SUMMARY OF SAFETY AND EFFECTIVENESS DATA
FOR A SUPPLEMENTAL PREMARKET APPROVAL APPLICATION

I. GENERAL INFORMATION

Device Generic Name:	Ophthalmic Medical Laser System (193 nanometer laser wavelength)
Device Trade Name:	VISX STAR S2 Excimer Laser System
Applicant's Name and Address:	VISX, Incorporated 3400 Central Expressway Santa Clara, CA 95051-0703 408-733-2020
Premarket Approval (PMA) Application Supplement Number:	P930016/S007
Date of Panel Recommendation:	July 23, 1998
Date of Notice of Approval to Applicant:	November 2, 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. This clinical indication was expanded in supplements 3 (approved on April 24, 1997) and 5 (approved on January 29, 1998) to include PRK in patients 21 years of age or 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.

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 approved indications, the summaries of safety and effectiveness data (SSED) 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 (original PMA and S3) and Docket # 99M-0293 (S5) or you may download the file from the internet site http://www.fda.gov/cdrh/pdf/p900036.pdf.

II. INDICATIONS FOR USE

Photorefractive Keratectomy (PRK) procedure using the VISX STAR S2 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 21 years of age or older in PRK treatments of naturally occurring hyperopia between +1.00 and +6.00 D spherical equivalent, on eyes with no more than 1.0 D of refractive astigmatism:

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: see the labeling

C. Precautions: see the labeling

IV. DEVICE DESCRIPTION

The device used in the clinical study was the VISX STAR (formerly Model C) Excimer Laser System for which a full description can be found in the SSED for supplement 5.

On March 20, 1998, in supplement 6, the VISX STAR S2 was approved for the previously approved indications of PRK for myopia with and without astigmatism. The following changes to the STAR were approved for the STAR S2: laser removal of the epithelium, visibility upgrade, swivel mounted vacuum nozzle, integrated hyperopia

11

hardware module, variable Hertz rate from 1.5 to 10 Hertz, smoothing, and installation of software Version 2.2.

On August 31, 1998, VISX, Inc. submitted a request that the VISX STAR S2 be considered comparable to the VISX STAR for PRK treatments of hyperopia based on PMMA ablation profiles and descriptions of the two models. FDA engineers met with VISX on August 20, 1998 to discuss comparability issues relating to the STAR and STAR S2 Laser Systems. After requesting and examining lensometer readings obtained from measurements of PMMA ablations from both systems for all indications, FDA reviewers concluded that the two models were equivalent for correction of hyperopia. VISX requested approval for only the STAR S2 for the indication discussed in this SSED.

V. ALTERNATIVE PRACTICES OR PROCEDURES

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

VI. MARKETING HISTORY

VISX has over 500 Excimer Laser Systems located in approximately 50 countries. The VISX STAR S2 Excimer Laser System has not been withdrawn from any country or market for reasons of safety or effectiveness.

VII. POTENTIAL 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 124 patients was conducted at eight investigation sites in the United States with a supplementary data of 53 eyes from a Canadian study.

A. Study objective

The objective of the U.S. clinical investigation of the VISX STAR S2 Excimer Laser System was to treat naturally occurring hyperopia between +1.0 and +4.0 D with no more than 1 D of astigmatism. Additionally, supplemental clinical data from the Canadian study with refractive errors from +4.0 to +6.0 D was evaluated.

B. Study design

This was a prospective, non-randomized, unmasked, multicenter clinical study where the primary control was the preoperative state of the treated eye (i.e., comparison of pretreatment and post-treatment visual parameters in the same eye).

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: naturally occurring refractive hyperopia between +1.0 and +4.0 diopters spherical equivalent, and no more than 1.0 diopter of refractive astigmatism; best corrected visual acuity of 20/40 or better in both eyes; the difference between the manifest and cyclopegic refractions may be no more than 0.75 D; 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 (2 weeks for soft lenses, 3 weeks for hard lenses) and have 3 central keratometry readings and manifest refractions taken at 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.

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, 9 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: distance and near 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.

Procedure effectiveness was evaluated based on improvement in uncorrected visual acuity, the ability of eyes to achieve predictability, and achieve stability of manifest refraction spherical equivalent 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.

E. Study period, investigational sites and demographic data

1. Study period

Table 1
Summary of First and Last Treatment Dates
Eyes (n=222)

	Patients	First Treatment	Last Treatment
8 U.S. Sites	124	2/20/97	5/18/98

2. Investigational Sites

Table 2
Investigators/Investigation Sites (Eyes=222)

Investigator	Site	Eyes Treated
James Salz, MD	American Eye Institute Los Angeles, CA 90048	43
James Auran, MS	Columbia-Presbyterian Eastside New York, NY 10021	5
Jonathan Talamo, MD	Cornea Consultants Boston, MA 02114	34*
Colman Kraff, MD	Kraff Eyes Institute Chicago, IL 60602	67
Nada Jabbur, MD	Wilmer Eye Institute Lutherville, MD 21093	26
Michael W. Belin, MD	LCA Laser Center Albany, NY 12211	15
James C. Liu, MD	LCA Laser Center Mountain View, CA 94040	15
R. Wayne Bowman, MD	UT Southwestern Medical Center Dallas, TX 75235	17

*An additional 2 fellow eyes with >1.00 pre-operative cylinder were treated in violation of protocol guidelines and excluded from all group analyses as their data inclusion would not be indicative of the result that might be expected in the appropriately selected patient population.

3. Demographics and Baseline Characteristics

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

Table 3
Demographic Information
(Patients=124)

Category	Classification	n	%
Sex	Female	61	49.2
	Male	63	50.8
Eye	Right	112	50.5
	Left	110	49.5
Race	Caucasian	108	87.1
	Black	3	2.4
	Asian	0	0.0
	Other*	13	10.5
Age (in Years)	Average	52.9	
	Standard Deviation	9.0	
	Minimum	31	
	Maximum	76	

*Hispanic, Spanish, or Latino

F. Data Analysis and Results

1. Preoperative Characteristics

Table 4 contains a summary of the preoperative refraction for eyes treated in the U.S. study.

Table 4
Pre-Operative Refractive Parameters
(N=222*)

	Primary Eyes (n=124)		Fellow Eyes (n=98)*	
Spherical Equivalent	n	%	n	%
1.0 to 1.99 DSE	47	37.9	45**	45.9
2.0 to 2.99 DSE	47	37.9	35	35.7
3.0 to 4.00 DSE	30	24.2	18	18.4
Cylinder				
0.00 DC	44	35.5	28	28.6
0.25 DC	18	14.5	12	12.2
0.50 DC	33	26.6	32	32.7
0.75 DC	17	13.7	19	19.4
1.00 DC	12	9.7	7	7.1

*2 Fellow Eyes with > 1.00 D pre-operative cylinder were treated in violation of protocol guidelines (ID#'s 3219, 3220) and excluded from all group analyses as their data inclusion would not be indicative of the result that might be expected in the appropriately selected patient population.
**2 Fellow Eyes with <+1.00 D pre-operative spherical equivalent are included.

2. 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
Study Accountability
All Eyes (N=222)

Category	1 Month	3 Months	6 Months	9 Months	12 Months
Eyes Enrolled	222	222	221	204	124
Not Due/Required	0	1	17	80*	7
Unable To Locate (dropped)	0	0	0	0	0
Eyes Eligible	222	221	204	124	117
Not Examined (or Missed Visit)	0	8	3	7	2
Accountability					
# Follow-Up Exams	220	213	201	117	115
% Follow-Up	**100%**	**96.4%**	**98.5%**	**94.4%**	**98.3%**

*9-month exam not required for Fellow Eyes.

b. Effectiveness Results

(1) Stability of Outcome

Table 6 presents the mean change in manifest refraction spherical equivalent for all eyes that had 1, 3, 6, 9 and 12-month visits (n=107). Stability of treatment appears to be reached by 9 months postoperative, based on MRSE data.

Table 6
Refractive Stability: Mean of the Differences in MRSE
All US Eyes with 1, 3, 6, 9, and 12-Month Visits (n=107)

Mean Pre SE +2.47 D	1 and 3 Months		3 and 6 Months		6 and 9 Months		9 and 12 Months	
	n	%	n	%	n	%	n	%
< 1.00 D	87	81.3	98	91.6	102	95.3	104	97.2
Mean Difference	0.41		0.32		0.16		0.10	
SD	0.74		0.56		0.49		0.45	
95% CI	0.55 0.26		0.42 0.21		0.25 0.07		0.19 0.02	

In consideration of the unique accommodative patterns of hyperopic subjects, refractive stability was further analyzed as a function of corneal power stability and resultant non corneal power variation. The mean of the two meridians measured by standard keratometry (Mean K) was analyzed for the pre-operative, 1, 3, 6, 9 and 12-month post-operative follow up visits to demonstrate corneal stability (Table 7).

Table 7 Mean of the Differences in Keratometry All US Eyes with 1, 3, 6, 9, and 12-Month Visits (n=105)								
	1 and 3 Months		3 and 6 Months		6 and 9 Months		9 and 12 Months	
< 1.00 D	78	74.3	90	85.7	97	92.4	105	100
Mean Difference	-0.54		-0.22		-0.11		-0.03	
SD	0.88		0.69		0.47		0.35	
95% CI	-0.38 -0.71		-0.09 -0.35		-0.02 -0.20		0.04 -0.09	

The stability of the keratometry means when compared to their corresponding manifest spherical equivalent means and the predictive value of age are most significant and indicate the role of accommodative variation as the most probable factor in the apparent instability of measurement of the refractive state. This supports the overall stability of the induced corneal change. Based on both MRSE and K data, stability of the PMA cohort is achieved by 9 months postoperative.

Table 8 presents a combination of eyes with pre-operative refractive errors between +1.00 D and +6.00 D (n=145) from both the US and Canadian studies that were treated identically and had follow-up visits at 3, 6, 9, and 12 months post-operatively. The Canadian data further confirmed that stability was reached by 9 months.

Table 8 Refractive Stability: Mean of the Differences in MRSE All Eyes (1 to 6 D) with Visits 3 to 12 Months (n=145)						
Mean Pre SE +2.54 D	3 to 6 M		6 to 9 M		9 to 12	
	n	%	n	%	n	%
< 1.00 D	134	92.4	140	96.6	142	97.9
Mean Difference	0.34		0.15		0.11	
SD	0.53		0.46		0.42	
95% CI	0.25 0.42		0.08 0.22		0.04 0.18	

(2) Distance Uncorrected Visual Acuity (UCVA)

The distance UCVA among eyes targeted for emmetropia that had a pre-operative BSCVA of 20/20 or better (n=166) was used to establish effectiveness of the procedure, because only eyes able to be refracted to at least 20/20 pre-operatively could be expected to produce an uncorrected acuity of 20/20 or better. Table 9 presents the distance UCVA pre-operatively and at 1, 3, 6, 9 and 12 months post-operatively.

The percentage of eyes with UCVA of 20/20 or better increased from 5.4% pre-operatively to over 60% at 9 months or later post-operatively, and over 94% of eyes had UCVA of 20/40 or better at 9 months or later post-operatively. These improvements in UCVA support the effectiveness of the device.

Table 9
Distance Uncorrected Visual Acuity Over Time
Eyes Targeted for Emmetropia with a Pre-Operative BSCVA of 20/20 or Better

	Pre-Op (n=166)		1 Month (n=166)		3 Months (n=158)		6 Months (n=150)		9 Months (n=99)		12 Months (n=97)	
	n	%	n	%	n	%	n	%	n	%	n	%
20/20 or better	9	5.4	22	13.3	52	32.9	80	53.3	69	69.7	62	63.9
20/25 or better	13	7.8	44	26.5	96	60.8	110	73.3	84	84.8	78	80.4
20/32 or better	20	12.0	79	47.6	126	79.7	135	90.0	93	93.9	91	93.8
20/40 or better	29	17.5	100	60.2	139	88.0	144	96.0	97	98.0	92	94.8

(3) Refractive Error

All investigators were instructed to use a full plus refracting technique to assure measurement of maximum manifest hyperopia without cycloplegia. Cycloplegia was performed on all patients pre-operatively to confirm the full plus refraction and preclude any patient with a large amount of latent hyperopia from being treated. Cycloplegic refractions were repeated at the 6 and 12-month visits. Table 10 presents the mean manifest refraction spherical equivalent pre-operatively, and at 1, 3, 6, 9, and 12 months post-operatively.

Table 10
Manifest Refraction Spherical Equivalent Over Time
All Eyes Targeted for Emmetropia

	Pre-Op	1 Month	3 Months	6 Months	9 Months*	12 Months
n	192	192	183	175	116	115
Mean (D)	2.28	-0.86	-0.50	-0.18	0.00	0.11
StDev	0.84	0.68	0.60	0.51	0.51	0.58
Min	0.38	-3.50	-2.88	-2.00	-1.50	-1.63
Max	4.00	1.00	1.00	1.38	1.75	2.25
Mean + 95% CI	2.40	-0.76	-0.41	-0.10	0.10	0.21
Mean - 95% CI	2.16	-0.95	-0.59	-0.25	-0.09	0.00

*One patient did not have a manifest refraction at this visit.

Table 11 presents the cycloplegic and manifest refractions found pre-operatively and at the 6 and 12-month visits.

Table 11 Manifest vs. Cycloplegic Refraction (MRSE vs CRSE) All Eyes Targeted for Emmetropia						
	Pre-Operative		6 Months		12 Months	
	MRSE	CRSE	MRSE	CRSE	MRSE	CRSE
n	192	192	171	171	72	72
Mean	2.28	2.44	-0.18	0.02	0.02	0.24
StDev	0.84	0.94	0.50	0.56	0.50	0.48
Min	0.38	0.38	-2.00	-1.63	-1.63	-1.13
Max	4.00	4.88	1.38	1.88	1.38	1.88
Mean + 95% CI	2.40	2.57	-0.11	0.10	0.14	0.35
Mean - 95% CI	2.16	2.31	-0.26	-0.06	-0.10	0.13

(4) Predictability of Outcome

Predictability of outcome was determined by comparing the intended MRSE with the achieved MRSE at each visit. Table 12 presents predictability of outcome as measured by post-operative manifest refraction spherical equivalent within ± 1.00 D and ± 0.50 D.

Table 12 Predictability of Outcome: Intended versus Achieved All Eyes										
	1 Month (n=222)		3 Months (n=213)		6 Months (n=201		9 Months* (n=116)		12 Months (n=115)	
Within 0.50 D	78	35.1	119	55.9	149	74.1	91	78.4	87	75.7
Within 1.00 D	144	64.9	172	80.8	182	90.5	111	95.7	106	92.2

*One eye did not have a refraction at this visit.

c. Adverse Events

There was no patient death related to the use of the VISX STAR S2 Excimer Laser System. Adverse events for visits at 6 and 12 months are presented in the table below.

Table 13
Adverse Events

DESCRIPTION	6 Months (n=201) n	(%)	12 Months (n=115) n	(%)
Decrease in BSCVA:				
>2 Lines	2	1.0	1	0.9
2 Lines	0	0	3	2.6
Worse than 20/40	0	0	1	0.9
Overcorrection > 1.0 D	4	2.0	3	2.6
Pre-treatment BSCVA 20/20 or Better with:				
Post-treatment BSCVA worse than 20/50	0	0	2	2.1*
Post-treatment Worse than 20/40	0	0	0	0
Increase > 2.0 D cylinder	0	0	1	0.9
Corneal haze > grade 2	0	0	1	0.9
IOP Increase				
>5 to 10 mm Hg	1	0.5	1	0.9
> 10 mm Hg	0	0	0	0
Subjective Patient Responses^				
Double/Ghost Images^				
Somewhat Worse	6	3.0	6	5.2
Much Worse	4	2.0	1	0.9
Sensitivity to Bright Lights**^				
Somewhat Worse	11	5.5	7	6.1
Much Worse	1	0.5	1	0.9
Difficulty with Night Vision**^				
Somewhat Worse	8	4.0	5	4.3
Much Worse	2	1.0	2	1.7

*The percentage reflects the actual number of occurrences reported divided by the number of data points available for each visit. Therefore, the % reported is different from the apparent value due to missing data points.
**Extensive contrast sensitivity and glare testing under mesopic and photopic conditions did not yield any statistically significant losses, nor any losses that could be interpreted as clinically significant.
^Reflects patient responses obtained from subjective questionnaires

Other adverse events might be expected 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. Conclusions

The key safety and effectiveness variables from the U.S. study are presented in Table 14 below.

Table 14
Summary of Key Safety and Effectiveness Variables
US Eyes

	1 Month		3 Months		6 Months		9 Months		12 Months		FDA
	n	%	n	%	n	%	n	%	n	%	Guidance
Effectiveness*	**195**		**187**		**175**		**99**		**97**		
UCVA 20/40 or Better	100	60.2	139	88.0	144	96.0	97	98.0	92	94.8	**85%**
Predictability[β]	**222**		**213**		**201**		**116**		**115**		
MRSE within ± 0.500	78	35.1	119	55.9	149	74.1	91	78.4	87	75.7	**50%**
MRSE within ± 1.00 D	144	64.9	172	80.8	182	90.5	111	95.7	106	92.2	**75%**
Refractive Stability[φ]	**107**		**107**		**107**		**107**		**107**		
Change ≤1.00 D between Visits	na		87	81.3	98	91.6	102	95.3	104	97.2	**95%**
SAFETY[Δ]	**222**		**213**		**201**		**117**		**115**		
Loss of > 10 Letters BSCVA	20	9.0	7	3.3	2	1.0	0	0.0	1	0.9	**<5%**
BSCVA Worse than 20/40	8	3.6	1	0.5	0	0.0	1	0.9	1	0.9	**<1%**
Increase > 2.0 D Cylinder	1	0.5	0	0.0	0	0.0	1	0.9[φ]	1	0.9	**<5%**

*Effectiveness analyses reflect eyes targeted for emmetropia with Pre-Op BSCVA of 20/20 or better.
[β]Predictability analyses reflect all eyes treated. One eye had no refraction at the 9-month visit.
[φ]Refractive stability analysis reflects those eyes with visits at 1, 3, 6, 9, and 12 months.
[Δ]Safety analyses reflect all eyes treated. The percentage of events reported reflects the actual number of occurrences reported divided by the number of data points available for each visit. Therefore, the % reported may differ from the apparent value due to missing data points.

e. Additional Confirmatory Canadian Data

Table 15 contains a summary of the preoperative refraction for eyes treated in the Canadian study.

Table 15
Pre-Operative Refractive Parameters
(n=53)

Spherical Equivalent	n	%
1.00 to 1.99 DSE	13	24.5
2.00 to 2.99 DSE	12	22.6
3.00 to 3.99 DSE	14	26.4
4.00 to 4.99 DSE	6	11.3
5.00 to 6.00 OSE	8	15.1
Cylinder		
0.00 DC	28	52.8
0.25 DC	1	1.8
0.50 DC	15	28.3
0.75DC	6	11.3
1.00 DC	3	5.6

Stability of outcome is presented by the mean of the differences in MRSE over time. Table 16 below refers only to those 36 eyes that were examined at all visits (1, 3, 6, 9, and 12-month). Stability of treatment appears to be reached by 9 months postoperative, based on MRSE data.

Table 16 Stability: Mean of the Differences in Manifest Refraction Spherical Equivalent All Eyes with Visits at 1, 3, 6, 9, and 12 Months (n=36)								
Change in SE Between (Mean Pre-Op SE +3.13)	**1to 3 Months**		**3 to 6 Months**		**6 to 9 Months**		**9 to 12 Months**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
≤1.00 D	28	77.8	34	94.4	36	100	36	100
Mean Difference	0.43		0.38		0.09		0.13	
SD	0.72		0.46		0.34		0.31	
95% CI	0.67 0.19		0.53 0.23		0.21 -0.02		0.23 0.03	

The key safety and effectiveness variables from the Canadian study are presented in Table 17 below. These data from a parallel study of 53 eyes conducted at Ottawa General Hospital further support the U.S. refractive stability data and the decision to approve treatments of patients with refractive errors up to +6.0 D.

Table 17 Summary of Key Safety and Effectiveness Variables Ottawa General Hospital Eyes										
	1 Month		3 Months		6 Months		9 Months		12 Months	
	n	%	n	%	n	%	n	%	n	%
Effectiveness Variables	**53**		**52**		**49**		**43**		**40**	
UCVA 2W40 or Better	34	64.2	41	78.8	43	87.8	40	93.0	37	92.5
MRSE within ± 0.50 D	7	13.2	23	44.2	34	69.4	33	76.7	35	87.5
MRSE within ± 1.00 D	26	49.1	9	75.0	41	83.7	38	88.4	37	92.5
Refractive Stability*	**36**		**36**		**36**		**36**		**36**	
Change of ≤1.00 D between visits	na		28	77.8	34	94.4	36	100	36	100
Safety Variables	**53**		**52**		**49**		**43**		**40**	
Loss of > 2 Lines BSCVA	8	15.1	2	3.8	0	0.0	0	0.0	0	0.0
BSCVA Worse than 20/40	3	5.7	1	1.9	0	0.0	0	0.0	1	2.5
increase > 2.0 D cylinder	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

*Refractive stability analysis reflects those eyes with visits at 1, 3, 6, 9, and 12 months.

f. Device Failures

Failure of the system monitor color occurred once. The video portion was unaffected. The video graphics adapter (VGA) video printed circuit board was replaced.

X. CONCLUSIONS DRAWN FROM THE CLINICAL STUDIES

The clinical results based on 124 hyperopic eyes treated with a 9.0 mm ablation zone and between +1.0 and +4.0 D spherical equivalent with no more than 1.0 D of refractive astigmatism together with clinical data from 53 Canadian study eyes with refractive errors from +4.0 to +6.0 D demonstrated that the VISX STAR S2 Excimer Laser System is safe and effective when used in accordance with the indications for use.

XI. PANEL RECOMMENDATIONS

On July 23, 1998, the Ophthalmic Devices Panel recommended that the PMA supplement for the excimer laser be conditionally approved for +1.0 to +6.0 D. The recommendations by the panel were:

- Additional follow-up data at 1 year or later on both cohorts to include standard error calculations to support stability claims.
- Addition of the precaution/warning to the labeling to state that: Patients on hormone replacement therapy or antihistamines may have delayed re-epithelialization of the cornea following surgery.
- Addition of the precaution/warning to the labeling to state that: Patients with 4.0-6.0 D of hyperopia may be at greater risk of regression of correction.
- Resubmission of the patient questionnaire to include reports of moderate as well as severe complaints postoperatively.

XII. FDA DECISION

CDRH concurred with the Ophthalmic Devices Panel's recommendation of July 23, 1998 and issued a major deficiency letter to VISX, Inc. on August 18, 1998 requesting the additional clinical follow-up data and their agreement to the other three conditions. In amendments received by FDA on August 28 and October 6, 1998, VISX submitted the required changes, clarification and information.

FDA determined that the data were sufficient to justify an approved indication range of up to +6 D with the condition that the labeling clearly indicate the low number of eyes studied and the greater regression and stability problems above +4 D. These statements were added to the General Precautions section of the labeling.

FDA issued an approval order on November 2, 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

Patient Assistance Information

Primary Eye Care Professional

Name: _____

Address: _____

Phone: _____

PRK 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

Facts You Need to Know About Photorefractive Keratectomy (PRK) Surgery

Patient Information Booklet

Nearsighted Patients (-1.0 to -12.0 diopters) or
Nearsighted Patients (0 to -12.0 diopters) with 0.75 to 4.0 Diopters of Astigmatism
Farsighted Patients (+1.0 to +6.0 diopters) with no more than 1.0 Diopter of Astigmatism

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

Table of Contents

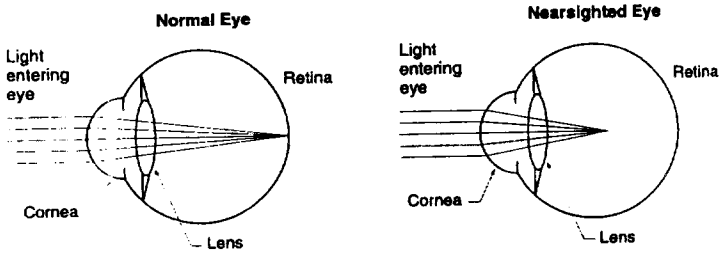
Introduction

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

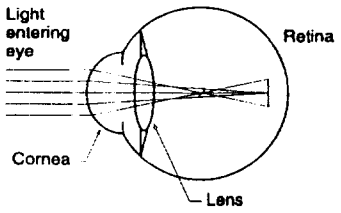
If both of your eyes are nearsighted and/or astigmatic or farsighted, your doctor may recommend PRK surgery for both eyes. However, sometimes it is better to have PRK done on only one eye. Talk with your doctor about whether it would be better to treat one or both of your eyes.

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

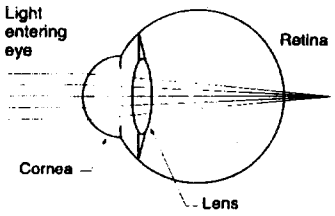
How the Eye Functions



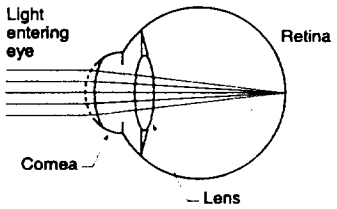
Nearsighted and Astigmatic Eye



Farsighted Eye



Eye After Treatment



The cornea and lens of the eye focus light like a camera lens to form an image on the retina at the back of the eye. The cornea, where light first enters the front of the eye, provides about two thirds of the eye's focusing power, and the lens inside the eye provides the other third. Some eyes focus, or refract, the light too much, so that the images of distant objects are formed in front of the retina, and the image on the retina is blurred. This condition is called nearsightedness, or myopia. Myopia usually starts in childhood and gets progressively worse through adolescence. It usually stops changing by the late teens, but it can sometimes continue to get worse into the mid-twenties. In astigmatism the image is not evenly focused

to a single point in front of the retina but the light rays are divided into two parts that focus along two lines with opposite orientations that are different distances from the retina.

In farsightedness the image focuses beyond the retina. In our youth, the innate accommodating (focusing) power of the eyes often compensates for farsightedness. But as we age, our eyes become less able to accommodate. For this reason, farsightedness most commonly becomes a problem later in life. Many farsighted eyes do not need correction until the individuals reach their forties or fifties.

Nearsightedness can be corrected by any method that reduces the total refractive power of the eye. Astigmatism correction makes all of the rays of light focus at the same distance so that they all fall right on the retina. Eyeglasses and contact lenses do this by putting in front of the eye "negative" lenses that are thicker at the edge than in the center. PRK corrects nearsightedness by flattening the central part of the cornea, and it corrects astigmatism by flattening the central cornea by different amounts at different orientations to correct for the uneven focus of the rays of light.

Farsightedness can be corrected by any method that increases the total refractive power of the eye. Eyeglasses and contact lenses do this by putting in front of the eye "positive" lenses that are thicker in the center than at the edge. PRK does it by making the central part of the cornea more steeply curved.

During a regular eye examination, your doctor uses lenses to measure your nearsightedness, astigmatism, or farsightedness in units called "diopters." The VISX STAR S2™ Excimer Laser System is approved for correcting eyes with up to 12 diopters of nearsightedness and from 0.75 to 4.0 diopters of astigmatism. For farsightedness, the system is approved for correcting eyes with up to 6.0 diopters of farsightedness and no more than 1.0 diopter of astigmatism. No astigmatism is corrected with a hyperopia treatment.

What is PRK?

PRK is laser surgery to correct nearsightedness (myopia), nearsightedness with astigmatism, or farsightedness (hyperopia). For nearsightedness with or without astigmatism, 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. For farsightedness, the excimer laser beam is used to steepen the front of the cornea. To do this, the laser beam removes small amounts of tissue from a ring-shaped area 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 surgery is 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 clinical studies of the VISX STAR Excimer Laser System, the results at 12 months after surgery were:

A. Without the help of glasses

- 94% mildly nearsighted eyes could see 20/40 or better
- 91% mildly nearsighted eyes with astigmatism could see 20/40 or better
- 90% highly nearsighted eyes with or without astigmatism could see 20/40 or better
- 95% moderately farsighted eyes could see 20/40 or better

B. With the help of glasses*

- 99% mildly nearsighted eyes could see 20/40 or better
- 98% mildly nearsighted eyes with astigmatism could see 20/40 or better
- 99% highly nearsighted eyes with or without astigmatism could see 20/40 or better
- 99% moderately farsighted eyes could see 20/40 or better

Even though their vision without glasses improved, some patients still needed glasses or contact lenses after PRK. PRK 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 STAR S2, is effective in reducing nearsightedness between 0 and -12.0 diopters and/or astigmatism between 0.75 and 4.0 diopters.
- PRK may reduce overall nearsightedness and astigmatism, while also reducing or eliminating dependency upon contact lenses or glasses.
- PRK surgery, as performed with the VISX STAR S2, is effective in reducing farsightedness between +1.0 and +6.0 diopters with no more than 1.0 diopter of astigmatism.

Risks

As with any surgical procedure there are risks associated with PRK surgery. It is important to discuss these risks with your doctor before you make the decision to have the surgery. If the results of the surgery are not satisfactory, you may need to have additional PRK surgery in the same eye.

* *Data collected from eyes that could see 20/20 or better with glasses before surgery.*

The First Week Following Surgery

- Pain and discomfort may last for up to 3 days after surgery.
- Blurred vision and tearing will occur as the cornea heals.
- You will be sensitive to bright lights.

The First Two To Six Months Following Surgery

- Your intraocular pressure may increase due to use of anti-inflammatory medications. This is usually resolved by drug therapy or by stopping the anti-inflammatory medication.
- Your cornea may become hazy or cloudy enough to affect your vision. This haze typically disappears over time, but some patients continue to experience haze over 2 - 3 years.

One or More Years After Surgery

Some patients report visual complaints at one or more years after surgery. These problems are discussed in detail later in this booklet (see the section titled Long Term Post-Treatment Safety Problems).

Contraindications

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

- You have collagen vascular, autoimmune or immunodeficiency diseases (for example, lupus or 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, astigmatism, or farsightedness is changing.
- You are diabetic or have severe allergies.
- You have a history of *Herpes simplex* or *Herpes zoster* of the eye.

Precautions

The clinical trials included only 21 out of 200 eyes with nearsightedness between 10 and 12 diopters and 13 out of 275 eyes with farsightedness between 4 and 6 diopters. These populations may not have been sufficient to determine the level of effectiveness and complication rate for patients with severe nearsightedness and severe farsightedness.

If you have more than +4.0 D of farsightedness, you may be at a greater risk of regression of correction.

The effects of PRK on visual performance under poor lighting conditions have not been determined. Following PRK treatment, you may 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. If you are under age 30 and have PRK treatment of astigmatism, you will be more likely to experience problems with your vision than older people because your pupils are larger under poor lighting conditions.

The safety and effectiveness of the VISX STAR S2 Excimer Laser System have **NOT** been established:

- In eyes with corneal disease or abnormality (for example, scar, infection, etc.).
- In eyes with previous surgery or injury to the center of the cornea where PRK will be performed.
- For hyperopia (farsightedness) treatment of patients with refractions less than +1.0 D.

- In eyes with progressive nearsightedness, astigmatism, or farsightedness.
- In eyes with abnormal blood vessels within 1.0 mm of the cornea area where PRK will be performed.
- In patients under 18 years of age for mild nearsightedness and under 21 years of age for high nearsightedness with or without astigmatism and farsightedness.
- In patients over the long term (more than 2 years after the surgery).
- In patients who are taking sumatripin (Imitrex) for migraine.
- In patients who have a tendency to form scars.
- For refractive treatments greater than -12.0 D of nearsightedness, -4.0 D of astigmatism or +6.0 D of farsightedness.
- In patients taking hormone replacement therapy or antihistamines who may have delayed re-epithelialization of the cornea following surgery.

Are You a Good Candidate for PRK?

If you are considering PRK, you must:

- Be at least 18 years of age for treatment of mild nearsightedness, or 21 years of age for treatment of high nearsightedness with or without astigmatism, or moderate farsightedness.
- Have healthy eyes that are free from eye disease or corneal abnormality (for example: scar, infection, etc.).
- Have nearsightedness (myopia) up to -12.0 diopters and/or between 0.75 and 4.0 diopters of astigmatism, or have farsightedness (hyperopia) between +1.0 and +6.0 diopters with no more than 1.0 diopter of astigmatism.

- 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 risks and benefits as compared to other available treatments for nearsightedness (myopia) with or without astigmatism and farsightedness (hyperopia).
- Be able to lie flat without difficulty.
- Be able to tolerate local or topical anesthesia.
- Be able to keep your eye accurately on the fixation light for the entire PRK procedure.
- 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, you will need to have a pre-surgical examination to determine if your eye is healthy and suitable for PRK. 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.

WARNING:

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 may 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. You will be asked to look directly at a blinking red light. Try to keep both eyes open without squinting, as this makes it easier to keep looking at the blinking red light. Small amounts of tissue will then be removed from your cornea using the VISX STAR S2 Excimer Laser.

PRECAUTION:

It is very important that you keep looking at the blinking red light during the procedure, even if the light fades or becomes dim. Your surgical results depend upon your looking at this red, blinking light throughout the treatment.

You will be under the laser less than 1 minute and, overall, the surgery takes about 10 minutes.

After the laser surgery is complete, some eye drops, a bandage contact lens or a patch will be placed on your eye. The surgery is painless because of the anesthetic drops.

When the anesthetic drops wear off (about 45 to 60 minutes), your eye may hurt for 1 to 3 days. Most patients describe this pain as moderate to severe. To promote healing and to lessen the risk of infection, do **NOT** rub your eyes for the first 3 to 5 days. Your doctor can prescribe pain medication to make you more comfortable during this time after the surgery.

IMPORTANT:

Your doctor will monitor you for any side-effects if topical steroids were used. Possible side-effects of prolonged topical steroid use are ocular hypertension, glaucoma, or cataract formation.

After Surgery

You will be mildly sensitive to light and have the feeling that something is in your eye for the first few days. Sunglasses may make you more comfortable during this time.

Your vision should become stable within the first several weeks after surgery. However, you may experience some small changes (for example, improvement or worsening of your vision). These changes may occur up to six months or more after surgery.

A haze or cloudiness is typically seen in the cornea following surgery, but usually does not affect your vision. This haze tends to decrease over time and usually disappears completely over a 12 to 24-month period.

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 who are **mildly nearsighted (MN), mildly nearsighted with astigmatism (MNA), highly nearsighted with or without astigmatism (HN), or moderately farsighted (MF)** at approximately 1 year after treatment:

Problems	MN (%)	MNA (%)	HN (%)	MF (%)
Worsening of Best Spectacle Corrected Vision: Significant (loss of more than 2 lines of vision) worsening of vision in the operated eye with the help of glasses	0.4	3.5	2.5	0
Overcorrection: May need to be corrected with glasses, contact lenses, or additional laser vision correction				
By more than 1 diopter	1.2	1.2	5.1	2.6
By more than 2 diopters	0.2	1.2	1.9	0
Increase in Astigmatism: Uneven curving of the cornea of 1 or more diopters that may distort vision and require corrective glasses or contact lenses	3.1	NA*	NA	0.9
Double/Ghost Images: Shadows or ghost images around objects, judged by the patient after surgery compared to vision before surgery:				
Somewhat Worse	0.6	1.1	NA	5.2
Much Worse	1.0	4.3	NA	0.9
Sensitivity to Bright Lights: Difficulty tolerating bright lights, judged by the patient after surgery compared to vision before surgery:				
Somewhat Worse	3.7	6.5	NA	6.1
Much Worse	1.6	6.5	NA	0.9
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 after surgery compared to vision before surgery:				
Somewhat Worse	2.7	9.8	NA	4.3
Much Worse	2.5	8.7	NA	1.7

*Not available.

Questions to Ask Your Doctor

You may want to ask the following questions to help you decide if PRK is right for you:

- What other options are available for correcting my nearsightedness with or without astigmatism or farsightedness?
- Will I have to limit my activities after surgery, and for how long?
- What are the benefits of PRK for my amount of nearsightedness with or without astigmatism or farsightedness?
- What vision can I expect in the first few months after surgery?
- If PRK does not correct my vision, what is the possibility that my glasses will need to be stronger than before? Could my need for glasses increase over time?
- Will I be able to wear contact lenses after PRK if I need them?
- How is PRK likely to affect my need to wear glasses or contact lenses as I get older?
- Will my cornea heal differently if injured after having PRK?
- Should I have PRK surgery in my other eye?
- How long will I have to wait before I can have surgery on my other eye?
- What vision problems might I experience if I have PRK only on one eye?

Discuss the cost of surgery and follow-up care requirements with your doctor, as laser treatment is not covered by most health insurance policies.

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.	[ ]	[ ]

Answers to SELF-TEST are found on page 16.

Summary of Important Information

- PRK is a permanent operation to the cornea and is irreversible.
- PRK does not eliminate the need for reading glasses, even if you never have worn them before.
- Your vision must be stable for at least one year before PRK surgery. You will need written evidence that your nearsightedness and/or astigmatism or farsightedness has changed less than 0.50 diopters.
- Pregnant and nursing women should wait until they are not nursing and not pregnant to have the surgery.
- You are not a good candidate if you have degenerative or auto-immune diseases, or have a condition that makes wound healing difficult.
- PRK surgery may result in some discomfort. The surgery is not risk-free. Please read this entire booklet, especially the sections on Benefits and Risks before you agree to the surgery.
- PRK is not a laser version of radial keratotomy (RK) or automated lamellar keratectomy (ALK). These operations are completely different from each other.
- Alternatives to PRK include, but are not limited to, glasses, contact lenses, RK, and ALK.
- Some people, such as military pilots, have job-related vision requirements that cannot be met by having RK or PRK.
- Before considering PRK surgery you should:
  a. Have a complete eye examination.
  b. Talk with one or more eye care professionals about the potential benefits of PRK surgery, and the complications, risks, and time required for healing.

Answers to Self-Test Questions:

1. False (see Risks on page 5); **2.** False (see What Is PRK? on page 3); **3.** False (see Before The Surgery on page 9); **4.** False (see The Day of Surgery on page 10); **5.** True (see Benefits on page 5); **6.** True (see What Is PRK? on page 3); **7.** True (see Risks on page 5); **8.** False (see Contraindications on page 6); **9.** False (see Contraindications on page 6).