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SUMMARY OF SAFETY AND EFFECTIVENESS DATA

ViewPoint[®] CK System

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1. GENERAL INFORMATION

Device Generic Name:	RF Electrosurgical Device
Device Trade Name:	ViewPoint™ CK System
Applicant's Name and Address:	Refractec, Inc. 3 Jenner, Suite 140 Irvine, California 92618 U.S. (949) 784-2600 (949) 784-2601 (fax)
Date of Panel Recommendation:	TBD
PMA Number:	PMA #P010018
Date of GMP Inspection:	TBD
Date of Notice of Approval to Applicant:	TBD

2. INDICATIONS FOR USE

The ViewPoint™ CK System/Conductive Keratoplasty (CK) Procedure is indicated for the reduction of previously untreated spherical hyperopia in patients 40 years of age or greater, who have 0.75 D to 3.25 D of cycloplegic spherical hyperopia, with less than or equal to 0.75 D of refractive astigmatism (minus cylinder format), a cycloplegic spherical equivalent of 0.75 D to 3.00 D, and no more than 0.50 D difference between pre-operative manifest refraction spherical equivalent (MRSE) and cycloplegic refraction spherical equivalent (CRSE). Some regression of the initial effect following the CK procedure is observed over time.

3. CONTRAINDICATIONS

CK treatment with the ViewPoint™ CK System is contraindicated in patients:

- With a peripheral pachymetry reading, measured at the 6 mm optical zone, of less than 560 microns
- Who have had previous strabismus surgery or are likely to develop strabismus following the CK procedure
- With a history of Herpes zoster or Herpes simplex keratitis
- Who have diabetes, diagnosed autoimmune disease, connective tissue disease, or clinically significant atopic syndrome

- Who are being treated with chronic systemic corticosteroid or other immunosuppressive therapy that may affect wound healing, and any immunocompromised patients
- Who are pregnant or lactating
- With keratoconus
- With a history of keloid formation
- With intractable keratoconjunctivitis sicca

4. WARNINGS AND PRECAUTIONS

A. Warnings

Special medical consideration should be given to patients with any of the following conditions:

- Nystagmus, or other condition that prevents a steady gaze, which is required during surgery.
- Unstable refraction over the year prior to examination.

B. Precautions

The safety and effectiveness of the ViewPoint[™] CK System have **NOT** been established in:

- Patients under 40 years of age
- Patients with progressive hyperopia, ocular disease, corneal abnormality, or trauma in the treatment area
- Patients with greater than 3.25 D of hyperopia, 0.75 D of astigmatism, or CRSE > 3.0 D.
- Patients who have had prior intraocular or corneal surgery.
- Retreatments.

5. DEVICE DESCRIPTION

The ViewPoint[™] CK System is designed to treat spherical, previously untreated spherical hyperopia of 0.75 to 3.25 D through a procedure known as Conductive Keratoplasty (CK).

Conductive Keratoplasty utilizes low energy, delivered directly into the corneal stroma through a handpiece and Keratoplast[™] Tip, to effect refractive change in the cornea. As a result of conducting a precise amount of RF energy into the corneal stroma, the desired collagen shrinkage temperature is achieved. The peripheral application of this treatment in a predetermined pattern creates a band of tightening and results in a steepening of the central cornea. This steepening creates a safe, predictable and lasting modification to the topographical curvature of the cornea, for the desired refractive effect.

Overview of the ViewPoint[™] CK System

The ViewPoint[™] CK System used to perform the CK procedure consists of the following components:

- Radio frequency energy-generating console
- Reusable corneal marker
- Reusable lid speculum with cable and connector
- Reusable hand-held, pen-shaped handpiece with cable and connector
- Footpedal
- Disposable Keratoplast[™] Tip
- Patient treatment card

The ViewPoint[™] CK System conforms to the following standards:

- ISO/EN 60601-1 Electrical Safety
- ISO/EN 60601-1-2 EMC
- ISO/EN 60601-2-2 Electrical Safety For RF
- ISO/EN 60601-1-4 Programmable Electrical Medical Systems
- ISO 10993 Biocompatibility
- ISO 10993-7 ETO Residuals
- ISO 11135 ETO Sterilization

ViewPoint[™] CK System Console

The ViewPoint[™] CK System console is an AC powered, portable, low power, energy source, which provides regulated RF energy through the handpiece and to the Keratoplast[™] Tip. A treatment card is inserted into the console to activate the system. The energy level is selectable in the range of 30% to 99% (default = 60% or 0.6 W) with exposure time of 0.3 to 0.99 sec. (default = 0.6 sec).

Handpiece

The handpiece is a hand-held, reusable, pen-shaped instrument attached by a cable and connector to the console. The RF energy is delivered by means of the Keratoplast[™] Tip, which attaches to the handpiece.

Keratoplast[™] Tip

A single-use, disposable, stainless steel Keratoplast[™] Tip, 90 µm in diameter and 450 µm long, delivers RF energy directly to the corneal stroma and is attached to the handpiece. The Keratoplast[™] Tip has a proximal bend of 45 degrees and a distal bend of 90 degrees to allow access to the cornea over the patient's brow and nasal regions. A Teflon[®] stop at the very distal portion of the stainless steel tip assures correct depth of penetration.

Lid Speculum

The lid speculum serves as the return (dispersive) electrode for the RF energy being delivered through the Keratoplast[™] Tip. Two types of specula are offered: Barraquer type and Lancaster type. The Barraquer type is a small, malleable wire-speculum and the Lancaster is a locking speculum. Alternate specula may be offered in response to future customer requests.

Footpedal

The footpedal attaches to the console and controls the release of RF energy.

Patient Treatment Card

A patient treatment card is inserted into the console to activate the system.

Safety Features

The ViewPoint[™] CK System has numerous features to assure proper operation. The ViewPoint[™] CK System includes safety checks at start-up and monitors output during treatment.

Software

The ViewPoint[™] CK System software controls user interface, and provides the user with system diagnostics and error messages in the event of a device anomaly. Additionally, the software saves all error messages to the patient treatment card to assist in the diagnosis of technical issues.

6. ALTERNATIVE PRACTICES OR PROCEDURES

Alternative methods of correcting farsightedness (hyperopia) include: spectacles, contact lenses, Laser *in situ* Keratomileusis (LASIK), photorefractive keratectomy (PRK), and Laser Thermal Keratoplasty (LTK).

7. MARKETING HISTORY

The ViewPoint[™] CK System has not been marketed in the United States.

8. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

A. Adverse Effects of the Device on Health

The following adverse effects were reported in the Refractec, Inc. clinical study of the ViewPoint™ CK System.

Table 1
Adverse Event Summary

	Month 1	Month 3	Month 6	Month 9	Month 12
Decrease in BSCVA of > 10 letters not due to irregular astigmatism as shown by hard contact lens refraction at 6 months or later	0%	0%	0%	0%	<1%
IOP >25 mm Hg	0%	0%	1%	<1%	<1%
Secondary Surgical Intervention other than CK treatment	0%	0%	0%	0%	<1%
Other	1%	1%	<1%	1%	1%

In clinical studies of the ViewPoint™ CK System, a complication was reported on the day of surgery: corneal scratch, with a reported rate of <1%. The following adverse events were reported on the day of surgery at a rate of <1%: corneal perforation; surgery could not be performed and had to be rescheduled due to technical difficulties with the CK device.

Each of the following complications was reported at the one week visit at a rate of less than 1%: blurred vision; conjunctivitis; double vision; eyelid inflammation; stye. The following adverse reaction was reported at one week at a rate of less than 1%: mild iritis.

During the first week following surgery patients may experience: pain, discomfort, a feeling of something in the eye lasting from one up to three days after surgery, mild light sensitivity, and swelling of the cornea.

B. Potential Adverse Effects of the Device on Health

Although the following adverse events were not noted in the clinical studies of the ViewPoint™ CK System, the potential exists for these events to occur following the CK procedure. These events include:

- Late onset of haze beyond 6 months with loss of 2 lines (10 letters) or more BSCVA
- A corneal epithelial defect involving the treatment site

- Corneal edema
- Corneal microbial infection
- Corneal decompensation
- Corneal scar in the visual axis
- Intraocular infection
- Hypopyon
- Hyphema
- Onset of cataract unrelated to age, systemic disease, or trauma
- Retinal detachment
- Retinal vascular accidents

9. SUMMARY OF PRECLINICAL STUDIES

A. Objectives

Preclinical studies were conducted to establish the safety and performance of the ViewPoint™ CK System.

B. Design Verification

Upon completion of the assembly and testing of prototype units, the output of the device was evaluated to assess the waveform and to verify that the output met the original design intent. This report concluded that the waveform generated by the prototype device meets the design intent.

C. Electrical Safety Tests

The device has been designed to comply with electrical standards that are recognized domestically and internationally. EN 60601-1 and EN 60601-2-2 Test Reports completed by Intertek Testing Service concluded that the device meets all of the applicable elements of these standards.

D. EMC Compliance

The device has been designed and tested to assure that the unit meets the applicable elements on EN 60601-1-2. The test report completed by Intertek Testing Service concluded that the device meets this standard for EMC compliance.

E. Physical Tests

1. Treatment probe dimensional/physical properties testing:
Qualification of the manufacturing and assembly process was conducted to verify that dimensional specifications were met and that process variability was within acceptable limits. Testing included dimensional analysis, visual inspection of the tip after repeated insertions and activation of RF energy, and evaluation of the glue bond between the Teflon® stop and the tip. The test report shows that the tip dimensions fall within an acceptable tolerance range, the glue bond is sufficient to withstand forces encountered during the procedure, and that repeated insertion and conductance of RF energy does not adversely affect the tip.
2. Return Electrode Heat Transfer Study:
A study was conducted to confirm that there are no adverse heating effects at the return electrode (the lid speculum). This study confirmed that the RF energy applied to the treatment probe caused localized heating at the treatment site and that there was no evidence of heating at the return electrode.

F. Physical Safety Tests

Sterility Validation and Expiration Dating: The device is terminally sterilized in its package utilizing a 100% ETO cycle that has been validated. The sterilization cycle provides a 10^{-6} Sterility Assurance Level (SAL). Accelerated and Real Time aging studies confirm the labeled expiration date.

G. Biocompatibility

The contact material of the tip is a medical grade 420 series Stainless Steel. This material is of known biocompatibility.

H. Performance Testing

Each device is evaluated against a Final Test Procedure as part of the manufacturing/assembly process. This Test Procedure includes calibration and verification of the critical waveform parameters as well as other performance criteria. The Test Procedure has been completed as part of the manufacturing process validation on five prototype units. The results of these tests are on file with the contract manufacturer and as part of the Design History File at Refractec.

I. Electrical and Thermal Simulation

Computer simulation of the ViewPoint[™] CK System was performed in order to analyze the power deposition pattern and thermal profile surrounding the needle tip. This simulation consisted of two steps. First, the needle tip was assigned a voltage with respect to the return electrode; other boundary conditions were defined on the surface of a rectangular volume as required. This information was analyzed by using a computer program to solve the Laplace equation to calculate the potential distribution within the volume. The electric field, power density and circuit impedance were then calculated. Once power density was identified, this value was used as the heating source input into a program that solved a bioheat equation, calculating the temperature distribution within the volume as a function of time. The applied power was then modified to simulate the effect of tissue coagulation or desiccation that occurs over time.

Temperature distributions were computed throughout the entire simulation volume. Based on the power deposition patterns computed from the electric field modeling program, the highest temperatures were predicted to be achieved along the axis of the needle and near the needle tip. At a distance from the needle, where power deposition was insignificant, increase in temperature was due to thermal conduction effects. While initially, maximum heating occurred near the needle tip, with increasing temperature, heating extended along the needle shaft, and ultimately spread at later points to tissue elements located further away from the tip. The extent of the thermal lesion produced was shown to be a function of both time and temperature.

J. Histopathology

As part of the clinical evaluation of the ViewPoint[™] CK System, six subjects scheduled for penetrating keratoplasty underwent the CK procedure 24 to 48 hours prior to penetrating keratoplasty (PK). Histology was performed on the corneal tissue obtained from these subjects.

Initially, the corneal tissue was examined to determine the exact location of the radio frequency applications, and to ensure that the section selected for histopathologic processing did not have any evidence of the underlying pathology that necessitated penetrating keratoplasty. The selected specimen was then processed and stained, and evaluated under high-powered light microscopy.

Histopathologic examination revealed a V-shaped or U-shaped stromal thermal footprint at the site of the radio frequency application that clearly demarcated the shrunken collagen from the surrounding preserved lamellae. A bullous-like separation of epithelium from the underlying Bowman's layer, or a total absence of epithelium at the site of the CK application was observed. Epithelial cells at the site of the CK application were abnormal, with necrotic, shrunken nuclei. Bowman's layer remained intact in all of the sections examined. The keratocyte population was decreased or shrunken, with edema between the stromal lamellae, and collagen disorganization. The surrounding stroma maintained its normal staining properties, with preservation of collagen structure and keratocyte nuclei. No inflammatory cells were observed within the area of the CK application. Descemet's membrane was continuous, with no folds.

Based on this histological study of human corneas, it can be concluded that Conductive Keratoplasty was not associated with an inflammatory response, and no damage to either Bowman's layer or Descemet's membrane in the areas of application was observed.

K. Conclusions

The preclinical testing 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).

10. SUMMARY OF CLINICAL STUDIES

Refractec, Inc. conducted a clinical study of the ViewPoint[™] CK System in the U.S. under IDE #G980224. The data from this study served as the basis for the approval decision. Safety and effectiveness outcomes through 12 months post-treatment were evaluated for confirmation.

A. Objectives

The ViewPoint[™] CK System / Conductive Keratoplasty (CK) Procedure was indicated for the correction of spherical hyperopia in patients with 0.75 D to 3.25 diopters spherical hyperopia, with less than or equal to 0.75 D of refractive astigmatism (cylinder) and a cycloplegic refractive spherical equivalent of 0.75 D to 3.00 D.

B. Study Design

This study was a prospective, multi-center clinical study where the primary control was the preoperative status of the treated eye.

1. Inclusion and Exclusion Criteria

Enrollment in the Refractec clinical study was limited to patients who:

- Had 0.75 to 3.25 D of manifest spherical hyperopia, ≤ 0.75 D of refractive astigmatism, and ≥ 0.75 D of spherical equivalent by cycloplegic refraction in the eye to be treated.
- Had spherical equivalent manifest refraction and spherical equivalent cycloplegic refraction that did not differ by more than 0.50 D.
- Discontinued using hard or rigid gas permeable contact lenses for at least 3 weeks and discontinued using soft contact lenses for at least 2 weeks prior to the preoperative evaluation in the eye to be treated.
- For hard contact lens wearers – had 2 central keratometry readings and 2 manifest refractions taken at least one week apart, the last of which did not differ from the previous values by more than 0.50 D in either meridian; mires were regular in the eye to be treated.
- Had visual acuity correctable to at least 20/40 in both eyes.
- Were at least 21 years of age.
- Were willing and able to return for scheduled follow-up examinations for 24 months after surgery.
- Provided written informed consent.
- Were able to tolerate their full cycloplegic correction while not under cycloplegia.

Patients with the following conditions were excluded from the study:

- Previous strabismus surgery, or who would have been likely to develop strabismus following the CK procedure.
- Anterior segment pathology, including cataracts (in the operative eye).
- Any corneal abnormality (in the operative eye).
- Progressive or unstable hyperopia (in the operative eye).
- Latent hyperopia.
- Distorted or unclear corneal mires.

- Blind in the fellow eye.
- Previous intraocular or corneal surgery.
- History of herpes zoster or herpes simplex keratitis.
- History of steroid-responsive rise in IOP, glaucoma, or preoperative IOP > 21 mm Hg.
- At risk for angle closure or with a potentially occludable angle.
- Diabetes, diagnosed autoimmune disease, connective tissue disease, or clinically significant atopic syndrome.
- Chronic systemic corticosteroid or other immunosuppressive therapy, and any immunocompromised patients.
- Using ophthalmic medication(s) other than artificial tears for treatment of any ocular pathology.
- Using systemic medications with significant ocular side effects.
- History of keloid formation.
- Intractable keratoconjunctivitis sicca.
- Pregnant, planning to be pregnant, or lactating during the course of the study.
- Known sensitivity to planned study concomitant medications.
- Participating in any other ophthalmic drug or device clinical trial during the time of this clinical investigation.
- Peripheral pachymetry reading of less than 560 microns.
- Distance UCVA better than 20/32.

2. Study Endpoints

The following primary study parameters were evaluated in the determination of safety and effectiveness of the Refractec ViewPointTM CK System.

Primary Safety Parameter:

- Preservation of best corrected visual acuity: less than 5% of eyes should lose more than two lines of best corrected visual acuity at the postoperative interval at which stability has been established.

Primary Effectiveness Parameter:

- Predictability: 75% of eyes should have a manifest refraction spherical equivalent within ± 1.00 D of the attempted correction at the postoperative interval at which stability has been established.

The following secondary study parameters were evaluated in the determination of safety and effectiveness of the Refractec ViewPoint[™] CK System.

Secondary Safety Parameters:

- Preservation of best corrected visual acuity: less than 1% of eyes with preoperative BSCVA of 20/20 should have a visual acuity outcome worse than 20/40 BSCVA at the postoperative interval at which stability has been established.
- Mean extent of induced manifest refractive astigmatism: less than 5% of eyes should have a postoperative manifest refractive astigmatism that varies from target amount by greater than 2.00 D at the postoperative interval at which stability has been established.
- Results of slit lamp examination: less than 1% of eyes should have clinically significant haze, defined as a decrease in BSCVA of >2 lines not due to irregular astigmatism, at the postoperative interval at which stability has been established.
- Central endothelial cell loss: mean endothelial cell loss should be no more than 10% at the postoperative interval at which stability has been established.
- Cumulative incidence of adverse events. Adverse events should occur in less than 5% of eyes and any single adverse event should occur in less than 1% of eyes.

Secondary Effectiveness Parameters:

- Predictability: 50% of eyes should have a manifest refraction spherical equivalent within ± 0.50 D of attempted correction at the postoperative interval at which stability has been established.
- Stability (absence of change in refractive outcome over time): 95% of eyes should have a change of ≤ 1.00 D in manifest refraction spherical equivalent between two refractions performed at least three months apart.
- Improvement in uncorrected visual acuity: 85% of eyes who had 20/20 or better spectacle-corrected visual acuity preoperatively, and for whom the intended target correction was emmetropia should have an uncorrected visual acuity of 20/40 or better at the postoperative interval at which stability has been established. For those eyes which had spectacle-corrected visual acuity of worse than 20/20 but at least 20/40 preoperatively, and for which the intended target correction was emmetropia, 75% should have an uncorrected visual acuity of 20/40 or better at the postoperative interval at which stability has been established.
- Decrease in manifest refraction spherical equivalent and astigmatism: 75% of eyes should be within ± 1.00 D of attempted spherical and

astigmatism correction at the postoperative interval at which stability has been established.

- Subject satisfaction as measured by subjective questionnaire.

C. Study Plan and Subject Assessments

1. Study Plan

All subjects were expected to return for follow-up examinations at one day, one week, and 1, 3, 6, 9, 12, and 24 months post-treatment. After the first 50 eyes were evaluated, the option to perform simultaneous bilateral surgery was left to the discretion of the investigator. Retreatments were not attempted in this study.

2. Subject Assessments and Efficacy Criteria

- Distance visual acuity, uncorrected and best spectacle-corrected, using ETDRS charts
- Manifest refraction (no auto-refraction)
- Cycloplegic refraction
- Pachymetry
- Intraocular pressure (applanation)
- Slit lamp examination
- Fundus examination (dilated)
- Specular microscopy of the central and peripheral corneal endothelium (in a subgroup of 100 subjects)
- Mesopic Contrast Sensitivity, with and without glare (subgroup)
- Computerized corneal topography (postoperatively in eyes with anomalous refractive outcomes)
- Central keratometry
- Subject self-evaluation/questionnaire

D. Study Period and Investigational Sites

Subjects were treated between 2/10/1999 and 12/01/2000 at 12 investigational sites. The database for this PMA Cohort reflected data collected through 4/17/2001 and included 401 eyes: 233 primary eyes and 168 fellow eyes.

E. Demographic Data

Of the 233 subjects, 58% were female and 42% were male. The mean age for all enrolled subjects was 55.3 years, with a range from 40 to 73 years. The study population consisted primarily of Caucasians (81%). Mean hyperopia (CRSE) prior to surgery was 1.86 diopters.

Table 2
Demographics
All Eyes Enrolled

401 Eyes of 233 Enrolled Subjects

Gender	Male	42%
	Female	58%
Race	Caucasian	81%
	Black	9%
	Asian	2%
	Other	9%
Eye	Left	49%
	Right	51%
Age (yrs)	N	233
	Mean	55.3
	95% Confidence Interval	54.5,56.1
	Standard Deviation	6.36
	Median	55.6
	Range	40.2,73.9
Range of Treatment - CRSE	N	401
	Mean	1.86
	95% Confidence Interval	1.80,1.92
	Standard Deviation	0.628
	Median	1.75
	Range	0.75,4.00
Range of Treatment - MRSE	N	401
	Mean	1.80
	95% Confidence Interval	1.74,1.86
	Standard Deviation	0.637
	Median	1.75
	Range*	-0.38,3.75

F. Data Analysis and Results

1. Pre-Treatment Characteristics

Table 3 presents a summary of the pre-treatment visual acuity and refraction. The treatment goal for all eyes was emmetropia.

Table 3
Preoperative Refractive Parameters
Eyes Treated with Current Nomogram

		Primary Eyes		Fellow Eyes		All Eyes	
Spherical Equivalent (MRSE) *	0.0-0.99 D	11	6%	11	7%	22	6%
	1.0-1.99 D	121	61%	84	52%	205	57%
	2.0-2.99 D	62	31%	63	39%	125	35%
	3.0-4.00 D	5	3%	4	2%	9	2%
	Total	199	100%	162	100%	361	100%
Cylinder (manifest) **	0.00 D	69	35%	57	35%	126	35%
	0.25 D	41	21%	38	23%	79	22%
	0.50 D	59	30%	49	30%	108	30%
	0.75 D	28	14%	18	11%	46	13%
	1.00 D	3	2%	1	1%	4	1%
	1.25 D	0	0%	0	0%	0	0%
	Total	200	100%	163	100%	363	100%
Spherical Equivalent (CRSE) **	0.0-0.99 D	8	4%	9	6%	17	5%
	1.0-1.99 D	117	59%	85	52%	202	56%
	2.0-2.99 D	65	33%	60	37%	125	34%
	3.0-4.00 D	10	5%	9	6%	19	5%
	Total	200	100%	163	100%	363	100%
Cylinder (cycloplegic) **	0.00 D	69	35%	67	41%	136	37%
	0.25 D	29	15%	36	22%	65	18%
	0.50 D	75	38%	39	24%	114	31%
	0.75 D	26	13%	21	13%	47	13%
	1.00 D	1	1%	0	0%	1	<1%
	1.25 D	0	0%	0	0%	0	0%
	Total	200	100%	163	100%	363	100%

* Excludes two ineligible eyes with minus MRSE; these eyes are included in the cylinder analysis.

** Includes one ineligible eye with >0.75 D cycloplegic cylinder.

2. Subject Accountability

Of the 401 eyes enrolled in the study, follow-up data through 6 months postoperative are available for 387 eyes (97%). Of the remaining eyes, one (<1%) was discontinued from the study; 11 (3%) missed the visit; and 2 (<1%) were not yet eligible for the visit.

Table 4
Accountability
Eyes Treated with Current Nomogram

	Month 1		Month 3		Month 6		Month 9		Month 12	
Available for Analysis	354/363	98%	358/363	99%	350/363	96%	340/363	94%	171/363	47%
Discontinued	1/363	<1%	1/363	<1%	1/363	<1%	1/363	<1%	1/363	<1%
Missed Visit	8/363	2%	4/363	1%	10/363	3%	8/363	2%	0/363	0%
Not yet eligible for interval	0/363	0%	0/363	0%	2/363	1%	12/363	3%	187/363	52%
Lost to Follow-up	0/363	0%	0/363	0%	0/363	0%	2/363	1%	4/363	1%
Accountability	354/363	98%	358/363	99%	350/361	97%	340/351	97%	171/176	97%

3. Summary of Key Effectiveness Variables

Table 5 demonstrates that the key effectiveness outcomes at 6 months postoperative meet or exceed the outcomes recommended in the October 10, 1996 *FDA Guidance for Refractive Surgery Lasers*.

Table 5
Summary of Key Efficacy Variables
Eyes Treated with Current Nomogram

	Month 1	Month 3*	Month 6	Month 9	Month 12
Efficacy Variables					
UCVA 20/20 or better	29%	40%	46%	50%	51%
UCVA 20/25 or better	51%	63%	65%	74%	73%
UCVA 20/40 or better	79%	86%	90%	93%	91%
MRSE 0.50 D	47%	56%	61%	64%	58%
MRSE 1.00 D	75%	83%	88%	87%	91%
MRSE 2.00 D	94%	97%	99%	99%	99%

* Two eyes were excluded from the 3 Month MRSE efficacy variables due to manifest refraction and BSCVA not performed.

Table 6
Summary of Key Efficacy Variables at 9 Months
Preoperative MRSE Stratified by Dioptric Group
Eyes Treated with Current Nomogram

	0.00 to 0.99 D	1.00 to 1.99 D	2.00 to 3.25 D
Efficacy Variables			
UCVA 20/20 or better	52%	54%	43%
UCVA 20/25 or better	76%	74%	72%
UCVA 20/40 or better	90%	92%	94%
MRSE 0.50 D	81%	65%	60%
MRSE 1.00 D	100%	90%	80%
MRSE 2.00 D	100%	99%	98%

Table 7
Summary of Key Efficacy Variables at 9 Months
Stratified by Treatment Spots Applied
Eyes Treated with Current Nomogram

	8 Spots*	16 Spots*	24 Spots*	32 Spots*
Efficacy Variables				
UCVA 20/20 or better	50%	58%	44%	45%
UCVA 20/25 or better	79%	79%	67%	73%
UCVA 20/40 or better	93%	95%	90%	93%
MRSE 0.50 D	93%	70%	57%	59%
MRSE 1.00 D	100%	93%	87%	73%
MRSE 2.00 D	100%	99%	98%	99%

* 8 spots = CRSE 0.75 to 0.875 D

16 spots = CRSE 1.00 to 1.625 D

24 spots = CRSE 1.75 to 2.25 D

32 spots = CRSE 2.375 to 3.00 D

a. Factors Associated with Outcomes

Statistical modeling performed on the data generated in the CK clinical study found no effect of age, race, sex or clinical site on outcomes.

b. Subject Satisfaction

Subjects were asked to rate their quality of vision compared to before the Conductive Keratoplasty (CK) procedure. Table 8 shows the percentage of subjects that rated each condition as improvement that was “extreme,” “marked,” “moderate,” “slight,” or “no improvement”.

**Table 8
Quality of Vision**

	Month 1		Month 3		Month 6		Month 9		Month 12	
Extreme Improvement	83/353	24%	87/361	24%	108/368	29%	111/357	31%	45/198	23%
Marked Improvement	149/353	42%	159/361	44%	163/368	44%	141/357	39%	97/198	49%
Moderate Improvement	68/353	19%	78/361	22%	57/368	15%	66/357	18%	33/198	17%
Slight Improvement	37/353	10%	22/361	6%	28/368	8%	28/357	8%	13/198	7%
No Improvement	16/353	5%	15/361	4%	12/368	3%	11/357	3%	10/198	5%

Overall subject satisfaction was assessed on a subject survey at 1, 3, 6, 9, and 12 months post-treatment using a 5-point grading scale from “very satisfied” to “very dissatisfied”.

**Table 9
Subject Satisfaction**

	Month 1		Month 3		Month 6		Month 9		Month 12	
Very Satisfied	161/356	45%	168/362	46%	170/369	46%	176/357	49%	92/198	46%
Satisfied	112/356	31%	118/362	33%	134/369	36%	107/357	30%	62/198	31%
Neutral	57/356	16%	55/362	15%	34/369	9%	42/357	12%	22/198	11%
Dissatisfied	16/356	4%	12/362	3%	20/369	5%	21/357	6%	15/198	8%
Very Dissatisfied	10/356	3%	9/362	2%	11/369	3%	11/357	3%	7/198	4%

4. Summary of Key Safety Variables

The following table demonstrates that the key safety outcomes meet or exceed the outcomes recommended in the October 10, 1996 *FDA Guidance for Refractive Surgery Lasers*.

Table 10
Summary of Key Safety Variables
All Eyes Treated

	Month 1	Month 3	Month 6	Month 9	Month 12
Safety Variables*					
Loss of 2 lines BSCVA	6%	5%	4%	3%	<1%
Loss of > 2 lines BSCVA	2%	1%	1%	1%	0%
BSCVA worse than 20/40	0%	0%	0%	0%	0%
Increase > 2.00 D cylinder	3%	2%	1%	<1%	<1%
BSCVA worse than 20/25 if 20/20 or better preoperatively	4%	2%	1%	1%	0%

* Two eyes were excluded from all safety variables due to manifest refraction and BSCVA not performed.

Table 11
Summary of Key Safety Variables at 9 Months
Preoperative MRSE Stratified by Dioptric Group
All Eyes Treated

	0.00 to 0.99 D	1.00 to 1.99 D	2.00 to 3.25 D*
Safety Variables			
Loss of 2 lines BSCVA	0%	4%	1%
Loss of > 2 lines BSCVA	0%	<1%	1%
BSCVA worse than 20/40	0%	0%	0%
Increase > 2.00 D cylinder	0%	0%	1%
BSCVA worse than 20/25 if 20/20 or better preoperatively	0%	1%	0%

* Safety variables shown for all treated eyes; includes 2 eyes with preoperative MRSE > 3.25. Neither of these eyes lost 2 lines BSCVA, had BSCVA worse than 20/40, or increased > 2.00 D cylinder.

Table 12
Summary of Key Safety Variables at 9 Months
Stratified by Treatment Spots Applied
All Eyes Treated

Safety Variables	8 Spots*	16 Spots*	24 Spots*	32 Spots*
Loss of 2 lines BSCVA	0%	4%	3%	1%
Loss of > 2 lines BSCVA	0%	0%	1%	0%
BSCVA worse than 20/40	0%	0%	0%	0%
Increase > 2.00 D cylinder	0%	0%	0%	1%
BSCVA worse than 20/25 if 20/20 or better preoperatively	0%	1%	1%	0%

* 8 spots = CRSE 0.75 to 0.875 D
 16 spots = CRSE 1.00 to 1.625 D
 24 spots = CRSE 1.75 to 2.25 D
 32 spots = CRSE 2.375 to 3.00 D

Table 13 presents a summary of the complications reported in the clinical study.

Table 13
Complication Summary
All Eyes Treated

	Month 1	Month 3	Month 6	Month 9	Month 12
Recurrent corneal erosion at one month or later	0%	1%	0%	0%	0%
Double/ghost images in the operative eye	1%	1%	2%	1%	<1%
Foreign body sensation at one month or later	0%	0%	0%	<1%	0%
Pain at one month or later	0%	1%	0%	0%	0%
Other	2%	3%	2%	1%	1%

The following complications were not reported in the clinical study, but could potentially occur following CK procedure: peripheral corneal epithelial defect; corneal edema.

Table 14 below shows the absolute change in refractive cylinder for all eyes treated.

Table 14
Absolute Change in Refractive Cylinder
All Eyes Treated

Astigmatism	Month 1	Month 3	Month 6	Month 9	Month 12
Increase >2.00 D	3%	2%	1%	<1%	<1%
Increase 2.00 D	3%	1%	1%	1%	<1%
Increase 1.75 D	3%	2%	2%	1%	<1%
Increase 1.50 D	4%	4%	2%	1%	2%
Increase 1.25 D	8%	6%	7%	4%	2%
Increase 1.00 D	13%	11%	10%	7%	6%
No Change (± 0.75 D)	66%	73%	75%	86%	87%
Decrease 1.00 D	1%	<1%	<1%	0%	<1%
Decrease >1.00 D	0%	0%	0%	0%	0%
Not Recorded	0%	1%	0%	0%	0%
Total	100%	99%	100%	100%	100%

Subjects were asked to complete a questionnaire that allowed them to report any symptoms or complaints they had regarding their vision or ocular comfort following the surgery. Results for the subjective responses to these questionnaires at 6, 9, and 12 months post treatment are provided in Table 15.

Table 15
Subject Symptoms
All Eyes Treated

	None	Mild	Moderate	Marked	Very Severe
Light Sensitivity					
Preop	69%	17%	9%	4%	1%
Month 6	52%	33%	11%	3%	1%
Month 9	57%	27%	12%	3%	1%
Month 12	60%	28%	11%	1%	1%
Headache					
Preop	84%	12%	2%	1%	1%
Month 6	84%	10%	4%	1%	1%
Month 9	84%	9%	4%	1%	2%
Month 12	88%	7%	3%	2%	1%
Pain					
Preop	95%	4%	1%	0%	0%
Month 6	91%	7%	1%	1%	1%
Month 9	92%	5%	1%	0%	1%
Month 12	98%	1%	0%	1%	1%
Redness					
Preop	83%	13%	3%	<1%	1%
Month 6	82%	13%	4%	1%	1%
Month 9	77%	15%	6%	2%	1%
Month 12	85%	12%	2%	1%	0%
Dryness					
Preop	77%	15%	8%	1%	0%
Month 6	58%	28%	7%	6%	1%
Month 9	60%	26%	8%	5%	1%
Month 12	68%	25%	6%	2%	0%
Excessive Tearing					
Preop	87%	6%	4%	2%	1%
Month 6	85%	9%	3%	2%	1%
Month 9	83%	11%	3%	1%	2%
Month 12	90%	5%	3%	2%	0%
Burning					
Preop	88%	9%	2%	1%	<1%
Month 6	83%	12%	2%	2%	<1%
Month 9	82%	11%	5%	2%	<1%
Month 12	90%	9%	1%	0%	0%
Gritty, Scratchy, or Sandy Feeling					
Preop	83%	14%	2%	0%	0%
Month 6	79%	13%	4%	3%	0%
Month 9	81%	14%	3%	1%	1%
Month 12	87%	11%	2%	0%	0%

Table 15
Subject Symptoms
All Eyes Treated
(Continued)

	None	Mild	Moderate	Marked	Very Severe
Glare					
Preop	74%	18%	6%	1%	1%
Month 6	55%	28%	11%	5%	1%
Month 9	58%	28%	8%	4%	2%
Month 12	62%	26%	11%	2%	0%
Halos					
Preop	90%	7%	2%	2%	<1%
Month 6	63%	22%	8%	5%	2%
Month 9	65%	21%	9%	2%	2%
Month 12	65%	21%	9%	4%	1%
Blurred Vision					
Preop	67%	13%	11%	7%	2%
Month 6	51%	28%	12%	6%	3%
Month 9	58%	23%	12%	5%	2%
Month 12	66%	20%	9%	6%	0%
Double Vision					
Preop	90%	5%	5%	1%	0%
Month 6	66%	17%	8%	6%	3%
Month 9	74%	13%	7%	5%	1%
Month 12	76%	14%	6%	3%	1%
Fluctuation of Vision					
Preop	84%	12%	3%	1%	0%
Month 6	54%	29%	8%	7%	1%
Month 9	60%	25%	7%	5%	3%
Month 12	60%	29%	8%	3%	1%
Variation in Vision in Bright Light					
Preop	74%	16%	8%	2%	<1%
Month 6	55%	30%	10%	3%	1%
Month 9	63%	24%	8%	5%	1%
Month 12	60%	27%	9%	4%	0%
Variation in Vision in Normal Light					
Preop	85%	11%	4%	<1%	<1%
Month 6	70%	19%	9%	1%	1%
Month 9	71%	17%	8%	3%	1%
Month 12	71%	21%	6%	2%	0%
Variation in Vision in Dim Light					
Preop	75%	14%	8%	1%	1%
Month 6	54%	26%	13%	5%	1%
Month 9	60%	19%	12%	5%	3%
Month 12	56%	26%	11%	5%	2%

Table 15
Subject Symptoms
All Eyes Treated
(Continued)

	None	Mild	Moderate	Marked	Very Severe
Night Driving Vision Problems					
Preop	64%	19%	12%	2%	2%
Month 6	54%	24%	12%	6%	4%
Month 9	59%	23%	8%	6%	4%
Month 12	58%	25%	8%	6%	3%
Other Symptom					
Preop	96%	1%	2%	1%	0%
Month 6	96%	2%	1%	<1%	1%
Month 9	97%	2%	1%	0%	<1%
Month 12	93%	3%	3%	1%	1%

11. CONCLUSIONS DRAWN FROM THE STUDIES

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.

12. PANEL RECOMMENDATION

13. CDRH DECISION

14. APPROVAL SPECIFICATIONS

See device labeling.

15. REFERENCES

1. Ariyasu R, Sand B, Menefee R, Hennings D, Rose C, Berry M, Garbus J, McDonnell P. Holmium laser thermal keratoplasty of 10 poorly sighted eyes. *Journal of Refractive Surgery* 1995;11:358-365.
2. Caster A. The Fyodorov technique of hyperopia correction by thermal coagulation: a preliminary report. *Journal of Refractive Surgery* 1988;4:105-108.
3. Charpentier D, Nguyen-Khoa J, Duplessix M, Colin J, Denis P. Intrastromal thermokeratoplasty for correction of spherical hyperopia: a 1-year prospective study. *Journal of French Ophthalmology* 1995;18:200-206.
4. Feldman S, Ellis W, Frucht-Pery J, Chayet A, Brown S. Regression of effect following radial thermokeratoplasty in humans. *Journal of Refractive and Corneal Surgery* 1989;5:288-291.
5. Koch D, Kohnen T, McDonnell P, Menefee R, Berry M. Hyperopia correction by noncontact holmium:YAG laser thermal keratoplasty. *Ophthalmology* 1997;104:1938-1947.
6. Lans LJ. Experimentelle Untersuchungen über Entstehung von Astigmatismus durch nicht-perforierende Corneawunden. *Graefes Arch Ophthalmol* 1889;44-117-152.
7. Mendez A, Mendez Noble A. Conductive keratoplasty for the correction of hyperopia. In: Neal A. Sher, M.D., F.A.C.S. *Surgery for Hyperopia and Presbyopia*. Williams and Wilkins 1997;163-171.
8. Neumann A, Fyodorov S, Sanders D. Radial thermokeratoplasty for the correction of hyperopia. *Journal of Refractive and Corneal Surgery* 1990;6:404-412.
9. Neumann A, Sanders D, Raanan M, DeLuca M. Hyperopic thermokeratoplasty: clinical evaluation. *Journal of Cataract and Refractive Surgery* 1991;17:830-838.
10. Neumann A, Sanders D, Salz J. Radial thermokeratoplasty for hyperopia. *Journal of Refractive and Corneal Surgery* 1989;5:50-54.
11. Parel J, Ren Q, Simon G. Noncontact laser photothermal keratoplasty I: Biophysical principles and laser beam delivery system. *Journal of Refractive and Corneal Surgery* 1994;10:511-518.

12. Ren Q, Simon G, Parel J. Noncontact laser photothermal keratoplasty III: Histological study in animal eyes. *Journal of Refractive and Corneal Surgery* 1994;10:529-539.
13. Simon G, Ren Q, Parel J. Noncontact laser photothermal keratoplasty II: Refractive effects and treatment parameters in cadaver eyes. *Journal of Refractive and Corneal Surgery* 1994;10:519-528.
14. Stringer H, Parr J. Shrinkage temperature of eye collagen. *Nature* 1964;204:1307.
15. Walline J, Kinney K, Zadnik K, Mutti D. Repeatability and validity of astigmatic measurements. *Journal of Refractive Surgery* 1999;15:23-31.
16. Zadnik K, Mutti D, Adams A. The repeatability of measurement of the ocular components. *Investigative Ophthalmology & Visual Science* 1992;33:2325-2333.