DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

APR 24 1997

Ms. Eleanor V. Chiu
Manager, Regulatory Affairs
VISX, Inc.
3400 Central Expressway
Santa Clara, CA 95051

Re: P930016/S3
VISX Excimer Laser System Models "B" and "C" for
Photorefractive Keratectomy for Astigmatism (PRKa)
Filed: August 26, 1996
Amended: September 5, October 23, November 26 (2 amendments) and 27, and December 16 and 17, 1996; January 6 and 7, and February 11, 25 and 26, and April 15, 1997

Dear Ms. Chiu:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the VISX Excimer Laser System (Models B and C). This device is indicated for myopic astigmatic photorefractive keratectomy (PRKa) using an ablation zone with a 6.0 mm major axis. PRKa is intended for use:

1. in PRKa treatments for the reduction or elimination of mild to moderate myopia between 0 and - 6.0 D spherical myopia at the spectacle plane (with a vertex distance of 12.5 mm), and concomitant reduction or elimination of refractive cylinder of not less than 0.75 D and not more than 4.0 D at the spectacle plane (with a vertex distance of 12.5 mm) as determined by minus cylinder refraction;

2. in patients with documented evidence of a change in manifest refraction of less than or equal to 0.5 D (in both cylinder and sphere components) per year for at least one year prior to the date of pre-operative examination; and,

3. in patients who are 21 years of age or older.

We are pleased to inform you that the PMA supplement is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

These restrictions on the use, labeling, promotion, and advertising of the device are applicable to VISX, Incorporated, as well as device purchasers and users. VISX must notify the purchasers and users of these restrictions and include them in your training programs.

1. Only practitioners who are experienced in the medical management and surgical treatment of the cornea, who have been trained in laser refractive surgery (for myopia and astigmatism) including laser system calibration and operation, may use the device as approved in this order.

2. Prospective patients, as soon as they express an interest in myopic astigmatic PRKa and prior to undergoing surgery, must receive from the treatment provider the Patient Information Booklet (as described in your final submission to this PMA Supplement).

3. Prior to undergoing surgery, prospective patients must be informed of the alternatives for correcting their astigmatism including eyeglasses, contact lenses and other refractive surgeries such as automated lamellar keratectomy.

4. Comparison of the safety and effectiveness of this laser with any other method of refractive correction is prohibited. This prohibition is based on the fact that the data submitted for PMA supplemental approval of the VISX Excimer Laser System do not compare the clinical outcome of this device with any other method of refractive correction. Such comparisons of safety and effectiveness are misleading and would misbrand your laser in accordance with section 502(a) of the act. All promotion and advertising for this device must include the following information on indications, risks and benefits:

a. Approval is for the VISX, Incorporated application for the VISX Excimer Laser System (Models B and C) to correct mild to moderate myopia between 0 and -6.0 D spherical myopia at the spectacle plane (with a vertex distance of 12.5 mm), and concomitant reduction or elimination of refractive cylinder of not less that 0.75 D and not more than 4.0 D at the spectacle plane (with a vertex distance of 12.5 mm) as determined by minus cylinder refraction in a procedure called photorefractive keratectomy for nearsightedness with astigmatism (PRKa) using an excimer laser that emits light at a wavelength of 193 nm.

b. PRKa is an elective procedure with the alternatives including eyeglasses, contact lenses, astigmatic keratotomy or automated lamellar keratectomy.

c. Approval of the application is based on clinical trials in the United States with 116 eyes treated, of which 84 eyes were followed for two years, together with supplemental safety and effectiveness information from international trials with 625 eyes through 12 months of follow up.

d. The studies found that of the 82 eyes with refractive data at 2 years of follow up, 91.5% were corrected to 20/40 or better, and 81.7% were corrected to 20/30 or better without spectacles or contact lenses.

e. The clinical trials showed the following adverse events occurred in at least 1% of the subjects at two years post-treatment: corneal haze ≥ grade 2 (1.2%); intraocular pressure (IOP) increase of > 5mm Hg (2.4%); loss of ≥2 lines Best Spectacle Corrected Visual Acuity (BSCVA) due to corneal causes (4.8%); worsening of double vision (5.9%); pre-treatment BSCVA of 20/20 or better with post-treatment BSCVA worse than 20/25 (6.1%); worsening of sensitivity to bright lights (15.5%); and increased difficulty with night vision (22.6%).

f. Long term risks of PRKa beyond 2 years have not been studied.

g. This laser is not indicated to correct high myopia (nearsightedness >- 6 D), high astigmatism (>4 D), or farsightedness. It is not to be used in procedures other than PRKa as described in the approved Operator's Manual.

h. Note that the complete name for this ophthalmic laser is "VISX Excimer Laser (Models B and C) for Photorefractive Keratectomy for the Correction of Nearsightedness with Astigmatism (PRKa) (0 to - 6.0 D myopia with 0.75 to 4.0 D astigmatism)". An acceptable alternate version of this official name is "PRKa laser correction of nearsightedness with astigmatism". The word excimer, ultraviolet, or UV may be used instead of PRKa. Also, these names do not have to contain the qualifiers mild to moderate nearsightedness (0 to - 6.0 D) or mild to moderate astigmatism (0.75 to 4.0 D) if the adjacent text provides this information. Names other than those appearing above require approval in a PMA supplement.

In addition to the postapproval requirements in the enclosure, you must report to FDA CDRH's Office of Compliance at the address below of any instances of device tampering or usage outside of the approved indication, and any excimer systems that were exported under an 801(e) order and are now back in the U.S.

OC/Division of Enforcement (HFZ-331)
Center for Devices and Radiological Health
Food and Drug Administration
2098 Oakgrove Drive
Rockville, MD 20850

CDRH will publish a notice of its decision to approve your PMA supplement in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA supplement submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Ms. Jan C. Callaway at (301) 594-2018.

Sincerely yours,

Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure
"Conditions of Approval"

SUMMARY OF SAFETY AND EFFECTIVENESS
FOR A SUPPLEMENTAL PREMARKET APPROVAL (PMA) APPLICATION

I. GENERAL INFORMATION

Device Generic Name:	Ophthalmic Medical Laser System (193 nanometer laser wavelength)
Device Trade Name:	VISX Excimer Laser Systems, Model B and Model C ("STAR")
Applicant's Name and Address:	VISX, Incorporated 3400 Central Expressway Santa Clara, CA 95051-0703 (408) 733-2020
Date of Panel Recommendation:	Approvable with Conditions on January 14, 1997
PMA Application Supplement Number	P930016/S3
Date of Notice of Approval to Applicant:	April 24, 1997

This device was originally approved on March 27, 1996, for the limited indication for myopic photorefractive keratectomy (PRK) using a 6.0 mm ablation zone in patients 18 years of age or older with 1.0 to 6.0 diopters of myopia with astigmatism of $\leq$ 1.0 diopters whose refractive change for one year prior to treatment is within $\pm$ 0.5 diopter.

The sponsor submitted this supplement to expand the clinical indications. The updated clinical data to support the expanded indication is provided in this summary. The preclinical test results were presented in the original PMA application. For more information on the data which supported the original indication, the summary of safety and effectiveness data (SSED) to the original PMA should be referenced. Written requests for copies of the SSED can be obtained from the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Drive, rm. 1-23, Rockville, MD 20857 under Docket # 97M-0084.

II. INDICATIONS FOR USE

The Photorefractive Keratectomy for nearsightedness with astigmatism (PRKa) procedure using the VISX Excimer Laser System is intended for use:

- In PRKa treatments for the reduction or elimination of mild to moderate myopia between 0 and -6.0 D spherical myopia at the spectacle plane (with a vertex distance of 12.5 mm), and concomitant reduction or elimination of refractive cylinder of not less than 0.75 D and not more than 4.0 D at the spectacle plane (with a vertex distance of 12.5 mm) as determined by minus cylinder refraction.

- In patients with documented evidence of a change in manifest refraction of less than or equal to 0.5 D (in both cylinder and sphere components) per year for at least one year prior to the date of pre-operative examination.

- In patients who are 21 years of age or older.

III. CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

A. Contraindications:

PRKa surgery is contraindicated:

- In patients with collagen vascular, autoimmune or immunodeficiency diseases.

- In pregnant or nursing women.

- In patients with signs of keratoconus.

- In patients who are taking one or both of the following medications:
  - isotretinoin (Accutane)
  - amiodarone hydrochloride (Cordarone)

B. Warnings:

- The decision to perform PRKa surgery in patients with systemic disease likely to affect wound healing, such as connective tissue disease, diabetes, severe atopic disease or an immunocompromised status, should be approached cautiously. The safety and effectiveness of the VISX Excimer Laser System has not been established in patients with these conditions.

- PRKa is not recommended in patients with ophthalmic *Herpes simplex* or *Herpes zoster*.

C. Precautions:

General

The safety and effectiveness of the VISX Excimer Laser System have **NOT** been established:

- In patients with refractive cylinder of less than 0.75 D.
- In patients with progressive myopia, ocular disease, corneal abnormality, and previous corneal surgery or trauma in the ablation zone.
- In patients with corneal neovascularization within 1.0 mm of the ablation zone.
- Over the long term (approximately 2 years after surgery).
- In patients with a history of keloid formation.
- In patients who are taking sumatripin (Imitrex).

The effects of PRKa on visual performance under poor lighting conditions have not been determined. Patients between the ages of 21 and 30 should be reminded that due to larger pupils, they are more likely than the over 30-year old population to experience a degradation in visual performance after PRKa under poor lighting conditions (e.g., fog, rain, snow, or glare from bright lights at night).

Patient Selection

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

- Complete examination, including, but not limited to, 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 abstaining from contact lens use for at least 2 weeks for soft lenses and at least 3 weeks for hard lenses. Prior to treatment and after at least 3 weeks of contact lens abstinence, patients who wear rigid gas permeable or hard (PMMA) lenses must have 3 central keratometry readings and manifest refractions taken at 1 week intervals, the last 2 of which must not differ by more than 0.50 diopter in either meridian. All mires must be regular. Any patient with keratometry or a clinical picture that is suggestive of keratoconus is specifically contraindicated as described above.

- Glaucoma is more common in myopic patients than in the general population. Evaluation of the optic nerve and measurement of the intraocular pressure are necessary. If there are any concerns regarding the appearance of the optic nerve, a Humphrey 24-2 Fastpac or equivalent threshold test of the visual field should be performed. 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 PRKa 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.

- Baseline evaluation of patients requesting refractive surgery should be performed within 30 days of the PRKa surgery.

- 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 PRKa procedure.

- The patient must be able to understand and give an informed consent.

- In patients who have been clearly informed of all alternatives for the correction of their myopia and/or astigmatism, including but not limited to spectacles, contact lenses and other refractive surgeries such as radial keratotomy.

IV. DEVICE DESCRIPTION

The VISX Excimer Laser System is available in two models: B and C. Although the Model C is a technological upgrade of the Model B, the energy output and the delivery mechanism from both models remains the same.

Each model combines a 193 nm laser with a computer-controlled optics system. Srinivasan was the first to describe the unique non-thermal chemical bond breaking properties of the newly developed excimer lasers starting in 1979.[1] He pointed out the potential of the 193 nm laser for sculpting organic materials and with Trokel and Braren applying this new technology to ophthalmic surgery, specifically to the cornea in 1983.[2]

VISX, in cooperation with Srinivasan, Trokel, and L'Esperance, developed the Excimer Laser System. The laser system produces its surgical effect by ablative photodecomposition. Short, intense pulses of laser energy allow precise control of the depth of the corneal incision. The clinical application is used for reshaping the cornea for a variety of refractive corrections. This procedure is known as Photorefractive Keratectomy, and is the subject of this PMA supplement.

A. The Excimer Laser System consists of the following components:

1. Excimer Laser:

Laser wavelength:	193 nanometers
Laser pulse duration:	20 nanoseconds (FWHM)
Repetition rate:	5 hertz
Fluence :	160 mJ/cm^2
PRKa ablation zone:	6 mm diameter ablation zone (major axis) 4.5 mm diameter ablation zone (minor axis - minimum)

Composition of gases:

ArF Premix	Argon Fluorine (< 1.0%) Helium Neon
For internal purging:	Helium (99.9995% purity)
For purifying (Model B):	Liquid Nitrogen

2. Gas Management System: This system includes the housing for gas cylinders, a gas alarm for fluorine, a gas discharge system that uses an activated charcoal filter to ensure that no fluorine is exhausted into the atmosphere, and an emergency safety system that automatically seals the ArF Premix cylinder in the event of a natural disaster or power failure.

3. Laser Beam Delivery System: Before reaching the eye, the raw rectangular beam of an excimer laser is directed by mirrors to pass sequentially through; homogenizing optics that convert the raw beam into a uniform and coaxial profile beam; a spatial and temporal integrator that minimizes variations in the average treatment beam profile; and a beam-shaping module (iris diaphragm and rotatable slit blades) that controls the size and shape of the exiting beam.

4. Patient Management System: Components under this category include an operating microscope that allows the physician to view the eye; a halogen illuminator that illuminates the patient's eye; a blinking fixation LED upon which the patient focuses during the procedure; a reticle for aligning the eye to the system; a patient chair and a vacuum pillow; and a video camera and monitor for recording and viewing a procedure.

5. Computer Control and Software System: Provided with the laser is an IBM or equivalent PC system that contains a monitor, a keyboard, a trackball, and a printer. The PC drives the excimer system's components, calculates ablation algorithms, and prompts the user through the surgical procedure. Additionally, the PC is equipped with the VISX VisionKey optical memory cards. Each card stores patient information and treatment data, provides standardization of ablations, and controls treatment selection.

   The VisionKey cards available to U.S. users will allow only PRKa myopia treatment from 0 to -6.0 D spherical myopia at the spectacle plane (with a vertex distance of 12.5 mm), and concomitant reduction or elimination of astigmatism of not less than 0.75 D and not more than 4.0 D at the spectacle plane (with a vertex distance of 12.5 mm) as determined by minus cylinder refraction.

B. Regulations

The Excimer System contains a Class IV laser that conforms with US/FDA 21 CFR 1040.10 and 1040.11 Radiological Health requirements. The laser system was designed to meet the following safety standards:

UL544
CSA C22.2 No. 125M1984
IEC 601-1: 1988
IEC 601-2-22P: 1991
IEC 825: 1984
EN 60601-1-2
EN 55011
IEC 801-2,3,4,5

V. ALTERNATIVE PRACTICES OR PROCEDURES

Conventional methods in correcting astigmatism are: spectacles, contact lenses or refractive surgery.

VI. MARKETING HISTORY

VISX has over 200 Excimer Systems located in approximately 35 countries. The VISX Excimer 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 reactions associated with PRKa include: loss of best spectacle corrected visual acuity, worsening of patient symptoms including double vision, sensitivity to bright lights, and increased difficulty with night vision, increase in intraocular pressure, corneal haze, and secondary surgical intervention.

VIII. SUMMARY OF PRECLINICAL STUDIES

Please refer to the SSED for the original PMA for PRK.

IX. SUMMARY OF CLINICAL STUDIES

A prospective study with 116 eyes was conducted at five investigational sites in the United States, and two international retrospective studies were used to supplement the U.S. prospective study: 95 eyes from University of Ottawa Eye Institute (Ottawa, Canada), and 530 eyes from Moorfields Eye Hospital (London, England). All eyes from the international studies met the U.S. indications for use criteria.

U.S. Study

A. Study objective

The objectives of the multicenter, clinical investigation of the VISX excimer system for PRKa, conducted under IDE G910064, were to assess the ability of the device to: 1) safely improve uncorrected visual acuity, and 2) to predictably reduce cylindrical manifest refraction (0.75 to -4.5 D) in healthy eyes.

B. Study design

This was a prospective, non-randomized, unmasked, multicenter clinical study with the subjects acting as their own controls.

C. Inclusion and exclusion criteria

Study subjects were 18 years or older and must have signed an informed consent form. Enrollment occurred if the subject met these conditions: 1.0 to 6.0 diopters of myopia, spherical equivalent, best corrected visual acuity of 20/40 or better in both eyes, cylindrical component of the manifest refraction is not less than 0.75 diopters or greater than 4.50 diopters and stable spherical or cylindrical portion of manifest refraction as documented by ≤0.5 D change within the previous twelve months. Contact lens wearers had to abstain from contact lens use prior to baseline examination [two (2) weeks for soft lenses, three (3) weeks for hard lenses] and have three (3) central keratometry readings and manifest refractions taken at one (1) week intervals, the last two of which must not differ by more than 0.50 diopter in either meridian; furthermore, the mires had to be regular.

Subjects not meeting the above inclusion criteria were excluded from the study. In addition, subjects who exhibited any of the following conditions were excluded: progressive myopia, keratoconus, active ocular disease or corneal abnormality, patent corneal neovascularization within 1 mm of the intended ablation zone, previous corneal surgery or trauma within the intended ablation zone, systemic disease likely to affect wound healing, unstable central keratometry readings with irregularly shaped mires or corneascope photographs with broken central rings, use of systemic medications likely to affect wound healing or immunodeficiency, under 18 years of age, spherical or

cylindrical portion of manifest refraction which had progressed at a rate of more than 0.50 diopter per year from date of baseline exam, cylindrical component of the manifest refraction less than 0.75 diopters or greater than 4.5 diopters.

D. Study Plan, Patient Assessments, and Efficacy Criteria

Subjects were evaluated preoperatively, every 24 to 48 hours post-operatively until re-epithelialization, and at 1, 3-4, 6, 12, 18 and 24 months post-treatment.

Pre-operatively the subject's medical and ocular histories were recorded. Post-operatively, subjects were questioned about any visual symptoms and their satisfaction with the procedure. Objective measurements included: uncorrected and best corrected visual acuity, manifest refraction, keratometry, intraocular pressure, pachymetry, clinical assessment of corneal clarity, clinical assessment of anterior chamber, vitreal, retinal and lens status, assessment of complications or adverse reactions.

Additional post-operative evaluations were performed in subsets of subjects as follows: cycloplegic refraction, corneal topography, glare testing, contrast sensitivity, endothelial cell counts and visual fields.

Procedure effectiveness was evaluated based on improvement in uncorrected visual acuity and reduction in spherical equivalent, reduction in astigmatic component, and patient acceptance of the procedure. The stability of the procedure was defined in terms of the change in manifest refraction over time, starting one month after treatment.

Statistical analyses were performed at the 0.05 significance level against two-sided alternatives. Descriptive statistics were generally provided on data up to 24 months. For continuous data, changes between time periods were analyzed using appropriate t-tests. For categorical data, differences in proportions between time periods were tested using the McNemar's test, while differences in groups of eyes and/or patients were tested using the Chi-squared test, or Fischer's Exact test. The surgically induced refractive change (SIRC) was assessed by vector analysis and compared to the intended refractive change (IRC) to produce a mean vector axis and magnitude of error.

E. Study period, investigational sites and demographic data

1. Study period

Table 1 Summary of First and Last Treatment Dates Cohort Eyes (n=116)			
Group	**n**	**First Treatment**	**Last Treatment**
Primary Eyes	71	12/16/92	8/16/93
Fellow Eyes	45	7/19/93	6/14/95
Retreated Eyes	9*	9/21/93	11/7/95

*One eye was retreated after completing 24 months of follow-up.

There were 76 patients enrolled in the protocol and 133 eyes treated. The 76th patient was enrolled due to a communication error with one site. Treatment of the 76 primary eyes was completed on 8/16/93; fellow eyes were treated through 6/14/95. Of the 133 eyes that were treated in this study, a total of 17 did not meet the refractive criteria of the refined indications. There were nine (9) eyes that exceeded the upper limit of spherical myopia (-6.0 D) at the spectacle plane, nine (9) eyes failed to meet the refractive requirements for cylinder at the spectacle plane of 0.75 to 4.0 D. This exclusion based upon the refined indications resulted in a new cohort of 116 eyes for analysis of safety and effectiveness. The effectiveness data for all initial treatments were analyzed together with the retreated eyes being carried until retreated. All retreated eyes were then examined separately. This report presents an analysis of the clinical results without overestimating effectiveness results. The analysis of safety was not segregated; all complications and adverse events are reported regardless of retreatment.

2. Investigational Sites

The following table presents the five sites that participated in the clinical investigation.

Table 2 Investigators/Investigation Sites (n=116)	
Investigator/Site	**Primary Eyes (Fellow Eyes)**
Paul Pender, MD Catholic Medical Center 100 McGregor Street Manchester, NH 03102	21 (13)
Peter J McDonnell, MD Doheny Eye Institute 1450 San Pablo Street Los Angeles, CA 90033	12 (8)
Charles H. Cozean, Jr., MD 56 Doctors' Park Cape Girardeau, MO 63701	8 (4)
Alan Spigelman, MD Sinai Hospital of Detroit 6767 West Outer Drive Detroit, MI 48235	21 (14)
J. James Rowsey, MD University of South Florida Eye Institute 2020 Laurel Drive, Box 21 Tampa, FL 33612	9 (6)

3. Demographics and Baseline Characteristics

Demographic characteristics with respect to patient age and sex are shown below.

Table 3
Cohort Demographics: Sex (n=116)

	Male	Female	p-value
Primary Eye Only	69.2%	30.8%	0.680
Primary and Fellow Eye	64.4%	35.6%	

Table 4
Cohort Demographics: Age (n=116)

	Mean	SD	Range	p-value
Primary Eye Only	37.5	9.35	24 to 62	0.270
Primary and Fellow Eye	39.9	8.75	26 to 71	

Baseline Characteristics:

Baseline characteristics for the eyes evaluated were as follows:

Table 5
Cohort Spherical Equivalent (n=116)

	Mean	SD	Range	p-value
Primary Eye Only	-3.76	1.56	-6.00 to -1.25	0.739
Primary and Fellow Eye	-3.64	1.44	-6.00 to -0.50	

Table 6
Cylinder (n=116)

	Mean	SD	Range	p-value
Primary Eye Only	-1.51	0.81	-4.00 to -0.75	0.293
Primary and Fellow Eye	-1.69	0.67	-3.50 to -0.80	

Table 7
UCVA (n=116)

	Primary Eye Only	Primary and Fellow Eye	p-value*
CF or worse	19.7%	22.4%	0.510
20/200 to 20/800	51.0%	44.8%	
20/100 to 20/200	19.7%	20.7%	
Better than 20/100	9.9%	12.1%	

*p-value does not change significantly

Table 8
Cohort BSCVA

	Primary Eye Only	Primary and Fellow Eye	p-value*
20/20 and better	71.8%	73.3%	0.993
20/30 and worse	28.2%	26.7%	

*p-value does not change significantly

The following table summarizes the pre-operative refractive characteristics of the cohort:

Table 9 Cohort Pre-Operative Refractive Characteristics (n=116)			
Primary Eyes (n=116)	Spherical Equivalent	Sphere (MRSE)	Astigmatism
Mean	-4.46 D	-3.64 D	-1.63 D
SD	1.39 D	1.47 D	0.74 D
Range	-1.75 to -8.63 D	-0.5 to -8.00 D	-0.75 to -4.00 D
Fellow Eyes (n=48)			
Mean	-4.16 D	-3.33 D	-1.66
SD	1.46	1.59	0.65
Range	-1.38 to -8.50 D	0.00 to 5.75	-0.75 to -3.25 D
All Cohort Eyes (n=164)			
Mean	-4.34 D	-3.52	-1.64 D
SD	1.41	1.52	0.71
Range	-1.38 to -8.63	0.00 to -8.00 D	-0.75 to -4.00 D

F. Data Analysis and Results

1. Postoperative Characteristics and Results

a. Patient Accountability

Any retreated patient was considered eligible for examination and inclusion in effectiveness analyses until retreatment; after retreatment they are followed in the retreatment analysis. All eyes treated are included in the accountability table (Table 10). The final visit characterizes the available long term follow-up on these patients. All but one patient had 24-month or longer follow-up in this group.

Table 10 Accountability of All Eyes Eyes Eligible for Follow-Up (as of 8/7/96)			
Category	**6 Month**	**12 Month**	**Final Visit**
Eyes Enrolled	**116** **^Cohort**	**116** **^Cohort**	**116** **^Cohort**
Drop-Outs			
Retreated*	0	5	8
Withdrew**	3	6	13
Other Treatment (AK)	0	0	0
Not Yet Due for Exam	0	0	4
Total Eyes Eligible	**113**	**105**	**91**
(Minus) **Not Examined** (or Missed Visit)	**5**	**13**	**7**
Accountability			
# Follow-Up Exams	**108**	**92**	**82**
% Follow-up			
of Eligible Eyes	**95.6%** **108/113**	**87.6%** **92/105**	**90.1% 82/91**
of Enrolled Eyes	**93.1%** **108/116**	**79.3%** **92/116**	**70.7% 82/116**

FINAL VISIT=At least 24±3 months follow-up from the date of initial treatment. In the case of 1 retreatment, the eye completed 24 months follow-up after the date of the initial treatment before the date of retreatment. One follow-up at 20 months is also included.

*Follow-up and accountability after retreatment is summarized and presented in Tables 11 and 12.

**Drop-outs at patient request, patient moved or was unable to be contacted - all with documentation.

^Cohort indicates those eyes that qualify under the refractive eligibility criteria of the requested indications (n=116) and denoted by shaded areas.

One eye that underwent epithelial debridement for anterior stromal haze was included in the analysis and not withdrawn from study or considered retreated.

Table 11 Cohort Retreatments (n = 9)	
Time of Retreatment	**# Eyes**
After 6-Month Follow-Up	4
After 12-Month Follow-Up	4
After 24-Month Follow-Up	1*

*Although retreated, this eye is included in all efficacy reports since 24 months of follow-up was completed before retreatment occurred.

Table 12 Accountability for Retreatment of Cohort Eyes (n=9)	
Current Status	# of Eyes
Completed Study Requirements	8
Missed Visit	0
Retreated After Completion of Study Requirements	1*

Completion of Study Requirements=At least 6 months of follow-up after retreatment and a total of at least 24 months of follow-up after initial treatment.
*Although retreated, this eye is included in all efficacy reports since 24 months of follow-up was completed before retreatment occurred.

Two of these retreated eyes were fellow eyes and seven were primary eyes.

b. Effectiveness Results

(1) **Uncorrected Visual Acuity (UCVA)**

Table 13 is a distribution of uncorrected visual acuities (UCVA) for the primary and fellow eyes stratified by pre-operative refractive cylinder (PE = primary eye, FE = fellow eye). At the final visit 91.5% (75/82) of eyes treated attained 20/40 or better vision without correction and the majority (81.7% or 67/82) attained an uncorrected visual acuity of 20/30 or better. No eye was able to attain 20/40 uncorrected acuity pre-operatively. The improvement of uncorrected visual acuity following treatment is stable and significant.

This analysis shows the effectiveness of one laser treatment for astigmatism. Refer to d. for a summary of retreatment data.

Table 13 Final Visit UCVA of Cohort Eyes Stratified by Diopter of Pre-Operative Cylinder (n=82*)												
	0.75-1.0			1.1-2.0			2.1-3.0			3.1-4.0		
	PE	FE	All	PE	FE	All	PE	FE	All	PE	FE	All
20/20	0	1	1	0	0	0	0	0	0	0	0	0
20/25-20/30	16	8	24	28	16	44	4	8	12	2	0	2
20/40-20/50	0	0	0	0	0	0	0	0	0	0	0	0
<20/40-20/50	0	1	1	2	0	2	0	1	1	0	0	0
<20/50-20/60	0	0	0	0	0	0	0	0	0	0	0	0
<20/60-20/70	0	0	0	0	0	0	0	0	0	0	0	0
<20/70-20/100	0	1	1	1	0	1	0	1	1	0	0	0
<20/100-20/200	0	0	0	0	0	0	0	0	0	0	0	0
<20/200-20/800	0	0	0	0	0	0	0	0	0	0	0	0
CF or Worse	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	16	9	24	28	16	44	4	8	12	2	0	2

*UCVA data for 2 eyes were not available at this visit.

(2) BSCVA

Best spectacle corrected visual acuity (BSCVA) was compared at the Pre-Operative and final visit by amount of pre-operative cylinder. No eye was worse than 20/40 pre-treatment. At the final visit, 98.8% (81/82) were 20/40 or better and no eye was worse than 20/40-1.

Table 14
Final Visit BSCVA of Cohort Eyes Stratified by Diopter of Pre-Operative Cylinder (n=82*)

	0.75-1.0			1.1-2.0			2.1-3.0			3.1-4.0		
	PE	FE	All	PE	FE	All	PE	FE	All	PE	FE	All
20/20	10	7	17	22	12	34	3	4	7	2	0	2
20/25-20/30	4	2	6	5	4	9	0	3	3	0	0	0
20/30-20/40	1	0	1	0	2	2	1	0	1	0	0	0
<20/40-20/50	0	0	0	1	0	1	0	0	0	0	0	0
<20/50-20/60	0	0	0	0	0	0	0	0	0	0	0	0
<20/60-20/70	0	0	0	0	0	0	0	0	0	0	0	0
<20/70-20/100	0	0	0	0	0	0	0	0	0	0	0	0
<20/100-20/200	0	0	0	0	0	0	0	0	0	0	0	0
<20/200-20/800	0	0	0	0	0	0	0	0	0	0	0	0
CF or Worse	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	15	9	24	28	16	44	4	8	12	2	0	2

*BSCVA for 2 eyes were not available at this visit

(3) Vector Analysis

A vector analysis of refractive corrections was performed for the pre-treatment and post-treatment manifest refraction data. The final visit results are summarized in Tables 15, 16 and 17, and the mean correction and errors for the 6-month, 12-month and final visits are listed in Table 18.

The final visit analysis compares pre-treatment and final visit refractions for the 82 eyes that were examined at both time points. The mean surgically induced refractive vector change (SIRC) was 3.22 D ± 1.56 (standard deviation) of sphere while the mean intended refractive vector change (IRC) was 3.31 D ± 1.34 . The mean SIRC for cylinder was 1.14 D ± 0.61 while the mean IRC was 1.44 D ± 0.59. As is demonstrated in Table 17 the mean absolute vector axis error is 11.5 degrees with a mean vector magnitude error of -0.30 D.

Table 15
Vector Analysis of the Cohort at Final Visit

	Pre-Treatment (n=116)		Final Visit (n=82)ξ		SIRC (n=82)ξ		Intended Change (IRC) (n=82) ξ	
	Sph	Cyl	Sph	Cyl	Sph	Cyl	Sph	Cyl
Mean	-3.52	-1.64	-0.10	-0.55	3.22	1.14	3.31	1.44
Median	-3.75	-1.50	0.00	-0.50	3.14	1.05	3.30	1.35
SD	1.52	0.71	0.83	0.54	1.56	0.61	1.34	0.59
Min	-6.00	-4.00	-4.00	-2.25	-0.90	0.14	0.00	0.56
Max	0.00	-0.75	2.25	0.00	7.83	3.16	5.60	3.16
p value					<0.001	<0.001		

SIRC=Surgically induced refractive vector change
IRC=Intended refractive vector change
p value (two-sided z-test to determine if mean change is different from 0)
ξ The refractive data for 2 eyes are not available for this visit. The total number of patient visits at Final Visit was 84

Table 16
Vector Analysis of the Cohort Stratified by Pre-operative Cylinder at Final Visit (n=82)ξ

Pre-op Cyl	Pre Sph	Pre Cyl	Final Visit Sph	Final Visit Cyl	SIRC Sph	SIRC Cyl	IRC Sph	IRC Cyl	V Mag Error	Abs Vector Axis Error
0.75 - 1.0	-4.06	-0.91	-0.59	-0.55	3.08	0.66	3.64	0.83	-0.17	24.3
1.1 - 2.0	-3.63	-1.60	0.11	-0.48	3.51	1.17	3.39	1.46	-0.29	6.30
2.1 - 3.0	-2.58	-2.58	0.10	-0.83	2.50	1.74	2.49	2.32	-0.58	6.67
3.1 - 4.0	-2.04	-3.5	-0.13	-0.50	2.64	2.65	2.77	3.13	-0.48	1.00

ξ The refractive data for 2 eyes are not available for this visit. The total number of patient visits at Final Visit was 84

Table 17
Vector Errors of the Cohort at Final Visit

	V Ax Error (n=82) ξ	V Mag Error (n=82) ξ
Mean	11.5	-0.3
Median	3.5	-0.23
SD	18.77	0.45
Min	0.00	-2.09
Max	79	1

V Ax Error = Vector error in astigmatic axis
V Mag Error = Vector error in astigmatic magnitude
ξ The refractive data for 2 eyes are not available for this visit. The total number of patient visits at Final Visit was 84

Table 18 Cohort (n=116) Summary of Sphere, Cylinder Magnitude and Axis						
	6 Months (n=106)*		12 Months (n=89)ϕ		Final Visit (n=82)ϒ	
Sphere (SIRC/IRC)	3.18/3.27	(97.2%)	3.30/3.36	(98.2%)	3.22/3.31	(97.3%)
Cylinder (SIRC/IRC)	1.25/1.47	(85.0%)	1.18/1.43	(82.5%)	1.14/1.44	(79.2%)
Mean absolute vector axis error	7.2 degrees		10.49 degrees		11.5 degrees	
Mean vector magnitude error	-0.22 D		-0.25 D		-0.3 D.	

*The refractive data for 2 eyes are not available for this visit
ϕThe refractive data for 3 eyes are not available for this visit
ϒThe refractive data for 2 eyes are not available for this visit

(4) Reduction of Mean Spherical Equivalent

The mean spherical equivalent (S.E.) was reduced at all time periods examined. Not all eyes were targeted for emmetropia; the mean target was -0.10 D with a standard deviation of 0.24. The mean pre-treatment manifest refractive S.E. was -4.34 D. The mean S.E. was reduced by 4.06 D or 93.5% at 6 months, 4.15 D or 95.6% at 12 months and 4.03 D or 92.9% at the final visit.

Table 19 (n=116) Reduction of Mean Spherical Equivalent of the Cohort			
	6-Month (n=106 Ψ)	12-Month (n=89∝)	Final Visit (n=82 ξ)
Mean	4.06	4.15	4.03
Median	4.19	4.13	4.13
SD	1.72	1.60	1.64
Min	-0.88	0.88	0.00
Max	8.00	8.63	8.63

ΨThe refractive data for 2 eyes are not available for this visit. (See Table 10)
∝The refractive data for 3 eyes are not available for this visit. (See Table 10)
ξThe refractive data for 2 eyes are not available for this visit. (See Table 10)

(5) Deviation From Intended Correction (Predictability of Outcome)

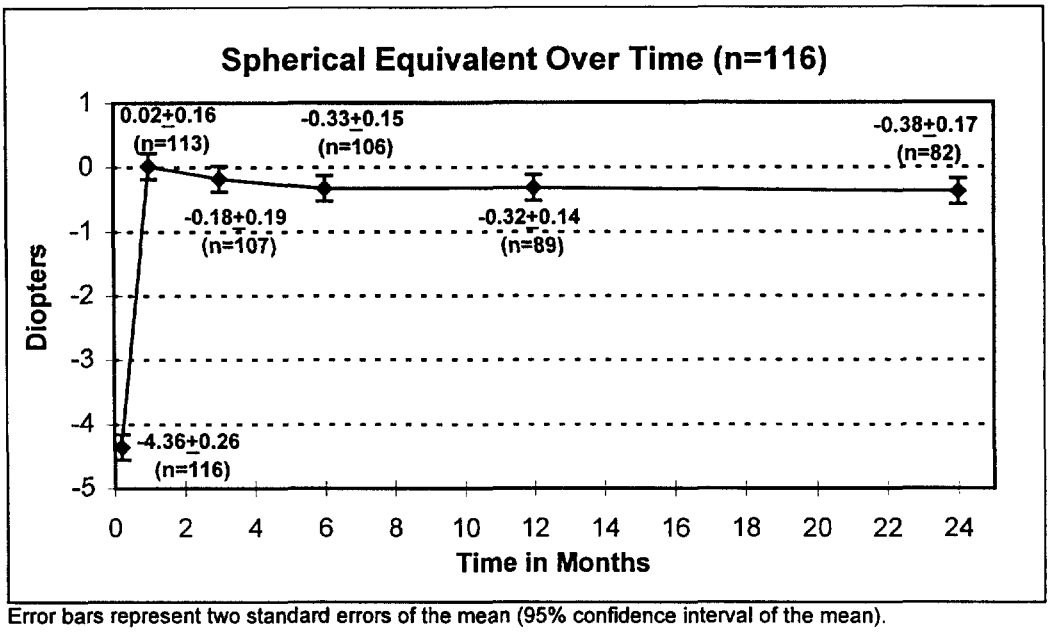
The predictability of outcome has been assessed as the extent of deviation from intended correction (i.e., difference between achieved correction and intended correction) by considering mean reduction in spherical equivalent and cylinder over time. The intended final refractive error was not plano in all cases (i.e., intended undercorrection for monovision); the resultant mean intended result was -0.10 D, spherical equivalent. As shown in Table 19 the mean spherical equivalent was reduced by 93.5% at 6 months, 95.6% at 12 months, and 92.9% at the final visit. The reduction in absolute cylinder over time was 67% at 6 months, 64% at 12 months, and 62% at the final visit.

Predictability of outcome was also examined by performing vector analyses of the refractive data from follow-up visits. Because astigmatic corrections have three components (sphere, cylinder and axis), an accurate outcomes assessment can be obtained only with a vector analysis to determine the magnitude and direction of change. The close agreement between the mean SIRC and IRC values for sphere, cylinder magnitude, and axis indicate a low deviation from intended correction. The mean vector axis error and the mean vector magnitude error are also well correlated. A summary of the results is included in Table 18.

In summary, the mean vector analyzed values at 6 months, 12 months and the final visit for the Surgically Induced Refractive Change (SIRC) and Intended Refractive Change (IRC) in sphere, cylinder magnitude, and axis are evidence of the predictability of the correction of myopia and astigmatism.

(6) Stability of Outcome

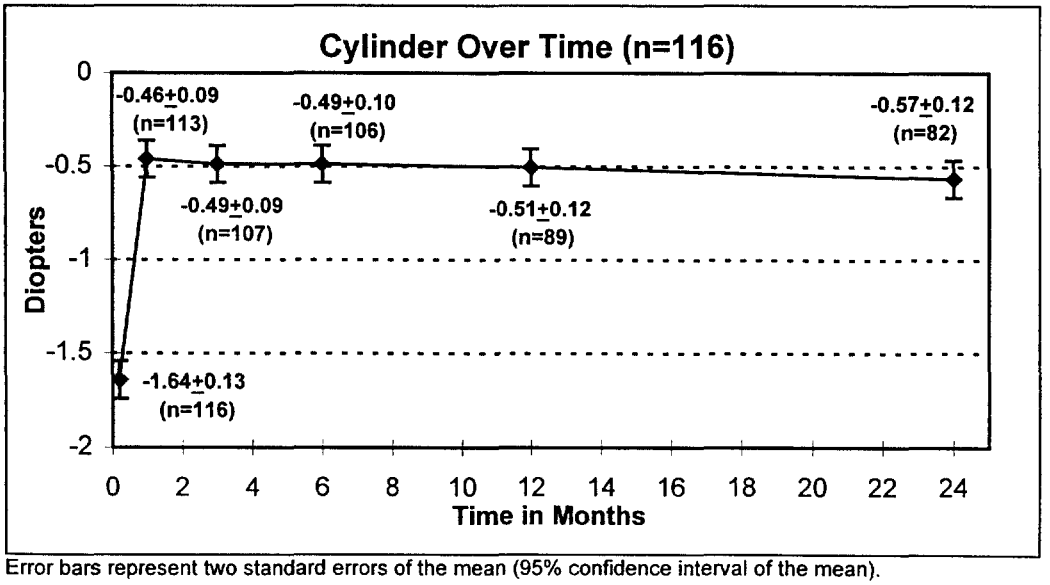
Stability of outcome is presented by assessment of UCVA, spherical equivalent refractive error and refractive cylinder over time. Over the course of the study, a significant number of eyes (86.7%, 86.6%, and 91.5% at the 6-month, 12-month and final visit, respectively) achieved and maintained uncorrected visual acuity of 20/40 or better. The mean reduction in spherical equivalent was 4.06 D (SD 1.72) at 6 months, 4.15 D (SD 1.60) at 12 months, and 4.03 D (SD 1.64) at the final visit. Graphic depiction of this reduction and maintenance in spherical equivalent over time is presented in Figure 1 below:



Error bars represent two standard errors of the mean (95% confidence interval of the mean).

Figure 1

Both the observed mean cylinder and reduction in absolute mean cylinder were also stable over the course of study. The mean pre-treatment cylinder was -1.64 (SD 0.71). The mean observed cylinder was -0.49 D (SD 0.54) at 6 months, -0.51 D (SD 0.58) at 12 months, and -0.55 D (SD 0.54) at the final visit. The reduction in absolute mean cylinder was 1.15 (SD 0.79) at 6 months, 1.08 (SD 0.81) at 12 months, and 1.05 (SD 0.73) at the final visit. This represents a 67%, 64% and 62% reduction in cylinder at each time point, respectively. Graphic depiction of this reduction and maintenance in cylinder over time is presented in Figure 2.



Error bars represent two standard errors of the mean (95% confidence interval of the mean).

Figure 2

The above two graphs (Figures 1 and 2) demonstrate stability over the entire course of the study with no significant regression. The reduction and maintenance of both spherical equivalent and cylinder, and achievement and maintenance of uncorrected visual acuity of 20/40 or better represent evidence of stability of the procedure.

c. Adverse Events

There was no patient death related to the use of the VISX Excimer Laser System.

Adverse events for visits 6 months and later are presented in Table 20. They are ordered by frequency at final visit.

The following transient complications might be expected with patients undergoing the PRKa procedure: pain (24-48 hrs), foreign body sensation, tearing, photophobia, redness, itching/scratchiness, burning, dryness, headache, blurred vision, corneal swelling and pupil enlargement.

Other adverse events might be expected with patients undergoing the PRKa procedure but have not been observed in the VISX clinical studies are: corneal perforations, intraocular infections, hyphemas, hypopyon, post-treatment lens abnormalities with vision loss, significant overcorrections, persistent corneal decompensation/edema, or cystoid macular edema.

Excimer laser energy has the potential to induce micromechanical damage to endothelial cells, induce cataracts, and cause mutations. These effects have not been observed in any clinical use, nor have they been reproducible in various animal and *in vitro* test systems.

Table 20 Adverse Events (n=116)						
Adverse Events	6M (n=108)		12M (n=92)		Final Visit* (n=82)	
	n	%	n	%	n	%
1. Increased Difficulty with Night Vision♦	28	25.9%	17	18.5%	19	22.6%
2. Worsening of Patient Symptoms♣: "Sensitivity to Bright Lights"	18	16.7%	12	13.0%	13	15.5%
3. Loss of ≥2 lines BSCVA Due to Any Cause	5	4.8%	6	6.7%	7	8.5%♠
Due to Corneal Causes	4	3.8%	4	4.5%	4	4.8%♠
4. Pre-treatment BSCVA 20/20 or Better with Post-treatment BSCVA Worse than 20/25⊗	5	4.8%	4	4.5%	5	6.1%
5. Worsening of Patient Symptoms♣: "Double Vision"	6	5.6%	5	5.4%	5	5.9%
6. Secondary Surgical Intervention Retreatments	0	0.0%	4	4.3%	5	5.9%
7. IOP Increase > 5 mm Hg < 10 mm Hg	8	7.4%	2	2.2%	2	2.4%
8. Corneal Haze ≥ Grade 2	2	1.9%	4	4.3%	1	1.2%
9. Pre-treatment BSCVA 20/20 or Better with Post-treatment BSCVA Worse than 20/40⊗	0	0.0%	2	2.2%	0	0.0%
10. Secondary Surgical Intervention Other Refractive Procedures	0	0.0%	1	1.1%	0	0.0%

Percentages of adverse events are reported as:

$$\frac{\text{number of eyes with at least one occurrence observed/reported at the specified study visit}}{\text{number of eyes examined at the specified study visit}}$$

♠ Includes two eyes in one patient who had cataract formation upon enrollment and one eye of one patient who had a stroke; these losses of BSCVA were not attributed to corneal wound healing. One of these eyes was reported to be 20/20 pre-operatively in error (misread value discovered when Investigator was asked to explain 2 line loss). Actually, the eye was 20/25 pre-operatively; therefore the eye did never actually lose 2 lines of BSCVA. The data throughout this report continue to reflect the erroneous pre-op BSCVA of 20/20 for consistency. One eye was retreated after the final exam so that the last BSCVA data are not reflective of the last examination for this eye. At the final examination (4 months after retreatment on 3/19/96), this eye had a BSCVA of 20/15 which technically represents a 2.0 line loss from the original BSCVA (20/10). If the three eyes contributing non-corneal losses of BSCVA and the eye that was retreated after completion of the study are eliminated from this analysis, only 4 eyes (4.8%) experienced a ≥ 2 line loss and no eye was worse than 20/40-1 at the Final Visit. However, one eye was 20/20 at the Final Visit and one eye was not 20/20 pre-operatively. Therefore, only 1 (1.2%) of the seven (7) eyes that completed the study follow-up without retreatment and were 20/20 or better pre-operatively, experienced a ≥ 2 line loss of BSCVA that could be attributed to corneal causes and was worse than 20/20 at the Final Study Visit. **At no time did any eye lose BSCVA beyond 20/50 and at the Final Visit no eye was worse than 20/40-1.**

⊗ Visual acuities were taken from the ETDRS standard and may have (+) and (-) designations.

♣ Reflects the number of eyes where these symptoms as occurring 'often or always' post-treatment and worse than pre-treatment. Post-retreatment data are not included.

♦ Reflects the number of eyes where this symptom was reported as significantly worse than pre-treatment. Post-retreatment data are not included.

* The final visit occurred at 24 ± 3 months after treatment.

Visual Acuity. The Adverse Events table (Table 20) lists the number and percentages of eyes that lost two or more lines of BSCVA at the 6-month, 12-month and final visits. At the final visit, 2 eyes were noted to have lost BSCVA of ≥ to 2 lines of BSCVA for reasons unrelated to the laser procedure. At no time did any eye lose BSCVA beyond 20/50 and that at the last visit no eye was worse than 20/40-1. The losses of BSCVA appear related, in at least three eyes, to the formation of cataracts, two of which were present prior to ablation. The other causes are topographic irregularity and haze formation. Also significant is a large overlap between this group and the reported adverse event group (8/13 eyes).

Contrast Sensitivity was evaluated using the VectorVision CSV-1000 contrast sensitivity test system. This system employs a constant illumination intensity background (85 cd/mm as recommended by the US National Academy of Science Committee on Vision). The unit detects sensitivity over the a wide range of ambient light levels. Contrast sensitivity was evaluated at 4 spatial frequencies (3, 6, 12 and 18 cycles per degree). The CSV-1000 grading system was then used to characterize contrast sensitivity into one of four categories: normal or mild, moderate or large loss.

Table 21
Contrast Sensitivity of Cohort Eyes*

Categories	6 Month Visit (n=90)				12 Month Visit (n=74)				Final Visit (n=66)			
	Pre-Op		Post-Op		Pre-Op		Post-Op		Pre-Op		Post-Op	
	n	%	n	%	n	%	n	%	n	%	n	%
Normal	83	92.2	78	86.7	67	90.5	59	79.7	62	93.9	57	86.4
Mild Loss	5	5.6	8	8.9	4	5.4	11	14.9	3	4.5	4	6.1
Mod Loss	1	1.1	3	3.3	0	0.0	2	2.7	0	0.0	4	6.1
Large Loss	1	1.1	1	1.1	3	4.1	2	2.7	1	1.5	1	1.5

*The totals at each post-op visit vary by 1 due to the categorization of 1 eye that tested as a "large loss" pre-operatively and was considered "not available" in the original table.

Glare response was evaluated using the brightness acuity tester (BAT) in conjunction with a high contrast acuity chart. Loss of two or more lines of acuity, as presented on the age-normalized scoring table for this system, was considered to be an abnormal glare response. Investigators were asked to grade the patient's glare response as being either normal or abnormal based on the above criteria. The results are presented in the table below:

Table 22 Glare Testing of Cohort Eyes												
Categories	6 Month Visit (n=87)				12 Month Visit (n=74)				Final Visit (n=67)			
	Pre-Op		Post-Op		Pre-Op		Post-Op		Pre-Op		Post-Op	
	n	%	n	%	n	%	n	%	n	%	n	%
Normal	85	97.7	83	95.4	73	98.6	69	93.2	66	98.5	67	100
Abnormal	2	2.3	4	4.6	1	1.4	5	6.8	1	1.5	0	0.0

Patient Satisfaction. Patients were given questionnaires at the 6-month, 12-month and final visit and asked to grade their level of satisfaction with the procedure on a scale from one (dissatisfied) to ten (most satisfied). The table below reports the results of this questionnaire:

Table 23 Satisfaction Among Cohort Eyes												
Visit	# Responses	≤ 2		≤ 4		≤ 6		7-8		9-10		Avg Score
		n	%	n	%	n	%	n	%	n	%	
6-Month (n=113)	90	3	3.3	5	5.6	11	12.2	24	26.7	55	61.1	8.3
12-Month (n=92)	81	2	2.5	5	6.2	14	17.3	13	16.0	54	66.7	8.5
Final Visit (n=84)	67	1	1.5	1	1.5	11	16.4	15	22.4	41	61.2	8.5

The # of responses reflects data missing from questionnaires.

d. Retreatments

Nine eyes were retreated (9/116 or 7.8%) during the study (Table 24). The majority were retreated for initial undercorrection of refractive error. Videokeratography was examined for each of these patients. Initial treatment of two eyes (Patients # 6 and 8) also resulted in ghost images and/or night vision disturbances that warranted retreatment. One eye (Patient #7) underwent a PTK ablation to correct decentration, with a post retreatment UCVA of 20/25+1, and BSCVA of 20/20, resolution of the ghosting, and a satisfaction score of 9 (10 being most satisfied). Included in Table 24 are comparisons for all retreated eyes.

Table 24 Reason for Retreatment of Cohort Eyes (n=9)		
	Patient	Reason for Retreatment
After 6 Months	1	Undercorrection
	2	Undercorrection
	3	Undercorrection
	4	Undercorrection
	5	Undercorrection, central island on videokeratography
After 12 Months	6	Decentered ablation, ghost images
	7	Undercorrection, Decentered ablation
	8	Severe ghost images, night vision disturbance, haze
After 24 Months	9	Undercorrected

Table 25 Retreatment Visual Acuity for Cohort Eyes (n=9)						
	Pre-Treatment		Pre-Retreatment		Post-Retreatment@	
Patient	UCVA	BSCVA	UCVA	BSCVA	UCVA	BSCVA
1	80-2	20/15	50	20/12	25	20
2	400	20/15	80+4	25	60	20
3	CF	20	40	20	20	20
4	CF	25	50+3	25	25-3	25-1
5	400	20/12	50-2	20/15	30	20/15
6	CF	20	25+2	20	25+1	20
7	80	20/20	50	20	30	20
8	200	15	20-1	20/15	30	15
9	125	20	50	20/15	30	15

*The data listing indicates this BSCVA to be 20/80+4 in error; the correct value is included for accuracy.
@Last visit available.

The uncorrected visual acuities before retreatment were better than before initial treatment. All but two cases (Patients #6 and 8) had uncorrected visual acuities that were better after retreatment. With one exception, BSCVA either improved or remained the same after retreatment. In one case, BSCVA dropped from 20/12 to 20/15 after initial treatment, then dropped further to 20/20-3 after retreatment. No patient had a BSCVA worse than 20/25-1 post-retreatment; baseline BSCVA in this case (Patient #4) was 20/25.

Risks. The risks for patients requiring retreatment are the same as for the original procedure with the additional caveat that patients who are prone to haze formation and an accompanying loss of BSCVA and/or UCVA are similarly prone to healing with haze after retreatment. Doctors are encouraged to wait for significant reduction in haze and concomitant refractive stability prior to retreating patients. There is no evidence that undercorrection by the laser system is causative for these retreatments. VISX believes that variable healing response is the major causative factor for retreatment.

e. Cylinder Axis Shift

Table 26 Distribution of Axis Shift Between Pre-Op and 6 Months Stratified by Pre-Op Cylinder (n=106)*				
Axis Shift (degrees)	0.75 - 1.0 (n=26)	1.1 - 2.0 (n=60)	2.1 - 3.0 (n=14)	3.1 - 4.0 (n=6)
0-15	19	50	8	6
16-30	3	3	4	0
31-45	0	1	1	0
46-60	0	2	0	0
61-75	3	2	0	0
76-90	1	2	0	0

*The refractive data for 2 eyes are not available for this visit.

Table 27 Distribution of Axis Shift Between Pre-Op and 12 Months Stratified by Pre-Op Cylinder (n=89)[α]				
Axis Shift (degrees)	0.75 - 1.0 (n=25)	1.1 - 2.0 (n=49)	2.1 - 3.0 (n=12)	3.1 - 4.0 (n=3)
0-15	19	38	10	3
16-30	4	4	1	0
31-45	0	3	1	0
46-60	0	3	0	0
61-75	1	0	0	0
76-90	1	1	0	0

[α]The refractive data for 3 eyes are not available for this visit.

Table 28 Distribution of Axis Shift between Pre-Op and Final Visit Stratified by Pre-Op Cylinder (n=82)[ξ]				
Axis Shift (degrees)	0.75 - 1.0 (n=24)	1.1 - 2.0 (n=44)	2.1 - 3.0 (n=12)	3.1 - 4.0 (n=2)
0-15	21	33	9	2
16-30	1	7	2	0
31-45	1	2	0	0
46-60	1	1	0	0
61-75	0	0	0	0
76-90	0	1	1	0

[ξ]The refractive data for 2 eyes are not available for this visit.

f. Endothelial Cell Counts

Endothelial cell count data were available for 80 eyes where data were available at least 6 months following treatment. Incomplete data sets were deleted from the analysis. In two cases, there were no data for a follow-up visit until after retreatment, so the baseline pre-operative data were used as the pre-operative and the post-retreatment as the follow-up. The post-retreatment date was used to calculate the post-treatment interval. There were also cases where the last post-operative data before retreatment were also used as pre-treatment data. The number of these exceptions is small. In a separate analysis not presented in this document, the outcome of this analysis was not changed if alternate methods of data handling were used.

Table 29 presents the results of the analysis of endothelial cell counts. The change from pre-treatment to post-treatment was tested using a paired two-tailed Student's t-test for all visits, 6 months, 12 months, 24 months, and 36 months. At all time points the change from pre-treatment to post-treatment was not statistically significant ($p = 0.608$ for all visits, $p = 0.058$ at 6 months, $p = 0.676$ at 12 months, $p = 0.176$ at 24 months, and $p = 0.562$ at 36 months).

At 6 months post-treatment, the time point which most closely approaches statistical significance (p = 0.058), the mean difference between pre- and post-treatment shows a mean increase of 100 cells. Since the safety concern associated with PRKa centers on an abnormal *reduction* in post surgical endothelial cell count, this change in mean cell counts is not clinically important.

A review of the 5 time points evaluated indicates that the mean change in cell counts showed an increase at two of the time points and a decrease at the other three, with the mean change ranging from a decrease of 152 cells to an increase of 104 cells. The difference is not clinically important.

Table 29
Endothelial Cell Counts (Subset of 133 Eyes Enrolled in Protocol)

	All Visits (n=80*)		6 M (n=25)		12 M (n=20)		24 M (n=18)		36 M (n=7)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Mean	2378	2354	2332	2432	2385	2338	2376	2224	2400	2504
SD	431	386	347	320	498	421	526	482	200	336
Mean Diff	-24		100		-47		-152		104	
p-value	0.608		0.058		0.676		0.176		0.562	

Mean Diff = Hypthesized Mean Difference
p-value = paired two-tailed t-test
*The total number 80 for all visits includes 10 eyes with pre- to post-op intervals of at least 6M that are not also included in the designated follow-up cohorts (6, 12, 24 and 36M).

International Studies

The protocols used in the international studies conducted at University of Ottawa Eye Institute and Moorfields Eye Hospital were approved by Research Ethics Board of the respective insititution. All patients received and signed a consent form. The patients were followed by corneal specialists.

Table 30
International Eyes Enrolled and Percentage Follow-Up

	Eyes Enrolled	% Follow-Up @ 12-Mon
Ottawa	95	100% (95/95)
Moorfields	530	85.7% (454/530)

Table 31
Pre-Operative & Post-Operative Refractive Characteristics

	Pre-Op Sph	Pre-Op Cyl	Pre-Op SE	Post-Op Sph	Post-Op Cyl	Post-Op SE
Ottawa	-3.75D	-1.33 D	-4.41 D	-0.16 D	-0.26 D	-0.29 D
Moorfields	-3.74 D	-1.49 D	-4.48 D	-0.14 D	-0.75 D	-0.51 D

Table 32
Percent of Intended Corrections at 12 Months

	Mean Sph	Mean Cyl	Mean SE
Ottawa	95.7%	80.5%	93.4%
Moorfields	96%	50%	89%

Table 33 Astigmatism Results at 12 Months			
	UCVA 20/20 or Better	UCVA 20/40 or Better	BSCVA Loss ≥ 2 Lines
Ottawa	64/95 (67%)	91/95 (96%)	1/95 (1%)
Moorfields	267/454 (59%)	392/454 (86%)	3/454 (1%)

Comparison of U.S., Canadian and British PRKa Studies

Table 34 Comparison of Astigmatism Studies at 12-Month			
	U.S.	Canada	U.K.
# Eyes Treated	116	95	530
# Eyes Examined (12 m)	92	95	454
% Follow-up (12 m)	87.6^	100	85.7
Mean Pre-Op Sph	-3.52	-3.75	-3.74
Mean Post-Op Sph	-0.07	-0.16	-0.14
% Intended Sph Corr	98	95.7	96.3
Mean Pre-Op Cyl	-1.64	-1.33	-1.49
Mean Post-Op Cyl	-0.51	-0.26	-0.75
% Intended Cyl Corr	68.9	80.5	49.7
Mean Pre-Op SE	-4.34	-4.41	-4.48
Mean Post-Op SE	-0.32	-0.29	-0.51
% Intended SE Corr	92.6*	93.4	88.6
% UCVA ≥ 20/20	45.6	67.4	58.8
% UCVA ≥ 20/40	86.7	95.8	86.3
% ≥ 2-line BSCVA Loss	4.5	1.1	0.7

^Reflects # examined/# eligible for follow-up at the 12-month visit (excludes dropouts and retreatments).

*The percentage of Intended SE Correction presented in Table 34 reflects the calculated mean post-op Sphere (-0.07 D) and Cylinder (-0.51 D) as generated by vector analysis and expressed in diopters. These numbers are consistent with the mean Spherical Equivalent (-0.32 D) at 12 months post-operatively, but different from the percentage Reduction of Mean SE (95.6%) presented in the Professional Use Manual (see Section 3.4.2.2 Stability of Outcome). The Reduction of Mean SE was generated by averaging the differences between each subject's pre-operative and post-operative SE (mean 4.34 D - 0.19 D = 4.15 ± 1.60 D) and expressed as the absolute value of the reduction in diopters.

X. CONCLUSIONS DRAWN FROM THE CLINICAL STUDIES

The clinical results based on 116 eyes in the U.S. and 625 eyes internationally (from Canada and England) treated with a 6.0 mm ablation zone and 0 to 6 D of spherical myopia at the spectacle plane and concomitant reduction or elimination of astigmatism of not less than 0.75 D and not more than 4.0 D at the spectacle plane provides reasonable assurance that the VISX Excimer Laser System is safe and effective for improving uncorrected visual acuity and predictably reducing mild to moderate myopia with astigmatism.

XI. PANEL RECOMMENDATIONS

On January 14, 1997, the Ophthalmic Devices Panel recommended that the premarket approval supplement for the excimer laser be conditionally approved with changes in labeling. The conditions recommended by the panel were:

- To change the age limitation statement in their indications for use from 18 years of age to 21 years of age.
- To include a statement in their labeling to advise that for ages 21-30 , due to large pupil size, there is an increased chance that they will experience greater problems with night vision, contrast sensitivity and glare.
- To have a specific training program for astigmatic correction methods and issues.

XII. FDA DECISION

CDRH concurred with the Ophthalmic Devices Panel's recommendation of January 14, 1997 and issued a letter to VISX, Inc. on February 10, 1997 advising that the PMA was approvable subject to submission of the required labeling changes, several data clarifications, and additional contrast sensitivity and glare information.

In an amendment received by FDA on February 25, 1997, VISX submitted the required changes, clarifications, and information. FDA issued an approval order on April 24, 1997.

XIII. 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
- Directions for Use: see the labeling

REFERENCES

1. Srinivasan R, Wynne JJ, Blum SE, Far-UV Photo Etching of Organic Material. *Laser Focus* 1983; 19:62.

2. Trokel SL, Srinivasan R, and Braren B. Excimer Laser Surgery of the Cornea. *Am J Ophthal.* 96 (6):710-15, 1983.

FACTS YOU NEED TO KNOW ABOUT PHOTOREFRACTIVE KERATECTOMY SURGERY FOR NEARSIGHTEDNESS (PRK) OR NEARSIGHTEDNESS WITH ASTIGMATISM (PRKa)

PATIENT INFORMATION BOOKLET

Mildly to Moderately Nearsighted Patients (-1.0 to -6.0 diopters) (PRK)
or
Nearsighted Patients (0 to -6.0 diopters) With 0.75 to 4.0 Diopters of Astigmatism (PRKa)

Please read this entire booklet. Discuss its contents with your doctor so that all your questions are answered to your satisfaction. Ask any questions you may have before you agree to the surgery.

VISX, INCORPORATED
3400 CENTRAL EXPRESSWAY
SANTA CLARA, CA 95051-0703
U.S.A.

Tel: 408.733.2020

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INTRODUCTION

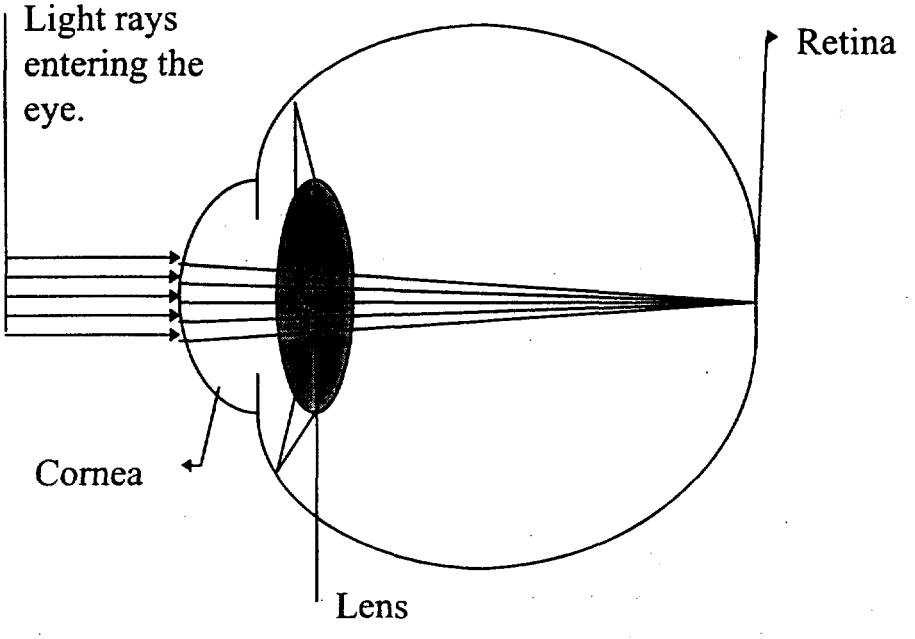
The information in this booklet is to help you decide whether or not to have Photorefractive Keratectomy (PRK or PRKa) laser surgery to correct or partly correct your nearsightedness (myopia) and/or astigmatism. Some other ways to correct nearsightedness and astigmatism are glasses, contact lenses and other kinds of refractive surgery such as radial keratotomy (RK) or automated lamellar keratectomy (ALK). PRK or PRKa is a completely different type of surgery from RK or ALK.

If both of your eyes are nearsighted and/or astigmatic, your doctor may recommend PRK or PRKa surgery for both eyes. However, sometimes it is better to have PRK or PRKa done on only one eye. Talk with your doctor about whether it would be better to treat one or both of your eyes.

Please read this booklet completely. Discuss any questions with your doctor before you decide if PRK or PRKa is right for you. Only an eye care professional trained and certified in PRK and PRKa can determine whether or not you are a suitable candidate. The vision requirements of some occupations, such as military pilots, cannot be met by having RK, ALK, PRK or PRKa.

HOW THE EYE FUNCTIONS

Normal Eye



of the cornea. PRKa flattens the central cornea by different amounts at different orientations to correct for the uneven focus of the rays of light.

During a regular eye examination, your doctor uses lenses to measure your nearsightedness and astigmatism in units called "diopters". The VISX Excimer Laser System is approved for correcting up to six diopters of nearsightedness and from 0.75 to 4.0 diopters of astigmatism.

WHAT ARE PRK AND PRKa?

PRK and PRKa are laser surgeries to correct nearsightedness (myopia) and nearsightedness with astigmatism, respectively. An excimer laser beam is used to flatten the front of the cornea. The laser beam removes small amounts of tissue from the front of the cornea. This differs from RK, which uses a knife to make deep cuts around the center of the cornea.

An excimer laser produces a powerful beam of ultraviolet light. The laser is controlled by the doctor. It produces a series of rapid pulses that removes small amounts of corneal tissue. Excimer laser light does not penetrate the eye and leaves other eye structures (iris, lens, retina) undisturbed.

PRK and PRKa surgery are performed on one eye at a time. The second eye can be treated if all goes well and vision stabilizes without complications or adverse reactions. Laser surgery of the second eye is usually done three months after the first eye, if needed.

In the U.S. clinical studies of the VISX Excimer Laser System for nearsightedness and astigmatism, 58% of eyes could see 20/20 or better without glasses after PRK and 33% of eyes could see 20/20 or better without glasses after PRKa. Ninety-four percent could see 20/40 or better after PRK and 87% could see 20/40 or better after PRKa. Even though their vision without glasses improved, some patients still needed glasses or contact lenses after PRK or PRKa. PRK or PRKa does not eliminate the need for reading glasses. NOTE: You may need reading glasses after laser surgery even if you did not wear them before.

BENEFITS

- PRK surgery, as performed with the VISX Excimer Laser System, is effective in reducing nearsightedness between -1.0 and -6.0 diopters in patients with less than or equal to 1.0 diopter of astigmatism.

The studies also showed that the following vision-threatening events happened less than 1% of the time after PRK surgery:

- Losing a significant amount of vision even with glasses
- Too large a correction (causing farsightedness)
- Visually significant corneal haze

For Astigmatism:

• Increased difficulty with night vision	22.6%
• Increased sensitivity to bright light	15.5%
• Double vision worse after surgery if present before surgery	5.9%
• Losing a significant amount of vision even with glasses	4.8%
• Visually significant corneal haze	1.2%

CONTRAINDICATIONS

You should **NOT** have PRK or PRKa surgery if:

- You have collagen vascular, autoimmune or immunodeficiency diseases (for example, lupus, AIDS).
- You are pregnant or nursing.
- You show signs of keratoconus (corneal disease).
- You are taking one or both of the following medications:
  Accutane (isotretinoin)
  Cordarone (amiodarone hydrochloride)

WARNINGS

Discuss with your doctor if:

- Your nearsightedness or astigmatism is changing.
- You are diabetic or have severe allergies.

between 0 and -6.0 diopters and between 0.75 and 4.0 diopters of astigmatism for PRKa.

- Have documented evidence that your refraction did not change by more than 0.50 diopter during the year before your pre-operative examination.
- Be informed of PRK or PRKa risks and benefits as compared to other available treatments for nearsightedness (myopia) and astigmatism.
- Be willing to sign an informed consent form, if provided by your eye care professional.

BEFORE THE SURGERY

If you are interested in having PRK or PRKa, you will need to have a pre-surgical examination to determine if your eye is healthy and suitable for PRK or PRKa. This will include a complete physical and eye history, and thorough examination of both eyes. In addition, computerized mapping of your cornea will be done to determine if it is smooth and properly shaped.

IMPORTANT:
If you wear contact lenses, it is very important to stop wearing them 2 - 4 weeks before the evaluation. Failure to do this will produce poor surgical results.

Before the surgery, please tell your doctor whether you take any medications or have any allergies. Also, talk with your doctor about eating or drinking immediately before the surgery. You should also arrange for transportation, since you must not drive immediately after the surgery. You can resume driving only after receiving permission from your doctor.

THE DAY OF SURGERY

Before the surgery you will be asked to listen to the sounds of the treatment so that you will be prepared for the noise the laser makes during surgery. Anesthetic (numbing) drops will be placed into the eye to be treated and you will be escorted into the room with the laser. You will lie on your back in a reclining chair and look up at a microscope that will deliver the laser light to your cornea. An instrument will be placed between your eyelids to hold them open during the surgery. There will also be a temporary shield covering the eye not having surgery.

The surgery begins with removal of the outermost layer of the cornea. This is done either with the laser or with a small spatula. After this has been completed, the doctor will reposition your head in the chair, and refocus the microscope.

IMPORTANT:

Use the anti-inflammatory eye drops and lubricants as directed by your doctor. Your surgical results depend upon your following your doctor's directions.

Long Term Post-Treatment Safety Problems

The following is a list of the adverse events and complications that occurred in patients **at approxmately 2 years** after treatment (the exact percentages are given in parentheses):

- **Overcorrection (by more than 1 diopter):** Farsightedness, which may need to be corrected with glasses or contact lenses (1.0% for nearsightedness).
- **Overcorrection (by more than 2 diopters):** Farsightedness, which may need to be corrected by glasses or contact lenses (0.6% for nearsightedness).
- **Worsening of Best Spectacle Corrected Vision :** Significant worsening of vision in the operated eye with the help of glasses (1.3% for nearsightedness, 4.8% for astigmatism).
- **Double Vision:** Shadows or ghost images around objects, judged by the patient to be worse than before the surgery (1.3% for nearsightedness, 5.9% for astigmatism).
- **Sensitivity to Bright Lights:** Difficulty tolerating bright lights, judged by the patient to be worse than before the surgery (1.7% for nearsightedness, 15.5% for astigmatism).
- **Increase in Astigmatism:** Uneven curving of the cornea of 1 or more diopters that may distort vision and require corrective glasses or contact lenses (2.9% for nearsightedness).
- **Difficulty with Night Vision:** Difficulty performing visual tasks in low light or at night that are performed without difficulty during the day, judged by the patient to be worse than before the surgery (3.1% for nearsightedness, 22.6% for astigmatism).
- **Increase in Intraocular Pressure:** Increase of pressure in the eye greater than 5 mm Hg that could, but may not necessarily, cause damage (3.6% for nearsightedness, 2.4% for astigmatism).
- **Corneal Haze:** A scar or cloudy cornea surface that may affect vision (0.2% for nearsightedness, 1.2% for astigmatism).

SELF-TEST

ARE YOU AN INFORMED AND EDUCATED PATIENT?

Take the test below and see if you can correctly answer these questions after reading this booklet.

	TRUE	FALSE
1. Excimer laser refractive surgery is risk free.	[ ]	[ ]
2. Excimer laser surgery is the same as radial keratotomy (RK).	[ ]	[ ]
3. It doesn't matter if I wear my contact lenses when my doctor told me not to.	[ ]	[ ]
4. The laser does all the work; I just have to lie on the chair.	[ ]	[ ]
5. After the surgery, there is a good chance that I will be less dependent on eye glasses.	[ ]	[ ]
6. I may need reading glasses after laser surgery.	[ ]	[ ]
7. There is a risk that I may lose some vision after laser surgery.	[ ]	[ ]
8. It doesn't matter if I am pregnant.	[ ]	[ ]
9. If I have an auto-immune disease, I am still a good candidate for PRK or PRKa.	[ ]	[ ]

Answers to SELF-TEST are found at the bottom of page 12.

PATIENT ASSISTANCE INFORMATION

PRIMARY EYE CARE PROFESSIONAL

Name: _____

Address: _____

Phone: _____

PRK/PRKa DOCTOR

Name: _____

Address: _____

Phone: _____

TREATMENT LOCATION

Name: _____

Address: _____

Phone: _____

LASER MANUFACTURER:

VISX, Incorporated
3400 Central Expressway
Santa Clara, CA 95051
U.S.A.

Tel: 408.733.2020

VISX™ EXCIMER LASER SYSTEM
PHOTOREFRACTIVE KERATECTOMY
for Nearsightedness with Astigmatism
(PRKa)

PROFESSIONAL USE INFORMATION

RESTRICTED DEVICE: U.S. Federal Law restricts this device to sale, distribution, and use by or on the order of a physician or other licensed eye care practitioner. U.S. Federal Law restricts the use of this device to practitioners who have been trained in its calibration and operation, and who have experience in the surgical management and treatment of refractive errors.

This document provides information concerning the intended clinical use of the VISX Excimer Laser System. For complete information concerning system components, safety instructions, installation, maintenance, and troubleshooting, refer to the VISX Excimer Laser System *Operator's Manual.*

Carefully read all instructions prior to use. Observe all contraindications, warnings, and precautions noted in these instructions. Failure to do so may result in patient and/or user complications.

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Tel. 408.733.2020

*Revision	Description	Date	ECN #
A	Product Release	04/22/97	5807

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GENERAL WARNINGS

- **RESTRICTED DEVICE:** U.S. Federal Law restricts this device to sale, distribution, and use by or on the order of a physician or other licensed eye care practitioner. U.S. Federal Law restricts the use of this device to practitioners who have been trained in its calibration and operation, and who have experience in the surgical treatment and management of refractive errors.

- Performance of procedures, use of controls, or any other adjustments other than those specified herein may result in a hazardous condition.

- Never operate the laser in the presence of flammable anesthetics or other volatile substances, such as alcohol.

- All patients must be given the opportunity to read and understand the Patient Information Booklet, and to have all their questions answered to their satisfaction before giving consent for Photorefractive Keratectomy for nearsightedness with astigmatism (PRKa) surgery.

- **GAS HANDLING:** High pressure gas cylinders are contained in a protected compartment within the VISX Excimer Laser System. Storage of additional cylinders and the replacement of used cylinders must be done in accordance with the Safe Operating Procedures outlined in the *Operator's Manual* (Section 3.7, Chapter 3).

  The premix (argon/fluorine) gas mixture used in this laser system is highly toxic. VISX, Incorporated recommends that anyone working with the gas cylinders: 1) be trained in the proper handling of toxic and compressed gases, 2) know the location of the emergency exhaust fan/room purifier switch, 3) have easy access to protective respirators, and 4) be familiar with safety procedures provided by the site's safety officer. Gas discharge into the atmosphere may be evidenced by a sharp, penetrating odor, and eye, nose, and throat irritation.

- **SKIN AND EYE EXPOSURE:** The VISX Excimer Laser System contains a Class IV laser with an output at 193 nm, which is potentially hazardous to the skin and the surface layers of the cornea. This laser radiation will not enter the eye and poses no threat to retinal structures or the crystalline lens. The fixed optical system restricts the beam path which is bounded by the operating table or the floor. Reflectivity from objects in operating rooms, including surgical instruments, is extremely low for 193 nm radiation.

  The area of potential hazard (Nominal Hazard Zone) for production of a photochemical keratitis has been determined to be less than 40 cm from the primary beam. All healthcare personnel should avoid direct exposure to the skin or eye by the primary beam. While no hazard may exist further than 40 cm from the beam, the use of protective eyewear is recommended if the possibility exists that healthcare personnel will approach closer than this distance from the primary beam.

1.0 DEVICE DESCRIPTION

The VISX Excimer Laser System is designed to create a superficial lamellar keratectomy on exposed corneal tissue. Corneal tissue is removed by a process known as *Ablative Photodecomposition.* Ablative Photodecomposition occurs when far-ultraviolet radiation reacts with organic molecules, resulting in the photochemical breakdown of the molecular bonds without a significant local thermal effect. The source of the far-ultraviolet photons is a high efficiency, gas discharge excimer laser that electronically excites a combination of argon and fluorine, producing an ultraviolet wavelength of 193 nm.

Features and components of the VISX Excimer Laser System include:

Excimer Laser — An argon-fluoride excimer laser module, with an output wavelength of 193 nm.

Gas Management System — A gas cabinet containing a working gas cylinder for laser operation; a gas cleaning system; a gas leak audio alarm with a sensor to detect fluorine (one part-per-million); a gas discharge system, using an activated charcoal filter to absorb fluorine; an emergency safety system using a positive-action solenoid safety valve, which automatically seals the premix cylinder in the event of a power failure; and a second charcoal scrubber to neutralize fluorine in case of a leak.

Laser Beam Delivery System — Beam shaping and homogenizing optics designed to produce a uniform, coaxial beam profile; a spatial integrator and beam rotator for temporal integration; and an iris diaphragm and rotating slit blades used to shape the beam.

Patient Management System — An operating microscope with reticle, used to observe a patient procedure and to facilitate accurate focus and laser beam alignment; a debris-removal system designed to evacuate the debris plume that occurs during ablation; a patient operating chair used to align the patient for treatment; a video camera and monitor used to record and monitor patient treatment; an illumination device used to illuminate the patient's eye for observation and treatment; and a fixation LED used by the patient to maintain proper alignment during treatment.

Computer Control — An IBM-compatible computer and video monitor; a computer keyboard with trackball (MODEL C) or mouse (MODEL B) for user interface; a printer; a VisionKey card driver; and system software.

VisionKey Card — A write-once-read-many (WORM) optical memory card designed to allow compilation, storage, and printout of essential patient data and procedural information.

2.0 INDICATIONS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS AND ADVERSE EVENTS

2.1 INDICATIONS FOR USE

Photorefractive Keratectomy for Nearsightedness with Astigmatism (PRKa) procedure using the VISX Excimer Laser System is intended for use:

- In PRKa treatments for the reduction or elimination of mild to moderate myopia between 0 and -6.0 D spherical myopia at the spectacle plane (with a vertex distance of 12.5 mm), and concomitant reduction or elimination of refractive cylinder of not less than 0.75 D and not more than 4.0 D at the spectacle plane (with a vertex distance of 12.5 mm) as determined by minus cylinder refraction.

- In patients with documented evidence of a change in manifest refraction of less than or equal to 0.5 D (in both cylinder and sphere components) per year for at least one year prior to the date of pre-operative examination.

- In patients who are 21 years of age or older.

Caution must be used to calculate treatment in MINUS CYLINDER at the spectacle plane (vertex distance 12.5 mm) before entering the refraction information into the laser in order to conform with the Indications for Use.

Refer to the preceding General Warnings section of this *Professional Use Information Manual,* in addition to the warnings and precautions found in this section.

2.2 CONTRAINDICATIONS

PRKa surgery is contraindicated:

- In patients with collagen vascular, autoimmune or immunodeficiency diseases.

- In pregnant or nursing women.

- In patients with signs of keratoconus.

- In patients who are taking one or both of the following medications:
  - isotretinoin (Accutane)
  - amiodarone hydrochloride (Cordarone)

2.3 WARNINGS

- The decision to perform PRKa surgery in patients with systemic disease likely to affect wound healing, such as connective tissue disease, diabetes, severe atopic disease or an immunocompromised status, should be approached cautiously. The safety and

- Glaucoma is more common in myopic patients than in the general population. Evaluation of the optic nerve and measurement of the intraocular pressure are necessary. If there are any concerns regarding the appearance of the optic nerve, a Humphrey 24-2 Fastpac or equivalent threshold test of the visual field should be performed. If elevated intraocular pressure and/or evidence of glaucomatous damage are found, topical steroids should be used only with careful medical supervision or the patient should not undergo PRKa 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.

- Baseline evaluation of patients requesting refractive surgery should be performed within 30 days of the PRKa surgery.

- 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 PRKa procedure.

- The patient must be able to understand and give an informed consent.

- The patient should be clearly informed of all alternatives for the correction of myopia and/or astigmatism, including but not limited to spectacles, contact lenses and other refractive surgeries such as radial keratotomy.

2.4.3 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. The area of potential hazard (Nominal Hazard Zone) for production of a photochemical keratitis has been determined to be less than 40 cm from the primary beam. All healthcare personnel should avoid direct exposure to the skin or eye by the primary beam. While no hazard may exist further than 40 cm from the beam, the use of protective eyewear is recommended if the possibility exists that healthcare personnel will approach closer than this distance to the primary beam.

2.4.4 POST-PROCEDURE

A slit-lamp examination should be performed on a daily basis until re-epithelialization is complete. After re-epithelialization, the following examinations are recommended at a schedule of at least 1, 3, 6, and 12 months:

- Uncorrected Visual Acuity (UCVA or VA-sc).

- Manifest refraction with the Best Spectacle Corrected Visual Acuity (BSCVA or VA-cc).

Table 2-1
Adverse Events
(n=116)

Adverse Events	6M (n=108)		12M (n=92)		Final Visit* (n=82)	
	n	%	n	%	n	%
1. Increased Difficulty with Night Vision♦	28	25.9%	17	18.5%	19	22.6%
2. Worsening of Patient Symptoms♠: "Sensitivity to Bright Lights"	18	16.7%	12	13.0%	13	15.5%
3. Loss of ≥2 lines BSCVA						
Due to Any Cause	5	4.8%	6	6.7%	7	8.5%♠
Due to Corneal Causes	4	3.8%	4	4.5%	4	4.8%♠
4. Pre-treatment BSCVA 20/20 or Better with Post-treatment BSCVA Worse than 20/25⊗	5	4.8%	4	4.5%	5	6.1%
5. Worsening of Patient Symptoms♠: "Double Vision"	6	5.6%	5	5.4%	5	5.9%
6. Secondary Surgical Intervention Retreatments	0	0.0%	4	4.3%	5	5.9%
7. IOP Increase > 5 mm Hg < 10 mm Hg	8	7.4%	2	2.2%	2	2.4%
8. Corneal Haze ≥ Grade 2	2	1.9%	4	4.3%	1	1.2%
9. Pre-treatment BSCVA 20/20 or Better with Post-treatment BSCVA Worse than 20/40⊗	0	0.0%	2	2.2%	0	0.0%
10. Secondary Surgical Intervention Other Refractive Procedures	0	0.0%	1	1.1%	0	0.0%

Percentages of adverse events are reported as:

$$\frac{\text{number of eyes with at least one occurrence observed/reported at the specified study visit}}{\text{number of eyes examined at the specified study visit}}$$

♠ Includes two eyes in one patient who had cataract formation upon enrollment and one eye of one patient who had a stroke; these losses of BSCVA were not attributed to corneal wound healing. **At no time did any eye lose BSCVA beyond 20/50 and at the Final Visit no eye was worse than 20/40-1.**

⊗ Visual acuities were taken from the ETDRS standard and may have (+) and (-) designations.

♣ Reflects the number of eyes where these symptoms as occurring 'often or always' post-treatment and worse than pre-treatment. Post-retreatment data are not included.

♦ Reflects the number of eyes where this symptom was reported as significantly worse than pre-treatment. Post-retreatment data are not included.

* The final visit occurred at 24 ± 3 months after treatment.

3.0 CLINICAL RESULTS

3.1 INTRODUCTION

A prospective, non-randomized, unmasked, multicenter PRKa clinical study was conducted. The refractive inclusion criteria specified that the primary eye have myopia of 1.0 to 6.0 D spherical equivalent with between -0.75 and -4.5 D of refractive astigmatism. There were a total of 116 eyes treated (71 primary eyes and 45 fellow eyes). Patients who exhibited any of the following conditions were excluded: keratoconus; active ocular disease likely to affect wound healing; unstable central keratometry readings with irregularly shaped mires; use of systemic medications likely to affect wound healing; or immunocompromise.

3.2 ABOUT THE STUDY

One hundred and sixteen (116) eyes were treated. These eyes were treated between August 1993 and June 1995. The patients were evaluated pre-operatively, every 24 to 48 hours post-operatively until re-epithelialization, and at 1, 3, 6, 12, and 21 months or later after-treatment. Eyes were analyzed for: reduction of astigmatism, vector analysis of intended versus achieved refractive correction, residual refractive cylinder, stability of refractive correction over time and uncorrected visual acuity. Additional parameters were analyzed by closely examining best spectacle visual acuity losses of two lines or more (significant losses), endothelial cell counts, contrast sensitivity results, glare results, patient subjective symptoms (e.g., worsening of double vision, sensitivity to bright lights and night vision disturbances), clinical signs (e.g., haze) and IOP increases in addition to the adverse events as reported by the investigators and monitored throughout the course of the study.

3.3 PATIENT ACCOUNTABILITY

One hundred and sixteen (116) eyes of 71 subjects, treated at five centers in the United States, were used for safety and effectiveness analyses. Eighty two eyes out of 91 were available for followup visits at 24 months or longer.

3.4 DATA ANALYSIS AND RESULTS

3.4.1 PRE-OPERATIVE CHARACTERISTICS

Pre-operative characteristics for the 116 eyes are presented in Table 3-1.

Table 3-3
Final Visit UCVA of Cohort Eyes Stratified by Diopter of Pre-Operative Cylinder (n=82*)

	0.75-1.0			1.1-2.0			2.1-3.0			3.1-4.0		
	PE	FE	All	PE	FE	All	PE	FE	All	PE	FE	All
≥20/20	6	6	12	11	7	18	2	1	3	0	0	0
<20/20-20/30	7	1	8	13	6	19	2	4	6	1	0	1
<20/30-20/40	2	0	2	1	3	4	0	1	1	1	0	1
<20/40-20/50	0	1	1	2	0	2	0	1	1	0	0	0
<20/50-20/60	0	0	0	0	0	0	0	0	0	0	0	0
<20/60-20/70	0	0	0	0	0	0	0	0	0	0	0	0
<20/70-20/100	0	1	1	1	0	1	0	1	1	0	0	0
<20/100-20/200	0	0	0	0	0	0	0	0	0	0	0	0
<20/200-20/800	0	0	0	0	0	0	0	0	0	0	0	0
CF or Worse	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	15	9	24	28	16	44	4	8	12	2	0	2

*UCVA data for 2 eyes were not available at this visit.

Table 3-4
Summary of Sphere, Cylinder Magnitude and Axis (n=116)

	6 Months (n=106)*		12 Months (n=89)◆		Final Visit (n=82)†	
Sphere (SIRC/IRC)	3.18/3.27	(97.2%)	3.30/3.36	(98.2%)	3.22/3.31	(97.3%)
Cylinder (SIRC/IRC)	1.25/1.47	(85.0%)	1.18/1.43	(82.5%)	1.14/1.44	(79.2%)
Mean absolute vector axis error	7.2 degrees		10.49 degrees		11.5 degrees	
Mean vector magnitude error	-0.22 D		-0.25 D		-0.3 D.	

*The refractive data for 2 eyes are not available for this visit.
◆The refractive data for 3 eyes are not available for this visit.
†The refractive data for 2 eyes are not available for this visit.

3.4.2.2 Reduction of Mean Spherical Equivalent

The mean spherical equivalent (S.E.) was reduced at all time periods examined (Table 3-5). Not all eyes were targeted for emmetropia; the mean target was -0.10 D. The mean pre-treatment manifest refractive S.E. was -4.34 D. The mean S.E. was reduced by 92.9% at the final visit.

Table 3-5
Reduction of Mean Spherical Equivalent

	6-Month (n=106)Ψ	12-Month (n=89)"	Final Visit (n=82)§
Mean	4.06	4.15	4.03
Median	4.19	4.13	4.13
SD	1.72	1.60	1.64
Min	-0.88	0.88	0.00
Max	8.00	8.63	8.63

ΨThe refractive data for 2 eyes are not available for this visit.
"The refractive data for 3 eyes are not available for this visit.
§The refractive data for 2 eyes are not available for this visit.

Table 3-6
Retreatment Visual Acuity for Cohort Eyes (n=9)

	Pre-Treatment		Pre-Retreatment		Post-Retreatmentφ	
Patient	UCVA	BSCVA	UCVA	BSCVA	UCVA	BSCVA
1	80-2	25+3	50	20-2	25	20
2	400	20-2	80+4	25	60	20
3	CF	20	40	20	20	20
4	CF	25	50+3	25-1	25-3	25-1
5	400	12	50-2	15	30	20-3
6	CF	20	25+2	20	25+1	20
7	80	20	50	20	30	20
8	200	15	20-1	15	30	15
9	125	10	50	15	30	15

*The data listing indicates this BSCVA to be 20/80+4 in error; the correct value is included for accuracy.
φLast visit available.

3.4.4 CYLINDER AXIS SHIFT

Table 3-7
Distribution of Axis Shift between Pre-Op and Final Visit Stratified by Pre-Op Cylinder (n=82)[ξ]

Axis Shift (degrees)	0.75 - 1.0 (n=24)	1.1 - 2.0 (n=44)	2.1 - 3.0 (n=12)	3.1 - 4.0 (n=2)
0-15	21	33	9	2
16-30	1	7	2	0
31-45	1	2	0	0
46-60	1	1	0	0
61-75	0	0	0	0
76-90	0	1	1	0

[ξ]The refractive data for 2 eyes are not available for this visit.

3.4.5 ADVERSE EVENTS

Refer to Table 2-1 in Section 2.5.

4.0 SURGICAL PLANNING AND PROCEDURES

After reading this section, please refer to the step-by-step procedure provided in Section 5, *Step-By-Step Procedure*, before proceeding with the surgery.

4.1 INTRODUCTION

PRKa is a procedure using the energy of the excimer laser to create a superficial lamellar keratectomy of a shape designed to correct or ameliorate a specific refractive error. It is essential that the refractive information upon which this surgical procedure is based is accurate and is correctly transmitted to the laser. **It is the sole responsibility of the operating doctor to ensure the information for each individual patient is accurate.**

4.2 PRE-OPERATIVE (EXAMINATION OF THE PATIENT)

A complete examination, including, but not limited to, cycloplegic evaluation, must be performed. The lens must be evaluated to assure that nuclear sclerosis or any other lens opacity is not present prior to laser surgery, as these opacities may adversely affect the end surgical result. Direct and indirect ophthalmoscopy through a dilated pupil are essential. Evaluation of the optic nerve and measurement of IOP are necessary. If there are any concerns regarding the appearance of the optic nerve, a Humphrey 24-2 Fastpac or equivalent threshold test of the visual field should be performed. Pre-operative corneal mapping is essential on all patients to exclude topographical abnormalities. Baseline evaluation of patients with myopia desiring refractive surgery should be performed within 30 days of PRKa surgery.

Patients who wear soft contact lenses must discontinue their use for at least 2 weeks and those who wear gas permeable or hard lenses must discontinue their use for at least 3 weeks. Failure to do so will adversely affect the end surgical result.

4.3 PERI-OPERATIVE (ANESTHESIA AND ANALGESIA)

Extensive clinical experience has shown that PRKa excimer surgery is well tolerated and rarely causes significant pain. For this reason, systemic sedatives and injected local anesthetics are not required. Topical anesthesia applied just before insertion of the lid speculum will provide adequate control of pain during the surgery. For those patients with a high degree of anxiety, appropriate medication may be given pre-operatively.

4.4 INTRA-OPERATIVE (EPITHELIAL REMOVAL)

4.4.1 MECHANICAL TECHNIQUE

This technique for epithelial removal is accomplished with a blunt instrument such as a Paton spatula. The region of epithelial removal should be at least 6.0 mm in diameter. After the stromal bed is cleaned of debris, a non-fragmenting sponge should be saturated with balanced sterile saline and squeezed out and wiped over the ablation bed. The PRKa treatment can then be performed.

5.0 VISX EXCIMER LASER SURGICAL PROCEDURES

Before proceeding, please refer to the laser preparation and shut-down procedures presented in the VISX Excimer Laser System *Operator's Manual*, Chapter 7, *Operating Instructions*.

The VISX Excimer Laser System contains a Class IV laser with an output at 193 nm, which is potentially hazardous to the skin and the surface layers of the cornea. This laser radiation will not enter the eye, and poses no threat to retinal structures or the crystalline lens. However, the fixed optical system restricts the beam path, which is bounded by the operating table or the floor. Reflectivity from objects in operating rooms (including surgical instruments) is extremely low for 193 nm radiation.

The area of potential hazard (Nominal Hazard Zone) for production of a photochemical keratitis has been determined to be less than 40 cm from the primary beam. All healthcare personnel should avoid direct exposure to the skin or eye by the primary beam. While no hazard may exist further than 40 cm from the beam, the use of protective eyewear is recommended if there is a possibility that healthcare personnel will approach closer than this distance from the primary beam.

The *Professional Use Information Manual* is to be used in conjunction with the VISX Excimer Laser System *Operator's Manual*. Refer to the *Operator's Manual* regarding designated sections listed in Section 5.1.

5.1 STEP-BY-STEP PROCEDURE

1. Power ON the system.

2. Complete all daily calibrations, as described in the VISX Excimer Laser System, *Operator's Manual*, Section 6, *Daily Calibrations*.

3. Prepare a VisionKey card with patient information and parameters for the PRK or PRKa procedure as described in the *Operator's Manual*, Chapter 2, *Device Description—Interactive Computer Menus*. This may be done in advance of treatment.

Ablate a -4.0 D, 6.0 mm lens after every THIRD treatment to verify the calibration of the VISX Excimer Laser System. Refer to the *Operator's Manual*, Chapter 6, *Daily Calibrations*, for additional information on the calibration procedure.

4. Ensure that all persons in the operating room obey all safety regulations. Caution all attendees in the operating room against touching the laser, patient, or patient chair during the procedure. Movement of personnel in the operating room should be minimized during the procedure. It is recommended that all attendees, including the doctor, wear surgical masks and protective eyewear.

5. Allow the patient the opportunity to become familiar with the sounds of the laser during the calibration procedure.

6. Insert the VisionKey card into the card drive when prompted by the system software. Follow the system software prompts. If the card has been preprogrammed, **verify that the card corresponds with the patient to be treated.** Add any additional data to the PRKa

several seconds, the pillow will harden and conform to the patient's head. This creates a comfortable, stable platform for the patient. Disconnect the tubing after the pillow has hardened.

16. Position the patient with the microscope set at low zoom magnification. When the cornea is visible in the microscope, focus the image of the cornea and increase the magnification. Refer to the *Operator's Manual*, Chapter 2, *Device Description—Microscope*. Instruct the patient to begin fixating on the blinking red fixation light.

17. Move the patient so the microscope reticle is centered over the patient's pupil. Chair movement is controlled by the doctors keypad. Refer to the *Operator's Manual*, Chapter 2, *Device Description*, for information regarding chair movement.

The microscope oculars must be properly focused to accommodate the Doctor's refraction. This will assure that the microscope focal plane and the laser focal plane are coincident.

18. Continually encourage the patient to maintain fixation on the blinking red fixation light throughout the procedure.

19. Verify that all color status bars are green in the procedure screen of the system software. If a yellow status bar is displayed, you may continue with the procedure; however, a condition exists that warrants attention as soon as possible after completion of treatment. A red status bar will prevent system operation. Therefore, any interlock must be cleared prior to a treatment.

20. After verification of green system status bars, warn all attendees to stand clear of the laser, patient, and patient chair. Accidental bumping of the laser, patient, or patient chair during the surgery can cause decentering of the treatment area. Movement in the operating room must be kept to a minimum during patient treatment.

21. Insert a closed blade speculum into the eye to hold the eyelid open. If using mechanical epithelial removal, a 6.0 or 6.5 mm marker can be used centered over the entrance pupil and gently depressed onto the epithelial surface. If the laser scrape technique is to be used then there is no need to mark the epithelium.

22. Epithelial removal is best performed using the ring illuminator, with the illumination on the lowest setting that allows good visualization of the epithelial surface while not causing the patient discomfort. This is accomplished by setting the ring illuminator on low power and gradually increasing illumination until the epithelial surface is comfortably in view. Visibility of the the red blinking fixation light by the patient is facilitated by low operating illumination.

23. After confirming the pupillary centration of the 6.0 or 6.5 mm marker, mechanical removal is facilitated by placing one or two drops of anesthetic in the operative eye prior to commencing the surgical procedure. Many light even strokes at a fixed site may be necessary to start the mechanical epithelial removal process. Avoid hard pressure that deforms the cornea. Use rapid, even strokes until the epithelium is completely removed. Mechanical epithelial removal can be accomplished with either a blunt spatula or a small blade such as a Beaver 64. If a sharp instrument is used take care not to disrupt Bowman's layer. If the patient has not had adequate pre-operative topical anesthesia, place a 6.0 mm anesthetic soaked pledget on the cornea prior to removal of the epithelium. Remove the pledget after 60 seconds. If laser scrape epithelium removal is to be used, place one or two drops of anesthetic in the operative eye prior to commencing

The doctor may interrupt the procedure for any reason, at any time, by releasing the laser footswitch. This may be done if the patient should move and the treatment area becomes decentered. The doctor then realigns the eye and continues the procedure by depressing the laser footswitch again. The procedure will automatically start from the point of interruption.

29. Lower the patient chair to its lowest position, then rotate the patient chair from under the laser while carefully monitoring patient clearance. Remove the eye shield from the untreated eye.

30. Place appropriate post-operative medications in the treated eye. Following application of medication, apply a firm pressure patch to the eye.

31. Raise the chair backrest to a sitting position. Assist the patient in putting on any spectacles, and escort them to a waiting area.

32. Ensure that the patient is given post-operative instructions. An analgesic may be given to the patient prior to leaving the facility.

33. Review post-operative instructions, confirm the first follow-up appointment, and discharge the patient when stable.

34. Clean the debris removal nozzle with isopropanol wipes and prepare the system for the next patient.

WARNING! Never operate the laser in the presence of flammable anesthetics or other volatile substances, such as alcohol.

WARNING! Warn the patient about the hazards of driving immediately after surgery. The combination of analgesic and eye patch can be very dangerous.

6.0 EMERGENCY STOP

If a system emergency situation arises, press the **Emergency Stop** button located on the front control panel (Model B) or the **Laser Stop** button located on the doctor's panel (Model C). This will power OFF the system; however, the gas cleaning and gas detector systems will continue to operate. When the emergency condition no longer exists, turn the button in the direction of the arrows; turn the System Power Key first OFF and then ON; then power ON the system using the **System Power** button, which will re-energize the laser.

If the emergency appears to involve the electrical system (visible smoke, fire, etc.), switch OFF the wall mounted electrical disconnect switch.