

Premarket Approval (PMA) Package for  
Dockets Management Branch

PMA Number P970005  
Docket # 00M-0811

Photomed, Inc.  
Kremer Excimer laser System (Serial#  
KEA940202)

Includes:

Approval Order  
Summary of Safety and Effectiveness Data (SSED)  
Labeling

00M-0811

AAV1

2722 '00 MAR -6 A9:44

# APPROVAL ORDER



Food and Drug Administration  
9200 Corporate Boulevard  
Rockville MD 20850

JUL 30 1998

Frederic B. Kremer, M.D.  
Photomed, Inc.  
200 Mall Boulevard  
King of Prussia, PA 19406

Re: P970005

Kremer Excimer Laser System Serial No. KEA940202 for Laser in situ Keratomileusis (LASIK) for the Correction of Primary Myopia, With and Without Astigmatism

Filed: January 31, 1997

Amended: February 7, March 7, 11, and 12, April 8, 14, and 21, May 8, July 7, August 1 and 7, September 29, October 1, 21, and 29, December 8, 19, and 23, 1997, January 26, 28, and 29, February 27, March 17 and 30, April 16, 21, 22, and 28, May 6, 7, 20 (2 amendments), 22, and 28, and June 8, 12, and 26, 1998

Dear Dr. Kremer:

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 a single laser, Kremer Excimer Laser System Serial No. KEA940202. This device, using a 6.0 mm ablation zone, is indicated for myopic and astigmatic laser in situ keratomileusis (LASIK) in patients:

1. with myopia ranging between -1.0 and -15.0 diopters (D) with or without astigmatism ranging from 0.0 D to 5.00 D;
2. who are 18 years of age or older; and,
3. with stable refraction over the 1-year period prior to surgery. Note: Patients between 18 and 20 years old should not demonstrate a shift in refraction greater than 0.5 D. Patients 21 years and older should not demonstrate a shift greater than 1.0 D.

We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). This PMA is for a single device and its approval does not authorize you or Photomed, Inc. to manufacture or distribute any additional devices. You may begin commercial use and treatment with this device of patients who fulfill the above stated indications after you submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

The sale and distribution of this device (Kremer Excimer Laser Serial No. KEA940202) 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. To ensure the safe and effective use of the device, FDA also has determined 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 must 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 and distribution must not violate sections 502(q) and (r) of the act.

These restrictions on the device are applicable to you and Photomed, Incorporated (hereafter, collectively referred to as "Photomed"), as well as any users or purchasers of this device. Photomed must notify any purchasers or users of these restrictions and include them in your training programs.

1. Kremer Excimer Laser Serial No. KEA940202 has only been approved to perform LASIK, using a 6.0 mm ablation zone, to treat myopia ranging from -1.0 D to -15.0 D, with or without astigmatism ranging from 0.0 D to 5.0 D. The device has not been approved to perform photorefractive keratectomy (PRK) (surface ablation), and it has not been approved to correct extreme myopia (nearsightedness >-15.0 D), high astigmatism (>5.0 D), or farsightedness. Labeling, promotion, and advertising are restricted to the LASIK modality because no data on the safety and effectiveness of this device for these unapproved indications were submitted to FDA for review and evaluation.
2. Only licensed practitioners who are experienced in the medical management and surgical treatment of the cornea, and who have been trained in laser system calibration and operation to perform laser refractive surgery (for myopia and astigmatism), may use the device as approved in this order.
3. Prospective patients, as soon as they express an interest in myopic or astigmatic LASIK and prior to undergoing surgery, must receive the Patient Information Booklet (as described in your final submission to this PMA) from the treatment provider.
4. Prior to undergoing surgery, prospective patients must be informed of the alternatives for correcting their myopia and/or astigmatism including eyeglasses, contact lenses, and other refractive surgeries such as PRK, radial keratotomy, and automated lamellar keratectomy.
5. 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 approval of Kremer Excimer Laser System Serial No. KEA940202 do not compare the clinical outcome of LASIK as performed with this single laser with any other laser or method of refractive correction. Such comparisons of safety and effectiveness are misleading and would cause your laser to be misbranded under section 502(a) of the act.

6. All promotion and advertising for this device must include the following information on indications, risks and benefits:

The Kremer Excimer Laser System Serial No. KEA940202 is approved to perform laser in situ keratomileusis (LASIK) for the correction of mild to high myopia between -1.0 and -15.00 D with up to 5.0 D of astigmatism. Alternatives to LASIK include: eyeglasses, contact lenses, PRK, radial keratotomy or automatic lamellar keratoplasty. In studies of 665 eyes after final treatment with refractive data at 6 months, 90.3% were corrected to 20/40 or better and 40.5% were corrected 20/20 or better with eyeglasses or contact lenses. The following adverse events were reported during the clinical trial at 6 months post final treatment: halos (1.1%); night driving problems (1.1%); epithelium in the interfaces (1.2%); double vision/ghosts (1/3%); loss of >2 lines best spectacle corrected visual acuity (BSCVA) (2.1%); and, pretreatment BSCVA 20/20 or better with post-treatment BSCVA worse than 20/25 (3.9%). Long term risk of LASIK for high myopia with or without astigmatism has not been studied.

CDRH will notify the public of its decision to approve your PMA by making available a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at <http://www.fda.gov/cdrh/pmapage.html>. Written requests for this information can also be made to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., Rm. 1-23, Rockville, MD 20857. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, 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).

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

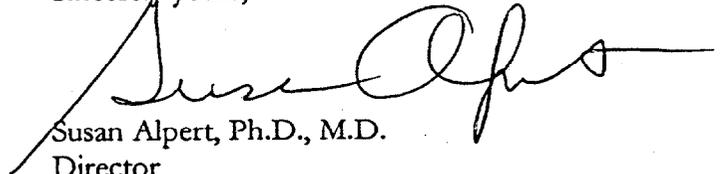
In addition to the postapproval requirements in the enclosure, the following information must also be submitted to the Agency:

1. in your annual report, for two years following approval, you must report on unscheduled maintenance visits (i.e., those beyond the usual laser maintenance schedule) to monitor laser performance and reliability; and,
2. you must immediately submit reports to FDA CDRH's Office of Compliance at the address below of any instances of device tampering.

OC/Division of Enforcement (HFZ-331)  
Center for Devices and Radiological Health  
Food and Drug Administration  
2098 Gaither Road  
Rockville, MD 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"

Issued: 3-4-98

#### CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

- (1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).
- (2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:
  - (a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and
  - (b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

- (1) A mix-up of the device or its labeling with another article.
- (2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and
  - (a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984. This regulation was replaced by the reporting requirements of the Safe Medical Devices Act of 1990 which became effective July 31, 1996 and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to the FDA whenever they receive or otherwise become aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer or importer:

- (1) May have caused or contributed to a death or serious injury; or
- (2) Has malfunctioned and such device or similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for a PMA, the manufacturer shall submit the appropriate reports required by the MDR Regulation within the time frames as identified in 21 CFR 803.10(c) using FDA Form 3500A, i.e., 30 days after becoming aware of a reportable death, serious injury, or malfunction as described in 21 CFR 803.50 and 21 CFR 803.52 and 5 days after becoming aware that a reportable MDR event requires remedial action to prevent an unreasonable risk of substantial harm to the public health. The manufacturer is responsible for submitting a baseline report on FDA Form 3417 for a device when the device model is first reported under 21 CFR 803.50. This baseline report is to include the PMA reference number. Any written report and its envelope is to be specifically identified, e.g., "Manufacturer Report," "5-Day Report," "Baseline Report," etc.

Any written report is to be submitted to:

Food and Drug Administration  
Center for Devices and Radiological Health  
Medical Device Reporting  
PO Box 3002  
Rockville, Maryland 20847-3002

Copies of the MDR Regulation (FOD # 336&1336) and FDA publications entitled "An Overview of the Medical Device Reporting Regulation" (FOD # 509) and "Medical Device Reporting for Manufacturers" (FOD #987) are available on the CDRH WWW Home Page. They are also available through CDRH's Fact-On-Demand (F-O-D) at 800-899-0381. Written requests for information can be made by sending a facsimile to CDRH's Division of Small Manufacturers Assistance (DSMA) at 301-443-8818.

SUMMARY OF SAFETY AND  
EFFECTIVENESS DATA (SSED)

## SUMMARY OF SAFETY AND EFFECTIVENESS DATA

### I. GENERAL INFORMATION

Device Generic Name: Ophthalmic Medical Laser System  
(193 nanometer wavelength)

Device Trade Name: Kremer Excimer Laser  
Serial No. KEA940202

Applicant's Name and Address: Photomed, Inc.  
Frederic B. Kremer, M.D.  
200 Mall Boulevard  
King of Prussia, PA 19406  
(610) 337-1580

Date of Panel Recommendation: February 13, 1998

Premarket Approval (PMA) Application Number: P970005

Date of Notification of Approval to Applicant: July 30, 1998

### II. INDICATIONS FOR USE

The Kremer Excimer Laser Serial No. KEA940202, using a 6.0 mm ablation zone, is indicated for myopic and astigmatic laser assisted in-situ keratomileusis (LASIK) in patients:

- with myopia ranging between -1.0 and -15.0 diopters (D) with or without astigmatism ranging from 0.0 D to 5.00 D;
- who are 18 years of age or older; and,
- with stable refraction over the 1-year period prior to surgery. Note: Patients between 18 and 20 years old should not demonstrate a shift in refraction greater than 0.5 D. Patients 21 years and older should not demonstrate a shift greater than 1.0 D.

### III. CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS

CONTRAINDICATIONS - Patients with the following conditions should not be considered for this procedure:

- Active ocular / systemic infection
- Fuchs' corneal dystrophy
- Keratoconus

- Central corneal scars affecting visual acuity
- Cornea too thin to achieve the desired correction
- Pregnant or nursing women

**WARNINGS** - Patients presenting with the following condition(s) should be considered for this treatment only after careful assessment of the potential risk and benefit to the specific patient:

- Previous herpetic keratitis<sup>1</sup>
- Collagen vascular disorders<sup>2</sup>
- Ablation of corneal stroma to less than 200 $\mu$ m from the endothelium
- Ablation depths within less than 250 microns from the endothelium may result in the loss of two or more lines of BSCVA.

**PRECAUTIONS** - The safety and effectiveness of this procedure has not been established in patients presenting with the following conditions:

- Severe dry eye syndrome
- Glaucoma
- Uveitis
- Blepharitis
- Psoriasis
- Immunosuppression
- Systemic or topical use of steroids
- History of keloid formation
- Due to the small sample of eyes treated in the investigational device exemptions (IDE) study with myopia of -13.0 D or more (1%, 6/665) or astigmatism of -4.0 D or more (1.8%, 13/720), the reported safety and effectiveness for this refractive range is less reliable than for eyes with less severe myopia or astigmatism.
- Patients with high myopia greater than -7.0 D whose BSCVA was 20/20 preoperatively have a 9% chance of being worse than 20/25 postoperatively at the 6 month postoperative interval.
- The effects of the LASIK procedure on visual performance under poor lighting conditions have not been determined. It is possible, following LASIK treatment, that patients may find it difficult to see in conditions such as very dim light, rain, snow, fog or glare from bright lights at night.
- Patients may still need glasses or contact lenses.
- There is no safety and effectiveness data for surface ablation performed with this laser.

- 
1. Patient needs to understand risks associated with corneal trauma and possible re-activation of herpetic keratitis.
  2. Patient needs to understand the risks associated with collagen vascular disorders and their associated corneal involvement. The patient may be included if sufficient understanding of possible complications is demonstrated. Consideration should be given to treatment on a monocular basis.

#### IV. DEVICE DESCRIPTION

##### A. The KEA940202 consists of the following system components:

*Excimer Laser:* An argon-fluorine excimer laser provides the following characteristics:

Laser wavelength:	193 nm
Laser pulse duration:	8-30 ns (FWHM)
Repetition rate:	10 Hz
Fluence (at the eye):	134 mJ/cm <sup>2</sup>
Ablation zone:	6.0 mm diameter
Composition of gases:	
ArF Premix	Argon (97.73%) Fluorine (2.17%)
Buffer:	Helium (99.999% purity)
For internal purging:	Helium

##### *Laser Beam Delivery System:*

Before reaching the eye, the raw rectangular beam of the excimer laser is directed sequentially through homogenizing optics that condense the long beam axis and modify the short axis to reduce effects of the Gaussian distribution.

The laser beam is continually monitored by an automatic fail-safe energy detector which evaluates each pulse to determine if it falls within predetermined energy limits.

##### *Gas Management System:*

The laser automatically mixes the correct proportion of halogen and buffer gases in the laser cavity to produce the 193 nm laser wavelength.

##### *Patient Management System:*

Patient management components include an operating microscope that allows the physician to view the eye; a fiber optic light source that illuminates the patient's eye; a fixation light source upon which the patient focuses during the procedure; a patient operating table with an adjustable V-shaped headrest to stabilize the patient's head; and a video camera and monitor for recording and viewing the procedure.

##### *Computer Control System:*

The KEA 940202 Laser has two PC-based computer systems with monitors and keyboards. The first system is the calibration computer which is used for daily calibration of the laser and to calculate an adjusted refractive correction. The second system is the laser computer. Its function is to accept the adjusted refractive correction and convert it into corresponding ablation profile

tables, and thereafter manage treatment by controlling the number of laser pulses and aperture size and shape for each ablation layer.

*Note:* Details regarding the operation of Kremer Excimer Laser Serial No. KEA940202 can be found in the operator's manual.

#### **B. Microkeratome:**

The complete system consists of an instrument tray which includes the shaper head, an adjustable height suction ring, handle, wrenches and test shaft. The instrument motor, handpiece, disposable blades, power supply with footswitches and power cords, applanation lens set, tonometer, optical zone marker, spatula, stop attachment, and digital thickness gauge are provided as separate components which complete the system

#### **V. ALTERNATIVE PRACTICES**

Conventional methods of correcting nearsightedness are: spectacles, contact lenses, or refractive surgery involving radial keratotomy (RK), or laser photorefractive keratotomy (PRK).

#### **VI. MARKETING HISTORY**

The Kremer Excimer Laser Serial No. KEA940202 is a single laser unit.

#### **VII. ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

Potential adverse reactions associated with LASIK include: loss of best spectacle-corrected visual acuity, overcorrection, undercorrection, increase in refractive cylinder, abnormal glare, halos, double vision, difficulty with night vision, corneal haze, epithelial ingrowth, corneal infection/ulcer/infiltrate, corneal decompensation/edema, lens abnormality, anxiety, and possible need for secondary surgical intervention.

#### **VIII. SUMMARY OF PRECLINICAL STUDIES**

Prior to clinical investigation, photoablations were performed in plastic materials, animal eyes, and human cadaver eyes with the Kremer Excimer Laser. The shape and surface of the ablations were analyzed under the electron microscope.

The laser was bench tested to assess the stability and reliability of the laser emissions and beam quality. Testing in plastic (PMMA) was performed to establish reliability and predictability of the shape and depth of the ablation for given beam settings and pulse sequences.

Test results showed that the laser could make smooth and reproducible ablations, primarily perpendicular to the surface, which were of controlled depth and geometry. Photoablation of the plastics showed that refractive correction were reproducible and predictable.

## **IX. SUMMARY OF CLINICAL STUDIES**

### **A. Study Objectives**

The objectives of this clinical investigation of the LASER-K<sup>sm</sup> LASIK procedure using the Kremer Excimer Laser were to:

- Reduce myopia and myopic astigmatism predictably and safely in eyes with myopia ranging between -1.0 D and -15.0 D, with or without astigmatism up to 5.0 D;
- Improve uncorrected visual acuity to reduce patients' dependence on spectacles and/or contact lenses.

### **B. Study Design**

This was a prospective, non-randomized, unmasked, single-center clinical study performed by two surgeons, with the participants acting as their own controls.

### **C. Inclusion/Exclusion Criteria**

Participants were eligible for the study if they met the following inclusion criteria:

- $\geq 18$  years old;
- primary myopia between -1.0 D and -15.0 D with or without astigmatism up to 5.0 D;
- stable refraction defined as  $< 1.0$  D shift over the one year prior to surgery;
- demonstrated desire for independence from spectacles or contact lenses;
- no soft contact lens wear for 2 weeks prior to surgery or no hard contact lens wear for 3 weeks prior to surgery;
- willingness to comply with all postoperative follow-up visits.

All patients were required to sign an informed consent form, were instructed about the risks associated with LASIK, and were clearly informed of all alternatives for the correction of their refractive error.

Patients who did not meet all of the above inclusion criteria were excluded from the study. Patients with any of the following conditions were also excluded: active ocular or systemic infection; severe dry eye syndrome; Fuchs' dystrophy; anterior basement membrane dystrophy; keratoconus associated with thinning; and chronic topical steroid use. Patients who had central corneal scars that affected visual acuity or whose corneas were too thin to permit the desired correction were also excluded.

### **D. Study Plan, Patient Assessments, and Efficacy Criteria**

From May 1, 1993 through June 30, 1996, the study was conducted under Institutional Review Board approval. This study population is known as Cohort 1. Beginning July 1, 1996, the study was conducted under a slightly modified, FDA-approved protocol (IDE G960101). This study

group is known as the Cohort 2 population. A second investigator joined the study during this IDE phase.

In essence, the protocols for both cohorts were the same, with one notable exception. Initially, the intended correction was typically calculated by subtracting 20% from the ideal correction. With time and experience, this 'safety factor' was progressively reduced. As a result, some patients in the Cohort 1 population were intentionally undercorrected by some degree. All patients in the Cohort 2 population, however, were treated using an intended correction that was equivalent to the ideal correction, with no safety factor included. The only other protocol change was a slight verbiage modification of the informed consent form. It should also be noted that, with time and experience, the primary operating surgeon improved the centering strategy and the operating technique.

Patients were evaluated preoperatively; 1 day postoperatively; 1 week postoperatively; 1, 3, and 6 months postoperatively, and 1 year postoperatively. Whenever an enhancement was performed, the follow-up schedule started over from the date of the retreatment.

Preoperatively, complete ocular and medical histories were taken, and visual acuity measurements, brightness acuity testing, cycloplegic refraction, and pupil examinations were performed. Refractive and ocular stability was documented.

Objective postoperative measurements performed at the 1-week visit and each visit thereafter included keratometry, uncorrected and best spectacle-corrected visual acuities, manifest refraction, and a thorough slit lamp examination for assessment of corneal clarity, anterior chamber, and lens status. All patient complaints, complications, and adverse reactions were recorded. Additional evaluations were performed at the 6-month and 1-year visits as outlined in the protocol. Cycloplegic refractions were performed at the 1-year visit.

The effectiveness of the procedure was based on uncorrected visual acuity (UCVA) improvement, reduction in the spherical equivalent (SE) [including independent analyses of both the spherical and cylindrical components], and accuracy of the achieved SE (as compared with the intended SE). The predictability of the procedure and device was evaluated by assessing the proportion of eyes experiencing a deviation from intended correction within  $\pm 0.5$  D,  $\pm 1$  D, and  $\pm 2$  D. Stability was defined as a change of less than or equal to 1 D for two consecutive visits three months apart. Stability evaluation also included analysis of the mean differences between the two visits.

Safety was evaluated in terms of loss of >2 lines of best spectacle-corrected visual acuity (BSCVA), BSCVA worse than 20/40, increase in cylinder of >2 D (eyes treated for myopia only), BSCVA worse than 20/25 in eyes that were 20/20 or better preoperatively, and all patient symptoms/complaints and adverse events.

All safety and efficacy analyses were performed on the population following a single treatment, and after retreatment (final result). Retreatment results were also evaluated separately.

Statistical analyses were performed at the 0.05 significance level at the point of stability (defined as the 6-month interval) for the key safety and efficacy variables. The following between-group comparisons were conducted for all of these key variables: Cohort 1 versus Cohort 2; myopes versus astigmatic myopes; eyes with <7 D versus eyes with  $\geq 7$  D preoperative SE; and eyes receiving a single treatment versus those that received at least one enhancement.

### E. Study Period, Investigational Site, and Demographic Data/Baseline Characteristics

#### *Study period*

A total of 2,482 eyes were treated under both protocols, beginning on May 1, 1993. The database was closed for purposes of this analysis on November 20, 1997.

#### *Investigational site*

All procedures were performed at the Kremer Laser Eye Center. Patients were evaluated postoperatively at the Kremer Laser Eye Center and at co-managing sites, provided the referring caregiver was qualified as a co-managing investigator.

#### *Demographics*

Demographics of both cohorts were quite similar. Slightly fewer females than males were treated, and mean age was in the upper 30s for both cohorts. Slightly more eyes for myopic astigmatism were treated than for myopia only. Table 1 summarizes these key demographic characteristics.

**Table 1.** Summary of Key Demographic Characteristics

	Male	Female	Mean Age (years)	Myopia (eyes)	Myopic Astigmatic (eyes)
Cohort 1 Population	329/616 (53.4%)	285/616 (46.3%)	38.1	487/1140 (42.7%)	653/1140 (57.3%)
Cohort 2 Population	359/704 (51.0%)	342/704 (48.6%)	36.3	630/1342 (46.9%)	712/1342 (53.1%)

#### *Baseline characteristics*

The majority of eyes treated in both cohorts for spherical myopia had moderate myopia from -2 D to -7 D spherical equivalent with no astigmatism, although some eyes did require spherical corrections up to just under -15 D.

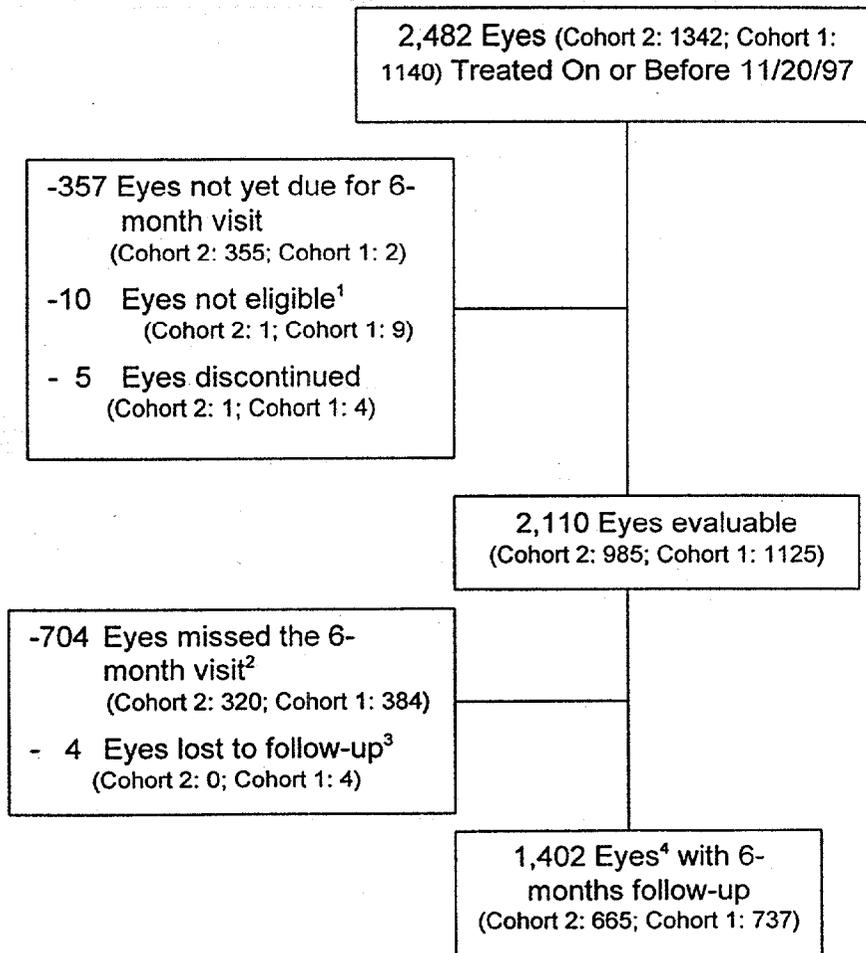
The majority of eyes treated for myopic astigmatism had low to moderate myopia with low to moderate astigmatism. Nearly 72% of eyes in Cohort 2 had preoperative sphere < -7 D; 58.5% of eyes in the Cohort 1 had preoperative sphere < -7 D. The remaining eyes had preoperative sphere ranging from  $\geq -7$  D to just under -15 D. Approximately 94% and 96% of eyes in the Cohort 2 and Cohort 1 populations, respectively, had preoperative cylinder < 3 D.

## F. Data Analysis and Results

### *Patient accountability*

Primary data analysis was performed using 6-month follow-up, as recommended by the October 10, 1996 CDRH FDA guidance for refractive surgery lasers performing LASIK. There were 2,482 enrolled eyes in the study on the cutoff date of November 20, 1997. There were 1,402 eyes with one or more LASIK treatments available for analysis at 6 months. Table 1 shows the 6-month status of all eyes that entered the study.

**Table 1.** Status of All Eyes at 6 Months



1. Not eligible due to non-myopic enhancement.
2. Note that 403 of these eyes (Cohort 2: 235; Cohort 1: 168) missed the 6-month visit *and* were not yet due for the 12-month visit or missed the 12-month visit. Also, 301 of these eyes (Cohort 2: 85; Cohort 1: 216) were seen after 6-months.
3. Patients considered lost to follow-up 18 months after their last visit.
4. Following one or more LASIK treatments.

Data validity was verified by twenty-four separate intra-data-set statistical comparisons. Overall accountability at the 6-month visit was 77.5% (Cohort 2: 81.1%; Cohort 1: 73.9%), with a total of 1,402 eyes seen at 6-months (i.e., 1402/1809). Accountability was calculated by dividing the eyes available at 6-months (1,402) by the total eyes enrolled (2,482) after adjusting the denominator for discontinued eyes (5), eyes not yet due for the interval (357), eyes not eligible for analysis (10), and eyes that missed the interval but were seen subsequently (301). Additional data validity analyses were performed. Safety and efficacy variables of eyes (a) seen at 6-months, and (b) last status of eyes seen prior to 6-months were compared to (c) eyes seen at 6-months, and (d) eyes not yet due for 6-month follow-up. Similar comparisons were performed at the 12-month interval as well (24 comparisons in all). As a result of these analyses, it was determined that the data presented in the PMA application are reliable, unbiased, and therefore constitute valid scientific evidence.

#### *Key efficacy variables*

Table 2(a) presents a summary of efficacy results at the 6-and 12-month visits, stratified by protocol, for eyes having one or more LASIK treatments, and Table 2(b) for eyes after initial LASIK treatment only. Six-month UCVA was 20/40 or better in 88.4% of all eyes after the final LASIK treatment, and 84.1% following initial treatment only without regard to further enhancement. When the 6-month UCVA results were compared between cohorts 1 and 2, there was a statistically significant between-group difference. A greater proportion of eyes in the Cohort 2 population had UCVA of 20/40 or better and 20/20 or better. This is due to the intentional undercorrection performed in some of the Cohort 1 eyes. None of the other efficacy variables were significantly different when the two populations were compared.

**Table 2(a). Summary of Key Efficacy Results After Final<sup>1</sup> Treatment at 6 and 12 Months**

Efficacy Variable	Cohort 2 (%)		Cohort 1 (%)		P value <sup>2</sup>
	6 months	12 months	6 months	12 months	
UCVA: <sup>3</sup>					
20/20 or better	199/491 (40.5)	87/218 (39.9)	212/668 (31.7)	202/612 (32.7)	0.840
20/40 or better	446/491 (90.3)	201/218 (92.2)	579/668 (86.7)	535/612 (87.4)	0.523
MRSE: <sup>4</sup>					
±0.5 D	472/665 (71.0)	199/269 (74.0)	494/737 (67.0)	431/688 (62.6)	0.401
±1 D	584/665 (87.8)	249/269 (92.6)	631/737 (85.6)	588/688 (85.5)	0.231
±2 D	650/665 (97.7)	266/269 (98.9)	710/737 (96.3)	669/688 (97.2)	0.091

1. Final treatment includes all eyes treated after their last LASIK procedure.
2. Cochran-Mantel-Haenszel statistic comparing 6 and 12 months, controlling for protocol.
3. All eyes treated for monovision were excluded from this analysis, since undercorrection is intentional in this sub-population
4. Manifest refraction spherical equivalent.

**Table 2(b). Summary of Key Efficacy Results After Initial<sup>1</sup> Treatment at 6 and 12 Months**

Efficacy Variable	Cohort 2 (%)		Cohort 1 (%)		P value <sup>2</sup>
	6 months	12 months	6 months	12 months	
UCVA: <sup>3</sup>					
20/20 or better	195/493 (39.6)	87/219 (39.7)	192/657 (29.2)	185/563 (32.9)	0.262
20/40 or better	440/493 (89.3)	201/219 (91.8)	527/657 (80.2)	481/563 (85.4)	0.009
MRSE: <sup>4</sup>					
±0.5 D	461/670 (68.8)	199/271 (73.4)	421/724 (58.2)	387/637 (60.8)	0.102
±1 D	579/670 (86.4)	249/271 (91.9)	556/724 (76.8)	530/637 (83.2)	0.001
±2 D	655/670 (97.8)	268/271 (98.9)	675/724 (93.2)	614/637 (96.4)	0.003

1. Initial treatment includes all eyes after their first LASIK treatment without regard to further enhancement.
2. Cochran-Mantel-Haenszel statistic comparing 6 and 12 months, controlling for protocol.

3. All eyes treated for monovision were excluded from this analysis, since undercorrection is intentional in this sub-population
4. Manifest refraction spherical equivalent.

There was a statistically significant difference between all key efficacy variables when eyes with preoperative SE <7 D were compared with those with preoperative SE ≥7 D, thus indicating that the LASIK procedure produced better results in eyes with low to moderate preoperative myopia. Table 3(a) summarizes the key efficacy variables and statistical comparisons for patient eyes after their final LASIK treatment, and Table 3(b) summarizes key efficacy variables and statistical comparisons for patient eyes after their initial LASIK treatment without regard to further enhancement.

**Table 3(a).** Summary of Key Efficacy Results After Final<sup>1</sup> Treatment at 6 Months Stratified by Preoperative SE

Efficacy Variable	Cohort 2 (%)		Cohort 1 (%)		P value <sup>2</sup>
	<7 D	≥7 D	<7 D	≥7 D	
UCVA: <sup>3</sup>					
20/20 or better	185/371 (49.9)	14/120 (11.7)	176/447 (39.4)	36/221 (16.3)	0.001
20/40 or better	358/371 (96.5)	88/120 (73.3)	407/447 (91.1)	172/221 (77.8)	0.001
MRSE: <sup>4</sup>					
±0.5 D	374/477 (78.4)	98/188 (52.1)	356/483 (73.7)	138/254 (54.3)	0.001
±1 D	446/477 (93.5)	138/188 (73.4)	439/483 (90.9)	192/254 (75.6)	0.001
±2 D	475/477 (99.6)	175/188 (93.1)	480/483 (99.4)	230/254 (90.6)	0.001

1. Final treatment includes all eyes treated after their last LASIK procedure.
2. Cochran-Mantel-Haenszel statistic comparing preoperative SE (<7 D vs. ≥7D), controlling for protocol.
3. All eyes treated for monovision were excluded from this analysis, since undercorrection is intentional in this sub-population.
4. Manifest refraction spherical equivalent.

**Table 3(b).** Summary of Key Efficacy Results After Initial<sup>1</sup> Treatment at 6 Months Stratified by Preoperative SE

Efficacy Variable	Cohort 2 (%)		Cohort 1 (%)		P value <sup>2</sup>
	<7 D	≥7 D	<7 D	≥7 D	
UCVA: <sup>3</sup>					
20/20 or better	181/371 (48.8)	14/122 (11.4)	160/441 (36.3)	32/216 (14.8)	0.001
20/40 or better	356/371 (96.8)	84/122 (68.9)	382/441 (86.6)	145/216 (67.1)	0.001
MRSE: <sup>4</sup>					
±0.5 D	367/479 (76.6)	94/191 (49.2)	316/476 (66.4)	105/248 (42.3)	0.001
±1 D	445/479 (92.9)	134/191 (70.2)	401/476 (84.2)	155/248 (62.5)	0.001
±2 D	477/479 (99.6)	178/191 (93.2)	467/476 (98.1)	208/248 (83.9)	0.001

1. Initial treatment includes all eyes after their first LASIK treatment without regard to further enhancement.
2. Cochran-Mantel-Haenszel statistic comparing preoperative SE (<7 D vs. ≥7D), controlling for protocol.
3. All eyes treated for monovision were excluded from this analysis, since undercorrection is intentional in this sub-population.
4. Manifest refraction spherical equivalent.

Table 4 summarizes the key efficacy variables and statistical comparisons for myopic eyes versus myopic astigmatic eyes at 6-months after the final LASIK treatment in the Cohort 2 study. When controlling for high vs. low myopia, a comparison of efficacy results between eyes treated for myopia only and eyes treated for both myopia and astigmatism showed no statistically significant differences, with the lone exception being a reduction in the number of high myopic astigmatic eyes achieving UCVA of 20/20 or better.

**Table 4.** Summary of Key Efficacy Results<sup>1</sup> at 6 Months Stratified by Spherical vs. Astigmatic Myopia Controlling for Preoperative SER

Efficacy Variable	< 7 D		≥ 7 D		P value <sup>2</sup>
	Spherical Myopia	Astigmatic Myopia	Spherical Myopia	Astigmatic Myopia	
UCVA: <sup>3</sup>					
20/20 or better	111/213 (52.1)	74/158 (46.8)	12/61 (19.7)	2/59 (3.4)	0.057
20/40 or better	204/213 (95.8)	154/158 (97.5)	47/61 (77.1)	41/59 (69.5)	0.808
MRSE: <sup>4</sup>					
±0.5 D	192/243 (79.0)	182/234 (77.8)	36/76 (47.4)	62/112 (55.4)	0.703
±1 D	228/243 (93.8)	218/234 (93.2)	52/76 (68.4)	86/112 (76.8)	0.456
±2 D	242/243 (99.6)	233/234 (99.6)	68/76 (89.5)	107/113 (95.4)	0.141

1. Includes all eyes in the IDE study after the last LASIK treatment.
2. Cochran-Mantel-Haenszel statistic comparing spherical and astigmatic myopia, controlling for Preoperative SER group.
3. All eyes treated for monovision were excluded from this analysis, since undercorrection is intentional in this sub-population.
4. Manifest refraction spherical equivalent.

*Other efficacy results after final LASIK treatment:*

- **Stability of manifest refraction.** A total of 451 eyes were examined at three (3) consecutive visits (1, 3 & 6 months) in Cohort 2, of which 89.3% achieved stability (defined as a change in SE of ≤1.00 D across consecutive visits) between the month-1 and month-3 visits, increasing to 93.3% stability between the 3-month and 6-month visits. When analyzing those eyes evaluated at all four (4) consecutive visits in the Cohort 2 study, (n=139) 90.6% achieved stability between the 1- and 3-month visits, 95.0% between the 3- and 6-month visits, and 96.4% between the 6- and 12-month visits. Between 6 and 12 months the mean difference in refractive error was 0.05 D per month.

**Table 4(a).** Stability of Manifest Refraction - Cohort 2 - All Eyes Treated

Change in Spherical Equivalent Between	1 and 3 Months n/N (%)	3 and 6 Months n/N (%)	6 and 12 Months n/N (%)
≤ 1.00 D	126/139 (90.6)	132/139 (95.0)	134/139 (96.4)
Mean Difference	0.45	0.38	0.31
SD	0.44	0.38	0.34
95% CI	(0.42 - 0.48)	(0.36 - 0.40)	(0.29 - 0.33)

Only those subjects with all 1,3,6, and 12 months visits are included in the analysis.

Accuracy of sphere and cylinder for astigmatic myopes.

*Sphere.* For all eyes treated under Cohort 2, mean intended spherical correction was -4.95 D and mean actual correction at the sixth postoperative month was -4.94 D. For eyes treated under the Cohort 1, mean intended spherical correction was -5.58 D and mean actual correction at month 6 was -5.34 D.

Over 80% of those eyes treated for myopic astigmatism achieved correction within  $\pm 1$  D of intended sphere at 1 month. This level of accuracy was maintained throughout the 1-year study period.

*Cylinder.* Over 80% of all eyes treated for myopic astigmatism achieved cylinder correction within  $\pm 1$  D of zero cylinder at 1 month. This level of accuracy was maintained throughout the 1-year study period. For myopic astigmatism, there was a mean undercorrection of just 0.1 D in Cohort 2. The procedure most effectively reduced cylinder magnitude in eyes with  $>1$  D preoperative cylinder. Table 5 presents the accuracy of cylinder correction (to zero) for eyes in Cohort 2, stratified by high versus low dioptric group.

**Table 5.** Accuracy of Cylinder Correction (to Zero) for Eyes Treated in IDE Study

Sphere	Preoperative SER <sup>1</sup> < -7 D			
	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	12 Months n/N (%)
$\leq 0.50$ D	252/365 (69.0)	208/327 (63.6)	153/234 (65.4)	63/95 (66.3)
$\leq 1.00$ D	329/365 (90.1)	287/327 (87.8)	209/234 (89.3)	84/95 (88.4)
Sphere	Preoperative SER $\geq -7$ D			
	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	12 Months n/N (%)
$\leq 0.50$ D	58/149 (38.9)	53/135 (39.3)	43/112 (38.4)	18/43 (41.9)
$\leq 1.00$ D	105/149 (70.5)	94/135 (69.9)	77/112 (68.8)	25/43 (58.1)

1. Spherical Equivalent Refraction.

*Manifest versus Cycloplegic Refraction:* Table 6 compares manifest refraction and cycloplegic refraction at 12 months for the Cohort 2 study group. There were no statistical differences in the proportion of eyes within 0.5 D or 2.0 D of target correction. There was a statistical difference between manifest and cycloplegic refractions when looking at proportions of eyes within 1.0 D of target. This is attributed to a higher proportion of hyperopic overcorrections in the  $\pm 1.0$  D group than in the  $\pm 0.5$  D group. However, 89% of eyes within 1.0 D of target correction meets current FDA guidelines for this parameter.

**Table 6.** Comparison of Manifest and Cycloplegic Refractions at 12 Months

Spherical Equivalent	Manifest Refraction	Cycloplegic Refraction	p-value <sup>1</sup>
SE $\pm$ 0.5 D	158/224 (70.5)	160/224 (71.4)	0.7440
SE $\pm$ 1.0 D	221/224 (94.2)	199/224 (88.8)	0.0075
SE $\pm$ 2.0 D	222/224 (99.1)	221/224 (98.7)	1.000

1. P-value for proportions derived from McNemar's test.

- **Stability of cylinder.** The manifest cylinder refraction was considered stable when cylinder did not change by more than 1 D between any two postoperative visits. Stability of cylinder was achieved in approximately 93.5% of all eyes between the month 1 and 3 visits, increasing to 94.7% between the 3 and 6 month visits, and 95.5% had a stable cylinder between 6 and 12 months.

*Key safety variables*

Table 7(a) presents a summary of key safety variables for all eyes after their final LASIK treatment at the 6- and 12-month visits, stratified by protocol. Table 7(b) summarizes key safety variables for all eyes after their initial LASIK treatment without regard to further enhancement. The overall proportion of eyes for both studies combined losing  $\geq 2$  lines of BSCVA at 12-months was 2.3% after final LASIK treatment, and 1.4% after initial LASIK treatment. When these key safety results are compared between Cohorts 1 and 2, there are no statistically significant differences.

**Table 7(a).** Summary of Key Safety Results After Final<sup>1</sup> Treatment at 6 and 12 Months

Safety Variable	Cohort 2 (%)		Cohort 1 (%)		P value <sup>2</sup>
	6 months	12 months	6 months	12 months	
<b>BSCVA:</b>					
Loss of >2 lines	14/665 (2.1)	2/269 (0.7)	20/737 (2.7)	20/688 (2.9)	0.593
Worse than 20/40	4/665 (0.6)	3/269 (1.1)	11/737 (1.5)	12/688 (1.7)	0.480
Worse than 20/25 with 20/20 or better preop	26/665 (3.9)	10/269 (3.7)	33/737 (4.5)	28/688 (4.1)	0.696
Increase of >2D cylinder <sup>3</sup>	2/319 (0.6)	2/131 (1.5)	1/315 (0.3)	2/283 (0.7)	0.258

1. Final treatment includes all eyes treated after their last LASIK procedure.
2. Cochran-Mantel-Haenszel statistic comparing 6 and 12 months, controlling for protocol.
3. Eyes treated for spherical correction only.

**Table 7(b).** Summary of Key Safety Results After Initial<sup>1</sup> Treatment at 6 and 12 Months

Safety Variable	Cohort 2 (%)		Cohort 1 (%)		P value <sup>2</sup>
	6 months	12 months	6 months	12 months	
BSCVA:					
Loss of >2 lines	14/670 (2.1)	2/271 (0.7)	16/724 (2.2)	11/637 (1.7)	0.754
Worse than 20/40	5/670 (0.8)	3/271 (1.1)	9/724 (1.2)	10/637 (1.6)	0.472
Worse than 20/25 with 20/20 or better preop	27/670 (6.6)	10/271 (3.7)	29/724 (4.0)	20/637 (3.1)	0.411
Increase of >2D cylinder <sup>3</sup>	2/319 (0.6)	2/131 (1.5)	1/306 (0.3)	3/264 (0.7)	0.140

1. Initial treatment includes all eyes after their first LASIK treatment without regard to further enhancement.
2. Cochran-Mantel-Haenszel statistic comparing 6 and 12 months, controlling for protocol.
3. Eyes treated for spherical correction only.

There was a statistically significant difference in favor of SE <7 D in several of the key safety variables when eyes with preoperative SE <7 D were compared with those with preoperative SE ≥7 D. Table 8(a) summarizes the key safety variables and statistical comparisons for patient eyes after final LASIK treatment, and Table 8(b) summarizes key safety variables after initial LASIK treatment.

**Table 8(a).** Summary of Key Safety Variables After Final<sup>1</sup> Treatment at 6 Months Stratified by Preoperative SE

Safety Variable	Cohort 2 (%)		Cohort 1 (%)		P value <sup>2</sup>
	<7 D	≥7 D	<7 D	≥7 D	
BSCVA:					
Loss of >2 lines	2/477 (0.4)	12/188 (6.3)	2/483 (0.4)	18/254 (7.1)	0.001
Worse than 20/40	1/477 (0.2)	3/188 (1.6)	0/483 (0)	11/254 (4.3)	0.001
Worse than 20/25 with 20/20 or better preop	9/477 (2.0)	17/188 (9.0)	8/469 (2.0)	17/183 (9.0)	0.001
Increase of >2D cylinder <sup>3</sup>	0/243 (0)	2/76 (2.6)	0/252 (0)	1/63 (1.6)	0.001

1. Final treatment includes all eyes treated after their last LASIK procedure.
2. Cochran-Mantel-Haenszel statistic comparing preoperative SE (<7D vs. ≥7D), controlling for protocol.
3. Eyes treated for spherical correction only.

**Table 8(b).** Summary of Key Safety Variables After Initial<sup>1</sup> Treatment at 6 Months Stratified by Preoperative SE

Safety Variable	Cohort 2 (%)		Cohort 1 (%)		P value <sup>2</sup>
	<7 D	≥7 D	<7 D	≥7 D	
BSCVA:					
Loss of >2 lines	2/479 (0.4)	12/191 (6.3)	0/476 (0)	16/248 (6.5)	0.001
Worse than 20/40	1/479 (0.2)	4/191 (2.1)	0/476 (0)	9/248 (3.6)	0.001
Worse than 20/25 with 20/20 or better preop	9/479 (1.9)	18/191 (9.4)	8/476 (1.7)	21/248 (8.5)	0.001
Increase of >2D cylinder <sup>3</sup>	0/242 (0)	2/77 (2.6)	0/247 (0)	1/59 (1.7)	0.001

1. Initial treatment includes all eyes after their first LASIK treatment without regard to further enhancement.

2. Cochran-Mantel-Haenszel statistic comparing preoperative SE (<7D vs. ≥7D), controlling for protocol.

3. Eyes treated for spherical correction only.

*Adverse events/complications after final LASIK treatment:*

Adverse events / Complications

Adverse events included corneal infiltrate (1 eye in Cohort 1 population), 1 case of cap malalignment (repositioned without sequelae), 1 retinal detachment in each cohort, and several early cataracts. The retinal detachments occurred at 11 months and >1 year postoperatively, indicating that these detachments were unrelated to surgery. The early cataracts were noted prior to surgery and were not induced. There were no corneal infections, lost or melted caps, or retinal vascular accidents recorded.

Corneal edema was noted between 1 week and 1 month in 5.3% of the Cohort 1 population and 3.4% of the Cohort 2 population. These cases resolved with further healing. The following complications - transient corneal central and peripheral epithelial defects, epithelium in the central interface that required removal, aborted procedures due to an incomplete cap, and cap striae - each occurred with ≤ 1% incidence. Epithelium in the periphery, which did not influence vision and did not require removal, occurred somewhat more frequently in the Cohort 1 population, as compared with the Cohort 2 population. Hingeless flap, an intraoperative complication, occurred in 1.8% of cases in the Cohort 1 population and 0.7% of cases in the Cohort 2 population. There were no associated sequelae with a hingeless flap. Interface foreign bodies at each interval which were observed under slit-lamp, but had no clinical sequelae, ranged between 14.5% and 8.8%.

Recorded patient complaints included glare, halos, trouble with night driving, double vision/ghosting, foreign body sensation, anxiety, and pain. The incidence of complaints considered by patients to be bothersome ranged from 0% to 4.1% for both protocol populations. Difficulty with night driving that was of a bothersome nature occurred at a rate of 4.1% in the Cohort 1 population and 1.1% in the Cohort 2 population. Complaints of a similar nature but not considered bothersome by the patients occurred at a somewhat higher incidence.

All of these complaints tended to be less prevalent in the Cohort 2 population than in the earlier Cohort 1 population, likely because of improvements in centering strategy and surgical technique. As expected, complaints were also less prevalent in the <7 D group as compared with the  $\geq 7$  D group in both protocol populations. Eyes with residual refractive errors also had a higher incidence of symptoms than those with SEs within  $\pm 0.5$  D. The study did not measure the extent to which the complaints may have resolved in the presence of spectacle correction, as would be expected. Tables 9(a) and (b) summarize the bothersome complaints reported by patients in both studies.

**Table 9(a).** Summary of Adverse Events and Complications Experienced in Cohort 2.

Adverse Events / Complications	Cohort 2 (%)				
	Operative <sup>1</sup>	1 month	3 months	6 months	12 months
Corneal infiltrate		0/873 (0)	0/814 (0)	0/657 (0)	0/308 (0)
Corneal edema $\geq 1$ mo		2/873 (0.2)	1/814 (0.1)	0/657 (0)	0/308 (0)
Flap misalignment		1/873 (0.1)	0/814 (0)	0/657 (0)	0/308 (0)
Retinal detachment		0/873 (0)	0/814 (0)	0/657 (0)	1/308 (0.3)
Corneal Edema < 1 mo	30/873 (3.4)				
Incomplete cap-abort procedure	4/1342 (0.3)				
No hinge on flap	9/1342 (0.7)				
Epithelial defect - Central		1/873 (0.1)	1/814 (0.1)	0/657 (0)	0/308 (0)
Epithelial defect - Peripheral		1/873 (0.1)	0/814 (0)	1/657 (0.2)	0/308 (0)
Epithelium in interface-Central		1/873 (0.1)	0/814 (0)	1/657 (0.2)	0/308 (0)
Epithelium in interface-Periph.		8/873 (0.9)	10/814 (1.2)	8/657 (1.2)	1/308 (0.3)
Interface foreign bodies		126/873 (14)	128/814 (14)	95/657 (15)	27/308 (9)
Cap striae		9/873 (1.0)	6/814 (0.7)	5/657 (0.8)	1/308 (0.3)
Pain		4/873 (0.5)	4/814 (0.5)	3/657 (0.5)	2/308 (0.7)
Glare <sup>2</sup>				5/661 (0.8)	4/269 (1.5)
Halos <sup>2</sup>				7/661 (1)	0/269 (0)
Night Driving Problems <sup>2</sup>				7/661 (1)	2/269 (0.7)
Double Vision / Ghosts <sup>2</sup>				10/661 (1.5)	2/269 (0.7)
Foreign Body Sensation <sup>2</sup>				5/661 (0.8)	0/269 (0)
Anxiety <sup>2</sup>				0/661 (0)	0/269 (0)

1. Adverse events occurring operatively and up to 1 month postoperatively.
2. These events were reported 6 and 12 months after final treatment.

**Table 9(b).** Summary of Adverse Events and Complications Experienced in Cohort 1.

Adverse Events	Operative <sup>1</sup>	Cohort 1 (%)			
		1 month	3 months	6 months	12 months
Corneal infiltrate		0/804 (0)	0/910 (0)	1/788 (0.1)	0/752 (0)
Corneal edema $\geq$ 1 mo		14/804 (1.7)	4/910 (0.4)	0/788 (0)	0/752 (0)
Flap misalignment		0/804 (0.1)	0/910 (0)	0/788 (0)	0/752 (0)
Retinal detachment		0/804 (0)	0/910 (0)	0/788 (0)	1/752 (0.1)
<b>Complications</b>					
Corneal Edema < 1 mo	43/741 (5.8)				
Incomplete cap-abort procedur	1/1141 (0.1)				
No hinge on flap	20/1141 (1.8)				
Epithelial defect - Central		2/741 (0.3)	1/859 (0.1)	2/750 (0.3)	0/687 (0)
Epithelial defect - Peripheral		1/741 (0.1)	1/859 (0.1)	0/750 (0)	2/687 (0.3)
Epithelium in interface-Central		2/741 (0.3)	0/859 (0)	1/750 (0.1)	0/687 (0)
Epithelium in interface-Periph.		8/741 (1.1)	12/859 (1.4)	15/750 (2)	10/687 (1.5)
Interface foreign bodies		71/741 (9.6)	78/859 (9.1)	50/750 (6.7)	43/687 (6.3)
Cap striae		3/741 (0.4)	7/859 (0.8)	5/750 (0.7)	3/687 (0.4)
Pain		4/741 (0.5)	1/859 (0.1)	3/750 (0.4)	2/687 (0.3)
Glare <sup>2</sup>				23/726 (3.2)	16/678 (2.4)
Halos <sup>2</sup>				14/726 (1.9)	6/678 (0.9)
Night Driving Problems <sup>2</sup>				30/726 (4.1)	15/678 (2.2)
Double Vision / Ghosts <sup>2</sup>				6/726 (0.8)	5/678 (0.7)
Foreign Body Sensation <sup>2</sup>				1/726 (0.1)	0/678 (0)
Anxiety <sup>2</sup>				1/726 (0.1)	1/678 (0.1)

1. Adverse events occurring operatively and up to 1 month postoperatively.

2. These events were reported 6 and 12 months after final treatment.

*Other safety results after final LASIK treatment*

- **Residual cylinder.** Both Cohort 2 and 1 populations had slight cylindrical overcorrections when the intended correction was taken into consideration (mean overcorrections: 0.18 D and 0.21 D, respectively). These overcorrections, or surgically induced residual astigmatism, were greater in eyes treated for myopia only. The mean cylinder overcorrection was approximately one-half of a diopter among eyes treated for myopia only in both populations.

Of eyes treated for myopic astigmatism, 68.8% of those treated under the Cohort 2 and 70.9% of those treated under the Cohort 1 had residual cylinder <1 D at the point of stability (6 months postoperatively). The number of these eyes with residual cylinder >2 D is low (n=15/346 [4.3%] for the Cohort 2 population and n=21/422 [4.9%] for the Cohort 1 population). Table 11 summarizes the residual astigmatic error observed at 6-months postoperatively in eyes treated for astigmatic myopia.

**Table 10.** Summary of Residual Astigmatic Error at 6 Months Postoperative in Eyes Treated for Myopic Astigmatism

Residual Cylinder Magnitude	Cohort 2 (%)	Cohort 1 (%)
0.0 D to < 0.5 D	148/346 (42.8)	156/422 (37)
≥ 0.5 D to < 1.0 D	90/346 (26)	141/422 (33.4)
≥ 1.0 D to < 2.0 D	90/346 (26)	87/422 (20.6)
≥ 2.0 D to < 3.0 D	11/346 (3.2)	15/422 (3.6)
>3.0 D	4/346 (1.2)	6/422 (1.4)
Unknown	3/346 (0.8)	17/422 (4.0)

- Change in cylinder axis. The median shift in cylinder axis among all eyes treated was 25° for the Cohort 2 population and 35° for the Cohort 1 population. The highest shifts in astigmatic axes tended to occur in eyes with the lowest degrees of residual cylinder. A shift in axis has no clinical significance, and is analogous to a compass needle showing multiple directions at the North Pole. Table 12 summarizes the observed shift in axis.

**Table 11.** Summary Statistics of Shift in Cylinder Axis in Eyes Treated for Myopic Astigmatism

	Cohort 2 Shift in Axis	Cohort 1 Shift in Axis
N	655	712
Mean	42.55	46.64
Median	25.00	35.99
Std Dev	40.27	40.32
Min	0.00	0.00
Max	147.00	149.00

### *Retreatments*

Under Cohort 2, 47 eyes were retreated for undercorrection, for an overall enhancement rate of 3.5% (n=47/1342) under this protocol. In Cohort 2, 1 of 13 eyes that had a BSCVA of 20/20 or better preoperatively exhibited a BSCVA of worse than 20/25 at 6-months postoperative.

Under Cohort 1, 162 eyes were retreated for undercorrection, for an overall enhancement rate of 14.2% (n=162/1140). The higher retreatment rate in this earlier population is attributable to the earlier Cohort 1 requirement of intentional undercorrection. Four (4) retreated eyes had a decrease of BSCVA greater than 2 lines at 3 months which persisted out to 12 months postoperatively. Two eyes (2.1%) at 6 months and 3 eyes (3.9%) at 12 months had a BSCVA worse than 20/40. Eight eyes (8.3%) at 6 months and 8 eyes (10.4%) at 12 months that had a BSCVA of 20/20 or better preoperatively exhibited a BSCVA of 20/25 or worse.

## **X. CONCLUSIONS**

The laboratory and clinical results based on 665 eyes treated and followed for six months provide reasonable assurance that the Kremer Excimer Laser is safe and effective for LASIK procedures when used as indicated and in accordance with the directions for use. The results of this study have been complemented and supported by safety and effectiveness information from an additional 737 eyes also followed for six months and 957 eyes followed for 12 months.

## **XI. PANEL RECOMMENDATIONS**

On February 13, 1998, the Ophthalmic Devices Panel recommended that the premarket approval application for this excimer laser be considered not approvable. The major concerns raised by the panel related to:

- accountability;
- use of Snellen charts;
- hyperopic retreatments;
- induced cylinder;
- cycloplegic refraction;
- stability of cylinder;
- clarification of 250 $\mu$  versus 200 $\mu$  residual thickness; and,
- labeling (retreatments, indications, contraindications and precautions)

## **XII. FDA DECISION**

This laser was originally developed for the use of Dr. Kremer for his patients. It was developed to perform what has come to be referred to as the Laser K<sup>SM</sup> LASIK procedure. The device was first used for the LASIK treatment of patients in 1993 and until 1996 under studies approved by an Investigational Review Board (IRB). In late 1995, FDA requested that an IDE be submitted to, and approved by, the Agency if Dr. Kremer was to continue to study human subjects with his laser. Dr. Kremer received approval for his IDE on June 7, 1996. This PMA was filed on January 31, 1997.

Following the February 13, 1998 panel meeting, CDRH met with the sponsor on February 24, 1998 to discuss clinical issues and on March 10, 1998 to discuss engineering and software concerns. Subsequently, CDRH issued a major deficiency letter on March 12, 1998 which requested the information and clarifications specified by the panel and FDA.

The sponsor provided FDA with detailed responses to each of the deficiencies in subsequent amendments to the PMA. The major concerns raised by the panel were resolved in the following manner:

**Accountability:** The sponsor performed the required analyses and demonstrated that those patients not available at 6 months are no different in their safety when compared to those that were available. Also, they had a somewhat better effectiveness outcome.

**Use of Snellen charts:** FDA accepted the sponsor's explanation of the constant error introduced by the use of the Snellen charts instead of ETDRS charts. The sponsor re-calculated the key safety variables using the conventional definition of lines lost with respect to loss of >2 lines of visual acuity. Moreover, FDA acknowledges that the IDE study was approved by FDA using Snellen charts so that there would be comparability with the IRB protocol.

**Hyperopic retreatments:** All key safety and effectiveness variables were recalculated by the sponsor after eliminating hyperopic retreatments. The outcomes are satisfactory. Dataline listings of retreated eyes were provided by the sponsor. These data did not reveal a problem with the device.

**Induced cylinder:** The sponsor demonstrated that after correcting for decentration early in the clinical trial, there was minimal induction of cylinder.

**Cycloplegic refraction:** The sponsor compared cycloplegic refraction with manifest refraction at one year and found minimal overcorrection when cyclopleged.

**Stability of cylinder:** The sponsor reanalyzed the residual cylinder in a manner requested by FDA. There is reasonable assurance of effectiveness of the laser with regard to cylinder correction.

**Clarification of 250 $\mu$  versus 200 $\mu$  residual thickness:** Only six eyes were treated with a residual depth of 200 $\mu$ . FDA expressed its concerns to the sponsor about future ectasia in these eyes. This issue was addressed in the Warnings section of the labeling.

**Labeling:** Labeling revisions concerning retreatment, indications, contraindications and precautions were recommended by FDA and agreed to in a meeting with the sponsor held on May 26, 1998 and in subsequent facsimile correspondence.

This PMA approval is for a single device and does not authorize the PMA applicant to manufacture or distribute any additional units. Therefore, no preapproval Good Manufacturing Practices (GMP) inspection was required. However, the Office of Compliance did recommend a postmarket approval inspection.

### **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

# LABELING

**KREMER EXCIMER LASER SERIAL NO. KEA940202**

**PHYSICIAN MANUAL**

Document P970005 - PM

**CAUTION:** Federal Law restricts this device to commercial use and treatment of patients by or on the order of a physician or other licensed practitioner.

This document provides information concerning the intended clinical use of the Kremer Excimer Laser Serial No. KEA940202. For complete information concerning system components, safety instructions, maintenance, and troubleshooting, refer to the Kremer Excimer Laser Serial No. KEA940202 Operator Instruction Manual (Document KEA0100).

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.



**KREMER LASER EYE CENTER  
200 MALL BOULEVARD  
KING OF PRUSSIA, PA 19406**

**PHONE (610) 337-1580**

# **Kremer Excimer Laser Serial No. KEA940202**

## **Physician Manual**

### **GENERAL WARNINGS**

The following warnings need to be read and fully understood before operating this laser refractive surgical system. Each warning identifies conditions or practices that may cause personal injury, loss of life or cause damage to this equipment or surrounding property:

**WARNING! RESTRICTED DEVICE:** U.S. Federal Law restricts the commercial use of this equipment to treatment of patients by physicians or other licensed eye care practitioners. Practitioners who use this device must have prior corneal surgical experience and be trained in laser system calibration.

**WARNING!** Do not operate this laser in the presence of flammable anesthetics or volatile substances such as alcohol.

**WARNING! TOXIC AND COMPRESSED GAS HANDLING** The air, argon-fluorine premix and helium gases used in this system are stored in high pressure gas cylinders. Improper handling, storage, adjustments or modifications to the gas cylinder or any gas carrying line or component can result in a high pressure gas leak or possible explosion. Additionally the argon fluorine premix is highly toxic and can be sensed by its sharp, penetrating odor and eye, nose and throat irritation.

Before anyone works with either the gas cylinders or gas handling equipment, it is recommended that the person be trained in the proper handling of toxic and compressed gases. Gas safety instructions provided in the operator's manual shall be fully understood and followed.

**WARNING!** Hazardous conditions may result if this equipment is used in a manner other than that described in the manual. This use includes but is not limited to performance of procedures, control usage and adjustments.

**WARNING! POTENTIAL SKIN AND/OR EYE EXPOSURE** The Kremer Excimer Laser Serial No. KEA940202 is classified as a Class IV laser with a 193 nanometer output. Although this class of laser is potentially hazardous to the skin and surface layers of the cornea, the laser energy will not enter the eye and will not damage the retina or crystalline lens. The beam path is enclosed except for the area of the optics extension located vertically immediately below the microscope and above the operating table. Laser beam reflectivity from objects in the operating room including surgical instruments is relatively low.

# Kremer Excimer Laser Serial No. KEA940202

## Physician Manual

### TABLE OF CONTENTS

	<u>Contents</u>	<u>Page No</u>
I.	Device Description .....	1
II.	Indications for Use .....	1
III.	Contraindications, Warnings, and Precautions .....	2
IV.	Patient Selection .....	3
V.	Preoperative Examination and Surgical Planning .....	13
VI.	LASER-K <sup>SM</sup> LASIK Procedure for Myopia and/or Astigmatism	17
	References .....	23

# Kremer Excimer Laser Serial No. KEA940202

## Physician Manual

### I. DEVICE DESCRIPTION

The Kremer Excimer Laser Serial No. KEA940202 operates on the principle that radiation at the 193 nm wavelength is highly absorbed by the cornea.<sup>4</sup> The 193 nm wavelength photon energy disrupts the intramolecular collagen bonds of corneal tissue,<sup>4</sup> causing the ablated tissue to denature. The 193 nm wavelength disruption is precise in that, for a given intensity (or energy per pulse), the depth of an ablated area corresponds with the number of laser pulses and the area of tissue removal corresponds with the diameter of the incident laser beam on the tissue.<sup>1,2</sup> In addition, the non-thermal 193 nm wavelength results in minimal damage to surrounding tissue.<sup>1,2,3,5</sup>

The Kremer Excimer Laser Serial No. KEA940202 consists of the following system components:

- *Excimer Laser:*

An argon-fluorine excimer laser provides the following characteristics:

Laser wavelength:	193 nm
Laser pulse duration:	8-30 ns (FWHM)
Repetition rate:	10 Hz
Fluence (at the eye):	134 mJ/cm <sup>2</sup>
Ablation zone:	6.0 mm diameter
Composition of gases:	
ArF Premix	Argon (97.73%) Fluorine (2.17%)
Buffer:	Helium (99.999% purity)
For internal purging:	Helium

- *Laser Beam Delivery System:*

- *Gas Management System:*

- *Patient Management System:*

- *Computer Control System:*

Note: Additional details regarding the operation of this laser can be found in the Kremer Excimer Laser Serial No. KEA940202 Operator Instruction Manual (Document KEA0100).

### II. INDICATIONS FOR USE

The Kremer Excimer Laser Serial No. KEA940202, using a 6.0 mm ablation zone, is indicated for myopic and astigmatic laser assisted in-situ keratomileusis (LASIK) in patients:

**Physician Manual**

- with myopia ranging between -1.0 and -15.0 diopters (D) with or without astigmatism ranging from 0.0 D to 5.00 D;
- who are 18 years of age or older; and,
- with stable refraction over the 1-year period prior to surgery. Note: Patients between 18 and 20 years old should not demonstrate a shift in refraction greater than 0.5 D. Patients 21 years and older should not demonstrate a shift greater than 1.0 D.

**III. CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS**

**CONTRAINDICATIONS** - Patients with the following conditions should not be considered for this procedure:

- Active ocular / systemic infection
- Fuchs' corneal dystrophy
- Keratoconus
- Central corneal scars affecting visual acuity
- Cornea too thin to achieve the desired correction
- Pregnant or nursing women

**WARNINGS** - Patients presenting with the following condition(s) should be considered for this treatment only after careful assessment of the potential risk and benefit to the specific patient:

- Previous herpetic keratitis<sup>1</sup>
- Collagen vascular disorders<sup>2</sup>
- Ablation of corneal stroma to less than 200 $\mu$ m from the endothelium
- Ablation depths within less than 250 microns from the endothelium may result in the loss of two or more lines of BSCVA.

**PRECAUTIONS** - The safety and effectiveness of this procedure has not been established in patients presenting with the following conditions:

- Severe dry eye syndrome
- Glaucoma
- Uveitis
- Blepharitis
- Psoriasis
- Immunosuppression
- Systemic or topical use of steroids
- History of keloid formation

# **Kremer Excimer Laser Serial No. KEA940202**

## **Physician Manual**

- Due to the small sample of eyes treated in the Cohort 2 study with myopia of  $-13.0$  D or more (1%, 6/665) or astigmatism of  $-4.0$  D or more (1.8%, 13/720), the reported safety and effectiveness for this refractive range is less reliable than for eyes with less severe myopia or astigmatism.
  - Patients with high myopia greater than  $-7.0$  D whose BSCVA was 20/20 preoperatively have a 9% chance of being worse than 20/25 postoperatively at the 6 month postoperative interval.
  - The effects of the LASIK procedure on visual performance under poor lighting conditions have not been determined. It is possible, following LASIK treatment, that patients may find it difficult to see in conditions such as very dim light, rain, snow, fog or glare from bright lights at night.
  - Patients may still need glasses or contact lenses.
  - There is no safety and effectiveness data for surface ablation performed with this laser.
- 
1. Patient needs to understand risks associated with corneal trauma and possible re-activation of herpetic keratitis.
  2. Patient needs to understand the risks associated with collagen vascular disorders and their associated corneal involvement. The patient may be included if sufficient understanding of possible complications is demonstrated. Consideration should be given to treatment on a monocular basis.

### **IV. PATIENT SELECTION**

#### **A. INCLUSION / EXCLUSION CRITERIA**

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

- $\geq 18$  years old;
- primary myopia between  $-1.0$  D and  $-15.0$  D with or without astigmatism up to 5.0 D;
- with stable refraction over the 1-year period prior to surgery. Note: Patients between 18 and 20 years old should not demonstrate a shift in refraction greater than 0.5 D. Patients 21 years and older should not demonstrate a shift greater than 1.0 D.
- demonstrated desire for independence from spectacles or contact lenses;
- no soft contact lens wear for 2 weeks prior to surgery or no hard contact lens wear for 3 weeks prior to surgery;
- willingness to comply with all postoperative follow-up visits.

Patients should sign an informed consent form, and be instructed about the risks associated with LASIK, and be informed of all alternatives for the correction of their refractive error.

Patients who do not meet all of the above inclusion criteria should not be treated. Patients with any of the following conditions should also be excluded: active ocular or systemic infection; severe dry eye syndrome; Fuchs' dystrophy; anterior basement membrane dystrophy; keratoconus associated with thinning; and chronic topical steroid use. Patients with central corneal scars that affect visual acuity or whose corneas are too thin to permit the desired correction should also be excluded from treatment.

# Kremer Excimer Laser Serial No. KEA940202

## Physician Manual

### B. ADVERSE EVENTS AND COMPLICATIONS

**Table 1. Summary of Adverse Events and Complications Experienced in Cohort 2.**

Adverse Events / Complications	Cohort 2 (%)				
	Operative <sup>1</sup>	1 month	3 months	6 months	12 months
Corneal infiltrate		0/873 (0)	0/814 (0)	0/657 (0)	0/308 (0)
Corneal edema > 1 mo		2/873 (0.2)	1/814 (0.1)	0/657 (0)	0/308 (0)
Flap misalignment		1/873 (0.1)	0/814 (0)	0/657 (0)	0/308 (0)
Retinal detachment		0/873 (0)	0/814 (0)	0/657 (0)	1/308 (0.3)
Corneal Edema < 1 mo	30/873 (3.4)				
Incomplete cap-abort procedure	4/1342 (0.3)				
No hinge on flap	9/1342 (0.7)				
Epithelial defect - Central		1/873 (0.1)	1/814 (0.1)	0/657 (0)	0/308 (0)
Epithelial defect - Peripheral		1/873 (0.1)	0/814 (0)	1/657 (0.2)	0/308 (0)
Epithelium in interface-Central		1/873 (0.1)	0/814 (0)	1/657 (0.2)	0/308 (0)
Epithelium in interface-Periph.		8/873 (0.9)	10/814 (1.2)	8/657 (1.2)	1/308 (0.3)
Interface foreign bodies		126/873 (14)	128/814 (14)	95/657 (15)	27/308 (9)
Cap striae		9/873 (1.0)	6/814 (0.7)	5/657 (0.8)	1/308 (0.3)
Pain		4/873 (0.5)	4/814 (0.5)	3/657 (0.5)	2/308 (0.7)
Glare <sup>2</sup>				5/661 (0.8)	4/269 (1.5)
Halos <sup>2</sup>				7/661 (1)	0/269 (0)
Night Driving Problems <sup>2</sup>				7/661 (1)	2/269 (0.7)
Double Vision / Ghosts <sup>2</sup>				10/661 (1.5)	2/269 (0.7)
Foreign Body Sensation <sup>2</sup>				5/661 (0.8)	0/269 (0)
Anxiety <sup>2</sup>				0/661 (0)	0/269 (0)

1. Adverse events occurring operatively and up to 1 month postoperatively.
2. These events were reported 6 and 12 months after final treatment.

# Kremer Excimer Laser Serial No. KEA940202

## Physician Manual

**Table 2. Summary of Adverse Events and Complications Experienced in Cohort 1.**

Adverse Events	Cohort 1 (%)				
	Operative <sup>1</sup>	1 month	3 months	6 months	12 months
Corneal infiltrate		0/804 (0)	0/910 (0)	1/788 (0.1)	0/752 (0)
Corneal edema ≥ 1 mo		14/804 (1.7)	4/910 (0.4)	0/788 (0)	0/752 (0)
Flap misalignment		0/804 (0.1)	0/910 (0)	0/788 (0)	0/752 (0)
Retinal detachment		0/804 (0)	0/910 (0)	0/788 (0)	1/752 (0.1)
<b>Complications</b>					
Corneal Edema < 1 mo	43/741 (5.8)				
Incomplete cap-abort procedure	1/1141 (0.1)				
No hinge on flap	20/1141 (1.8)				
Epithelial defect - Central		2/741 (0.3)	1/859 (0.1)	2/750 (0.3)	0/687 (0)
Epithelial defect - Peripheral		1/741 (0.1)	1/859 (0.1)	0/750 (0)	2/687 (0.3)
Epithelium in interface-Central		2/741 (0.3)	0/859 (0)	1/750 (0.1)	0/687 (0)
Epithelium in interface-Periph.		8/741 (1.1)	12/859 (1.4)	15/750 (2)	10/687 (1.5)
Interface foreign bodies		71/741 (9.6)	78/859 (9.1)	50/750 (6.7)	43/687 (6.3)
Cap striae		3/741 (0.4)	7/859 (0.8)	5/750 (0.7)	3/687 (0.4)
Pain		4/741 (0.5)	1/859 (0.1)	3/750 (0.4)	2/687 (0.3)
Glare <sup>2</sup>				23/726 (3.2)	16/678 (2.4)
Halos <sup>2</sup>				14/726 (1.9)	6/678 (0.9)
Night Driving Problems <sup>2</sup>				30/726 (4.1)	15/678 (2.2)
Double Vision / Ghosts <sup>2</sup>				6/726 (0.8)	5/678 (0.7)
Foreign Body Sensation <sup>2</sup>				1/726 (0.1)	0/678 (0)
Anxiety <sup>2</sup>				1/726 (0.1)	1/678 (0.1)

1. Adverse events occurring operatively and up to 1 month postoperatively.
2. These events were reported 6 and 12 months after final treatment.

- Adverse events

Adverse events included corneal infiltrate (1 eye in the Cohort 1 population), 1 case of cap malalignment (repositioned without sequelae), 1 retinal detachment in each Cohort, and several early cataracts. The retinal detachments occurred at 11 months and >1 year postoperatively, indicating that these detachments were unrelated to surgery. The early cataracts were noted prior to surgery and were not induced. There were no corneal infections, lost or melted caps, or retinal vascular accidents recorded.

- Complications

Corneal edema was noted between 1 week and 1 month in 5.3% of the Cohort 1 population and 3.4% of the Cohort 2 population. These cases resolved with further healing. The following complications - transient corneal central and peripheral epithelial defects, epithelium in the

**Physician Manual**

central interface that required removal, aborted procedures due to an incomplete cap, and cap striae - each occurred with  $\leq 1\%$  incidence. Epithelium in the periphery, which did not influence vision and did not require removal, occurred somewhat more frequently in the Cohort 1 population, as compared with the Cohort 2 population. Hingeless flap, an intraoperative complication, occurred in 1.8% of cases in the Cohort 1 population and 0.7% of cases in the Cohort 2 population. There were no associated sequelae with a hingeless flap. Interface foreign bodies at each interval which were observed under slit-lamp, but had no clinical sequelae, ranged between 14.5% and 8.8%.

In addition, glare, halos, trouble with night driving, double vision/ghosting, foreign body sensation, and anxiety, and pain were also reported. The incidence of these events considered by patients to be bothersome ranged from 0% to 4.1% for both protocol populations. Difficulty with night driving that was of a bothersome nature occurred at a rate of 4.1% in the Cohort 1 population and 1.1% in Cohort 2. Events of a similar nature, but not considered bothersome by the patients, occurred at a somewhat higher incidence.

All of these events tended to be less prevalent in Cohort 2 than in the earlier Cohort 1, likely because of improvements in centering strategy and surgical technique. As expected, these events were also less prevalent in the  $<7$  D group as compared with the  $\geq 7$  D group in both protocol populations. Eyes with residual refractive errors also had a higher incidence than those with SEs within  $\pm 0.5$  D. The study did not measure the extent to which the events may have resolved in the presence of spectacle correction, as would be expected.

**C. STUDY PERIOD AND INVESTIGATIONAL SITE**

*Study design*

This was a prospective, non-randomized, unmasked, single-center clinical with the participants acting as their own controls. Surgery was performed by two physicians.

*Study period*

A total of 2,482 eyes were treated under both protocols, beginning on May 1, 1993. The database was closed for purposes of this analysis on November 20, 1997.

*Investigational site*

All procedures were performed at the Kremer Laser Eye Center. Patients were evaluated postoperatively at the Kremer Laser Eye Center and at co-managing sites, provided the referring caregiver was qualified as a co-managing investigator.

# Kremer Excimer Laser Serial No. KEA940202

## Physician Manual

### D. Data Analysis and Results

#### *Key efficacy variables*

Table 3 presents a summary of efficacy results at the 6-and 12-month visits, stratified by protocol, for eyes having one or more LASIK treatments. Six-month UCVA was 20/40 or better in 88.4% of all eyes after the final LASIK treatment, and 84.1% following initial treatment only without regard to further enhancement. When the 6-month UCVA results were compared between Cohorts 1 and 2, there was a statistically significant between-group difference. A greater proportion of eyes in the Cohort 2 population had UCVA of 20/40 or better and 20/20 or better. This is due to the intentional undercorrection performed in some of the Cohort 1 eyes. None of the other efficacy variables were significantly different when the two populations were compared.

**Table 3 . Summary of Key Efficacy Results After Final<sup>1</sup> Treatment at 6 and 12 Months**

Efficacy Variable	Cohort 2 (%)		Cohort 1 (%)		P value <sup>2</sup>
	6 months	12 months	6 months	12 months	
UCVA: <sup>3</sup> 20/20 or better	199/491 (40.5)	87/218 (39.9)	212/668 (31.7)	202/612 (32.7)	0.840
	446/491 (90.3)	201/218 (92.2)	579/668 (86.7)	535/612 (87.4)	0.523
MRSE: <sup>4</sup> ±0.5 D	472/665 (71.0)	199/269 (74.0)	494/737 (67.0)	431/688 (62.6)	0.401
	584/665 (87.8)	249/269 (92.6)	631/737 (85.6)	588/688 (85.5)	0.231
	650/665 (97.7)	266/269 (98.9)	710/737 (96.3)	669/688 (97.2)	0.091

1. Final treatment includes all eyes treated after their last LASIK procedure.
2. Cochran-Mantel-Haenszel statistic comparing 6 and 12 months, controlling for protocol.
3. All eyes treated for monovision were excluded from this analysis, since undercorrection is intentional in this sub-population
4. Manifest refraction spherical equivalent.

***Physician Manual***

There was a statistically significant difference between all key efficacy variables when eyes with preoperative SE  $<7$  D were compared with those with preoperative SE  $\geq 7$  D, thus indicating that the LASIK procedure produced better results in eyes with low- to moderate preoperative myopia. Table 4 summarizes the key efficacy variables and statistical comparisons for patient eyes after their final LASIK treatment.

# Kremer Excimer Laser Serial No. KEA940202

## Physician Manual

Table 4. Summary of Key Efficacy Results After Final<sup>1</sup> Treatment at 6 Months Stratified by Preoperative SE

Efficacy Variable	Cohort 2 (%)		Cohort 1 (%)		P value <sup>2</sup>
	<7 D	>7 D	<7 D	≥7 D	
UCVA: <sup>3</sup>					
20/20 or better	185/371 (49.9)	14/120 (11.7)	176/447 (39.4)	36/221 (16.3)	0.001
20/40 or better	358/371 (96.5)	88/120 (73.3)	407/447 (91.1)	172/221 (77.8)	0.001
MRSE: <sup>4</sup>					
±0.5 D	374/477 (78.4)	98/188 (52.1)	356/483 (73.7)	138/254 (54.3)	0.001
±1 D	446/477 (93.5)	138/188 (73.4)	439/483 (90.9)	192/254 (75.6)	0.001
±2 D	475/477 (99.6)	175/188 (93.1)	480/483 (99.4)	230/254 (90.6)	0.001

1. Final treatment includes all eyes treated after their last LASIK procedure.
2. Cochran-Mantel-Haenszel statistic comparing preoperative SE (<7D vs. ≥7D), controlling for protocol.
3. All eyes treated for monovision were excluded from this analysis, since undercorrection is intentional in this sub-population.
4. Manifest refraction spherical equivalent.

Table 5 summarizes the key efficacy variables and statistical comparisons for myopic eyes versus myopic astigmatic eyes at 6-months after the final LASIK treatment in Cohort 2. When controlling for high vs. low myopia, a comparison of efficacy results between eyes treated for myopia only and eyes treated for both myopia and astigmatism showed no statistically significant differences, with the lone exception being a reduction in the number of high myopic astigmatic eyes achieving UCVA of 20/20 or better.

# Kremer Excimer Laser Serial No. KEA940202

## Physician Manual

**Table 5.** Summary of Key Efficacy Results<sup>1</sup> at 6 Months Stratified by Spherical vs. Astigmatic Myopia Controlling for Preoperative SER

Efficacy Variable	< 7 D		> 7 D		P value <sup>2</sup>
	Spherical Myopia	Astigmatic Myopia	Spherical Myopia	Astigmatic Myopia	
UCVA: <sup>3</sup>					
20/20 or better	111/213 (52.1)	74/158 (46.8)	12/61 (19.7) 47/61 (77.1)	2/59 (3.4)	0.057
20/40 or better	204/213 (95.8)	154/158 (97.5)		41/59 (69.5)	0.808
MRSE: <sup>4</sup>					
±0.5 D	192/243 (79.0)	182/234 (77.8)	36/76 (47.4) 52/76 (68.4)	62/112 (55.4)	0.703
±1 D	228/243 (93.8)	218/234 (93.2)	68/76 (89.5)	86/112 (76.8)	0.456
±2 D	242/243 (99.6)	233/234 (99.6)		107/113 (95.4)	0.141

1. Includes all eyes in Cohort 2 after the last LASIK treatment.
2. Cochran-Mantel-Haenszel statistic comparing spherical and astigmatic myopia, controlling for Preoperative SER group.
3. All eyes treated for monovision were excluded from this analysis, since undercorrection is intentional in this sub-population.
4. Manifest refraction spherical equivalent.

*Other efficacy results after final LASIK treatment:*

Additional efficacy measures are summarized below.

- Stability of manifest refraction.

A total of 451 eyes were examined at three (3) consecutive visits (1, 3 & 6 months) in Cohort 2, of which 89.3% achieved stability (defined as a change in SE of  $\leq 1.00$  D across consecutive visits) between the month-1 and month-3 visits, increasing to 93.3% stability between the 3-month and 6-month visits. When analyzing those eyes evaluated at all four (4) consecutive visits in Cohort 2, (n = 139) 90.6% achieved stability between the 1- and 3-month visits, 95.0% between the 3- and 6-month visits, and 96.4% between the 6- and 12-month visits.

- Accuracy of sphere and cylinder for astigmatic myopes.

*Sphere.* For all eyes treated in Cohort 2, mean intended spherical correction was -4.95 D and mean actual correction at the sixth postoperative month was -4.94 D. For eyes treated in Cohort 1, mean intended spherical correction was -5.58 D and mean actual correction at month 6 was -5.34 D.

# Kremer Excimer Laser Serial No. KEA940202

## Physician Manual

Over 80% of those eyes treated for myopic astigmatism achieved correction within  $\pm 1$  D of intended sphere at 1 month. This level of accuracy was maintained throughout the 1-year study period.

*Cylinder.* Over 80% of all eyes treated for myopic astigmatism achieved cylinder correction within  $\pm 1$  D of zero cylinder at 1 month. This level of accuracy was maintained throughout the 1-year study period. For myopic astigmatism, there was a mean undercorrection of just 0.1 D in Cohort 2. The procedure most effectively reduced cylinder magnitude in eyes with  $>1$  D preoperative cylinder. Table 6 presents the accuracy of cylinder correction (to zero) for eyes in Cohort 2, stratified by high versus low dioptric group.

**Table 6.** Accuracy of Cylinder Correction (to Zero) for Eyes Treated in Cohort 2

Sphere	Preoperative SER <sup>1</sup> < -7 D			
	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	12 Months n/N (%)
$\leq 0.50$ D	252/365 (69.0)	208/327 (63.6)	153/234 (65.4)	63/95 (66.3)
$\leq 1.00$ D	329/365 (90.1)	287/327 (87.8)	209/234 (89.3)	84/95 (88.4)
Sphere	Preoperative SER > -7 D			
	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	12 Months n/N (%)
$\leq 0.50$ D	58/149 (38.9)	53/135 (39.3)	43/112 (38.4)	18/43 (41.9)
$\leq 1.00$ D	105/149 (70.5)	94/135 (69.9)	77/112 (68.8)	25/43 (58.1)

1. Spherical Equivalent Refraction.

- **Stability of cylinder.**

The manifest cylinder refraction was considered stable when cylinder did not change by more than 1 D between any two postoperative visits. Stability of cylinder was achieved in approximately 93.5% of all eyes between the month 1 and 3 visits, increasing to 94.7% between the 3 and 6 month visits, and 95.5% had a stable cylinder between 6 and 12 months.

*Key safety variables*

Table 7 presents a summary of key safety variables for all eyes after their final LASIK treatment at the 6- and 12-month visits, stratified by protocol. The overall proportion of eyes for both studies combined losing  $\geq 2$  lines of BSCVA at 12-months was  $\leq 2.3\%$  after final LASIK treatment, and 1.4% after initial LASIK treatment. When these key safety results are compared between Cohorts 1 and 2, there are no statistically significant differences.

# Kremer Excimer Laser Serial No. KEA940202

## Physician Manual

**Table 7. Summary of Key Safety Results After Final<sup>1</sup> Treatment at 6 and 12 Months**

Safety Variable	Cohort 2 (%)		Cohort 1 (%)		P value <sup>2</sup>
	6 months	12 months	6 months	12 months	
<b>BSCVA:</b>					
Loss of >2 lines	14/665 (2.1)	2/269 (0.7)	20/737 (2.7)	20/688 (2.9)	0.593
Worse than 20/40	4/665 (0.6)	3/269 (1.1)	11/737 (1.5)	12/688 (1.7)	0.480
Worse than 20/25 with 20/20 or better preop	26/665 (3.9)	10/269 (3.7)	33/737 (4.5)	28/688 (4.1)	0.696
Increase of >2D cylinder <sup>3</sup>	2/319 (0.6)	2/131 (1.5)	1/315 (0.3)	2/283 (0.7)	0.258

1. Final treatment includes all eyes treated after their last LASIK procedure.
2. Cochran-Mantel-Haenszel statistic comparing 6 and 12 months, controlling for protocol.
3. Eyes treated for spherical correction only.

There was a statistically significant difference in favor of SE <7 D in several of the key safety variables when eyes with preoperative SE <7 D were compared with those with preoperative SE ≥7 D. Table 8 summarizes the key safety variables and statistical comparisons for patient eyes after final LASIK treatment.

**Table 8. Summary of Key Safety Variables After Final<sup>1</sup> Treatment at 6 Months Stratified by Preoperative SE**

Safety Variable	Cohort 2 (%)		Cohort 1 (%)		P value <sup>2</sup>
	<7 D	≥7 D	<7 D	≥7 D	
<b>BSCVA:</b>					
Loss of >2 lines	2/477 (0.4)	12/188 (6.3)	2/483 (0.4)	18/254 (7.1)	0.001
Worse than 20/40	1/477 (0.2)	3/188 (1.6)	0/483 (0)	11/254 (4.3)	0.001
Worse than 20/25 with 20/20 or better preop	9/477 (2.0)	17/188 (9.0)	8/469 (2.0)	17/183 (9.0)	0.001
Increase of >2D cylinder <sup>3</sup>	0/243 (0)	2/76 (2.6)	0/252 (0)	1/63 (1.6)	0.001

1. Final treatment includes all eyes treated after their last LASIK procedure. Cochran-Mantel-Haenszel statistic comparing preoperative SE (<7D vs. ≥7D), controlling for protocol.
2. Eyes treated for spherical correction only.

**Physician Manual**

*Other safety results after final LASIK treatment*

- Residual cylinder.

Both the Cohort 2 and Cohort 1 populations had slight cylindrical overcorrections when the intended correction was taken into consideration (mean overcorrections: 0.18 D and 0.21 D, respectively). These overcorrections, or surgically induced residual astigmatism, were greater in eyes treated for myopia only. The mean cylinder overcorrection was approximately one-half of a diopter among eyes treated for myopia only in both populations.

Of eyes treated for myopic astigmatism, 68.8% of those treated in Cohort 2 and 70.9% of those treated in Cohort 1 had residual cylinder <1 D at the point of stability (6 months postoperatively). The number of these eyes with residual cylinder >2 D is low (n=15/346 for the Cohort 2 population and n=21/422 for the Cohort 1 population). Table 11 summarizes the residual astigmatic error observed at 6-months postoperatively in eyes treated for astigmatic myopia.

- Change in cylinder axis

The median shift in cylinder axis among all eyes treated was 25° for the Cohort 2 population and 35° for the Cohort 1 population. The highest shifts in astigmatic axes tended to occur in eyes with the lowest degrees of residual cylinder. A shift in axis has no clinical significance, and is analogous to a compass needle showing multiple directions at the North Pole.

*Retreatments*

In Cohort 2, 47 eyes were retreated for undercorrection, for an overall enhancement rate of 3.5% (n=47/1342) under this protocol. This retreatment rate compares very favorably with those cited in the literature for other refractive procedures. From 6% to 10% or more of eyes that undergo surface photorefractive keratectomy require at least one enhancement, and retreatment rates for radial keratotomy procedures run as high as 30%.

In Cohort 1, 162 eyes were retreated for undercorrection, for an overall enhancement rate of 14.2% (n=162/1140). The higher retreatment rate in this earlier population is attributable to the earlier Cohort 1 protocol requirement of intentional undercorrection. Four (4) retreated eyes had a decrease of BSCVA greater than 2 lines at 3-months which persisted out to 12-months postoperatively.

Most key efficacy and safety variables differed significantly between eyes that received one (1) treatment and eyes that received two (2) or more treatments.

**Physician Manual**

**V. PRE-OPERATIVE EXAMINATION AND SURGICAL PLANNING**

Ocular Examination and History

**A. HISTORY**

Complete ocular and medical histories are obtained from the patient including primary reason for desiring the evaluation, patient's occupation, hobbies or activities patient enjoys. Work requirements on a visual basis, previous ocular history including the role of previous ocular injuries, ocular infections or previous ocular surgery. Contact lens history is taken detailing type of previous contact lens wear, how long the patient has continuously been wearing contact lenses and when the lenses were last worn, as well as documentation of absence or presence of contact lens intolerance or other complications. Complete medical history is obtained with specific rule outs for hypertension, heart/lung or breathing problems, thyroid or kidney problems or diabetes mellitus. Complete medical evaluation for pharmaceutical agents is reviewed as well as any known allergies to medications.

**B. VISUAL ACUITY MEASUREMENTS**

The patient is seated at 6 optical meters distance from the acuity chart. A standard occluder is held by the patient to block out the eye not being tested and the examiner must constantly ensure that the untested eye is completely covered to avoid inadvertent peeking. The patient is instructed to read the smallest line on the chart that is easily visible. This saves the monotonous reading of the entire chart.

When the patient cannot read a letter they are encouraged to guess at it. If the patient states that the letter is one of two letters, they are asked to choose only one letter, and if necessary, to guess. The patient may neither squint to achieve pinhole nor lean forward.

Visual Acuity and Refraction will be performed with the Snellen Eye Charts. Please refer to the Patient Data Collection Chart which describes at which visits Visual Acuity and Refraction are required on the operative eye (or both eyes at certain designated visits).

**C. METHOD OF REFRACTION**

The trial frame or phoropter is placed and adjusted in front of the patient's face so that the lens cells are parallel to the anterior plane of the orbits and centered in front of the pupils. Manifest retinoscopy is performed to obtain initial objective refraction prior to beginning subjective refraction. The left eye is occluded and subjective refraction begun on the right eye.

The patient is then asked to look at and read a Snellen acuity chart in the light box at an optical distance of 6 meters either directly or with a mirror.

Each refraction should be done without knowledge of the previous refraction results.

**Physician Manual**

The refraction should be performed until neither the power nor the axis of the cylinder can be improved. The power of the sphere is rechecked by adding +0.37 and -0.37 spheres and changing the spherical power by quarter diopter increments of the appropriate sign until the patient can perceive no improvement in vision. If the sphere is changed at this point, the cylinder should be rechecked. This process is repeated until no further significant lens changes are made. The lens corrections obtained in this way for the right eye are recorded. The entire process is repeated for the left eye and the lens corrections are recorded on the examination form.

**D. BRIGHTNESS ACUITY TESTING (BAT)**

This test is commonly referred to as glare testing. Currently BAT testing is being performed with a Mentor Brightness Acuity Testor. Performance of brightness acuity testing is being performed as described in the instructions found within the Operating Manual. (See Fig. 1) Brightness Acuity Testing is also performed at subsequent follow up visits until stabilization of vision, at which time results of brightness acuity testing pre- and post-operatively can be compared within our data analysis.

**E. CYCLOPLEGIC REFRACTION**

For Cycloplegic Refraction, Retinoscopy and Refraction are carried out as described above in the Section "Manifest Refraction". Cycloplegia is obtained by instilling 1 drop of 1% Mydracyl in each eye, three times each separated by 5 minutes. Cycloplegic refraction is performed 30 to 45 minutes after the last instillation of 1% Mydracyl.

**F. CONTRAST SENSITIVITY - OPTIONAL**

Contrast sensitivity is performed on both eyes with best corrected visual acuity (BCVA) with and without the BAT.

Contrast sensitivity is current being measured with a vector vision CSV 1000 Contrast Sensitivity Unit and is being performed as described in the Operations Manual.

**G. NATURAL PUPIL**

Pupil examination is performed at pre-op, 12 month, and 2 year intervals, or as needed based on symptoms from the patient or signs found within the clinical examination. Pupil findings are recorded on the chart in the standard PERRLA format, as well as scotopic and photopic pupil measured diameters are recorded.

**H. STABILITY OF CONTACT LENS WEARERS**

All patients who wear contact lenses will be asked to discontinue wearing them prior to LASER-K<sup>SM</sup> LASIK refractive evaluation and to continue absence of lens wearing prior to any surgical treatment.

- Soft lenses - discontinue wear for minimum of 2 weeks

# **Kremer Excimer Laser Serial No. KEA940202**

## **Physician Manual**

- Hard lenses - (including PMMA and all rigid gas permeable materials) discontinue wear for a minimum of 3 weeks

Review contact lens history with patient including total time wearing contact lenses, when last worn, and type of lenses worn, any complications with contact lens wear recorded.

### **I. INTRAOCULAR PRESSURE**

For measurement of intraocular pressure Goldmann Applanation Tonometry is performed after instillation of 1 drop 0.5% Proparacaine and application of fluorescein.

### **J. CORNEAL TOPOGRAPHY**

Corneal mapping is performed with the Tomey TMS-1 corneal topography unit as described in the Operations Manual.

### **K. CORNEAL THICKNESS TESTING**

Corneal thickness testing is performed with the Accutome Corneometer (ultrasound pachymetry) as described in the Operations Manual.

### **L. BIOMICROSCOPY**

A slit lamp examination of the cornea (operative eye/s) will be carried out at least every visit as part of a thorough ocular examination. The corneal cap will be evaluated for clarity and integrity at every visit, with and without fluorescein staining.

A detailed evaluation of the cornea in terms of the presence of haze will be performed.

**Visual Diagram: (Optional)** To assist in describing a patient's haze, a circle symbolizing the cornea (limbus to limbus) will be included on the Post-operative Report to allow the clinical investigator to include information regarding the location and extent of the haze. Please refer to the Clinical Evaluation forms included at the end of this Section.

Summary of Pre-operative report includes detailed discussion involving refractive options for the patient including contact lenses, spectacle lenses, refractive surgeries involving LASER-K<sup>SM</sup> LASIK ALK, HLK, PRK, PTK, CGK, keratophakia or other procedures that may be available to the patient on a case-specific basis.

Patients are given the option of having LASER-K<sup>SM</sup> LASIK performed on one eye or bilaterally.

**Physician Manual**

**M. PATIENT INSTRUCTIONS**

Pre-operative

Pre-operative LASER-K<sup>SM</sup> LASIK patients are notified the day prior to surgery to review pre-operative instructions. Pre-operative instructions include the following:

1. No food after midnight.
2. May have clear liquids up to 2 hours prior to arrival.
3. Patients are to take regular medication prior to arrival
4. Patient is instructed to shower, shampoo hair, and wash face with DIAL soap the morning of surgery.
5. Verify telephone number where patient may be reached evening of surgery for post-surgical follow-up call.
6. Name and telephone number of person to contact in case of emergency.
7. One day post-operative appointment given to patient.

**N. PATIENT INSTRUCTIONS/PROCEDURES**

Day of Surgery

The patient arrives at the Surgery Center at the designated time. He/she is asked to sign in at the front desk. At this time additional pre-operative testing is performed (i.e., repeat manifest refraction, corneal topography, etc.) if needed. Office staff then notifies the pre-operative area that the patient is ready. A transporter then assists patient to the pre-operative area with their office and surgical charts.

Once the patient arrives in the pre-operative area, they are assisted to a pre-operative lounge chair and identity is established along with surgical procedure and verified by nursing personnel. The Informed Consent is then given to the patient to read and, if they cannot read it, it is read to them by one of the nursing personnel. After the patient has read the Informed Consent, they are asked to sign it and the nursing personnel will witness their signature. If the patient has questions at this point, they are taken to a private exam room where they will see the surgeon and have their questions answered prior to signing the Informed Consent. Following the Informed Consent process, the patient is given the post-operative instructions form, they are asked to read and sign the form (the patient is given a copy of this form upon discharge). The patient is then asked to read and sign a General Surgical Consent form which lists the exact surgical procedure to be performed, with the designated eye or eyes, and the surgeon performing the procedure. Following the Consent process, the patient is asked to complete a review of medical systems questionnaire to aid us in assessing their general health. Finally they are given a Patient Bill of Rights form to read and sign. The patient is given a copy of this form upon discharge.

The pre-operative LASER-K<sup>SM</sup> LASIK patient is then asked to change into a disposable surgical jump suit that is worn over their street clothes and they are given shoe covers and a hair bonnet.

**Physician Manual**

This is a precaution to maintain sterile conditions in the Operative Suite. Personal effects are placed in a storage bag with the patient's name on it. A name tag with the procedure and eye(s) is then placed on the patient's jump suit. Identification stickers are placed over eye or eyes for verification. Next, the nurse will verify known allergies to medications with the patient and a drug allergy label is then applied to the patient's jump suit. If the patient has a known allergy to one of the medications used pre-, peri- or post-operatively, the surgeon is notified at once and a medication change is implemented. Allergy labels are then placed on the outside of both surgical and office charts (upper right hand corner) and in the appropriate places inside the charts (on the surgical form). Vital signs are taken and recorded. These include temperature, pulse, respirations, blood pressure and oximetry. Pre-operative sedation is given 45 to 60 minutes prior to procedure. The pre-operative sedation includes Ansaid 100 mg po and Halcion 0.125 mg sublingually. The patient is made comfortable in the lounge chair and offered a blanket if needed.

**VI. LASER-K<sup>SM</sup> LASIK PROCEDURE FOR MYOPIA AND/OR ASTIGMATISM**

Note: Before proceeding, please review the Operator Instruction Manual.

**A. ENTERING PATIENT DATA**

The LASER K<sup>SM</sup> procedure for correction of myopia is prefaced with careful review of the patient's medical record. Once the plan of correction has been established, the surgeon will instruct the Laser Technician in how the refractive data will be entered into the "Excimer Operative Computer Program". The technician enters the appropriate refractive data consisting of the following:

- Name
- Date
- Type of procedure
- Eye
- Central corneal thickness
- Pupil diameter (photopic and scotopic)
- Refraction
- Vertex distance
- Desired final refraction.

The program will then calculate the diopters of correction to be placed at the corneal plane.

Procedures for the correction of myopia may require the amount of myopic correction to be divided into more than one component. The total diopters of correction (obtained from the patient's medical record) placed in one component is 4.00 diopters. If the total amount of correction is above four diopters, then more than one component will be used.

# Kremer Excimer Laser Serial No. KEA940202

## Physician Manual

### B. COMPONENTS OF MYOPIC CORRECTION

In some cases, the amount of myopic correction may require more than one component. The maximum diopters of myopia corrected in one component is 4.00 diopters. This number is taken from the patient's refraction in minus cylinder. For example:

$$-4.00 - 1.00 \times 180$$

If the spherical portion of the refraction (in minus cylinder) is greater than 4, then more than one component will be used. To determine the number of components to be used, just look at the "Factored Correction" found on the Excimer Operative Computer Program. If the spherical portion of the correction is greater than 4 D (e.g. 6.50 D), then divide that number by 2, and ablation is done in two components. For example:

$$\frac{\{6.50\}}{2} - 1.00 @ 180$$

and

$$\frac{\{6.50\}}{2} = 3.25$$

The spherical correction would consist of two equal components of -3.25. If the spherical diopters of correction divided by 2 is greater than 4.00 diopters, then three components are to be used.

For example:

Incorrect:  $\frac{(9.00)}{2} = 4.50$  (greater than 4.00)

Correct:  $\frac{(9.00)}{3} = 3.00$  (less than 4.00)

In this case, there would be three components consisting of -3.00 diopters of correction in each component for a total correction of 9.00 diopters.

This information is then entered into the Excimer laser computer under the program for myopia correction. The following information is then entered:

Diopters of correction (-3.00)  
Starting iris diameter (1.0 mm)  
Final iris diameter (6.0 mm)  
Number of pulse intervals (120)  
Number of Hertz (10).

# **Kremer Excimer Laser Serial No. KEA940202**

## **Physician Manual**

The Excimer laser computer will then calculate the total number of pulses and total microns of tissue to be ablated. The laser technician then records this information on the Excimer Operative Computer Program data sheet as the patient's control numbers.

To perform astigmatic correction, enter the program for Astigmatic correction on the Excimer Laser and enter the following information:

- Diopters of correction (as determined from refraction)
- Angle of correction (as determined from patient position and refraction)
- Starting slot diameter (1.0 mm)
- Final slot diameter (6.0 mm)
- Slot intervals (maximum listed on screen)
- Starting iris diameter (6.0 mm)
- Final iris diameter (6.5 mm)
- Iris intervals (21)
- Fire laser at 10 Hertz.

The computer will then calculate the total microns of tissue to be ablated in a total number of pulses. Record this information on the patient data sheet. Place test paper under delivery system of Excimer laser and allow one pulse to be emitted. This is to ensure correct alignment of slot angle. In turn, during the course of the procedure, the laser technician will double check the pulses and total microns listed on the computer screen against the control numbers, to ensure the information had been entered correctly. The surgeon is then seated at the head of the operating room table and with the patient lying supine on the operating table, the height of the table is adjusted to bring the cornea to the level of the crossed HeNe beam. This is done under the highest magnification of the microscope, at the same time centering of the eye under the microscope is checked by ensuring that the cornea is appropriately located within the field of view of the microscope (patient fixating on coaxial light).

### **C. MARKING THE CORNEA**

A 6 mm corneal marker is then pressed into a methylene blue sponge and a circular mark is placed on the temporal corneal limbal area. This should be placed so that the microkeratome will bisect approximately half the circle when the flap is made. At this point, balanced salt solution is irrigated over the surface of the eye and excess balanced salt solution is removed via suction tubing.

### **D. USING THE MICROKERATOME**

The microkeratome is then brought into the field. The suction ring is placed onto the globe, decentered nasally approximately 0.50 to 1.0 mm. The foot pedal controlling the suction power supply unit is then depressed, activating the suction ring. Proper functioning of the suction ring at this point is verified in two ways: first, by a change in the pitch of the sound being emitted by the suction device, and second, by inserting mild upward pressure on the ring to ensure proper suction. Next, install the shaper head of the microkeratome onto the suction ring by engaging the dovetail

**Physician Manual**

side first, then rotate the shaper flat against the ring. Gently advance the shaper until the gears are engaged. Central placement of the microkeratome is checked by placing gentle upward pressure to be sure that both the foot plates are well seated. The microkeratome is then passed forward by depressing the forward foot switch, creating the corneal flap. When the stop is reached the foot pedal is released and again, the foot pedal which activates the forward direction of the microkeratome movement is tapped to ensure that the microkeratome has transversed the entire length of the tracks.

The microkeratome is then run in the reverse direction and, as soon as it reaches the end of the suction ring, the microkeratome is removed from the suction ring. The suction ring is immediately removed from the eye after suction has been broken and the cornea is inspected to ensure that the flap has been created properly, that the flap is indeed in place and has not become a cap which is still contained within the microkeratome.

**E. COMPLETING LASER APPLICATION**

A "T" forceps is then used to retract the flap onto the medial canthal area after the medial conjunctival and medial canthus have been dried thoroughly with a Weck cell sponge. The flap is smoothed using a Weck cell sponge and the microscope is placed on full zoom. Again, proper positioning is checked to ensure the pupil is directly in the center of the microscope field and with the HeNe beams aligned, the laser procedure continues.

The surgeon then verifies that the appropriate data have been entered into the computer and that the Excimer laser is ready for ablation. At this point, the laser technician will open the laser port and the surgeon will then depress the foot pedal controlling the Excimer laser. If more than one myopic application is to be applied, the second and/or third components will follow consecutively. At the end of the laser application(s), the stromal bed is irrigated with balanced salt solution and excess balanced salt solution is removed again, using suction tubing.

The flap is repositioned by gently pushing the flap back into position using the irrigating tip of the balanced salt solution bottle. The sphere edge of the flap is gently lifted and a space between the flap and the stromal bed is freely irrigated with copious amounts of balanced salt solution. At this time, flap positioning is checked using the pre-placed methylene blue marker, as well as checking to see that the distance between the flap and the surrounding corneal tissue is equal for 360 degrees. While dripping balanced salt solution on the center of the cornea, oxygen is directed at the cap interface using a 21 gauge anterior chamber cannula on the end of the oxygen tubing to thoroughly dry the epithelial junction between the corneal flap and the peripheral cornea. The flow of oxygen is applied starting at the hinged side of the flap and moving progressively towards the opposite side. This ensures that the edge of the flap will not be blown or lifted up during the drying process. Once the corneal junction is thoroughly dry, a forceps is used to check the adherence of the flap to the underlying stroma by gently pressing on both the corneal flap and the surrounding corneal tissue sides to be sure that the flap is adherent.

# **Kremer Excimer Laser Serial No. KEA940202**

## **Physician Manual**

The lid speculum is removed and the patient is asked to blink several times. The eye is then reopened and the flap checked to be sure the edges have not moved and the flap is intact.

A drop of Maxitrol ophthalmic solution is then placed in the eye and attention is turned to the opposite eye if a bilateral procedure is specified. An identical procedure is carried out with the opposite eye after which the first eye is again checked for cap position. A shield is placed over the patient's eye(s) and the patient is taken to the recovery room.

### **F. LASER-K<sup>SM</sup> LASIK PATIENT INSTRUCTIONS/PROCEDURES**

#### **Post-operative**

Following completion of the LASER-Ksm LASIK procedure, Maxitrol ophthalmic solution is instilled in one or both eyes depending on the procedure(s) performed, unilaterally or bilaterally. Clear shields are taped over the eye(s) and the patient is escorted to the recovery room via wheelchair. Once the patient has been received in the post-operative area, he/she is seated in a reclining chair and given his/her post-operative nourishment.

The post-operative instructions are then reviewed with the patient by the recovery room nurse. The patient is discharged with instructions to go home and lie quietly in a darkened room and to keep both eyes closed as much as possible. However, he/she is allowed to open his/her eyes to ambulate to the rest room.

The patient is given two prescriptions for eye drops. These include Pred Forte 1% ophthalmic solution, 1 drop in the operative eye(s) b.i.d. for 4 days and then discontinue and Tobrex ophthalmic solution 1 drop in the operative eye(s) q.i.d. for 4 days and then discontinue. The patient is instructed to bring the drops with him/her the next day for the one-day postoperative visit. He/she is to keep the shields in place until their postoperative visit. A patient with greater than 5 diopters of myopia is given prescriptions for Darvocet N-100 1 tablet p.o. q 4 hours prn for pain and Demerol 50 mg 1 tablet p.o. q 4 hours prn for pain. A patient with less than 5 diopters of myopia is given a prescription for Darvocet N-100 1 tablet p.o. q 4 hours prn for pain.

### **G. LASER SURGICAL PROCEDURES**

1. Turn the power on.
2. Check power levels and calibrate the laser as described in Section I of the Kremer Excimer Laser Serial No. KEA940202 Operator Instruction Manual (Document KEA0100). Note: recheck calibration with a film test firing and a -2.00 diopter plastic test firing after every fifth patient.
3. Check to be sure that the microscope zoom and focus are operating properly.
4. Be sure that the HeNe beam is on and operating properly.
5. Turn on video recorder and monitor.
6. Bring patient into the room and place them on the chair with their head under the operating microscope. Position the patient so that the microscope light and the HeNe

**Physician Manual**

- beam are both centered over the right eye of the patient. Test the lateral movement of the chair to be sure that the left eye can be accessed for the second half of the treatment without difficulty.
7. Prep the patient's eyelid skin with a small amount of iodine, being sure not to get any iodine into the eyes. When the iodine has dried, place a plastic adhesive drape over the patient's face with both eyes cut out.
  8. Instill Tetracaine drops in the eye and place a lid speculum between the lids of the right eye.
  9. Raise the table so that the patient's eye is in good focus in the microscope and so that the HeNe beams line up over the center of the pupil.
  10. Have the patient fixate directly onto the microscope light and zoom the microscope to full power and note the position of the surgical limbus in relation to the microscope field, and use the relationship between the limbus and the microscope field to ensure proper alignment throughout the procedure.
  11. Once proper positioning is assured, reduce zoom, place a semicircle with a 4 mm radial keratotomy optical zone marker saturated with Gentian violet over the temporal half of the cornea, to insure proper cap repositioning.
  12. Rinse the corneal surface thoroughly with balanced salt solution to remove any debris.
  13. Check the surgical plan with the surgical parameters entered into the computer. If astigmatic treatment is involved, check the angle of the astigmatic treatment to be used with thermal paper just prior to the start of the procedure.
  14. When the surgical plan and the astigmatic angle have been confirmed, place the suction ring on the patient's eye and confirm a good seal with a slight upper pull.
  15. Make a pass with the microkeratome creating the corneal flap.
  16. Dry the nasal conjunctiva and using a T forceps, swing the flap and lay it over the nasal conjunctival area, being sure that the hinge is well out of the surgical field.
  17. Using a Weck sponge dry the area of the hinge, zoom to full power, center the patient's eye and encourage the patient to maintain the fixation throughout the procedure.
  18. While continually monitoring fixation, place the astigmatic treatment first followed by all myopic treatment components.
  19. At the conclusion of the laser treatment use balanced salt solution to vigorously clean the stromal bed upon which the laser treatment was applied. Also moisten both the surface and the underside of the cap.
  20. When all the debris have been removed from the stromal bed, use the nozzle of the balanced salt solution cannula to lay the corneal flap back onto the stromal bed. Position it using the pre-placed marks and squeegee all of the balanced salt solution from the cap-stroma interface by sweeping with a tying forceps from nasal to temporal on the flap.
  21. While keeping the center of the cornea moistened with balanced salt solution, use a moderate flow of oxygen through an 18 gauge cannula to dry the edge of the flap-stromal interface.
  22. When complete drying has been achieved, use a tying forceps to apply light pressure outside the flap edge on the cornea to be sure that striae go from the area of pressure onto the cap. This ensures that the cap is well sealed.

# Kremer Excimer Laser Serial No. KEA940202

## Physician Manual

23. Remove the speculum, have the patient blink several times to ensure that the flap is well sealed into position. Apply a drop of Maxitrol and repeat the procedure for the left eye.
24. At the end of the left eye treatment, recheck both the right and left eye again to be sure that the flap is in good position.
25. Place shields over both eyes and take the patient back to the recovery room where they should be checked again at the slit lamp before leaving the Center.
26. While in the recovery room, postoperative instructions should be reviewed in detail and any prescriptions should be reviewed with the patient at this time.

### References

1. Courant D, Fritsch P, Azema A, et al. Corneal wound healing after photokeratomileusis treatment on the primate eye. *Lasers and Light in Ophthalmology*. 1990; 3 (3):187-99.
2. Marshall J, Trokel SL, Rothery S, And Krueger RR. Photoablative reprofiling of the cornea using an excimer laser: Photorefractive keratectomy. *Lasers in Ophthalmol* 1986: 1:21-99.
3. Puliafito CA, Wong K, and Steinert RF. Quantitative and ultrastructural studies of excimer laser ablation of the cornea at 193 and 248 nanometers. *Lasers In Surgery And Medicine*, 1987; 7:155-59.
4. Srinivasan R, Wynne JJ, and Blum SE. Far - UV photo etching of organic material. *Laser Focus* 19:62,1983.
5. Trokel Sl, Srinivasan R, and Braren B. Excimer laser surgery of the cornea. *Am J of Ophthalmol*. 1983; 96 (6):710-15

# Patient Information on the LASER-K<sup>SM</sup> Surgery (LASIK)

Please speak with your doctor regarding the LASER-K<sup>SM</sup> process for the correction of myopia (nearsightedness) with or without astigmatism.

Use of any machine for a medical treatment  
requires discussion with a doctor.

It is important for you to read this booklet and  
then discuss its contents in detail with your doctor.

LASER-K<sup>SM</sup> is used to treat degrees of nearsightedness between  
-1.00 and -15.00 diopters with or without astigmatism up to 5.00 diopters.



200 Mall Boulevard  
King of Prussia, PA 19406  
(610) 337-1697

August 10, 1998

# Table of Contents

---

<u>Topic</u>	<u>Page Number</u>
Introduction	1
How The Eye Works	2
What Is LASER-K <sup>SM</sup> ?	3
What Is An Excimer Laser?	3
How Is Laser-K <sup>SM</sup> Performed?	3
Who Is Eligible For LASER-K <sup>SM</sup> Surgery?	4
Alternatives	5
Risks And Benefits of LASER-K <sup>SM</sup>	6
Contraindications To LASER-K <sup>SM</sup>	8
Warnings	8
Precautions	9
What You Need To Know Before And After LASER-K <sup>SM</sup>	10
What To Expect Before Surgery	10
What To Expect The Day Of Surgery	11
What To Expect After Surgery	12
Questions To Ask Your Doctor	13

# Introduction

---

We have prepared this booklet to help you make an informed decision about having LASER-K<sup>SM</sup> eye surgery. LASER-K<sup>SM</sup> is an abbreviation for Laser Keratomileusis. It is one form of Laser Assisted Intrastronal Keratomileusis (LASIK), developed at the Kremer Laser Eye Center.

Please take as much time as you wish to review this booklet before making your decision to have surgery. You may decide not to make any decision at this time. We welcome any questions you may have after reading this booklet.

# How The Eye Works

---

In a normal eye, light focuses on the retina (the back of the eye). This allows you to see a clear image.

If light is focused in front of or behind the back of the eye, it is referred to as a refractive error. Listed below are types of refractive errors.

- Myopia or nearsightedness is caused by light focusing in front of the back of the eye. Most nearsighted people can see close, but far objects seem blurry.
- Astigmatism causes light to be focused at two points. It may exist by itself or with nearsightedness. This may cause you to see objects blurry or double at distance and close up.

## What Is LASER-K<sup>SM</sup>?

---

LASER-K<sup>SM</sup> is a surgical procedure for correcting nearsightedness and astigmatism. An excimer laser reshapes the cornea so that light can focus on the back of the eye.

LASER-K<sup>SM</sup> is used to treat degrees of nearsightedness between -1.00 and -15.00 diopters with or without astigmatism. Your vision should be at least -1.00 diopter of nearsightedness (very mild) or greater. (A diopter is a unit used to measure the amount of nearsightedness and/or astigmatism.)

## What Is An Excimer Laser?

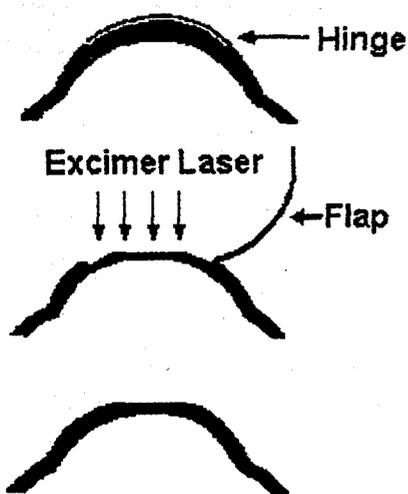
---

An excimer laser is a laser which removes very thin layers of corneal cells without damaging nearby layers. (The cornea is the clear surface over the colored part of the eye.)

A computer program controls the laser by telling it how much tissue to remove to correct a given refractive error. The program was written at the Kremer Laser Eye Center specifically for the LASER-K<sup>SM</sup> process.

## How Is LASER-K<sup>SM</sup> Performed?

---



The LASER-K<sup>SM</sup> process uses an excimer laser under the surface of the cornea. The doctor saves the surface cells by folding them to one side. The doctor uses a device called a microkeratome to create a 'flap' of the surface cells. The excimer laser reshapes the cornea by removing very thin layers of the underlying cells. Next, the flap is put back in its original position. This procedure is used to treat nearsightedness between -1.00 and -15.00 diopters with or without astigmatism.

The LASER-K<sup>SM</sup> process rarely requires strong pain medication.

## Who Is Eligible For LASER-K<sup>SM</sup> Surgery?

---

People thinking about the LASER-K<sup>SM</sup> process should:

- be at least 18 years of age or older; and,
- have stable vision for at least one year (If you are under 21 years old, your vision should not have changed by more than 0.5 diopters. If you are 21 years old or older, your vision should not have changed by more than one diopter);
- have between -1.00 diopter and -15.00 diopters of nearsightedness with or without astigmatism up to 5 diopters.

# Vision Correction Alternatives

---

## Non-Surgical

---

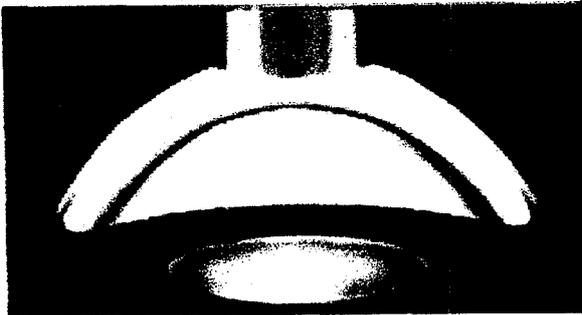
- Glasses
- Contact lenses

## Surgical

---

- RK (Radial Keratotomy)

This was the first surgical procedure available for vision correction. The doctor places spoke-like incisions on the front surface of the cornea to correct mild nearsightedness.



- PRK (Photo Refractive Keratectomy)  
The surface cells are removed and discarded. An excimer laser is used to change the shape of the cornea so light can focus directly on the back of the eye. The surface gradually heals. This procedure usually requires pain medication, and is effective for low and moderate degrees of nearsightedness with or without astigmatism.

- ALK ( Automated Lamellar Keratectomy)

A corneal flap is formed and part of the cornea under the surface is then removed with a blade.

# Risks and Benefits of LASER-K<sup>SM</sup> Surgery

## Potential Benefits:

1. LASER-K<sup>SM</sup> can reduce nearsightedness and reduce or eliminate your need for glasses or contact lenses.
2. LASER-K<sup>SM</sup> can be an alternative to glasses for patients who cannot wear contact lenses.

## Potential Risks:

1. **Temporary Changes in Vision**  
Temporary changes in vision are normal right after the surgery. These changes can occur in one or both eyes and may vary from patient to patient. Visual recovery for routine activities usually occurs within a few days. Your vision will become stable within 3 to 6 months
2. **May Require Repeat Procedures**  
Your LASER-K<sup>SM</sup> procedure may not fully correct your vision. About four percent (4 %) of our patients require a second procedure to reach the desired amount of correction. For those patients requiring a repeat procedure, the risks are increased and the results are not as good.
3. **May Develop Irregular Astigmatism**  
The surface of your cornea may become less smooth after surgery, which can produce irregular astigmatism. Some patients have experienced this problem, which can result in more glare, halos around lights and in some cases decreased vision. Irregular astigmatism is usually treated by glasses, contact lenses. However, these symptoms may persist regardless of method of treatment.

4. Decreased Vision at Night

You may have more difficulty seeing in conditions such as very dim light, rain, snow, fog or glare from bright lights at night. During the final study, about 1.1 percent (7 out of 661) of our patients have experienced this problem 6 months after the procedure.

5. May See Starbursts, Halos and/or Glare at Night

At night, your pupils may become larger than the treatment zone. This can lead to starbursts (noticeable streaks in lights), halos and/or glare at night. In our final study, about 0.8 percent (5 out of 661) of our patients experienced this problem and another 1.1% experienced halos up to 6 months after surgery. We may give you eye drops that make your pupils smaller at night. You can drive while using the eye drops. The effects of the eye drops last a few hours.

6. May Require a Pair of Glasses for Driving, Movies, Etc.

Some patients may need to wear a pair of glasses or contact lenses after the procedure.

7. May Require Reading Glasses for Near Vision

During the first 1-2 weeks after your surgery, your near vision may be blurred and you may temporarily require the use of reading glasses. This effect should go away with time. However, most people require reading glasses after the age of 40 to 45, whether or not they have this procedure.

8. Possible Risk of Decreased Vision or Loss of Vision

As with any surgery, there is a risk of infection after the surgery. This can lead to scarring, decreased vision, or loss of vision.

9. If your refraction is greater than 7 diopters, the accuracy is less and the possibility of complications is more than if your refraction is less than 7 diopters.

## Contraindications To LASER-K<sup>SM</sup>

---

You should not have LASER-K<sup>SM</sup> surgery if you:

- have an active ocular / systemic infection;
- are pregnant or nursing;
- have keratoconus (thinning, cone-like cornea);
- have scars on your eye affecting vision;
- have Fuch's corneal dystrophy;
- have a cornea which is too thin to achieve the desired correction.

## Warnings

---

You should discuss in detail with your surgeon if you:

- have an eye infection;
- have a history of Herpes simplex virus or Herpes zoster (clusters of small blisters on skin or eyes);
- have a collagen vascular disorder (e.g. Rheumatoid arthritis, Systemic lupus erythematosus, etc.);
- Situations where the remaining corneal thickness is insufficient (less than 250 microns) may result in the loss of 2 or more lines of visual acuity that can be corrected by spectacles.

## Precautions

---

The safety and effectiveness of the LASER-K<sup>SM</sup> procedure has not been established in patients who have:

- Severe dry eye syndrome (lack of a lot of tears);
- Glaucoma (disease of pressure in the eye);
- Uveitis (iris tissue is inflamed);
- Blepharitis (eyelid/eye lash area is inflamed);
- Psoriasis (skin disease-dry, flaky skin);
- Immunosuppression (immune system weakened);
- Systemic or topical use of steroids.
- Keloid formations
- If you have myopia between 13 and 15 diopters and /or astigmatism between 4 and 5 diopters, please note that the reported safety and effectiveness for these refractive ranges is less reliable due to the smaller numbers of eyes studied.
- For patients with myopia above 7 diopters, there is a 9% chance that your vision may be less than 20/25 if it was 20/20 or better previously
- There is no data for safety and effectiveness for this laser for surface ablation.

# **What You Need To Know Before And After LASER-K<sup>SM</sup>**

---

## **What To Expect Before Surgery**

---

If you are thinking about having LASER-K<sup>SM</sup> surgery, first discuss it with your doctor. Many times we are able to work with your doctor in order to decrease the number of visits to the surgery center.

You will first have pre-operative testing for surgery. This testing will include a complete medical history of the eye, a vision check and a mapping of the cornea and eye muscle movements. We will dilate your eyes, so you may prefer to have someone drive you to this visit. Other tests include checking for eye dominance, tear function and brightness acuity testing.

During your pre-operative testing, you will discuss your case with the doctor who will perform your surgery. The doctor will also review the risks and benefits of the surgery. If you decide to have surgery, we will schedule a date for you.

We will give you instructions to follow before having the surgery. We will also go over these with you at your pre-operative testing.

Please arrange for a friend or family member to bring you to and from the surgery center on the day of your procedure and your one day follow up visit.

## What To Expect The Day Of Surgery

---

When you arrive at the surgery center, you will check in. You will be taken to the pre-operative area. Here numbing eye drops are placed in your eye(s). You will be taken into the surgery suite on a wheelchair. You will be helped onto the patient chair. The nurses will help you to lay face up on the chair. You will receive more eye drops.

The surgery takes about 10 minutes per eye. Your eye(s) will be held open by an instrument called a lid speculum. You will be asked to look straight ahead at a light on the microscope. The doctor will place a suction ring on the eye to stabilize and raise the intraocular pressure. Then he will attach an instrument called a microkeratome to the suction ring which will create the flap. The excimer laser then removes very thin layers of the underlying cells without damaging the nearby layers. After the laser, the doctor will replace the surface cells to their original position.

After the surgery, your eye(s) will be covered with a clear eye shield for safety. Be careful after your surgery, and DO NOT rub your eye(s).

Please do not drive until your doctor gives you permission.

## What To Expect After Surgery

---

The eye shield(s) is removed at your one day follow up visit. However, you will wear them at bedtime for the first week after your surgery for safety.

We will give you prescriptions for eye drops to use after your surgery. One prescription is for an antibiotic which will help prevent infection. The second will control inflammation. If needed, you will also have a prescription for pain.

You are to use the eye drops for four days. After you finish these drops you can use artificial tears to help moisten your eyes, if needed.

Your vision after surgery will be changing over the next few weeks. Usually by 4 to 6 weeks after surgery, your vision will be stable. Generally, however, you can expect to return to normal daily activities within 1 to 2 days of your surgery. Some patients take longer, so we ask that you keep your schedule flexible.

During your healing time you may see glare around lights and/or starbursting at night (a streaking of lights). These side effects will decrease over time and usually stop.

Your post-operative visits are at: 1 day, 1 week, 1 month, 3 months, 6 months and 12 months.

Again, please do not drive until your doctor gives you permission.

## Questions To Ask Your Doctor

---

1. **Is the LASER-K<sup>SM</sup> process painful?** For most people there is little or no pain associated with the LASER-K<sup>SM</sup> process. Many report it feels scratchy and teary for about two hours after the process. In general, strong pain medication is not required.
2. **When can I return to work following the procedure?** Typically, you can return to work within 1 to 2 days. More time may be required, so we ask you to keep your schedule flexible.
3. **How long is the healing process?** Your visual recovery for routine activities usually occurs within a few days. Your vision will completely stabilize within 3 to 6 months.
4. **How will my post-operative care be handled if I come from out of town?** We see patients from all over the U.S. and other countries. We often work with your local doctor. The first post-operative visit will be performed at our center. Your local doctor will perform the rest of your post-operative visits. Information from these visits will be recorded and sent to our center.
5. **Who will perform the LASER-K<sup>SM</sup> process?** Dr. Frederic B. Kremer, Dr. George R. Pronesti and Dr. Michael Aronsky are the doctors who perform the LASER-K<sup>SM</sup> process at the Kremer Laser Eye Center.
6. **Are eye drops required after the LASER-K<sup>SM</sup> process?** The LASER-K<sup>SM</sup> process typically requires antibiotic and anti-inflammatory eye drops for four days.
7. **What about eye shields or bandage lenses?** After the LASER-K<sup>SM</sup> process, we provide eye shield(s) for use at bedtime for the first week for safety. No bandage contact lenses are required.

8. **Will I need glasses after the process?** You should be able to do all or most things without glasses. Some patients may require glasses for some activities like driving at night. In some cases, glasses or contact lenses may still be required. Most people who are older than 40-45 will need reading glasses for near work regardless of whether these procedures are done. Talk to your doctor.