SUMMARY OF SAFETY AND EFFECTIVENESS
FOR A SUPPLEMENTAL 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® Regulatory Consultants, Inc. 5 Timber Lane North Reading, MA 01864
Panel Recommendation:	None (see Section XII.)
Premarket Approval (PMA) Application Number:	P030008/S004
Date of Notice of Approval to Applicant:	APR 19 2006

The WaveLight ALLEGRETTO WAVE™ was originally approved on October 7, 2003, under PMA P020050, for the limited indication for laser assisted in situ keratomileusis (LASIK); using optical zones of 6.0 and 6.5 mm with an ablation/treatment zone up to 9.0 mm; for the reduction or elimination of myopia up to -12.0 diopers (D) of sphere and up to -6.0 D of astigmatism at the spectacle plane; in patients 18 years of age or older with documentation of a stable manifest refraction defined as ≤ 0.50 D of preoperative spherical equivalent shift over one year prior to surgery.

This clinical indication was expanded in P030008 (approved on October 10, 2003) for LASIK treatments for the reduction or elimination of hyperopic refractive errors up to +6.0 D of sphere with and without astigmatic refractive errors up to 5.0 D at the spectacle plane, with a maximum manifest refraction spherical equivalent (MRSE) of +6.0 D; in patients 18 years of age of older with documentation of a stable manifest refraction defined as ≤ 0.50 D of preoperative spherical equivalent shift over one year prior to surgery, exclusive of changes due to unmasking latent hyperopia.

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(SSED) for P030008 and P020050 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 # 03M-0491 (P020050) and Docket # 03M-0492 (P030008) or you may download the files from the internet sites http://www.fda.gov/cdrh/pdf/p020050.pdf and http://www.fda.gov/cdrh/pdf/p030008.pdf.

II. INDICATIONS FOR USE

The WaveLight Allegretto Wave Excimer Laser System is indicated for laser assisted in situ keratomileusis (LASIK) for:

- the reduction or elimination of naturally occurring mixed astigmatism of up to 6.00 diopters (D) at the spectacle plane;
- patients who are 21 years of age or older; and
- patients with documentation of a stable manifest refraction defined as ≤0.50 D preoperative spherical equivalent shift over one year prior to surgery.

III. CONTRAINDICATIONS

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 of keratoconus; and
- patients who are taking one or both of the following medications: isotretinoin (Accutane®[1]); amiodarone hydrochlorid (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.

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

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. In addition, the ablation profiles are "Wavefront Optimized" meaning that the initial profiles, which can be mathematically calculated, were refined by empirical research with a wavefront aberrometer.

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.

The operative laser parameters are summarized as follows:

Pulse repetition rate:	200 Hz
Fluence:	200 mJ/cm^2 (average)
	400 m J/cm^2 (peak)
Optical zone:	6.0 - 7.0 mm for mixed astigmatism treatments
Ablation zone:	9.0 mm for mixed astigmatism treatments
Ablation spot diameter:	0.95 + 0.10 mm

During the clinical study, a 6.5 mm optical zone was used.

The software versions in the laser system during the clinical trial were as follows:

a. Notebook Software	1.208
b. Firmware Software	PR034901
c. Treatment Lists	NG-041301
d. Eyetracker	4.08
e. Laser Head Firmware	H4.2 / G3.6 / E3.8 / M3.3 / P3.7

The software versions in the laser system at approval are as follows:

a. Notebook Software	NB-PSW 2.0xx
b. Firmware Software	PR-V2-1.00
c. Treatment Lists	NG-051701
d. Eyetracker	4.08 or 4.10
e. Laser Head Firmware	H4.2 / G3.6 / E3.8 / M3.3 / P3.7

Laboratory testing was performed which compared the software versions used in the clinical study to the software version being requested for approval. This testing showed functional comparability (the new software met the same specifications as the version used in the clinical study). Both the clinical study

software and the proposed software met all specifications. Therefore, the clinical data also apply to the use of the new software.

B. Microkeratome

The LASIK procedure requires the use of a commercially available microkeratome that has been cleared for marketing via premarket notification. Treatments in this study were conducted with both a mechanical microkeratome as well as a laser microkeratome.

Mechanical keratomes consist 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. Laser keratomes include a transparent applanation plate used to flatten the cornea and establish a known reference plane. The laser is a femtosecond laser that is operated through a software interface and is activated by use of a foot pedal. The laser keratome used in this series was operated at a 15 KHz repetition rate.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Conventional methods in correcting mixed 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 53 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, United States, Egypt, Algeria, Argentina, Chile, Columbia, Curacao, Finland, Iran, Jordan, Kenya, La Reunion, Malaysia, New Zealand, Poland, Serbia, Slovakia, South Africa, Sweden, Taiwan, Thailand, Czech Republic, Dubai). The WaveLight ALLEGRETTO WAVE™ has not been withdrawn from any country or market for reasons of safety or effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse effects associated with LASIK include: loss of best spectacle corrected visual acuity, 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, problems associated with the flap including a lost, misplaced or misaligned flap, retinal detachment, and retinal vascular accidents. The occurrence of many of these events may involve the necessity of secondary (additional) surgical intervention.

Please refer to the complete list of adverse events and complications observed during the clinical study, which are presented in the clinical study section.

IX. SUMMARY OF PRECLINICAL STUDIES

Please refer to the SSED for PMA P020050.

Additionally, the final software versions in this approval are different than the software used in the clinical trial. Bench testing was performed with both software versions to ensure identical behavior of the software in all functions which may affect treatment outcomes. Tests included laser pulse characterization, beam profilometry and eye tracking tests. Specifications have been met with both software versions. No differences were found.

Verification and validation testing was applied to laser systems with the clinical trial software and the proposed software to analyze possible differences in treatment profiles. A large series of corrections were cut in PMMA disks for all optical zones. Treatment types included myopic and hyperopic spheres, myopic and hyperopic astigmatic treatments, myopic and hyperopic spherocylindrical treatments and mixed astigmatism treatments. Cuts were measured and results were compared with nominal profiles. All specifications were met with both software versions and no differences in ablation properties and ablation profiles were found between the software versions.

X. SUMMARY OF CLINICAL STUDIES

The sponsor performed a clinical study of the WaveLight ALLEGRETTO WAVE™ Excimer Laser System at six U.S. clinical sites under the auspices of an Investigational Device Exemption (IDE) G040113. 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 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 mixed astigmatism errors up to 6.0 D.

B. Study Design

The study was a prospective, non-randomized, 6 center, 7 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 mixed astigmatism was limited to:

- Subjects undergoing LASIK surgery for the correction of mixed astigmatism in either or both eyes
- Subjects with intended treatment from 0.5 to 6 D of manifest mixed astigmatism. (All refractions measured at the spectacle plane).
- BSCVA of 20/40 or better in each eye.
- Subjects with a stable refraction (0.5 D or less change in spheroequivalent) for the last twelve (12) months, objectively documented (by previous clinical records, eyeglass prescriptions, etc.).
- Subjects who are contact lens wearers must have had hard or gas permeable lenses discontinued for 3 weeks and soft lenses discontinued for 3 days prior to the preoperative evaluation.
- Subjects at least eighteen (18) years of age.
- Corneal topography must be normal, as judged by the operating investigator.
- Subjects must sign 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 which conform to the standard of care for Informed Consent practices.
- Subjects must be able to return for scheduled follow-up examinations for 6 months after surgery.

Subjects with the following conditions will not be eligible for enrollment in the LASIK for mixed astigmatism study:

- Subjects with anterior segment pathology.

- Subjects with residual, recurrent or active ocular disease.
- Subjects who have undergone previous intraocular or corneal surgery involving the stroma in the eye to be operated.
- Subjects who have 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 are pregnant or nursing or who plan to become pregnant over the course of their participation in this investigation.
- Participation 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, and 6 months. 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, measurement of angle kappa, 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 spherical equivalent was 0.5 D or greater (myopic or hyperopic), the manifest 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 162 eyes in 96 subjects were treated between September 14, 2004 and July 29, 2005. All follow-up received by SurgiVision prior to September 29, 2005 was included in this PMA Supplement.

2. Demographics

More males than females were treated with 67.3% (109/162) of the cases being male and 32.7% (53/162) being female. Overall, 85.8% (139/162) of eyes treated were in Caucasian subjects, 8.0% (13/162) in Hispanics, 3.7% (6/162) in Blacks, 1.2% (2/162) in Arabs, and 1.2% (1/162) in American Indians. The mean age of the patients treated was 39.0±9.4 years with a range from 22 to 70.

Table 1
Demographic Characteristics
(N=162)

Category	Classification	%	n
Gender	Female	32.7	53
	Male	67.3	109
Race	Caucasian	85.8	139
	Black	3.7	6
	Asian	0.0	0
	Hispanic	8.0	13
	Other	2.4	4
	Not Reported	0.0	0
Eyes	OD	50.6	82
	OS	49.4	80
CL History	Soft	22.3	36
	RGP	2.5	4
	PMMA	0.0	0
	Glasses	74.1	120
	Unknown	1.2	2
Age (in Years)	Average	39.0	
	Standard Deviation	9.4	
	Minimum	22.0	
	Maximum	70.0	

F. Data Analysis and Results

1. Baseline characteristics

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

Table 2
Preoperative Refractive Error Stratified by Sphere and Cylinder (N=162)

Sphere	Cylinder (Minus Cylinder Notation)													
	0 to ≤1 D		>1 to ≤2 D		>2 to ≤3 D		>3 to ≤4 D		>4 to ≤5 D		>5 to ≤6 D		Total	
	%	n												
0 to ≤1 D	6.8	11	31.5	51	21.6	35	6.2	10	1.2	2	0.6	1	67.9	110
>1 to ≤2 D	0.0	0	4.9	8	6.2	10	6.2	10	1.9	3	0.0	0	19.1	31
>2 to ≤3 D	0.0	0	0.0	0	1.9	3	4.9	8	3.1	5	0.6	1	10.5	17
>3 to ≤4 D	0.0	0	0.0	0	0.0	0	0.0	0	1.2	2	0.6	1	1.9	3
>4 to ≤5 D	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.6	1	0.6	1
>5 to ≤6 D	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0
Total	6.8	11	36.4	59	29.7	48	17.3	28	7.4	12	2.4	4	100	162

2. Postoperative Characteristics and Results

a. Patient Accountability

There were 162 eyes treated. Accountability information is provided in Table 3. Accountability was 99.4% (161/162) at 1–month, 96.0% (142/148) at 3-months, and 100% (111/104) at 6-months. The following cohorts were used for analysis:

- Safety-all eyes (162)
- Effectiveness-all eyes (162)
- Stability-subset of all eyes seen at any two consecutive visits, and subset of all eyes seen at 1, 3 and 6-months (142 and 105)

Table 3 Subject Accountability (N=162)					
		1 Day	1 Month	3 Months	6 Months
Available for Analysis	%	98.8	99.4	87.7	68.5
	n	160	161	142	111
Discontinued-Deceased	%	0.0	0.0	0.0	0.0
	n	0	0	0	0
Discontinued-Retreated	%	0.0	0.0	0.0	1.9
	n	0	0	0	3
Discontinued-Total (Cumulative)	%	0.0	0.0	0.0	1.9
	n	0	0	0	3
Not Yet Eligible for Interval	%	0.0	0.0	8.6	34.0
	n	0	0	14	55
Expected	%	100	100	91.4	64.2
	n	162	162	148	104
Lost to Follow-Up (Cumulative)	%	0.0	0.0	0.0	0.0
	n	0	0	0	0
Missed Visit	%	1.2	0.6	3.7	0.0
	n	2	1	6	0
% Accountability	%	98.8	99.4	96.0	100
	n	160	161	142	111

b. Stability of Outcome

In the 1-3 and 3-6 month windows, greater than 98% of eyes experienced a change of MRSE not exceeding 1.0 D. Furthermore, the mean of the paired difference of MRSE was 0.07 D in the 1 to 3-month time period and 0.01 D in the 3 to 6-month time period. Thus, stability was demonstrated at 3-months postoperatively.

Table 4 Refractive Stability (Eyes with 1, 3 and 6 Month Visits (n=105)		
Change in MRSE	**1 and 3 Months**	**3 and 6 Months**
	% n **95% CI**	**% n** **95% CI**
≤1.00 D **95% CI for %**	99.0 104 98.1%, 100%	98.1 103 96.8%, 99.4%
MRSE (D)		
Mean	+0.07 D	+0.01 D
SD	0.34	0.32
95% CI for Mean	0.00, +0.13	-0.05, +0.07

c. Effectiveness Outcomes

The analysis of effectiveness was based on the 142 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**
Efficacy Variables	**N=161**	**N=142**	**N=111**
UCVA 20/20 or better*	59.6 96 55.8%, 63.5%	67.6 96 63.7%, 71.5%	69.4 77 65.0%, 73.7%
UCVA 20/40 or better*	96.9 156 95.5%, 98.3%	95.8 136 94.1%, 97.5%	97.3 108 95.8%, 98.8%
MRSE ± 0.50 D	91.3 147 89.1%, 93.5%	95.8 136 94.1%, 97.5%	91.0 101 88.3%, 93.7%
MRSE ± 1.00 D	99.4 160 98.8%, 100%	100 142 100%, 100%	97.3 108 95.8%, 98.8%
MRSE ± 2.00 D	100 161 100%, 100%	100 142 100%, 100%	100 111 100%, 100%

*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 1.0 D % n 95% CI	>1.0 to 2.0 D % n 95% CI	>2.0 to 3.0 D % n 95% CI	>3.0 to 4.0 D % n 95% CI	>4.0 to 5.0 D % n 95% CI	>5.0 to 6.0 D % n 95% CI	>6.0 to 7.0 D % n 95% CI	Total ≤7 D % n 95% CI
Efficacy Variables	**N=132**	**N=10**	**N=0**	**N=0**	**N=0**	**N=0**	**N=0**	**N=142**
UCVA 20/20 or better*	68.9 91 64.9%,73.0%	50.0 5 34.2%,65.8%	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%	67.6 96 63.7%,71.5%
UCVA 20/40 or better*	96.2 127 94.6%,97.9%	90.0 9 80.5%,99.5%	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%	95.8 136 94.1%,97.5%
MRSE ± 0.50 D	97.0 128 95.5%,98.5%	80.0 8 67.4%,92.7%	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%	95.8 136 94.1%,97.5%
MRSE ± 1.00 D	100 132 100%, 100%	100 10 100%, 100%	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%	100 142 100%, 100%
MRSE ± 2.00 D	100 132 100%, 100%	100 10 100%, 100%	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%	100 142 100%, 100%

*For all eyes minus those intentionally treated for monovision.

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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 Panel considered 64% as an acceptable mean reduction in absolute cylinder at the point of stability. Therefore, the 85.0% reduction at 3 months achieved with this device is acceptable.

Table 7
Cylinder Correction Efficacy Stratified by Preoperative Cylinder
(N=132)

	3 Months
Preoperative Cylinder	**% Reduction of Absolute Cylinder**
≤ 1.00 D	83.3%
> 1.00 to ≤ 2.00 D	84.1%
> 2.00 to ≤ 3.00 D	85.4%
> 3.00 to ≤ 4.00 D	87.5%
> 4.00 to ≤ 5.00 D	88.3%
> 5.00 to ≤ 6.00 D	72.5%
Total	85.0%

Looking at the intended versus achieved vector magnitude cylinder, the Intended Refractive Correction ("IRC") had a mean of –2.44 ± 1.10 D. The Surgically Induced Refractive Correction ("SIRC") had a mean of –2.50 ± 1.10 D. The vector magnitude ratio (SIRC/IRC) was 1.04 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 (N=142)	
Preoperative Cylinder	**Achieved vs. Intended Vector Magnitude Ratio (Achieved/Intended) Mean**	
	n	**Mean**
ALL	142	1.04
0 to 0.50 D	NA	NA
>0.50 to ≤ 1.00 D	9	0.90
>1.00 to ≤ 2.00 D	51	1.09
>2.00 to ≤ 3.00 D	45	1.03
>3.00 to ≤ 4.00 D	24	1.03
>4.00 to ≤ 5.00 D	10	0.98
>5.00 to ≤ 6.00 D	3	0.88

Table 9
Comparison of Key Outcomes in Eyes with >4.00 D Preoperative Cylinder to the Remaining Eyes, at 3 Months

Preoperative Cylinder		Postoperative Cylinder (D)			Postoperative BSCVA			Postoperative UCVA		
	N	Mean	SD	p	Mean	SD	p	Mean	SD	p
≤4.00 D	129	0.35	0.43	<0.05	20/17	0.9 lines	NS	20/20	1.5 lines	NS
>4.00 to 6.00 D	13	0.77	0.68		20/17.7	0.7 lines		20/21.9	1.5 lines	

In cylinder amounts >4 to ≤6 D due to the lack of large numbers of patients in the general population, there are few subjects with cylinder amounts in this range to be studied. Not all complications, adverse events, and levels of effectiveness may have been determined.

As can be seen in Table 9, the mean residual postoperative cylinder amount was higher in this group, however, no significant differences were seen in UCVA and BSCVA outcomes for the 13 eyes in the >4 to 6.00 D range compared with the remainder of eyes in the study.

Table 10 presents the accuracy of the sphere and cylinder components in a non-vector analysis, for each postoperative interval. Sphere accuracy is rated against the target sphere while cylinder accuracy is rated against zero.

Table 10
Accuracy of Sphere (To Target) and Cylinder (To Zero) Component (For Eyes Treated for Astigmatic Myopia)

	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI
CYLINDER	**N=161**	**N=142**	**N=100**
<= 0.50 D	73.9 119 70.5%, 77.4%	77.5 110 74.0%, 81.0%	78.4 87 74.5%, 82.3%
<=1.00 D	96.9 156 95.5%, 98.3%	95.1 135 93.3%, 96.9%	91.9 102 89.3%, 94.5%
SPHERE			
± 0.50 D	91.3 147 89.1%, 93.5%	95.8 142 94.1%, 97.5%	91.0 101 88.3%, 93.7%
± 1.00 D	99.4 160 98.8%, 100%	100 142 100%, 100%	97.3 108 95.8%, 98.8%

d. Safety Outcomes

The analysis of safety was based on the 142 eyes that have had the 3-month examination. The key safety results for this study are presented in Tables 11 and 12, with all adverse events reported in Table 13. Overall the device was deemed reasonably safe.

Table 11
Summary of Key Safety Variables Over Time

	1 Month % n 95% CI	3 Months % n 95% CI	6 Months % n 95% CI
Safety Variables	**N=161**	**N=142**	**N=111**
Loss of ≥ 2 lines BSCVA	2.5 4 1.3%, 3.7%	0.7 1 0.0%, 1.4%	0.9 1 0.0%, 1.8%
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%
	N=145	**N=128**	**N=97**
BSCVA worse than 20/25 if 20/20 or better preoperatively	1.4 2 0.4%, 2.4%	0.0 0 0.0%, 0.0%	0.0 0 0.0%, 0.0%

Table 12
Summary of Key Safety Variables
at 3 Months (Stratified by Preoperative MRSE)

	0 to 1.0 D % n 95% CI	>1.0 to 2.0 D % n 95% CI	>2.0 to 3.0 D % n 95% CI	>3.0 to 4.0 D % n 95% CI	>4.0 to 5.0 D % n 95% CI	>5.0 to 6.0 D % n 95% CI	>6.0 to 7.0 D % n 95% CI	Cum Total ≤7 D % n 95% CI
Safety Variables	**N=132**	**N=10**	**N=0**	**N=0**	**N=0**	**N=0**	**N=0**	**N=142**
Loss of ≥ 2 lines BSCVA	0.8 1 0.0%,1.5%	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%	0.7 1 0.0%,1.4%
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=119	**N=9**	**N=0**	**N=0**	**N=0**	**N=0**	**N=0**	**N=128**
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%	0.0 0 0.0%,0.0%

Table 13 presents a summary of adverse events. The benchmark for each adverse event is a rate of less than 1% per event.

Table 13
Adverse Events

Adverse Event	1 Month % n N=161	3 Months % n N=142	6 Months % n N=111
Corneal infiltrate or ulcer requiring treatment	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	0.0 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
Any complication leading to intraocular surgery	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
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
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
Retinal detachment or retinal vascular accident	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

No protocol-defined adverse events occurred during this clinical trial. Two events were reported to FDA and the IRB as adverse events during the follow-up period of this clinical trial. The first event involved a patient who postoperatively was

subject to blunt trauma to the treatment eye 6 days after surgery. The second event involved the treatment of an incorrect axis of astigmatism. After retreatment, the UCVA was 20/20, the manifest refraction was plano with a BSCVA of 20/20.

Table 14
Complications Summary Table

Complications	1 Month % (N=161)	n	3 Months % (N=142)	n	6 Months % (N=111)	n
Corneal edema between 1 week and 1 month after the procedure	0.0	0	0.0	0	0.0	0
Corneal epithelial defect at 1 month or later	0.0	0	0.0	0	0.0	0
Any epithelium in the interface	0.0	0	0.0	0	0.0	0
Foreign body sensations at 1 month or later	1.2	2	0.0	0	0.0	0
Pain at 1 month or later	0.0	0	0.0	0	0.0	0
Ghosting or double images in the operative eye at stability or beyond			0.0	0	1.8	2
Need for lifting and/or reseating of the flap/cap prior to 1 month	0.0	0	0.0	0	0.0	0

Table 15
Change in Patient Symptoms at 6 Months

	Worse %	n	No Change %	n	Better %	n
	N=142		N=142		N=142	
Glare from Bright Lights	16.2	23	48.6	69	35.2	3
Halos	29.6	42	42.3	60	28.2	40
Light Sensitivity	21.1	30	58.5	83	20.4	29
Visual Fluctuations	23.2	33	64.1	91	12.7	18
Night Driving Glare	14.8	21	56.3	80	28.9	41

e. Retreatments

A total of 3 eyes were retreated with the study laser. Table 16 contains the outcomes for retreated eyes.

Table 16
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
Efficacy Variables	**N=3**	**N=2**	**N=0**
UCVA 20/20 or better*	100 3 100%, 100%	100 2 100%, 100%	0 0 0%, 0%
UCVA 20/40 or better*	100 3 100%, 100%	100 2 100%, 100%	0 0 0%, 0%
	N=3	**N=2**	**N=0**
MRSE ± 0.50 D	100 3 100%, 100%	100 2 100%, 100%	0 0 0%, 0%
MRSE ± 1.00 D	100 3 100%, 100%	100 2 100%, 100%	0 0 0%, 0%
MRSE ± 2.00 D	100 3 100%, 100%	100 2 100%, 100%	0 0 0%, 0%
Safety Variables	**N=3**	**N=2**	**N=0**
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%
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%
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%

*For all eyes minus those intentionally treated for monovision.

f. Factors Associated with Outcomes

An extensive analysis was performed to determine what influences, if any, affected outcomes in this series. Potential influences examined include gender, race, age, history of contact lens wear, effect of the preoperative refraction, pupil diameter, laser room temperature and humidity, and the keratome used to make the flap. Because this was a LASIK-only study, epithelial factors applicable to surface procedures were not considered. As all eyes in this series were targeted for distance outcomes, monovision analysis could not be performed.

The results of the analysis mirrored prior studies (PMA 020050 and PMA 030008) with the device used in this study, the WaveLight Allegretto Wave Excimer Laser. No detectable effect was found for any potential influence (sex, age, prior contact lens history, preoperative refraction, pupil diameter, laser room temperature and humidity or keratome) on major outcomes targets.

It is worthwhile to note that some of these influences were controlled within relatively narrow tolerances – e.g., laser room temperature and humidity. The conclusion should not be drawn that these potential influences cannot affect outcomes, nor should it be said that the major targets completely describe outcomes. Other studies have shown that, for example, low contrast acuity may be affected by pupil size. Rather, the valid statement is that when used under the conditions of the study, these influences had no detectable effect on the major targeted outcomes.

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 and night driving glare improved after LASIK.

Table 17 Patient Symptoms									
	Preoperative						3 Months					
	None-Mild		Moderate		Marked-Severe		None-Mild		Moderate		Marked-Severe	
	%	n	%	n	%	n	%	n	%	n	%	n
	N=162		N=162		N=162		N=142		N=142		N=142	
Glare from Bright Lights	40.1	65	32.7	53	27.2	44	45.8	65	37.3	53	16.9	24
Halos	63.0	102	17.9	29	19.1	31	57.8	82	16.9	24	25.4	36
Light Sensitivity	56.8	92	19.8	32	23.5	38	47.2	67	25.4	36	27.5	39
Visual Fluctuations	67.9	110	19.1	31	13.0	21	57.0	81	24.7	35	18.3	26
Night Driving Glare	45.7	74	27.8	45	26.5	43	58.5	83	21.8	31	19.7	28

h. Device Failures

There were no device failures reported during this study.

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 RECOMMENDATIONS

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

XIII. CDRH DECISION

FDA issued an approval order on APR 19 2006

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

XIV. APPROVAL SPECIFICATIONS

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