SUMMARY OF SAFETY AND EFFECTIVENESS DATA
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
PMA Application Supplement Number:	P930016/S5
Date of Notice of Approval to Applicant:	January 29, 1998

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 (D) of myopia with astigmatism of ≤ 1.0 D whose refractive change for one year prior to treatment is within ± 0.5 D.

On April 24, 1997 the expanded indication for PRK with astigmatism (PRKa) was approved in 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 21 years of age or older 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.

The sponsor submitted this supplement to further 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, 5630 Fishers Lane, rm. 1061, Rockville, MD 20857 under Docket # 97M-0084 or you may download the file from the internet site *http://www.fda.gov/cdrh/pdf/p930016.pdf.*

II. INDICATIONS FOR USE

Photorefractive Keratectomy (PRK) procedure using the VISX Excimer Laser System is intended for use:

- 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

- in patients 18-20 years of age in PRK treatments for the reduction or elimination of myopia (nearsightedness) of less than or equal to -6.0 D spherical equivalent at the corneal plane with less than or equal to -1.0 D of astigmatism; or

- in patients 21 years of age of older in PRK treatments for the reduction or elimination of myopia (nearsightedness) of between 0 and -12.0 D spherical myopia at the spectacle plane and up to -4.0 D of astigmatism.

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

III. CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

A. Contraindications:

PRK 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 PRK 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.

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

C. Precautions:

General

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

- For PRK treatment of astigmatism in patients with refractive cylinder of less than 0.75 D.

- In patients with progressive myopia or astigmatism, 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.

- For patients under 21 years of age with myopia greater than 6.0 D and astigmatism greater than 1.0 D.

- For patients under 18 years of age.

- Over the long term: More than 3 years after surgery for low myopia and more than 1 year after surgery for high myopia with astigmatism.

- In patients with a history of keloid formation.

- In patients who are taking sumatripin (Imitrex)

Because of the low numbers of patients (10.5%, 21/200) with myopia between the 10 and 12 diopters treated in these trials, there may not have been a sufficient population to determine the level of effectiveness or the complication rates for this refractive error range.

There is no safety and effectiveness information for refractive treatments greater than –12.0 D of myopia or greater than –4.0 of astigmatism

Ablation of corneal stroma to less than 200 μm from the endothelium may result in corneal ectasia.

The effects of PRK on visual performance under poor lighting conditions have not been determined. It is possible, following PRK treatment, that patients will find it more difficult than usual to see in conditions such as very dim light, rain, snow, fog, or glare from bright lights at night. Astigmatic 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 under these conditions.

Patient Selection

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

- 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, an adequate 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 PRK surgery.

- Pre-operative corneal mapping is essential on all patients to exclude topographical abnormalities. This is especially important when astigmatism or steep keratometry readings are present, which may indicate the presence of keratoconus or other irregularities.

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

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

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

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 remain 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 or 6 hertz
Fluence :	160 mJ/cm^2
PRK 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 PRK myopia treatment from 0 to -12.0 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 nearsightedness with or without astigmatism are: spectacles, contact lenses or refractive surgery.

VI. MARKETING HISTORY

VISX has over 450 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 PRK include: loss of best spectacle corrected visual acuity, worsening of best spectacle corrected visual acuity, 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 200 eyes was conducted at two international investigation sites: 155 eyes from University of Ottawa Eye Institute (Ottawa, Canada), and 45 eyes from Moorfields Eye Hospital (London, England).

A. Study objective

The objectives of the clinical investigation of the VISX Excimer System for PRK 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 21 years or older and must have signed an informed consent form. Enrollment occurred if the subject met these conditions: -1.0 to -20.0 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; mires 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 21 years of age, spherical or cylindrical portion of manifest refractive has progressed at a rate of more than 0.50 diopter per year from date of baseline exam, cylindrical component of the manifest refraction is greater than 4.0 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, 6 and 12 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 distance 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.

Treatment 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 treatment 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 12 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 Fisher'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
Eyes (n=200)

	n	First Treatment	Last Treatment
Ottawa Eye Inst.	155	3/1/94	9/3/96
Moorfields Eye Hosp	45	7/5/95	5/22/96

2. Investigational Sites

Table 2 Investigators/Investigation Sites (N=200)		
Investigator	Site	Primary Eyes (Fellow Eyes)
W. Bruce Jackson	Ottawa Eye Institute Ottawa, Canada	113 (42)
Julian D. Stevens	Moorfields Eye Hospital London, England	44 (1)

3. Demographics and Baseline Characteristics

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

Table 3 Patient Demographic Information			
157 Patients	Male	Female	All Patients
# Eyes	60	97	157
Mean Age (years)	39.0 ± 9.2	38.5 ± 9.2	38.7 ± 9.2
Age Range (years)	20 to 61	20 to 58	20 to 61

Baseline Characteristics:

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

Table 4 Pre-Op Refractive Error Stratified by Diopter Sphere and Cylinder (N=200)							
Pre-Op Cylinder	Pre-Operative Sphere						Total n (%)
	6.1 to 7.0 n=87	7.1 to 8.0 n=49	8.1 to 9.0 n=27	9.1 to 10.0 n=20	10.1 to 11.0 n=10	11.1 to 12.0 n=7	
0.00	20	10	4	3	1	1	39 (19.5)
0.01 to 1.00	36	20	13	10	4	4	87 (43.5)
1.01 to 2.00	23	14	9	4	4	2	56 (28.1)
2.01 to 3.00	7	2	0	2	1	0	12 (6.0)
3.01 to 4.00	1	3	1	1	0	0	6 (3.0)

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. All eyes treated are included in the accountability table below (Table 5).

Table 5
Accountability of All Eyes
Eyes Eligible for Follow-Up (as of 5/31/97)
N=200

Category	6 Months	12 Months
Eyes Enrolled	**200**	**200**
Drop-Outs		
Retreated	0	3
Withdrew	0	1
Not Yet Due/Overdue for Exam	0	25
Total Eyes Eligible	**200**	**171**
(Minus)		
Not Examined (or Missed Visit)	1	15
Accountability		
# Follow-Up Exams	199	156
% Follow-up		
of Eligible Eyes	199/200 (99.5%)	156/171 (91.2%)
of Enrolled Eyes	199/200 (99.5%)	156/200 (78.0%)

b. Effectiveness Results

(1) Uncorrected Visual Acuity (UCVA)

163 eyes (81.5%) had a pre-operative spherical component between 6 and 9 diopters, however, 37 eyes (18.5%) had between 9 and 12 diopters of sphere. All eyes were worse than 20/200 without correction prior to treatment and 72% (144/200) had an uncorrected visual acuity of 20/800 or worse before treatment. At 12 months following treatment, 140/156 (89.7%) of eyes were 20/40 or better, 125/156 (80.1%) were 20/30 or better and 79/156 (50.6%) were 20/20 or better without correction. No eye was worse than 20/200 unaided. Table 6 presents the 12-month post-treatment uncorrected visual acuity (UCVA) data sorted by pre-operative sphere.

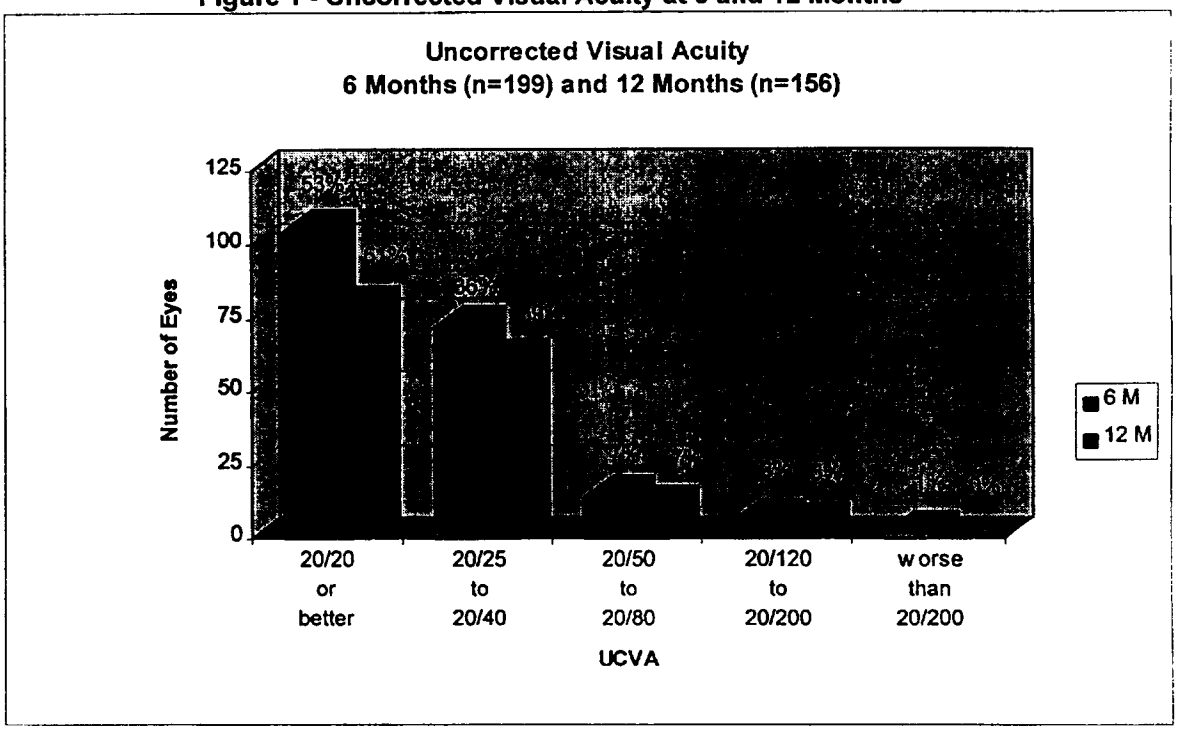
Figure 1 presents the Uncorrected Visual Acuity at 6 and 12 months in the following groups: 20/20 or better, 20/25 to 20/40, 20/50 to 20/80, 20/120 to 20/200 and 20/400 or worse. At 6 months, 89% (177/199) of

eyes were 20/40 or better uncorrected, and at 12 months this proportion rose to 90% (140/156). No eye had a UCVA worse than 20/200 at 12 months.

Table 6
12-Month UCVA Stratified by Diopter of Pre-Operative Sphere (N=156)

12-Month UCVA	Pre-Operative Sphere						Total n (%)
	6.1 to 7.0 n=71	7.1 to 8.0 n=38	8.1 to 9.0 n=20	9.1 to 10.0 n=15	10.1 to 11.0 n=7	11.1 to 12.0 n=5	
20/12-15	13	4	6	1	0	0	24 (15.4)
20/20	24	23	5	2	0	1	55 (35.3)
20/25	11	2	1	3	1	2	20 (12.8)
20/30	10	7	2	2	3	2	26 (16.7)
20/40	5	1	3	3	3	0	15 (9.6)
20/50-60	3	0	2	4	0	0	9 (5.8)
20/70-80	2	0	0	0	0	0	2 (1.3)
20/120-160	1	1	1	0	0	0	3 (1.9)
20/200	2	0	0	0	0	0	2 (1.3)

Figure 1 - Uncorrected Visual Acuity at 6 and 12 Months



(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 12-month visit, 126/156 (80.8%) are 20/20 or better and 153/156 (98.1%) are 20/40 or better. Three eyes had a postoperative BSCVA that was worse than 20/40, although none was worse than 20/80. One of these eyes had progressive nuclear sclerosis which decreased the BSCVA from 20/20 to 20/80 (this patient later recovered BSCVA to 20/20 following lens extraction). The reduction of BSCVA in the other two eyes were attributed to an anomalous refraction and decentered ablation (which later recovered to 20/30) in one eye and an irregular astigmatism in the other eye (this eye was 20/40 at pre-op).

Table 7
12-Month BSCVA Stratified by Diopter of Pre-Operative Sphere (N=156)

Post-Op BSCVA	Pre-Operative Sphere						Total n (%)
	6.1 to 7.0 n=71	7.1 to 8.0 n=38	8.1 to 9.0 n=20	9.1 to 10.0 n=15	10.1 to 11.0 n=7	11.1 to 12.0 n=5	
20/10-12	13	2	4	2	0	0	21 (13.5)
20/15-16	25	12	6	1	0	0	44 (28.2)
20/20	25	19	5	7	3	2	61 (39.1)
20/25	4	3	3	1	2	2	15 (9.6)
20/30	2	2	0	3	2	1	10 (6.4)
20/40	0	0	2	0	0	0	2 (1.3)
< 20/40	2^	0	0	1*	0	0	3 (1.9)

* 6885115-2 (20/40 to 20/60—due to irregular astigmatism)
^ 0189 (20/16 to 20/60—due to an anomalous refraction and decentered ablation) and 9411-1 (20/20 to 20/60—due to progressive nuclear sclerosis)

(3) **Vector Analysis**

A vector analysis of refractive corrections was performed for the pre-treatment and post-treatment manifest refraction data.

The 12-month analysis compares 156 eyes pre-treatment to 12 months post-treatment. The mean surgically induced refractive vector magnitude change (SIRC) was -6.78 D ± 1.57 (standard deviation) of sphere while the mean intended refractive vector magnitude change (IRC) was -7.04 D ± 1.11. The mean SIRC for cylinder was -0.85D ± 0.67 while the mean IRC was -0.71 D ± 0.70. As demonstrated below, the mean absolute vector axis error is 12.78 degrees with mean vector magnitude error of 0.03 D.

Table 8
Vector Analysis of the Cohort at 12-Month Visit

	Pre-Treatment (n=200)		12-Month (n=156)		Induced Change (SIRC) (n=156)		Intended Change (IRC) (n=156)	
	Sph	Cyl	Sph	Cyl	Sph	Cyl	Sph	Cyl
Mean	-7.78	-0.99	-0.05	-0.41	-6.78	-0.85	-7.04	-0.82
Median	-7.50	-0.75	0.00	-0.25	-6.63	-0.75	-6.74	-0.71
SD	1.39	0.85	1.00	0.56	1.57	0.67	1.11	0.70
Min	-11.50	-4.00	-4.00	-3.25	-10.60	-3.68	-10.05	-3.23
Max	-6.25	0.00	-3.00	0.00	-1.66	0.00	-5.80	0.00
p value					p<0.0001	p=0.0002		

SIRC=Surgically induced refractive vector magnitude change
IRC=Intended refractive vector magnitude change
p value (two-sided z-test to determine if mean change is different from 0)

Table 9
Vector Errors of the Cohort at 12-Month Visit

	Absolute V Ax Error (n=118[∝])	V Mag Error (n=156)
Mean	12.78	0.03
Median	5.50	0.00
SD	20.01	0.46
Min	0.00	-1.43
Max	90.00	2.88

[∝]The total number of patient visits at 12 months was 156; however, as some of these patients had no astigmatic treatments and had no pre operative astigmatism and little or no post operative astigmatism the number of eyes for the vector axis error is less (118) than the number of visits.
Absolute V Ax Error=Absolute vector error in astigmatic axis
V Mag Error =Vector error in astigmatic magnitude
α This value represents the most undercorrection encountered in this group of 156 eyes; however, the standard deviation (SD) validates the consistency of the data.
β This value represents the most overcorrection encountered in this group of 156 eyes; however, the standard deviation (SD) validates the consistency of the data.

(4) Reduction of Mean Spherical Equivalent

The mean spherical equivalent was reduced at all time periods examined. The mean pre-treatment manifest refractive spherical equivalent was -8.27 D. At 6 months -0.16 D was the mean spherical equivalent or a reduction of 8.11 D (a mean reduction of 98%). At 12 months the mean spherical equivalent was -0.25 D which represents a mean spherical equivalent reduction of 8.02 D (a mean reduction of 97%).

Table 10 Mean Spherical Equivalent Over Time			
	Pre Op (n=200)	6 Month (n=199)	12 Month (n=156)
Mean	-8.27	-0.16	-0.25
Median	-7.88	0.00	-0.13
SD	1.47	1.12	1.02
Min	-12.00	-7.00	-4.25
Max	-6.25	3.00	2.50

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

The following table reflects the post-operative spherical equivalent at 12 months after treatment. Table 11 presents the post-operative spherical equivalent data stratified by diopter of pre-operative spherical equivalent. At 12 months post-operation, 127/156 (81.4%) are within one diopter of spherical equivalent and 144/156 (92.3%) are within two diopters. Over half, 88/156 (56.4%) are within 0.50 diopters of emmetropia.

Table 11 Spherical Equivalent at 12-Months Stratified by Diopter of Pre-Op Spherical Equivalent (N=156)							
Post-Op Spherical Equivalent	Pre-Operative Spherical Equivalent						Total n (%)
	6.1 to 7.0 n=43	7.1 to 8.0 n=45	8.1 to 9.0 n=33	9.1 to 10.0 n=13	10.1 to 11.0 n=13	11.1 to 12.0 n=9	
> +2.1	0	0	2	1	0	0	3 (1.9)
+1.1 to 2.0	2	0	1	0	2	0	5 (3.2)
+0.51 to 1.0	5	3	6	2	1	0	17 (10.9)
+0.1 to 0.50	5	6	3	2	0	2	18 (11.5)
0.00	7	11	9	0	2	3	32 (20.5)
-0.1 to -0.50	12	7	8	3	4	4	38 (24.4)
-0.51 to -1.0	7	10	0	3	2	0	22 (14.1)
-1.1 to -2.0	3	4	2	1	2	0	12 (7.7)
>-2.1	2	4	2	1	0	0	9 (5.8)

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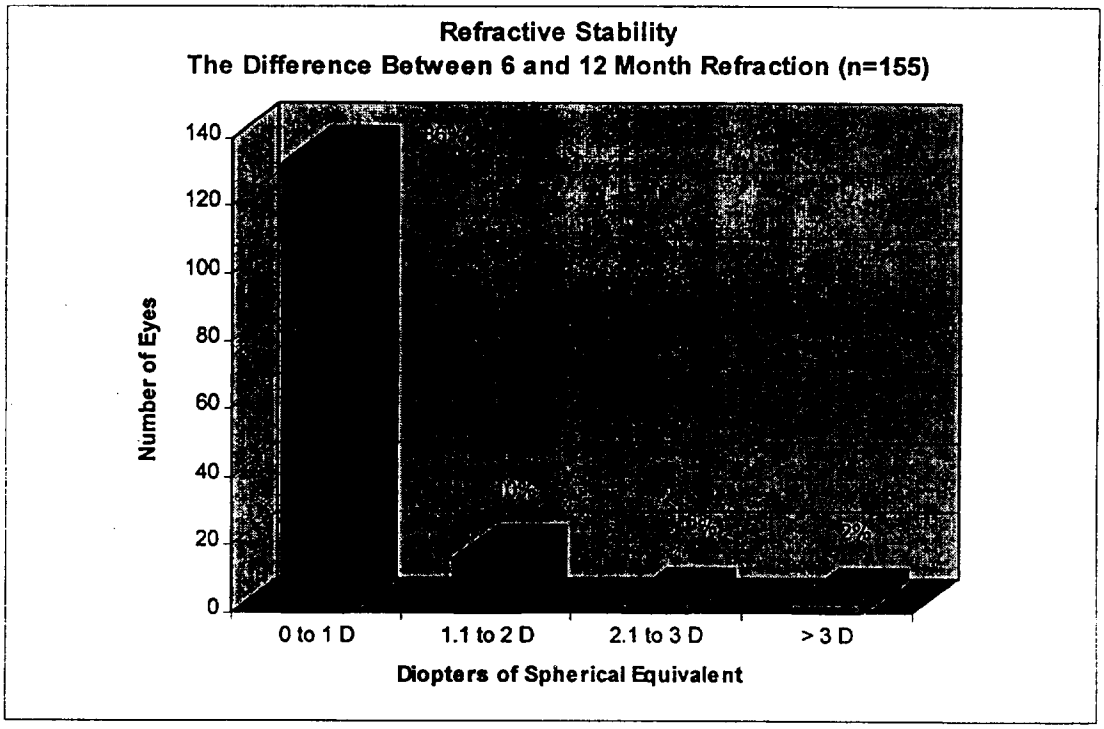
(6) Stability of Outcome

The stability of outcome is demonstrated by a change of 1 D or less in manifest spherical equivalent between the 6 and 12-month visits. Of the 200 eyes initially treated, 155 had both a 6 and 12-month refraction. Of these, there were 133/155 eyes (85.8%) that had a change of not more than 1 D of manifest spherical equivalent between the 6 and 12-month visit.

FIGURE 2 - REFRACTIVE STABILITY



c. Adverse Events

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

Adverse events for visits 6 and 12 months are presented in the table below. They are ordered by frequency at final visit.

Table 13 Summary of Adverse Events During Post-Treatment Follow-Up* (N=200)				
Safety Endpoint	6M (n=199)		12M (n=156)	
	n	%	n	%
1. Loss of ≥ 2 lines BSCVA due to				
All Causes	17	8.5%	9	5.8%
Corneal Causes	15	7.5%	8	5.1%
2. Pre-treatment BSCVA 20/20 or Better with a				
Post-treatment BSCVA Worse than 20/25	14	7.0%	7	4.5%
Post-treatment BSCVA Worse than 20/40	0	0.0%	2	1.3%
3. IOP Increase^				
> 5 mm Hg from baseline	5	2.7%	1	0.7%
> 10 mm Hg from baseline	2	1.1%	0	0.0%
> 25 mm Hg	1	0.5%	0	0.0%
4. Corneal Haze^^				
with loss of ≥ 2 lines BSCVA	7	3.5%	2	1.3%
with loss of > 2 lines BSCVA	4	2.0%	2	1.3%
5. Retreatments not for primary undercorrection	0	0.0%	3	1.5%

^ There is a lower "n" for IOP data due to missing values (6M n=185 and 12M n=148)
^^There is a lower "n" for Haze data due to missing values (12M n=153)
* Patient survey not conducted for subjective evaluation of vision after surgery

Other adverse events that may occur with patients undergoing the PRK 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.

d. Retreatments

Three eyes were retreated (3/200 or 1.5%) during the study during the initial 12 months after primary treatment. In each case retreat resulted in visual recovery to at least the pre-operative level. Table 14 below summarizes the 3 retreatment cases that occurred during the 12-month follow-up period. Retreatment was performed to address post-operative irregular videokeratographic maps, regression and haze, and irregular astigmatism. These patients did not undergo other additional refractive procedures (AK, ALK, etc.) even though the investigators were not restricted in their choice of surgery.

Table 14 Re-Treatment Summary						
	Pre-Treatment		Pre-Retreatment		Post-Retreatment at Last Visit	
Patient	UCVA	BSCVA	UCVA	BSCVA	UCVA	BSCVA
1	800	20	200	40	100	15
2	800	20	400	40	200	20
3	800	20	200	30	25	20

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.

X. CONCLUSIONS DRAWN FROM THE CLINICAL STUDIES

The clinical results based on 200 eyes treated with a 6.0 mm ablation zone and 0 to -12 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 high myopia with astigmatism.

XI. PANEL RECOMMENDATIONS

This PMA supplement was not referred to the Ophthalmic Devices Panel because the information in the application substantially duplicated information previously reviewed by this panel using the refractive surgery laser guidelines issued October 10, 1996 and information from the previous VISX astigmatism approval (P930016/S3), and no new issues of safety and effectiveness were identified.

XII. FDA DECISION

After primary in-house and panel member review, a minor deficiency letter dated November 26, 1997 was sent to the sponsor. VISX, Inc. met with CDRH on December 8, 1997 to clarify issues and discuss their response.

In an amendment received by FDA on December 12, 1997, VISX submitted the requested information. FDA issued an approval order on January 29, 1998.

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.