SUMMARY OF SAFETY AND EFFECTIVENESS
FOR A PREMARKET APPROVAL APPLICATION

I. GENERAL INFORMATION

Device Generic Name:	Ophthalmic Medical Laser System (193 nanometer wavelength)
Device Trade Name:	WaveLight ALLEGRETTO WAVE™ Excimer Laser System
Applicant's Name and Address:	SurgiVision® Refractive Consultants, LLC 5 Timber Lane North Reading, MA 01864
Date of Panel Recommendation:	None (see Section XII.)
Premarket Approval (PMA) Application Number:	P020050
Date of Notice of Approval to Applicant:	OCT - 7 2003

II. INDICATIONS FOR USE

The WaveLight ALLEGRETTO WAVE™ Excimer Laser System is indicated for use in Laser Assisted in situ Keratomileusis (LASIK) treatments for:

- the reduction or elimination of myopia of up to -12.0 diopters (D) of sphere and up to -6.0 D of astigmatism at the spectacle plane;
- patients who are 18 years of age or older; and
- patients with documentation of a stable manifest refraction defined as $\leq$0.50 D of preoperative spherical equivalent shift over one year prior to surgery.

III. CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

LASIK surgery is contraindicated in:

- pregnant or nursing women;
- patients with a diagnosed collagen vascular, autoimmune or immunodeficiency disease;
- patients with diagnosed keratoconus or any clinical pictures suggestive to keratoconus; and
- patients who are taking one or both of the following medications: isotretinoin (Accutane®[1]); amiodarone hydrochloride (Cordarone®[2]).

IV. WARNINGS AND PRECAUTIONS

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

V. DEVICE DESCRIPTION

A. Laser System

The WaveLight ALLEGRETTO WAVE Excimer Laser System is a scanning-spot excimer laser system which includes an excimer laser with high pulse repetition rate, a pair of precise galvanometer scanners for positioning the laser spots and an eye-tracker for determining eye location and laser-beam position. The integrated eye-tracker permits the system to accurately track fast eye movements or to interrupt the treatment when the eye moves out of a predetermined range.

The specially shaped profile of the treatment beam and the small spot diameter assure the necessary accuracy to achieve the desired contour of the treated surface. The spot patterns for all treatment parameters are stored in memory inside the laser. The ablation contours are based on sophisticated numerical algorithms. Since the small spot diameter allows for a low pulse energy, a compact excimer laser source with a small gas volume and low gas consumption is integrated into the laser console.

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[1] Accutane® is a registered trademark of Hoffmann-La Roche Inc.
[2] Cordarone® is a registered trademark of Sanofi-Synthelabo Inc.

The operative laser parameters for Model 1008 are summarized as follows:

Pulse repetition rate: 200 Hz
Fluence: 200 mJ/cm^2 (average)
400 m J/cm^2 (peak)
Optical zone: 4.5 - 8.0 mm (only a 6.5 mm OZ was studied in the clinical trial)
Ablation zone: 5.2 - 8.7 mm for spherical treatments
7.0 - 9.0 mm for cylindrical and spherocylindrical treatments

The software versions in the laser system are as follows:

a. Notebook Software NB_032101
b. Firmware Software PR-020501
c. Treatment Lists NG_032101
d. Eyetracker 4.03

B. Microkeratome

The LASIK procedure requires the use of a commercially available microkeratome that has been cleared for marketing via premarket notification. The device used in this study consists of a sterilization/storage tray which includes the shaper head, a left/right eye adapter, suction ring, suction handle, blade handling pin, and corneal reference marker. The instrument motor, tonometer, cleaning brush, disposable blades, power/suction supply unit with vacuum and motor footswitches and power cords are provided as separate components in an accessory stand and equipment suitcase which complete the system.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Conventional methods in correcting nearsightedness with and without astigmatism are: spectacles, contact lenses, photorefractive keratectomy (PRK), or other types of refractive surgery.

VII. MARKETING HISTORY

The ALLEGRETTO WAVE™ Excimer Laser Systems has been commercially distributed in approximately 31 countries (Austria, Australia, Bahrain, Belgium, Brazil, Canada, China, France, Germany, Great Britain, Greece, Hong Kong, India, Ireland, Israel, Italy, Japan, Korea, Lebanon, Mexico, Netherlands, Norway, Russia, Saudi Arabia, Singapore, Slovenia, Spain, Sri Lanka, Sweden, Switzerland). The WaveLight ALLEGRETTO WAVE™ has not been withdrawn from any country or market for reasons of safety or effectiveness of the device.

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VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

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

IX. SUMMARY OF PRECLINICAL STUDIES

A. Gas Lifetime

To measure the static gas lifetime, the energy immediately after a gas change, after 24 hours and after 48 hours was measured. The standard deviation was below 3% with a target energy of 6 mJ.

Measurement of dynamic gas lifetime with one gas fill showed that the standard deviation was below 2% for more than 1E6 pulses when using constant high voltage (HV-const-mode). However since energy decreases with the number of pulses, the high voltage has to be raised accordingly (energy-const-mode). When energy and standard deviation were measured in the energy-const-mode (settings: 20,000 warm-up pulses, 10,000 pulses (treatment simulation) with 5 minute breaks), the resulting standard deviation was below 4%.

B. Electrical safety and electromagnetic compatibility validation

These measurements determined the compliance of the ALLEGRETTO WAVE™ Excimer Laser System with regulatory standards for electrical safety and electromagnetic compatibility. The ALLEGRETTO WAVE™ was found to be in compliance with 21 CFR 1040.10, 21 CFR 1040.11, IEC 825, IEC 601.

C. Ablation profile testing for software validations using PMMA targets

These tests validated the ability of the ALLEGRETTO WAVE™ to ablate predefined refractive shapes. Treatment profiles for various prescriptions were ablated into flat PMMA discs at precisely defined conditions and examined using tactile measurements. Measured profile curvatures were in good agreement with intended shapes, and profile depths were a direct linear function of prescription magnitude.

D. Energy control and pulse stability

Measurements of the beam energy were performed with a video based, calibrated beam profile analyzer and the same laser data (frequency, pulse energy) as used for a treatment. These measurements were used to assess the stability of the laser beam energy distribution at the treatment plane for repetitive excimer laser operation. The reaction properties of the energy control were measured in two ways. Short term shows the ability of the control to compensate for even artificially generated extreme large step deviations of the output energy. The controller becomes active when the energy deviation is larger than 1 % averaged over 200 pulses. Long-term: This was tested by measuring the reproducibility of 8 ablations on flat PMMA discs of a nominal ablation depth of 40um. The measurements even without external closed loop control showed nearly constant depths for all 8 tests.

E. Variation of ablation depth in different treatment planes

Experiments showed that the central ablation depth is nearly constant within +/- 1 mm range of the treatment plane. Therefore an accuracy of alignment in z-direction of < +/-1 mm is demanded, ensured by alignment of the eye with the two distance diodes.

F. Measurement of thermal warm-up behavior of the laser

At 200Hz pulse repetition rate, the laser was warmed-up at least after 20,000 pulses. In the standard warm-up procedure for the ALLEGRETTO WAVE™, 24,000 pulses are used for the warm-up of the laser. With the energy-const-mode and only 1,000 low energy warm-up-pulses as worst case the target energy was reached after 55 pulses. As a safety measure, 2,000 pulses are released into the safety shutter before every treatment and a few pulses are released into the safety shutter when the laser pedal is pressed (when starting or restarting the treatment).

G. Animal and Biological Testing of Excimer Laser Photoablation of the Cornea

Prior animal studies of histologic changes after 193 nm excimer laser photoablation report that most histologic changes occur in PRK, and are limited to the epithelium and sub-epithelial stroma. Epithelial changes may persist beyond 18 months and permanent architectural changes are present, including absence of Bowman's membrane and undulating and spiked basement membrane with irregular collagen lamellae in the sub-epithelial stroma.

In contrast, histologic changes after LASIK were minimal, with no stromal disorganization observed. No report suggested histologic evidence of carcinomatous changes after exposure to excimer ablation. The shock wave effects of broad beam lasers were not found with small diameter beams similar to that used in the ALLEGRETTO WAVE™.

The body of literature regarding animal and tissue effects of excimer laser treatments raises few safety concerns for this PMA application and point out the minimal tissue impact of LASIK, rapid healing with minimal haze and light scattering (if any), limited thermal effects, lack of shock wave damage with a small diameter beam, and lack of oncologic transformation.

X. SUMMARY OF CLINICAL STUDIES

The sponsor performed a clinical study of the WaveLight ALLEGRETTO WAVE™ Excimer Laser System at eleven U.S. clinical sites under the auspices of an Investigational Device Exemption (IDE) G990317. The data from this study served as the basis for the approval decision. Specifically, safety and effectiveness outcomes at 3 months postoperatively were assessed, as stability was reached at that time. Outcomes at 6 and 12 months postoperatively were also evaluated for confirmation of stability. The IDE study is described in detail as follows.

A. Study Objective

The objective of the study was to determine the safety and effectiveness of the WaveLight ALLEGRETTO WAVE™ Excimer Laser System for LASIK treatment of myopic refractive errors up to -14.0 D with and without astigmatic refractive errors up to -6.0 D.

B. Study Design

The study was a prospective, non-randomized, 11 center, 11 surgeon study where the primary control was the preoperative status of the treated eye (i.e., comparison of pretreatment and post-treatment visual parameters in the same eye).

C. Inclusion and Exclusion Criteria

Enrollment in the WaveLight LASIK for myopia and myopic astigmatism study was limited to:

- Subjects undergoing LASIK surgery for the correction of myopia.
- Intended treatment from 0 to -14 D of spherical equivalent myopia or myopia with astigmatism, with up to -14 D of spherical component and up to -6.0 D of astigmatic component. (All refractions measured at the spectacle plane).
- Subjects with bilateral physiologic myopia.
- Subjects with BSCVA of 20/40 or better in each eye.
- Subjects with a stable refraction (0.5 D or less change in MRSE) for the last 12 months, objectively documented (by previous clinical records, eyeglass prescriptions, etc.).

- Subjects who were contact lens wearers must have hard or gas permeable lenses discontinued for 3 weeks and soft lenses discontinued for 3 days prior to the preoperative evaluation.
- Subjects at least 18 years of age.
- Subjects with normal corneal topography, as judged by the operating investigator.
- Subjects who signed a written Informed Consent form acknowledging their awareness of their participation in this study, the alternative treatments available, the risks involved, and the investigative nature of LASIK, and other issues that conform to the standard of care for Informed Consent practices.
- Subjects able to return for scheduled follow-up examinations for 12 months after surgery.

Subjects with the following conditions were not eligible for enrollment in the LASIK for myopia and myopic astigmatism study:

- Subjects with anterior segment pathology.
- Subjects with residual, recurrent or active ocular disease.
- Subjects who had undergone previous intraocular or corneal surgery involving the stroma in the eye to be operated.
- Subjects having a history of herpes keratitis.
- Subjects with diagnosed autoimmune disease, systemic connective tissue diseases or atopic syndrome, diabetes mellitus, or taking systemic medications (i.e., corticosteroids or antimetabolites) likely to affect wound healing.
- Subjects with unstable central keratometry/topography readings with irregular topography patterns or keratometry mires, including signs of keratoconus.
- Subjects with known sensitivity to study medications.
- Subjects with intraocular pressure of > 23 mm Hg by Goldmann applanation tonometry, a history of glaucoma, or glaucoma suspect.
- Women who were pregnant or nursing or who planned to become pregnant over the course of their participation in this investigation.
- Subjects who intended to participate in other ophthalmic clinical trials during this clinical investigation
- Subjects with colobomas of the iris or other irregularities of the pupil margin.

D. Study Plan, Patient Assessments, and Efficacy Criteria

Subjects were evaluated preoperatively and postoperatively at 1 day, 1 month, 3 months, 6 months, and 1 year. Preoperative objective measurements included: uncorrected distance and near visual acuity, manifest refraction, distance best spectacle corrected visual acuity, cycloplegic refraction, applanation tonometry,

slit lamp examination, pupil size measurement in photopic and scotopic conditions, central keratometry, computerized corneal topography, pachymetry, dilated fundus examination, and patient questionnaire.

Postoperatively, objective measurements included: uncorrected distance and near visual acuity, manifest refraction, distance best spectacle corrected visual acuity, cycloplegic refraction, applanation tonometry, slit lamp examination, central keratometry, computerized corneal topography, dilated fundus examination, and patient questionnaire.

Subjects were permitted to have second eyes (fellow eyes) treated at the same time as the first eye (primary treatment). Subjects were eligible for retreatment no sooner than 3 months after surgery. Subjects were eligible for retreatment if the manifest refractive myopia (spherical equivalent) was 0.5 D or greater, the manifest myopic astigmatism was 0.5 D or more, the distance visual acuity was 20/30 or less, or due to any subjective complaints by the patient with treatable cause as determined by the investigator.

Effectiveness was evaluated based on improvement in uncorrected visual acuity and predictability of the manifest refraction spherical equivalent (MRSE).

E. Study Period, Investigational Sites and Demographic Data

1. Study Period

A total of 901 eyes in 459 subjects were treated between 2/20/01 and 10/11/02. All follow-up received by SurgiVision prior to March 24, 2002 was included in this PMA.

2. Demographics

The demographics for this study are very typical of a contemporary refractive surgery trial performed in the U.S. Gender of subjects treated was almost equally split with 51.6% (465/901) of the cases being female and 48.4% (436/901) being male. Overall, 92.6% (834/901) of eyes treated were in Caucasian subjects, 2.9% (26/901) in Hispanics, 1.8% (16/901) in Asians, 1.3% (12/901) were in Black subjects, and 1.2% (11/901) were categorized as "other" races. The mean age of the patients treated was 38.07 ± 9.7 years with a range from 18 to 67.

Table 1 Demographic Characteristics (N=901)			
Category	**Classification**	**%**	**n**
Gender	Female	51.6	465
	Male	48.4	436
Race	Caucasian	92.6	834
	Black	1.3	12
	Asian	1.8	16
	Hispanic	2.9	26
	Other	1.2	11
	Not Reported	0.2	2
Eyes	OD	50.1	451
	OS	49.9	450
CL History	Soft	55.6	500
	RGP	8.3	75
	PMMA	1.0	9
	Glasses	34.8	313
	Unknown	0.2	2
Age (in Years)	Average	38.07	
	Standard Deviation	9.7	
	Minimum	18.0	
	Maximum	67.0	

F. Data Analysis and Results

1. Preoperative characteristics

Table 2 contains a summary of the preoperative refractive errors of the entire cohort.

Table 2 Baseline Characteristics-All Eyes (n=901)		
Spherical Equivalent Refraction	**%**	**n**
0.00 to 1.00 D	2.0	18
1.01 to 2.00 D	13.2	119
2.01 to 3.00 D	15.4	139
3.01 to 4.00 D	16.6	150
4.01 to 5.00 D	16.4	148
5.01 to 6.00 D	12.8	115
6.01 to 7.00 D	9.8	88
7.01 to 8.00 D	4.7	42
8.01 to 9.00 D	4.7	42
9.01 to 10.00 D	2.6	23
10.01 to 11.00 D	0.4	4
11.01 to 12.00 D	1.2	11
12.01 to 13.00 D	0.2	2
>13.00 D	0.0	0
Cylinder		
0.00 D	19.4	175
0.25 D	13.5	122
0.50 D	17.1	154
0.75 D	14.4	130
1.00 D	9.5	86
1.25 D	6.6	59
1.50 D	4.1	37
1.75 D	3.3	30
2.00 D	3.3	30
2.25 D	1.7	15
2.50 D	1.8	16
2.75 D	1.6	14
3.00 D	1.3	12
3.25 D	0.4	4
3.50 D	0.7	6
3.75 D	0.3	3
4.00 D	0.3	3
4.25 D	0.1	1
4.50 D	0.0	0
4.75 D	0.1	1
>5.00 D	0.3	3

2. Postoperative results

a. Patient Accountability

There were 901 eyes treated. Accountability information is provided in Table 3. Accountability for All Eyes treated was 97.2% (876/901) at 1-month, 93.8% (844/900) at 3-months, 91.9% (818/890) at 6-months, and 93.9% (813/866) at 1-year. The following cohorts were used for analysis:

- Safety-all eyes (901)
- Effectiveness-all eyes (901)
- Stability-subset of all eyes seen at any two consecutive visits, and subset of all eyes seen at 1, 3 and 6-months (765 and 833)

Table 3
Accountability

		1 Day (N=901)	1 Month (N=901)	3 Months (N=901)	6 Months (N=901)	1 Year (N=901)
Available for Analysis	%	98.7	97.2	93.7	90.8	90.2
	n	889	876	844	818	813
Discontinued-Deceased	%	0.0	0.0	0.0	0.0	0.0
	n	0	0	0	0	0
Discontinued-Retreated	%	0.0	0.0	0.1	1.1	2.4
	n	0	0	1	10	22
Discontinued-Total (Cumulative)	%	0.0	0.0	0.1	1.2	3.7
	n	0	0	1	11	33
Not Yet Eligible for Interval	%	0.0	0.0	0.0	0.0	0.2
	n	0	0	0	0	2
Expected	%	100	100	99.9	98.8	96.1
	n	901	901	900	890	866
Lost to Follow-Up (Cumulative)	%	0.0	0.4	0.7	0.9	1.1
	n	0	4	6	8	10
Missed Visit	%	1.3	2.3	5.6	7.1	4.8
	n	12	21	50	64	43
% Accountability	%	98.7	97.2	93.8	91.9	93.9
	n	889	876	844	818	813

b. Stability of Outcome

In the 1-3 month window, greater than 95% of eyes experienced a change of MRSE not exceeding 1.0 D. Furthermore, the mean of the paired difference of MRSE was -0.01 D in the 1 to 3-month time period. Thus, stability was demonstrated at 3-months postoperatively.

Table 4
Refractive Stability
(Eyes with 1, 3 and 6 Month Visits (n=765)

Change in MRSE	1 and 3 Months	3 and 6 Months
	% n 95% CI	% n 95% CI
≤1.00 D	97.6 747	99.0% 757
95% CI for %	97.1%, 98.2%	98.6%, 99.4%
MRSE (D)		
Mean	-0.01 D	-0.05 D
SD	0.34	0.30
95% CI for Mean	-0.03, 0.01	-0.07, -0.02

c. Effectiveness Outcomes

The analysis of effectiveness was based on the 844 eyes evaluable at the 3-month stability time point. Key efficacy outcomes over the course of the study and at the point of stability stratified by diopter of MRSE are presented in Tables 5 and 6.

Table 5
Summary of Key Efficacy Variables Over Time

	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI	1 Year % n 95% CI
Efficacy Variables	N=841	N=813	N=782	N=780
UCVA 20/20 or better*	82.8 696 81.5%, 84.1%	84.4 686 83.1%,85.7%	87.7 686 86.6%,88.9%	87.4 682 86.3%,88.6%
UCVA 20/40 or better*	97.6 821 97.1%, 98.2%	98.0% 797 97.5%,98.5%	98.3% 769 97.9%,98.8%	99.0 772 98.6%,99.3%
	N=876	N=844	N=818	N=813
MRSE ± 0.50 D	85.6 750 84.4%,86.8%	84.8 716 83.6%,86.1%	85.3 698 84.1%,86.6%	85.1 692 83.9%,86.4%
MRSE ± 1.00 D	96.8 848 96.2%,97.4%	96.7 816 96.1%,97.3%	97.3 796 96.7%,97.9%	97.7 794 97.1%,98.2%
MRSE ± 2.00 D	99.4 871 99.2%,99.7%	99.5 840 99.3%,99.8%	99.6 815 99.4%,99.8%	99.5 809 99.3%,99.8%

*For all eyes minus those intentionally treated for monovision.

Table 6 Summary of Key Efficacy Variables at 3 Months (Stratified by Preoperative MRSE)								
	0 to 1 D % n 95% CI	>1 to 2 D % n 95% CI	>2 to 3 D % n 95% CI	>3 to 4 D % n 95% CI	>4 to 5 D % n 95% CI	>5 to 6 D % n 95% CI	>6 to 7 D % n 95% CI	Total ≤7 D % n 95% CI
Efficacy Variables	**N=17**	**N=110**	**N=126**	**N=138**	**N=130**	**N=101**	**N=82**	**N=704**
UCVA 20/20 or better*	94.1 16 88.4%, 99.8%	87.3 96 84.1%, 90.5%	92.9 117 90.6%, 95.2%	92.0 127 89.7%, 94.3%	83.1 108 79.8%, 86.4%	79.2 80 75.2%, 83.3%	79.3 65 74.8%, 83.8%	86.5 609 85.2%, 87.8%
UCVA 20/40 or better*	100 17 100%, 100%	97.3 107 95.7%, 98.8%	98.4 124 97.3%, 99.5%	99.3 137 98.6%, 100%	98.5 128 97.4%, 99.5%	97.0 98 95.3%, 98.7%	97.6 80 95.9%, 99.3%	98.2 691 97.7%, 98.7%
	N=17	**N=114**	**N=131**	**N=141**	**N=135**	**N=106**	**N=84**	**N=728**
MRSE ± 0.50 D	94.1 16 88.4%, 99.8%	91.2 104 88.6%, 93.9%	84.7 111 81.6%, 87.9%	95.0 134 93.2%, 96.9%	84.4 114 81.3%, 87.6%	84.0 89 80.4%, 87.5%	78.6 66 74.1%, 83.1%	87.1 634 85.9%, 88.3%
MRSE ± 1.00 D	100 17 100%, 100%	98.3 112 97.0%, 99.5%	98.5 129 97.4%, 99.5%	99.3 140 98.6%, 100%	98.5 133 97.5%, 99.6%	96.2 102 94.4%, 98.1%	96.4 81 94.4%, 98.5%	98.1 714 97.6%, 98.6%
MRSE ± 2.00 D	100 17 100%, 100%	100 114 100%, 100%	100 131 100%, 100%	100 141 100%, 100%	100 135 100%, 100%	100 106 100%, 100%	100 84 100%, 100%	100 728 100%, 100%

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	>7 to 8 D % n 95% CI	>8 to 9 D % n 95% CI	>9 to 10 D % n 95% CI	>10 to 11 D % n 95% CI	>11 to 12 D % n 95% CI	>12 to 13 D % n 95% CI	Cum Total >7 D % n 95% CI
Efficacy Variables	**N=34**	**N=38**	**N=22**	**N=4**	**N=10**	**N=1**	**N=109**
UCVA 20/20 or better*	70.6 24 62.8%,78.4%	73.7 28 66.5%,80.8%	68.2 15 58.3%,78.1%	50.0 2 25.0%,75.0%	70.0 7 55.5%,85.5%	100 1 100%,100%	70.6 77 66.3%,75.0%
UCVA 20/40 or better*	100 34 100%,100%	100 38 100%,100%	95.5 21 100%,100%	100 4 100%,100%	80.0 8 67.4%,92.7%	100 1 100%,100%	97.3 106 95.7%,98.8%
	N=37	**N=40**	**N=22**	**N=4**	**N=11**	**N=2**	**N=116**
MRSE ± 0.50 D	86.5 32 80.9%,92.1%	72.5 29 65.4%,79.6%	59.1 13 48.6%,69.6%	75.0 3 53.4%,96.7%	45.5 5 30.4%,60.5%	0.0 0 0.0%,0.0%	70.7 82 66.5%,74.9%
MRSE ± 1.00 D	94.6 35 90.9%,98.3%	87.5 35 82.3%,92.7%	86.4 19 79.1%,93.7%	100 4 100%,100%	72.7 8 59.3%,86.2%	50.0 1 14.6%,85.4%	87.9% 102 84.9%,91.0%
MRSE ± 2.00 D	97.3 36 94.6%,100%	100 40 100%,100%	100 22 100%,100%	100 4 100%,100%	81.8 9 70.2%,93.5%	50.0 1 14.6%,85.4%	96.6% 112 94.9%,98.3%

*For all eyes minus those intentionally treated for monovision.

Analysis of the correction of the cylindrical component of the astigmatic eyes is presented in Tables 7 and 8. The Ophthalmic Devices Panel (the Panel), at the January 14, 1997 meeting, assessed outcomes from a myopic astigmatic treatment and provided FDA with recommendations as to acceptable effectiveness rates. The mean reduction in absolute cylinder at 3-months is consistent with what the Panel considered acceptable mean reduction in absolute cylinder at the point of stability.

Table 7
Cylinder Correction Efficacy Stratified by Preoperative Cylinder

	3 Months	
Preoperative Cylinder	**Reduction of Absolute Cylinder**	
	% Reduction Mean[1]	**Ratio Mean[2]**
≤ 1.00 D	76.9%	0.56
> 1.00 to ≤ 2.00 D	79.6%	0.21
> 2.00 to ≤ 3.00 D	83.1%	0.17
> 3.00 to ≤ 4.00 D	82.1%	0.18
> 4.00 to ≤ 5.00 D	92.1%	0.08
> 5.00 to ≤ 6.00 D	93.9%	0.06
Total	78.2%	0.44

[1] [(Postoperative cylinder – Preoperative cylinder) / Preoperative cylinder] x 100
[2] Postoperative cylinder / Preoperative cylinder]

Looking at the intended versus achieved vector magnitude cylinder, the Intended Refractive Correction ("IRC") had a mean of –1.02 ± 0.76 D. The Surgically Induced Refractive Correction ("SIRC") had a mean of –1.14 ± 0.86 D. The vector magnitude ratio (SIRC/IRC) was 1.18 at 3-months. The Panel has found 0.82 acceptable for correction efficacy (SIRC/IRC) at stability.

Table 8
Cylinder Correction Efficacy Stratified by Preoperative Cylinder

	3 Months
Preoperative Cylinder	**Achieved vs. Intended Vector Magnitude Ratio (Achieved/Intended) Mean**
ALL	1.18
0 to 0.50 D	1.36
>0.50 to ≤ 1.00 D	1.13
>1.00 to ≤ 2.00 D	1.09
>2.00 to ≤ 3.00 D	1.11
>3.00 to ≤ 4.00 D	1.08
>4.00 to ≤ 5.00 D	1.07
>5.00 to ≤ 6.00 D	0.90

d. Safety Outcomes

The analysis of safety was based on the 844 eyes that have had the 3-month examination. The key safety results for this study are presented in Tables 9 and 10, with all adverse events reported in Table 11. Overall the device was deemed reasonably safe.

Table 9
Summary of Key Safety Variables Over Time

	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI	1 Year % n 95% CI
Safety Variables	**N=876**	**N=844**	**N=818**	**N=813**
Loss of ≥ 2 lines BSCVA	0.9 8 0.6%,1.2%	0.6 5 0.3%,0.9%	0.7 6 0.4%,1.0%	0.5 4 0.3%,0.7%
BSCVA worse than 20/40	0.1 1 0.0%,0.2%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%
	N=263	**N=251**	**N=242**	**N=249**
Increase > 2 D Cylinder#	0.4 1 0.0%,0.8%	0.4 1 0.0%,0.8%	0.0 0 0.0%,0.0%	0.4 1 0.0%,0.8%
	N=833	**N=800**	**N=779**	**N=771**
BSCVA worse than 20/25 if 20/20 or better preoperatively	0.2 2 0.1%,0.4%	0.1 1 0.0%,0.3%	0.3 2 0.1%,0.4%	0.1 1 0.0%,0.3%

#For eyes treated for spherical correction only.

Table 10 Summary of Key Safety Variables at 3 Months (Stratified by Preoperative MRSE)								
	0 to 1 D % n 95% CI	>1 to 2 D % n 95% CI	>2 to 3 D % n 95% CI	>3 to 4 D % n 95% CI	>4 to 5 D % n 95% CI	>5 to 6 D % n 95% CI	>6 to 7 D % n 95% CI	Total ≤7 D % n 95% CI
Safety Variables	**N=17**	**N=114**	**N=131**	**N=141**	**N=135**	**N=106**	**N=84**	**N=728**
Loss of ≥ 2 lines BSCVA	0.0 0 0.0%,0.0%	0.9 1 0.0%,1.8%	0.0 0 0.0%,0.0%	0.7 1 0.0%,1.4%	2.2 3 1.0%,3.5%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.7 5 0.4%,1.0%
BSCVA worse than 20/40	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%
	N=2	**N=41**	**N=49**	**N=46**	**N=38**	**N=29**	**N=22**	**N=227**
Increase >2 D cylinder#	0.0 0 0.0%,0.0%	2.4 1 0.0%,4.9%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.4 1 0.0%,0.9%
	N=17	**N=114**	**N=130**	**N=138**	**N=130**	**N=96**	**N=77**	**N=702**
BSCVA worse than 20/25 if 20/20 or better preoperatively	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.8 1 0.0%,1.5%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.1 1 0.0%,0.3%

	>7 to 8 D % n 95% CI	>8 to 9 D % n 95% CI	>9 to 10 D % n 95% CI	>10 to 11 D % n 95% CI	>11 to 12 D % n 95% CI	>12 to 13 D % n 95% CI	Cum Total >7 D % n 95% CI
Safety Variables	N=37	N=40	N=22	N=4	N=11	N=2	N=116
Loss of ≥ 2 lines BSCVA	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%
BSCVA worse than 20/40	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%
	N=10	N=6	N=4	N=2	N=2	N=0	N=24
Increase >2 D cylinder#	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%
	N=32	N=34	N=19	N=3	N=9	N=1	N=98
BSCVA worse than 20/25 if 20/20 or better preoperatively	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%	0.0 0 0.0%,0.0%

#For eyes treated for spherical correction only.

Table 11 presents a summary of adverse events. The benchmark for each adverse event is a rate of less than 1% per event.

Table 11
Adverse Events

Adverse Event	1 Month % n N=876	3 Months % n N=844	6 Months % n N=818	1 Year % n N=813
Corneal infiltrate or ulcer requiring treatment	0.0 0	0.0 0	0.0 0	0.0 0
Lost, misplaced, or misaligned flap, or any flap/cap problems requiring surgical intervention beyond 1 month	0.2 2	0.0 0	0.0 0	0.0 0
Corneal edema at 1 month or later visible in the slit lamp exam	0.0 0	0.0 0	0.0 0	0.0 0
Any complication leading to intraocular surgery	0.0 0	0.0 0	0.0 0	0.0 0
Melting of the flap of >1 mm sq	0.0 0	0.0 0	0.0 0	0.0 0
Epithelium of > 1 mm2 in the interface with loss of 2 lines or more of BSCVA	0.0 0	0.0 0	0.0 0	0.0 0
Uncontrolled IOP rise with increase of > 5 mm Hg or any reading above 25 mm Hg	0.0 0	0.0 0	0.0 0	0.0 0
Retinal detachment or retinal vascular accident	0.0 0	0.0 0	0.0 0	0.0 0
Decrease in BSCVA of > 10 letters not due to irregular astigmatism as shown by hard contact lens refraction	0.0 0	0.0 0	0.0 0	0.0 0

Table 12 Complications Summary Table								
Complications	**1 Month**		**3 Months**		**6 Months**		**1 Year**	
	%	**n**	**%**	**n**	**%**	**n**	**%**	**n**
	N=876		**N=844**		**N=818**		**N=813**	
Corneal edema between 1 week and 1 month after the procedure	0.0	0	0.0	0	0.0	0	0.0	0
Corneal epithelial defect at 1 month or later	0.7	6	0.8	7	0.1	1	0.3	2
Any epithelium in the interface	0.2	2	0.1	1	0.0	0	0.0	0
Foreign body sensations at 1 month or later	0.5	4	0.1	1	0.0	0	0.0	0
Pain at 1 month or later	0.0	0	0.2	2	0.0	0	0.0	0
Ghosting or double images in the operative eye at stability or beyond			0.7	6	0.9	7	0.3	2
Need for lifting and/or reseating of the flap/cap prior to 1 month	0.0	0	0.0	0	0.0	0	0.0	0

e. Retreatments

A total of 33 eyes were retreated with the study laser due primarily to undercorrection. One eye was retreated for overcorrection. Table 13 contains the outcomes for retreated eyes.

Table 13 Summary of Key Safety and Efficacy Variables Over Time for Retreated Eyes				
	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI	1 Year % n 95% CI
Efficacy Variables	N=25	N=16	N=21	N=1
UCVA 20/20 or better*	56.0 14 46.1%, 65.9%	87.5 14 79.2%, 95.8%	66.7 14 56.4%, 77.0%	100 1 100%, 100%
UCVA 20/40 or better*	96.0 24 92.1%, 99.9%	100 16 100%, 100%	100 21 100%, 100%	100 1 100%, 100%
	N=25	N=15	N=21	N=1
MRSE ± 0.50 D	64.0 16 54.4%, 73.6%	100 15 100%, 100%	85.7 18 78.1%, 93.4%	100 1 100%, 100%
MRSE ± 1.00 D	96.0 24 92.1%, 99.9%	100 15 100%, 100%	100 21 100%, 100%	100 1 100%, 100%
MRSE ± 2.00 D	100 25 100%, 100%	100 15 100%, 100%	100 21 100%, 100%	100 1 100%, 100%
Safety Variables	N=25	N=16	N=21	N=1
Loss of ≥ 2 lines BSCVA	4.0 1 0.1%, 7.9%	0.0 0 0.0%, 0.0%	4.8 1 0.1%, 9.4%	0.0 0 0.0%, 0.0%
BSCVA worse than 20/40	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%
BSCVA worse than 20/25 if 20/20 or better preoperatively	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	4.8 1 0.1%, 9.4%	0.0 0 0.0%, 0.0%
	N=7	N=5	N=6	N=0
Increase >2 D cylinder#	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%

*For all eyes minus those intentionally treated for monovision.
#For eyes treated for spherical correction only.

f. Factors Associated with Outcomes

The following are the results of the testing for association between several baseline characteristics and 3 month outcomes. In summary, no significant differences in enrollment characteristics or outcomes were found between the sexes. Significant preoperative and outcomes differences were seen with age. Older patients had significantly lower preoperative MRSE and significantly worse preoperative BSCVA. Accuracy of manifest refraction and UCVA outcomes were best in

patients under 40. Patients over 60 experienced a significantly higher amount of residual myopia, and had correspondingly lower UCVA. Despite these variations in efficacy measures, safety among the groups was similar, with change in BSCVA showing no differences with age. Preoperative MRSE was significantly associated with effectiveness outcomes. UCVA results were worse in eyes with higher preoperative MRSE. UCVA was more sensitive to preoperative spheroequivalent than MRSE, showing a fall-off in results at the 4 D level. Association of preoperative spheroequivalent with MRSE was limited to rates of overcorrection by more than 0.50 D, which showed a significant difference beyond the 6 D level. Preoperative spheroequivalent was not found to be associated with gain or loss of BSCVA.

No direct correlations for pupil size with preoperative and main postoperative target measures were found.

g. Patient Satisfaction

Subjects were asked to complete a patient questionnaire preoperatively and at 3-months, 6-months, and 1-year postoperatively. Responses were made by placing a mark or an "x" through the provided line. Each end of the line was marked with opposing answers such as "Never" versus "All the Time". A mark on either end of the bar represented an extreme answer (never on one end, all the time on the other end) and a mark in the middle indicated a scaled response between the extremes.

Patient reports of glare from bright lights, light sensitivity, night driving glare and visual fluctuations all improved after LASIK. The percent of subjects reporting "none" or "mild" of these symptoms improved after treatment.

Table 14 Patient Symptoms						
	Preoperative (N=892)			3 Months (N=832)		
	None-Mild % n	Moderate % n	Marked-Severe % n	None-Mild % n	Moderate % n	Marked-Severe % n
Glare from Bright Lights	48.1 429	34.5 308	17.4 155	61.4 511	26.2 218	12.4 103
Halos	71.0 635	15.8 141	13.2 118	67.9 565	13.2 110	9.1 76
Light Sensitivity	61.8 552	26.0 232	12.3 110	73.2 609	18.5 154	8.3 69
Night Driving Glare	50.5 450	32.2 287	17.4 155	64.1 533	24.0 200	11.9 99
Visual Fluctuations	87.3 780	10.3 92	2.5 22	71.4 594	22.5 187	6.1 51

h. Device Failure

In one case, reported to FDA on April 5, 2001, the laser ceased firing after 18% of the treatment had been completed. The attempted correction was –1.50 –0.50 x 79. At one day postoperatively, the patient's UCVA was 20/15. This event was determined by FDA to be a device malfunction but not an unanticipated adverse event. No further action was required.

XI. CONCLUSIONS DRAWN FROM THE CLINICAL STUDY

The data in this application support reasonable assurance of the safety and effectiveness of this device when used in accordance with the approved indications for use.

XII. PANEL RECOMMENDATION

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

XIII. CDRH DECISION

CDRH issued an approval order on OCT - 7 2003.

An inspection of the manufacturing facility determined that the applicant was in compliance with the Quality System Regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

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