Summary of Safety and Effectiveness Data

I. GENERAL INFORMATION

Device Generic Name:	Ophthalmic Excimer Laser System
Device Trade Name:	Nidek EC-5000 Excimer Laser System
Device ProCode:	LZS
Applicant's Name and Address:	Nidek Co. LTD 34-14 Maehama Hiroishi-cho Gamagori, Aichi Japan 443-0038
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P970053/S011
Date of FDA Notice of Approval:	September 30, 2013

The Nidek EC-5000 CX Excimer Laser System was originally approved on December 17, 1998 under PMA P970053 for the limited indication for myopic photorefractive keratectomy (PRK) uncomplicated by astigmatism (≤ -0.75 D) in patients 21 years of age or older with -0.75 to -13.0 D of myopia whose refractive change for one year prior to treatment is within ±0.5 D for low myopia (≤ -7.0 D MRSE) or within ± 1.0 D for high myopia (> -7.0 D MRSE). For more information, please see our website at: http://www.accessdata.fda.gov/cdrh_docs/pdf/P970053b.pdf.

The clinical indication was expanded in Supplement 1 (approved September 29, 1999) to include PRK treatment of myopic astigmatism (-1.00 to -8.00 D MRSE with -0.5 to -4.00 D cylinder). Supplement 6 (approved September 4, 2001) further expanded the clinical indication to include laser assisted in-situ keratomilieusis (LASIK) for the treatment of myopic astigmatism (-1.00 to -14.00 D MRSE with up to -4.00 D astigmatism) using an optical zone between 5.0 and 6.5 mm in patients 21 years of age or older. Supplement 9 further expanded the clinical indication to include hyperopia and hyperopic astigmatism

(+0.5 D to +5.00 D with up to +2.00 D astigmatism and up to +5.00 D MRSE). Supplement 11 further expands the approved clinical indications to custom topography-assisted LASIK treatments. The clinical data to support the expanded indication are provided in this summary.

II. INDICATIONS FOR USE

The Nidek EC-5000 Excimer Laser System is indicated for topography-assisted Laser-Assisted In-Situ Keratomileusis (LASIK) treatment using the Final Fit™ custom ablation treatment planning software:

- for the reduction or elimination of myopic refractive errors from -1.0 to -4.0 D of sphere with astigmatic refractive errors from >-0.5 to -2.0 D at the spectacle plane with manifest refraction spherical equivalent (MRSE) of >-1.0 to -5.0 D;
- in patients 21 years of age or older; and,
- in patients with documented stability of manifest refraction over the prior year, demonstrated by a change in MRSE not greater than ±0.5 D.

III. CONTRAINDICATIONS

LASIK surgery is contraindicated in:

- Patients with severe dry eye;
- Patients with recurrent corneal erosion;
- Patients with advanced Glaucoma;
- Patients with collagen vascular, autoimmune or immunodeficiency diseases;
- Pregnant or nursing women;
- Patients with signs of keratoconus, keratoconus suspect, or unstable central keratometry readings with irregular mires;
- Uncontrolled Diabetes;
- Eyes that have a calculated residual stromal bed thickness that is less than 250 microns; or
- Eyes for which a preoperative OPDScan that contains the torsional error detection measurements for eye orientation cannot be obtained.
- Patients with uncontrolled eye movements (nystagmus) or another condition that prevents a steady gaze.

IV. WARNINGS AND PRECAUTIONS

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

V. DEVICE DESCRIPTION

The Nidek EC-5000 Excimer Laser System is an ophthalmic laser system for refractive surgery of the cornea designed to correct the vision of patients with a variety of refractive errors (myopia, myopic astigmatism, hyperopia, and hyperopic astigmatism).

The EC-5000 System consists of an argon fluoride (ArF) excimer laser and beam delivery system, a diode aiming laser; the laser optical viewing system including the microscope, fixation light, and illumination lamps; the mechanical systems used for positioning, focusing, and gas handling; and microprocessor controllers. The EC-5000 Excimer uses a 193 nm ArF laser beam to recontour the cornea by ablation of corneal tissue using a scanning beam delivery system.

The Nidek EC-5000 Excimer Laser System is identical to the marketed version approved under P970053 for LASIK with the exception that the Nidek EC-5000 now includes additional software, called Final Fit™. This simulation software uses corneal topography data obtained from the OPD-Scan Model ARK-1000 aberrometer device to simulate the postoperative corneal shape and generate shot data to perform the simulated ablation. Minor asymmetric irregularities detected in the corneal topography data can be treated using the Multipoint Ablation Module feature on the EC-5000 Excimer Laser System.

The Final Fit™ simulation software has three simulation modes available to the approved EC-5000 System:

- **Spherical Ablation:** This is the traditional technique that uses sphere, cylinder, and axis to determine the amounts of spherical and cylindrical ablations. The optical zone (OZ) is ablated as a spherical lens.

- **Optimized Aspheric Treatment Zone Ablation (OATz):** This ablation mode is different than the spherical mode in that the treatment zone (TZ) area that lies between the outer edge of the optical zone and the outermost area of the entire ablation zone, is adjustable, based on the diameter of the OZ and TZ that are selected. In the TZ, the amount of ablation gradually decreases in such a manner that this outer TZ is very smooth with no abrupt changes in curvature. This contributes to a reduction in nighttime glare and halo that can result from abrupt curvature changes.

- **Customized Aspheric Treatment Zone Ablation (CATz):** This ablation mode consists of the performance of an OATz ablation plus the performance of an additional ablation using the Multipoint Ablation Module to treat the corneal irregularities detected by corneal topography.

The Final Fit™ software allows the user to select one of the three available simulation modes. Corneal irregularities can be treated in the CATz mode using the Multipoint Ablation Module feature of the EC-5000 Excimer Laser, which consists of a linear arrangement of six different 1 mm beams that can be used independently or together to provide localized ablation patterns. Shot data can be generated from the Final Fit™ software using diagnostic data from the Nidek OPD-Scan (Refractive Power/Corneal Analyzer ARK-10000) and Final Fit™ simulation software.

The Final Fit™ software accepts the measurement data from the OPD-scan device via a floppy disk. These data are then used to simulate the postoperative topography using the approved optical zone and treatment zone diameters and the #5 CATz treatment zone profile. CATz treatment uses the preoperative corneal shape as the basis of ablation algorithms. Once the treatment parameters are selected, the software creates the operation data (shot file) by calculating the difference between the preoperative corneal shape and the desired postoperative corneal shape. The Final Fit ™ software is loaded on a stand-alone computer. If the CATz mode is selected, the shot file that is created is separated into three parts: sphere, cylinder, and irregularity. The scanning slit of the NIDEK-EC-5000 corrects the spherical and cylindrical components in its usual fashion using the selected OATz profile followed by the irregularity treatment using the Multipoint Ablation Module.

Final Fit™ software can be used to generate CATz treatment plans for the treatment of myopic astigmatism with the following parameters that are operational in the approved system:

- OATz profile #5
- Optical Zone = 5.0 mm
- Manifest Cylinder -0.5 to -2.0 D
- Manifest Sphere -1.0 to -4.0 D
- Torsion Error Detection (TED) data are present on the preoperative OPD-Scan topography that is used for treatment simulation and planning

Nidek EC-5000 Laser Specifications

Model	EC-5000 (Model EC2B)
Pulse Repetition Rate	40 Hz
Fluence (nominal)	300 mJ/cm^2/scan (mean at the cornea)
Slit Beam	2 mm by 10 mm (FWHM)
Iris Diaphragm Diameter	10 mm (Max)
Multipoint Segmental Unit	linear array of six 1 mm spot beams (1.8 mm center-to-center spacing on the cornea)
Optical Zone/Ablation Zone	5.0 mm/8.5 mm (spherocylindrical) 6.0 mm/8.5 mm (irregularity)
Ablation Rate in Cornea	0.6 μm/scan
Ablation Rate in PMMA	0.315 μm/scan

The software versions in the laser system are as follows:

Laser Operating System	Windows 2000 v.5.26(a)
200 Hz Eye tracker	ETC v.4.10
Dragon Eye Software	v.3.20
Final Fit™ Software	v.1.11

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative methods of correcting nearsightedness (myopia) with astigmatism include: glasses, contact lenses, surface procedures such as photorefractive keratectomy (PRK), LASIK, and phakic IOLs approved within the same refractive range.

VII. MARKETING HISTORY

The EC-5000 Excimer Laser System has been distributed worldwide in more than 50 countries including Algeria, Argentina, Australia, Bahrain, Belgium, Bolivia, Brazil, Canada, Chile, China, Costa Rica, Croatia, Czech Republic, Dominican Republic, Ecuador, Egypt, Finland, France, Germany, Greece, India, Indonesia, Iran, Ireland, Israel, Italy, Korea, Kuwait, Japan, Jordan, Lebanon, Malaysia, Mexico, New Zealand, Oman, Norway, Pakistan, Paraguay, Peru, Poland, Puerto Rico, Romania, Russia, Saudi Arabia, Singapore, Slovakia, South Africa, Spain, Sweden, Switzerland, Syria, Taiwan, Thailand, Tunisia, Turkey, UAE, UK, Ukraine, United States, Uruguay, and Venezuela. The Nidek EC-5000 Excimer Laser 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

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device. Potential adverse effects associated with LASIK include: loss of best spectacle-corrected visual acuity (BSCVA), double vision, sensitivity to bright lights, difficulty with night vision, fluctuations in vision, increased 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, and retinal vascular accidents.

For the specific adverse events that occurred in the clinical study, see Section X below.

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory/Animal Studies

No preclinical in-vivo studies were conducted or required to demonstrate safety and effectiveness.

B. Additional Studies

1. Hazard Analysis and Software Validation

   Hazard analysis and software validation testing were conducted for the Nidek EC-5000 Excimer Laser System, including the MultiPoint Ablation module and the Windows-based system operating software, and the Final Fit™ custom treatment planning software. The hazard analysis includes risk assessment of hazards to the patient, operator, service personnel, bystanders, manufacturing personnel, and the environment. The software validation procedures covered all aspects of new software specifications and design, development, testing, functionality and performance. The hazard analysis and software validation testing indicated no new hazards affecting safety or effectiveness. Refer to the EC-5000 Excimer Laser System Operator's Manual, MultiPoint Ablation Module Operator's Manual, and the Final Fit™ Operator's Manual for safety precautions for the use of the excimer laser system and the Final Fit™ system.

2. Profilometry of Ablation

   As a part of this PMA, Nidek validated the accuracy of the myopic astigmatic corrections by performing a variety of test ablations on flat and curved plastic surfaces. All ablations were scanned with a surface profilometer or the OPDScan corneal analyzer and showed good agreement to theoretical targets.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of topography-guided LASIK treatment with the Nidek EC-5000 Excimer Laser System using the Customized Aspheric Treatment Zone (CATz) mode of Final Fit™ custom treatment planning software for the correction of myopia with astigmatism was conducted under IDE G040194 in the United States (3 sites) and Mexico (1 site). Safety and effectiveness outcomes at 3 months postoperatively were assessed, as refractive stability is reached by that time. Data from this clinical study were the basis for the PMA approval.

A. Study Design

Subjects were treated between December 14, 2005 and September 28, 2006. The database for this PMA submission reflects postoperative visits completed through May 15, 2008 and includes clinical data for 136 enrolled and 135 treated eyes. On December 18, 2007, in response to IDE G040194/S009, FDA approved study termination subject follow up at the 12-month postoperative visit instead of the 24-month visit. This contributed to a limited number of 18 and 24-month postoperative visits available for reporting. Four investigational sites provided eligible data for analysis.

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

The objective of this clinical study was to demonstrate that topography-guided LASIK treatment with the Nidek EC-5000 and Final Fit™ treatment planning software is safe and effective for the correction of myopia with astigmatism.

The sample size for this study was based on having a high probability the confidence interval for the mean refractive error is wholly contained in the interval (-0.5D, 0.5D).
A sample size of 125 evaluable eyes was deemed sufficient to estimate the mean refractive error to within ± 0.5 D.

Since historically there is a 10% discontinuation rate, the sample size was adjusted for a 10% rate of discontinued and lost-to-follow-up eyes. The adjusted sample size calculations accounting for this 10% lost-to-follow-up resulted in an estimated sample size of 138 eyes.

Rounding upwards, up to a total of 140 eyes assured that there are 125 evaluable eyes at the time point of stability.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the clinical study entitled: "The Safety and Effectiveness of the Nidek EC-5000 Excimer Laser System Using Customized Aspheric Treatment zone (CATz) Assisted LASIK for the Treatment of Myopic Astigmatism in Virgin Eyes with Corneal Irregularity" was limited to subjects who met the selection criteria listed in tables 1 and 2 below:

Inclusion
21 years of age or older
Had an uncorrected refractive error that could be surgically treated by LASIK consisting of myopic astigmatism with a spherical component of -0.5 D to -7.0 D, and an astigmatic component of -0.50 D to -4.0 D, based on the manifest refraction in the operative study eye
Target postoperative refraction of 0.00 D sphere and 0.00 D cylinder in the operative study eye
BSCVA distance of 20/25 or better in each eye
0.75 D SE or less difference between the manifest or cycloplegic refractions and the OPD-Scan refraction used for the Final Fit™ treatment calculation

Inclusion
15 degrees or less difference between the axes of the manifest or cycloplegic refractions and the OPD-Scan refraction used for the Final Fit™ treatment calculation
OPD-Scan image with a 5 mm or larger pupil diameter that was without artifacts and 10 microns or less of corneal irregularity
A stable correction (± 0.5 D) in the operative study eye, as determined by MRSE for a minimum of 12-months prior to surgery
For contact lens wearers, demonstration of a stable refraction (± 0.5 D MRSE) of the manifest refraction and topography on two consecutive exam dates at least 7 days apart after discontinuation of contact lens wear
Normal topography
Signed written informed consent
Willingness and ability to comply with schedule for follow-up visits.

Table 1: Inclusion Criteria

Exclusion
An acute or chronic disease or illness that would increase the operative risk or confound the outcome(s) of the study (e.g., severe dry eyes, immunocompromised, connective tissue disease with ocular involvement, clinically significant atopic disease, diabetes with ocular involvement, etc.)
Use of systemic medications that may confound the outcome of the study or increase the risk to the subject, including, but not limited to steroids, antimetabolites, etc.
Previous ocular condition (other than refractive error) that may predispose the eye for future complications, for example: history of corneal disease (e.g., herpes simplex, herpes zoster keratitis, recurrent erosion syndrome or corneal dystrophy, etc.)
Evidence of retinal vascular disease
Keratoconus or unstable central keratometry readings with irregular mires
Glaucoma or glaucoma suspect by exam findings
Previous intraocular or corneal surgery, except strabismus surgery
Pregnancy or lactation during the course of the study
A known sensitivity to study medications
Mixed astigmatism in the operative study eye, based on the screening manifest refraction
Surgical treatment plan in the study eye(s) for monovision or intentional undercorrection or overcorrection
Residual corneal bed thickness remaining after laser ablation is calculated preoperatively to be less than 250 microns in the operative study eye
Preoperative central corneal thickness of less than 475 microns in the operative study eye
Concurrent participation in other ophthalmic clinical trials
Contact lens intolerance in subjects who are not undergoing bilateral treatment
Mesopic pupil size $\geq$ 8mm

Table 2: Exclusion Criteria

2. Follow-Up Schedule

Subjects completed follow-up examinations at 1 day, 1 week, and 1, 3, 6, 9, and 12-months post-LASIK. The objective parameters measured both preoperatively and postoperatively, along with their respective time schedule are detailed in Table 3, below:

Procedure	Screen	Surgery	POSTOPERATIVE VISITS								
			1 DAY	1 WK	1 MO	3 MO	6 MO	9 MO	12 MO	18 MO	24 MO
Medical History	X	X	X	X	X	X	X	X	X	X	X
Ocular History	X	X	X	X	X	X	X	X	X	X	X
Medication History	X	X	X	X	X	X	X	X	X	X	X
Demographics	X										
BCVA Distance	X			X	X	X	X	X	X	X	X
BCVA Near	X			X	X	X	X	X	X	X	X
UCVA Distance	X		X	X	X	X	X	X	X	X	X
UCVA Near	X					X	X	X	X	X	X
Manifest Refraction	X	X		X	X	X	X	X	X	X	X
Cycloplegic Refraction	X						X	X	X	X	X
Intraocular Pressure Measurement	X			X	X	X	X	X	X	X	X
Slit Lamp Exam	X		X	X	X	X	X	X	X	X	X
Pupil Size Measurement	X		X[7]	X[7]	X[7]	X[7]	X	X	X	X	X
Dilated Fundus Examination	X						X	X	X	X	X
Pachymetry, Keratometry	X						X	X	X	X	X
OPD-Scan Topography and Power Analysis	X				X	X	X	X	X	X	X
Contrast sensitivity	X						X				
RSVP Questionnaire	X				X	X	X	X	X	X	X
Subjective Complaint Questionnaire	X				X	X	X	X	X	X	X
Sign Consent	X										
Complications		X	X	X	X	X	X	X	X	X	X
Adverse Events		X	X	X	X	X	X	X	X	X	X

Table 3: Follow-Up Schedule – Postoperative Visits

Subjects were permitted to have second eyes (fellow eyes) treated at the discretion of the investigator at the same time as the first eyes (primary eyes) or after the primary eye treatment. There was one (1) retreatment/ secondary surgical intervention. One subject experienced a small hemorrhage under the flap, a traumatic injury with diffuse lamellar keratitis (DLK), and a retreatment in the right eye (OD). This subject has a resultant BSCVA of 20/20, and has not suffered any significant loss of visual acuity compared to baseline. Subjects were ineligible for retreatment unless specific permission was obtained from the applicant, Food and Drug Administration (FDA), and the Institutional Review Board (IRB).

3. Clinical Endpoints

Safety and Effectiveness Criteria

The primary safety endpoints were:

1) Percentage of eyes that had a loss of two or more lines in BSCVA
2) Percentage of eyes that had a BSCVA worse than 20/25 if the BSCVA was 20/20 or better preoperatively
3) Percentage of eyes that had a BSCVA worse than 20/40

These endpoints were measured postoperatively at 1, 3, 6, 9 and 12-months. Specifically, safety outcomes were assessed, at 3-months postoperatively, the time of refractive stability.

Other safety endpoints included adverse events (AEs), complications, evaluation of corneal haze and intraocular pressure, symptoms/problems/complaints assessed in subject questionnaires and contrast sensitivity.

Primary effectiveness endpoints that were evaluated over time include:

1) Refractive predictability
2) Uncorrected visual acuity
3) Refractive stability

Other effectiveness endpoints include Zernike analysis of topography data and a patient symptom questionnaire that assesses vision related quality of life factors.

These primary effectiveness endpoints were measured postoperatively at 1, 3, 6, 9 and 12-months. Specifically, effectiveness outcomes at 3-months postoperatively were assessed, as refractive stability is reached by that time.

Table 4 indicates target criteria for primary safety and effectiveness outcomes:

Target Criteria for Primary Safety and Effectiveness Outcomes

Criteria	Parameter	CATz-1 Myopic Astigmatism Target Criteria
Effectiveness	Percentage of eyes with UCVA of 20/40 or better (BSCVA 20/20 or better preop)	85%
	Percentage of eyes achieving refractive predictability (attempted versus achieved) that are within:	
	±0.50D	50%
	±1.00D	75%

Safety	Percentage of eyes losing 2 or more lines of BSCVA	<5%
	Percentage of eyes that have BSCVA worse than 20/25 if BSCVA 20/20 or better preoperatively	<1%

Table 4: Target Criteria for Primary Safety and Effectiveness Outcomes

B. Accountability of PMA Cohort

At the time of database lock, of the 136 eyes enrolled (135 eyes treated) in the CATz-1 PMA study, 94% (127/135) of treated eyes are available for analysis at the timepoint of refractive stability, the 3-month post-operative visit. Eighty-four percent (113/135) of treated eyes are available for analysis at the completion of the study, the 12-month post-operative visit.

A total of 135 eyes in 74 subjects were treated between December 14, 2005 and September 28, 2006. Main statistical analyses to determine safety and efficacy included clinical data for the 135 eyes treated.

Accountability for the 135 treated eye cohort is summarized below in Table 5 for all eyes treated. One enrolled eye was not treated due to a buttonhole created during the keratectomy. This eye did not undergo a primary LASIK treatment.

Accountability by Eye for All Treated Eyes							
Status	Day 1	Week 1	Month 1	Month 3	Month 6	Month 9	Month 12
Enrolled [Treated] (N)	135	135	135	135	135	135	135
Available for Analysis	135 (100%)	135 (100%)	135 (100%)	127 (94%)	133 (99%)	117 (87%)	113 (84%)
Discontinued	0	0	0	0	0	0	2 (1%)
Active (Not Eligible for Interval)	0	0	0	0	0	0	0
Lost to Follow-up	0	0	0	0	0	2 (1%)	16 (12%)
Missed Visit (Accounted for)	0	0	0	8 (6%)	2 (1%)	16 (12%)	4 (3%)
Accountability	100%	100%	100%	94%	99%	87%	85%

Table 5: Accountability by Eye for All Treated Eyes

C. Study Population Demographics and Baseline Parameters

Demographics

Table 6 presents demographic information at each site for the cohort of 74 subjects enrolled in the study.

Table 10: Subject Population Demographic Characteristics for All Treated Patients

		Site 1 (N=18)	Site 2 (N=21)	Site 3 (N=16)	Site 4 (N=19)	Total (N=74)	p-value[1]
Gender							0.759
	Male	9 (50%)	8 (38%)	8 (50%)	7 (37%)	32 (43%)	
	Female	9 (50%)	13 (62%)	8 (50%)	12 (63%)	42 (57%)	
Age							<.001
	n	18	21	16	19	74	
	mean (SD)	36.9 (7.1)	39.5 (7.9)	34.9 (9.5)	28.7 (5.6)	35.1 (8.5)	
	median	35.5	39.0	33.5	28.0	34.0	
	min,max	23.0 , 50.0	23.0 , 55.0	23.0 , 64.0	21.0 , 41.0	21.0 , 64.0	
Race							<.001
	Caucasian	18 (100%)	12 (57%)	12 (75%)	0 (0%)	42 (57%)	
	Black	0 (0%)	0 (0%)	3 (19%)	0 (0%)	3 (4%)	
	Asian	0 (0%)	3 (14%)	1 (6%)	0 (0%)	4 (5%)	
	Hispanic	0 (0%)	5 (24%)	0 (0%)	19 (100%)	24 (32%)	
	Other	0 (0%)	1 (5%)	0 (0%)	0 (0%)	1 (1%)	

[1] Chi-square test for categorical variables and t-test for continuous variables

Table 6: demographic information

There was a statistically significant difference in the distribution of races across the sites ($p<0.001$). This difference in race was due to the high proportion of Hispanic patients enrolled at Site 7. Published literature evaluating racial differences have demonstrated there are no significant differences between the Hispanic and Caucasian populations for corneal curvature, central corneal thickness, refractive measurements, preoperative astigmatism, or intraocular pressure[1,2]. Therefore, the outcomes would not be expected to be different between the two groups. Thus the predominance of Hispanic population should have no clinically significant effect on the outcomes that would affect poolability of the data.

Baseline Refractive Parameters

The preoperative bin distribution is based on the preoperative manifest refraction, specifically sphere and cylinder. All eyes were treated for myopia with astigmatism with a target refraction of emmetropia. All eyes enrolled and treated had -0.50 D or more of cylinder in the study. Table 7, below, provides the bin distribution stratified by preoperative sphere and by preoperative cylinder.

Bin Distribution for All Primary and Fellow Eyes			
Sphere	Primary n (%)	Fellow n (%)	Total
-1.00 to -2.00 D	26 (19%)	15 (11%)	41
-2.01 to -3.00 D	10 (7%)	16 (12%)	26
-3.01 to -4.00 D	21 (16%)	17 (13%)	38
-4.01 to -5.00 D[3]	9 (7%)	9 (7%)	18
-5.01 to -6.00 D[3]	8 (6%)	4 (3%)	12
Total	74	61	135
Cylinder			
-0.50 to -0.75 D	38 (28%)	34 (25%)	72
-0.76 to -1.00 D	13 (10%)	8 (6%)	21
-1.01 to -2.00 D	20 (15%)	13 (10%)	33
-2.01 to -3.00 D[1]	2 (1%)	5 (4%)	7
-3.01 to -4.00 D[2]	1 (1%)	1 (1%)	2
Total	74	61	135
[1] Outside range of approved indication for use: Flag warning [2] Outside range of approved indication for use: Locked out			

Table 7: Bin Distribution for All Primary and Fellow Eyes

The range of refractive error treated in the CATz-1 study is listed in Table 8, below:

	Minimum	Maximum
Sphere	-1.00	-6.00
Cylinder	-0.5	-3.5
MRSE	-1.25	-6.88

Table 8: The range of refractive error treated in the CATz-1 study

D. Safety and Effectiveness Results

Safety Results

The analysis of safety was based on the treated cohort of 136 study eyes available for analysis at the 3-month evaluation, the time point of refractive stability. The primary safety outcomes for this study and overall AEs are presented below Tables 10, 11 and 12. Given the device system did not raise any new safety issues in comparison to the previously approved system, it is appropriate to leverage the prior clinical data and experience from this device to require only 125 eyes to support approval; the minimum number of eyes needed to evaluate the primary effectiveness endpoint.

Comparison of LASIK Safety Criteria at 3 Months Post-LASIK (timepoint of stability)		
Parameter	CATz-1 Myopic Astigmatism Target Criteria	CATz-1 Myopic Astigmatism 3 Months Postop
Percentage of eyes losing 2 or more lines of BSCVA	<5%	2/123 (1.6%)
Percentage of eyes that have BSCVA worse than 20/25 if BSCVA 20/20 or better preoperatively	<1%	2/97 (2.1%)*

Table 9: Comparison of LASIK Safety Criteria at 3 Months Post-LASIK (timepoint of stability)

Table 10 lists all AEs (Table 11 lists AEs in descending order of overall incidence), including AEs both related and unrelated to the topography-assisted LASIK treatment, observed during the CATz-1 clinical study in descending order of the overall incidence rate. Any and all observations of the clinical reviewer are included in the table below. There were no AEs that led to any device design modifications during the PMA clinical study.

The most common AEs related to the topography-assisted LASIK treatment occurring in over 5% of study subjects overall reported at the 3-month visit are: dry eye, 13% (9/70); halo vision, 9% (6/70); glare, 7% (5/70); and punctate keratitis, 9% (6/70). At the 6-month visit, dry eye decreases to 8% (6/73); halo vision 73). At the 9-month visit, dry eye decreases to 6% (4/64); halo vision increases to 5% (3/64); glare increases to 3% decreases to 0% (0/73); glare decreases to 1% (1/73) and punctate keratitis decreases to 1% (1/ (2/64) and punctate keratitis decreases to 3% (2/64). At the 12-month visit, dry eye further decreases to 5% (3/63); halo vision decreases to 0% (0/63); glare decreases to 0% (0/63) and punctate keratitis remains at 3% (2/63). The table below lists AEs by severity for all treated subjects with at least 5% overall incidence rate.

Adverse Events by Severity for All Treated Subjects Preferred Terms with at Least 5% Overall Incidence Rate are Included					
Preferred Term	Severity	Mo 3 (N=70)	Mo 6 (N=73)	Mo 9 (N=64)	Mo 12 (N=63)
Any AE	Mild	23 (33%)	11 (15%)	11 (17%)	12 (19%)
	Moderate	3 (4%)	1 (1%)	3 (5%)	1 (2%)
	Severe	1 (1%)	2 (3%)	0	0
	Unknown	0	1 (1%)	0	2 (3%)
Corneal deposits	Mild	0	0	0	0
Corneal opacity	Mild	2 (3%)	1 (1%)	1 (2%)	0
Corneal striae	Mild	1 (1%)	0	0	0
	Moderate	0	0	0	0
Diplopia	Mild	0	0	1 (2%)	0
	Moderate	0	0	0	0
	Severe	0	0	0	0
Dry eye	Mild	8 (11%)	5 (7%)	4 (6%)	3 (5%)
	Moderate	2 (3%)	0	1 (2%)	0
	Severe	0	1 (1%)	0	0
Eye pain	Mild	0	0	2 (3%)	0
	Moderate	0	0	0	0
Foreign body sensation in eyes	Mild	0	0	1 (2%)	0
	Moderate	0	0	0	0
Glare	Mild	4 (6%)	0	2 (3%)	0
	Moderate	1 (1%)	0	0	0
	Severe	0	1 (1%)	0	0
Halo vision	Mild	4 (6%)	0	2 (3%)	0
	Moderate	1 (1%)	0	1 (2%)	0
	Severe	1 (1%)	0	0	0
Headache	Mild	1 (1%)	0	1 (2%)	0
Meibomian gland discharge	Mild	0	0	0	1 (2%)
Photophobia	Mild	0	1 (1%)	0	2 (3%)
	Moderate	0	0	0	0
	Severe	1 (1%)	0	0	0
Photopsia[1]	Mild	1 (1%)	1 (1%)	1 (2%)	2 (3%)
	Severe	0	0	0	0
Punctate keratitis	Mild	6 (9%)	1 (1%)	2 (3%)	2 (3%)
Vision blurred	Mild	2 (3%)	0	0	1 (2%)
Visual acuity reduced transiently	Mild	1 (1%)	0	0	0
[1] Photopsia denotes “starbursts”					

Table 10: **Adverse Events by Severity for All Treated Subjects**

Adverse Events in Descending Order of Overall Incidence for All Treated Patients											
Preferred Term	Intraop (N=74)	Day 1 (N=74)	Wk 1 (N=74)	Mo 1 (N=74)	Mo 3 (N=70)	Mo 6 (N=73)	Mo 9 (N=64)	Mo 12 (N=63)	Mo 18 (N=15)	Mo 24 (N=6)	Overall (N=74)
Any AE	3 (4%)	20 (27%)	34 (46%)	27 (36%)	27 (39%)	15 (21%)	14 (22%)	15 (24%)	7 (47%)	1 (17%)	59 (80%)
Dry eye	0	1 (1%)	5 (7%)	10 (14%)	10 (14%)	6 (8%)	5 (8%)	3 (5%)	3 (20%)	0	36 (49%)
Halo vision	0	6 (8%)	9 (12%)	8 (11%)	6 (9%)	0	3 (5%)	0	0	0	19 (26%)
Glare	0	5 (7%)	7 (9%)	5 (7%)	5 (7%)	1 (1%)	2 (3%)	0	0	0	15 (20%)
Corneal striae	1 (1%)	3 (4%)	5 (7%)	3 (4%)	1 (1%)	0	0	0	0	0	12 (16%)
Punctate keratitis	0	4 (5%)	3 (4%)	2 (3%)	6 (9%)	1 (1%)	2 (3%)	2 (3%)	2 (13%)	0	12 (16%)
Photopsia[1]	1 (1%)	0	5 (7%)	0	1 (1%)	1 (1%)	1 (2%)	2 (3%)	0	0	10 (14%)
Foreign body sensation in eyes	0	2 (3%)	3 (4%)	4 (5%)	0	0	1 (2%)	0	0	0	9 (12%)
Corneal opacity	0	3 (4%)	1 (1%)	1 (1%)	2 (3%)	1 (1%)	1 (2%)	0	0	0	8 (11%)
Vision blurred	0	2 (3%)	3 (4%)	0	2 (3%)	0	0	1 (2%)	0	1 (17%)	8 (11%)
Eye pain	0	0	2 (3%)	3 (4%)	0	0	2 (3%)	0	1 (7%)	0	7 (9%)
Visual acuity reduced transiently	0	2 (3%)	2 (3%)	1 (1%)	1 (1%)	0	0	0	1 (7%)	0	6 (8%)
Meibomian gland discharge	0	1 (1%)	3 (4%)	0	0	0	0	1 (2%)	0	0	5 (7%)
Corneal deposits	0	1 (1%)	3 (4%)	1 (1%)	0	0	0	0	0	0	4 (5%)
Diplopia	0	0	3 (4%)	1 (1%)	0	0	1 (2%)	0	1 (7%)	0	4 (5%)
Headache	0	0	1 (1%)	1 (1%)	1 (1%)	0	1 (2%)	0	0	0	4 (5%)
Photophobia	0	1 (1%)	1 (1%)	2 (3%)	1 (1%)	1 (1%)	0	2 (3%)	0	0	4 (5%)
Keratitis	0	2 (3%)	0	1 (1%)	0	0	0	0	0	0	3 (4%)
Visual acuity reduced	0	0	0	0	0	1 (1%)	1 (2%)	0	1 (7%)	0	3 (4%)
Asthenopia	0	0	1 (1%)	0	1 (1%)	0	0	0	0	0	2 (3%)
Blepharospasm	0	0	0	1 (1%)	1 (1%)	0	0	0	0	0	2 (3%)
Conjunctival haemorrhage	0	1 (1%)	1 (1%)	0	0	0	0	0	0	0	2 (3%)
Hypersensitivity	0	0	0	1 (1%)	0	1 (1%)	0	0	0	0	2 (3%)
Loss of visual contrast sensitivity	0	1 (1%)	1 (1%)	1 (1%)	1 (1%)	1 (1%)	1 (2%)	0	0	0	2 (3%)

Meibomian gland dysfunction	0	1 (1%)	0	0	0	0	1 (2%)	0	0	0	2 (3%)
Vitreous floaters	0	0	0	0	0	0	0	1 (2%)	1 (7%)	0	2 (3%)
Allergy to animal	0	0	0	0	0	0	0	1 (2%)	0	0	1 (1%)
Astigmatism	0	0	0	0	0	1 (1%)	0	0	0	0	1 (1%)
Cardiac disorder	0	0	1 (1%)	0	0	0	0	0	0	0	1 (1%)
Chalazion	0	0	0	0	0	0	0	1 (2%)	0	0	1 (1%)
Conjunctivitis viral	0	1 (1%)	1 (1%)	0	0	0	0	0	0	0	1 (1%)
Corneal abrasion	0	0	0	0	0	0	0	0	1 (7%)	0	1 (1%)
Corneal epithelium defect	0	0	0	1 (1%)	0	0	0	0	0	0	1 (1%)
Corneal infiltrates	0	0	0	1 (1%)	0	0	0	0	0	0	1 (1%)
Corneal scar	0	1 (1%)	0	0	0	0	0	0	0	0	1 (1%)
Depression	0	0	0	0	0	1 (1%)	0	0	0	0	1 (1%)
Dizziness	0	0	0	0	0	0	0	1 (2%)	0	0	1 (1%)
Eye injury	0	0	0	1 (1%)	0	0	0	0	0	0	1 (1%)
Eye irritation	0	0	0	0	1 (1%)	0	0	0	0	0	1 (1%)
Eye laser scar	0	0	0	1 (1%)	0	0	0	0	0	0	1 (1%)
Eye pruritus	0	0	0	0	1 (1%)	0	0	0	0	0	1 (1%)
Facial palsy	0	0	0	1 (1%)	0	0	0	0	0	0	1 (1%)
Hepatitis	0	0	0	0	0	1 (1%)	0	0	0	0	1 (1%)
Hypermetropia	0	0	0	1 (1%)	0	0	0	0	0	0	1 (1%)
Hypothyroidism	0	0	1 (1%)	0	0	0	0	0	0	0	1 (1%)
Injury corneal	1 (1%)	0	0	0	0	0	0	0	0	0	1 (1%)
Intraocular pressure increased	0	0	1 (1%)	0	0	0	0	0	0	0	1 (1%)
Migraine	0	0	0	0	0	0	0	1 (2%)	0	0	1 (1%)
Migraine with aura	0	0	0	0	0	0	0	0	1 (7%)	0	1 (1%)
Nasopharyngitis	0	0	0	0	1 (1%)	0	0	0	0	0	1 (1%)
Ocular hyperaemia	0	0	1 (1%)	0	0	0	0	0	0	0	1 (1%)
Pain	0	0	0	0	1 (1%)	0	0	0	0	0	1 (1%)
Pregnancy	0	0	0	0	0	1 (1%)	0	0	0	0	1 (1%)
Presbyopia	0	0	0	0	1 (1%)	0	0	0	0	0	1 (1%)
Pruritus allergic	0	0	0	1 (1%)	0	0	0	0	0	0	1 (1%)

Retinal pigment epitheliopathy	0	0	0	0	0	1 (1%)	0	0	0	0	1 (1%)
Rib fracture	0	0	0	0	0	0	1 (2%)	0	0	0	1 (1%)
Seasonal allergy	0	0	0	0	0	0	0	1 (2%)	0	0	1 (1%)
Syncope	0	0	0	0	0	0	0	1 (2%)	0	0	1 (1%)
Upper limb fracture	0	0	0	0	0	1 (1%)	0	0	0	0	1 (1%)
Urticaria	1 (1%)	0	0	0	0	0	0	0	0	0	1 (1%)
[1] Photopsia denotes "starbursts"											

Table 11: **Adverse Events in Descending Order of Overall Incidence for All Treated Patients**

Corneal Haze

Corneal haze was graded at each postoperative time point after observation on the slit lamp examination. Rare occurrences of haze were reported in the CATz-1 clinical trial, with only single reports of transient trace haze at the 1 and 3-month visits. Topography-assisted LASIK for the treatment of myopic astigmatism with the EC-5000 Excimer Laser does not induce corneal haze postoperatively.

Intraocular Pressure

Intraocular pressure was measured by Goldmann applanation tonometry at the slit lamp. There were no clinically significant changes (defined as > 10mmHg increase) between the intraocular pressure measurements obtained preoperatively and postoperatively.

Serious Adverse Events

There was one reported serious adverse event of corneal striae reported in the CATz-1 clinical study. Table 12 indicates the one serious adverse event reported.

Serious Adverse Events for All Treated Eyes

Page No.	AE No.	Description	Preferred Term	Visit	Start Date	End Date	SAE[A]	Sev[B]	Rel[C]	Act[D]	Out[E]
100.00	1	OS flap striae	Corneal striae	Surg	04/12/2006	04/13/2006	1	2	5	4	1

A=Yes, 2=No
B Severity: 1=Mild, 2=Moderate, 3=Severe
C Relationship: 1=None, 2=Unlikely, 3=Possible, 4=Probable, 5=Definite
D Action: 1=None, 2=Concomitant Medication, 3=Discontinued, 4=Other
E Outcome: 1=Resolved, 2=Not Resolved, 3=Death

Table 12: Serious Adverse Events for All Treated Eyes

The subject that experienced the serious adverse event was a 32 year old female subject (age at the time of CATz-1 screening) who underwent uneventful bilateral CATz-1 LASIK surgery for the treatment of myopic astigmatism. The postoperative course for the right eye is unremarkable. At the 1-day postop visit, the UCVA OS was 20/25 and striae were

observed at the slit lamp exam. The corneal flap was re-floated at the 1-day postop visit to remove the striae. The striae were no longer present at the 1-week slit lamp. At the 1-month visit, the subject reports fluctuation of vision on the patient subjective questionnaire. This was the only visit the fluctuation of vision was reported.

Complications

As summarized in table 13, the most commonly occurring postoperative complication at month-3, or later, was dry eye requiring chronic artificial tears or punctual plugs. Other (Surg) refers to two corneal flap refloats and one retreatment.

Complications for All Treated Subjects

Complication	Mo 3 (N=70)	Mo 6 (N=73)	Mo 9 (N=64)	Mo 12 (N=63)
Any Complications	15 (21%)	11 (15%)	4 (6%)	7 (11%)
Diffuse Lamellar Keratitis	0	0	0	0
Dry Eye Requiring Chronic Artificial Tears or Punctal Plugs	4 (6%)	3 (4%)	2 (3%)	2 (3%)
Foreign Body Sensation	0	0	0	0
Ghosts or Double Images	0	0	0	0
Loss of 2 lines BCVA	1 (1%)	0	0	0
Misaligned Flap	0	0	0	0
Miscreated Flap	0	0	0	0
Other (AE)	11 (16%)	8 (11%)	2 (3%)	5 (8%)
Other (Surg)	0	0	0	0
Pain	0	0	1 (2%)	1 (2%)

Table 13: Complications for All Treated Subjects

Patient Questionnaire

Subjective visual complaints were obtained from each subject using a self-administered 10-point questionnaire to record symptoms. Subjects were asked to rate the presence or absence of each visual complaint in their CATz-treated eye(s) at baseline before the CATz topography-assisted LASIK treatment and each postoperative visit, beginning at 1-month. Subjects were instructed to rate the absence of a complaint as “none,” and the presence of a complaint was rated as “mild,” “moderate,” “marked” or “severe.” Values stated as “Unknown” refer to questions where the subject did not provide an answer. Subjective visual complaints noted on the patient questionnaire were noted as either AEs or complications at the discretion of the clinical investigator. The results of the subjective questionnaire at baseline and at each postoperative examination are summarized by symptom in table 14.

Subject Symptoms Recorded via Self-Administered Symptom Questionnaire for All Treated Eyes									
Question	Response	Screening (N=135)	Mo 1 (N=135)	Mo 3 (N=127)	Mo 6 (N=133)	Mo 9 (N=117)	Mo 12 (N=113)	Mo 18 (N=24)	Mo 24 (N=10)
Light Sensitivity	None	93 (69%)	88 (65%)	95 (75%)	105 (79%)	94 (80%)	81 (72%)	14 (58%)	3 (30%)
	Mild	20 (15%)	28 (21%)	24 (19%)	21 (16%)	17 (15%)	23 (20%)	3 (13%)	2 (20%)
	Moderate	7 (5%)	18 (13%)	4 (3%)	7 (5%)	5 (4%)	5 (4%)	2 (8%)	0
	Marked	4 (3%)	0	2 (2%)	0	1 (1%)	0	1 (4%)	0
	Severe	2 (1%)	1 (1%)	0	0	0	0	0	0
	Unknown	9 (7%)	0	2 (2%)	0	0	4 (4%)	4 (17%)	5 (50%)
Difficulty Driving at Night	None	63 (47%)	111 (82%)	110 (87%)	117 (88%)	103 (88%)	93 (82%)	14 (58%)	3 (30%)
	Mild	15 (11%)	20 (15%)	13 (10%)	15 (11%)	14 (12%)	14 (12%)	4 (17%)	1 (10%)
	Moderate	18 (13%)	2 (1%)	2 (2%)	1 (1%)	0	2 (2%)	2 (8%)	1 (10%)
	Marked	21 (16%)	2 (1%)	0	0	0	0	0	0
	Severe	9 (7%)	0	0	0	0	0	0	0
	Unknown	9 (7%)	0	2 (2%)	0	0	4 (4%)	4 (17%)	5 (50%)
Reading Difficulty	None	112 (83%)	113 (84%)	98 (77%)	110 (83%)	102 (87%)	91 (81%)	13 (54%)	1 (10%)
	Mild	9 (7%)	16 (12%)	18 (14%)	15 (11%)	9 (8%)	13 (12%)	4 (17%)	2 (20%)
	Moderate	5 (4%)	3 (2%)	6 (5%)	6 (5%)	3 (3%)	4 (4%)	1 (4%)	0
	Marked	0	1 (1%)	2 (2%)	2 (2%)	3 (3%)	1 (1%)	2 (8%)	2 (20%)
	Severe	0	2 (1%)	1 (1%)	0	0	0	0	0
	Unknown	9 (7%)	0	2 (2%)	0	0	4 (4%)	4 (17%)	5 (50%)
Double Vision	None	124 (92%)	124 (92%)	120 (94%)	130 (98%)	114 (97%)	108 (96%)	16 (67%)	3 (30%)
	Mild	2 (1%)	8 (6%)	3 (2%)	2 (2%)	3 (3%)	1 (1%)	2 (8%)	1 (10%)
	Moderate	0	3 (2%)	2 (2%)	0	0	0	0	0
	Marked	0	0	0	1 (1%)	0	0	1 (4%)	1 (10%)
	Severe	0	0	0	0	0	0	1 (4%)	0
	Unknown	9 (7%)	0	2 (2%)	0	0	4 (4%)	4 (17%)	5 (50%)
Fluctuation in Vision	None	106 (79%)	93 (69%)	98 (77%)	99 (74%)	94 (80%)	91 (81%)	16 (67%)	1 (10%)
	Mild	14 (10%)	37 (27%)	22 (17%)	31 (23%)	22 (19%)	16 (14%)	2 (8%)	2 (20%)
	Moderate	6 (4%)	5 (4%)	5 (4%)	2 (2%)	0	2 (2%)	2 (8%)	1 (10%)
	Marked	0	0	0	1 (1%)	0	0	0	1 (10%)
	Unknown	9 (7%)	0	2 (2%)	0	1 (1%)	4 (4%)	4 (17%)	5 (50%)
Glare	None	108 (80%)	95 (70%)	94 (74%)	111 (83%)	98 (84%)	94 (83%)	16 (67%)	3 (30%)
	Mild	13 (10%)	34 (25%)	24 (19%)	16 (12%)	13 (11%)	15 (13%)	4 (17%)	1 (10%)
	Moderate	2 (1%)	6 (4%)	7 (6%)	6 (5%)	6 (5%)	0	0	1 (10%)
	Marked	3 (2%)	0	0	0	0	0	0	0
	Unknown	9 (7%)	0	2 (2%)	0	0	4 (4%)	4 (17%)	5 (50%)
Halos	None	111 (82%)	96 (71%)	88 (69%)	105 (79%)	94 (80%)	89 (79%)	16 (67%)	3 (30%)
	Mild	12 (9%)	33 (24%)	32 (25%)	28 (21%)	19 (16%)	20 (18%)	4 (17%)	2 (20%)
	Moderate	3 (2%)	6 (4%)	3 (2%)	0	2 (2%)	0	0	0

Subject Symptoms Recorded via Self-Administered Symptom Questionnaire for All Treated Eyes									
Question	Response	Screening (N=135)	Mo 1 (N=135)	Mo 3 (N=127)	Mo 6 (N=133)	Mo 9 (N=117)	Mo 12 (N=113)	Mo 18 (N=24)	Mo 24 (N=10)
	Marked	0	0	2 (2%)	0	2 (2%)	0	0	0
	Unknown	9 (7%)	0	2 (2%)	0	0	4 (4%)	4 (17%)	5 (50%)
Starbursts	None	112 (83%)	98 (73%)	95 (75%)	106 (80%)	101 (86%)	84 (74%)	16 (67%)	3 (30%)
	Mild	11 (8%)	27 (20%)	24 (19%)	27 (20%)	12 (10%)	23 (20%)	4 (17%)	0
	Moderate	2 (1%)	8 (6%)	4 (3%)	0	4 (3%)	2 (2%)	0	2 (20%)
	Marked	1 (1%)	2 (1%)	2 (2%)	0	0	0	0	0
	Unknown	9 (7%)	0	2 (2%)	0	0	4 (4%)	4 (17%)	5 (50%)
Dryness	None	94 (70%)	56 (41%)	48 (38%)	68 (51%)	62 (53%)	57 (50%)	12 (50%)	1 (10%)
	Mild	29 (21%)	57 (42%)	45 (35%)	44 (33%)	40 (34%)	43 (38%)	7 (29%)	2 (20%)
	Moderate	3 (2%)	14 (10%)	28 (22%)	20 (15%)	14 (12%)	7 (6%)	1 (4%)	2 (20%)
	Marked	0	2 (1%)	2 (2%)	1 (1%)	1 (1%)	2 (2%)	0	0
	Severe	0	6 (4%)	2 (2%)	0	0	0	0	0
	Unknown	9 (7%)	0	2 (2%)	0	0	4 (4%)	4 (17%)	5 (50%)
Pain	None	119 (88%)	119 (88%)	117 (92%)	127 (95%)	113 (97%)	106 (94%)	17 (71%)	4 (40%)
	Mild	6 (4%)	12 (9%)	8 (6%)	5 (4%)	4 (3%)	3 (3%)	3 (13%)	1 (10%)
	Moderate	0	4 (3%)	0	1 (1%)	0	0	0	0
	Unknown	10 (7%)	0	2 (2%)	0	0	4 (4%)	4 (17%)	5 (50%)
Foreign Body Sensation	None	111 (82%)	95 (70%)	105 (83%)	116 (87%)	103 (88%)	95 (84%)	17 (71%)	4 (40%)
	Mild	15 (11%)	34 (25%)	16 (13%)	15 (11%)	14 (12%)	14 (12%)	3 (13%)	1 (10%)
	Moderate	0	6 (4%)	2 (2%)	1 (1%)	0	0	0	0
	Severe	0	0	0	1 (1%)	0	0	0	0
	Unknown	9 (7%)	0	4 (3%)	0	0	4 (4%)	4 (17%)	5 (50%)
Other	None	35 (26%)	37 (27%)	30 (24%)	37 (28%)	29 (25%)	35 (31%)	10 (42%)	5 (50%)
	Mild	0	2 (1%)	2 (2%)	0	0	0	0	0
	Moderate	2 (1%)	0	0	0	2 (2%)	0	0	0
	Marked	2 (1%)	0	1 (1%)	0	0	1 (1%)	0	0
	Unknown	96 (71%)	96 (71%)	94 (74%)	96 (72%)	86 (74%)	77 (68%)	14 (58%)	5 (50%)

Table 14: Subject Symptoms Recorded via Self-Administered Symptom Questionnaire for All Treated Eyes

Visual symptoms after topography-assisted LASIK were generally mild in severity. Eye dryness was the most commonly reported subject complaint that occurred in the early 1 or 3-month postoperative period, with 4% of the eyes (6/135) reporting severe dry eye at 1-month and 2% (2/127) reporting severe dry eye at the 3-month visit. This is not an atypical finding after LASIK surgery.

The single report of severe light sensitivity at 1-month postoperatively also reported severe light sensitivity at screening. Light sensitivity improved to "marked" at 3-months, "moderate" at 6-months and was "marked" at 9-months. This subject had the fellow eye

treated with an alternative laser and reported the same severity of light sensitivity before and after LASIK treatment in both eyes.

Reports of "marked" or "severe" reading difficulty are all in middle-aged presbyopic subjects who require reading glasses for their presbyopia and this finding is not unexpected for the age of these patients. The mean age for the 30 study subjects reporting any type of reading difficulty postoperatively was 40.3 years.

Reports of "marked" double vision and fluctuation in one study eye accompanied a report of dry eye and are considered to be related to the subject's eye dryness. One study subject reported "marked" double vision OD and "severe" double vision OS in the patient subjective questionnaire at the 18-month visit. At the 18-month visit, this study subject reported UCVA was 20/40 OU and manifest refraction was +0.25 sphere OD, +0.50 +0.25 x 140 OS. This subject reported a BCVA of 20/20 OU at the 18-month visit.

A single report of severe foreign body sensation occurred at 6-months was completely resolved at the 9-month visit. One study subject reported "marked" starbursts at the 1-month and 3-month postoperative visits OU. Starbursts completely resolved at all further visits through the 12-month visit.

Changes in the degree of severity of patient symptoms reported via the self-administered questionnaire at 3-months compared to baseline are summarized in Table 15.

Change in Degree of Severity of Subject Symptoms at 3 Months After Topography-Assisted LASIK Compared to Before LASIK for All Treated Eyes (N=116)

Question	Preop Marked-Severe n (%)	Month 3 Marked-Severe n (%)	Percent Difference	p-value[1]
Difficulty Driving at Night	25 (21.6%)	0	-21.6%	<.001
Double Vision	0	0	0.0%	*
Dryness	0	4 (3.4%)	3.4%	0.125
Fluctuation in Vision	0	0	0.0%	*
Foreign Body Sensation	0	0	0.0%	*
Glare	3 (2.6%)	0	-2.6%	0.250
Halos	0	0	0.0%	*
Light Sensitivity	6 (5.2%)	2 (1.7%)	-3.4%	0.219
Other	0	1 (3.0%)	3.0%	1.000
Pain	0	0	0.0%	*
Reading Difficulty	0	3 (2.6%)	2.6%	0.250
Starbursts	1 (0.009%)	0	-0.009%	1.000

[1] McNemar's test. * indicates that the p-value cannot be calculated.

Table 15: Change in Degree of Severity of Subject Symptoms at 3 Months post-LASIK Compared to Before LASIK for All Treated Eyes (N=116)

The greatest change is the improvement in night driving which showed about a 21.6% decrease in the number of eyes that had "marked" or "severe" difficulty driving at night after the CATz topography-assisted LASIK procedure compared to baseline. The improvement in difficulty with night driving was clinically significant, defined as a change of ±10% or more in the proportion of eyes reporting symptoms that were moderate to severe postoperatively compared to baseline.

Contrast Sensitivity

Contrast sensitivity was evaluated preoperatively and at 6-months after the topography-assisted LASIK procedure with and without glare under mesopic (3cd/m^2) and photopic (85cd/m^2) chart luminance conditions. Testing was performed using the StereoOptical Optec® 6500 Vision Tester and the Functional Acuity Contrast test (FACT™) Chart with Sine Wave Grating Chart, which tests at five spatial frequencies (1.5, 3, 6, 12 and 18 cycles/degree) and nine levels of contrast, that increase in contrast in equal 0.15 log units from Column 1 through Column 9 for each spatial frequency. The Optec® 6500 is calibrated by the manufacturer to provide photopic and mesopic test conditions and has a built-in glare source that is preset to deliver 10 lux glare luminance under photopic test conditions and 1 lux glare luminance under mesopic conditions.

To perform the test, the subject reports the orientation of the grating (right, up or left). The test is scored by assigning the corresponding percentage contrast value for the target to the last correct grating (target) seen for each spatial frequency.

The change in contrast sensitivity is then determined by calculating the difference between the contrast percentage at baseline and 6-months after the topography assisted LASIK for each spatial frequency.

For the CATz-1 study, study eyes were tested at each of the five spatial frequencies using the manufacturer's preset glare under the following test conditions:

- Photopic (85 cd/m2) without glare
- Photopic (85 cd/m^2) with glare (10 lux)
- Mesopic (3 cd/m^2) without glare
- Mesopic (3 cd/m^2) with glare (1 lux)

Clinically Significant Change in Contrast Sensitivity for All Treated Eyes Tested Monocularly With Data at Pre-op and Post-op Month 6						
			Clinically Significant Decrease		Clinically Significant Increase	
Luminance	Glare	N	n	%	n	%
Mesopic	Yes	69	5	7.2	14	20.3
	No	104	4	3.8	11	10.6
Photopic	Yes	69	2	2.9	15	21.7
	No	104	7	6.7	10	9.6

Table 16: Clinically Significant Change in Contrast Sensitivity for All Treated Eyes

The changes in logarithmic contrast sensitivity, based on the last correct grating seen for each spatial frequency reveal that there is a gain in photopic mean contrast sensitivity, both with and without glare, at most spatial frequencies tested. Spatial frequencies that show a mean loss in photopic contrast sensitivity, (1.5-cpd, 6-cpd (without glare), and 12 cpd (without glare)) are not statistically significant.

Eyes treated with the CATz-1 topography-assisted LASIK procedure also showed a gain in mesopic mean contrast sensitivity with and without glare at all but the highest spatial frequencies of 12-cpd without glare and 18-cpd with and without glare at 6-months after the treatment.

Clinically significant changes in contrast sensitivity are defined as a greater than 0.3 log unit increase (gain) or decrease (loss) at two or more spatial frequencies. Table 16 summarizes clinically significant changes in contrast sensitivity.

Effectiveness Results

The effectiveness analyses were based on 127 eyes that were available for analysis 3 months postoperatively. A comparison of the primary effectiveness parameters 3 months postoperatively (the time point for refractive stability) for the eyes treated in the cohort with the target effectiveness criteria from the CATz-1 Protocol is provided in Table 17 . The outcomes exceed the target criteria for each effectiveness parameter specified in the protocol and combined with the safety profile, serve as the basis of approval.

Comparison of LASIK Effectiveness Criteria at 3 Months Post-LASIK (timepoint of stability)		
Parameter	CATz-1 Myopic Astigmatism Target Criteria	CATz-1 Myopic Astigmatism 3 Months Postop
Percentage of eyes with UCVA of 20/40 or better	85%	127/127 (100.0%)
Percentage of eyes achieving refractive predictability (attempted versus achieved) that are within:		
±0.50D	50%	118/127 (92.9%)
±1.00D	75%	127/127 (100.0%)
±2.00D	NA	127/127 (100.0%)

Table 17: Comparison of LASIK Effectiveness Criteria at 3 Months Post-LASIK

A summary of primary effectiveness variables is provided in Table 18 for the eyes treated in this myopia with astigmatism cohort.

Primary Effectiveness Variables for All Treated Eyes									
	Statistic	Week 1	Month 1	Month 3	Month 6	Month 9	Month 12	Month 18	Month 24
Effectiveness Variables									
MRSE +/- 0.50 D	n/N	117/133	126/135	118/127	113/124	108/117	94/109	18/21	5/7
	%	88.0%	93.3%	92.9%	91.1%	92.3%	86.2%	85.7%	71.4%
	CI[1]	(81.2, 93.0)%	(87.7, 96.9)%	(87.0, 96.7)%	(84.7, 95.5)%	(85.9, 96.4)%	(78.3, 92.1)%	(63.7, 97.0)%	(29.0, 96.3)%
MRSE +/- 1.00 D	n/N	132/133	135/135	127/127	123/124	116/117	109/109	21/21	7/7
	%	99.2%	100.0%	100.0%	99.2%	99.1%	100.0%	100.0%	100.0%
	CI[1]	(95.9, 100.0)%	(97.3, 100.0)%	(97.1, 100.0)%	(95.6, 100.0)%	(95.3, 100.0)%	(96.7, 100.0)%	(83.9, 100.0)%	(59.0, 100.0)%
MRSE +/- 2.00 D	n/N	133/133	135/135	127/127	124/124	117/117	109/109	21/21	7/7
	%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	CI[1]	(97.3, 100.0)%	(97.3, 100.0)%	(97.1, 100.0)%	(97.1, 100.0)%	(96.9, 100.0)%	(96.7, 100.0)%	(83.9, 100.0)%	(59.0, 100.0)%
UCVA 20/20 or better	n/N	104/133	108/135	110/127	118/133	108/117	95/111	18/21	5/7
	%	78.2%	80.0%	86.6%	88.7%	92.3%	85.6%	85.7%	71.4%
	CI[1]	(70.2, 84.9)%	(72.3, 86.4)%	(79.4, 92.0)%	(82.1, 93.5)%	(85.9, 96.4)%	(77.6, 91.5)%	(63.7, 97.0)%	(29.0, 96.3)%
UCVA 20/40 or better	n/N	133/133	135/135	127/127	133/133	117/117	111/111	21/21	7/7
	%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	CI[1]	(97.3, 100.0)%	(97.3, 100.0)%	(97.1, 100.0)%	(97.3, 100.0)%	(96.9, 100.0)%	(96.7, 100.0)%	(83.9, 100.0)%	(59.0, 100.0)%
[1] Exact 95% confidence Interval									

Table 18: Primary Effectiveness Variables for All Treated Eyes

86.6% (110/127) of eyes in this cohort achieved a postoperative uncorrected visual acuity (UCVA) of 20/20 or better at the 3-month postoperative visit. Additionally, 92.9% (118/127) study eyes were within ±0.5D of attempted MRSE and 100% (127/127) of the eyes were within ±1.0D of attempted MRSE at 3 months after the topography-assisted procedure.

The time point to refractive stability is 3 months for the CATz-1 cohort. The summary of effectiveness variables was stratified by preoperative manifest sphere and preoperative manifest cylinder for the cohort at 3-months to encompass the time point of refractive stability. The results of this stratification are summarized in the Tables 19 and 20.

Primary Effectiveness Variables at Month 3 for All Treated Eyes by Preoperative Manifest Sphere							
	Statistic	-1.00 to -2.00 D	-2.01 to -3.00 D	-3.01 to -4.00 D	-4.01 to -5.00 D[2]	-5.01 to -6.00 D[2]	Total
MRSE +/- 0.50 D	n/N	39/41	22/22	34/35	14/17	9/12	118/127
	%	95.1%	100.0%	97.1%	82.4%	75.0%	92.9%

Primary Effectiveness Variables at Month 3 for All Treated Eyes by Preoperative Manifest Sphere							
	Statistic	-1.00 to -2.00 D	-2.01 to -3.00 D	-3.01 to -4.00 D	-4.01 to -5.00 D[2]	-5.01 to -6.00 D[2]	Total
	CI[1]	(78.6, 99.2)%	(84.6, 100.0)%	(85.1, 99.9)%	(56.6, 96.2)%	(42.8, 94.5)%	(87.0, 96.7)%
MRSE +/- 1.00 D	n/N	41/41	22/22	35/35	17/17	12/12	127/127
	%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	CI[1]	(88.8, 100.0)%	(84.6, 100.0)%	(90.0, 100.0)%	(80.5, 100.0)%	(73.5, 100.0)%	(97.1, 100.0)%
MRSE +/- 2.00 D	n/N	41/41	22/22	35/35	17/17	12/12	127/127
	%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	CI[1]	(88.8, 100.0)%	(84.6, 100.0)%	(90.0, 100.0)%	(80.5, 100.0)%	(73.5, 100.0)%	(97.1, 100.0)%
UCVA 20/20 or better	n/N	38/41	19/22	31/35	16/17	6/12	110/127
	%	92.7%	86.4%	88.6%	94.1%	50.0%	86.6%
	CI[1]	(78.6, 99.2)%	(65.1, 97.1)%	(73.3, 96.8)%	(71.3, 99.9)%	(21.1, 78.9)%	(79.4, 92.0)%
UCVA 20/40 or better	n/N	41/41	22/22	35/35	17/17	12/12	127/127
	%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	CI[1]	(88.8, 100.0)%	(84.6, 100.0)%	(90.0, 100.0)%	(80.5, 100.0)%	(73.5, 100.0)%	(97.1, 100.0)%
[1] Exact 95% confidence Interval [2] Outside range of approved indication for use: Flag warning							

Table 19: Primary Effectiveness Variables at Month 3 for All Treated Eyes by Preoperative Manifest Sphere

Primary Effectiveness Variables at Month 3 for All Treated Eyes by Preoperative Manifest Cylinder							
	Statistic	-0.50 to -0.75 D	-0.76 to -1.00 D	-1.01 to -2.00 D	-2.01 to -3.00 D[2]	**-3.01 to -4.00 D[3]**	Total
Effectiveness Variables							
MRSE +/- 0.50 D	n/N	60/65	20/21	31/33	5/6	**2/2**	118/127
	%	92.3%	95.2%	93.9%	83.3%	**100.0%**	92.9%
	CI[1]	(83.0, 97.5)%	(76.2, 99.9)%	(79.8, 99.3)%	(35.9, 99.6)%	**(15.8, 100.0)%**	(87.0, 96.7)%
MRSE +/- 1.00 D	n/N	65/65	21/21	33/33	6/6	**2/2**	127/127
	%	100.0%	100.0%	100.0%	100.0%	**100.0%**	100.0%
	CI[1]	(94.5, 100.0)%	(83.9, 100.0)%	(89.4, 100.0)%	(54.1, 100.0)%	**(15.8, 100.0)%**	(97.1, 100.0)%
MRSE +/- 2.00 D	n/N	65/65	21/21	33/33	6/6	**2/2**	127/127
	%	100.0%	100.0%	100.0%	100.0%	**100.0%**	100.0%

Primary Effectiveness Variables at Month 3 for All Treated Eyes by Preoperative Manifest Cylinder							
	Statistic	-0.50 to -0.75 D	-0.76 to -1.00 D	-1.01 to -2.00 D	-2.01 to -3.00 D[2]	**-3.01 to -4.00 D[3]**	Total
	CI[1]	(94.5, 100.0)%	(83.9, 100.0)%	(89.4, 100.0)%	(54.1, 100.0)%	**(15.8, 100.0)%**	(97.1, 100.0)%
UCVA 20/20 or better	n/N	61/65	18/21	25/33	4/6	**2/2**	110/127
	%	93.8%	85.7%	75.8%	66.7%	**100.0%**	86.6%
	CI[1]	(85.0, 98.3)%	(63.7, 97.0)%	(57.7, 88.9)%	(22.3, 95.7)%	**(15.8, 100.0)%**	(79.4, 92.0)%
UCVA 20/40 or better	n/N	65/65	21/21	33/33	6/6	**2/2**	127/127
	%	100.0%	100.0%	100.0%	100.0%	**100.0%**	100.0%
	CI[1]	(94.5, 100.0)%	(83.9, 100.0)%	(89.4, 100.0)%	(54.1, 100.0)%	**(15.8, 100.0)%**	(97.1, 100.0)%
[1] Exact 95% confidence Interval [2] Outside range of approved indication for use: Flag warning [3] Outside range of approved indication for use: Locked out							

Table 20: Primary Effectiveness Variables at Month 3 for All Treated Eyes by Manifest Cylinder

Change in Best Spectacle Corrected Visual Acuity (BSCVA)

Best spectacle corrected visual acuity was measured in the CATz-1 study using an early treatment diabetic retinopathy study (ETDRS) visual acuity chart. BSCVA was recorded as the total number of letters that was correctly identified by the subject. The number of letters identified was converted to lines of visual acuity by dividing the total number of letters observed by five (1 line/5 letters). Changes in the number of lines of BSCVA were then calculated. In the tables below, a decrease in lines of BSCVA represents a loss of BSCVA, whereas an increase in lines of BSCVA represents a gain or improvement in BSCVA.

The changes in lines of best spectacle corrected visual acuity from screening to each postoperative visit are summarized in Table 21 for the cohort.

Changes in Lines of BCVA From Preop to Postop for All Treated Eyes									
	Statistic	Week 1	Month 1	Month 3	Month 6	Month 9	Month 12	Month 18	Month 24
Decrease > 2 lines	n/N	0/131	0/133	0/123	0/127	0/109	0/103	0/21	0/6
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	CI[1]	(0.0, 2.8)%	(0.0, 2.7)%	(0.0, 3.0)%	(0.0, 2.9)%	(0.0, 3.3)%	(0.0, 3.5)%	(0.0, 16.1)%	(0.0, 45.9)%
Decrease 2 lines	n/N	0/131	0/133	2/123	0/127	0/109	0/103	0/21	0/6
	%	0.0%	0.0%	1.6%	0.0%	0.0%	0.0%	0.0%	0.0%
	CI[1]	(0.0, 2.8)%	(0.0, 2.7)%	(0.2, 5.8)%	(0.0, 2.9)%	(0.0, 3.3)%	(0.0, 3.5)%	(0.0, 16.1)%	(0.0, 45.9)%
Decrease 1 line	n/N	13/131	12/133	8/123	4/127	7/109	9/103	4/21	0/6
	%	9.9%	9.0%	6.5%	3.1%	6.4%	8.7%	19.0%	0.0%

Changes in Lines of BCVA From Preop to Postop for All Treated Eyes									
	Statistic	Week 1	Month 1	Month 3	Month 6	Month 9	Month 12	Month 18	Month 24
	CI[1]	(5.4, 16.4)%	(4.7, 15.2)%	(2.8, 12.4)%	(0.9, 7.9)%	(2.6, 12.8)%	(4.1, 15.9)%	(5.4, 41.9)%	(0.0, 45.9)%
No change	n/N	57/131	57/133	43/123	65/127	45/109	38/103	5/21	0/6
	%	43.5%	42.9%	35.0%	51.2%	41.3%	36.9%	23.8%	0.0%
	CI[1]	(34.9, 52.4)%	(34.3, 51.7)%	(26.6, 44.1)%	(42.2, 60.1)%	(31.9, 51.1)%	(27.6, 47.0)%	(8.2, 47.2)%	(0.0, 45.9)%
Increase 1 line	n/N	50/131	49/133	44/123	38/127	33/109	34/103	4/21	0/6
	%	38.2%	36.8%	35.8%	29.9%	30.3%	33.0%	19.0%	0.0%
	CI[1]	(29.8, 47.1)%	(28.6, 45.6)%	(27.3, 44.9)%	(22.1, 38.7)%	(21.8, 39.8)%	(24.1, 43.0)%	(5.4, 41.9)%	(0.0, 45.9)%
Increase 2 lines	n/N	10/131	14/133	22/123	16/127	21/109	15/103	7/21	6/6
	%	7.6%	10.5%	17.9%	12.6%	19.3%	14.6%	33.3%	100.0%
	CI[1]	(3.7, 13.6)%	(5.9, 17.0)%	(11.6, 25.8)%	(7.4, 19.7)%	(12.3, 27.9)%	(8.4, 22.9)%	(14.6, 57.0)%	(54.1, 100.0)%
Increase > 2 lines	n/N	1/131	1/133	4/123	4/127	3/109	7/103	1/21	0/6
	%	0.8%	0.8%	3.3%	3.1%	2.8%	6.8%	4.8%	0.0%
	CI[1]	(0.0, 4.2)%	(0.0, 4.1)%	(0.9, 8.1)%	(0.9, 7.9)%	(0.6, 7.8)%	(2.8, 13.5)%	(0.1, 23.8)%	(0.0, 45.9)%
[1] Exact 95% confidence Interval									

Table 21: Changes in Lines of BCVA From Preop to Postop for All Treated Eyes

Two eyes (2/123, 1.6%) had a transient two-line loss in BSCVA at the 3-month postoperative visit and none of the eyes had a two or more line loss at any other postoperative visit. 56.9% (70/123) eyes gained at least one or more lines of BSCVA.

Both eyes of one subject had a transient 2-line loss of BSCVA at the 3-month postoperative visit, resulting in a BSCVA of 20/32. Data documented in the database indicates that at the 3-month postoperative visit, this study subject had 1+ PEK (Punctate Epithelial Keratitis) as well as a few meibomian gland secretions in the right eye. BSCVA at the 1-month postoperative visit was 20/20 in the right eye (OD) and 20/16 in the left eye (OS). At the 6, 9 and 12-month postoperative visits, the BSCVA was 20/20 OU.

Uncorrected Visual Acuity

Uncorrected visual acuity was measured using an ETDRS visual acuity chart. Uncorrected visual acuity across time is summarized in Table 22. Eyes treated for myopic astigmatism with CATz topography-assisted LASIK uncorrected visual outcomes at the 3-month postoperative visit were: 86.6% (110/127) eyes achieving an UCVA of 20/20 or better; 48.8% (62/127) eyes achieving an UCVA of 20/16 or better; and 7.9% (10/127) eyes achieving an UCVA or 20/12.5 or better. 99.2% (126/137) reported an UCVA of 20/32 or better, and 100% (127/127) reported an UCVA of 20/40 or better at the 3-month postoperative visit.

UCVA for All Treated Eyes

	Statistic	Preop	Month 1	Month 3	Month 6	Month 9	Month 12	Month 18	Month 24
20/12.5 or better	n/N	0/135	8/135	10/127	10/133	22/117	17/111	2/21	0/7
	%	0.0%	5.9%	7.9%	7.5%	18.8%	15.3%	9.5%	0.0%
	CI[1]	(0.0, 2.7)%	(2.6, 11.3)%	(3.8, 14.0)%	(3.7, 13.4)%	(12.2, 27.1)%	(9.2, 23.4)%	(1.2, 30.4)%	(0.0, 41.0)%
20/16 or better	n/N	0/135	45/135	62/127	65/133	57/117	57/111	10/21	3/7
	%	0.0%	33.3%	48.8%	48.9%	48.7%	51.4%	47.6%	42.9%
	CI[1]	(0.0, 2.7)%	(25.5, 42.0)%	(39.9, 57.8)%	(40.1, 57.7)%	(39.4, 58.1)%	(41.7, 61.0)%	(25.7, 70.2)%	(9.9, 81.6)%
20/20 or better	n/N	1/135	108/135	110/127	118/133	108/117	95/111	18/21	5/7
	%	0.7%	80.0%	86.6%	88.7%	92.3%	85.6%	85.7%	71.4%
	CI[1]	(0.0, 4.1)%	(72.3, 86.4)%	(79.4, 92.0)%	(82.1, 93.5)%	(85.9, 96.4)%	(77.6, 91.5)%	(63.7, 97.0)%	(29.0, 96.3)%
20/25 or better	n/N	1/135	130/135	123/127	127/133	113/117	106/111	19/21	5/7
	%	0.7%	96.3%	96.9%	95.5%	96.6%	95.5%	90.5%	71.4%
	CI[1]	(0.0, 4.1)%	(91.6, 98.8)%	(92.1, 99.1)%	(90.4, 98.3)%	(91.5, 99.1)%	(89.8, 98.5)%	(69.6, 98.8)%	(29.0, 96.3)%
20/32 or better	n/N	3/135	132/135	126/127	133/133	117/117	111/111	19/21	5/7
	%	2.2%	97.8%	99.2%	100.0%	100.0%	100.0%	90.5%	71.4%
	CI[1]	(0.5, 6.4)%	(93.6, 99.5)%	(95.7, 100.0)%	(97.3, 100.0)%	(96.9, 100.0)%	(96.7, 100.0)%	(69.6, 98.8)%	(29.0, 96.3)%
20/40 or better	n/N	7/135	135/135	127/127	133/133	117/117	111/111	21/21	7/7
	%	5.2%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	CI[1]	(2.1, 10.4)%	(97.3, 100.0)%	(97.1, 100.0)%	(97.3, 100.0)%	(96.9, 100.0)%	(96.7, 100.0)%	(83.9, 100.0)%	(59.0, 100.0)%
20/80 or better	n/N	22/135	135/135	127/127	133/133	117/117	111/111	21/21	7/7
	%	16.3%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	CI[1]	(10.5, 23.6)%	(97.3, 100.0)%	(97.1, 100.0)%	(97.3, 100.0)%	(96.9, 100.0)%	(96.7, 100.0)%	(83.9, 100.0)%	(59.0, 100.0)%
20/200 or better	n/N	135/135	135/135	127/127	133/133	117/117	111/111	21/21	7/7
	%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	CI[1]	(97.3, 100.0)%	(97.3, 100.0)%	(97.1, 100.0)%	(97.3, 100.0)%	(96.9, 100.0)%	(96.7, 100.0)%	(83.9, 100.0)%	(59.0, 100.0)%
[1] Exact 95% confidence Interval									

Table 22: UCVA for All Treated Eyes

Eyes treated in the study also showed improvement in functional vision after the topography-assisted LASIK procedure. As shown in Table 23, 20.4% (26/127) of study eyes reported an uncorrected visual acuity at 3-months of at least one line less than the baseline best spectacle corrected visual acuity (BSCVA) before CATz-1 LASIK treatment; and 79.5% (101/127) of study eyes achieved an uncorrected visual acuity at 3-months equal to or greater than the baseline BSCVA before CATz-1 LASIK treatment.

Postop UCVA Compared to Preop BCVA for All Treated Eyes

	Statistic	Week 1	Month 1	Month 3	Month 6	Month 9	Month 12	Month 18	Month 24
> 2 lines better	n/N	0/133	1/135	1/127	1/133	2/117	6/111	0/21	0/7
	%	0.0%	0.7%	0.8%	0.8%	1.7%	5.4%	0.0%	0.0%
	CI[1]	(0.0, 2.7)%	(0.0, 4.1)%	(0.0, 4.3)%	(0.0, 4.1)%	(0.2, 6.0)%	(2.0, 11.4)%	(0.0, 16.1)%	(0.0, 41.0)%
2 lines better	n/N	8/133	6/135	15/127	15/133	19/117	14/111	7/21	1/7
	%	6.0%	4.4%	11.8%	11.3%	16.2%	12.6%	33.3%	14.3%
	CI[1]	(2.6, 11.5)%	(1.6, 9.4)%	(6.8, 18.7)%	(6.5, 17.9)%	(10.1, 24.2)%	(7.1, 20.3)%	(14.6, 57.0)%	(0.4, 57.9)%
1 line better	n/N	33/133	41/135	47/127	46/133	37/117	31/111	3/21	4/7
	%	24.8%	30.4%	37.0%	34.6%	31.6%	27.9%	14.3%	57.1%
	CI[1]	(17.7, 33.0)%	(22.8, 38.9)%	(28.6, 46.0)%	(26.6, 43.3)%	(23.3, 40.9)%	(19.8, 37.2)%	(3.0, 36.3)%	(18.4, 90.1)%
Equal	n/N	56/133	53/135	38/127	49/133	40/117	39/111	5/21	0/7
	%	42.1%	39.3%	29.9%	36.8%	34.2%	35.1%	23.8%	0.0%
	CI[1]	(33.6, 51.0)%	(31.0, 48.0)%	(22.1, 38.7)%	(28.6, 45.6)%	(25.7, 43.5)%	(26.3, 44.8)%	(8.2, 47.2)%	(0.0, 41.0)%
1 line worse	n/N	22/133	29/135	20/127	17/133	16/117	17/111	4/21	0/7
	%	16.5%	21.5%	15.7%	12.8%	13.7%	15.3%	19.0%	0.0%
	CI[1]	(10.7, 24.0)%	(14.9, 29.4)%	(9.9, 23.3)%	(7.6, 19.7)%	(8.0, 21.3)%	(9.2, 23.4)%	(5.4, 41.9)%	(0.0, 41.0)%
2 lines worse	n/N	10/133	3/135	5/127	4/133	2/117	2/111	0/21	2/7
	%	7.5%	2.2%	3.9%	3.0%	1.7%	1.8%	0.0%	28.6%
	CI[1]	(3.7, 13.4)%	(0.5, 6.4)%	(1.3, 8.9)%	(0.8, 7.5)%	(0.2, 6.0)%	(0.2, 6.4)%	(0.0, 16.1)%	(3.7, 71.0)%
> 2 lines worse	n/N	4/133	2/135	1/127	1/133	1/117	2/111	2/21	0/7
	%	3.0%	1.5%	0.8%	0.8%	0.9%	1.8%	9.5%	0.0%
	CI[1]	(0.8, 7.5)%	(0.2, 5.2)%	(0.0, 4.3)%	(0.0, 4.1)%	(0.0, 4.7)%	(0.2, 6.4)%	(1.2, 30.4)%	(0.0, 41.0)%
[1] Exact 95% confidence Interval									

Table 23: Postop UCVA Compared to Preop BCVA for All Treated Eyes

Treatment Accuracy for Manifest Sphere and Manifest Cylinder

The descriptive statistics for the predictability (accuracy) of the attempted versus achieved manifest sphere and magnitude of cylinder are summarized in Table 24 for this cohort of myopic astigmatic eyes.

At the timepoint of refractive stability (3-months), the eyes in the entire myopic astigmatic cohort (see table below) achieved at least 72% of the attempted magnitude of cylinder treatment and 103% of the attempted spherical treatment. The percentage of magnitude of cylinder achieved remains constant through the 18-month visit, as does the percentage of spherical treatment achieved. 92% of study eyes were within ±0.50D of the attempted magnitude of cylinder treatment at the 3-month visit.

Treatment Accuracy for Sphere and Cylinder Magnitude for All Treated Eyes									
	Preop	Week 1	Month 1	Month 3	Month 6	Month 9	Month 12	Month 18	Month 24
Sphere	N = 135	N = 133	N = 135	N = 127	N = 133	N = 117	N = 111	N = 21	N = 7
Mean (SD)	-3.06 (1.40)	0.11 (0.38)	0.08 (0.31)	0.06 (0.31)	0.05 (0.32)	0.03 (0.33)	0.02 (0.37)	0.11 (0.35)	0.07 (0.35)
Attempted (SD)	-3.06 (1.40)	-3.08 (1.39)	-3.06 (1.40)	-3.04 (1.43)	-3.05 (1.41)	-3.04 (1.40)	-3.22 (1.41)	-3.83 (1.62)	-3.96 (1.43)
Achieved (SD)		-3.19 (1.52)	-3.13 (1.44)	-3.10 (1.48)	-3.10 (1.46)	-3.07 (1.45)	-3.24 (1.45)	-3.94 (1.61)	-4.04 (1.57)
% Achieved		103	103	103	102	102	101	105	101
Within +/- 0.5D, n (%)		115 (86%)	127 (94%)	121 (95%)	124 (93%)	109 (93%)	100 (90%)	19 (90%)	7 (100%)
Within +/- 1.0D, n (%)		131 (98%)	134 (99%)	126 (99%)	133 (100%)	117 (100%)	111 (100%)	21 (100%)	7 (100%)
Cylinder	N = 135	N = 133	N = 135	N = 127	N = 133	N = 117	N = 111	N = 21	N = 7
Mean (SD)	-1.03 (0.64)	-0.21 (0.27)	-0.23 (0.25)	-0.24 (0.24)	-0.24 (0.27)	-0.22 (0.24)	-0.19 (0.24)	-0.30 (0.27)	-0.75 (0.54)
Attempted (SD)	-1.03 (0.64)	-1.02 (0.64)	-1.03 (0.64)	-1.04 (0.64)	-1.03 (0.64)	-0.97 (0.56)	-1.01 (0.59)	-0.88 (0.37)	-0.75 (0.29)
Achieved (SD)		-0.81 (0.66)	-0.80 (0.66)	-0.80 (0.64)	-0.79 (0.66)	-0.74 (0.62)	-0.82 (0.63)	-0.58 (0.37)	0.00 (0.61)
% Achieved		76	73	72	71	71	77	65	-12
Within +/- 0.5D, n (%)		123 (92%)	125 (93%)	117 (92%)	121 (91%)	111 (95%)	103 (93%)	18 (86%)	3 (43%)
Within +/- 1.0D, n (%)		133 (100%)	135 (100%)	127 (100%)	133 (100%)	117 (100%)	111 (100%)	21 (100%)	5 (71%)

Table 24: Treatment Accuracy for Sphere and Cylinder Magnitude for All Treated Eyes

At 3-months postoperatively, the surgically induced refractive correction (SIRC) of 0.89 for the myopic astigmatism cohort closely approximates the intended refractive correction (IRC) of 0.95 for all eyes treated. This is confirmed by the correction ratio (CR) of 0.95 for all treated eyes in the cohort. At 3-months postoperatively, the error of magnitude for the myopic astigmatism cohort is 0.06 with an error of angle of -2.33. Subjects with preoperative cylinder greater than -2.0D experienced a higher error of magnitude and error of angle. For subjects with preoperative cylinder greater than -2.0D to -3.0D, the error of magnitude was 0.39 and the error of angle was -2.48. For subjects with preoperative cylinder greater than -3.0D to -4.0D, the error of magnitude was 0.36 and the error of angle was 0.73.

Accuracy of Manifest Refraction Attempted vs Achieved

The number of eyes that are within ±0.5 D, ±1.00 D, and ±2.00 D of attempted versus achieved manifest refraction spherical equivalent (MRSE) is summarized in Table 25. Also included in the table is a summary of eyes that were overcorrected or undercorrected by 1.00 D and by 2.00 D.

Refractive Predictability in All Treated Eyes									
	Statistic	Preop	Month 1	Month 3	Month 6	Month 9	Month 12	Month 18	Month 24
+/- 0.50 D	n/N	0/135	126/135	118/127	113/124	108/117	94/109	18/21	5/7
	%	0.0%	93.3%	92.9%	91.1%	92.3%	86.2%	85.7%	71.4%
	CI[1]	(0.0, 2.7)%	(87.7, 96.9)%	(87.0, 96.7)%	(84.7, 95.5)%	(85.9, 96.4)%	(78.3, 92.1)%	(63.7, 97.0)%	(29.0, 96.3)%
+/- 1.00 D	n/N	0/135	135/135	127/127	123/124	116/117	109/109	21/21	7/7
	%	0.0%	100.0%	100.0%	99.2%	99.1%	100.0%	100.0%	100.0%
	CI[1]	(0.0, 2.7)%	(97.3, 100.0)%	(97.1, 100.0)%	(95.6, 100.0)%	(95.3, 100.0)%	(96.7, 100.0)%	(83.9, 100.0)%	(59.0, 100.0)%
+/- 2.00 D	n/N	32/135	135/135	127/127	124/124	117/117	109/109	21/21	7/7
	%	23.7%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	CI[1]	(16.8, 31.8)%	(97.3, 100.0)%	(97.1, 100.0)%	(97.1, 100.0)%	(96.9, 100.0)%	(96.7, 100.0)%	(83.9, 100.0)%	(59.0, 100.0)%
Overcorrected > 1 D	n/N	0/135	0/135	0/127	0/124	0/117	0/109	0/21	0/7
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	CI[1]	(0.0, 2.7)%	(0.0, 2.7)%	(0.0, 2.9)%	(0.0, 2.9)%	(0.0, 3.1)%	(0.0, 3.3)%	(0.0, 16.1)%	(0.0, 41.0)%
Overcorrected > 2 D	n/N	0/135	0/135	0/127	0/124	0/117	0/109	0/21	0/7
	%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	CI[1]	(0.0, 2.7)%	(0.0, 2.7)%	(0.0, 2.9)%	(0.0, 2.9)%	(0.0, 3.1)%	(0.0, 3.3)%	(0.0, 16.1)%	(0.0, 41.0)%
Undercorrected < -1 D	n/N	135/135	0/135	0/127	1/124	1/117	0/109	0/21	0/7
	%	100.0%	0.0%	0.0%	0.8%	0.9%	0.0%	0.0%	0.0%
	CI[1]	(97.3, 100.0)%	(0.0, 2.7)%	(0.0, 2.9)%	(0.0, 4.4)%	(0.0, 4.7)%	(0.0, 3.3)%	(0.0, 16.1)%	(0.0, 41.0)%
Undercorrected < -2 D	n/N	103/135	0/135	0/127	0/124	0/117	0/109	0/21	0/7
	%	76.3%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	CI[1]	(68.2, 83.2)%	(0.0, 2.7)%	(0.0, 2.9)%	(0.0, 2.9)%	(0.0, 3.1)%	(0.0, 3.3)%	(0.0, 16.1)%	(0.0, 41.0)%
[1] Exact 95% confidence Interval									

Table 25: Refractive Predictability in All Treated Eyes

Refractive outcomes of 92.9% (118/127) of study eyes were within ±0.5 D of attempted versus achieved MRSE and 100% or study eyes (127/127) were within ±1.00 D of attempted versus achieved MRSE at 3-months after the topography-assisted LASIK procedure. These

refractive outcomes correlate well with the uncorrected visual acuities reported by study subjects.

Zernike Analysis

The CATz (Customized Aspheric Treatment zone) mode of the Final Fit software is a topography-assisted treatment and not a wavefront-assisted treatment. The treatment is calculated to first reduce the refractive error (spherocylindrical correction) based on the manifest refraction using OATz Profile #5 and then treats a portion of the residual corneal irregularities based on the raw topographic data.

Zernike polynomial data were obtained in all eyes using the Nidek OPD-Scan topographer/aberrometer. The OPD-Scan calculates the whole eye aberrometry Zernike coefficients according to the methods described in ANSI Z80.28[3]. An analysis of the Zernike coefficients was performed to evaluate the effect of the topography-assisted LASIK treatment on whole eye aberrations. The analysis is based on a consistent cohort of eyes that had an OPD-Scan with 5 mm pupil diameter data at all time points evaluated.

RMS Aberration Magnitudes Before and After Topography-Assisted LASIK Mean (μm) ±SD for All Treated Eyes 6-Month Consistent Cohort									
		Pre-op		Month 1		Month 3		Month 6	
Aberration	N	Mean	SD	Mean	SD	Mean	SD	Mean	SD
RMS Defocus	101	2.799	1.234	0.344	0.318	0.370	0.300	0.389	0.303
RMS Astigmatism	101	0.493	0.292	0.300	0.378	0.292	0.270	0.275	0.190
RMS >2nd Order	101	0.243	0.101	0.354	0.447	0.373	0.371	0.324	0.225
RMS Coma	101	0.102	0.058	0.125	0.097	0.135	0.085	0.129	0.086
RMS Trefoil	101	0.167	0.093	0.199	0.110	0.219	0.138	0.197	0.121
RMS Spherical Aberration	101	0.051	0.036	0.078	0.056	0.080	0.052	0.070	0.051
RMS Secondary Astigmatism	101	0.037	0.024	0.051	0.055	0.053	0.054	0.053	0.047
RMS Tetrafoil	101	0.053	0.046	0.096	0.216	0.107	0.252	0.086	0.141
RMS >4th Order	101	0.073	0.055	0.142	0.396	0.148	0.270	0.117	0.159

Table 26: RMS Aberration Magnitudes Before and After LASIK Mean (μm) ±SD for All Treated Eyes 6-Month Consistent Cohort

The mean defocus amplitude and signed astigmatism horizontal amplitude is reduced at all timepoints compared to baseline (see Table 27). Spherical aberrations show an increase that is no greater than that observed with conventional LASIK treatments.

Signed Aberration Amplitudes Before and After Topography-Assisted LASIK Mean (μm) ±S.D.									
		Pre-op		Month 1		Month 3		Month 6	
Aberration	N	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Signed Defocus	101	2.799	1.234	0.204	0.422	0.237	0.414	0.283	0.405
Signed Astigmatism Horizontal	101	-0.135	0.485	0.008	0.439	-0.013	0.340	-0.015	0.265
Signed Astigmatism Vertical	101	-0.006	0.278	-0.070	0.189	-0.043	0.267	-0.068	0.195
Signed Coma Horizontal	101	-0.009	0.092	-0.036	0.127	-0.043	0.123	-0.030	0.119
Signed Coma Vertical	101	-0.005	0.072	-0.018	0.087	-0.015	0.092	-0.014	0.095
Signed Spherical Aberration	101	0.014	0.061	0.049	0.083	0.045	0.084	0.052	0.069

Table 27: Signed Aberration Amplitudes Before and After LASIK Mean (μm) ±S.D.

A paired analysis was performed for each eye in the consistent cohort to determine the change in aberration magnitudes and the percentage change in magnitudes at each postoperative visit compared to baseline as expected, the changes in defocus and astigmatism were significant ($p<0.05$). The increases in spherical aberration and coma were also significant ($p<0.05$). Significant percentage changes should be interpreted cautiously for those Zernike coefficients, such as trefoil, that have very small values in which small incremental changes in value will result in a seemingly large percentage change.

The proportion of eyes with reduced, overcorrected, or increased aberrations is analyzed. The changes in aberrations are defined as follows:

- ***Reduced:*** Aberrations reduced in magnitude by an order that is greater than or equal to the repeated-measures standard deviation and of the same sign (orientation), or reversed in sign (orientation) with magnitude less than or equal to the repeated-measures standard deviation,

- ***Overcorrected:*** Aberrations with reversed sign (orientation) and magnitude that is greater than the repeated measures standard deviation; or,

- ***Increased:*** Aberrations increased in magnitude by an order that is greater than or equal to the repeated-measures standard deviation and of the same sign (orientation).

At 3 and 6-months, each aberration evaluated is either reduced or unchanged in at least two-thirds of eyes that underwent the topography-assisted LASIK procedure.

The proportion of eyes that have increased and overcorrected aberrations is low for astigmatism (horizontal, vertical, secondary horizontal, secondary vertical), with 12% or fewer of the eyes that showed an increase and/or overcorrection.

A paired difference analysis was performed to evaluate the stability of the aberrations across time.

Stability of Manifest Refraction

Refractive stability was evaluated in the eyes that completed one or more pairs of successive postoperative visits. The mean changes (paired differences) in MRSE (±S.D. and 95% C.I.) between pairs of successive refractions for eyes in a consistent cohort (i.e., 114 eyes that each completed all consecutive visits from 1-week through 6-month) are reported in Table 28 and depicted graphically in Figure 1.

Refractive Stability for All Treated Eyes that Have Paired Differences at All of Specified Visit Intervals From Week 1 to Month 6				
Measure	Statistic	Week 1 to Month 1	Month 1 to Month 3	Month 3 to Month 6
Absolute Change of MRSE <= 1D	n/N	112/114	114/114	114/114
	%	98.2%	100.0%	100.0%
	CI[1]	(93.8, 99.8)%	(96.8, 100.0)%	(96.8, 100.0)%
Absolute Change of MRSE <= 0.5D	n/N	100/114	107/114	109/114
	%	87.7%	93.9%	95.6%
	CI[1]	(80.3, 93.1)%	(87.8, 97.5)%	(90.1, 98.6)%
Change of MRSE in diopters	Mean	-0.051	-0.023	-0.025
	Std	0.365	0.270	0.245
	CI[1]	(-0.118, 0.017)	(-0.073, 0.027)	(-0.071, 0.020)
Change of MRSE per year	Mean	-0.876	-0.138	-0.102
	Std	6.331	1.623	0.981
	CI[1]	(-2.050, 0.299)	(-0.439, 0.163)	(-0.284, 0.080)
Change of MRSE per month	Mean	-0.067	-0.011	-0.008
	Std	0.487	0.135	0.082
	CI[1]	(-0.158, 0.023)	(-0.037, 0.014)	(-0.024, 0.007)
[1] Exact 95% confidence Interval				

Table 28: Refractive Stability for All Treated Eyes that Have Paired Differences at All of Specified Visit Intervals From Week 1 to Month 6

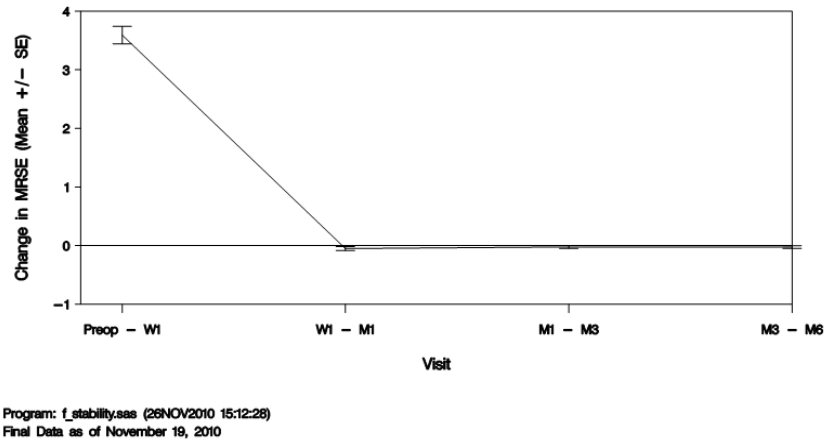

Figure 1: Refractive Stability for all Treated Eyes with Paired Differences at All Specified Visit Intervals From Week 1 to Month 6

Refractive stability, as defined in Protocol CATz-1, is achieved at 3-months and confirmed at 6-months postoperatively for this cohort of eyes treated with topography-assisted LASIK. The stability criteria are summarized in the Refractive Stability Criteria table below, based on the data for the consecutive cohort of eyes presented in the Table 29.

CATz-1 Refractive Stability Criteria		
Criteria	CATz-1 Stability Outcomes	Meets Criteria
At least 95% of treated eyes have a change ≤1.00D MRSE between manifest refractions performed at 3 and 6 months after surgery (and confirmed at 6 and 9 months)	Month 1 to Month 3: All paired visits: 114/114 (100%) Missing visits: 127/127 (100%) Month 3 to Month 6: All paired visits: 114/114 (100%) Missing visits: 116/116 (100%)	Yes at 3 months Confirmed at 6 months
Mean rate of change (paired analysis) is ≤0.04D/month	Month 1 to Month 3: All paired visits: -0.011D/month Missing visits: -0.006D/month Month 3 to Month 6: All paired visits: -0.008D/month Missing visits: -0.009D/month	Yes at 3 months Confirmed at 6 months
Mean rate of change decreases monotonically over time	Month 1 to Month 3: All paired visits: -0.011D/month Missing visits: -0.006D/month Month 3 to Month 6: All paired visits: -0.008D/month Missing visits: -0.009D/month	Change consistent with usual stability pattern for myopic astigmatism

	Missing Visits: Month 6 to Month 9: -0.006 D/month Month 9 to Month 12: 0.005 D/month	
95% confidence interval for the mean rate of change includes zero	Month 1 to Month 3: All paired visits: (-0.073, 0.027) Missing visits: (-0.059, 0.035) Month 3 to Month 6: All paired visits: (-0.071, 0.020) Missing visits: (-0.071, 0.019)	Yes at 3 months Confirmed at 6 months

Table 29: CATz-1 Refractive Stability Criteria

Manifest Sphere and Manifest Cylinder Descriptive Statistics

Descriptive statistics for manifest sphere and manifest cylinder for each study visit are summarized in Tables 30, 31. Descriptive statistics for the MRSE are summarized in Table 32. As shown in the tables, the topography-assisted LASIK achieves good accuracy for all three parameters. At 3-months postoperatively, the mean sphere, cylinder, and MRSE are 0.06 D (±0.31), -0.24 D (±0.24), and -0.06 D (±0.29), which is well within the accepted standards for variability of these manifest refraction measurements.

Descriptive Statistics for Manifest Refraction Sphere For All Treated Eyes					
Visit	N	Mean	Standard Deviation	95% Lower CL	95% Upper CL
Screening	135	-3.03	1.40	-3.27	-2.80
Preop	135	-3.06	1.40	-3.29	-2.82
Postop Week 1	133	0.11	0.38	0.05	0.18
Postop Month 1	135	0.08	0.31	0.02	0.13
Postop Month 3	127	0.06	0.31	0.00	0.11
Postop Month 6	133	0.05	0.32	-0.01	0.10
Postop Month 9	117	0.03	0.33	-0.03	0.09
Postop Month 12	111	0.02	0.37	-0.05	0.09
Postop Month 18	21	0.11	0.35	-0.05	0.27
Postop Month 24	7	0.07	0.35	-0.25	0.39

Table 30: Descriptive Statistics for Manifest Refraction Sphere for All Treated Eyes

Descriptive Statistics for Manifest Refraction Cylinder For All Treated Eyes					
Visit	N	Mean	Standard Deviation	95% Lower CL	95% Upper CL
Screening	135	-1.01	0.63	-1.12	-0.90
Preop	135	-1.03	0.64	-1.14	-0.92
Postop Week 1	133	-0.21	0.27	-0.26	-0.16

Descriptive Statistics for Manifest Refraction Cylinder For All Treated Eyes					
Visit	N	Mean	Standard Deviation	95% Lower CL	95% Upper CL
Postop Month 1	135	-0.23	0.25	-0.27	-0.19
Postop Month 3	127	-0.24	0.24	-0.28	-0.20
Postop Month 6	133	-0.24	0.27	-0.29	-0.20
Postop Month 9	117	-0.22	0.24	-0.27	-0.18
Postop Month 12	111	-0.19	0.24	-0.24	-0.15
Postop Month 18	21	-0.30	0.27	-0.42	-0.17
Postop Month 24	7	-0.75	0.54	-1.25	-0.25

Table 31: Descriptive Statistics for Manifest Refraction Cylinder for All Treated Eyes

Descriptive Statistics for Manifest Refraction MRSE For All Treated Eyes					
Visit	N	Mean	Standard Deviation	95% Lower CL	95% Upper CL
Screening	135	-3.54	1.45	-3.78	-3.29
Preop	135	-3.57	1.45	-3.82	-3.32
Postop Week 1	133	0.01	0.37	-0.05	0.07
Postop Month 1	135	-0.04	0.31	-0.09	0.02
Postop Month 3	127	-0.06	0.29	-0.11	-0.01
Postop Month 6	124	-0.08	0.33	-0.14	-0.02
Postop Month 9	117	-0.08	0.31	-0.14	-0.02
Postop Month 12	109	-0.08	0.37	-0.15	-0.01
Postop Month 18	21	-0.04	0.35	-0.20	0.12
Postop Month 24	7	-0.30	0.33	-0.60	0.00

Table 32: Descriptive Statistics for Manifest Refraction MRSE for All Treated Eyes

Treatment Accuracy for Manifest Sphere and Manifest Cylinder

The descriptive statistics for the predictability (accuracy) of the attempted versus achieved manifest sphere and magnitude of cylinder are summarized in Table 33 for this cohort of myopic astigmatic eyes.

At the timepoint of refractive stability (3-months), the eyes in the entire myopic astigmatic cohort (see table below) achieved at least 72% of the attempted magnitude of cylinder treatment and 103% of the attempted spherical treatment. The percentage of magnitude of cylinder achieved remains constant through the 18-month visit, as does the percentage of spherical treatment achieved. 92% of study eyes were within ±0.50D of the attempted magnitude of cylinder treatment at the 3-month visit.

Treatment Accuracy for Sphere and Cylinder Magnitude for All Treated Eyes									
	Preop	Week 1	Month 1	Month 3	Month 6	Month 9	Month 12	Month 18	Month 24
Sphere	N = 135	N = 133	N = 135	N = 127	N = 133	N = 117	N = 111	N = 21	N = 7
Mean (SD)	-3.06 (1.40)	0.11 (0.38)	0.08 (0.31)	0.06 (0.31)	0.05 (0.32)	0.03 (0.33)	0.02 (0.37)	0.11 (0.35)	0.07 (0.35)
Attempted (SD)	-3.06 (1.40)	-3.08 (1.39)	-3.06 (1.40)	-3.04 (1.43)	-3.05 (1.41)	-3.04 (1.40)	-3.22 (1.41)	-3.83 (1.62)	-3.96 (1.43)
Achieved (SD)		-3.19 (1.52)	-3.13 (1.44)	-3.10 (1.48)	-3.10 (1.46)	-3.07 (1.45)	-3.24 (1.45)	-3.94 (1.61)	-4.04 (1.57)
% Achieved		103	103	103	102	102	101	105	101
Within +/- 0.5D, n (%)		115 (86%)	127 (94%)	121 (95%)	124 (93%)	109 (93%)	100 (90%)	19 (90%)	7 (100%)
Within +/- 1.0D, n (%)		131 (98%)	134 (99%)	126 (99%)	133 (100%)	117 (100%)	111 (100%)	21 (100%)	7 (100%)
Cylinder	N = 135	N = 133	N = 135	N = 127	N = 133	N = 117	N = 111	N = 21	N = 7
Mean (SD)	-1.03 (0.64)	-0.21 (0.27)	-0.23 (0.25)	-0.24 (0.24)	-0.24 (0.27)	-0.22 (0.24)	-0.19 (0.24)	-0.30 (0.27)	-0.75 (0.54)
Attempted (SD)	-1.03 (0.64)	-1.02 (0.64)	-1.03 (0.64)	-1.04 (0.64)	-1.03 (0.64)	-0.97 (0.56)	-1.01 (0.59)	-0.88 (0.37)	-0.75 (0.29)
Achieved (SD)		-0.81 (0.66)	-0.80 (0.66)	-0.80 (0.64)	-0.79 (0.66)	-0.74 (0.62)	-0.82 (0.63)	-0.58 (0.37)	0.00 (0.61)
% Achieved		76	73	72	71	71	77	65	-12
Within +/- 0.5D, n (%)		123 (92%)	125 (93%)	117 (92%)	121 (91%)	111 (95%)	103 (93%)	18 (86%)	3 (43%)
Within +/- 1.0D, n (%)		133 (100%)	135 (100%)	127 (100%)	133 (100%)	117 (100%)	111 (100%)	21 (100%)	5 (71%)

Table 33: Treatment Accuracy for Sphere and Cylinder Magnitude for All Treated Eyes

Data on seven eyes of four subjects are reported at the last recorded postoperative visit (24-months). These seven eyes (see table directly above) achieved -12% of the attempted magnitude of cylinder treatment and 101% of the attempted spherical treatment.

The two eyes that showed an increase in myopic astigmatism of 0.75D during the 18 and 24-month time interval were of the same subject. The right eye had an increase in cylinder of -0.75D and the left eye had an increase in cylinder of -0.75D during this time interval. Both eyes of this subject had 1+ PEK reported at the18 month visit. This subject complained of dry eyes in both eyes and Artificial Tears were prescribed throughout the postoperative reporting period, including the 24 month visit. At the 24 month postoperative visit, the right eye UCVA was 20/40 and BCVA was 20/16; the left eye UCVA was 20/20 and BCVA was 20/16.

A summary of the IRC, SIRC, error of magnitude, error of angle and correction ratio at 3-months postoperatively (timepoint of stability) is provided below in Table 34.

Vector Cylinder Correction Parameters at 3 Months Stratified by Preop Cylinder for All Treated Eyes						
Preop Cylinder	N	|IRC| Mean (SD)	|SIRC| Mean (SD)	Error of Magnitude Mean (SD)	Error of Angle Mean (SD)	Correction Ratio Mean (SD)
All	127	0.95 (0.57)	0.89 (0.54)	0.06 (0.22)	-2.33 (12.29)	0.95 (0.28)
0 to -0.5 D	40	0.46 (0.02)	0.45 (0.19)	0.02 (0.19)	-4.31 (17.92)	0.96 (0.41)
-0.5 D to -1.0 D	46	0.80 (0.12)	0.76 (0.19)	0.04 (0.17)	-1.85 (10.07)	0.95 (0.21)
> -1.0 D to -2.0 D	34	1.38 (0.24)	1.30 (0.32)	0.09 (0.22)	-0.80 (6.98)	0.94 (0.16)
> -2.0 D to -3.0 D	5	2.48 (0.31)	2.09 (0.49)	0.39 (0.40)	-2.48 (3.91)	0.84 (0.15)
> -3.0 D to -4.0 D	2	3.17 (0.13)	2.81 (0.38)	0.36 (0.52)	0.73 (1.03)	0.89 (0.16)

Table 34: Vector Cylinder Correction Parameters at 3 Months Stratified by Preop Cylinder for All Treated Eyes

At 3-months postoperatively, the SIRC of 0.89 for the myopic astigmatism cohort closely approximates the IRC of 0.95 for all eyes treated. This is confirmed by the correction ratio (CR) of 0.95 for all treated eyes in the cohort. At 3-months postoperatively, the error of magnitude for the myopic astigmatism cohort is 0.06 with an error of angle of -2.33. Subjects with preoperative cylinder greater than -2.0D experienced a higher error of magnitude and error of angle. For subjects with preoperative cylinder greater than -2.0D to -3.0D, the error of magnitude was 0.39 and the error of angle was -2.48. For subjects with preoperative cylinder greater than -3.0D to -4.0D, the error of magnitude was 0.36 and the error of angle was 0.73.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XII. PANEL MEETING 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. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness analyses were based on 127 eyes that were available for analysis at 3 months postoperatively. Ninety-two and nine-tenths percent (92.9%; 118/127) of the eyes were within 0.5 D of attempted versus achieved MRSE and 100% of the eyes (127/127) within 1.0 D of attempted versus achieved MRSE at 3 months after the topography-guided LASIK procedure. These refractive outcomes are reflected in the uncorrected visual acuities reported by the subjects. Refractive stability has been established at 3-months postoperatively for the entire cohort and confirmed at 6-months postoperatively. At 3 months postop, the SIRC of 0.97 for the myopic astigmatism cohort closely approximates the intended refractive correction of 1.04 for all eyes treated. This is confirmed by the CR of 0.94 for all treated eyes in the cohort. All cylinder treatment outcomes demonstrated a high degree of accuracy. At 3 and 6 months, each aberration treated was either reduced or unchanged in at least three-fourths of eyes that underwent the topography-guided LASIK procedure. Very few eyes (9 or less) had an increase in astigmatism of any type at any of the postoperative time points.

Eyes treated with the topography-guided LASIK procedure also showed a gain in mesopic mean contrast sensitivity with and without glare at all but the highest spatial frequencies of 12 cpd without glare and 18 cpd with and without glare at 6 months after the treatment. The increases in mesopic mean contrast percent were statistically significant at 3 and 6 cpd with glare, which were the same spatial frequencies and glare conditions that reached statistical significance under photopic conditions.

B. Safety Conclusions

Only a small percentage of adverse events occurred in the study, which included dry eye, a transient loss of 2 lines of BSCVA in one patient at 3 months postoperatively due to eye tiredness and eye dryness and optical aberrations (e.g., halo, starbursts, glare). The most commonly occurring postoperative complication at 1 month or later was dry eyes requiring the use of prescribed artificial tears in 8 eyes (5.9%) at 1 month and 2 eyes (1.5%) at 6 months postoperatively. Prescribed usage was discontinued at the next postoperative visit in most cases. Visual symptoms after topography-guided CATz LASIK were generally mild in severity. Eye dryness was the most commonly reported patient complaint that occurred in the early 1 or 3 month postoperative period, with 4% of the eyes (6/135) reporting severe dry eye at 1 month and 2% (2/122) reporting severe dry eye at 3 months. This is not an atypical finding after LASIK surgery.

Changes in the degree of severity of patient symptoms reported via the self-administered questionnaire are summarized in Table 14 on page 20. Clinically significant changes were defined as a change of ±10% or more in the proportion of eyes reporting symptoms that were moderate to severe postoperatively compared to baseline. The 23% improvement in difficulty with night driving was statistically ($p<0.05$) and clinically significant. The 3.3% increase in eye dryness at 3 months was statistically significant ($p<0.05$) but not clinically significant.

C. Benefit-Risk Conclusions

The study was able to predict benefit based upon past experience with this device. There is at least a 95% probability of a patient for experiencing the benefit. Subpopulations were not evaluated. Duration of the effect was evaluated only within the time the study was conducted. Refractive error changes over the lifespan; therefore, it is expected that the effect of the treatment will change with age, but this varies with the individual. Patients are informed of this in the informed consent process. This benefit and its duration are valued by the patient as refractive surgery, LASIK, is very popular.

Summary of benefits: There were 86.6% (110/127) eyes achieving an UCVA of 20/20 or better; 48.8% (62/127) eyes achieving an UCVA of 20/16 or better; and 7.9% (10/127) eyes achieving an UCVA or 20/12.5 or better. 99.2% (126/137) reported an UCVA of 20/32 or better, and 100% (127/127) reported an UCVA of 20/40 or better at the 3-month postoperative visit.

Summary of risks: Five percent (5%) or less of the intended population would expect to experience a harmful event. In this study**,** 5% (4/74) study subjects had an AE marked as "severe." AEs marked as severe included: diplopia (1%, 1/74, 1-month visit); dry eye (1%, 1/74, 1-month visit; 1%, 1/74, 6-month visit); glare (1%, 1/74, 6-month visit); halo (1%, 1/74, 3-month visit); photophobia (1%, 1/74, 3-month visit); photopsia [starbursts] (1%, 1/74, 1-week visit) and difficulty driving at night (1%, 1/74, 1-month visit).

Risk mitigation: The risks are surgical in nature. As with all surgeries, there are known risks. Surgeons are trained corneal refractive specialists. This device is not new, nor is the procedure of LASIK. The labeling of refractive lasers properly addresses the known risks in an effort to mitigate the risks involved.

D. Overall Conclusions

The results consistently meet or exceed all of the CATz-1 protocol target safety and effectiveness criteria. At the 3-month postoperative visit, 86.6% (110/127) eyes achieved an UCVA of 20/20 or better; 48.8% (62/127) eyes were at 20/16 or better; and 7.9% (10/127) eyes achieved UCVA or 20/12.5 or better. Refractive stability has been established at 3-months postoperatively for the entire cohort and confirmed at 6-months postoperatively. The incidence of severe adverse events, complications, and other ocular or vision-related observations is small. The adverse events, complications and other ocular or vision-related observations are common to the LASIK procedure and the observed rates are well within the range of outcomes expected with this procedure. These adverse events and complications are not uniquely related to the topography-assisted LASIK procedure that is the subject of this PMA application.

XIV. CDRH DECISION

CDRH issued an approval order on September 30, 2013.

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

XV. APPROVAL SPECIFICATIONS

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

XVI. REFERENCES

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3. ANSI Standard Z80.28:-2010: Methods for Reporting Optical Aberrations of Eyes