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:	VISX STAR S4™ Excimer Laser System and WaveScan WaveFront® System
Applicant's Name and Address:	VISX, Incorporated 3400 Central Expressway Santa Clara, CA 95051-0703
Date of Panel Recommendation:	None
Premarket Approval (PMA) Application Number:	P930016/S016
Date of Notice of Approval to Applicant:	May 23, 2003

The STAR Excimer Laser was originally approved on March 27, 1996, under PMA P930016, for the limited indication for myopic photorefractive keratectomy (PRK) using a 6.0 mm ablation zone in patients 18 years of age or older with 1.0 to 6.0 diopters (D) of myopia with astigmatism of ≤ 1.0 D whose refractive change for one year prior to treatment is within ± 0.5 D.

This clinical indication was expanded in supplements 3 (approved on April 24, 1997), 5 (approved on January 29, 1998), 7 (approved November 2, 1998), and 10 (approved October 18, 2000) to include PRK in patients 21 years of age or older in PRK treatments for the reduction or elimination of myopia (nearsightedness) of between 0 and -12.0 D spherical myopia at the spectacle plane and up to -4.0 D of astigmatism, hyperopia (sphere only) of between +1.0 and +6.0 D spherical equivalent with no more than 1.0 D of refractive astigmatism, and hyperopia between +0.5 and +5.0 D sphere at the spectacle plane with refractive astigmatism from +0.5 to +4.0 D with a maximum manifest refraction spherical equivalent (MRSE) of +6.0 D. On November 19, 1999 (P990010), the clinical indication was further expanded to include laser insitu keratomileusis (LASIK) treatments in patients 18 years of age or older for the reduction or elimination of myopia (nearsightedness) from 0 to -14.0 D with or without -0.50 to -5.0 D of astigmatism. Supplement 12 (approved April 27, 2001) expanded the indication to include patients 21 years of age or older in treatments for the reduction or elimination of naturally hyperopia between +0.5 D and +5.0 D sphere at the spectacle plane with or without refractive astigmatism up to +3.0 D with a maximum manifest refraction spherical equivalent (MRSE) of +6.0 D. Supplement 14 (approved November 16, 2001) expanded the indication for the reduction or elimination of naturally occurring mixed astigmatism where the magnitude of cylinder (≤ 6.0 D at the spectacle plane) is greater than the magnitude of sphere and the cylinder and sphere have opposite signs. Supplement 15 (approved August 7, 2002) added an auto-centering function to the ActiveTrak™ eye tracking system and changed the trade name to the STAR S4.

The sponsor submitted this supplement to further expand the clinical indications. The updated clinical data to support the expanded indication is provided in this summary. The preclinical test results were presented in the original PMA application. For more information on the data which supported the approved indications, the summaries of safety and effectiveness data (SSED) for P930016 and P990010 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 # 97M-0084 (P930016 and S3), Docket # 99M-0293 (S5), Docket # 00M-1391 (S7), Docket # 01M-0015 (S10), Docket # 01M-0305 (S12), Docket # 01M-0522 (S14), and Docket # 00M-1447 (P990010) or you may download the files from the internet sites http://www.fda.gov/cdrh/pdf/p930016.pdf and http://www.fda.gov/cdrh/pdf/p990010.pdf.

II. INDICATIONS FOR USE

The STAR S4™ Excimer Laser System with Variable Spot Scanning (VSS™) and WaveScan® System is indicated for wavefront-guided laser assisted in situ keratomileusis (LASIK):

- for the reduction or elimination of myopic astigmatism up to - 6.00 D MRSE, with cylinder between 0.00 and -3.00 D;
- in patients 21 years of age or older; and
- in patients with documented evidence of a change in manifest refraction of no more than 0.50 D (in both cylinder and sphere components) for at least one year prior to the date of pre-operative examination.

III. CONTRAINDICATIONS

Laser refractive surgery is contraindicated:

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

IV. WARNINGS AND PRECAUTIONS

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

V. DEVICE DESCRIPTION

A. WaveScan WaveFront® System

The WaveScan WaveFront System is an integral part of this approval. It is a class III assessory and has a separate user manual. It is a diagnostic instrument indicated for the automated measurement, analysis, and recording of refractive errors of the eye: including myopia, hyperopia, astigmatism, coma, spherical aberration, trefoil, and other higher order aberrations through sixth order, and for displaying refractive data of the eye to assist in prescribing refractive correction.

The WaveScan WaveFront System measures the refractive error and wavefront aberrations of the human eye using a Hartmann-Shack wavefront sensor. The measurements can be used to determine regular (sphero-cylindrical) refractive errors and irregularities (aberrations) that cause decreased or blurry vision in the human eye.

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The function of the Hartmann-Shack sensor is to measure the refractive error of the eye by evaluating the deflection of rays emanating from a small beam of light projected onto the retina. To control the natural accommodation of the eye during WaveScan® imaging, the system incorporates a fogged fixation target.

The WaveScan System optical head projects a beam of light onto the retina. The light reflects back through the optical path of the eye and into the wavefront device. The reflected beam is imaged by a lenslet array onto the charge-coupled device (CCD). Each lens of the array gathers light information (deflection information) from a different region of the pupil to form an image of the light that passes through that region of the pupil. An array of spots are imaged on the CCD sensor. The system compares the locations of the array of spots gathered from the CCD to the theoretical ideal (the ideal plane wave).

The WaveScan System software uses these data to compute the eye's refractive errors and wavefront aberrations using a polynomial expansion. The system displays the refractive errors and wavefront aberrations as the optical path difference (OPD) between the measured outgoing wavefront and the ideal plane wave. The WaveScan system software subtracts the refractive errors from the wavefront errors map and displays the higher order aberrations as OPD errors. Regions of the pupil with positive OPD are in front of the ideal plane wave and areas with negative OPD are behind the ideal plane wave.

1. Data Collection

   The eye of the patient is centered in the instruments field of view and the image of the eye is brought in focus. As the patient fixates on the target, the fogging system is engaged to optically adjust the position of the target beyond the far point of the patient. This forces the patient to relax their accommodative system, so that the refraction of the eye is measured accurately. There is no pharmaceutical eye dilation required for the patient.

2. Wavefront Measurement

   During the data capture, four images are captured from the Hartmann-Shack camera within a short interval of time. The pupil camera of the instrument captures the image of the eye during the same time interval. The spot pattern images are processed to reconstruct the wavefront and if two or more of them pass the acceptance criteria, the valid measurements are averaged to yield the final measurement for the examination.

3. Registration

   Internal instrument calibration establishes the coordinate transformation between the pupil imaging camera and the Hartmann-Shack camera, so that the wavefront map can be correctly centered at the center of the pupil during the measurement.

4. Treatment Design

   The target treatment shape is automatically calculated by the WaveScan instrument from the wavefront data. Once the target shape is established, VSS™ software module generates the commands for the laser to create the target shape on the cornea. Corneal geometry, represented by the keratometry values, is taken into account in computing the laser instructions.

CustomVue™ ablations are approved for an optical zone of 6.0 mm, and a blend zone of 1.0 mm for a total ablation zone of 8 mm. No treatments with optical zones greater than 6.0 mm were attempted in the U.S. Clinical Trial. CustomVue ablations for this PMA are locked out above -6.0 D MRSE and -3.0 D cylinder as measured by manifest refraction.

The final commercial release versions for CustomVue are WaveScan software version 3.07 together with STAR software version 4.6. The WaveScan software is capable of calculating optical zone up to 9.0 mm with total ablation zone up to 9.5 mm.

5. Data Transfer

The treatment files produced by the WaveScan® instrument contain information about the patient, such as name, ID and refractive data and the set of instructions for the VISX STAR™ laser. They are copied onto a floppy disc for transfer to the laser. The files are encrypted to prevent data tampering or data corruption.

Features and components of the WaveScan WaveFront System include:

- Computer Control
- PC and Monitor
- Isolation Transformer
- Power Supply
- LED
- Optical Head
- Printer
- Motorized table

B. Microkeratome

The LASIK procedure required 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 sterilization/storage tray which includes the shaper head, a left/right eye adapter, suction ring, suction handle, blade handling pin, and corneal reference marker. The instrument motor, tonometer, cleaning brush, disposable blades, power/suction supply unit with vacuum and motor footswitches and power cords are provided as separate components in an accessory stand and equipment suitcase which complete the system.

C. STAR S4™ Excimer Laser System

The STAR S4 laser system is a 193nm excimer laser system that delivers spatially scanning ultraviolet pulses of variable diameters and slits on to the cornea. The range of diameters and slits available during treatments are 0.65mm to 6mm. An auto-centering dual camera infrared eye tracking system, together with the delivery system, compensates for eye movements during laser correction to maximize the corneal reshaping accuracy.

The variable spot scanning (VSS™) feature of the laser, used for CustomVue™ treatments delivers variable diameter ultraviolet pulses to precise locations by the scanning delivery system. The VSS algorithm optimizes the ablation pattern by choosing the best combination of beam diameters and locations to achieve a target shape. VSS expands the laser capability to achieve a broader spectrum of ablation shapes than conventional treatments because the conventional algorithm optimizes only the diameter for myopic treatments and slits for hyperopic treatments.

Conventional STAR™ treatments utilize sphere, cylinder and axis components which are entered manually into the laser by the operator to generate the ablation treatment. CustomVue™ treatment information is generated on the WaveScan® system and transferred to the STAR S4 Excimer Laser System. The transferred information includes patient information, eye and refraction information, image of the eye, and ablation instructions to the laser for beam diameters and the exact locations of the beam on the cornea.

Features and components of the STAR S4 System include:

- Excimer Laser
- Gas Management System
- Laser Beam Delivery System
- Patient Management System
- Computer Control
- VISX Treatment Card

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are currently several other alternatives for the correction of myopia with or without astigmatism:

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 VISX STAR™ Excimer Laser System has been distributed in 47 countries (Argentina, Aruba, Australia, Belgium, Bolivia, Brazil, Bulgaria, Canada, Chile, China, Colombia, Cyprus, Czech Republic, Ecuador, Egypt, Finland, France, Germany, Greece, Hong Kong, Hungary, Israel, Italy, Jamaica, Japan, Korea, Mexico, The Netherlands, New Zealand, Norway, Pakistan, Paraguay, Peru, Philippines, Portugal, Russia, Russia-Kazakhstan, Singapore, Slovak Republic, Spain, Sweden, Switzerland, Taiwan, Turkey, United Kingdom, the United States, and Uruguay). The

VISX STAR Excimer Laser System has not been withdrawn from any country or market for reasons of safety or effectiveness.

The WaveScan WaveFront® System has been distributed in approximately 16 countries (Argentina, Aruba, Brazil, Canada, Colombia, Finland, Germany, Korea, The Netherlands, Portugal, Russia, Spain, Taiwan, United Kingdom, and the United States). The WaveScan WaveFront System has not been withdrawn from any country or market for reasons of safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse reactions 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 21-22 of the clinical study section.

IX. SUMMARY OF PRECLINICAL STUDIES

A. Star™ Excimer Laser System

For a summary of non-clinical studies (excluding hazard analysis and software testing) for the STAR Excimer Laser System, refer to the SSED of the original PMA #P930016.

B. WaveScan Wavefront® System

1. Hazard Analysis

Hazard Analysis and Software Testing was conducted for the combined use of the WaveScan WaveFront System and the STAR Excimer Laser System. Hazard Analysis includes 3 separate fault tree analyses (FTAs): WaveScan 3.00, Topographer Measurement for Custom Contoured Ablation Patterns Method (C-CAP) Treatments and Star software 4.60 version with C-CAP and WavePrint treatment. The WaveScan FTA encompasses the process from patient measurement to the generation of treatment table files. The Topographer FTA encompasses the process from patient measurement to treatment printout. The Star FTA encompasses all previously identified fault and mitigating circumstances identified with any given treatment process. The software test procedures covered all aspects of new software functionality and performance. All test procedures were completed. The Hazard Analysis and software test report indicated no known hazards affecting safety or effectiveness.

2. Testing for Measurement of Refractive Errors of the Eye with WaveScan Wavefront System

Benchtop Study for the measurement of total refractive errors of the eye, including myopia, astigmatism, coma, spherical aberrations, trefoil and other higher order aberrations through sixth order, and Software Testing was conducted for the WaveScan

WaveFront® System. The tests were designed to measure conventional aberration in a VISX model eye and in 8 phase plates with different combinations of Zernike aberrations. The data from this study indicated the VISX WaveScan WaveFront System provides an adequate and reliable measurement of total refractive errors of the eye, including myopia, astigmatism, coma, spherical aberration, trefoil and other higher order aberration through sixth order.

3. Profilometry of Corneal Ablation

A series of preclinical tests were conducted on the VISX STAR™ Excimer Laser System using the VSS™ algorithms before these entered human clinical trials for the first time. The tests involved algorithm simulations, measuring ablation profile on plastic blocks and enucleated porcine eyes. The data obtained from these tests allowed the validation of the VSS algorithm by recording the dioptric power and three dimensional interferometry of ablated plastics, and detailed optical surface profilometry for plastic and porcine eye ablations. The profilometry tests confirmed the validation of the VSS algorithms and provided sufficient evidence to proceed to human studies.

X. SUMMARY OF CLINICAL STUDIES

A clinical study of LASIK treatment, with the VISX STAR Excimer Laser System with Variable Spot Scanning and WaveScan derived ablation targets for the correction of myopia with and without astigmatism, was conducted under IDE G010048. The data from this study is presented as a basis for consideration and approval. Specifically, safety and effectiveness outcomes at 3 months postoperatively were assessed as stability is reached by that time. Outcomes at 6 months postoperatively were also evaluated for confirmation. The IDE study is described in detail as follows:

A. Study Objective

The objectives of this clinical investigation were to:

- Study the effect of LASIK treatment with the VISX STAR Excimer Laser System using Variable Spot Scanning technology with WaveScan derived ablation targets on human subjects
- Determine the feasibility of study procedures
- Define the method of data collection
- Assess the relationship of pre-operative to post-operative wavefront aberrations
- Identify any safety concerns related to VSS™ technology

B. Study Design

This was a prospective, multi-center, open-label, non-randomized study where the primary control was the preoperative state of the treated eye (i.e., comparison of pretreatment and post-treatment visual parameters in the same eye).

C. Inclusion and Exclusion Criteria

Enrollment in the study on the effect of LASIK treatment with the VISX STAR™ Excimer Laser System using Variable Spot Scanning technology with WaveScan® derived ablation targets, was limited to:

- Male or female subjects of any race, and at least 21 years old at the time of the pre-operative examination.
- Subjects who had a best spectacle corrected visual acuity of at least 20/20 in both eyes.
- Eyes that had a manifest refractive error from –0.50 D to –6.00 D, a cylinder component up to -3.00 D, and a maximum manifest spherical equivalent of –6.00 D.
- Eyes that had higher order aberrations that did not exceed 8 μm (peak-to-valley) of wavefront error.
- Eyes that had a minimum pupil size of at least 6.0mm in dim illumination.
- Eyes that had a difference between WaveScan and manifest sphere or cylinder powers (WaveScan power – manifest power) no more minus than 0.50 diopters or no more plus than 0.75 diopters, or whose difference between WaveScan and manifest cylinder axis was greater than 15 degrees (if manifest cylinder power is greater than 0.50 diopters).
- Eyes that had a minimal WavePrint™ Corrected Visual Acuity (WCVA) of at least half the letters (3) on the 20/16 ETDRS acuity line while looking through a plastic (PreVue) lens ablated with the WavePrint treatment.
- Eyes that had a planned treatment not closer than 250 microns from the corneal endothelium.
- Eyes that had a difference between the manifest and cycloplegic refractions (sphere or cylinder) of no more than 0.75 D and no more than 15 degrees (axis) for eyes with cylinder greater than 0.50 D.
- Eyes that demonstrated refractive stability confirmed by a change of less than or equal to 0.50 diopter (sphere and cylinder) at an exam at least 12 months prior to the baseline examination.
- Contact lens wearers who removed soft lenses at least 1 week prior and rigid (Gas permeable and PMMA) lenses at least 2 weeks prior to baseline measurements. At that baseline examination, cycloplegic and manifest refractions as well as corneal topography were obtained on both eyes. If the investigator determined that the topography was within normal limits, surgery was scheduled at least one week after the initial exam, with no contact lens wear permitted prior to the surgery. If on the day of scheduled surgery, for the operative eye, central keratometry readings and manifest refraction spherical equivalents did not differ significantly from the initial exam measurements (by more than 0.50 diopter), surgery proceeded. If the refractive change exceeded this criterion, the surgery was rescheduled after refractive stability was achieved.
- Subjects willing and capable of returning for follow-up examinations for the duration of the study.

Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

- Female subjects who were pregnant, breast-feeding or intended to become pregnant over the course of the study.

- Subjects who used concurrent topical or systemic medications which might impair healing, including but not limited to: antimetabolites, isotretinoin (Accutane®) within 6 months of treatment, and amiodarone hydrochloride (Cordarone®) within 12 months of treatment.

  NOTE: The use of topical or systemic corticosteroids, whether chronic or acute, was deemed to adversely affect healing and subjects using such medication were specifically excluded from eligibility.

- Subjects with a history of any of the following medical conditions, or any other condition that could affect wound healing: collagen vascular disease, autoimmune disease, immunodeficiency diseases, ocular herpes zoster or simplex, endocrine disorders (including, but not limited to unstable thyroid disorders and diabetes), lupus, and rheumatoid arthritis.

  NOTE: The presence of diabetes (either type 1 or 2), regardless of disease duration, severity or control, specifically excluded subjects from eligibility.

- Subjects with a history of prior intraocular or corneal surgery (including cataract extraction), active ophthalmic disease or abnormality (including, but not limited to, blepharitis, recurrent corneal erosion, dry eye syndrome, neovascularization > 1mm from limbus), clinically significant lens opacity, clinical evidence of trauma (including scarring), or with evidence of glaucoma or propensity for narrow angle glaucoma as determined by gonioscopic examination in either eye.

  NOTE: This included any subject with open angle glaucoma, regardless of medication regimen or control. Additionally, any subject with an IOP greater than 21 mm Hg at baseline is specifically excluded from eligibility.

- Subjects with evidence of keratoconus, corneal irregularity, or abnormal videokeratography in either eye.

- Subjects with known sensitivity or inappropriate responsiveness to any of the medications used in the post-operative course.

- Subjects who were participating in any other clinical trial.

D. Study Plan, Patient Assessments, and Efficacy Criteria

All subjects were expected to return for follow-up examinations at 1 and 7 days, and 1, 3, 6, 9, 12, and 24 months postoperatively.

Subjects were permitted to have second eyes (fellow eyes) treated at the same time as the first eye (primary eyes). In addition, subjects were eligible for retreatment no sooner than 3 months after treatment. To qualify for retreatment, eyes must have had a uncorrected visual acuity (UCVA) of 20/32 (or worse) with no significant loss of BSCVA (2 lines or less) with concomitant refractive error. Post retreatment data for these eyes are not included in the safety and effectiveness analysis.

All study treatments were conducted using a 6mm optical zone and an 8mm ablation zone with intention of full correction of emmetropia.

The objective parameters measured during the study were:

- At 24 hours and 1-week- subjective patient symptoms, UCVA, and anterior segment examination by biomicroscopy. Manifest refraction and BSCVA were also conducted on each patient at the 1-week visit. Adverse events, complications, medications and other clinical findings were also noted.

- At 1 and 3 months- visual acuity (uncorrected and best spectacle corrected), manifest refraction, keratometry, videokeratography, WaveScan® measurement, contrast sensitivity, applanation tonometry, slit lamp examination, and a subjective questionnaire. Adverse events, complications, medications and other clinical findings were also noted.

- At 6, 9, and 12 months- visual acuity (uncorrected and best spectacle corrected), manifest refraction, keratometry, corneal videokeratography, WaveScan measurement, contrast sensitivity, applanation tonometry, slit lamp examination, and a subjective questionnaire. After cycloplegia, a refraction, dilated media and fundoscopic examination were performed. Adverse events, complications, medications, and other clinical findings were noted as appropriate. During the 9-month post-operative examination, contrast sensitivity, the subjective questionnaire, cycloplegia and post-cycloplegia testing were not required.

- The primary efficacy variables for this study were: improvement of UCVA, predictability of manifest refraction spherical equivalent (MRSE), and refractive stability.

E. Study Period, Investigational Sites, and Demographics

1. Study Period and Investigational Sites

One hundred and eighty-nine subjects were treated between April 10, 2001 and November 20, 2002. The database for this PMA supplement reflected data collected through December 2, 2002 and included 351 eyes: 189 first eyes and 162 second eyes. There were 6 investigational sites that provided eligible data for analysis.

2. Demographics

Of the 351 treated eyes, 59% (209/351) were from male subjects and 41% (142/351) were from female subjects. Furthermore, 88% (309/351) were from Caucasians, 1% (3/351) were from African Americans, 1% (4/351) were from Asian/Pacific Islanders, and 10% (35/351) were of other races. The right eye was treated in 52% (184/351) of the cases and the left eye was treated in 48% (167/351) of the cases. The mean age of the subjects treated was 35.9 years with a range from 21 to 62. Preoperative patient characteristics that were found to associate with outcomes are discussed in section F.2.f.

Table 1 presents demographic information for the 351 eyes treated.

Table 1:
Demographic Information
All Eyes (N=351)

Category	Classification	n	% Eyes
Gender	Male	209	59.5
	Female	142	40.5
Race	Caucasian	309	88.0
	Asian/Pacific Islander	4	1.1
	African American	3	0.9
	American Indian/Aleut Eskimo	0	0.0
	Other*	35	10.0
Eyes	Right	184	52.4
	Left	167	47.6
CL History	None	171	48.7
	Soft	170	48.4
	RGP/PMMA	10	2.8
Age (in Years)	Average	35.9	
	Standard Deviation	±8.3	
	Minimum	21	
	Maximum	62	

*"Other" classifications of race include: Hispanic, "White-Asian", "Black-White", Arabic, and Thai

F. Data Analysis and Results

1. Preoperative Characteristics

Table 2 contains a summary of the preoperative manifest refractive error stratified by sphere and cylinder, expressed in plus cylinder notation.

Table 2:

Pre-Operative Refractive Error Stratified by Sphere and Cylinder

All Eyes (N=351)

	Cylinder											
	0 D		**0.25 to 0.5D**		**0.75 to 1.0D**		**>1 to ≤ 2 D**		**>2 to ≤ 3 D**		**Total**	
Sphere	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
<0 to ≥ -1 D	4	1.1	2	0.6	0	0.0	0	0.0	0	0.0	6	1.7
<-1 to ≥ -2 D	13	3.7	35	10.0	5	1.4	2	0.6	0	0.0	55	15.7
<-2 to ≥ -3 D	22	6.3	31	8.8	14	4.0	12	3.4	3	0.9	82	23.4
<-3 to ≥ -4 D	12	3.4	29	8.3	10	2.8	12	3.4	12	3.4	75	21.4
<-4 to ≥ -5 D	17	4.8	21	6.0	18	5.1	16	4.6	5	1.4	77	21.9
<-5 to ≥ -6 D	12	3.4	12	3.4	18*	5.1	10*	2.8	4*	1.1	56	16.0
Total	80	22.8	130	37.0	65	18.5	52	14.8	24	6.8	351	100

* Includes six eyes with a pre-operative sphere (*in plus cylinder*) of –6.25 D (n=2), –6.5 D (n=2), –6.75 D (n=1), and –7.0 D (n=1).

2. Postoperative Results

a. Patient Accountability

During the study, accountability was excellent. Of the 351 eyes treated, over 95% accountability was achieved at the 1, 3, 6, 9, and 12-month visits. Table 3 presents subject accountability over time.

The following cohorts were used for analysis:

- Safety and Effectiveness
  -All Eyes
  -Spherical Myopia
  -Astigmatic Myopia
- Stability Analysis
  -Eyes with visits at 1, 3, and 6 months
  -Eyes with two consecutive exams
- Patient Questionnaire - Eyes with completed questionnaires at pre-op, 3 and 6 months

Table 3:

Subject Accountability

All Eyes (N=351)

	1 Month		3 Months		6 Months		9 Months		12 Months	
	n	%	n	%	n	%	n	%	n	%
Available for Analysis	331	94.3	318	90.6	277	78.9	102	29.1	86	24.5
Discontinued^	0	0.0	0	0.0	12	3.4	13	3.7	13	3.7
Missed Visit	2	0.6	4	1.1	9	2.6	5	1.4	4	1.1
Not yet eligible	18	5.1	29	8.3	53	15.1	231	65.8	248	70.7
Lost to Follow-Up	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
% Accountability*	**99.4%**		**98.8%**		**96.9%**		**95.3%**		**95.6%**	

^12 of 13 eyes were discontinued due to retreatment in the study, 1 eye was exited from the study and retreated commercially.
*% Accountability=[Available for Analysis/(enrolled-discontinued-not yet eligible)] x 100

b. Stability of Outcome

Stability of outcome is evaluated both by the cohort of eyes with a refraction at each visit through 6 months as well as by the cohort of eyes with refractions at two consecutive exams, but not every follow-up exam through 12 months.

1) Eyes with exams at 1, 3, and 6 months post-operatively (n=275)

Between the 1 and 3-month visits, 96.4% (265/275) of eyes experienced a change in MRSE of 0.5 diopters or less. This percentage was maintained between the 3 and 6 month visits. Refractive stability is reached at 3 months and confirmed at the 6-month visit. The difference in percentage of eyes with less than or equal to 0.5 D change at 1 and 3 months and 3 and 6 months is not statistically significantly different from zero.

Table 4a presents refractive stability of eyes with visits at 1, 3, and 6 months post-operatively.

Table 4a:

Refractive Stability

Eyes that Underwent 1, 3, and 6 Month Visits

	Between 1 and 3 Months			**Between 3 and 6 Months**		
	All Eyes n=275	**Sphere n=71**	**Astig n=204**	**All Eyes n=275**	**Sphere n=71**	**Astig n=204**
Change in MRSE by ≤ 0.5 D	265	69	196	266	69	197
%	96.4	97.2	96.1	96.7	97.2	96.6
95% CI %	(93.4, 98.2)	(90.2, 99.7)	(92.4, 98.3)	(93.9, 98.5)	(90.2, 99.7)	(93.1, 98.6)
Change in MRSE by ≤ 1.0 D	274	71	203	273	71	202
%	99.6	100	99.5	99.3	100	99.0
95% CI %	(98.0, 100)	(95.9, 100)	(97.3, 100)	(97.4, 99.9)	(95.9, 100)	(96.5, 99.9)
Mean Change in MRSE	-0.04	-0.04	-0.04	0.00	0.00	0.00
SD	0.24	0.24	0.24	0.26	0.24	0.26
95% CI	(-0.07, -0.01)	(-0.10, 0.01)	(-0.07, -0.01)	(-0.03, 0.03)	(-0.05, 0.06)	(-0.04, 0.04)

2) Eyes with two consecutive exams

Between the 1 and 3-month visits, 96.5% (305/316) of eyes experienced a change in MRSE of 0.5 diopters or less, and 99.7% (315/316) of eyes experienced a change in MRSE of 1.0 diopters or less. Refractive stability was maintained between the 3 and 6-month visits with 96.8% (268/277) of eyes experiencing a change in MRSE of 0.5 diopters or less, and 99.3% (275/277) experiencing a change in MRSE of 1.0 diopters or less. Table 4b presents refractive stability over time for those eyes with two consecutive exams, but not every follow up exam.

Table 4b:

Refractive Stability

Eyes with Two Consecutive Exams

	Between 1 and 3 Months			Between 3 and 6 Months			Between 6 and 9 Months			Between 9 and 12 Months		
	All Eyes n=316	Sphere n=79	Astig n=237	All Eyes n=277	Sphere n=71	Astig n=206	All Eyes n=102	Sphere n=29	Astig n=73	All Eyes n=83	Sphere n=22	Astig n=61
Change in MRSE by ≤ 0.5 D	305	77	228	268	69	199	99	28	71	83	22	61
%	96.5	97.5	96.2	96.8	97.2	96.6	97.1	96.6	97.3	100	100	100
95% CI %	(93.9, 98.2)	(91.2, 99.7)	(92.9, 98.2)	(93.9, 98.5)	(90.2, 99.7)	(93.1, 98.6)	(91.6, 99.4)	(82.2, 99.9)	(90.5, 99.7)	(96.5, 100)	(87.3, 100)	(95.2, 100)
Change in MRSE by ≤ 1.0 D	315	79	236	275	71	204	102	29	73	83	22	61
%	99.7	100	99.6	99.3	100	99.0	100	100	100	100	100	100
95% CI %	(98.2, 100)	(96.3, 100)	(97.7, 100)	(97.4, 99.9)	(95.9, 100)	(96.5, 99.9)	(97.1, 100)	90.2, 100)	(96.0, 100)	(96.5, 100)	(87.3, 100)	(95.2, 100)
Mean change in MRSE	-0.05	-0.05	-0.05	0.00	0.00	0.00	0.03	0.03	0.03	-0.03	-0.03	-0.03
SD	±0.25	±0.25	±0.25	±0.26	±0.24	±0.26	±0.23	±0.26	±0.22	±0.24	±0.31	0.21
95% CI	(-0.08, -0.02)	(-0.11, 0.00)	(-0.08, -0.02)	(-0.03, 0.03)	(-0.05, 0.06)	(-0.04, 0.03)	(-0.01, 0.08)	(-0.06, 0.12)	(-0.02, 0.08)	(-0.08, 0.02)	(-0.16, 0.10)	(-0.08, 0.02)

c. Effectiveness Outcomes

The analysis of effectiveness was based on 318 eyes evaluable at the 3-month stability time point. Key effectiveness variables over the course of the study and at the point of stability for all eyes, stratified by diopter of pre-operative manifest spherical equivalent, are presented in Table 5a and Table 6a. Corresponding effectiveness variables for spherical myopia and astigmatic myopia cohorts are presented in Tables 5b to 5c and 6b to 6c, respectively.

Table 5a:

Summary of Key Effectiveness Variables

All Eyes (N=351)

Criteria	1 Month n % (95% CI)	3 Months n % (95% CI)	6 Months n % (95% CI)	9 Months n % (95% CI)	12 Months n % (95% CI)	FDA Targets
	n=331	n=318	n=277	n=102	n=86	
UCVA 20/20 or better	304 91.8 (88.4, 94.6)	281 88.4 (84.3, 91.7)	260 93.9 (90.4, 96.4)	101 99.0 (94.7, 100)	84 97.7 (91.9, 99.7)	
UCVA 20/40 or better	324 97.9 (95.7, 99.1)	306 96.2 (93.5, 98.0)	276 99.6 (98.0, 100)	102 100 (97.1, 100)	86 100 (96.6, 100)	≥85%
MRSE ± 0.50 D	307 92.7 (89.4, 95.3)	277 87.1 (82.9, 90.6)	250 90.3 (86.1, 93.5)	98 96.1 (90.3, 98.9)	80 93.0 (85.4, 97.4)	≥50%
MRSE ± 1.00 D	326 98.5 (96.5, 99.5)	309 97.2 (94.7, 98.7)	275 99.3 (97.4, 99.9)	102 100 (97.1, 100)	86 100 (96.6, 100)	≥75%
MRSE ± 2.00 D	331 100 (99.1, 100)	318 100 (99.1, 100)	277 100 (98.9, 100)	102 100 (97.1, 100)	86 100 (96.6, 100)	

Table 5b:

Summary of Key Effectiveness Variables

Eyes with Spherical Myopia (by manifest) (N=80)

Criteria	1 Month n % (95% CI)	3 Months n % (95% CI)	6 Months n % (95% CI)	9 Months n % (95% CI)	12 Months n % (95% CI)	FDA Targets
	n=80	n=79	n=71	n=29	n=23	
UCVA 20/20 or better	73 91.3 (82.8, 96.4)	72 91.1 (82.6, 96.4)	68 95.8 (88.1, 99.1)	29 100 (90.2, 100)	23 100 (87.8, 100)	
UCVA 20/40 or better	79 98.8 (93.2, 100)	76 96.2 (89.3, 99.2)	71 100 (95.9, 100)	29 100 (90.2, 100)	23 100 (87.8, 100)	≥85%
MRSE ± 0.50 D	74 92.5 (84.4, 97.2)	68 86.1 (76.5, 92.8)	65 91.5 (82.5, 96.8)	28 96.6 (82.2, 99.9)	20 87.0 (66.4, 97.2)	≥50%
MRSE ± 1.00 D	79 98.8 (93.2, 100)	79 100 (96.3, 100)	70 98.6 (92.4, 100)	29 100 (90.2, 100)	23 100 (87.8, 100)	≥75%
MRSE ± 2.00 D	80 100 (96.3, 100)	79 100 (96.3, 100)	71 100 (95.9, 100)	29 100 (90.2, 100)	23 100 (87.8, 100)	

Table 5c:

Summary of Key Effectiveness Variables

Eyes with Astigmatic Myopia (by manifest) (N=271)

Criteria	1 Month n % (95% CI)	3 Months n % (95% CI)	6 Months n % (95% CI)	9 Months n % (95% CI)	12 Months n % (95% CI)	FDA Targets
	n=251	n=239	n=206	n=73	n=63	
UCVA 20/20 or better	231 92.0 (88.0, 95.1)	209 87.4 (82.6, 91.4)	192 93.2 (88.9, 96.2)	72 98.6 (92.6, 100)	61 96.8 (89.0, 99.6)	
UCVA 20/40 or better	245 97.6 (94.9, 99.1)	230 96.2 (93.0, 98.3)	205 99.5 (97.3, 100)	73 100 (96.0, 100)	63 100 (95.4, 100)	≥85%
MRSE ± 0.50 D	233 92.8 (88.9, 95.7)	209 87.4 (82.6, 91.4)	185 89.8 (84.8, 93.6)	70 95.9 (88.5, 99.1)	60 95.2 (86.7, 99.0)	≥50%
MRSE ± 1.00 D	247 98.4 (96.0, 99.6)	230 96.2 (93.0, 98.3)	205 99.5 (97.3, 100)	73 100 (96.0, 100)	63 100 (95.4, 100)	≥75%
MRSE ± 2.00 D	251 100 (98.8, 100)	239 100 (98.8, 100)	206 100 (98.6, 100)	73 100 (96.0, 100)	63 100 (95.4, 100)	

Table 6a:

Summary of Key Effectiveness Variables at Stability Endpoint of 3 Months (Stratified by Pre-Operative MRSE)

All Eyes (N=318)

Criteria	0.0 to –1.0 n/N, % (%CI)	<–1.0 to –2.0 n/N, % (%CI)	<–2.0 to –3.0 n/N, % (%CI)	<–3.0 to –4.0 n/N, % (%CI)	<–4.0 to –5.0 n/N, % (%CI)	<–5.0 to –6.0 n/N, % (%CI)	Cum Total n/N, % (%CI)
	n=10	n=67	n=80	n=71	n=58	n=32	N=318
UCVA 20/20 or better	9 90.0 (55.5, 99.7)	65 97.0 (89.6, 99.6)	72 90.0 (81.2, 95.6)	65 91.5 (82.5, 96.8)	47 81.0 (68.6, 90.1)	23 71.9 (53.3, 86.3)	281 88.4 (84.3, 91.7)
UCVA 20/40 or better	10 100 (74.1, 100)	67 100 (95.6, 100)	78 97.5 (91.3, 99.7)	69 97.2 (90.2, 99.7)	54 93.1 (83.3, 98.1)	28 87.5 (71.0, 96.5)	306 96.2 (93.5, 98.0)
MRSE ± 0.50 D	10 100 (74.1, 100)	64 95.5 (87.5, 99.1)	76 95.0 (87.7, 98.6)	60 84.5 (74.0, 92.0)	47 81.0 (68.6, 90.1)	20 62.5 (43.7, 78.9)	277 87.1 (82.9, 90.6)
MRSE ± 1.00 D	10 100 (74.1, 100)	67 100 (95.6, 100)	79 98.8 (93.2, 100)	70 98.6 (92.4, 100)	55 94.8 (85.6, 98.9)	28 87.5 (71.0, 96.5)	309 97.2 (94.7, 98.7)
MRSE ± 2.00 D	10 100 (74.1, 100)	67 100 (95.6, 100)	80 100 (96.3, 100)	71 100 (95.9, 100)	58 100 (95.0, 100)	32 100 (91.1, 100)	318 100 (99.1, 100)

Table 6b:
Summary of Key Effectiveness Variables at Stability Endpoint of 3 Months (Stratified by Pre-Operative MRSE)
Eyes with Spherical Myopia (by manifest) N=79

Criteria	0.0 to –1.0 n/N, % (%CI)	<–1.0 to –2.0 n/N, % (%CI)	<–2.0 to –3.0 n/N, % (%CI)	<–3.0 to –4.0 n/N, % (%CI)	<–4.0 to –5.0 n/N, % (%CI)	<–5.0 to –6.0 n/N, % (%CI)	Cum Total n/N, % (%CI)
	n=4	n=13	n=21	n=12	n=17	n=12	N=79
UCVA 20/20 or better	4 100 (47.3, 100)	12 92.3 (64.0, 99.8)	19 90.5 (69.6, 98.8)	12 100 (77.9, 100)	16 94.1 (71.3, 99.9)	9 75.0 (42.8, 94.5)	72 91.1 (82.6, 96.4)
UCVA 20/40 or better	4 100 (47.3, 100)	13 100 (79.4, 100)	20 95.2 (76.2, 99.9)	12 100 (77.9, 100)	16 94.1 (71.3, 99.9)	11 91.7 (61.5, 99.8)	76 96.2 (89.3, 99.2)
MRSE ± 0.50 D	4 100 (47.3, 100)	12 92.3 (64.0, 99.8)	19 90.5 (69.6, 98.8)	9 75.0 (42.8, 94.5)	16 94.1 (71.3, 99.9)	8 66.7 (34.9, 90.1)	68 86.1 (76.5, 92.8)
MRSE ± 1.00 D	4 100 (47.3, 100)	13 100 (79.4, 100)	21 100 (86.7, 100)	12 100 (77.9, 100)	17 100 (83.8, 100)	12 100 (77.9, 100)	79 100 (96.3, 100)
MRSE ± 2.00 D	4 100 (47.3, 100)	13 100 (79.4, 100)	21 100 (86.7, 100)	12 100 (77.9, 100)	17 100 (83.8, 100)	12 100 (77.9, 100)	79 100 (96.3, 100)

Table 6c:
Summary of Key Effectiveness Variables at Stability Endpoint of 3 Months (Stratified by Pre-Operative MRSE)
Eyes with Astigmatic Myopia (by manifest) N=239

Criteria	0.0 to –1.0 n/N, % (%CI)	<–1.0 to –2.0 n/N, % (%CI)	<–2.0 to –3.0 n/N, % (%CI)	<–3.0 to –4.0 n/N, % (%CI)	<–4.0 to –5.0 n/N, % (%CI)	<–5.0 to –6.0 n/N, % (%CI)	Cum Total n/N, % (%CI)
	n=6	n=54	n=59	n=59	n=41	n=20	N=239
UCVA 20/20 or better	5 83.3 (35.9, 99.6)	53 98.1 (90.1, 100)	53 89.8 (79.2, 96.2)	53 89.8 (79.2, 96.2)	31 75.6 (59.7, 87.6)	14 70.0 (45.7, 88.1)	209 87.4 (82.6, 91.4)
UCVA 20/40 or better	6 100 (60.7, 100)	54 100 (94.6, 100)	58 98.3 (90.9, 100)	57 96.6 (88.3, 99.6)	38 92.7 (80.1, 98.5)	17 85.0 (62.1, 96.8)	230 96.2 (93.0, 98.3)
MRSE ± 0.50 D	6 100 (60.7, 100)	52 96.3 (87.3, 99.5)	57 96.6 (88.3, 99.6)	51 86.4 (75.0, 94.0)	31 75.6 (59.7, 87.6)	12 60.0 (36.1, 80.9)	209 87.4 (82.6, 91.4)
MRSE ± 1.00 D	6 100 (60.7, 100)	54 100 (94.6, 100)	58 98.3 (90.9, 100)	58 98.3 (90.9, 100)	38 92.7 (80.1, 98.5)	16 80.0 (56.3, 94.3)	230 96.2 (93.0, 98.3)
MRSE ± 2.00 D	6 100 (60.7, 100)	54 100 (94.6, 100)	59 100 (95.0, 100)	59 100 (95.0, 100)	41 100 (93.0, 100)	20 100 (86.1, 100)	239 100 (98.8, 100)

d. Higher Order Aberrations

Although the WaveScan WaveFront® System measures the refractive error and wavefront aberrations of the human eyes, including myopia, hyperopia, astigmatism, coma, spherical aberration, trefoil, and other higher order aberrations through sixth order, in the clinical study for this PMA, the average higher order aberration did not decrease after CustomVue™ treatment.

e. Safety Outcomes

The analysis of safety was based on all 351 eyes. The key safety outcomes for all eyes in this study are presented in Tables 7a and 8a. Corresponding safety variables for spherical myopia and astigmatic myopia cohorts are presented in Tables 7b to 7c and 8b to 8c, respectively.

Table 9 presents the results of the contrast sensitivity analysis. Adverse Events are reported in Table 10a and Complications in Table 10b. Overall, the device was deemed reasonably safe.

Table 7a:

Summary of Key Safety Variables

All Eyes (N=351)

Criteria	1 Month n % (95% CI)	3 Months n % (95% CI)	6 Months n % (95% CI)	9 Months n % (95% CI)	12 Months n % (95% CI)	FDA Targets
	n=331	n=318	N=277	n=102	n=86	
Loss of ≥ 2 lines BSCVA	0 0.0 (0.0, 0.9)	1 0.3 (0.0, 1.7)	0 0.0 (0.0, 1.1)	0 0.0 (0.0, 2.9)	0 0.0 (0.0, 3.4)	
Loss of > 2 lines BSCVA	0 0.0 (0.0, 0.9)	0 0.0 (0.0, 0.9)	0 0.0 (0.0, 1.1)	0 0.0 (0.0, 2.9)	0 0.0 (0.0, 3.4)	<5%
BSCVA worse than 20/25	0 0.0 (0.0, 0.9)	1 0.3 (0.0, 1.7)	0 0.0 (0.0, 1.1)	0 0.0 (0.0, 2.9)	0 0.0 (0.0, 3.4)	
BSCVA worse than 20/40	0 0.0 (0.0, 0.9)	0 0.0 (0.0, 0.9)	0 0.0 (0.0, 1.1)	0 0.0 (0.0, 2.9)	0 0.0 (0.0, 3.4)	

Table 7b:

Summary of Key Safety Variables

***Eyes with Spherical Myopia (by manifest)* (N=80)**

Criteria	1 Month n % (95% CI)	3 Months n % (95% CI)	6 Months n % (95% CI)	9 Months n % (95% CI)	12 Months n % (95% CI)	FDA Targets
	n=80	n=79	n=71	n=29	n=23	
Loss of ≥ 2 lines BSCVA	0 0.0 (0.0, 3.7)	0 0.0 (0.0, 3.7)	0 0.0 (0.0, 4.1)	0 0.0 (0.0, 9.8)	0 0.0 (0.0, 12.2)	
Loss of > 2 lines BSCVA	0 0.0 (0.0, 3.7)	0 0.0 (0.0, 3.7)	0 0.0 (0.0, 4.1)	0 0.0 (0.0, 9.8)	0 0.0 (0.0, 12.2)	<5%
BSCVA worse than 20/25	0 0.0 (0.0, 3.7)	0 0.0 (0.0, 3.7)	0 0.0 (0.0, 4.1)	0 0.0 (0.0, 9.8)	0 0.0 (0.0, 12.2)	
BSCVA worse than 20/40	0 0.0 (0.0, 3.7)	0 0.0 (0.0, 3.7)	0 0.0 (0.0, 4.1)	0 0.0 (0.0, 9.8)	0 0.0 (0.0, 12.2)	
Increase > 2 D cylinder	0 0.0 (0.0, 3.7)	0 0.0 (0.0, 3.7)	0 0.0 (0.0, 4.1)	0 0.0 (0.0, 9.8)	0 0.0 (0.0, 12.2)	<5%

Table 7c:

Summary of Key Safety Variables

Eyes with Astigmatic Myopia (by manifest) (N=271)

Criteria	1 Month n % (95% CI)	3 Months n % (95% CI)	6 Months n % (95% CI)	9 Months n % (95% CI)	12 Months n % (95% CI)	FDA Targets
	n=251	n=239	n=206	n=73	n=63	
Loss of ≥ 2 lines BSCVA	0 0.0 (0.0, 1.2)	1 0.4 (0.0, 2.3)	0 0.0 (0.0, 1.4)	0 0.0 (0.0, 4.0)	0 0.0 (0.0, 4.6)	
Loss of > 2 lines BSCVA	0 0.0 (0.0, 1.2)	0 0.0 (0.0, 1.2)	0 0.0 (0.0, 1.4)	0 0.0 (0.0, 4.0)	0 0.0 (0.0, 4.6)	<5%
BSCVA worse than 20/25	0 0.0 (0.0, 1.2)	1 0.4 (0.0, 2.3)	0 0.0 (0.0, 1.4)	0 0.0 (0.0, 4.0)	0 0.0 (0.0, 4.6)	
BSCVA worse than 20/40	0 0.0 (0.0, 1.2)	0 0.0 (0.0, 1.2)	0 0.0 (0.0, 1.4)	0 0.0 (0.0, 4.0)	0 0.0 (0.0, 4.6)	

Table 8a:

Summary of Key Safety Variables at Stability Endpoint of 3 Months (Stratified by Pre-Operative MRSE)

All Eyes (N=318)

Criteria	0.0 to –1.0 n/N, % (%CI)	<–1.0 to –2.0 n/N, % (%CI)	<–2.0 to –3.0 n/N, % (%CI)	<–3.0 to –4.0 n/N, % (%CI)	<–4.0 to –5.0 n/N, % (%CI)	<–5.0 to –6.0 n/N, % (%CI)	Cum Total n/N, % (%CI)
N=318	**n=10**	**n=67**	**n=80**	**n=71**	**n=58**	**n=32**	**n=318**
Loss of ≥ 2 lines BSCVA	0 0.0 (0.0, 25.9)	0 0.0 (0.0, 4.4)	1 1.3 (0.0, 6.8)	0 0.0 (0.0, 4.1)	0 0.0 (0.0, 5.0)	0 0.0 (0.0, 8.9)	1 0.3 (0.0, 1.7)
Loss of > 2 lines BSCVA	0 0.0 (0.0, 25.9)	0 0.0 (0.0, 4.4)	0 0.0 (0.0, 3.7)	0 0.0 (0.0, 4.1)	0 0.0 (0.0, 5.0)	0 0.0 (0.0, 8.9)	0 0.0 (0.0, 0.9)
BSCVA worse than 20/25	0 0.0 (0.0, 25.9)	0 0.0 (0.0, 4.4)	1 1.3 (0.0, 6.8)	0 0.0 (0.0, 4.1)	0 0.0 (0.0, 5.0)	0 0.0 (0.0, 8.9)	1 0.3 (0.0, 1.7)
BSCVA worse than 20/40	0 0.0 (0.0, 25.9)	0 0.0 (0.0, 4.4)	0 0.0 (0.0, 3.7)	0 0.0 (0.0, 4.1)	0 0.0 (0.0, 5.0)	0 0.0 (0.0, 8.9)	0 0.0 (0.0, 0.9)

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Table 8b:
Summary of Key Safety Variables at Stability Endpoint of 3 Months (Stratified by Pre-Operative MRSE)
Eyes with Spherical Myopia (by manifest) N=79

Criteria	0.0 to –1.0 n/N, % (%CI)	<–1.0 to –2.0 n/N, % (%CI)	<–2.0 to –3.0 n/N, % (%CI)	<–3.0 to –4.0 n/N, % (%CI)	<–4.0 to –5.0 n/N, % (%CI)	<–5.0 to –6.0 n/N, % (%CI)	Cum Total n/N, % (%CI)
N=79	n=4	n=13	n=21	n=12	n=17	n=12	n=79
Loss of ≥ 2 lines BSCVA	0 0.0 (0.0, 52.7)	0 0.0 (0.0, 20.6)	0 0.0 (0.0, 13.3)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 16.2)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 3.7)
Loss of > 2 lines BSCVA	0 0.0 (0.0, 52.7)	0 0.0 (0.0, 20.6)	0 0.0 (0.0, 13.3)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 16.2)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 3.7)
BSCVA worse than 20/25	0 0.0 (0.0, 52.7)	0 0.0 (0.0, 20.6)	0 0.0 (0.0, 13.3)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 16.2)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 3.7)
BSCVA worse than 20/40	0 0.0 (0.0, 52.7)	0 0.0 (0.0, 20.6)	0 0.0 (0.0, 13.3)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 16.2)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 3.7)
Increase > 2 D cylinder	0 0.0 (0.0, 52.7)	0 0.0 (0.0, 20.6)	0 0.0 (0.0, 13.3)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 16.2)	0 0.0 (0.0, 22.1)	0 0.0 (0.0, 3.7)

Table 8c:
Summary of Key Safety Variables at Stability Endpoint of 3 Months (Stratified by Pre-Operative MRSE)
Eyes with Astigmatic Myopia (by manifest) N=239

Criteria	0.0 to –1.0 n/N, % (%CI)	<–1.0 to –2.0 n/N, % (%CI)	<–2.0 to –3.0 n/N, % (%CI)	<–3.0 to –4.0 n/N, % (%CI)	<–4.0 to –5.0 n/N, % (%CI)	<–5.0 to –6.0 n/N, % (%CI)	Cum Total n/N, % (%CI)
N=239	N=6	n=54	n=59	n=59	n=41	n=20	N=239
Loss of ≥ 2 lines BSCVA	0 0.0 (0.0, 39.3)	0 0.0 (0.0, 5.4)	1 1.7 (0.0, 9.1)	0 0.0 (0.0, 5.0)	0 0.0 (0.0, 7.0)	0 0.0 (0.0, 13.9)	1 0.4 (0.0, 2.3)
Loss of > 2 lines BSCVA	0 0.0 (0.0, 39.3)	0 0.0 (0.0, 5.4)	0 0.0 (0.0, 5.0)	0 0.0 (0.0, 5.0)	0 0.0 (0.0, 7.0)	0 0.0 (0.0, 13.9)	0 0.0 (0.0, 1.2)
BSCVA worse than 20/25	0 0.0 (0.0, 39.3)	0 0.0 (0.0, 5.4)	1 1.7 (0.0, 9.1)	0 0.0 (0.0, 5.0)	0 0.0 (0.0, 7.0)	0 0.0 (0.0, 13.9)	1 0.4 (0.0, 2.3)
BSCVA worse than 20/40	0 0.0 (0.0, 39.3)	0 0.0 (0.0, 5.4)	0 0.0 (0.0, 5.0)	0 0.0 (0.0, 5.0)	0 0.0 (0.0, 7.0)	0 0.0 (0.0, 13.9)	0 0.0 (0.0, 1.2)

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Table 9 presents the results of the contrast sensitivity analysis. When analyzed using the paired-t for the means, the difference of the means from Pre-Op to 1, 3, and 6 months consistently demonstrated a statistically significant improvement in all three test conditions (dim with and without glare and bright without glare).

Table 9

Contrast Sensitivity

All Eyes (N=351)

	Pre-Op				Change from Pre-Op to 1 Months				Change from Pre-Op to 3 Months				Change from Pre-Op to 6 Months				Change from Pre-Op to 12 Months			
CPD	3	6	12	18	3	6	12	18	3	6	12	18	3	6	12	18	3	6	12	18
Dim w/ Glare	n=351				n=329^				n=318				n=277				n=86			
Mean	1.54	1.56	1.04	0.61	0.04	0.10	0.14	0.15	0.05	0.10	0.12	0.14	0.07	0.12	0.17	0.17	0.02	0.04	0.11	0.13
(SE)	0.012	0.017	0.021	0.021	0.013	0.019	0.024	0.025	0.013	0.019	0.024	0.024	0.016	0.020	0.025	0.026	0.024	0.036	0.036	0.041
P Value* ≤					**0.002**	**0.000**	**0.000**	**0.000**	**0.001**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	0.419	0.236	**0.004**	**0.002**
Dim w/o Glare	n=351				n=329^				n=318				n=277				n=86			
Mean	1.60	1.69	1.20	0.74	0.04	0.05	0.10	0.11	0.05	0.04	0.08	0.07	0.06	0.06	0.16	0.13	0.04	0.01	0.01	0.04
(SE)	0.011	0.013	0.020	0.021	0.012	0.014	0.022	0.024	0.013	0.016	0.024	0.024	0.013	0.016	0.024	0.025	0.024	0.029	0.036	0.040
P Value* ≤					**0.003**	**0.000**	**0.000**	**0.000**	**0.000**	**0.010**	**0.000**	**0.003**	**0.000**	**0.000**	**0.000**	**0.000**	0.101	0.787	0.762	0.274
Bright w/o Glare	n=351				n=329^				n=318				n=277				n=86			
Mean	1.76	1.97	1.65	1.22	0.02	0.02	0.04	0.03	0.04	0.04	0.04	0.03	0.05	0.05	0.06	0.04	0.02	0.02	0.02	0.02
(SE)	0.009	0.010	0.011	0.013	0.010	0.011	0.013	0.014	0.010	0.013	0.014	0.015	0.011	0.013	0.014	0.017	0.020	0.022	0.024	0.033
P Value* ≤					**0.012**	**0.025**	**0.003**	**0.043**	**0.000**	**0.002**	**0.004**	**0.023**	**0.000**	**0.000**	**0.000**	**0.013**	0.321	0.328	0.373	0.637

*Two tailed paired t test for the means.
^Two eyes of 1 subject did not undergo contrast sensitivity testing at the 1-month visit

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e. Safety Outcomes (continued)

Table 10a presents a summary of adverse events that occurred at the 1, 3, 6, 9, and 12-month visits. The benchmark for each adverse event is a rate of less than 1 % per type of event.

Table 10a:
Summary of Adverse Events
All Eyes (N=351)

	1 Month (n=331)		3 Months (n=318)		6 Months (n=277)		9 Months (n=102)		12 Months (n=86)	
	n	%	n	%	n	%	n	%	n	%
Corneal Infiltrate/Ulcer	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Corneal epithelial defect involving the keratectomy at 1 month or later	2	0.6	0	0.0	0	0.0	0	0.0	0	0.0
Corneal edema at 1 month or later (specify "flap" or "bed" or both)	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Epithelium in the interface with loss of 2 or more lines of BSCVA	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Miscreated Flap	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
Melting of the flap (LASIK only)	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Uncontrolled IOP >10 mm Hg or any reading > 25 mm Hg	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Late onset of haze beyond 6 months with loss of 2 lines (10 letters) or more BSCVA	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Decrease in BSCVA of > 10 letter not due to irregular astigmatism as shown by hard contact lens refraction, at 6 months or later	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Retinal Detachment	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Retinal Vascular Accidents	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Prior to the 1 month visit, five eyes of four subjects developed diffuse lamellar keratitis (DLK) on post-operative day 1 and day 7. Each case resolved within 8 days of onset with no loss of vision. Additionally, one eye experienced a corneal erosion at 18 months post-operatively. This case resolved within 7 days of onset with no loss of vision.

e. Safety Outcomes (continued)

Table 10b presents a summary of complications reported before 1 month, and at the 1, 3, 6, 9, and 12 month visits.

Table 10b:
Summary of Complications
All Eyes (N=351)

	<1 Month (n=351)		1 Month (n=331)		3 Months (n=318)		6 Months (n=277)		9 Months (n=102)		12 Months (n=86)	
	n	%	n	%	n	%	n	%	n	%	n	%
Misaligned flap	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Corneal edema between 1 week and 1 month	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Corneal abrasion	5	1.4	0	0.00	0	0.00	0	0.0	0	0.0	0	0.0
Peripheral corneal epithelial defect at 1 month or later			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Epithelium in the interface	1	0.3	1	0.3	2	0.6	1	0.4	0	0.0	0	0.0
Foreign body sensation at 1 month or later			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Pain at 1 month or later			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Diplopia (ghost images)	5	1.4	2	0.6	2	0.6	2	0.7	0	0.0	0	0.0

f. Retreatment

Twelve eyes of 10 subjects (12/351 or 3.4%) underwent wavefront-guided LASIK retreatment due to initial undercorrection. Twelve retreatments are insufficient to yield clinically useful information; however, caution should be taken to assure refractive stability before performing additional procedures.

g. Factors Associated with Outcomes

To evaluate the consistency of results and effect of treatment by study site and baseline characteristics, results at 3 months post-operatively were analyzed. The key safety and effectiveness variables were compared to FDA target percentages to determine if the results were significantly different.

No eye had a BSCVA loss of > 2 lines and no eye had a BSCVA worse than 20/40, so there were no detectable differences between study sites and baseline characteristics relative to safety outcomes.

For each effectiveness criterion, comparisons between the actual and target outcomes (MRSE ± 0.50, MRSE ± 1.00, UCVA 20/40 or better) were made using a chi-square goodness-of-fit test. A Mantel-Haenszel one degree of freedom chi-square test was used to compare the observed percentages across categories. Those p-values are used to identify situations where there are differences between categories.

Specifically, the analyses of effect included: sex, race, investigational site, age group, pre-operative contact lens use, pre-operative MRSE, laser room humidity, laser room temperature and surgeon. In these analyses, statistically significant differences in outcomes were identified by comparing actual outcomes with FDA target values (MRSE ± 0.50 / 50%, MRSE ± 1.00 / 75%, UCVA 20/40 or better / 85%). Throughout all of these analyses, there are only three cases where the observed value does not meet the target value. For the measure UCVA 20/40 or better (target = 85%), one site had an observed value of 81%. One surgeon at that site had an observed value of 78% for UCVA 20/40 or better. For the contact lens group of GP/PMMA, five eyes (83%) had a UCVA 20/40 or better. None of these three values is statistically significantly worse than the target value ($p = 0.4626$, 0.2249, and 0.9090 respectively).

h. Patient Satisfaction

Patients were asked to complete a questionnaire for each eye to evaluate vision pre-operatively and post-operatively. Upon completion of the questionnaire, both the patient and the investigator reviewed the form. To be included in the analysis, a pre-operative questionnaire had to have been completed. While the point of stability occurred at 3 months, patient questionnaire responses are presented pre-operatively and at 3 and 6 months post-operatively. Tables 11a and 11b presents a summary of questionnaire responses and patient symptoms.

Table 11a:

Summary of Questionnaire Responses

All Eyes (N=332*)

	Very Satisfied			Satisfied			Not Sure			Somewhat Dissatisfied			Very Dissatisfied			Not Reported		
	Pre n=332	3M n=297	6M n=258	Pre n=332	3M n=297	6M n=258	Pre n=332	3M n=258	6M n=262	Pre n=332	3M n=297	6M n=258	Pre n=332	3M n=297	6M n=258	Pre n=332	3M n=297	6M n=258
	n % 95%CI	n % 95%CI	n % 95% CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n	n	n
Sharpness and Clarity	87 26.2 (21.6, 31.3)	177 59.6 (53.8, 65.2)	171 66.3 (60.2, 72.0)	205 61.7 (56.3, 67.0)	80 26.9 (22.0, 32.4)	68 26.4 (21.1, 32.2)	10 3.0 (1.5, 5.5)	14 4.7 (2.6, 7.8)	6 2.3 (0.9, 5.0)	29 8.7 (5.9, 12.3)	22 7.4 (4.7, 11.0)	11 4.3 (2.1, 7.5)	1 0.3 (0.0, 1.7)	4 1.3 (0.4, 3.4)	2 0.8 (0.1, 2.8)	0	0	0
Overall Visual Comfort	105 31.6 (26.7, 36.9)	205 69.0 (63.4, 74.2)	178 69.0 (63.0, 74.6)	157 47.3 (41.8, 52.8)	78 26.3 (21.3, 31.7)	68 26.4 (21.1, 32.2)	15 4.5 (2.6, 7.3)	9 3.0 (1.4, 5.7)	6 2.3 (0.9, 5.0)	48 14.5 (10.9, 18.7)	4 1.3 (0.4, 3.4)	4 1.6 (0.4, 3.9)	7 2.1 (0.9, 4.3)	1 0.3 (0.0, 1.9)	2 0.8 (0.1, 2.8)	0	0	0
Consistency of Vision	90 27.1 (22.4, 32.2)	156 52.5 (46.7, 58.3)	147 57.0 (50.7, 63.1)	190 57.2 (51.7, 62.6)	106 35.7 (30.2, 41.4)	90 34.9 (29.1, 41.0)	14 4.2 (2.3, 7.0)	23 7.7 (5.0, 11.4)	13 5.0 (2.7, 8.5)	38 11.4 (8.2, 15.4)	10 3.4 (1.6, 6.1)	8 3.1 (1.3, 6.0)	0 0.0 (0.0, 0.9)	2 0.7 (0.1, 2.4)	0 0.0 (0.0, 1.2)	0	0	0
Daylight Vision	108 32.5 (27.5, 37.9)	197 66.3 (60.6, 71.7)	189 73.3 (67.4, 78.6)	205 61.7 (56.3, 67.0)	82 27.6 (22.6, 33.1)	59 22.9 (17.9, 28.5)	6 1.8 (0.7, 3.9(	2 0.7 (0.1, 2.4)	5 1.9 (0.6, 4.5)	13 3.9 (2.1, 6.6)	13 4.4 (2.4, 7.4)	5 1.9 (0.6, 4.5)	0 0.0 (0.0, 0.9)	3 1.0 (0.2, 2.9)	0 0.0 (0.0, 1.2)	0	0	0
Night Vision	39 11.7 (8.5, 15.7)	122 41.1 (35.4, 46.9)	114 44.2 (38.0, 50.5)	176 53.0 47.5, 58.5)	117 39.4 (33.8, 45.2)	105 40.7 (34.6, 47.0)	33 9.9 (6.9, 13.7)	18 6.1 (3.6, 9.4)	16 6.2 (3.6, 9.9)	80 24.1 (19.6, 29.1)	34 11.4 (8.1, 15.6)	19 7.4 (4.5, 11.3)	4 1.2 (0.3, 3.1)	6 2.0 (0.7, 4.3)	4 1.6 (0.4, 3.9)	0	0	0
Night Vision with Glare	25 7.5 (4.9, 10.9)	98 33.0 (27.7, 38.7)	91 35.3 (29.4, 41.4)	174 52.4 (46.9, 57.9)	134 45.1 (39.4, 51.0)	118 45.7 (39.5, 52.0)	37 11.1 (8.0, 15.0)	29 9.8 (6.6, 13.7)	29 11.2 (7.7, 15.7)	81 24.4 (19.9, 29.4)	30 10.1 (6.9, 14.1)	16 6.2 (3.6, 9.9)	15 4.5 (2.6, 7.3)	6 2.0 (0.7, 4.3)	4 1.6 (0.4, 3.9)	0	0	0

*The protocol did not include a provision for patient questionnaires at the time the first 19 patients (19 eyes) were enrolled and treated in the study.

Table 11b:
Summary of Patient Symptoms
All Eyes (N=332*)

	Never			Rarely			Sometimes			Often			Always			Not Reported		
	Pre n=332	3M n=297	6M n=258	Pre n=332	3M n=297	6M n=258	Pre n=332	3M n=297	6M n=258	Pre n=332	3M n=297	6M n=258	Pre n=332	3M n=297	6M n=258	Pre n=332	3M n=297	6M n=258
	n % 95%CI	n % 95%CI	n % 95% CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n % 95%CI	n	n	n
Dryness	90 27.1 (22.4, 32.2)	45 15.2 (11.3, 19.7)	44 17.1 (12.7, 22.2)	140 42.2 (36.8, 47.7)	86 29.0 (23.9, 34.5)	111 43.0 (36.9, 49.3)	81 24.4 (19.9, 29.4)	132 44.4 (38.7, 50.3)	79 30.6 (25.1, 36.6)	19 5.7 (3.5, 8.8)	28 9.4 (6.4, 13.3)	15 5.8 (3.3, 9.4)	2 0.6 (0.1, 2.2)	6 2.0 (0.7, 4.3)	9 3.5 (1.6, 6.5)	0	0	0
Blurry Vision	124 37.3 (32.1, 42.8)	96 32.3 (27.0, 38.0)	83 32.2 (26.5, 38.2)	136 41.0 (35.6, 46.5)	104 35.0 (29.6, 40.7)	119 46.1 (39.9, 52.4)	65 19.6 (15.4, 24.3)	80 26.9 (22.0, 32.4)	52 20.2 (15.4, 25.6)	2 0.6 (0.1, 2.2)	12 4.0 (2.1, 7.0)	2 0.8 (0.1, 2.8)	5 1.5 (0.5, 3.5)	5 1.7 (0.5, 3.9)	2 0.8 (0.1, 2.8)	0	0	0
Fluctuation of vision	149 44.9 (39.4, 50.4)	101 34.0 (28.6, 39.7)	101 39.1 (33.2, 45.4)	133 40.1 (34.7, 45.6)	125 42.1 (36.4, 47.9)	98 38.0 (32.0, 44.2)	42 12.7 (9.3, 16.7)	58 19.5 (15.2, 24.5)	51 19.8 (15.1, 25.2)	8 2.4 (1.0, 4.7)	9 3.0 (1.4, 5.7)	6 2.3 (0.9, 5.0)	0 0.0 (0.0, 0.9)	4 1.3 (0.4, 3.4)	2 0.8 (0.1, 2.8)	0	0	0
Glare	102 30.7 (25.8, 36.0)	123 41.4 (35.8, 47.2)	98 38.0 (32.0, 44.2)	135 40.7 (35.3, 46.2)	116 39.1 (33.5, 44.9)	115 44.6 (38.4, 50.9)	87 26.2 (21.6, 31.3)	46 15.5 (11.6, 20.1)	34 13.2 (9.3, 17.9)	8 2.4 (1.0, 4.7)	8 2.7 (1.2, 5.2)	10 3.9 (1.9, 7.0)	0 0.0 (0.0, 0.9)	4 1.3 (0.4, 3.4)	1 0.4 (0.0, 2.1)	0	0	0
Halos Around Lights	137 41.3 (35.9, 46.8)	121 40.7 (35.1, 46.6)	106 41.1 (35.0, 47.4)	110 33.1 (28.1, 38.5)	90 30.3 (25.1, 35.9)	89 34.5 (28.7, 40.6)	67 20.2 (16.0, 24.9)	65 21.9 (17.3, 27.0)	45 17.4 (13.0, 22.6)	9 2.7 (1.2, 5.1)	15 5.1 (2.9, 8.2)	11 4.3 (2.1, 7.5)	9 2.7 (1.2, 5.1)	6 2.0 (0.7, 4.3)	7 2.7 (1.1, 5.5)	0	0	0
Difficulty at Night W/Glare	78 23.5 (19.0, 28.4)	102 34.3 (29.0, 40.0)	92 35.7 (29.8, 41.8)	117 35.2 (30.1, 40.6)	105 35.4 (29.9, 41.1)	91 35.3 (29.4, 41.4)	93 28.0 (23.2, 33.2)	65 21.9 (17.3, 27.0)	59 22.9 (17.9, 28.5)	31 9.3 (6.4, 13.0)	17 5.7 (3.4, 9.0)	14 5.4 (3.0, 8.9)	13 3.9 (2.1, 6.6)	8 2.7 (1.2, 5.2)	2 0.8 (0.1, 2.8)	0	0	0
Ghost or Double Images	260 78.3 (73.5, 82.6)	228 76.8 (71.5, 81.5)	200 77.5 (71.9, 82.5)	62 18.7 (14.6, 23.3)	53 17.8 (13.7, 22.7)	36 14.0 (10.0, 18.8)	8 2.4 (1.0, 4.7)	7 2.4 (1.0, 4.8)	19 7.4 (4.5, 11.3)	0 0.0 (0.0, 0.9)	7 2.4 (1.0, 4.8)	1 0.4 (0.0, 2.1)	2 0.6 (0.1, 2.2)	2 0.7 (0.1, 2.4)	2 0.8 (0.1, 2.8)	0	0	0

*The protocol did not include a provision for patient questionnaires at the time the first 19 patients (19 eyes) were enrolled and treated in the study.

i. Device Failure

There were no reported device failures during this study.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

Preclinical studies completed for this device did not raise any new safety or effectiveness concerns. Clinical studies demonstrated that safety and effectiveness parameters fell within acceptable FDA criteria providing reasonable assurance that the device is safe and effective, when used in accordance with the directions for use, for wavefront-guided LASIK treatment with the VISX STAR S4™ Excimer Laser System with Variable Spot Scanning and WaveScan® derived ablation targets for the correction of myopia with and without astigmatism.

XII. PANEL RECOMMENDATION

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.

XIII. CDRH DECISION

CDRH issued an approval order on May 23, 2003.

XIV. APPROVAL SPECIFICATIONS

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