SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name:	Ophthalmic Excimer Laser System
Device Trade Name:	Bausch & Lomb Technolas® 217z Zyoptix System for Personalized Vision Correction
Applicant's Name and Address:	Bausch & Lomb Incorporated 1400 North Goodman Street Rochester, New York 14603-0450 (585) 338-8731
Date of Panel Recommendation:	None
PMA Number:	P990027/S6
Date of Notice of Approval to Applicant:	October 10, 2003

Background

The Technolas 217A Excimer Laser System was approved on February 23, 2000, for the indication of laser in-situ keratomileusis (LASIK) for the reduction or elimination of myopia (nearsightedness) from –1.00 to –7.00 diopters (D) with less than –3.00 D astigmatism, the combination which must result in a manifest refraction of less than or equal to 0.5 D (in both cylinder and sphere components (P990027). On May 17, 2002, the device was also approved for the indication of laser in-situ keratomileusis (LASIK) for the reduction or elimination of myopic astigmatism up to –12.00 D MRSE, with sphere between >-7.00 D to –10.99 D and cylinder between 0.00 and <-3.00 D (P990027/S2). On February 25, 2003, the device was approved for the indication of LASIK treatments or the reduction or elimination of low-to-moderate naturally occurring hyperopia up to +4.00 D MRSE, with sphere between +1.00 to 4.00 D with or without refractive astigmatism up to +2.00 D at the spectacle plane.

The sponsor submitted this supplement to further expand the clinical indications. The updated pre-clinical and clinical work to support this expanded indication is provided in this summary. For more information on the data that supported the approved indications, the summaries of safety and effectiveness data (SSED) for the original PMA or supplement should be referenced. Written requests for copies of the SSED can be obtained from the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20857 under Docket # _____ or you may download the files from the internet site Http://www.fda.gov/cdrh/pdf/p990027.pdf.

II. A. INDICATIONS FOR USE

The Bausch & Lomb TECHNOLAS 217z Zyoptix System for Personalized Vision Correction (Zyoptix System) is indicated for wavefront-guided laser-assisted in-situ keratomileusis (LASIK) treatments:

- for the reduction or elimination of myopia with sphere up to -7.00 D, cylinder up to -3.00 D, and $\leq$ -7.50D MRSE at the spectacle plane;
- in patients with documented evidence of a change in manifest refraction of less than or equal to ± 0.50 diopters (in both cylinder and sphere components) for at least one year prior to the date of the pre-operative examination; and,
- in patients who are 21 years of age or older.

B. CONTRAINDICATIONS

LASIK surgery is contraindicated in:

- Patients with collagen vascular, autoimmune, or immunodeficiency diseases;
- Pregnant or nursing women;
- Patients with signs of keratoconus;
- Patients who are taking one or both of the following medications: isotretinoin (Accutane[1]), or amiodarone hydrochloride (Cordarone[2]).

C. WARNING AND PRECAUTIONS

Please refer to the Professional Use information and the Patient Information booklet for a complete list of warning and precautions.

III. DEVICE DESCRIPTION

A. WAVEFRONT ABERROMETER (Zywave or Zywave II)

The first step in performing Zyoptix LASIK surgery is to perform a wavefront examination on the patient using a wavefront detector (Zywave or Zywave II) compatible with the Zyoptix Excimer Laser System. The only compatible wavefront detector is the Bausch & Lomb™ Zywave® Wavefront System. This wavefront detector is available as a stand-alone aberrometer, the Zywave or Zywave II models, or as part of the Zyoptix Diagnostic Workstation (ZDW). The ZDW incorporates the Zywave II aberrometer and the Orbscan IIz anterior segment analyzer in one workstation. The ZDW allows the user to operate both the Zywave II and the Orbscan IIz from a single

[1] Accutane is the registered trademark of Hoffman La Roche Inc.
[2] Cordarone is the registered trademark of Sanofi-Synthlabo

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workstation. The Zywave II and the Orbscan IIz each has its own measurement head, and the software for the two systems are installed on one shared computer to facilitate viewing of the diagnostic information generated by these systems.

Essential features of Bausch & Lomb ™ Zywave® Wavefront System are as follows:

PATIENT FIXATION AND FOGGING

The Zywave includes a fixation optical subsystem that provides the patient with a fixation point. In addition, the fixation subsystem includes adjustable optics to compensate for the patient's inherent refractive error. The optics are used to "fog" the eye, first clarifying the fixation target and then it optically adjusts beyond the patient's far point to minimize accommodation.

WAVEFRONT MEASUREMENT

The Zywave Wavefront detector measures the Wavefront profile of the eye with a high degree of accuracy and characterizes the profile using Zernike polynomials up to and including the 5th Order.

DATA EXPORT

The Zywave sensor has the ability to export the Wavefront examination data as an electronic file to floppy disk for transfer to the Zyoptix system. The electronic file is structured in a specific format and contains essential patient information, and the detailed aberration data. In addition, the electronic file is encrypted in a manner that prohibits any data alteration or tampering prior to import into the Zylink Custom Treatment Planning Software.

B. MICROKERATOME

A microkeratome is used to achieve a partial thickness cut of the cornea, which creates a "flap" as part of the LASIK procedure. The microkeratome is a precision instrument used in performing lamellar corneal resections. This instrument cuts a corneal disc of pre-selected thickness and diameter. The system generally consists of a head, plates, ring, handle, wrenches, shaft, motor, hand-piece, disposable blades, and power supply with footswitches and power cords. The system is completed with the applanation lens set, tonometer, corneal storage jar, optical zone marker, spatula, stop attachment, and digital thickness gauge.

MICROKERATOME USED IN THE CLINICAL TRIAL:

The microkeratome used in the clinical trial was the Hansatome® (manufactured by Bausch & Lomb).

C. LASER SYSTEM with ACTIVE TRACKER

The specifications for the Bausch & Lomb TECHNOLAS Zyoptix 217z Laser are provided below.

Laser Type:	Argon Fluoride
Laser Wavelength:	193 nanometers
Laser Pulse Duration:	18 nanoseconds
Laser Head Repetition Rate:	50 Hz
Effective Corneal Repetition Rate:	12.5 Hz
Fluence (at the treatment area):	120 mJ/cm^2
Range of Ablation Diameter:	2 mm hard aperture: 2.0 to 2.05 mm
	2 mm soft aperture: 2.0 to 2.05 mm
	1 mm soft aperture: 1.0 to 1.05 mm
Active Eye Tracker	
- Tracking frequency	120 Hz

Bausch & Lomb recommends use of the largest possible optic zone size based on the patient's wavefront data, while ensuring residual stromal thickness of 250 microns. The optic zone should be selected from between 6.0 mm and 7.0 mm with a blend zone being held constant at 0.875 mm. A flag warning will appear when an optic zone of <6.0 mm is selected, and in the event that the selected optic zone would result in residual stromal thickness of less than 250 microns. The ablation (treatment) zone is the sum of the optical zone selected plus the blend zone. This blend zone is smaller than that used in Planoscan Conventional LASIK, and results in a central ablation depth approximately 25% less than is required by the Planoscan Conventional LASIK procedure for a -7.00 D sphere, -3.00 D cylinder, and MRSE $\leq$ -7.50D correction at the spectacle plane for each of the optic zone diameters.

It should be noted that the optic zone cannot be selected to be larger than the patient's pupil size during the Wavefront measurement. Dilation to ensure a large optic zone is available to the surgeon during treatment planning is recommended.

FEATURES AND COMPONENTS OF THE ZYOPTIX 217Z LASER SYSTEM

Laser Unit	The laser unit consists of the laser head (discharge system), which contains the optical resonator and a discharge chamber, which is filled with a premix of argon, fluorine, and a buffer of other noble gases.
Control Unit	The control unit contains the personal computer that uses a software algorithm to calculate the number and location of laser pulses required to achieve the desired correction.
Tower Unit	The tower unit provides the stable holding construction for the optical system of the Zyoptix 217z Laser. The tower unit contains the optical elements that condition the laser beam to the appropriate characteristics. The tower also contains the visualization optics (the operating microscope) and the positioning and fixation optics for properly locating and monitoring the progress of the ablation. There is a distance of 21 cm ("working distance") between the focusing point on the cornea and the laser arm.
Zyoptix Aperture Treatment Card	The Zyoptix Aperture Treatment Card (Aperture Card) softens the treatment laser beam edges to the truncated Gaussian formed beam through two different aperture diameters (1 mm and 2 mm).
Robotic Arm	The mechanical robotic arm provides the physical movement of the Aperture Card into the correct position of the laser's optical path.
Active Eye Tracker	The active eye tracker attaches to the laser to ensure the centration of the treatment on the cornea compensating for patient eye movement during treatment.
Operating Elements	The operating elements of the Bausch & Lomb Zyoptix Laser consist of two joysticks for movement of the patient bed in all axes and other operating elements and external connectors.
Bed Unit and Chair	The bed unit allows for accurate positioning of the patient during the surgical procedure while the operating chair allows the surgeon to adjust his/her position at the operating microscope.

D. TRACKING SYSTEM

The Zyoptix laser system includes a 120 Hz active eye-tracker. The eye tracking system enables the surgeon to select the treatment center of the ablation, and compensate for horizontal eye movements (x and y directions) by the patient during surgery. The overall reaction time of the laser system to eye movement is 10.7 milliseconds, allowing the laser to actively compensate for eye movements up to 24 mm per second. If the eye-tracker detects movement greater than 24 mm per second during the treatment, the laser pulse will be paused momentarily until the rapid eye movements come back within the active range of the eye-tracker.

IV. ALTERNATIVE PRACTICES OR PROCEDURES

Alternative methods of correcting nearsightedness (myopia) include: glasses, contact lenses, photorefractive keratectomy (PRK), incisional refractive keratotomy (RK), and lamellar refractive keratotomy.

V. MARKETING HISTORY

Over 250 Bausch & Lomb TECHNOLAS®217z Zyoptix Systems have been installed in the following countries: Argentina, Australia, Austria, Belgium, Brazil, Canada, China, Colombia, Finland, France, Germany, Greece, Hong Kong, India, Indonesia, Iran, Ireland, Israel, Italy, Japan, Jordan, Kuwait, Korea, Malaysia, Mexico, Netherlands, New Zealand, Norway, Philippines, Portugal, Singapore, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, Turkey, United Kingdom, and USA.

The Bausch & Lomb TECHNOLAS®217z Zyoptix Laser System has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

VI. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse reactions associated with LASIK include: loss of best spectacle corrected visual acuity, worsening of patient complaints such as double vision, sensitivity to bright lights, increased difficulty with night vision, fluctuations in vision, increase in intraocular pressure, corneal haze, secondary surgical intervention, corneal infiltrate or ulcer, corneal epithelial defect, corneal edema, problems associated with the flap including a lost, misplaced or misaligned flap, retinal detachment, and retinal vascular accidents. Please refer to Tables 10 and 11 (pages 20 and 21) for a summary of adverse events observed in the clinical study.

VII. SUMMARY OF PRECLINICAL STUDIES

A. TECHNOLAS® 217A Excimer Laser System

For a summary of the preclinical testing performed with the Technolas® 217A Excimer Laser System, refer to the SSED for the original PMA #P990027.

B. TECHNOLAS®217z Zyoptix Laser System

1. Hazard Analysis

   Hazard Analysis and Software Testing was conducted for the combined use of the components of the Bausch & Lomb TECHNOLAS 217z Zyoptix System for Personalized Vision Correction. Hazard Analysis includes 3 separate assessments for potential hazards/failure modes for the (a) Zyoptix System, which includes

assessment of the entire treatment system composed of the Technolas 217z laser, the Zyoptix Diagnostic Workstation that integrates the Orbscan IIz anterior segment analysis system and the Zywave II Wavefront System onto one unit, and the Zylink Customized Treatment Calculation Software; (b) the TECHNOLAS 217z excimer laser system; and (c) the Zylink Customized Treatment Calculation Software. The overall Zyoptix System hazard analysis encompasses all previously identified fault and mitigating circumstances identified with any given treatment process. The software test procedures covered all aspects of tnew software functionality and performance. All test procedures were completed. The Hazard Analysis and software test report indicated no known hazards affecting safety or effectiveness.

2. Testing for Measurement of Refractive Errors of the Eye with the Zywave Aberrometer.

   Benchtop testing for the measurement of total refractive errors of the eye, including myopia, astigmatism, coma, spherical aberrations, trefoil and other higher order aberrations through the fifth order, and software testing was conducted for the Zywave® Wavefront System. The tests were designed to measure lower and higher order wavefront aberrations created in a series of convex, single surface, plexiglass "model eyes" with different combinations of lower and higher order Zernike aberrations. The data from these tests indicated that the Zywave Wavefront System provides an adequate and reliable measurement of total refractive errors of the eye, including myopia, astigmatism, coma, spherical aberration, trefoil and other higher order aberration through the fifth order.

3. Profilometry of Corneal Ablation

   A series of preclinical tests were conducted on the Technolas 217z Laser System using the Zyoptix algorithm before initiating human clinical trials. The tests involved algorithm simulations, and measuring ablation profile on plastic blocks. The data obtained from these tests allowed the validation of the Zyoptix algorithm by recording the detailed optical surface profilometry for plastic ablations. The profilometry tests confirmed the validation for the Zyoptix algorithm and provided sufficient evidence to proceed to human studies.

VIII. SUMMARY OF CLINICAL STUDIES

A. OBJECTIVES

The objective of this study was to demonstrate the safety and effectiveness of the Bausch & Lomb TECHNOLAS 217z Zyoptix System for Personalized Vision Correction (Zyoptix System) for the correction of low-to-moderate myopia up to -7.00 diopters sphere (defocus) with astigmatism up to –3.50 diopters when used as part of the LASIK surgical procedure.

B. STUDY DESIGN

The data for this report were gathered from a prospective, open-label, non-randomized, multi-center clinical evaluation of the use of the Orbscan™ IIz Corneal Topographer and the Zywave™ II Wavefront Aberrometer as the basis for determining the appropriate LASIK-based treatment parameters for the correction of myopia up to -7.00 D of sphere (defocus) and up to -3.50 D of astigmatism using the Zyoptix System conducted in the United States of America. All eyes in the study were treated with the Zyoptix System. A total of 342 eyes were enrolled in this study. In this report, effectiveness results are provided for 340 eyes with at least 6 months of follow-up data.

C. INCLUSION AND EXCLUSION CRITERIA

In order to be enrolled in the study, patients needed to meet these conditions: have the required amount of myopia and astigmatism; have a stable refraction for the past year; discontinue use of contact lenses prior to surgery; have normal, healthy eyes with visual acuity correctable to at least 20/40; be at least 21 years of age; be willing and able to return for scheduled follow-up examinations; and provide written informed consent.

Patients not meeting the above inclusion criteria were excluded from the study. In addition, subjects who exhibited any of the following conditions were excluded: history of anterior segment pathology, including cataracts; residual, recurrent, active ocular or uncontrolled eyelid disease, or any corneal abnormality (specifically, recurrent corneal erosion, severe basement membrane disease); ophthalmoscopic signs of progressive or unstable myopia or keratoconus; required ablation is deeper than 250 microns from the corneal endothelium; unstable corneal mires on central keratotomy readings; blind in the fellow eye; previous ocular surgery; history of herpes zoster or herpes simplex keratitis, diabetes, autoimmune disease, connective tissue disease, or clinically significant atopic syndrome; taking chronic systemic corticosteroid or other immunosuppressive therapy; immunocompromised; pregnant, lactating, or of child-bearing potential and not practicing a medically approved form of birth control; sensitivity to planned evaluation medications; simultaneous participation in any other ophthalmic drug or device clinical trial.

D. STUDY PLAN, PATIENT ASSESSMENTS AND EFFICACY CRITERIA

All subjects were expected to return for follow-up examinations at 1 day, 1 week, 1 month, 3 months and 6 months postoperatively. Retreatment would not be performed as a part of the protocol.

Preoperatively, the subjects' medical and ocular histories were recorded. The objective parameters measured during the study included: uncorrected visual acuity, best spectacle corrected visual acuity, pupil size, manifest refraction, cycloplegic refraction, dilated aberrometer refraction, intraocular pressure, corneal pachymetry,' slit lamp examination of the anterior segment, fundus examination, computerized corneal topography, wavefront determination, and subjective self evaluation questionnaire.

The primary efficacy variables for this study were improvement of UCVA based on the pre-treatment goal of the procedure and predictability of manifest refraction.

E. STUDY PERIOD, INVESTIGATIONAL SITES AND DEMOGRAPHICS DATA

1. STUDY PERIOD AND INVESTIGATIONAL SITES

Subjects were treated between March 2001 to December 2001. The database for this PMA reflected data collected through June 14, 2002. A total of 342 eyes were treated at three sites, however 2 eyes were discontinued at the time of surgery due to intraoperative problems associated with the flap creation.

2. DEMOGRAPHICS

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

TABLE 1
DEMOGRAPHICS – ALL TREATED EYES

		Total
Number of eyes*		342
Number of Enrolled Subjects		191
Age (yrs)	Mean	34.4
	SD	8.29
	Range	21-61
Gender	Male	46.1%
	Female	53.9%
Race	White	90.6%
	Black	1.1%
	Asian	5.2%
	Other	3.1%
Operative Eye	OD	49.7%
	OS	50.3%

*Two surgery aborted/not attempted eyes (170-1621-BOFO, 170-1616-BO) are included in the total number of eyes.

F. DATA ANALYSIS AND RESULTS

1. PREOPERATIVE CHARACTERISTICS

Presented in Table 2 are the preoperative attempted refraction corrections for all treated eyes.

TABLE 2
ATTEMPTED SPHERICAL (DEFOCUS) AND CYLINDRICAL (ASTIGMATISM) CORRECTION* ALL TREATED EYES, N = 340

SPHERE	CYLINDER Mean = 0.71D; S.D. = 0.56D; Range = 0.02D – 3.12D					
Mean = 3.17D S.D. = 1.60D Range = 0.46D – 7.13D	0.00-0.49D % (n)	0.50-0.99D % (n)	1.00-1.99D % (n)	2.00-2.99D % (n)	3.00-3.99D % (n)	Total % (n)
0.00-0.99D	0.3% (1)	0.6% (2)	1.8% (6)	0.3% (1)	0.3% (1)	3.2% (11)
1.00-1.99D	11.5% (39)	7.6% (26)	4.7% (16)	2.1% (7)	0.0% (0)	25.9% (88)
2.00-2.99D	10.9% (37)	6.5% (22)	3.8% (13)	0.6% (2)	0.0% (0)	21.8% (74)
3.00-3.99D	7.4% (25)	7.9% (27)	3.2% (11)	0.6% (2)	0.0% (0)	19.1% (65)
4.00-4.99D	5.6% (19)	6.5% (22)	2.6% (9)	0.6% (2)	0.0% (0)	15.3% (52)
5.00-5.99D	4.4% (15)	2.9% (10)	0.3% (1)	0.3% (1)	0.0% (0)	7.9% (27)
6.00-6.99D	2.9% (10)	2.9% (10)	0.6% (2)	0.0% (0)	0.0% (0)	6.5% (22)
7.00-7.99D	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Total	43.2% (147)	35.0% (119)	17.1% (58)	4.4% (15)	0.3% (1)	100.0% (340)

* Attempted correction was the complete refractive error generated using the Zywave device.

2. POST-OPERATIVE CHARACTERISTICS AND RESULTS

a. ACCOUNTABILITY

Accountability for all treated eyes across the study visit schedule is presented in Table 3.

Accountability was excellent with no patients lost to follow-up, and no missed visits from 1 month forward. Two eyes were discontinued at the time of surgery due to intraoperative problems associated with the flap creation. No patients were retreated and no eyes were discontinued from the study due to visual symptoms.

TABLE 3
ACCOUNTABILITY
ALL TREATED EYES

	VISITS				
	DAY 1 % (n)	DAY 7 % (n)	1 MONTH % (n)	3 MONTHS % (n)	6 MONTHS % (n)
Eyes Enrolled	342	342	342	342	342
Eyes Treated	340	340	340	340	340
Available for Efficacy Analysis†	100.0% (340)	99.4% (338)	100.0% (340)	100.0% (340)	100.0% (340)
Discontinued/Terminated*	0.6% (2)	0.6% (2)	0.6% (2)	0.6% (2)	0.6% (2)
Lost To Follow-Up	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Missed Visit**	0.0% (0)	0.6% (2)	0.0% (0)	0.0% (0)	0.0% (0)
Active (Not Yet Eligible For The Interval)	0.0%(0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)

† The denominator for the percent is all eyes treated.

* One eye could not be treated due to a small flap and the patient was exited prior to the laser surgery. The other eye was also exited at time surgery due to creation of a flap that was too thin and epithelium on the cornea that was loose.

** Missed visit: Eyes not examined at the scheduled visit, but were then seen at a subsequent visit

b. STABILITY OF OUTCOME

Table 4 presents the results for the stability of the manifest refraction spherical equivalent for the consistent cohort (all treated eyes examined at 1, 3, and 6 months). The results indicate that refractive stability is achieved in the interval from 1 to 3 months and further confirmed between 3 and 6 months based upon the point estimator of 95% of eyes being within 1.00 D of the previous visit's spherical equivalent refraction value. The refraction was demonstrated to be stable by 3 months postoperative based upon 96.2% of all treated eyes remaining within 1.00 D of the previous visit's refraction. This was confirmed by the 3-6 month data.

TABLE 4
STABILITY OF MANIFEST REFRACTION SPHERICAL EQUIVALENT FOR ALL TREATED EYES: 6-MONTH

Change in Spherical Equivalent Between	1 AND 3 MONTHS	3 AND 6 MONTHS
≤ ±0.50 Diopter (%, n/N)	86.8% (295/340)	90.9%, (309/340)
≤ ±1.00 Diopter (%, n/N)	96.2% (327/340)	98.5% (335/340)
Mean Difference ± Standard Deviation	0.00 ± 0.41	0.00 ± 0.35
95% Confidence Interval	-0.054, 0.054	-0.046, 0.046

c. SAFETY AND EFFECTIVENESS OUTCOMES

The primary cohort consisted of 340 eyes including 117 eyes with less than -0.50D of astigmatism and 223 eyes with -0.50D to -3.5D of astigmatism based on manifest refraction.

Tables 5A-D present the summary of the key safety and effectiveness parameters for the 340 treated eyes, the 117 spherical eyes and the 223 spherocylindrical eyes respectively and stratified by preoperative MRSE at all available postoperative visits. Table 6 provides the summary of the key safety and effectiveness parameters at 6 months as a function of the optic zone size used in the treatment.

Preoperatively none of the eyes had uncorrected visual acuity of 20/40 or better. Postoperative UCVA of 20/20 or better was reported in ≥ 90% of eyes from the point of stability (3 months) forward (Table 5A). Approximately 70% of eyes had UCVA of 20/16 or better.

TABLE 5A

SUMMARY OF KEY EFFICACY VARIABLES OVER TIME (N=340)

Efficacy Variables		1 Month	3 Months	6 Months
UCVA 20/16 or better	%	61.2%	69.4%	70.3%
	(n/N)	208/340	236/340	239/340
	CI	54.8, 67.6	63.4, 75.4	64.4, 76.2
UCVA 20/20 or better	%	85.6%	90.3%	91.5%
	(n/N)	291/340	307/340	311/340
	CI	81.3, 89.9	86.7, 93.9	88.0, 95.0
UCVA 20/25 or better	%	94.4%	95.0%	95.3%
	(n/N)	321/340	323/340	324/340
	CI	91.4, 97.4	92.0, 98.0	92.7, 97.9
UCVA 20/32 or better	%	98.2%	98.2%	98.5%
	(n/N)	334/340	334/340	335/340
	CI	96.6, 99.8	96.6, 99.8	97.3, 99.8
UCVA 20/40 or better	%	99.4%	99.1%	99.4%
	(n/N)	338/340	337/340	338/340
	CI	97.9, 99.9	97.8, 100	97.9, 99.9
MRSE ≤ ±0.50D of intended	%	73.8%	77.6%	75.9%
	(n/N)	251/340	264/340	258/340
	CI	68.3, 79.3	72.4, 82.9	70.2, 81.6
MRSE ≤ ±1.00D of intended	%	93.8%	93.8%	93.8%
	(n/N)	319/340	319/340	319/340
	CI	90.8, 96.8	91.1, 96.6	91.1, 96.6
Safety Variables		**1 Month**	**3 Months**	**6 Months**
Loss of >2 Lines BSCVA	%	0.6%	0.0%	0.0%
	(n/N)	2/340	0/340	0/340
	CI	0.1, 2.1	0.0, 1.1	0.0, 1.1
Loss of ≥ 2 Lines BSCVA	%	1.5%	1.2%	0.6%
	(n/N)	5/340	4/340	2/340
	CI	0.2, 2.7	0, 2.6	0, 2.1
BSCVA worse than 20/40	%	0.3%	0	0
	(n/N)	1/340	0/340	0/340
	CI	0.0, 1.6	0, 1.1	0. 1, 1.1
BSCVA worse than 20/25 if 20/20 or better preoperatively	%	0.6%	0.3%	0
	(n/N)	2/335	1/335	0/335
	CI	0.1, 2.1	0. 1.7	0, 1.1

BSCVA = Best spectacle corrected visual acuity
MRSE = Manifest refraction spherical equivalent
CI = 95% Confidence interval for percentage
UCVA = Uncorrected visual acuity

TABLE 5B

SUMMARY OF KEY EFFICACY VARIABLES OVER TIME SPHERICAL EYES (N=117)

Efficacy Variables		1 Month	3 Months	6 Months
UCVA 20/16 or better	%	65.8%	73.5%	74.4%
	(n/N)	77/117	86/117	87/117
	CI	55.8, 75.8	63.4, 82.7	65.3, 83.5
UCVA 20/20 or better	%	92.3%	90.6%	94.0%
	(n/N)	108/117	106/117	110/117
	CI	86.9, 97.7	84.8, 96.4	89.1, 98.9
UCVA 20/25 or better	%	97.4%	96.6%	95.7%
	(n/N)	114/117	113/117	112/117
	CI	92.7, 99.5	92.5, 100	91.3, 100
UCVA 20/32 or better	%	98.3%	98.3%	98.3%
	(n/N)	115/117	115/117	115/117
	CI	94.0, 99.8	94.0, 99.8	94.0, 99.8
UCVA 20/40 or better	% (n/N)	100.0%	100.0%	100.0%
	CI	117/117	117/117	117/117
		96.9, 100	96.9, 100	96.9, 100
MRSE ≤±0.50D of intended	%	81.2%	84.6%	84.6%
	(n/N)	95/117	99/117	99/117
	CI	73.2, 89.2	77.4, 91.9	77.4, 91.9
MRSE ≤ ±1.00D of intended	%	94.0%	94.9%	96.6%
	(n/N)	110/117	111/117	113/117
	CI	89.1, 98.9	89.2, 98.1	91.5, 99.1
Safety Variables		**1 Month**	**3 Months**	**6 Months**
Loss of >2 Lines BSCVA	%	0%	0%	0%
	(n/N)	0/117	0/117	0/117
	CI	0.0, 3.1	0.0, 3.1	0.0, 3.1
Loss of ≥ 2 Lines BSCVA	%	0.0%	0.9%	0.9%
	(n/N)	0/117	1/117	1/117
	CI	0.0, 3.1	0.0, 4.7	0.0, 4.7
BSCVA worse than 20/40	%	0%	0%	0%
	(n/N)	0/117	0/117	0/117
	CI	0.0, 3.1	0.0, 3.1	0.0, 3.1
Increase >2D cylinder magnitude	%	0.0%	0.0%	0.0%
	(n/N)	0	0	0
BSCVA worse than 20/25 if 20/20 or better preoperatively	%	0%	0%	0%
	(n/N)	0/115	0/115	0/115
	CI	0.0, 3.2	0.0, 3.2	0.0, 3.2

BSCVA = Best spectacle corrected visual acuity
MRSE = Manifest refraction spherical equivalent
CI = 95% Confidence interval for percentage
UCVA = Uncorrected visual acuity

TABLE 5C

SUMMARY OF KEY EFFICACY VARIABLES OVER TIME SPHEROCYLINDRICAL EYES (N=223)

Efficacy Variables		1 Month	3 Months	6 Months
UCVA 20/16 or better	% (n/N)	58.7%	67.3%	68.2%
	CI	131/223	150/223	152/223
		50.9, 66.6	59.8, 74.7	60.9, 75.4
UCVA 20/20 or better	%	82.1%	90.1%	90.1%
	(n/N)	183/223	201/223	201/223
	CI	76.3, 87.9	85.6, 94.6	85.6, 94.6
UCVA 20/25 or better	%	92.8%	94.2%	95.1%
	(n/N)	207/223	210/223	212/223
	CI	88.6, 97.1	90.3, 98.1	92.0, 98.1
UCVA 20/32 or better	%	98.2%	98.3%	98.7%
	(n/N)	219/223	219/223	220/223
	CI	96.1, 100	96.1, 100	97.2, 100
UCVA 20/40 or better	%	99.1%	99.1%	99.1%
	(n/N)	221/223	220/223	221/223
	CI	96.8, 99.9	96.7, 100	96.8, 99.9
MRSE ≤±0.50D of intended	%	70.0%	74.0%	71.3
	(n/N)	156/221	165/223	159/223
	CI	63.0, 77.0	67.5, 80.5	64.2, 78.4
MRSE ≤±1.00D of intended	%	93.7%	93.3%	92.4%
	(n/N)	209/223	208/223	206/223
	CI	90.2, 97.3	89.8, 96.7	88.2, 96.5
Safety Variables		**1 Month**	**3 Months**	**6 Months**
Loss of >2 Lines BSCVA	%	0.9%	0.0%	0.0%
	(n/N)	2/223	0/223	0/223
	CI	0.1, 3.2	0.0, 1.6	0.0, 1.6
Loss of ≥ 2 Lines BSCVA	%	2.2%	1.3%	0.4%
	(n/N)	5/223	3/223	1/223
	CI	0.3, 4.2	0.0, 3.3	0.0, 2.5
BSCVA worse than 20/40	%	0.4%	0.0%	0.0%
	(n/N)	1/223	0/223	0/223
	CI	0.0, 2.5	0.0, 1.6	0.0, 1.6
BSCVA worse than 20/25 if 20/20 or better preoperatively	%	0.9%	0.5%	0.0%
	(n/N)	2/220	1/220	0/220
	CI	0.1, 3.2	0.0, 2.5	0.0, 1.7

BSCVA = Best spectacle corrected visual acuity
MRSE = Manifest refraction spherical equivalent
CI = 95% Confidence interval for percentage
UCVA = Uncorrected visual acuity

d. Influence Of Optic Zone Size Selection and Preoperative MRSE On Clinical Results

In the clinical trial, the investigators had the opportunity to select the optic zone size to use, with an effort made to keep the size at 6.0 mm or larger. There were only 3 eyes in the study with an optical zone of less than 6.0 mm, each of which was based on the medical judgment of the surgeon at the time of the treatment. All three eyes had an optic zone of 5.8 mm and had UCVA of 20/20 or better at the 6-month postoperative evaluation.

An evaluation of the clinical results as a function of the optic zone size selected indicates that the results favor use of the largest possible optic zone size based on the patient's wavefront data, while ensuring residual stromal thickness of 250 microns. The optic zone can be selected between 6.0 mm and 7.0 mm with a blend zone being held constant at 0.875 mm. This blend zone is smaller than that used in Planoscan Conventional LASIK, and results in a central ablation depth approximately 25% less than is required by the Planoscan Conventional LASIK procedure for a -7.00 D sphere, -3.00 D cylinder, and MRSE $\leq$ -7.50D correction at the spectacle plane for each of the optic zone diameters.

The effectiveness results by optical zone size are found in Table 5D below. No statistically significant differences among the optic zone groups were found on the parameters of MRSE within 0.5 and 1.0 diopters of emmetropia, or on achievement of UCVA of 20/16 or better, and 20/25 or better. Significant differences, favoring larger optic zones were found on the parameters of UCVA 20/20 or better, 20/32 or better and 20/40 or better.

Extensive analyses were performed to evaluate the effect of both treatment (i.e., sphere only or spherocylindrical corrections) and of optical zone size on safety and efficacy outcomes following treatment with the Zyoptix System. At both 3 months and 6 months, in the cohort of all treated eyes and in spherocylindrical eyes, smaller optical zones (less than 6.25 mm) were associated with lower proportions of eyes with UCVA of 20/20, 20/25, 20/32 and 20/40. No statistically significant differences in UCVA were observed across the optical zones for sphere only eyes, however, at 6 months, the proportion of spherical eyes with MRSE within 0.50 D of emmetropia was significantly lower for eyes treated with smaller optical zone (less than 6.25 mm). Notwithstanding these differences, all efficacy targets established in FDA guidance for clinical trials of excimer lasers were achieved or exceeded for all three cohorts (all treated eyes, sphere only eyes, spherocylindrical eyes) and for all optical zone sizes.

With regard to stratification of key safety variables by optical zone, because of the small number of adverse events and complications in the study population, stratification of these data by optical zone would not

provide any statistically meaningful information. For this reason, this analysis was limited to stratification of BCVA by treatment and by optical zone. Significantly fewer eyes with smaller optical zone (less than 6.25 mm) achieved BCVA of 20/20 or better at 3 months and 20/16 or better at 6 months in the population of all treated eyes. In spherocylindrical eyes, at 3 and 6 months, the proportion of eyes with BCVA of 20/16 or better was smaller for eyes with smaller optical zone (less than 6.25 mm). No differences were observed across the three optical zone groups for the sphere only eyes, and it should be noted that all eyes (100%) achieved BCVA of 20/25 or better at 6 months, and nearly all eyes (95% or greater) achieved BCVA of 20/20 or better at 6 months.

Optic zone can be selected between 6.0 mm to 7.0 mm. A warning flag will appear when an optical zone <6.0 mm is selected and when the selected optic zone would result in residual stromal thickness of less than 250 microns. Optic zone cannot be selected to be larger than the patient's pupil size during the wavefront measurement. Dilation to ensure a large optic zone is available to the surgeon during treatment planning is recommended.

TABLE 5D
SUMMARY OF KEY EFFICACY VARIABLES AT 6 MONTHS STRATIFIED BY OPTICAL ZONE SIZE ALL TREATED EYES

	OPTICAL ZONE SIZE (mm)			
KEY EFFICACY VARIABLES	**5.75-6.24** % (n)	**6.25-6.74** % (n)	**6.75-7.24** % (n)	**p-value**
Total Eyes Reported*	73	246	20	
UCVA 20/16 or Better	60.3% (44)	73.6% (181)	65.0% (13)	0.0802
UCVA 20/20 or Better	83.6% (61)	93.5% (230)	95.0% (19)	0.0249
UCVA 20/25 or Better	90.4% (66)	96.7% (238)	95.0% (19)	0.0798
UCVA 20/32 or Better	94.5%(69)	99.6% (245)	100.0% (20)	0.0054
UCVA 20/40 or Better	97.3% (71)	100.0% (246)	100.0% (20)	0.0237
MRSE ≤ ± 0.5 D	67.1% (49)	78.9% (194)	70.0% (14)	0.1004
MRSE ≤ ± 1.0 D	91.8% (67)	94.7% (233)	90.0% (18)	0.5152

* Number of CRFs received with non-missing values.
** p-value for comparison of optical zone strata (Cochran-Mantel-Haenszel test, stratified by primary and fellow eye designations).

As shown in Table 6, efficacy outcomes for eyes with MRSE ≥ -7.0D were slightly lower than for the remaining study eyes, with lower proportions of eyes achieving UCVA of 20/32 or better and MRSE within ≤ ± 0.5D of emmetropia.

TABLE 6

SUMMARY OF KEY EFFICACY VARIABLES AT 6 MONTHS STRATIFIED BY PREOPERATIVE MANIFEST REFRACTIVE SPHERICAL EQUIVALENT ALL TREATED EYES

	PREOPERATIVE MANIFEST REFRACTIVE SPHERICAL EQUIVALENT						
KEY EFFICACY VARIABLES	1.00–1.99 D % (n)	2.00–2.99 D % (n)	3.00–3.99 D % (n)	4.00–4.99 D % (n)	5.00–5.99 D % (n)	6.00–6.99 D % (n)	7.00-7.99D % (n)
Total Eyes Reported*	41	86	82	57	39	27	8
UCVA 20/16 or Better	73.2% (30)	77.9% (67)	70.7% (58)	66.7% (38)	61.5% (24)	66.7% (18)	50.0% (4)
UCVA 20/20 or Better	97.6% (40)	95.3% (82)	92.7% (76)	91.2% (52)	84.6% (33)	81.5% (22)	75.0% (6)
UCVA 20/25 or Better	100.0% (41)	97.7% (84)	95.1% (78)	96.5% (55)	89.7% (35)	92.6% (25)	75.0% (6)
UCVA 20/32 or Better	100.0% (41)	100.0% (86)	97.6% (80)	100.0% (57)	97.4% (38)	96.3% (26)	87.5% (7)
UCVA 20/40 or Better	100.0% (41)	100.0% (86)	98.8% (81)	100.0% (57)	100.0% (39)	96.3% (26)	100.0% (8)
MRSE ≤± 0.50 D	95.1% (39)	82.6% (71)	72.0% (59)	75.4% (43)	69.2% (27)	66.7% (18)	12.5% (1)
MRSE ≤± 1.00 D	100.0% (41)	97.7% (84)	92.7% (76)	96.5% (55)	89.7% (35)	81.5% (22)	75.0% (6)

* Number of CRFs received with non-missing values

e. Cylinder Correction/Vector Analysis

Table 7 presents the results of the Mean percent reduction of astigmatism for spherocylindrical eyes, stratified by preoperative cylinder and the Correction Ratio of achieved vector versus intended vector magnitude.

TABLE 7

CYLINDER CORRECTION EFFICACY AT 3 MONTHS STRATIFIED BY PREOPERATIVE CYLINDER SPHEROCYLINDRICAL EYES

PREOPERATIVE CYLINDER	(n)	MEAN PERCENT REDUCTUON OF ABSOLUTE CYLINDER (NON-VECTOR)	CORRECTION RATIO ACHIEVED VS. INTENDED VECTOR MAGNITUDE RATIO (SIRC/IRC)
All	223	64.0% ± 43.0%	1.00 ± 0.40
0.50 to <1.00 D	134	58.8% ± 51.0%	1.03 ± 0.43
1.00 to < 2.00 D	69	70.1% ± 26.3%	0.98 ± 0.27
2.00 to < 3.00 D	18	78.0% ± 19.3%	1.00 ± 0.26
3.00 to < 4.00 D	2	76.9% ± 0.0%	0.89 ± 0.17

f. Correlation with Preoperative Best Corrected Visual Acuity

Table 8 shows that at 6 months after the surgery, about **78%** of the patients saw as well ***without*** glasses after Zyoptix surgery as *with* glasses before surgery.

TABLE 8

VISUAL ACUITY *WITHOUT* GLASSES AFTER SURGERY COMPARED TO *WITH* GLASSES BEFORE SURGERY (N=340)

Time after Surgery	3 Months % (n)	6 Months % (n)
Percent of eyes with UCVA ≥2 lines better than preoperative BCVA	13.5% (46)	14.1% (48)
Percent of eyes with UCVA 1 line better than preoperative BCVA	25.6% (87)	27.9% (95)
Percent of eyes with UCVA the same as preoperative BCVA	38.2% (130)	36.2% (123)
Percent of eyes with UCVA 1 line worse than preoperative BCVA	15.3% (52)	14.7% (50)
Percent of eyes with UCVA ≥2 lines worse than preoperative BCVA	7.4% (25)	7.1% (24)

g. Change in Best Corrected Vision After Surgery

At 6 months after the procedure, best-corrected visual acuity was unchanged or improved in 94.1% of eyes. No eyes lost more than 2 lines, and two eyes lost 2 lines. One of these eyes was 20/12.5 preop and 20/20 at 6 months; the other was 20/16 preop and 20/25 at 6 months.

TABLE 9

CHANGE IN BEST SPECTACLE CORRECTED VISUAL ACUITY
FOR ALL EYES

	1 Month	3 Months	6 Months
	% (n/N)	% (n/N)	% (n/N)
	N=340	N=340	N=340
Decrease >2 Lines	0.6% (2)	0.0% (0)	0.0% (0)
Decrease 2 Lines	0.9% (3)	1.2 % (4)	0.6% (2)
Decrease 1 Line	7.6% (26)	5.9% (20)	5.3% (18)
No change	37.6% (128)	38.8% (132)	33.8% (115)
Increase 1 Line	36.2% (123)	35.6% (121)	41.5% (141)
Increase 2 Lines	15.3% (52)	17.3% (59)	17.3% (59)
Increase >2 Lines	1.8% (6)	1.2% (4)	1.5% (5)

h. ADVERSE EVENTS AND COMPLICATIONS

Tables 10 and 11 present all the cumulative key safety, adverse events, and complications for all treated eyes reported in the study.

TABLE 10

ADVERSE EVENTS SUMMARY
ALL TREATED EYES

	VISITS		
ALL REPORTED ADVERSE EVENTS	1 MONTH	3 MONTHS	6 MONTHS
Total Eyes Reported*	340	340	340
Not Reported**	0	0	0
Distribution of Scores	% (n)	% (n)	% (n)
Decrease in BSCVA of ≥ 2 lines not due to irregular astigmatism at ≥ 6 months	0.0% (0)	0.0% (0)	0.6% (2)
Epithelial defect	0.0% (0)	0.0% (0)	0.0% (0)
Keratome stopped	0.0% (0)	0.0% (0)	0.0% (0)
Lamellar keratitis	0.0% (0)	0.0% (0)	0.3% (1)
Secondary surgical intervention other than Excimer laser treatment	0.0% (0)	0.0% (0)	0.0% (0)

* Number of CRFs received with non-missing values at each visit.
** Number of CRFs received with missing values at each visit.

TABLE 11

COMPLICATION SUMMARY
ALL TREATED EYES

	VISITS		
	1 MONTH	3 MONTHS	6 MONTHS
ALL REPORTED CONDITIONS	% (n)	% (n)	% (n)
Recurrent corneal erosion	0.0% (0)	0.0% (0)	0.3% (1)
Foreign body sensation	0.0% (0)	0.0% (0)	0.0% (0)
Pain	0.0% (0)	0.0% (0)	0.0% (0)
Size and shape of flap not as intended	0.0% (0)	0.0% (0)	0.0% (0)
Misplaced, misaligned, loose flap, or free cap with loss of ≤ 2 lines (≤ 10 letters) of BSCVA	0.0% (0)	0.3% (1)	0.0% (0)
Epithelium in the interface with loss of ≤ 2lines of BSCVA	0.3% (1)	0.0% (0)	0.0% (0)
Double vision	0.0% (0)	0.0% (0)	0.0% (0)
Ghost images	0.0% (0)	0.3% (1)	0.0% (0)
Peripheral corneal epithelial defect (on the flap)	0.0% (0)	0.0% (0)	0.0% (0)
Peripheral corneal epithelial defect (off the flap)	0.0% (0)	0.0% (0)	0.0% (0)
Peripheral corneal epithelial defect (across the junction)	0.0% (0)	0.0% (0)	0.0% (0)
Epithelial ingrowth	0.0% (0)	0.0% (0)	0.0% (0)
Other:			
Allergy	0.3% (1)	0.3% (1)	0.0% (0)
Bowmans wrinkle	0.0% (0)	0.0% (0)	0.6% (2)
Chalazion	0.3% (1)	0.3% (1)	0.0% (0)
Conjunctivitis	0.3% (1)	0.3% (1)	0.6% (2)
Corneal abrasion	0.0% (0)	0.0% (0)	0.3% (1)
Debris in interface	5.3% (18)	2.4% (8)	1.2% (4)
Debris in interface & Browns wrinkle	0.0% (0)	0.0% (0)	0.6% (2)
Debris in interface & Episcleritis	0.3% (1)	0.0% (0)	0.0% (0)
Episcleritis	0.3% (1)	0.0% (0)	0.0% (0)
Inflammation, interface	0.3% (1)	0.0% (0)	0.0% (0)

i. CHANGE IN CONTRAST SENSITIVITY AFTER SURGERY

A contrast sensitivity study was conducted to assess the effects of Zyoptix myopic LASIK surgery to help determine how well patients see in conditions such as very dim light, rain, snow, and fog. The method used was Vision Sciences CST 1500 with FACT charts. Under mesopic lighting the conditions were controlled within the CST 1500 unit itself.

Table 12 shows the change in contrast sensitivity measured under photopic and mesopic lighting conditions after Zyoptix surgery compared to preoperative levels. Nearly all patients (97.9%) had no change or improvements in Mesopic testing; 22.7% improved and only 2.1% were worse. Similarly, 96.5% of patients had no change or improvements in Photopic testing; 24.4% improved and only 3.5% were worse.

TABLE 12
PROPORTION OF THE POPULATION WITH CHANGE OF >2 LEVELS (> 0.3 LOG) ON CSV-1500 AT 2 OR MORE SPATIAL FREQUENCIES FOR SPHERICAL MYOPIC EYES AT 6 MONTHS

	Photopic Conditions		
Change > 0.3 (log unit)	**Decrease**	**No Change**	**Increase**
% (n/N)	3.5%	72.1%	24.4%
	Mesopic Conditions		
Change > 0.3 (log unit)	**Decrease**	**No Change**	**Increase**
% (n/N)	2.1%	75.2%	22.7%

j. RETREATMENT

No retreatments were performed as a part of the protocol.

k. CHANGE IN CLINICALLY SIGNIFICANT SYMPTOMS

The change from preoperative incidence of clinically significant symptoms (moderate, marked and severe) is found in Table 13A at the 3 and 6-month intervals. At 6 months significant differences in the incidence of clinically significant symptoms favoring improvement (reduced symptoms) occurred for the vision associated parameters of difficulties with night driving, variation of vision under bright light, and light sensitivity, and for the comfort associated parameters of headaches, pain, redness, and blurry vision. Significant differences in worsening symptoms occurred for the parameters of vision-associated parameters of double and fluctuating vision.

TABLE 13A

INCIDENCE OF CLINICALLY SIGNIFICANT* SYMPTOMS PREOPERATIVE AND POSTOPERATIVE

Patient Symptom	N**	Occurrence (%)+		P-value ++	N**	Occurrence (%)+		P-value ++
		Preop	3 Months			Preop	6 Months	
Light Sensitivity	340	18.5%	4.7%	<.0001	340	18.5%	2.6%	<.0001
Headache	340	9.7%	5.3%	0.0090	340	9.7%	4.1%	0.0004
Pain	340	2.4%	0.3%	0.0196	340	2.4%	0.0%	0.0047
Redness	340	3.5%	3.2%	0.8084	340	3.5%	1.5%	0.0896
Dryness	340	7.9%	16.5%	0.0003	340	7.9%	5.9%	0.2623
Excessive Tearing	340	2.4%	0.0%	0.0047	340	2.4%	0.6%	0.0578
Burning	340	2.1%	2.1%	1.0000	340	2.1%	0.6%	0.0956
Gritty Feeling	340	0.9%	1.5%	0.4795	340	0.9%	0.3%	0.3173
Glare	340	4.4%	5.0%	0.7150	340	4.4%	3.5%	0.5637
Halos	340	2.6%	5.0%	0.1025	340	2.6%	3.8%	0.3938
Blurring of Vision	340	11.5%	7.4%	0.0390	340	11.5%	7.1%	0.0287
Double Vision	340	0.3%	0.9%	0.3173	340	0.3%	2.4%	0.0196
Ghost Images	340	0.9%	1.5%	0.3173	339	0.9%	1.8%	0.1797
Fluctuation of Vision	336	0.9%	7.4%	<.0001	335	0.9%	5.4%	0.0011
Variation in Vision:								
In Bright Light	340	7.4%	0.6%	0.0025	339	7.4%	1.2%	<.0001
In Normal Light	340	1.5%	2.1%	0.5637	339	1.5%	2.9%	0.1967
In Dim Light	340	11.8%	6.5%	0.0162	339	11.5%	10.6%	0.6858
Night Driving Difficulty	340	18.5%	8.8%	<.0001	340	18.5%	7.1%	<.0001
Other+++	325	0.6%	2.2%	0.0956	324	0.6%	3.7%	0.0075

* Absent/Mild scores were considered clinically insignificant. Moderate/Marked/Severe scores were considered clinically significant.
** Number of eyes reporting scores at both visits. This number was used as the denominator for calculating percentages. Rates for eyes reporting data at both visits.
\+ Minor variations from sums are due to rounding.
++ McNemar's test comparing occurrence rates at preop and 3 months; and at preop and 6 months.
+++Other symptoms included difficulty reading, eye strain, itchiness, starburst, floaters, headache

I. CHANGE IN SYMPTOMS FROM BASELINE AT 3 AND 6 MONTHS

Patients were asked to rate their symptoms at 3 and 6 months compared to before Zyoptix LASIK surgery for the correction of spherical myopia. As shown in Table13B, patients rated symptoms as significantly better, better, no change, worse, or significantly worse than preoperative. At 6 months significant differences favoring improvement (reduced symptoms) compared to worsening occurred for the parameters of light sensitivity, headaches, pain, redness, excessive tearing, burning, variation of vision under bright light and dim light, and difficulties with night driving. Significant differences in worsening symptoms occurred for the parameters of dryness, and fluctuating vision.

TABLE 13B. COMPARISON OF SYMPTOMS BEFORE AND AFTER SURGERY

Symptom	Significantly Better	Better	No Change	Worse	Significantly Worse
3 Months (N=340)					
Light Sensitivity	8.2%	26.5%	54.4%	8.8%	2.1%
Headache	5.0%	19.4%	68.5%	5.3%	1.8%
Pain	2.4%	3.8%	92.1%	1.5%	0.3%
Redness	1.2%	17.4%	71.8%	7.9%	1.8%
Dryness	1.2%	11.8%	46.8%	30.6%	9.7%
Excessive Tearing	2.1%	8.8%	87.6%	1.5%	0.0%
Burning	0.3%	11.2%	75.6%	12.4%	0.6%
Gritty Feeling	0.6%	7.4%	81.5%	9.7%	0.9%
Glare	2.9%	12.9%	64.4%	16.5%	3.2%
Halos	1.5%	7.9%	69.1%	17.6%	3.8%
Blurring of Vision	7.9%	12.6%	60.3%	15.9%	3.2%
Double Vision	0.3%	1.2%	95.3%	2.4%	0.9%
Ghost Images**	0.3%	3.5%	91.8%	3.5%	0.9%
Fluctuation of Vision*	0.0%	7.4%	62.5%	24.1%	6.0%
Variation in Vision:					
In Bright Light	3.8%	17.9%	65.9%	10.9%	1.5%
In Normal Light	0.9%	8.2%	78.8%	10.6%	1.5%
In Dim Light	5.9%	18.2%	57.9%	15.6%	2.4%
Night Driving Difficulty	10.0%	24.4%	52.6%	12.1%	0.9%
6 Months (N=340)					
Light Sensitivity	9.4%	27.4%	55.6%	7.1%	0.6%
Headache	5.9%	19.4%	69.4%	4.1%	1.2%
Pain	2.4%	3.8%	91.8%	2.1%	0.0%
Redness	1.8%	21.5%	65.9%	9.7%	1.2%
Dryness	2.9%	16.8%	49.1%	28.8%	2.4%
Excessive Tearing	2.1%	10.0%	84.1%	3.2%	0.6%
Burning	1.2%	13.2%	77.6%	7.6%	0.3%
Gritty Feeling	0.6%	7.9%	85.3%	6.2%	0.0%
Glare	3.5%	17.4%	63.8%	12.1%	3.2%
Halos	1.8%	11.8%	72.1%	11.8%	2.6%
Blurring of Vision	8.5%	13.8%	59.1%	14.7%	3.8%
Double Vision	0.3%	1.2%	95.3%	0.9%	2.4%
Ghost Images**	0.3%	4.1%	91.2%	3.5%	0.9%
Fluctuation of Vision*	0.0%	7.5%	68.4%	20.0%	4.2%
Variation in Vision*:**					
In Bright Light	3.8%	20.1%	65.5%	10.3%	0.3%
In Normal Light	0.9%	8.6%	79.4%	8.8%	2.4%
In Dim Light	5.0%	20.4%	57.2%	14.7%	2.7%
Night Driving Difficulty	11.2%	29.1%	49.4%	9.1%	1.2%

* Fluctuation in vision only reported on for n=336 eyes at 3 months and n=335 eyes at 6 months

** Ghost images was reported on for n=339 eyes at 6 months

*** Variation in vision was reported on for only n=339 eyes at 6 months

m. PATIENT SUBJECTIVE EVALUATIONS

Presented in Table 1 are the results for the patient subjective assessments of their overall quality of vision after the surgery, whether or not they would choose to have the surgery again if given the choice, and their overall satisfaction with the surgery.

- Quality of vision was rated as improved in 99.7% of patients at 3 months and at 6 months.
- Nearly all study patients (98.2%) of patients at 3 months and 98.8% at 6 months reported they were moderately or very satisfied with their results.
- Patient satisfaction was consistently high with no patients (0.0%) reporting dissatisfaction at 3 and 6 months.
- The percentage indicating they would choose LASIK again was 98.2% at 6 months, with 1.2% being unsure and 0.6% indicating they would not (2 eyes, 1 patient). This patient was MRSE –1.63D and –1.25D with BCVA 20/16 preop. At 6 months the patient presented with MRSE +0.5D and +0.63D, 20/25 and 20/16 UCVA for OS and OS respectively. The patient indicated the reason for the response was the anticipation that corrective lenses might still be needed in the future.
- For the 25 year-old patient that reported no improvement in one eye at 6 months, the UCVA at this interval was 20/20 OU, and BCVA was 20/16 OU. For the eye in which "no improvement was reported the MRSE was +0.50D. In the LASIK treated fellow eye the MRSE was plano.

n. COMPARISON TO CONVENTIONAL LASIK (BASED ON MANIFEST PHOROPTER REFRACTION)

CENTRAL ABLATION DEPTH

Wavefront guided LASIK with the Zyoptix system can reduce the central ablation depth compared to conventional LASIK with the Planoscan system, with tissue savings of approximately 25% for a -7.00D/-3.00D spherocylindrical treatment and MRSE $\leq$-7.5 D at the spectacle plane over equivalent optic zones. Increased higher order aberrations can reduce this tissue sparing effect.

Wavefront-guided LASIK using the Zyoptix system has demonstrated superior optical quality (reduced monochromatic aberrations) compared to Conventional LASIK with the Planoscan system.

CHANGES IN AMOUNT OF HIGHER ORDER ABERRATION POSTOPERATIVE

In a contralateral study of 40 patients, the average increase in Higher Order Aberrations over a 6.0 mm Wavefront analysis diameter was evaluated. The amount of postoperative higher-order aberrations was less for Zyoptix LASIK eyes than for the Conventional LASIK eyes. The average increase in higher-order aberrations after surgery was:

- **13.4% at 6 months for Zyoptix LASIK eyes**
- **45.3% at 6 months for Conventional LASIK eyes.**

Eyes with greater preoperative Higher Order Aberrations (HOA) were more likely to have a reduction in HOA or less of an increase 6 months after surgery.

When evaluated as a function of the optic zone size used, the results indicated that Higher Order Aberration increases were less in eyes treated with larger optical zones.

PROPORTION OF THE POPULATION WITH A DECREASE IN HIGHER ORDER ABERRATIONS POSTOPERATIVE:

For most patients, the Zyoptix LASIK did not reduce Higher Order Aberrations from baseline. In the contralateral study of 40 patients, the proportion of the population with reduced Higher Order Aberrations over the 6.0mm Wavefront analysis diameter after surgery compared to before surgery is found below:

- **37.5% at 6 months for Zyoptix LASIK eyes.**
- **12.8% at 6 months for Conventional LASIK eyes.**

For the 40 patients in the study who received Zyoptix LASIK in one eye and Conventional LASIK in the other eye, there was no significant difference in subjective symptoms between the two treatments.

The analysis of the Higher Order Aberrations present preoperative and postoperative confirms that the Zyoptix LASIK procedure shows improvements to be primarily in 3rd order aberrations (coma and trefoil). The impact on reducing Higher Order Aberrations is directly correlated to the magnitude of the specific Order of Aberration present prior to treatment.

COMPARATIVE RESULTS FOR THE WAVEFRONT GUIDED LASIK VS. CONVENTIONAL LASIK

Table 14 compares the change in total Wavefront error and in higher-order aberrations for spherical myopic eyes treated with Wavefront-guided LASIK and Conventional LASIK with the Zyoptix System manifest refraction in the Subgroup Study with matched conventional and Zyoptix treatments (N=40 patients). On a percentage basis, the reduction in total Wavefront RMS error is essentially equivalent between the treatment types. On Third Order Aberrations (Coma) the Zyoptix LASIK results in a reduction of 16% whereas the Conventional LASIK causes an increase of 30%.

TABLE 14

CHANGE FROM BASELINE IN WAVEFRONT ABERRATION RMS AT 6 MONTH VISIT FOR MATCHED CONVENTIONAL AND ZYOPTIX EYES 6.0MM WAVEFRONT ANALYSIS DIAMETER

	Zyoptix		**Conventional**	
n	40		39	
Induced Aberration	um	%	um	%
Total RMS	-3.51	-81 ⇓	-3.40	-78 ⇓
Higher Order	0.06	14 ⇑	0.17	45 ⇑
2nd Order	-3.67	-85 ⇓	-3.59	-82 ⇓
3rd Order	-0.05	-16 ⇓	0.09	30 ⇑
4th Order	0.14	70 ⇑	0.17	84 ⇑
5th Order	0.02	28 ⇑	0.00	1 ⇑

o. DEVICE FAILURES AND REPLACEMENTS

There were four device failures/malfunctions and there were no device replacements during the course of the study. Of these, 2 were surgery aborted/not attempted due to microkeratome/flap problems, 1 was due to the interruption of the laser treatment due to energy problems with the laser, and 1 was due to damage beyond the treatment area resulting from a tear in the keratome flap at the hinge.

IX. CONCLUSIONS DRAWN FROM THE STUDIES

The data in this application provides reasonable assurance that the device is safe and effective when used in accordance with the approved directions for use.

X. PANEL RECOMMENDATION

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

XI. CDRH DECISION

CDRH issued an approval order on October 10, 2003. The applicant's manufacturing facility was inspected on February 11-14, 2002 and was found to be in compliance with the medical device Quality System Regulation.

XII. 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 labeling.

Post-approval requirements and restrictions: See Approval Order.