SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name:	Ophthalmic Medical Laser System (2120 nanometers laser wavelength)
Device Trade Name:	HYPERION™ LTK System
Applicant's Name and Address:	Sunrise Technologies International, Inc. 3400 W. Warren Avenue Fremont, CA 94538 (510) 623-9001
Date of Panel Recommendation:	January 13, 2000
Premarket Approval (PMA) Application Number:	P990078
Date of Notice of Approval to Applicant:	June 30, 2000

II. INDICATIONS FOR USE

The Sunrise HYPERION™ LTK System is indicated for:

Temporary reduction of hyperopia in patients with +0.75 to +2.5 diopters of manifest refraction spherical equivalent (MRSE) at the spectacle plane (with cylinder less than or equal to ± 0.75 diopters) who are 40 years of age or older with documented stability of refraction for the prior 6 months, as demonstrated by a change of less than or equal to 0.50D in spherical and cylindrical components of the manifest refraction. The magnitude of correction with this treatment diminishes over time, with some patients retaining some or all of their refractive correction.

III. CONTRAINDICATIONS

LTK is contraindicated:

- In pregnant or nursing women
- In patients with signs of keratoconus.

- In patients with clinically significant corneal dystrophy or scarring in the 6 or 7 mm central zone.

- In patients with a history of herpetic keratitis.

- In patients with an autoimmune disease, collagen vascular disease, clinically significant atopic syndrome, insulin dependent diabetes or an immune compromised status.

IV. WARNINGS AND PRECAUTIONS

- Based on existing information for the clinical parameters used in the clinical trial, approximately half of the effect seen at 6 months is gone at 2 years including the "initially" intended myopic overcorrection.

- Extrapolating from existing data, Sunrise Technologies has found that the effect of LTK may dissipate in 3-5 years. The effect of the procedure may last substantially longer in some patients.

- The safety and effectiveness of re-treatment procedures with the Hyperion™ LTK System or other refractive surgical devices have not been established. Limited data suggests that the reduction in refractive error following re-treatment may diminish over time.

The inclusive listing of the warnings and precautions can be found in the device labeling.

V. DEVICE DESCRIPTION

The HYPERION™ LTK System uses a non-contact Ho:YAG laser to perform Laser Thermal Keratoplasty (LTK). This device delivers laser light to precisely heat predetermined areas of the mid-peripheral cornea in order to obtain collagen shrinkage and thereby increase corneal curvature.

The HYPERION™ delivers eight simultaneous spots (0.6mm) on the cornea in a circular pattern; one ring at 6 mm diameter and one at 7 mm diameter for a total of 16 spots.

Seven pulses per ring are delivered at a rate of five pulses per second resulting in a treatment time of 2.8 seconds. The pattern can be rotated if necessary.

The HYPERION™ contains a Class IV laser. The company submitted declarations that the HYPERION™ LTK System conforms to the Radiological Health requirements of U.S./FDA 21 CFR 1040.10 and 1040.11 and to the following safety standards:

- EN 60601-1 Electrical Safety
- EN 60601-1-2 EMC
- EN 60601-2-22 Medical Laser Safety
- EN 60825 Laser Safety
- EN60601-1-4 Programmable Electrical Medical Systems

The HYPERION™ consists of the following components. The Operator's Manual provides a more in-depth device description.

- **Laser System:**

Laser wavelength:	2120 nm
Laser pulse duration:	160 µsec
Repetition rate:	5 Hz

There is also a low power (0.5 mW), red 635 nm laser diode for aiming and a low power (0.1 mW), green 532 nm laser for focus.

- **Delivery System:** A green 532 nm laser is used for focusing on the cornea and an illuminator provides additional light on the eye. A heads up display is available for the ophthalmologist and the LCD display shows the image seen through the microscope.

- **Power Supply:** The power supply components meet international standards and requirements.

- **Computer:** PC based system that contains a LCD monitor, keyboard, storage devices, I/O control board and power supply.

- **Cooling Module:** The laser is cooled by a custom built cooling system.

- **Table Assembly:** All of the components are contained in a single housing.

- **Safety Features and Interlocks:** The HYPERION™ has numerous safety features and interlocks to assure safe operation. The HYPERION™ includes safety checks at start-up, calibration, pre-treatment and monitors output during treatment.

- **Software:** The HYPERION™ LTK software is divided into two components, the Instrument Group Program (ICP) which includes the Graphical User Interface (GUI) and the 8032 firmware which controls many of the low-level hardware functions, and communicates with the ICP through the Dual Port RAM. The ICP handles the user interface, peripheral hardware, and all other operational functions.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative methods for correcting farsightedness include spectacles, contact lenses, and excimer laser for photorefractive keratectomy or laser assisted in situ keratomileusis.

VII. MARKETING HISTORY

Sunrise has LTK Systems in commercial distribution in 13 countries outside of the United States: Canada, Mexico, Argentina, United Kingdom, Germany, Italy, Belgium, South Africa, Croatia, Saudi Arabia, Spain, Turkey and Hong Kong. The Sunrise LTK system has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse events of this device include: corneal infiltrate or ulcer; uncontrolled intraocular pressure (IOP); late onset of haze > 6 months, with loss of ≥ 2 lines best spectacle corrected visual acuity (BSCVA); decrease in BSCVA of > 10 letters not due to irregular astigmatism as shown by hard contact lens refraction, at 6 months or later; retinal vascular accidents; retinal detachment.

There were no adverse events reported during the post-treatment visits.

IX. SUMMARY OF PRECLINICAL STUDIES

The HYPERION™ utilizes infrared laser energy, delivered into the cornea, to achieve a thermal profile within the stroma that allows for controlled collagen shrinkage. The effects of holmium:YAG lasers have been evaluated in a series of non-clinical laboratory studies conducted by Sunrise Technologies as well as by independent researchers.

A. IN VITRO STUDIES

A series of investigations using porcine eyes was conducted by Sunrise Technologies to confirm 6 and 7 mm as the appropriate ring diameters. Later experiments utilized varying energy settings and number of pulses, with either 8 or 16 spots per ring. Laser energies evaluated ranged from 25 mJ/spot (8.8 J/cm^2) to 48 mJ/spot (16.8 J/cm^2). Change in central corneal curvature was measured as a function of energy, number of pulses (4, 7, 10 or 13), number of spots and ring diameter.

Refractive change was inversely proportional to ring diameter. Change in corneal curvature was linear, and directly proportional to laser energy up to 40 mJ/spot. Refractive change was also directly dependent on the number of pulses, ranging from approximately 1.5 D to 5.5 D over the range of pulses from 4 to 13, delivered at fixed laser energy. There were no substantial differences in refractive change resulting from the various spot patterns evaluated.

B. ANIMAL STUDIES

The *in vivo* effects of LTK were evaluated in rabbits treated with 24 spots arranged on 4 and 6 mm diameter rings, with energy density ranging from 5 to 21 J/cm^2. Three pulses per spot were applied to the spots treated with 20 J/cm^2, with the goal of maximizing any possible deleterious effect. There was a transient increase in corneal thickness on the first day after laser treatment, but no other observations (i.e., aqueous flare, iris abnormalities, corneal neovascularization, change in

intraocular pressure) were noted during the 4-week follow-up period. Histological evaluation revealed that both at therapeutic and higher doses, the effects of the laser were well-delineated and confined to the cornea. At the maximum energy tested (approximately 40% higher than clinical setting), scanning electron microscopy showed the magnitude of endothelial cell loss to be approximately 1% with a 32 spot pattern.

In a study by Koch and collaborators, the Sunrise Technologies holmium:YAG laser (wavelength of 2120 nanometers) was utilized to evaluate acute histologic changes and wound healing response following LTK in rabbits. The energy (J/cm^2) evaluated ranged from the highest clinical settings to energy levels considerably greater than those under clinical study.

Early histological observations (immediately after LTK and 24 hours later) revealed stromal swelling, alterations in the stromal matrix, and epithelial, keratocyte and endothelial damage. At 3 weeks after treatment, new basement membrane was beginning to form and keratocyte activation was observed. At 2 and 3 months post-treatment, keratocytes were still activated, indicating an ongoing wound healing process.

C. CONCLUSIONS

The in vitro and animal studies provided evidence to support the conclusion that the device did not present an unreasonable risk to subjects and could proceed to clinical trials under an approved investigational device exemption (IDE).

X. SUMMARY OF CLINICAL STUDIES

Sunrise Technologies performed a clinical study of the Company's LTK system in the U.S. under the auspices of investigational device exemption application (IDE) #G910166. The data from this study served as the basis for the approval decision. Safety and

effectiveness outcomes through 24 months post-treatment were evaluated for confirmation. The IDE study is described in detail as follows:

A. STUDY OBJECTIVES

The overall reason for the Laser Thermal Keratoplasty (LTK) procedure was defined by this treatment goal: to evaluate the safety and effectiveness of the Company's LTK system in the correction of low to moderate hyperopia.

B. STUDY DESIGN

The study was a prospective, non-randomized, unmasked, multi-center clinical study where the primary control was the preoperative status of the treated eye.

C. INCLUSION AND EXCLUSION CRITERIA

Enrollment in the Sunrise Technologies Low to Moderate Hyperopia LTK clinical study was limited to patients: at least 40 years of age, unilateral or bilateral hyperopia of +0.75D to +2.50D (manifest refraction spherical equivalent) at the spectacle plane with 0.75D or less manifest cylinder, stable refraction (no more than 0.50D change in 6 months prior to treatment) and discontinuation of contact lens prior to LTK (2 weeks, soft/permeable lenses; 3 weeks, hard lenses).

Patients were not permitted to enroll in the Sunrise Technologies Low to Moderate Hyperopia LTK clinical study if they met any of the following exclusion criteria: monocular patients; unstable refraction; nystagmus; prior corneal trauma, ocular surgery or corneal disease; uncontrolled uveitis; severe blepharitis; lagophthalmos or dry eye; pregnant or lactating women; cloudy corneas or anterior chambers; or immunocompromised patients.

D. STUDY PLAN, PATIENT ASSESSMENTS, AND EFFICACY CRITERIA

All subjects were expected to return for follow-up examinations at 1 day, 1 week, and 1, 3, 6, 12, 18 and 24 months post-treatment.

By the end of the study, subjects were permitted to have second eyes (fellow eyes) treated the same day as treatment of the first eye. In addition, subjects were eligible for retreatment if uncorrected visual acuity (UCVA) was worse than 20/40 and patient was unhappy due to undercorrection. (See Section X.F.2.e. for information on the few eyes which were retreated.)

Pre-treatment, the subject's medical and ocular histories were recorded. The objective parameters measured during the study included: best spectacle corrected visual acuity (distance), uncorrected visual acuity (distance and near), manifest and cycloplegic refraction, intraocular pressure and status of the cornea, conjunctiva, anterior chamber, lens, vitreous, retina and externals. Additional subgroup testing included glare testing, contrast sensitivity under photopic and mesopic conditions, low illumination vision testing and pupil size, pachymetry and endothelial cell density. A patient questionnaire was to be administered to all subjects pre-treatment and post-treatment at 6, 12, 18 and 24 months.

The primary efficacy variables for this study were: improvement in distance UCVA and reduction in hyperopia (MRSE) based on the per eye treatment goal of the procedure.

E. STUDY PERIOD, INVESTIGATIONAL SITES, AND DEMOGRAPHICS

1. Study Period and Investigational Sites

Subjects were treated between 8/96 and 10/99. The database for this PMA Cohort reflected data collected through 10/99 and included 612 eyes: 379 first eyes and 233 second eyes. There were 11 investigational sites.

2. Demographics

The demographics of this study are typical for a contemporary refractive surgery trial performed in the U.S. Of the 612 treated eyes in 379 subjects, 40.4% (153/379) were from male subjects and 59.6% (226/379) from female subjects. Furthermore, 93.4% (354/379) were from Caucasians, 2.1% (8/379) were from Blacks and 4.5% (17/379) were from other races. The right eye was treated in 50.2% (307/612) cases and the left eye was treated in 49.8% (305/612) cases. The mean age of the subjects treated was 56.1 years with a range from 40 to 78. Preoperative patient characteristics that were found to associate with outcomes are discussed in Section X.E.4.f.

Table 1: Demographics # Eyes of # Enrolled Subjects

PMA Cohort
612 Eyes Treated of 379 Subjects

Gender:		
Female	**226**	**(59.6%)**
Male	**153**	**(40.4%)**
Race:		
American Indian	**0**	**(0.0%)**
Asian	**1**	**(0.3%)**
Black	**8**	**(2.1%)**
Hispanic	**16**	**(4.2%)**
White	**354**	**(93.4%)**
Eyes Treated:		
Right	**307**	**(50.2%)**
Left	**305**	**(49.8%)**
Age at First Surgery:		
Average	**56.1**	
Standard Deviation	**7.4**	
Minimum	**40**	
Maximum	**78**	

F. DATA ANALYSIS AND RESULTS

1. Pre-Treatment Characteristics

Table 2 contains a summary of the pre-treatment acuity and refraction. The treatment goal for all eyes was emmetropia.

Table 2: Pre-Treatment Characteristics

UCVA 20/40 or better	**19.3%**	**118/611**
UCVA 20/80 or better	**73.2%**	**447/611**
UCVA 20/200 or better	**100.0%**	**611/611**
Manifest Refraction Spherical Equivalent:	**1.69 D mean ± 0.45 D SD**	
range:	**0.75 D to 2.50 D**	

Postoperative Results

a. Accountability and Definition of the PMA Cohort

Subject compliance with follow-up visits (the % Accountability) was between 92.5% and 98.3% of eyes seen at between 1 and 24 months post-treatment. Safety and efficacy analyses were performed based on all eyes in the PMA Cohort available at each post-treatment visit. Eyes that were retreated are included in these analyses up until time of retreatment.

Table 3: Accountability
(Number of eyes enrolled = 612 eyes)

	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	12 Months n/N (%)	18 Months n/N (%)	24 Months n/N (%)
Study Cohort (N)	612	612	612	612	612	612
Available for Analysis	592/612 (96.7)	571/612 (93.3)	555/612 (90.7)	493/612 (80.6)	267/612 43.6)	72/612 11.8)
Discontinued:						
Deceased	0/612 (0.0)	0/612 (0.0)	0/612 (0.0)	0/612 (0.0)	2/612 (0.3)	2/612 (0.3)
Retreated	1/612 (0.2)	2/612 (0.3)	7/612 (1.1)	7/612 (1.1)	8/612 (1.3)	8/612 (1.3)
Missed Visit	10/612 (1.6)	27/612 (4.4)	29/612 (4.7)	25/612 (4.1)	15/612 (2.5)	4/612 (0.7)
Not Yet Eligible for the Interval/ Window Still Open/Data Not Available	9/612 (1.5)	12/612 (2.0)	14/612 (2.3)	72/612 (11.8)	314/612 (51.0)	524/612 (85.6)
Lost to Follow-Up	0/612 (0.0)	0/612 (0.0)	7/612 (1.1)	15/612 (2.5)	6/612 (1.3)	2/612 (0.3)
Available for Analysis ÷ (Enrolled–Discont.–Not Yet Elig.) = % Accountability	592 / (612–1–9) = 98.3	571 / (612–2–12) = 95.5	555 / (612–7–14) = 93.9	493 / (612–7–72) = 92.5	267 / (612–10–314) = 92.7	72 / (612–10–524) = 92.3

b. Change in Refraction Over Time

Table 4 documents the change in the manifest refraction spherical equivalent between pairs of sequential post-treatment visits for the PMA Cohort eyes.

Of the eyes with both 18 and 24 month visit data, 61.8% experienced a change in spherical equivalent of 0.25D or less and 35.3% had a change of less than 0.25D between the two examinations. The overall mean change in spherical equivalent during this interval was 0.14D with a mean rate of change of 0.02D/month.

Since the interval length differs, the most meaningful comparison between time periods is the mean rate of change per month. The mean rate of change per month drops from 0.27D (1-3 months), to 0.10D (3-6 months), 0.06D (6-12 months), to 0.04D (12 to 18 months) to 0.02D (18 to 24 months).

Table 4: Reduction in Manifest Refraction Over Time: PMA Cohort

Change in MRSE	1 WK-1M	1 M-3 M	3 M-6 M	6 M-12 M	12 M-18 M	18 M-24 M
Time Period Intervals						
Months between visits						
≤ +0.25 D	24.2%	17.5%	28.4%	27.7%	25.9%	35.3%
+/-0.25 D	41.1%	32.5%	51.0%	43.8%	49.0%	61.8%
+/- 0.50 D	66.8%	51.6%	76.3%	70.2%	81.7%	88.2%
+/- 0.75 D	83.3%	69.0%	89.5%	86.5%	93.2%	97.1%
+/- 1.0 D	90.1%	82.0%	94.8%	94.3%	96.8%	100.0%
Mean Change in SE	**0.26 D**	**0.54 D**	**0.30 D**	**0.36 D**	**0.25 D**	**0.14 D**
Mean Rate of Change per month	**0.34 D**	**0.27 D**	**0.10 D**	**0.06 D**	**0.04 D**	**0.02 D**

c. Effectiveness Outcomes

The analysis of effectiveness was based on the all eyes available at postoperative visits from 1 month through 24 months. The following tables are located in Appendix 1.

Table 5 provides a summary of safety and efficacy results over time (1 through 24 months post-treatment) for the PMA Cohort.

Table 6 presents the same parameters at 12 months post-treatment stratified by dioptric power.

Table 7 presents the same parameters at 12 months post-treatment stratified by age groups.

d. Safety Outcomes

The analysis of safety was based on the entire 612 eyes treated in the PMA Cohort. The key safety outcomes for this study are presented in Appendix 1, The rates of the adverse events are reported in table 8; complications are reported in table 9; table 10 shows the incidence of induced cylinder; and, tables 11a-c present patient symptom information.

Table 8 presents a summary of adverse events. The benchmark for each adverse event is a rate of less than 1% per event.

Table 8: Adverse Events: All Post-treatment Visits

Corneal Infiltrate or Ulcer	**0.0%**
Uncontrolled IOP	**0.0%**
Late Onset of Haze > 6 months with loss of ≥ 2 lines BSCVA	**0.0%**
Retinal Vascular Accidents	**0.0%**
Retinal Detachment	**0.0%**

All complications reported between 1 and 24 months post-treatment are presented in Table 9.

Table 9: Complications: All Post-treatment Visits

	1 Mth	3 Mths	6 Mths	12 Mths	18 Mths	24 Mths
Corneal Edema	**0.2%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**
Recurrent Corneal Erosion	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**
Foreign Body Sensation	**1.9%**	**0.4%**	**0.2%**	**0.8%**	**1.1%**	**0.3%**
Pain	**0.7%**	**0.4%**	**0.0%**	**0.2%***	**0.0%**	**0.0%**

***Isolated single visit; patient seen at 8 post-tx visits but only reported at 12 months**

Induced cylinder (> 2.0 D and > 1.0 D) is provided in Table 10 for all post-treatment visits.

Table 10: Induced Cylinder All Post-treatment Visits

	1 Mth	3 Mths	6 Mths	12 Mths	18 Mths	24 Mths
Increase > 2.00 D	**3.5%**	**1.4%**	**0.9%**	**0.2%**	**0.0%**	**0.0%**
Increase > 1.00 D	**14.2%**	**10.3%**	**9.8%**	**4.7%**	**1.9%**	**4.2%**

Tables 11a-c present patient symptom information reported at the 6, 12, 18 and 24 month post-treatment visits.

No subjective symptom data was collected during the post-treatment period prior to 6 months.

Table 11a. Patient Subjective Symptoms-Graded "Present" (vs. "Absent")

Symptom	Pre-Tx	6 Mths	12 Mths	18 Mths	24 Mths
Photophobia	0.0%	0.0%	2.0%	8.7%	6.8%
Itching	0.0%	0.0%	2.0%	0.0%	0.0%
Pain	0.0%	0.0%	2.0%	0.0%	0.0%
Pressure	0.0%	0.0%	0.0%	0.0%	0.0%
Tearing	0.0%	2.0%	0.0%	0.0%	0.0%
Foreign Body Sensation	0.0%	0.0%	2.0%	4.3%	4.5%
Night Vision Difficulty	24.1%	32.6%	28.6%	NR	17.1%

Table 11b. Patient Subjective Symptom "Severity"-Graded 0 to +4

Symptom	0	+1	+2	+3	+4
Photophobia:					
Pre-Tx	94.9%	3.0%	1.7%	0.0%	0.4%
6 Mths	89.4%	2.6%	5.4%	1.2%	1.4%
12 Mths	89.5%	4.4%	2.8%	1.2%	2.1%
24 Mths	78.6%	10.7%	7.1%	3.6%	0.0%

Table 11c. Patient Subjective Symptom "Incidence"

Symptom	N/R*	None	Very Little	Mild	Moderate	Marked	Severe
Glare:							
Pre-Tx	2.2%	90.3%	1.1%	3.2%	2.5%	0.7%	0.0%
6 Mths	4.4%	83.2%	2.0%	1.6%	5.6%	2.8%	0.4%
12 Mths	8.7%	81.4%	1.7%	2.6%	3.0%	1.7%	0.9%
24 Mths	11.1%	81.5%	3.7%	3.7%	0.0%	0.0%	0.0%

*N/R = Not Reported

Symptom	N/R*	None	Very Little	Mild	Moderate	Marked	Severe
Increased Sensitivity to Light (e.g. halos):							
Pre-Tx	2.9%	91.0%	1.1%	2.5%	1.1%	1.4%	0.0%
6 Mths	3.2%	83.2%	0.8%	2.0%	6.8%	2.4%	1.6%
12 Mths	6.9%	81.4%	0.9%	2.6%	5.6%	1.7%	0.9%
24 Mths	3.7%	85.2%	0.0%	7.4%	0.0%	3.7%	0.0%

*N/R = Not Reported

Symptom	N/R*	None	Very Little	Mild	Moderate	Marked	Severe
Night Vision Problems:							
Pre-Tx	4.3%	88.1%	1.1%	2.2%	2.2%	2.2%	0.0%
6 Mths	3.6%	83.2%	1.6%	2.8%	4.4%	2.4%	2.0%
12 Mths	10.0%	78.4%	0.4%	1.3%	3.9%	4.3%	1.7%
24 Mths	3.7%	92.6%	0.0%	0.0%	0.0%	3.7%	0.0%

*N/R = Not Reported

e. Retreatment

Five retreatments were performed between 6 and 12 months after the original treatment and 5 retreatments were performed between 12 and 24 months.

All retreatment procedures were repeat LTK's. There were no major safety concerns for these retreated eyes. There is not enough data to form any definitive conclusions regarding retreatment outcomes with this device due to the small number of eyes that underwent retreatment.

f. Factors Associated with Outcomes

An in-depth modeling analysis was performed to identify those factors that have a statistically significant impact on LTK clinical outcomes. Change in spherical equivalent (or the reduction in hyperopia-MRSE) was analyzed as a continuous variable as a function of AGE, RACE, GENDER, APPLIED ENERGY and CORNEAL CURVATURE at 6, 12, 18 and 24 months post-treatment.

The only variables found to be statistically significant were AGE and APPLIED ENERGY.

g. Patient Satisfaction and Spectacle Dependence

Patient satisfaction and patient dependence on spectacles were assessed on a patient survey at 6, 12 and 24 months post-treatment.

Table 12 represents patient satisfaction data from 6 to 24 months post-treatment, using a 5 point grading scale from "very disappointed" to "most satisfied". Table 13 presents information on pretreatment and post-treatment spectacle and contact lens wear; the reason for spectacle/contact lens usage (i.e., for distance *vs* near vision) was not requested.

Table 12 Patient Satisfaction

	Very Disappointed (1)	(2)	(3)	(4)	Most Satisfied (5)
6 Mths	7.7%	6.7%	18.0%	21.5%	46.1%
12 Mths	8.0%	10.9%	18.5%	26.9%	35.7%
24 Mths	14.8%	13.1%	14.8%	9.8%	47.5%

*No patients (0.0%) reported dissatisfaction due to visual symptoms. Primary reasons for dissatisfaction were undercorrection and poorly managed patient expectations (e.g., displeased to lose the immediate post-operative improvement in near visual acuity which occurs due to expected overcorrection, even when aware that near acuity improvement is not a treatment goal).

Table 13
Do You Wear Spectacles or Contact Lenses?

	Pre-TX	6 Mths	12 Mths	24 Mths
Yes	92.3%	31.5%	20.6%	21.1%

*Patients treated bilaterally (both eyes treated) were asked pre-treatment and 6, 12, and 24 months post-treatment if they wore spectacles or contacts lenses. Reason for spectacle/contact lens usage (i.e., for distance *vs* near vision) not requested.

h. Device Failure

No device failures were reported during the clinical trial.

XI. CONCLUSIONS DRAWN FROM THE CLINICAL STUDY

The data in this application support reasonable assurance of the safety and efficacy of this device when used in accordance with the indications for use.

XII. PANEL RECOMMENDATIONS

The Ophthalmic Devices Panel originally reviewed this device under PMA P980051 at the Panel meeting on July 22, 1999, and recommended a non-approvable decision. The Panel's decision was based on ~~initial~~ concerns regarding regression of refractive correction following the LTK procedure; however, there were no safety issues related to the device. The applicant submitted additional information to FDA to address the Panel's concerns, including longer-term follow-up of subjects and a revised indication for use statement addressing post-surgical regression. A new PMA number, P990078, was assigned. At an advisory panel meeting held on January 13, 2000, the Ophthalmic Devices Panel recommended that Sunrise Technologies International, Inc. PMA P990078 was approvable with conditions. The conditions were related to labeling issues regarding longevity of the treatment effect, patient symptoms and effect of retreatment. The conditions were:

1. Revise the Indications for Use to state that the device is for temporary reduction of hyperopic error.

2. Revise Patient and Physician Labeling:
   a. Add Warning: The treatment effect decreases over time.
   b. Add Warning: Data on effect of retreatments with the Sunrise laser or other refractive surgical procedures are insufficient at the

present time. Available data suggest that the retreatment effect with the Sunrise laser also decreases over time. Outcomes of multiple retreatments are unknown.

c. Add specific data on the numbers of patients needing spectacle or contact lenses refractive correction after having received LTK.
d. Add information on the likelihood of developing postoperative symptoms, e.g. difficulty with night driving, glare, and photophobia.
e. Clarify description in patient labeling regarding the anatomy of the eye, over-correction (induced myopia), and presbyopia.

3. Provide additional data on:
   a. Satisfaction levels and retreatment outcomes stratified by age.
   b. Retreatment outcomes.

All panel recommendations were included in the Indications for Use, in the Patient and Physician Labeling, and in the SSED.

XIII. FDA DECISION

CDRH concurred with the Panel's recommendation and the applicant satisfactorily addressed the Panel's and FDA's remaining deficiencies. CDRH issued an approval order on June 30, 2000. The applicant's manufacturing facility was inspected on May 24 through June 1, 2000 and was found to be in compliance with the device Quality System Regulation.

XIV. APPROVAL SPECIFICATIONS

Directions for use: See labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.

Post-approval Requirements and Restrictions: See approval order.

APPENDIX I
Table 5

Sunrise Technologies Inc.
LTK - SL61 / SL72 / SL73 and SF
as of 10/19/1999

Summary of Key Safety and Efficacy Variables

PMA Cohort

	1 month	3 month	6 month	12 month	18 month	24 month
Available for Analysis	592	571	555	493	267	72
EFFICACY VARIABLES						
UCVA 20/20 or better	131 / 592 (22.1%) [18.8-25.5%]	181 / 570 (31.8%) [27.9-35.6%]	216 / 554 (39.0%) [34.9-43.1%]	179 / 479 (37.4%) [33.0-41.7%]	90 / 261 (34.5%) [28.7-40.2%]	15 / 72 (20.8%) [11.5-30.2%]
UCVA 20/40 or better	387 / 592 (65.4%) [61.5-69.2%]	447 / 570 (78.4%) [75.0-81.8%]	477 / 554 (86.1%) [83.2-89.0%]	407 / 479 (85.0%) [81.8-88.2%]	214 / 261 (82.0%) [77.3-86.7%]	49 / 72 (68.1%) [57.3-78.8%]
UCVA not reported	0	1	1	14	6	0
Difference from Intended						
± 0.50 D	211 / 544 (38.8%) [34.7-42.9%]	341 / 565 (60.4%) [56.3-64.4%]	356 / 554 (64.3%) [60.3-68.3%]	275 / 481 (57.2%) [52.8-61.6%]	122 / 262 (46.6%) [40.5-52.6%]	24 / 72 (33.3%) [22.4-44.2%]
± 1.00 D	367 / 544 (67.5%) [63.5-71.4%]	502 / 565 (88.8%) [86.3-91.4%]	485 / 554 (87.5%) [84.8-90.3%]	401 / 481 (83.4%) [80.0-86.7%]	194 / 262 (74.0%) [68.7-79.4%]	45 / 72 (62.5%) [51.3-73.7%]
± 2.00 D	521 / 544 (95.8%) [94.1-97.5%]	559 / 565 (98.9%) [98.1-99.8%]	551 / 554 (99.5%) [98.8-100.0%]	474 / 481 (98.5%) [97.5-99.6%]	256 / 262 (97.7%) [95.9-99.5%]	69 / 72 (95.8%) [91.2-100.0%]
MRSE not reported	48	6	1	12	5	0
Undercorrected > 1.00 D	2.4%	4.2%	10.6%	16.4%	25.6%	37.5%
Overcorrected > 1.00 D	30.1%	6.9%	1.8%	0.2%	0.4%	0.0%

Sunrise Technologies Inc.
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Table 5 (Continued)
Summary of Key Safety and Efficacy Variables

PMA Cohort

	1 month	3 month	6 month	12 month	18 month	24 month
Available for Analysis	592	571	555	493	267	72
SAFETY VARIABLES						
BsCVA worse than 20/40	1 / 573 (0.2%) [0.0-0.5%]	1 / 567 (0.2%) [0.0-0.5%]	0 / 552 (0.0%) [0.0-0.0%]	0 / 481 (0.0%) [0.0-0.0%]	0 / 260 (0.0%) [0.0-0.0%]	0 / 72 (0.0%) [0.0-0.0%]
BsCVA not reported	19	4	3	12	7	0
Loss of 2 lines BsCVA	14 / 573 (2.4%) [1.2-3.7%]	8 / 567 (1.4%) [0.4-2.4%]	14 / 552 (2.5%) [1.2-3.8%]	11 / 481 (2.3%) [1.0-3.6%]	5 / 260 (1.9%) [0.3-3.6%]	0 / 72 (0.0%) [0.0-0.0%]
Loss of > 2 lines BsCVA	14 / 573 (2.4%) [1.2-3.7%]	7 / 567 (1.2%) [0.3-2.1%]	2 / 552* (0.4%) [0.0-0.9%]	1 / 48+ (0.2%) [0.0-0.6%]	1 / 260ϒ (0.4%) [0.0-1.1%]	0 / 72 (0.0%) [0.0-0.0%]
BsCVA worse than 20/25; 20/20 or better preop	20 / 573 (3.5%) [2.0-5.0%]	15 / 567 (2.6%) [1.3-4.0%]	5 / 552 (0.9%) [0.1-1.7%]	3 / 481 (0.6%) [0.0-1.3%]	4 / 260 (1.5%) [0.0-3.0%]	0 / 72 (0.0%) [0.0-0.0%]
BsCVA value missing preop or postop	19	4	3	12	7	0
Increase >2 D cylinder	19 / 544 (3.5%) [1.9-5.0%]	8 / 566 (1.4%) [0.4-2.4%]	5 / 554 (0.9%) [0.1-1.7%]	1 / 481 (0.2%) [0.0-0.6%]	0 / 262 (0.0%) [0.0-0.0%]	0 / 72 (0.0%) [0.0-0.0%]
Cylinder value missing preop or postop	48	5	1	12	5	0

* SL73-07-341-OS: Cataract development in 1 subject 61 years of age, BsCVA of 20/40

SL61-07-011-OS: Reduced VA at 6 months shows recovery at 12 months, preop BsCVA of 20/10, 6 month BsCVA of 20/20, and 12 month BsCVA of 20/13.

\+ SL73-05-305-OD: Vision recorded as 20/32, however, no manifest refraction performed. Patient returned at 18 months post-treatment with BsCVA of 20/16.

ϒ SL73-10-314-OD: Cataract development in 1 subject 63 years of age, BsCVA of 20/40

Table 6

Summary of Key Safety and Efficacy Variables at 12 months

Stratified by Preop MRSE; PMA Cohort

Sunrise Technologies Inc.
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	0.75 to 0.99 D	1.00 to 1.24 D	1.25 to 1.49 D	1.50 to 1.74 D	1.75 to 1.99 D	2.00 to 2.24 D	2.25 to 2.50 D
EFFICACY VARIABLES							
UCVA 20/20 or better	11 / 18 (61.1%) [36.6-83.6%]	27 / 47 (57.4%) [43.3-71.6%]	44 / 86 (51.2%) [40.6-61.7%]	28 / 80 (35.0%) [24.5-45.5%]	42 / 96 (43.8%) [33.8-53.7%]	15 / 71 (21.1%) [11.6-30.6%]	12 / 81 (14.8%) [7.1-22.6%]
UCVA 20/40 or better	18 / 18 (100.0 [100.0-100.0%	45 / 47 (95.7%) [90.0-100.0%]	82 / 86 (95.3%) [90.9-99.8%]	69 / 80 (86.3%) [78.7-93.8%]	85 / 96 (88.5%) [82.2-94.9%]	50 / 71 (70.4%) [59.8-81.0%]	(71.6%) 58 / 81 [61.8-81.4%]
UCVA not reported	1	4	2	11	7	8	6
Difference from Intended							
± 0.50 D	14 / 18 (77.8%) [58.6-97.0%]	38 / 47 (80.9%) [69.6-92.1%]	64 / 85 (75.3%) [66.1-84.5%]	56 / 82 (68.3%) [58.2-78.4%]	59 / 96 (61.5%) [51.7-71.2%]	21 / 71 (29.6%) [19.0-40.2%]	23 / 82 (28.0%) [18.3-37.8%]
± 1.00 D	18 / 18 (100.0 [100.0-100.0%	46 / 47 (97.9%) [93.7-100.0%]	81 / 85 (95.3%) [90.8-99.8%]	77 / 82 (93.9%) [88.7-99.1%]	85 / 96 (88.5%) [82.2-94.9%]	49 / 71 (69.0%) [58.3-79.8%]	45 / 82 (54.9%) [44.1-65.6%]
± 2.00 D	18 / 18 (100.0 [100.0-100.0%	47 / 47 (100.0 [100.0-100.0%	85 / 85 (100.0 [100.0-100.0%	82 / 82 (100.0 [100.0-100.0%	96 / 96 (100.0 [100.0-100.0%	68 / 71 (95.8%) [91.1-100.0%]	78 / 82 (95.1%) [90.5-99.8%]
MRSE not reported	1	4	3	9	7	8	5

Table 6 (Continued)

Sunrise Technologies Inc.
LTK - SL61 / SL72 / SL73 and SF
as of 10/19/1999

Summary of Key Safety and Efficacy Variables at 12 months

Stratified by Preop MRSE; PMA Cohort

	0.75 to 0.99 D	1.00 to 1.24 D	1.25 to 1.49 D	1.50 to 1.74 D	1.75 to 1.99 D	2.00 to 2.24 D	2.25 to 2.50 D
SAFETY VARIABLES							
BsCVA worse than 20/40	0 / 18 (0.0%) [0.0-0.0%]	0 / 47 (0.0%) [0.0-0.0%]	0 / 86 (0.0%) [0.0-0.0%]	0 / 81 (0.0%) [0.0-0.0%]	0 / 96 (0.0%) [0.0-0.0%]	0 / 71 (0.0%) [0.0-0.0%]	0 / 82 (0.0%) [0.0-0.0%]
BsCVA not reported	1	4	2	10	7	8	5
Loss of 2 lines BsCVA	1 / 18 (5.6%) [0.0-16.1%]	1 / 47 (2.1%) [0.0-6.3%]	2 / 86 (2.3%) [0.0-5.5%]	1 / 81 (1.2%) [0.0-3.6%]	2 / 96 (2.1%) [0.0-4.9%]	1 / 71 (1.4%) [0.0-4.1%]	3 / 82 (3.7%) [0.0-7.7%]
Loss of > 2 lines BsCVA	0 / 18 (0.0%) [0.0-0.0%]	0 / 47 (0.0%) [0.0-0.0%]	0 / 86 (0.0%) [0.0-0.0%]	1 / 81 (1.2%) [0.0-3.6%]	0 / 96 (0.0%) [0.0-0.0%]	0 / 71 (0.0%) [0.0-0.0%]	0 / 82 (0.0%) [0.0-0.0%]
BsCVA worse than 20/25; 20/20 or better preop	0 / 18 (0.0%) [0.0-0.0%]	0 / 47 (0.0%) [0.0-0.0%]	0 / 86 (0.0%) [0.0-0.0%]	1 / 81 (1.2%) [0.0-3.6%]	1 / 96 (1.0%) [0.0-3.1%]	0 / 71 (0.0%) [0.0-0.0%]	1 / 82 (1.2%) [0.0-3.6%]
BsCVA value missing preop or postop	1	4	2	10	7	8	5
Increase >2 D cylinder	0 / 18 (0.0%) [0.0-0.0%]	0 / 47 (0.0%) [0.0-0.0%]	0 / 85 (0.0%) [0.0-0.0%]	0 / 82 (0.0%) [0.0-0.0%]	1 / 96 (1.0%) [0.0-3.1%]	0 / 71 (0.0%) [0.0-0.0%]	0 / 82 (0.0%) [0.0-0.0%]
Cylinder value missing preop or postop	1	4	3	9	7	8	5

Table 7

Sunrise Technologies Inc.
LTK - SL61 / SL72 / SL73 and SF
as of 10/19/1999

Summary of Key Safety and Efficacy Variables at 12 months

PMA Cohort

	Age 40-49	Age 50-59	Age 60 and over
Available for Analysis	69	255	167
EFFICACY VARIABLES			
UCVA 20/20 or better	22 / 66 (33.3%) [22.0-44.7%]	99 / 247 (40.1%) [34.0-46.2%]	58 / 164 (35.4%) [28.0-42.7%]
UCVA 20/40 or better	54 / 66 (81.8%) [72.5-91.1%]	213 / 247 (86.2%) [81.9-90.5%]	138 / 164 (84.1%) [78.6-89.7%]
UCVA not reported	3	8	3
Difference from intended			
± 0.50 D	33 / 66 (50.0%) [37.9-62.1%]	140 / 250 (56.0%) [49.8-62.2%]	100 / 163 (61.3%) [53.9-68.8%]
± 1.00 D	53 / 66 (80.3%) [70.7-89.9%]	201 / 250 (80.4%) [75.5-85.3%]	145 / 163 (89.0%) [84.1-93.8%]
± 2.00 D	66 / 66 (100.0 [100.0-100.0%]	246 / 250 (98.4%) [96.8-100.0%]	160 / 163 (98.2%) [96.1-100.0%]
MRSE not reported	3	5	4

Table 7 (Continued)

Summary of Key Safety and Efficacy Variables at 12 months

PMA Cohort

	Age 40-49	Age 50-59	Age 60 and over
Available for Analysis	69	255	167
SAFETY VARIABLES			
BsCVA worse than 20/40	0 / 66 (0.0%) [0.0-0.0%]	0 / 249 (0.0%) [0.0-0.0%]	0 / 164 (0.0%) [0.0-0.0%]
BsCVA not reported	3	6	3
Loss of 2 lines BsCVA	3 / 66 (4.5%) [0.0-9.6%]	5 / 249 (2.0%) [0.3-3.8%]	3 / 164 (1.8%) [0.0-3.9%]
Loss of > 2 lines BsCVA	0 / 66 (0.0%) [0.0-0.0%]	1 / 249 (0.4%) [0.0-1.2%]	0 / 164 (0.0%) [0.0-0.0%]
BsCVA worse than 20/25; 20/20 or better preop	0 / 66 (0.0%) [0.0-0.0%]	1 / 249 (0.4%) [0.0-1.2%]	2 / 164 (1.2%) [0.0-2.9%]
BsCVA value missing preop or postop	3	6	3
Increase >2 D cylinder	0 / 66 (0.0%) [0.0-0.0%]	1 / 250 (0.4%) [0.0-1.2%]	0 / 163 (0.0%) [0.0-0.0%]
Cylinder value missing preop or postop	3	5	4