SUMMARY OF SAFETY AND EFFECTIVENESS

I. GENERAL INFORMATION

Device Generic Name:	Ophthalmic Medical Laser System (193 nanometer wavelength)
Device Trade Name:	LaserSight Excimer Laser System Model: LaserScan LSX
Applicant's Name and Address:	LaserSight Technologies, Inc. 3300 University Blvd., Suite 140 Winter Park, Florida 32792 (407) 678-9900

Premarket Approval (PMA) Application Number: P980008

Date of Panel Recommendation: Not Applicable (Not reviewed by Panel)

Date of Notice of Approval to Applicant: November 12, 1999

II. INDICATIONS FOR USE

The LaserScan LSX Excimer Laser is intended for myopic photorefractive keratectomy:

- for the reduction or elimination of myopia ranging from –1.0 to less than –6.0 diopters (D) with less than or equal to 1.00 D of astigmatism;
- in patients with documentation of a stable manifest refraction (± 0.5 D) over the prior one year; and
- in patients who are 18 years of age or older.

III. CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

A. CONTRAINDICATIONS

Patients with the following conditions should not be considered for PRK surgery:

- Active ocular / systemic infection
- Fuch's corneal dystrophy
- Keratoconous
- Central corneal scars affecting visual acuity
- Autoimmune or immunodeficiency diseases
- Pregnant or nursing women

Patients who are taking one or both of the following medications:

- Isotretinoin (Accutane)
- Amiodarone hydrochloride (Cordarone)

B. WARNINGS:

Patients presenting with the following condition(s) should be considered for PRK surgery only after careful assessment of the potential risk and benefit to the specific patient:

- Collagen vascular disorders
- Myopia progressing at a rate greater than 0.5 diopters per year
- Active systemic disease

PRK is not recommended in patients with a history of ophthalmic *Herpes simplex* or *Herpes zoster*.

PRK treatment of myopia from -6.00 to -10.00 D with this device has demonstrated risk of a loss of 2 lines or more of BSCVA approximately ten times that below -6.00 D at ≥ 12 months (5.9% vs. 0.6%). For treatment of myopic sphere between -6.00 and -10.00 D effectiveness is also reduced compared to treatments less than -6.00 D. No safety and effectiveness data above -10.00 D are available.

C. PRECAUTIONS

General

The safety and effectiveness of the LaserScan LSX excimer laser have not been established in patients presenting the following conditions:

- Severe dry eye
- Immunosuppression
- Glaucoma
- Uveitis
- History of keloid formation
- Blepharitis
- Psoriasis
- Systemic or topical use of steroids
- For patients under 18 years of age
- In patients who are taking sumatripin (Imitrex)

- Use of medications likely to affect wound healing
- In patients with corneal neovascularization within 1.0 mm of the ablation zone
- In patients with progressive myopia or astigmatism, ocular disease, corneal abnormality, and previous corneal surgery or trauma in the ablation zone
- For PRK treatment of < -1.0 diopters

Patient selection

Consideration should be given to the following in determining the appropriate patients for PRK:

- Complete examination, including cycloplegic evaluation, must be performed. The lens must be evaluated, especially in the older patient, to assure that nuclear sclerosis or any other lens opacity is not present prior to laser surgery. Myopic patients will have a higher incidence of retinal pathology, and indirect ophthalmoscopy through a dilated pupil is essential.
- To obtain accurate refractive information, contact lens wearers must be examined after a period of abstinence from contact lens use for at least 2 weeks for soft lenses and at least 3 weeks for rigid gas permeable or hard (PMMA) lenses. Prior to treatment, patients must have 3 separate central keratometry readings and manifest refractions each taken at one (1) week intervals, of which the last two must not differ by more than 0.5 diopter in either meridian. All mires must be regular.
- Glaucoma is more common in myopia patients than in the general population. Evaluation of the optic nerve and measurement of the intraocular pressure are necessary. If elevated intraocular pressure and/or evidence of glaucomatous damage are found, topical steroids should only be used with careful medical supervision or the patient should not undergo PRK surgery.
- Pre-operative corneal mapping is essential on all patients to exclude topographical abnormalities. This is especially important when astigmatism or steep keratometry readings are present, which may indicate the presence of keratoconus or other irregularities.
- The patient should have the ability to tolerate local or topical anesthesia.
- The patient should have the ability to lie flat without difficulty.
- The patient should be able to fixate steadily and accurately for the duration of the PRK procedure.
- The patient must be able to understand and give an informed consent.

- Patients must be clearly informed of all alternatives for the correction of myopia. These alternatives corrections include, but are not limited to spectacles, contact lenses, and other refractive surgeries such as radial keratotomy or automated lamellar keratoplasty.

Procedure

- The output of the laser is potentially hazardous only to the skin and the surface layers of the cornea. This radiation has not been shown to pose a threat to retinal structures or the crystalline lens.

- All healthcare personnel should avoid direct exposure to the skin or eye by the laser beam. The use of protective eyewear is recommended.

Post Procedure

- A slit lamp examination should be performed on the postoperative day one and as needed thereafter to ensure that healing of the cornea is complete. After re-epithelialization, the following examinations are recommended at a schedule of at least 1,3, and 6 months:

  - Uncorrected Visual Acuity (UCVA or VA-sc)
  - Manifest refraction with the Best Spectacle Corrected Visual Acuity (BSCVA or VA-cc)
  - Intraocular pressure (IOP)
  - Slit lamp examination, including corneal clarity evaluation
  - If topical steroids are used post-operatively, patients should be monitored for development of possible steroid side effects, including but not limited to ocular hypertension, glaucoma, and/or cataract.

V. DEVICE DESCRIPTION

The LaserScan LSX excimer laser is based on the principle that radiation at the 193 nm wavelength is highly absorbed by corneal tissue[1], and that 193 nm wavelength photon energy disrupts the intramolecular collagen bonds of corneal tissue[2], with the result being that the irradiated area is denatured. For any given intensity (or energy per pulse) of the 193 nm wavelength disruption, the depth of an ablated area corresponds with the number of laser pulses and the area of tissue removal corresponds with the diameter of the incident laser beam on the tissue[3, 4]. It has also been shown that the non-thermal chemical bond breaking of the 193 nm wavelength results in minimal collateral damage to surrounding tissue [5].

To control the ablation profile of the 193 nm beam on the corneal surface, the LaserScan LSX excimer laser employs an optical scanning delivery system. Reports of the scanning technique for the delivery of laser radiation for photoablation of corneal tissue began to appear in 1992[6]. By 1993 the results from preclinical tissue studies demonstrated that optical scanning delivery of excimer laser energy produces smooth and gradual ablations without step-like transition zones, and without thermal damage [7].

The LaserScan LSX consists of the following system components:

A. Excimer Laser Head:

The laser head provides the following output characteristics:

Laser medium:	ArF
Laser wavelength:	193 nm
Gas mixture:	F2 0.12% Vol. / Ar 3.17% Vol.
	He 1.9% Vol. / Ne 94.81% Vol.
Operating fill pressure:	7 bar
Pulse energy:	8 mJ
Repetition rate:	100 Hz
Power:	800 mW
Pulse width (duration):	9 to 11 ns
Emergent beam size (VxH):	6 x 3.5 mm
Beam divergence (VxH):	1 x 2 mrad

B. Laser Gas System:

Included in the laser system is a tank of the laser gas mixture with Argon, Neon, and Fluorine. The concentration of Fluorine is less than 0.2%. Additionally, there is another tank containing Helium gas, which is used for flushing the laser and gas system for installation and service. Components of the gas system include automatic valve manifold, vacuum pump, fluorine filter, computer controlled gas manifold drive, and valve position sensors.

C. System Control: Computer, software, and system control board

An IBM computer and proprietary software are used to coordinate the control of the system, as well as determine the ablation profile and algorithm for each patient eye to be treated. The system control board interfaces the computer and the controlling components of the system, e.g., the shutter.

D. Laser Beam Delivery System

The laser beam delivery system consists of a fixed aperture, attenuator, safety shutter, focusing lens, galvonometers with scanning mirrors, and 45° deflection mirror. The main

functions of the delivery system are to shape the laser beam to the proper size and beam profile, to attenuate the fluence to an appropriate level, and to scan the laser pulses to the locations on the eye determined by the computer and software.

E. Patient and Doctor Interface

The laser system components that comprise the patient-doctor interface include the patient chair and joystick, operating microscope with centration reticule, illumination light, diode fixation light, footswitch for shutter control, computer keyboard, touchscreen, laser emission indicator, and emergency stop

F. System Integration

The mechanical integrity of the system is provided by a welded metal frame, with plastic covers bolted to the frame. All components and sub-components are fastened to the plates and the frame. Covers with specified interlocks are used to protect the users from electric and radiation hazards. The electronic components are connected with shielded cable. Isolation transformers and line filters are used for the electric power lines.

G. Power Stability

The LaserScan LSX excimer laser has an on-line power stability module that reduces potential fluctuations in laser power. The power stability module maintains a constant laser power within +/- 5% by continuously sampling the laser beam transmitted through the aperture and attenuator. The transmitted beam is absorbed by a photo-detector that generates an electronic signal corresponding to the power of the incident beam. The electronic signal is then processed via an electronic feedback loop that subsequently controls the high voltage pulse placed on the laser electrodes. The high voltage on the laser electrodes determines the halogen gas discharge level and subsequently the beam power output.

Electrical Safety:

The LaserScan LSX excimer laser system meets UL 2601 electrical safety standard requirements, and has been tested to meet this standard by Intertek Testing Services (ITS), a third party testing laboratory.

V. ALTERNATIVE PRACTICES AND PROCEDURES

Conventional methods in correcting nearsightedness are: spectacles, contact lenses or refractive surgery. There are other commercially available excimer laser systems for PRK and LASIK treatment of myopia.

VI. MARKETING HISTORY

The LaserSight excimer laser system Model Compak 200 was introduced into international markets in April 1993. The LaserScan 2000 model was introduced in 1995, and an upgraded version of the Compak 200, Model LS-300, was sold internationally beginning in 1996. The LaserScan LSX model was introduced in February 1998. Currently there are over 240 LaserSight excimer laser systems located in 31 countries around the world. The LaserSight excimer laser system has not been withdrawn from any country or market for reasons of safety or effectiveness.

VII. ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse effects associated with PRK include: loss of best spectacle corrected visual acuity, overcorrection, increase in refractive cylinder, abnormal glare, double vision, sensitivity to bright lights, difficulty with night vision, increase in intraocular pressure, corneal haze, corneal infection/ulcer/infiltrate, corneal decompensation/edema, lens abnormality and secondary surgical intervention.

VIII. SUMMARY OF PRECLINICAL STUDIES

The Compak-200 / LaserScan 2000 / LaserScan LSX excimer laser systems have undergone various nonclinical laboratory tests and analyses in order to verify and validate that the systems perform as designed. Additionally, the LSX system has been found comparable to the earlier models (Compak-200, LaserScan 2000) which were used to perform the procedure on subjects in the clinical study. The studies are summarized below:

A. In-vitro testing of optical scanning delivery in PMMA

In-vitro testing of the Compak-200 excimer laser with an optical scanning system were performed in PMMA, and compared to commercially distributed broad beam excimer lasers without scanning delivery. In contrast to broad beam excimer lasers, scanning excimers require a beam energy per pulse of only 0.9 – 1.2 mJ on the corneal surface to achieve the same range of energy density (160 – 200 mJ/cm^2) as that of the broad beam excimer. The testing demonstrated: (1) 50% of initial beam energy was delivered to the corneal surface, (2) beam consistency, (3) smooth surface ablation, (4) smooth ablation boundary transitions, and (5) absence of a centrally located area of significant undercorrection (i.e., central islands). These results were reported in the *Society of Photo-optical Instrumentation Engineers Proceedings*[12].

B. In-vivo study of LSX scanning delivery system in rabbit corneas

In-vivo experiments were performed on rabbit corneas using the LaserSight LSX excimer laser to determine the amount of corneal tissue removed per laser pulse. Similar experiments were conducted on PMMA samples to determine the amount of PMMA material removed for the same energy and fluence. PTK (phototherapeutic keratectomy) was performed on 12 New Zealand white rabbits and on PMMA samples. Based on these experiments the ablation rate of both rabbit corneal tissue and PMMA were measured. A good linear correlation was found between the amount of material removed and the fluence for both materials. Equations for the amount of corneal tissue and PMMA material removed per fluence level were obtained. The rate of ablation for corneal tissue and PMMA is a linear function but the rates have a different slope. The study was done at the University of South Florida Eye Institute in January, 1999.

C. Laser head lifecycle

The end of the laser head life is defined as output energy falls below 2mJ or power stability is higher than $\pm$ 5%. In order to determine laser head lifecycle, five new laser heads were used to perform lifetime testing. Each of the five laser heads consistently demonstrated a useful life of 13 $\pm$ 1 million pulses. As the laser heads reached 13 $\pm$ 1 million pulses, either the laser energy dropped to about 2 mJ/pulse, or the laser output power was unstable. Since each surgery requires 6,000 to 10,000 pulses on average, 3,000 to 5,000 pulses for calibration and an equal number to perform corneal ablation, the laser head life exceeds 1,000 surgical procedures.

D. Laser power stability

Laser power at the corneal plane must be held constant during the course of the surgical procedure, as well as from one surgery to the next. Testing was performed to determine how gas depletion effects power over an extended duration. It was determined that laser power drops with time of operation due to gas depletion, and that power output decreases to an unacceptable level after 200 minutes running at the operating frequency 100 Hz. During a 10 minute interval of continuous pulses, laser power fluctuation is within $\pm$ 5%. A single refractive surgery typically requires less than one minute, and the number of surgeries performed in a day is less than 50. Since the operator must perform a gas refill at the beginning of each surgery day, laser power stability is sufficient to meet daily treatment requirements. In addition, there are mitigating mechanisms to maintain laser power within $\pm$ 2% throughout a surgical procedure, and from surgery to surgery.

E. Benchmark ablation test on PMMA (plexiglas)

LaserScan 2000 excimer ablation on PMMA was performed to study the ablation smoothness (roughness) and profile. Dioptric power, ablation diameter and depth measurements gave standard deviations of 0.2D, 0.21mm, and 0.99μm, respectively.

F. Feedback Control of Laser System

Two separate tests were performed to verify the repeatability of the power stability unit on the LSX using *Lase* 9.0 software. Myopia surgeries of –6.00 diopters were created on PMMA plastic and read using a calibrated lensometer. The surgeries used a value of 44D for the average keratometry and 12mm for the vertex distance. These tests verified the repeatability of power stability of this laser.

G. Additional Studies

The LaserScan LSX excimer laser contains a Class IV laser that conforms to 21 CFR 1040.10 & 1040.11, Light Emitting Products Requirements. The LaserScan LSX excimer laser complies with the requirements of the European Community (EC) Medical Directive 93/42/EEC and has been Type tested by Semko, AB, EC's Notified Body for the placement of the CE mark. The LaserScan LSX system was tested and found to be in compliance with following domestic and international standards:

UL2601-1
Medical Electrical Equipment, Part I General Requirements for Safety
CSA C22.2, No. 601.1-M90
Medical Electrical Equipment, Part I General Req. for Safety
EN60601-1: 1990 / A1 & A12: 1993 / A2: 1995 / A13: 1996
Medical Electrical Equipment, General Requirements for Safety
EN60601-1-2: 1993
Medical Electrical Equipment, Electromagnetic Compatibility
EN60601-2-22: 1996
Medical Elec. Equip., Specification for Diagnostic and Therapeutic Laser Equip.
EN60601-1-1: 1993 / A1: 1996
Medical Elec. Equip., Safety Requirements for Medical Electrical Equipment
EN60825-1: 1994
Safety of Laser Products

IX. SUMMARY OF CLINICAL STUDIES

PHASE I STUDY

A. Study Objectives

The objectives of the Phase I study were to determine the safety of the Compak 200, Mini-excimer laser with non-functional eyes, and to confirm the design and operating parameters of the LaserSight laser so appropriate adjustments could be made for PRK.

B. Study Design

The study was a prospective, non-randomized open study in 10 blind eyes.

C. Inclusion and Exclusion Criteria

The inclusion and exclusion criteria were: BSCVA of 20/200 or less that could not be improved by currently available treatment. These subjects are considered legally blind. Ten subjects were enrolled, all of whom gave informed consent.

D. Study Plan and Patient Assessments

The study plan and patient assessments involved: pre-operative evaluation, corneal re-shaping with the Compak 200 excimer laser, follow-up evaluations occurred immediately post-operative, daily until re-epithelialization, at 1 week, 1 month, 3 months, and at 6 months post-operative.

E. Results

All corneas healed completely without complications. There was minimal corneal haze, and that which was present decreased with time. Neither the ablation area nor the margins were detectable. Pre-and-post surgical endothelial cell counts were very similar. Evaluation of corneal topography showed the expected laser induced change of curvature.

F. Adverse Reactions and Complications

Adverse events included one transient rise in intraocular pressure which appeared to be secondary to steroid drops, and one corneal erosion. Both events resolved without sequelae and were not considered by the investigator to be related to laser treatment. One patient had increased corneal thickness related to the eye being pre-phthisical. This condition does not appear to be related to the laser surgery.

One patient did not come in for follow-up visits beyond one month as he had moved out of the state.

G. Conclusions

The LaserSight Compak 200 excimer laser was operated without difficulty and performed as expected in ablating corneal tissue. No apparent laser related adverse events occurred. This results were reported in *Investigative Ophthalmology & Visual Science* [8].

PHASE II AND III STUDIES

A. Study Objectives

The objectives of the Phase II and III studies were to determine the safety and effectiveness of the Compak 200 / LaserScan 2000 excimer laser when used to perform PRK treatment of myopia in healthy eyes, and to assess stability of the achieved visual outcome.

B. Study Design

The study was a prospective, non-randomized, multicenter study with the subjects acting as their own controls. The protocols of the two phases had minor differences identified below in [*italics*].

C. Inclusion and Exclusion Criteria

Study subjects were 18 years or older [*21 years or older for Protocol II(b), 18 years of age or older in Phase III*] and must have signed an informed consent form. Enrollment occurred if the subject met these conditions: -1.00 to –10.00 diopters (D) of myopia at the spectacle plane with $\leq$ 1.0 D astigmatism [*Protocol II(a) limited to 10 patients with –6.25 to –10.00 D myopia*]; best spectacle corrected visual acuity if 20/20 or better in both eyes [*Phase III included BSCVA of 20/25 or in both eyes*], and stable manifest refraction as documented by $\leq$ 0.5 D change within the previous twelve months. Contact lens wearers had to refrain from contact lens use prior to baseline examination (2 weeks for soft lenses, 3 weeks for rigid gas permeable and hard lenses).

Subjects not meeting the above inclusion criteria were excluded from the study. In addition, subjects who exhibited any of the following conditions were excluded: keratoconus, active ocular disease or corneal abnormality, patent corneal neovascularization within 1 mm of the intended ablation zone, systemic disease

likely to affect wound healing, unstable keratometry readings with irregular shaped mires or corneascope photographs with broken central rings, use of systemic medications likely to affect wound healing, immunodeficiency, contact lens intolerant [*Phase III did not exclude contact lens intolerant*], use of Norplant® contraception [*Phases II(b) and III did not exclude patients with Norplant® contraception; Phase III excluded subjects with pacemakers, and subjects with allergies to postoperative medications*].

D. Study Plan, Patient Assessments and Efficacy Criteria

Subjects were evaluated pre-operatively, every 24 to 48 hours post-operatively until re-epithelialization, and at 1, 3, 6, 12, 18 and 24 months post-treatment. Pre-operatively the subject's medical and ocular histories were recorded. Additionally pre-operatively a questionnaire was administered to determine frequency of problems such as glare and difficulty with night vision. Upon enrollment, PRK surgery was performed to ablate tissue from the stroma after manually removing the epithelium. Post-operatively, subjects were questioned about any visual symptoms (using the same questionnaire as pre-operatively) and about their satisfaction with the procedure. Objective measurements included: uncorrected and best corrected visual acuity, manifest and cycloplegic refraction, keratometry, intraocular pressure, pachymetry, clinical assessment of corneal clarity, clinical assessment of anterior chamber, vitreal, retinal and lens status, assessment of complications and adverse reactions.

Additionally, corneal topography was performed pre-operatively in all eyes to rule out corneal abnormalities, such as keratoconus, and post-operatively in a subset of eyes to verify centration of ablation. Effectiveness was evaluated based on improvement in uncorrected visual acuity, reduction in mean spherical equivalent refractive error, stability of refractive outcome through the post-operative period, and the percent of cases experiencing a deviation from the intended correction within 1.0 D.

Statistical analyses were performed at the 0.05 significance level against two-sided alternatives. Descriptive statistics were provided on data up to 12 months. For categorical data, differences in proportions between groups of eyes were tested using Chi-squared test, or Fisher's Exact test. Key efficacy criteria were evaluated for all eyes.

Study Period, Investigational Sites and Demographic Data

1. Study Period

In the group with pre-operative MRSE < -6.0 D, a total of 383 eyes were treated across 10 participating centers in three phases of study.

Table 3 Preop MRSE < - 6.0 D		
Phase	**Treatments Dates**	**Number of Eyes**
I USA	9/93 – 12/93	10 blind eyes
II(a) USA	6/95 – 01/99	65
II(a) FRA	9/95 – 12/95	27
II(b) USA	8/96 – 11/97	125
III USA	10/97 - 01/99	156

In the group with MRSE ≥ -6.00 D, a total of 161 eyes were treated in Phases II(a) , II(b), and III.

Table 4 Preop MRSE ≥ - 6.0 D		
Phase	**Treatments Dates**	**Number of Eyes**
II(a) USA	6/95 – 05/98	17
II(a) FRA	9/95 – 12/95	9
II(b) USA	8/96 – 9/98	87
III USA	10/97 – 01/99	48

Eyes enrolled in < -6.00 D and ≥ - 6.00 D groups for Phases II(a), II(b) and III

Phase II(a) of the US clinical study began at Mid-West Eye Center on June 20, 1995 and was expanded to include five investigational sites in the US and one in Europe. The French site began on September 26, 1995 at Robert Debré Hôpital in Paris. Conducted under Huriet Law (consistent with the Declaration of Helsinki), this study was approved by the *"Comtié Consultatif de Protection des Personnes dans la Recherche Biomedicale"(C.C.P.P.R.B.)*. All French subjects gave informed consent for the PRK treatment. One-hundred and eighteen (118) eyes (82 in the US, and 36 in France) were treated in this series of sighted subjects. Data from the Phase II(a) provided the basis for moving into the Phase II(b) study.

Phase II(b) began at Yavitz Eye Center on August 6, 1996 and was expanded to include a total of five sites. Two-hundred and twelve (212) eyes were treated in this series by September 22, 1998. Results from the Phase II(b) study formed the basis for expansion into a Phase III study.

Phase III study began on October 17, 1997 at Jupiter Eye Center Eye Center. Two hundred and four eyes were in the Phase III study by the time of this PMA application. With six-month follow-up on the majority of all eyes treated, the database was "frozen" for analysis on March 25, 1999. The results from Phase I, II and III studies are provided in this summary.

2. Investigational Sites

The following table presents the eleven (10 US, one foreign) sites that participated in the clinical study. Results are for both groups (pre-operative MRSE < - 6.00 D and ≥ -6.00 D) combined.

Table 5

Distribution of Eyes treated by Clinical Site
For Preop MRSE < -6.0 and ≥ -6.0 D

Site	10 Eyes Phase I Safety		330 Eyes Phase II Safety & Effectiveness (Percentages based on Total eyes-534)		204 Eyes Phase III Safety & Effectiveness (Percentages based on Total eyes-534)	
	n	%	n	%	n	%
Mount Sinai Medical Center	10	100	21	3.9	14	2.6
University of South Florida	0	0.0	7	1.3	0	0.0
Jupiter Eye Center	0	0.0	17	3.1	23	4.3
Lions Eye Institute	0	0.0	90	16.8	0	0.0
Yavitz Eye Center	0	0.0	71	13.2	25	4.7
Mid-West Eye Center	0	0.0	83	15.5	0	0.0
South Coast Eye Institute	0	0.0	5	0.9	0	0.0
Laser Surgery Center West	0	0.0	0	0.0	94	17.6
Sinai, Detroit	0	0.0	0	0.0	5	0.9
Bloomberg Eye Center	0	0.0	0	0.0	42	7.8
Robert Debré Hôpital	0	0.0	36	6.7	0	0.0

3. Demographics and Baseline Characteristics

Demographic characteristics with respect to patient age and sex are shown below for both groups whose preoperative myopia was up to - 10.0 D. Fifty-four percent of subjects were female, forty-six percent were male. No

differences in clinical outcomes with respect to gender are expected. The mean age was 37.1 years at the time of surgery.

Table 6

Demographic Characteristics

	(534 Eyes)*
Male	164
Female	196
Mean Age (Range)	37.1 18- 67

*Does not include Blind Phase subjects

Baseline Characteristics:

The majority of eyes treated had moderate myopia from -2.0 D to -8.0 D spherical equivalent with astigmatism under 1.0 D. Baseline characteristics for the eyes up to -10.0 D were as follows:

Table 7

Baseline Characteristics

	534*
Pre-treatment Myopia (Manifest Refraction-SE)	
< 1.00 D	1 (0.2%)
1.00 to <2.00 D	30(5.6 %)
2.00 to <3.00 D	105 (19.7%)
3.00 to <4.00 D	99(18.57%)
4.00 to <5.00 D	73(13.7%)
5.00 to <6.00 D	65(12.2%)
6.00 to <7.00 D	50 (9.4%)
7.00 to <8.00 D	56 (10.5%)
8.00 to <9.00 D	28 (5.2%)
9.00 to <10.00 D	27 (5.1%)
Mean SE± SD (Range)	-4.78 ±2.27 (-0.875 to –11.125)
Cylinder	
0.0 D	177 (33.1%)
0.25 D	68 (12.7%)
0.50 D	124 (23.2 %)
0.75 D	80(15.0%)
1.00 D	67 (12.5%)
1.25 D	13 (2.4%)
1.50 D	2 (0.4%)

* Includes eyes with preoperative myopia up to -10.00 D only. Refraction not possible for the 10 Phase I blind eyes.

F. Data Analysis and Results

1. Operative Characteristics

The maximum ablation zone diameter varied depending on the planned dioptric correction. The operative laser parameters are summarized as follows.

	Table 8 **LaserScan LSX Excimer Laser Parameters**			
	Pulse Rate: 100 Hz Fluence: 80 - 100 mJ/cm			
	Maximum Ablation Zone			
	6.2 mm	6.4 mm	6.5 mm	7.0 mm
# Eyes	151	40	133	210

2. Postoperative Characteristics and Results

a. Patient Accountability

The follow-up period reported in this application is one (1) year. Data analyses were performed using both the six and twelve month follow-up intervals. There were 544 enrolled eyes in the study on the cutoff date of March 25, 1999. Of these, 10 were blind eyes. Therefore a total of 534 eyes were studied for safety and effectiveness. There were 389 eyes available for analysis at six months (275 eyes with pre-operative MRSE < -6.0D, 114 eyes with pre-operative MRSE –6.0 to –10.0 D.) There were 249 eyes available for analysis at greater than or equal to 12 months (181 in the < -6.0 D group, 68 in the –6.0 to –10.0 D group). Accountability for the two groups is shown in Tables 9 and 10.

Table 9
Accountability
Preop MRSE < -6.0 D, Initial Treatment

	1 Month	3 Months	6 Months	12 Months	≥ 12 Months
Available for Analysis n/N (%)	340/ 373 (91.2%)	318/ 373 (85.3%)	275/ 373 (73.7%)	162/ 373 (43.4%)	181/ 373 (48.5%)
Not yet due for the interval n/N (%)	7/ 373 (1.9%)	29/ 373 (7.8%)	66/ 373 (17.7%)	142/ 373 (38.1%)	142/ 373 (38.1%)
Lost to Follow-up[1] n/N (%)	0/ 373 (0.0%)	0/ 373 (0.0%)	3/ 373 (0.8%)	38/ 373 (10.2%)	44/ 373 (11.8%)
Discontinued n/N (%)	1/ 373 (0.3%)	1/ 373 (0.3%)	10/ 373 (2.7%)	8/ 373 (2.1%)	4/ 373 (1.1%)
Missed Visit n/N (%)	25/ 373 (6.7%)	25/ 373 (6.7%)	19/ 373 (5.1%)	23/ 373 (6.2%)	6/ 373 (1.6%)
% Accountability = Available for Analysis (Enrolled – Discontinued - Not yet due)	340/ 365 (93.2%)	318/ 343 (92.7%)	275/ 297 (92.6%)	162/ 223 (72.6%)	181/ 227 (79.7%)

* N = Total eyes enrolled;
[1] A patient is considered lost to follow-up after 12 months from the last visit.

Table 10
Accountability
Preop MRSE –6.0 to –10.0 D
Initial Treatment

	1 Month	3 Months	6 Months	12 Months	≥12 Months
Available for analysis n/N (%)	144/161 (89.4%)	136/161 (84.5%)	114/161 (70.8%)	60/161 (37.3%)	68/161 (42.2%)
Not yet due for the interval n/N	4/161 (2.5%)	5/161 3.1%)	19/161 (11.8%)	48/161 (29.8%)	48/161 (29.8%)
Lost to Follow-up[1] n/N (%)	2/161 (1.2%)	3/161 (1.9%)	9/161 (5.6%)	20/161 (12.4%)	40/161 (24.8%)
Discontinued n/N(%)	0/161 (0.0%)	3/161 (1.9%)	8/161 (5.0%)	22/161 (13.7%)	9/161 (5.6%)
Missed Visit n/N(%)	11/161 (6.8%)	14/161 (8.7%)	11/161 (6.8%)	11/161 (6.8%)	5/161 (3.1%)
% Accountability = Available for Analysis Enrolled-Discontinued-Not yet Due	144/157 (91.7%)	136/153 (88.9%)	114/134 (85.1%)	60/91 (65.9%)	68/104 (65.4%)

* N = Total eyes enrolled
1 A patient is considered lost to follow-up after 12 months from the last visit

b. Summary of Key Safety and Efficacy Variables

Table 11 includes data on eyes with pre-operative MRSE < -6.0 D following initial treatment, prior to any retreatments. Table 12 includes data on eyes with pre-operative MRSE from –6.0 to –10.0 D, prior to any retreatments. Safety and efficacy outcomes for the –6.0 to –10.0 D group are poorer than those for the < -6.0 D group. Table 13 includes data on eyes with preoperative MRSE < -6.0 D, stratified by diopter. Eyes with pre-operative MRSE of –4.0 to <-6.0 had poorer results than eyes with pre-operative MRSE –1.0 to <-4.0 D.

Table 11
Safety and Efficacy Variables
Preop MRSE < -6.0 D
Initial Treatment

	1 Month n/N (%)	3 Months N/N (%)	6 Months n/N (%)	12 Months n/N (%)	≥ 12 Months n/N (%)
Efficacy Variables					
UCVA 20/20 or better*	113/327 (34.6)	143/308 (46.4)	147/265 (55.5)	83/159 (52.2)	94/177 (53.1)
UCVA 20/40 or better*	268/327 (82.0)	268/308 (87.0)	232/265 (87.5)	133/159 (83.6)	151/177 (85.3)
MRSE ± 0.50 D	170/340 (50.0)	165/318 (52.9)	161/275 (58.5)	91/162 (56.2)	105/181 (58.0)
MRSE ± 1.00 D	266/340 (78.2)	254/318 (79.9)	224/275 (81.5)	124/162 (76.5)	140/181 (77.3)
MRSE ± 2.00 D	320/340 (94.1)	307/318 (96.5)	266/275 (96.7)	158/162 (97.5)	177/181 (97.8)
Safety Variables					
Loss of > 2 lines BSCVA	4/340 (1.2)	0/318 (0.0)	0/275 (0.0)	1/162 (0.6)	1/181 (0.6)
BSCVA worse than 20/40	0/340 (0.0)	0/318 (0.0)	0/275 (0.0)	0/162 (0.0)	0/181 (0.0)
Increase of > 2 D cylinder	3/340 (0.9)	1/318 (0.3)	1/275 (0.4)	0/162 (0.0)	0/181 (0.0)
BSCVA worse than 20/25 if 20/20 or better preoperatively	12/340 (3.5)	1/318 (0.3)	3/275 (1.1)	1/162 (0.6)	2/181 (1.1)

* For all eyes minus those intentionally undercorrected (defined as greater than 0.5 D myopia).

Table 12
Safety and Efficacy Variables
Preop MRSE -6.0 to –10.0 D
All Eyes Treated - Initial Treatment

	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	12 Months n/N (%)	≥ 12 Months n/N (%)
Efficacy_Variables					
UCVA 20/20 or better*	37/139 (26.6)	36/130 (27.7)	35/109 (32.1)	12/55 (21.8)	14/63 (22.2)
UCVA 20/40 or better*	108/139 77.7)	95/130 (73.1)	73/109 (67.0)	38/55 (69.1)	42/63 (66.7)
MRSE ± 0.50 D	73/144 (50.7)	57/136 (41.9)	37/114 (32.5)	21/60 (35.0)	25/68 (36.8)
MRSE ± 1.00 D	104/144 (72.2)	86/136 (63.2)	60/114 (52.6)	36/60 (60.0)	41/68 (60.3)
MRSE ± 2.00 D	131/144 91.0)	121/136 (89.0)	103/114 (90.4)	52/60 (86.7)	59/58 (86.8)
Safety Variables					
Loss of> 2 lines BSCVA	4/144 (2.8)	3/136 (2.2)	1/114 (0.9)	2/60 (3.3)	4/68 (5.9)
BSCVA worse than 20/40	2/144 (1.4)	2/136 (1.5)	0/114 (0.0)	0/60 (0.0)	0/68 (0.0)
Increase of> 2 0 cylinder	1/144 (0.7)	1/136 (0.7)	0/114 (0.0)	1/60 (1.7)	1/68 (1.5)
BSCVA worse than 20/25 if 20/20 or better preoperatively	9/144 (6.3)	8/136 (5.9)	4/114 (3.5)	2/50 (3.3)	4/68 (5.9)

*For all eyes minus those intentionally undercorrected (defined as greater than 0.5 D myopia).

Table 13
Safety and Efficacy Variables
At ≥ 12 Months (Stratified by Preop MRSE)
Eyes with Preop < -6.0D
Initial Treatment

	<-1.0 D n/N (%)	-1.0 to -1.99 D n/N (%)	-2.0 to -2.99 D n/N (%)	-3.0 to -3.99 D n/N (%)	-4.0 to -4.99 D n/N (%)	-5.0 to -5.99 D n/N (%)	CUM TOTAL < 6.0 D n/N (%)
Efficacy Variables							
UCVA 20/20 or better*	----	5/9 (55.6)	17/33 (51.5)	36/53 (67.9)	21/46 (45.7)	15/36 (41.7)	94/177 (53.1)
UCVA 20/40 or better*	----	9/9 (100)	29/33 (87.9)	48/53 (90.6)	37/46 (80.4)	28/36 (77.8)	151/177 (85.3)
MRSE ± 0.50 D	----	8/9 (88.9)	25/33 (75.8)	35/55 (63.6)	18/46 (39.1)	19/38 (50.0)	105/181 (58.0)
MRSE ± 1.00 D	----	9/9 (100)	29/33 (87.9)	47/55 (85.5)	31/46 (67.4)	24/38 (63.2)	140/181 (77.3)
MRSE ± 2.00 D	----	9/9 (100)	33/33 (100)	54/55 (98.2)	44/46 (95.7)	37/38 (97.4)	177/181 (97.8)
Safety Variables	----						
Loss of > 2 lines BSCVA	----	0/9 (0.0)	0/33 (0.0)	0/55 (0.0)	1/46 (2.2)	0/38 (0.0)	1/181 (0.6)
BSCVA worse than 20/40	----	0/9 (0.0)	0/33 (0.0)	0/55 (0.0)	0/46 (0.0)	0/38 (0.0)	0/181 (0.0)
Increase of > 2 D cylinder	----	0/9 (0.0)	0/33 (0.0)	0/55 (0.0)	0/46 (0.0)	0/38 (0.0)	0/181 (0.0)
BSCVA worse than 20/25 if 20/20 or better preoperatively	----	0/9 (0.0)	0/33 (0.0)	0/55 (0.0)	1/46 (2.2)	1/38 (2.6)	2/181 (1.1)

For all eyes minus those intentionally undercorrected (defined as greater than 0.5 D myopia).

c. Stability of Manifest Refraction

Stability was reached between 6 and 12 months. As shown in Table 14, for those eyes available for their 1,3,6 and 12 month visits, 94.3% and 95.0% changed $\leq$ 1 diopter at 6 and 12 months, respectively.

Table 14
Stability of Manifest Refraction Through 12 Months
Eyes with Preop MRSE < -6.0 D
Initial Treatment

Change in Spherical Eqivalent Between	1 and 3 Months n/N (%)	3 and 6 Months n/N (%)	6 and 12 Months n/N (%)
$\leq$ 1.00 D	122/140 (87.1)	132/140 (94.3)	133/140 (95.0)
Mean Difference	0.50	0.42	0.38
SD	0.48	0.49	0.50
95% CI (Mean)	(0.47 - 0.52)	(0.40 - 0.45)	(0.35 - 0.41)
95% CI (Individual)	(-0.45 - 1.44)	(-0.55 - 1.39)	(-0.59 - 1.36)

Only those patients with 1,3,6, and 12 months data are included in the analysis.

d. Retreatments

Table 15 includes data on eyes (< - 6.0 D group) that were retreated. In the <-6.0 D group 20/373 eyes (5.4%) were retreated for undercorrection of myopia.

Table 15
Safety and Efficacy Variables
Preop MRSE < -6.0 D
All Eyes Retreated - Last Treatment

	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	12 Months n/N (%)	≥ 12 Months n/N (%)
Efficacy Variables					
UCVA 20/20 or better*	5/14 (35.7)	5/11 (45.5)	4/7 (57.1)	1/1 (100)	1/1 (100)
UCVA 20/40 or better*	11/14 (78.6)	9/11 (81.8)	7/7 (100)	1/1 (100)	1/1 (100)
MRSE ± 0.50 D	9/14 (64.3)	5/11 (45.5)	2/7 (28.6)	0/1 (0.0)	0/1 (0.0)
MRSE ± 1.00 D	12/14 (85.7)	9/11 (81.8)	6/7 (85.7)	1/1 (100)	1/1 (100)
MRSE ± 2.00 D	12/14 (85.7)	10/11 (90.9)	7/7 (100)	1/1 (100)	1/1 (100)
Safety Variables					
Loss of > 2 lines BSCVA	0/14 (0.0)	0/11 (0.0)	0/7 (0.0)	0/1 (0.0)	0/1 (0.0)
BSCVA worse than 20/40	0/14 (0.0)	0/11 (0.0)	0/7 (0.0)	0/1 (0.0)	0/1 (0.0)
Increase of > 2 D cylinder	0/14 (0.0)	0/11 (0.0)	0/7 (0.0)	0/1 (0.0)	0/1 (0.0)
BSCVA worse than 20/25 if 20/20 or better preoperatively	0/14 (0.0)	0/11 (0.0)	0/7 (0.0)	0/1 (0.0)	0/1 (0.0)

* For all eyes minus those intentionally undercorrected (defined as greater than 0.5D myopia).

e. Adverse events

Table 16 shows the number and percentage of eyes that experienced adverse events at specified intervals. One investigational site accounted for nearly half the incidence of early corneal ulcer, and was subsequently discontinued from the study. No adverse events were reported after any retreatment procedure.

Table 16
Adverse Events

Preop MRSE < -6.0 D Initial Treatment (%)					
	< 1 month[1]	1 month	3 months	6 months	12 months
Corneal infiltrate/ulcer > 1 mo		2/340 (0.6)	0/318 (0)	0/275 (0)	0/162 (0)
Corneal edema > 1 mo		0/340 (0)	0/318 (0)	1/275 (0.4)	0/162 (0)
Persistent Central Epithelial Defect		1/340 (0.3)	0/318 (0)	0/275 (0)	0/162 (0)
Corneal Edema < 1 mo	0/373 (0)				
Corneal Infiltrate/ulcer < 1 mo	5/373 (1.3)				
Late onset haze beyond 6 months with loss of > 2 lines[2]				0/275 (0)	1/162 (0.6)
Loss >2 lines beyond 6 months[2]				0/275 (0)	1/162 (0.6)
IOP Increase > 5 mmHg above baseli and any reading above 25 mmHg		1/340 (0.3)	1/318 (0.3)	0/275 (0)	0/162 (0)
IOP increase 6 to 10 mmHg		11/340 (3.2)	15/318 (4.7)	7/275 (2.5)	3/162 (1.9)
IOP increase > 10 mmHg		1/340 (0.3)	1/318 (0.3)	0/275 (0)	0/162 (0)
Recurrent Corneal Erosion		0/340 (0)	1/318 (0.3)	0/275 (0)	1/162 (0.6)
Foreign Body Sensation		0/340 (0)	0/318 (0)	4/275 (1.5)	0/162 (0)
Pain/Discomfort		0/340 (0)	1/318 (0.3)	2/275 (0.7)	2/162 (1.2)
Corneal Haze (Moderate to Marked)		4/340 (1.2)	2/318 (0.6)	0/275 (0)	2/162 (1.2)
Overcorrection > 1 D[3]				20/275 (7.3)	8/162 (4.9)
Overcorrection > 2 D[3]				3/275 (1.1)	1/162 (0.6)

[1]Adverse events occurring operatively and up to 1 month postoperatively.
[2]These events were reported 6 and 12 months after final treatment.
[3]Cycloplegic refractions taken at 6 and 12 months postoperative.

Patient events were recorded on a self-administered questionnaire preoperatively and at 3 or 6 months post-treatment (Table 17). Patients were asked to subjectively rate the presence or absence of these events. The most frequent findings were halos, double vision, clarity changes over time, and night vision problems.

Table 17
Patient Events at Preop and 6 months
Preop MRSE < -6.0 D
Initial Treatment

Subjective Patient Adverse Events	Preop	6 Months
Burning, Gritty Feeling[1]	12/338 (3.6%)	15/183 (8.2%)
Halos, Startbursts[1]	46/335 (13.7%)	43/184 (23.4%)
Watery Eyes[1]	10/337 (3.0%)	6/184 (3.3%)
Double Vision / Ghosts[1]	2/337 (0.6%)	6/182 (3.2%)
Clarity Changes Day to Day[1]	10/335 (3.0%)	22/182 (12.1%)
Night Vision Problems[2]	80/336 (23.8%)	43/173 (24.9%)
Problems with Colors[2]	9/336 (2.7%)	3/175 (1.7%)

[1]Rated as "Never", "Rarely", "Often" or "Always". Percent reported as "Often" or "Always" included here.
[2]Rated as "Yes" or "No". Percent reporting "Yes" included here.

X. CONCLUSIONS DRAWN FROM THE STUDIES

The non-clinical and clinical results provide reasonable assurance that the LaserSight LaserScan LSX Excimer Laser System is safe and effective for the reduction or elimination of myopia ranging from –1.0 to < -6.0 D.

XI. 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 Advisory Panel for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by the Panel.

XII. FDA DECISION

FDA issued an approval order on November 12, 1999.

The sponsor's manufacturing facility was inspected and found to be in compliance with the Quality System/Good Manufacturing Practice regulations. Final GMP approval was dated October 19, 1999.

XIII. APPROVAL SPECIFICATIONS

Post approval 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.

Directions for use: see the labeling

XIV. REFERENCES

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