria

To be eligible for inclusion into the study, the spectacle plane refraction must have had a sphere between +6 and -15D and a cylinder between 0 and -6D. The minimum manifest refraction spherical equivalent (MRSE) allowed was -15D. Enrollment of myopic eyes in the study occurred over the range of up to -7D of myopia and up to -4D of astigmatism. Documentation of stability

of refraction for the prior 12 months, as demonstrated by a change of less than or equal to 0.50D, was required.

The manifest refraction for myopic eyes could not differ by more than 1D in sphere or cylinder from the attempted correction determined by the wavefront measurement system. Subjects whose eyes could not be assessed by the WMD, including an inability to obtain a clear and complete image, were excluded from the study. In addition, the manifest and cycloplegic refraction measured at the preoperative examination must have been within 0.50 D of each other in the sphere and cylinder components.

Subjects must have been at least 18 years of age. Both eyes must have had a best spectacle corrected visual acuity (BSCVA) of 20/25 or better. Subjects must have been willing to return for scheduled follow-up examinations for 6 months after surgery and have their eyes pharmacologically dilated at each visit. Subjects who were contact lens wearers were requested to discontinue contact lens wear in both eyes at least 2 to 3 weeks, depending upon the lens type, prior to the preoperative examination. Subjects who had worn RGP and PMMA lenses were required to have two examinations conducted 2 to 3 weeks apart to assess the stability of refraction without lens wear. Keratometry mires must have been clear and regular to exclude eyes with irregular astigmatism.

All eyes were required to be treated for emmetropia (no monovision). All surgeries performed in the study were subject to approval by the sponsor. Central pachymetry must have been performed preoperatively to assess corneal thickness to ensure the calculated residual corneal thickness was at least 250 microns in all treated eye.

Since this U.S. protocol originally had a contralateral Conventional eye, the manifest refraction between the two eyes could not differ more than 1 D in sphere or cylinder in the initial protocol. In addition, subjects must have been willing to have LASIK correction in both eyes within a 2-week period of one another. However, when the U.S. protocol changed to bilateral CustomCornea® treatment for myopic subjects, these inclusion criteria were eliminated from the U.S. protocol.

Subjects with the following conditions could not be included in the study: previous intraocular, corneal or strabismus surgery; history of or active clinically or visually significant ocular disease or pathology; clinically significant corneal scars within the ablation zone or other corneal abnormality such as recurrent erosion or severe basement membrane disease; progressive or unstable myopia or keratoconus; irregular corneal astigmatism; history of herpes keratitis; autoimmune disease, connective tissue disease, clinically significant atopic syndrome, or diabetes; use of chronic systemic corticosteroids or other immunosuppressive therapy; pregnant or nursing; use of ophthalmic medications other than artificial tears for treatment of an ocular pathology; use of systemic medication with

significant ocular side effects; severe dry eye syndrome unresolved by treatment; allergy to study medications; glaucoma or glaucoma filtering surgery; pregnant or lactating females; or, participation in another ophthalmic clinical trial.

D. Study Plan, Patient Assessments, and Efficacy Criteria

All subjects were expected to return for follow-up on Day 1, at 1 week, and at 1, 3, 4, and 6 months postoperatively. The 4 month visit was removed from the U.S. protocol during the study and therefore, was not a required visit for all eyes.

Subjects were permitted to have their fellow eyes treated on the same day as the primary eye or any time thereafter provided there were no active complications or adverse reactions for the primary eye.

Retreatments were permitted after the 3 month follow-up visit. Retreatment criteria included:

(1) For retreatment of undercorrection or overcorrection, uncorrected visual acuity (UCVA) is worse than 20/25 or residual sphere or cylinder is greater than or equal to 0.50 D at both of the two most recent consecutive visits that are at least 1 month apart.

(2) Refraction is stable with the sphere and cylinder components within 0.50D on two most recent consecutive visits that are at least 1 month apart.

(3) UCVA is stable, i.e., within one line on two consecutive visits at least 1 month apart.

(4) The eligibility criteria are met and an ophthalmic evaluation (including visual acuity, manifest refraction, and slit lamp) is done to establish the preoperative condition of the eye.

(5) Prior written approval is obtained from the sponsor of the study.

(6) The subject signs a separate Retreatment Informed Consent document, wherein he/she is informed of the risks associated with retreatment.

Retreatment for the purpose of correcting residual refractive error was not considered a treatment failure. Results of retreated eyes were analyzed separately from the primary treatment population.

No other ocular surgery procedures were allowed unless deemed medically necessary by the investigator. The sponsor was required to be notified prior to any secondary surgical intervention, except in the case of an emergency in which case notification must occur as soon as possible.

In the event of a miscreated flap with the microkeratome, which is an adverse reaction in the study, a second cut with the microkeratome could be performed and the laser ablation procedure may be completed after a minimum of 3 months. Approval from the medical monitor was required prior to treating an eye with a miscreated flap.

Preoperatively, the subject's medical and ocular histories were recorded. The objective parameters measured during the study included: high and low contrast UCVA, high and low contrast BSCVA, photopic and mesopic pupil size, manifest and cycloplegic refraction, wavefront measurement, contrast sensitivity, intraocular pressure (IOP), angle assessment and status of the cornea, conjunctiva, anterior chamber, lens, vitreous, retina, and anterior segment. These parameters were collected preoperatively and only as needed postoperatively: corneal thickness, corneal topography, and keratometry. The subjective parameters measured during the study included a subjective questionnaire.

The primary efficacy variables for this study were improvement of UCVA, predictability and stability of MRSE, and reduction of wavefront error.

E. Study Period, Investigational Sites, and Demographics

1. Study period and investigational sites

Subjects were treated between October 12, 1999 and September 18, 2001. A series of algorithm modifications were made early on in the study to enhance effectiveness outcomes and 40 eyes were treated with the initial algorithms. The primary cohort treated with the last algorithm consisted of 426 eyes including 139 eyes with less than -0.50D of astigmatism and 287 eyes with -0.50D to -4D of astigmatism based on manifest refraction. The safety cohort consisted of all 426 eyes, and the effectiveness cohort consisted of the 139 eyes treated for spherical myopia. All eyes were treated based on the Zernike data from the wavefront measurement system including lower-order aberrations, such as sphere and cylinder and higher-order aberrations, such as spherical aberration and coma. There were five investigational sites including four U.S. sites and one Canadian site.

2. Demographics

The demographics of this study shown in Table 1 were very typical for a contemporary refractive surgery trial performed in the U.S. The study population was primarily Caucasians and no subjects were over 65 years old.

| Table 1. Demographics | | |
|---|---|---|
| 426 Eyes of 264 Enrolled Subjects | | |
| **Age (In Years)** | | |
| Average ± Standard Deviation | 38.1 ± 8.4 | |
| Minimum to Maximum | 20 to 64 | |
| **Race** | **Number** | **Percentage** |
| Asian | 10 | 2.3% |
| Black | 1 | 0.2% |
| Caucasian | 411 | 96.5% |
| Other* | 4 | 0.9% |
| **Gender** | | |
| Female | 184 | 43.2% |
| Male | 242 | 56.8% |
| **Eye: Custom Treatment** | | |
| Right | 216 | 50.7% |
| Left | 210 | 49.3% |
| **Contact Lens History** | | |
| None | 97 | 22.8% |
| PMMA | 2 | 0.5% |
| RGP | 18 | 4.2% |
| Soft | 309 | 72.5% |

*2 eyes (1 subject) Philippino; 2 eyes (1 subject) Guyanese.
PMMA = polymethyl methacrylate RGP = rigid gas permeable

F. Data analysis and Results

1. Preoperative characteristics

Table 2 contains the number of eyes stratified by the preoperative manifest refraction.

| Table 2. Preoperative Manifest Refraction Stratified By Sphere And Cylinder | | | | | | |
|---|---|---|---|---|---|---|
| | **CYLINDER** | | | | | |
| **SPHERE** | 0 to -0.49 | -0.50 to -0.99 | -1.0 to -1.99 | -2.0 to -2.99 | -3.0 to -4.0 | TOTAL |
| 0.0 to -0.99 | 1/426<br>0.2% | 2/426<br>0.5% | 7/426<br>1.6% | 4/426<br>0.9% | 5/426<br>1.2% | 19/426<br>4.5% |
| -1.0 to -1.99 | 23/426<br>5.4% | 23/426<br>5.4% | 24/426<br>5.6% | 2/426<br>0.5% | 4/426<br>0.9% | 76/426<br>17.8% |
| -2.0 to -2.99 | 40/426<br>9.4% | 22/426<br>5.2% | 20/426<br>4.7% | 2/426<br>0.5% | 2/426<br>0.5% | 86/426<br>20.2% |
| -3.0 to -3.99 | 31/426<br>7.3% | 55/426<br>12.9% | 24/426<br>5.6% | 7/426<br>1.6% | 0/426<br>0.0% | 117/426<br>27.5% |
| -4.0 to -4.99 | 27/426<br>6.3% | 34/426<br>8.0% | 18/426<br>4.2% | 5/426<br>1.2% | 0/426<br>0.0% | 84/426<br>19.7% |
| -5.0 to –5.99 | 13/426<br>3.1% | 17/426<br>4.0% | 5/426<br>1.2% | 0/426<br>0.0% | 0/426<br>0.0% | 35/426<br>8.2% |
| -6.0 to –7.0 | 4/426<br>0.9% | 2/426<br>0.5% | 3/426<br>0.7% | 0/426<br>0.0% | 0/426<br>0.0% | 9/426<br>2.1% |
| TOTAL | 139/426<br>32.6% | 155/426<br>36.4% | 101/426<br>23.7% | 20/426<br>4.7% | 11/426<br>2.6% | 426/426<br>100.0% |

2. Postoperative results

a. Accountability

Table 3 shows the accountability for the safety cohort in this study, which was 100% with 426 eyes available at 3 months and 424 eyes available at 6 months for analysis of safety. Table 4 shows the accountability for the effectiveness cohort, which was 100% with 139 eyes available at 3 and 6 months for analysis of effectiveness.

**Table 3. Accountability at Each Visit: Safety Cohort**

| | | 1 Day | 1 Week | 1 Month | 3 Months | 4 Months* | 6 Months |
|---|---|---|---|---|---|---|---|
| Total Enrolled: Primary | n | 264 | 264 | 264 | 264 | 264 | 264 |
| Fellow | n | 162 | 162 | 162 | 162 | 162 | 162 |
| **Available for Analysis:** | n | 426 | 426 | 426 | 426 | 235 | 424 |
| | % | 100.0% | 100.0% | 100.0% | 100.0% | 55.2% | 99.5% |
| Discontinued: | n | 0 | 0 | 0 | 0 | 0 | 0 |
| Retreated | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| Death† | n | 0 | 0 | 0 | 0 | 0 | 2 † |
| | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.5% |
| Not Eligible for Interval / | n | 0 | 0 | 0 | 0 | 0 | 0 |
| In Process: | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| Not Required: | n | - | - | - | - | 191 | - |
| (4 Month Visit Only)* | % | -- | -- | -- | -- | 44.8% | -- |
| Unavailable: Missed Visit | n | 0 | 0 | 0 | 0 | 0 | 0 |
| | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| Lost to Follow-up | n | 0 | 0 | 0 | 0 | 0 | 0 |
| | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| % Accountability=[available/ (available + unavailable)] | | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |

*Not a required visit for all eyes.

† A death of 1 subject (2 eyes) occurred after the 3-month visit due to colon cancer with no relationship to the device or study. Key parameters for this patient are provided in the section on Adverse Events.

| Table 4. Accountability at Each Visit: Effectiveness Cohort | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | **1 Day** | **1 Week** | **1 Month** | **3 Months** | **4 Months*** | **6 Months** |
| Total Enrolled: Primary | n | 85 | 85 | 85 | 85 | 85 | 85 |
| Fellow | n | 54 | 54 | 54 | 54 | 54 | 54 |
| Available for Analysis | n | 139 | 139 | 139 | 139 | 80 | 139 |
| | % | 100.0% | 100.0% | 100.0% | 100.0% | 57.6% | 100.0% |
| Discontinued: | n | 0 | 0 | 0 | 0 | 0 | 0 |
| Retreated | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| Not Eligible for Interval / | n | 0 | 0 | 0 | 0 | 0 | 0 |
| In Process: | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| Not Required: | n | 0 | 0 | 0 | 0 | 59 | 0 |
| (4 Month Visit Only)* | % | 0.0% | 0.0% | 0.0% | 0.0% | 42.4% | 0.0% |
| Unavailable: Missed Visit | n | 0 | 0 | 0 | 0 | 0 | 0 |
| | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| Lost to Follow-up | n | 0 | 0 | 0 | 0 | 0 | 0 |
| | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| % Accountability=[available/ (available + unavailable)] | | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |

*Not a required visit for all eyes.

b. Stability of Outcome

Between 1 and 3 months, 100% of spherical myopic eyes experienced a change of MRSE not exceeding ± 1.0D with a mean change per month of –0.035D (Table 5). The change in MRSE between 3 and 6 months was -0.01D per month with 100% of eyes having less than or equal to 1D change (Table 6). Thus, refractive stability was demonstrated by 3 months postoperative and confirmed between 3 and 6 months based on the FDA guidance document criterion of >95% having a change in MRSE of ≤ 1.0D between two intervals.

| Table 5. Stability of Manifest Refraction Spherical Equivalent for Spherical Myopic Eyes: 3 Month Cohort | |
|---|---|
| Change in Spherical Equivalent Between | 1 and 3 Months |
| ≤1.00 (% (n/N)) | 100.0% (139/139) |
| Mean Difference ± SD | -0.07 ± 0.27 |
| 95% Confidence Interval | (-0.12, -0.03) |
| Mean Change per month | -0.035 |

| Table 6. Stability of Manifest Refraction Spherical Equivalent for Spherical Myopic Eyes: 6 Month Cohort | | |
|---|---|---|
| Change in Spherical Equivalent Between | 1 and 3 Months | 3 and 6 Months |
| ≤1.00 (% (n/N)) | 100.0% (139/139) | 100.0% (139/139) |
| Mean Difference ± SD | -0.07 ± 0.27 | -0.03 ± 0.26 |
| 95% Confidence Interval | (-0.12, -0.03) | (-0.07, 0.02) |
| Mean Change per month | -0.035 | -0.01 |

c. Effectiveness Outcomes

The effectiveness outcomes for UCVA and MRSE by visit are shown in Table 7 for spherical myopic eyes (eyes with less than 0.50D astigmatism on preoperative manifest refraction). The same parameters are shown for spherical myopic eyes stratified by diopter at 3 months (Table 8) and 6 months (Table 9).

**Table 7. Summary of Key Efficacy Variables Over Time for Spherical Myopic Eyes Based on Manifest Refraction (N=139)**

| Efficacy Variables | | 1 MONTH | 3 MONTHS | 6 MONTHS |
|---|---|---|---|---|
| UCVA 20/20 or better | n | 120/139 | 112/139 | 111/139 |
| | % | 86.3% | 80.6% | 79.9% |
| | CI | (79.5, 91.6) | (73.0, 86.8) | (72.2, 86.2) |
| UCVA 20/25 or better | n | 131/139 | 131/139 | 127/139 |
| | % | 94.2% | 94.2% | 91.4% |
| | CI | (89.0, 97.5) | (89.0, 97.5) | (85.4, 95.5) |
| UCVA 20/40 or better | n | 138/139 | 136/139 | 137/139 |
| | % | 99.3% | 97.8% | 98.6% |
| | CI | (96.1, 100.0) | (93.8, 99.6) | (94.9, 99.8) |
| MRSE ±0.50D of intended | n | 116/139 | 109/139 | 104/139 |
| | % | 83.5% | 78.4% | 74.8% |
| | CI | (76.2, 89.2) | (70.6, 84.9) | (66.8, 81.8) |
| MRSE ±1.00D of intended | n | 135/139 | 132/139 | 133/139 |
| | % | 97.1% | 95.0% | 95.7% |
| | CI | (92.8, 99.2) | (89.9, 98.0) | (90.8, 98.4) |

UCVA = Uncorrected Visual Acuity
CI = 95% Confidence Interval
MRSE = Manifest Refraction Spherical Equivalent
D = Diopter

**Table 8. Summary of Key Efficacy Variables at 3 Months for Spherical Myopic Eyes Stratified by Diopter of Preoperative Manifest Refraction Spherical Equivalent**

| Efficacy Variables | | 0 to –0.99 | -1 to –1.99 | -2 to –2.99 | -3 to –3.99 | -4 to –4.99 | -5 to –5.99 | -6 to –7.00 | Total |
|---|---|---|---|---|---|---|---|---|---|
| UCVA 20/20 or better | % | 100.0% | 91.3% | 80.0% | 74.2% | 88.9% | 61.5% | 75.0% | 80.6% |
| | (n) | (1/1) | (21/23) | (32/40) | (23/31) | (24/27) | (8/13) | (3/4) | (112/139) |
| UCVA 20/25 or better | % | 100.0% | 100.0% | 95.0% | 96.8% | 96.3% | 76.9% | 75.0% | 94.2% |
| | (n) | (1/1) | (23/23) | (38/40) | (30/31) | (26/27) | (10/13) | (3/4) | (131/139) |
| UCVA 20/40 or better | % | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 84.6% | 75.0% | 97.8% |
| | (n) | (1/1) | (23/23) | (40/40) | (31/31) | (27/27) | (11/13) | (3/4) | (136/139) |
| MRSE ±0.50D of intended | % | 100.0% | 95.7% | 75.0% | 77.4% | 70.4% | 76.9% | 75.0% | 78.4% |
| | (n) | (1/1) | (22/23) | (30/40) | (24/31) | (19/27) | (10/13) | (3/4) | (109/139) |
| MRSE ±1.00D of intended | % | 100.0% | 100.0% | 95.0% | 96.8% | 96.3% | 84.6% | 75.0% | 95.0% |
| | (n) | (1/1) | (23/23) | (38/40) | (30/31) | (26/27) | (11/13) | (3/4) | (132/139) |

UCVA = Uncorrected Visual Acuity D = Diopter MRSE = Manifest Refraction Spherical Equivalent

**Table 9. Summary of Key Safety and Efficacy Variables at 6 Months for Spherical Myopic Eyes Stratified by Diopter of Preoperative Manifest Refraction Spherical Equivalent**

| Efficacy Variables | | 0 to –0.99 | -1 to –1.99 | -2 to –2.99 | -3 to –3.99 | -4 to –4.99 | -5 to –5.99 | -6 to –7.00 | Total |
|---|---|---|---|---|---|---|---|---|---|
| UCVA 20/20 or better | % | 100.0% | 82.6% | 75.0% | 90.3% | 81.5% | 69.2% | 50.0% | 79.9% |
| | (n) | (1/1) | (19/23) | (30/40) | (28/31) | (22/27) | (9/13) | (2/4) | (111/139) |
| UCVA 20/25 or better | % | 100.0% | 95.7% | 87.5% | 93.5% | 92.6% | 92.3% | 75.0% | 91.4% |
| | (n) | (1/1) | (22/23) | (35/40) | (29/31) | (25/27) | (12/13) | (3/4) | (127/139) |
| UCVA 20/40 or better | % | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 92.3% | 75.0% | 98.6% |
| | (n) | (1/1) | (23/23) | (40/40) | (31/31) | (27/27) | (12/13) | (3/4) | (137/139) |
| MRSE ±0.50D of intended | % | 100.0% | 87.0% | 72.5% | 71.0% | 66.7% | 84.6% | 75.0% | 74.8% |
| | (n) | (1/1) | (20/23) | (29/40) | (22/31) | (18/27) | (11/13) | (3/4) | (104/139) |
| MRSE ±1.00D of intended | % | 100.0% | 100.0% | 97.5% | 96.8% | 96.3% | 84.6% | 75.0% | 95.7% |
| | (n) | (1/1) | (23/23) | (39/40) | (30/31) | (26/27) | (11/13) | (3/4) | (133/139) |

A comparison of **postoperative** uncorrected visual acuity (UCVA) to **preoperative** best spectacle corrected visual acuity (BSCVA) after CustomCornea® LASIK surgery is presented in Table 10. At 6 months, postoperative UCVA was equal to or better than preoperative BSCVA in 57.6% of subjects. However, postoperative UCVA was equal to or worse than preoperative BSCVA in 67.8% of subjects.

**Table 10. Postoperative Uncorrected Visual Acuity Compared to Preoperative Best Spectacle Corrected Visual Acuity for Spherical Myopic Eyes (N=139)**

| | 1 MONTH | 3 MONTHS | 6 MONTHS |
|---|---|---|---|
| 2 Lines Better | 2.2% | 1.4% | 2.2% |
| 1 Line Better | 12.2% | 13.7% | 15.1% |
| Equal | 44.6% | 40.3% | 35.3% |
| 1 Line Worse | 26.6% | 23.7% | 23.7% |
| 2 Lines Worse | 8.6% | 11.5% | 14.4% |
| >2 Lines Worse | 5.8% | 9.4% | 9.4% |

d. Wavefront Outcomes

Table 11 compares the change in total wavefront error and in higher-order aberrations for spherical myopic eyes treated with wavefront-guided CustomCornea® LASIK and Conventional LASIK with the LADARVision®4000 system using manifest refraction.

**Table 11. Change in Aberrations from Preoperative for Spherical Myopic Eyes (wavefront analysis diameter = 6.5mm)**

| Aberration | 3-MONTH MEAN VALUE | | | | 6-MONTH MEAN VALUE | | | |
|---|---|---|---|---|---|---|---|---|
| | CustomCornea® (N = 138) | | Conventional (N = 47) | | CustomCornea® (N = 139) | | Conventional (N = 50) | |
| | µm | % | µm | % | µm | % | µm | % |
| Total RMS | -3.90 | -80 | -3.30 | -69 | -3.88 | -79 | -3.21 | -67 |
| Higher Order | 0.10 | 27 | 0.31 | 77 | 0.08 | 20 | 0.33 | 82 |
| Coma | 0.07 | 31 | 0.15 | 71 | 0.05 | 22 | 0.17 | 78 |
| Trefoil | -0.01 | -8 | 0.09 | 52 | -0.02 | -11 | 0.07 | 38 |
| Spherical Aberration | 0.04 | 24 | 0.21 | 96 | 0.04 | 22 | 0.23 | 108 |
| Secondary Astigmatism | 0.06 | 83 | 0.07 | 92 | 0.05 | 73 | 0.07 | 105 |
| Tetrafoil | 0.07 | 108 | 0.09 | 124 | 0.05 | 81 | 0.09 | 119 |

RMS = Root Mean Square

The total higher-order RMS error was most significantly correlated with low contrast BSCVA with a correlation coefficient of -0.46 at 3 months and -0.16 at 6 months.

A vision simulation program (CTView by Sarver and Associates) was used to model the effect of various wavefront errors on the retinal point-spread function (i.e., the effective blur pattern) and a simulated eye chart image for CustomCornea® and Conventional LASIK eyes. Visual comparisons of letter charts blurred by defocus or higher-order aberrations suggest that the benefit of smaller amounts of higher-order aberrations after wavefront-guided CustomCornea® LASIK surgery compared to Conventional LASIK corresponds to approximately 0.2 D of defocus on average.

e. Safety Outcomes

The analysis of safety was based on all eyes in the primary cohort of 426 eyes. The key safety outcomes for this study are presented in Table 12 for all eyes by visit and in Tables 13 and 14 stratified by diopter at 3 and 6 months.

**Table 12. Summary of Key Safety Variables Over Time for All Myopic Eyes**

| Safety Variables | | 1 MONTH | 3 MONTHS | 6 MONTHS |
|---|---|---|---|---|
| Loss of >2 Lines BSCVA | %<br>(n)<br>CI | 0.5%<br>(2/426)<br>(0.1, 1.7) | 0.2%<br>(1/426)<br>(0.0, 1.3) | 0.0%<br>(0/424)<br>(0.0, 0.9) |
| Loss of 2 Lines BSCVA | %<br>(n)<br>CI | 1.4%<br>(6/426)<br>(0.5, 3.0) | 0.5%<br>(2/426)<br>(0.1, 1.7) | 0.7%<br>(3/424)<br>(0.1, 2.1) |
| BSCVA worse than 20/40 | %<br>(n)<br>CI | 0.0%<br>(0/426)<br>(0.0, 0.9) | 0.0%<br>(0/426)<br>(0.0, 0.9) | 0.0%<br>(0/424)<br>(0.0, 0.9) |
| Increase >2D cylinder magnitude | %<br>(n)<br>CI | 0.0%<br>(0/426)<br>(0.0, 0.9) | 0.0%<br>(0/426)<br>(0.0, 0.9) | 0.0%<br>(0/424)<br>(0.0, 1.6) |
| BSCVA worse than 20/25<br>if 20/20 or better preoperatively | %<br>(n)<br>CI | 0.2%<br>(1/423)<br>(0.0, 1.3) | 0.0%<br>(0/423)<br>(0.0, 0.9) | 0.2%<br>(1/421)<br>(0.0, 1.3) |

BSCVA = Best Spectacle Corrected Visual Acuity CI = 95% Confidence Interval
D = Diopter

**Table 13. Summary of Key Safety Variables at 3 Months for All Myopic Eyes Stratified by Diopter of Preoperative Manifest Refraction Spherical Equivalent**

| Safety Variables | | 0 to –0.99 | -1 to –1.99 | -2 to –2.99 | -3 to –3.99 | -4 to –4.99 | -5 to –5.99 | -6 to –7.00 | Total |
|---|---|---|---|---|---|---|---|---|---|
| Loss of >2 Lines BSCVA | % | 0.0% | 0.0% | 0.0% | 1.0% | 0.0% | 0.0% | 0.0% | 0.2% |
| | (n) | (0/2) | (0/60) | (0/95) | (1/103) | (0/97) | (0/58) | (0/11) | (1/426) |
| Loss of 2 Lines BSCVA | % | 0.0% | 0.0% | 1.1% | 0.0% | 1.0% | 0.0% | 0.0% | 0.5% |
| | (n) | (0/2) | (0/60) | (1/95) | (0/103) | (1/97) | (0/58) | (0/11) | (2/426) |
| BSCVA worse than 20/40 | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| | (n) | (0/2) | (0/60) | (0/95) | (0/103) | (0/97) | (0/58) | (0/11) | (0/426) |
| Increase >2D cylinder magnitude | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| | (n) | (0/2) | (0/60) | (0/95) | (0/103) | (0/97) | (0/58) | (0/11) | (0/426) |
| BSCVA worse than 20/25 if 20/20 or better preoperatively | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| | (n) | (0/2) | (0/60) | (0/95) | (0/102) | (0/97) | (0/56) | (0/11) | (0/423) |

**Table 14. Summary of Key Safety and Efficacy Variables at 6 Months for All Myopic Eyes Stratified by Diopter of Preoperative Manifest Refraction Spherical Equivalent**

| Safety Variables | | 0 to –0.99 | -1 to –1.99 | -2 to –2.99 | -3 to –3.99 | -4 to –4.99 | -5 to –5.99 | -6 to –7.00 | Total |
|---|---|---|---|---|---|---|---|---|---|
| Loss of >2 Lines BSCVA | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| | (n) | (0/1) | (0/59) | (0/95) | (0/103) | (0/97) | (0/58) | (0/11) | (0/424) |
| Loss of 2 Lines BSCVA | % | 0.0% | 1.7% | 0.0% | 1.0% | 0.0% | 1.7% | 0.0% | 0.7% |
| | (n) | (0/1) | (1/59) | (0/95) | (1/103) | (0/97) | (1/58) | (0/11) | (3/424) |
| BSCVA worse than 20/40 | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| | (n) | (0/1) | (0/59) | (0/95) | (0/103) | (0/97) | (0/58) | (0/11) | (0/424) |
| Increase >2D cylinder magnitude | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| | (n) | (0/1) | (0/59) | (0/95) | (0/103) | (0/97) | (0/58) | (0/11) | (0/424) |
| BSCVA worse than 20/25 if 20/20 or better preoperatively | % | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 1.8% | 0.0% | 0.2% |
| | (n) | (0/1) | (0/59) | (0/95) | (0/102) | (0/97) | (1/56) | (0/11) | (1/421) |

BSCVA = Best Spectacle Corrected Visual Acuity D = Diopter

BSCVA was measured using a standard (high-contrast) visual acuity chart under dim room illumination (10-12 cd/m$^2$). Change in BSCVA from preoperative is shown in Table 15.

**Table 15. Change in Best Spectacle Corrected Visual Acuity for Spherical Myopic Eyes (n=139)**

| | | 1 MONTH | 3 MONTHS | 6 MONTHS |
|---|---|---|---|---|
| Decrease >2 Lines | % | 0.0% | 0.0% | 0.0% |
| Decrease 2 Lines | % | 2.2% | 1.4% | 0.0% |
| Decrease 1 Line | % | 10.1% | 15.1% | 8.6% |
| No change | % | 58.3% | 52.5% | 53.2% |
| Increase 1 Line | % | 26.6% | 28.8% | 35.3% |
| Increase 2 Lines | % | 2.2% | 2.2% | 2.9% |
| Increase >2 Lines | % | 0.7% | 0.0% | 0.0% |

Low-contrast BSCVA was measured using a 10% low contrast visual acuity chart under dim room illumination. Change in low contrast BSCVA from preoperative is shown in Table 16.

**Table 16. Change in Low Contrast Best Spectacle Corrected Visual Acuity for Spherical Myopic Eyes (n=139)**

| | | 3 MONTHS | 6 MONTHS |
|---|---|---|---|
| Decrease >2 Lines | % | 0.0% | 0.0% |
| Decrease 2 Lines | % | 7.2% | 2.2% |
| Decrease 1 Line | % | 15.1% | 18.7% |
| No change | % | 42.4% | 40.3% |
| Increase 1 Line | % | 30.2% | 30.2% |
| Increase 2 Lines | % | 4.3% | 6.5% |
| Increase >2 Lines | % | 0.7% | 2.2% |

A summary of adverse events and complications that occurred at any interval up to 6 months is shown in Table 17.

**Table 17. Summary Of Adverse Events and Complications At Any Postoperative Visit**

| | | |
|---|---|---|
| **ADVERSE EVENTS** | | |
| | **%** | **(n/N)** |
| Miscreated flap (related to microkeratome) | 0.2% | (1/427)† |
| Recalcitrant Diffuse Lamellar Keratitis (DLK) with Blepharitis | 0.5% | (2/426)* |
| Retinal horseshoe tear (unrelated to device) | 0.2% | (1/426) |
| **COMPLICATIONS** | | |
| Conjunctivitis | 0.2% | (1/426) |
| Corneal edema 1 week to <1 month | 1.9% | (8/426) |
| Diffuse Lamellar Keratitis (includes rule out DLK vs. debris) | 3.5% | (15/426) |
| Double/ghost images | 2.1% | (9/426) |
| Epithelial defect by microkeratome | 0.2% | (1/426) |
| Epithelium in the interface | 3.3% | (14/426) |
| Focal inflammatory reaction in interface | 0.2% | (1/426) |
| Foreign body sensation at 1 month or later | 0.5% | (2/426) |
| Pain at 1 month or later | 0.2% | (1/426) |
| Striae | 0.5% | (2/426) |

* Includes both eyes of one subject

† One eye received conventional laser ablation three months after miscreated flap and was not included in primary cohort analysis.

Subjects were asked to rate symptoms compared to before surgery, as shown in Tables 18 for spherical myopic eyes. These events came from the self-evaluations performed at the 3- and 6-month visits.

**Table 18. Change in Subjective Symptoms From Preoperative**

| 3 MONTHS | | | | |
|---|---|---|---|---|
| **Symptom** | **Worse** | | **Significantly Worse** | |
| | **%** | **n/N** | **%** | **n/N** |
| Blurring of Vision | 21.2% | (29/137) | 1.5% | (2/137) |
| Burning | 5.8% | (8/137) | 0.7% | (1/137) |
| Double Vision | 7.3% | (10/137) | 0.7% | (1/137) |
| Dryness | 21.5% | (29/135) | 7.4% | (10/135) |
| Excessive Tearing | 0.0% | (0/137) | 0.0% | (0/137) |
| Fluctuation of Vision | 24.1% | (33/137) | 1.5% | (2/137) |
| Glare | 16.8% | (23/137) | 0.0% | (0/137) |
| Gritty Feeling | 10.9% | (15/137) | 0.7% | (1/137) |
| Halos | 19.0% | (26/137) | 0.7% | (1/137) |
| Headache | 5.1% | (7/137) | 0.0% | (0/137) |
| Light Sensitivity | 7.3% | (10/137) | 0.7% | (1/137) |
| Night Driving Difficulty | 13.9% | (19/137) | 3.6% | (5/137) |
| Pain | 5.1% | (7/137) | 0.0% | (0/137) |
| Redness | 8.0% | (11/137) | 0.0% | (0/137) |
| **6 MONTHS** | | | | |
| Blurring of Vision | 16.2% | (22/136) | 2.9% | (4/136) |
| Burning | 5.9% | (8/136) | 1.5% | (2/136) |
| Double Vision | 5.9% | (8/136) | 0.7% | (1/136) |
| Dryness | 20.6% | (28/136) | 2.2% | (3/136) |
| Excessive Tearing | 0.0% | (0/135) | 0.0% | (0/135) |
| Fluctuation of Vision | 16.9% | (23/136) | 0.7% | (1/136) |
| Glare | 14.7% | (20/136) | 0.0% | (0/136) |
| Gritty Feeling | 8.8% | (12/136) | 1.5% | (2/136) |
| Halos | 13.2% | (18/136) | 0.0% | (0/136) |
| Headache | 1.5% | (2/136) | 0.0% | (0/136) |
| Light Sensitivity | 4.4% | (6/136) | 0.0% | (0/136) |
| Night Driving Difficulty | 18.4% | (25/136) | 0.7% | (1/136) |
| Pain | 0.7% | (1/136) | 0.0% | (0/136) |
| Redness | 5.9% | (8/136) | 0.0% | (0/136) |

Contrast sensitivity was measured under both photopic conditions and mesopic conditions for spherical myopic eyes (Table 19).

**Table 19. Change of >2 Levels (> 0.3 Log) on CSV-1000 at 2 or More Spatial Frequencies for Spherical Myopic Eyes**

| | **Photopic Conditions** | | | |
|---|---|---|---|---|
| Change >0.3 (log unit) | **Decrease** | | **Increase** | |
| **Post-op Time** | **3 MONTHS** | **6 MONTHS** | **3 MONTHS** | **6 MONTHS** |
| n/N | 3/138 | 1/138 | 6/138 | 3/138 |
| % | 2.2% | 0.7% | 4.3% | 2.2% |
| | **Mesopic Conditions*** | | | |
| Change >0.3 (log unit) | **Decrease** | | **Increase** | |
| **Post-op Time** | **3 MONTHS** | **6 MONTHS** | **3 MONTHS** | **6 MONTHS** |
| n/N | 8/138 | 8/138 | 14/138 | 21/138 |
| % | 5.8% | 5.8% | 10.1% | 15.2% |

*Mesopic illumination with neutral density filters in front of eyes

f. Additional Safety Outcomes

None of the eyes had an IOP ≥ 25 mmHg or an increase in IOP > 7 mmHg above baseline at any scheduled visit 1 month or later. No corneal haze was noted in ≥ 95% of eyes at any visit and in 98.6% of eyes at 3 and 6 months. There was no BSCVA loss of ≥ 2 lines associated with haze.

Significant corneal and anterior segment findings that were reported at 1 month or later in ≥ 1% of eyes included superficial punctate keratitis (SPK), striae, cells under the flap, flap edge fibrosis, blepharitis, meibomian gland dysfunction, and papillary changes. All other significant corneal or anterior segment findings were reported in <1% of eyes. There were no clinically significant crystalline lens, vitreous, or fundus findings noted postoperatively that were not already reported preoperatively or as an adverse event. There was one subject (2 eyes) with an age-related trace nuclear sclerosis lens finding reported at 4 and 6 months that was considered to be within normal limits.

g. Retreatments

No data are available for CustomCornea® LASIK retreatments using the LADARVision®4000 system.

h. Statistical Analysis Outcomes

Statistical analysis at 3 months showed that spherical myopic eyes with a lower preoperative sphere were more likely to have a MRSE within 1.00 D of emmetropia. There were also statistical interactions for some of the effectiveness outcomes at 3 months, which are difficult to interpret in terms of

clinical significance. There were too few eyes with a loss of 2 or more lines of BSCVA to perform a statistical analysis on this outcome.

Statistical analysis at 6 months showed that spherical myopic eyes with a lower preoperative sphere were more likely to achieve an UCVA of 20/40 or better. Spherical myopic eyes treated in an operating room environment with lower humidity were more likely to have a MRSE within 0.50 D of emmetropia. In addition, eyes with a lower preoperative sphere were more likely to have a MRSE within 1.00 D of emmetropia.

i. Surgical Interruptions

There were 10 eyes with reported problems during surgery, including a brief interruption in ablation of one eye due to low energy, insufficient pupil dilation in 2 eyes, and microkeratome-related epithelial defects or limbal bleeding, and a miscreated flap. All eyes had complete laser ablation during the same surgery session and were tracked throughout the ablation. All eyes had a BSCVA of 20/16 or better at the last reported visit with no loss of BSCVA from preoperative, except for 1 eye with the microkeratome-related miscreated flap, which was 20/16 and within 1 line of preop.

## XI. CONCLUSIONS DRAWN FROM THE CLINICAL STUDY

The data in this application provide reasonable assurance of safety and effectiveness of the LADARVision® 4000 Excimer Laser System for wavefront-guided Laser In-Situ Keratomileusis (LASIK) correction of myopia up to -7.00D with less than -0.50D of astigmatism when used in accordance with the indications for use.

Regardless of the treatment of other higher-order aberrations, the accuracy of the correction for myopia is still the primary determinant of uncorrected image quality and visual acuity. There are no data to support improved functional performance (activities of daily living such as reading and driving) or satisfaction rates in patients with wavefront-guided LASIK as compared to the Conventional LASIK with the LADARVision® 4000 system.

The accuracy of the myopic correction is the primary determinant in patient satisfaction and subjective symptoms. In the clinical study, the wavefront-guided LASIK eyes showed slight myopic undercorrection on average relative to the Conventional LASIK eyes. For the 20 patients in the study who received wavefront-guided LASIK in one eye and Conventional LASIK in the other eye, there was no significant difference in subjective symptoms between the two treatments.

## XII. PANEL RECOMMENDATION

At an advisory meeting on August 1, 2002, the Ophthalmic Devices Panel recommended that Alcon LADARVision®4000 Excimer Laser System for wavefront-guided LASIK be conditionally approved, on the conditions that the following information are included in the labeling of the device:

- Note that Wavefront-guided LASIK has demonstrated slightly superior optical quality (reduced monochromatic aberrations) compared with conventional LADARVision® LASIK. Minor improvements were noted in visual acuity and contrast sensitivity relative to conventional LADARVision® LASIK.
- Note that the accuracy of the correction for myopia is still the primary determination of uncorrected image quality and vision.
- Note that study data has not supported improved functional performance (activities of daily living such as reading, driving) or satisfaction rates in patients with wavefront- guided LASIK as compared to the conventional LADARVision® LASIK.
- Discuss that the relative increase in higher-order aberrations after conventional LADARVision® LASIK was greater than after wavefront-guided LASIK.
- Note that no retreatment data using CustomCornea® are available.
- Note that the study population included only 4 eyes in the study above -6D of myopia and was primarily Caucasian with no patients being over 65 years old.
- Provide data for changes in high- and low-contrast BSCVA.
- Compare postoperative UCVA to preoperative BSCVA.
- Include postoperative patient symptom categories of significantly better, better, no change, worse, and significantly worse.
- Exclude patients with preoperative severe dry eye.
- Discuss pre-existing dry eye and/or large nighttime pupils may affect postoperative satisfaction with the LASIK procedure.
- Postoperatively, a patient's eyes should become stable after 1 month.
- Clarify results in the Patient Information Booklet regarding visual acuity at 6 months were recorded with patients wearing their best corrected glasses or contact lenses.

## XIII. CDRH DECISION

CDRH concurred with the panel's recommendation and worked interactively with the applicant to satisfactorily address FDA's remaining deficiencies. CDRH issued an approval order on October 18, 2002.

## XIV. APPROVAL SPECIFICATIONS

- Postapproval Requirements and Restrictions: see Approval Order
- Hazards to Health from Use of the Device: see Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.
- Directions for use: see labeling.