DMC

P910067

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date MAR 10 1995

From Director, Office of Device Evaluation (HFZ-400)
Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of Summit Technology, Inc.
ExciMed® UV200LA Excimer Laser System
SVS Apex Excimer Laser System (formerly the OmniMed Excimer Laser System)

To The Director, CDRH
Through: ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

(1) a premarket approval order for the above referenced medical device (Tab B); and

(2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

Susan Alpert, Ph.D., M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved ___ Disapproved ___ Date _____

Prepared by Emma Knight, M.D. and Quynh Hoang, CDRH, HFZ-460, 3/10/95, 594-2018.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
[DOCKET NO. _____]
SUMMIT TECHNOLOGY, INC.; PREMARKET APPROVAL OF EXCIMED® UV200LA AND SVS APEX (FORMERLY THE OMNIMED) EXCIMER LASER SYSTEMS

AGENCY: Food and Drug Administration, HHS.
ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by Summit Technology, Inc., Waltham, MA, for premarket approval, under section 515 of the Federal Food, Drug, and Cosmetic Act (the act), of the Excimed® UV200LA and SVS Apex (formerly the OmniMed) Excimer Laser Systems. After addressing the concerns of the Ophthalmic Devices Panel, FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter on MAR 10 1995 of the approval of the application.

DATE: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER); Written comments by (insert date 30 days after date of publication in the FEDERAL REGISTER).

ADDRESS: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review, to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 1-23, 12420 Parklawn Drive, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Debra Y. Lewis, O.D.
Center for Devices and Radiological Health (HFZ-460)
Food and Drug Administration
9200 Corporate Blvd.
Rockville, MD 20850
301-594-2018.

SUPPLEMENTARY INFORMATION: On February 20, 1992, Summit Technology, Inc., Waltham, MA 02154, submitted to CDRH an application for premarket approval of the Excimed® UV200LA and the SVS Apex (formerly the OmniMed) Excimer Laser Systems. The excimer laser in the two Systems delivers pulses at 193 nm wavelength. The excimer laser is indicated for use in the following Phototherapeutic Keratectomy (PTK) procedures which treat superficial pathology located in the anterior 100 microns of the cornea, where the proposed treatment area is at least 400 microns in thickness, and where other less invasive treatments have

failed or are not possible, such as contact lens intolerance. This indication is limited to patients with decreased visual acuity or symptoms of pain and discomfort of sufficient severity to cause disability for the patients with any of the following conditions:

1. superficial corneal dystrophies (granular, lattice, and Reis-Buckler's);

2. epithelial basement membrane dystrophy;

3. irregular corneal surfaces (secondary to Salzmann's degeneration, keratoconus nodules and other irregular surfaces); and,

4. corneal scars and opacities (post-traumatic, post-surgical, post-infectious and secondary to pathology).

On March 21, 1994, the Ophthalmic Devices Panel, an FDA advisory panel, reviewed and recommended conditional approval, of the application. The concerns of the panel have been adequately addressed by Summit Technology, Inc. in subsequent submissions to FDA.

On MAR 10 1995, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

OPPORTUNITY FOR ADMINISTRATIVE REVIEW

Section 515(d)(3) of the act (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act (21 U.S.C. 360e(g)), for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under part 12 (21 CFR part 12) of FDA's administrative practices and regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 10.33(b) (21 CFR 10.33(b)). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. This notice is issued under the Federal Food, Drug, and Cosmetic Act section 520(h), 90 Stat. 554-555, 571 (21 U.S.C. 360e(d), 360j(h)) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated:_____.

_____

D. Bruce Burlington, M.D.
Director
Center for Devices and
Radiological Health

CERTIFIED TO BE A TRUE COPY OF THE ORIGINAL

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

MAR 10 1995

Ms. Kimberley Doney
c/o Ms. Maureen O'Connell
Regulatory & Clinical Affairs
Summit Technology, Inc.
21 Hickory Drive
Waltham, MA 02154

RE: P910067
Excimed® UV200LA Excimer Laser System
SVS Apex Excimer Laser System (formerly the OmniMed Excimer Laser System)

Filed: February 20, 1992
Amended: March 23, April 24, May 20, and October 29, 1992; December 17 and 23, 1993; January 21 and 31, February 25, March 31, April 1, July 20, December 20 and 21, 1994; January 13, 17, 24, 27, and 30, February 1, and March 9, 1995

Dear Ms. Doney:

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 the Excimed® UV200LA and the SVS Apex (formerly the OmniMed) Excimer Laser Systems. The excimer laser in the two Systems is indicated for use in the following Phototherapeutic Keratectomy (PTK) procedures which treat superficial pathology located in the anterior 100 microns of the cornea, where the proposed treatment area is at least 400 microns in thickness, and where other less invasive treatments have failed or are not possible, such as contact lens intolerance. This indication is limited to patients with decreased visual acuity or symptoms of pain and discomfort of sufficient severity to cause disability for the patients with any of the following conditions:

1. superficial corneal dystrophies (granular, lattice, and Reis-Buckler's);

2. epithelial basement membrane dystrophy;

3. irregular corneal surfaces (secondary to Salzmann's degeneration, keratoconus nodules and other irregular surfaces); and,

4. corneal scars and opacities (post-traumatic, post-surgical, post-infectious and secondary to pathology).

The sale, distribution, and use of this device 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. FDA has also determined that to ensure the safe and effective use of the device 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 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, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the postapproval requirements in the enclosure, Summit must also report the following to the Agency if the information becomes available to Summit:

1. any instances of device tampering (such as the removal of the PRK lockout mechanisms) or device usage outside of the approved indications;

2. any excimer systems that were exported under the 801(e) order, but are now back in use in the U.S.; and,

3. all complications as part of your annual reporting.

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, 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).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that as soon as possible, and before commercial distribution of your device, that you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

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

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If you have any questions concerning this approval order, please contact Quynh Hoang 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

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 acknowledgement by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This acknowledgement 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 mixup 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.

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REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise became aware of information that reasonably suggests that one of its marketed devices

(1) may have caused or contributed to a death or serious injury or

(2) has malfunctioned and that the device or any other 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 this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Division of Surveillance Systems (HFZ-544)
Center for Devices and Radiological Health
Food and Drug Administration
1350 Piccard Drive, Room 3083
Rockville, Maryland 20850
Telephone (301) 594-2735

Events included in periodic reports to the PMA that have also been reported under the MDR Regulation must be so identified in the periodic report to the PMA to prevent duplicative entry into FDA information systems.

Copies of the MDR Regulation and an FDA publication entitled, "An Overview of the Medical Device Reporting Regulation," are available by written request to the above address or by telephoning (301) 594-2735.

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

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

Device Trade Name: ExciMed® UV200LA Excimer Laser System
SVS Apex Excimer Laser System (formerly the OmniMed Excimer Laser System)

Applicant's Name and Address: Summit Technology, Inc.
21 Hickory Drive
Waltham, MA 02154 USA
(617) 890-1234

Date of Panel Recommendation: Conditional Approval on March 21, 1994

Premarket Approval Application (PMA) Number: P910067

Date of Notice of Approval to Applicant: March 10, 1995

II. INDICATIONS FOR USE

The ExciMed^{R} UV200LA or SVS Apex (formerly the OmniMed) Excimer Laser System (hereinafter called the Excimer Laser System) is indicated for use in Phototherapeutic Keratectomy (PTK) procedures which treat superficial pathology located in the 100 microns of the cornea, where the proposed treatment area is at least 400 microns in thickness, and where other less invasive treatments have failed or are not possible, such as contact lens intolerance. This indication is limited to patients with decreased visual acuity or symptoms of pain and discomfort of sufficient severity to cause disability for the patients with any of the following conditions:

1. superficial corneal dystrophies (granular, lattice, and Reis-Buckler's);
2. epithelial basement membrane dystrophy;
3. irregular corneal surfaces (secondary to Salzmann's degeneration, keratoconus nodules and other irregular surfaces); and,
4. corneal scars and opacities (post-traumatic, post-surgical, post-infectious and secondary to pathology).

III. CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS

A. Contraindications

The Excimer Laser System when used for the PTK procedure is contraindicated in patients:

1. with uncontrolled vascular disease or autoimmune disease which is known to affect corneal healing or cause corneal melting.

2. who are immunocompromised or on drugs or therapy which suppress the immune system.

B. Warnings

Reactivation of herpes simplex virus has occurred after the Phototherapeutic Keratectomy procedure and is therefore **not** recommended in patients with a history of this ocular infection. However, if a patient's only alternative therapy is a penetrating keratoplasty and the patient is informed regarding the possibility of reactivation of the virus after the PTK procedure, PTK may be considered in these patients.

C. Precautions

1. The safety and effectiveness of the Excimer Laser System has not been established in:

   a. The treatment of superficial corneal erosion syndrome;

   b. Patients under 21 years of age;

   c. Pregnant women;

   d. Patients whose pathologic condition would require the area of ablation to be deeper than 100 microns;

   e. Patients whose proposed treatment area of the cornea is less than 400 microns thick.

2. Consideration should be given to the following in determining the appropriate patient for Phototherapeutic Keratectomy procedures:

   a. The potential induced refractive error would include significant, uncorrectable anisometropia and/or induced astigmatism; or

   b. The patient is unable to cooperate during the procedure because of the potential difficulty aligning the laser beam and keeping the eye steady during the procedure.

3. During the Phototherapeutic Keratectomy procedure:

   a. Do not use alcohol, cocaine or any other substances to remove the epithelium. Application of these substances may influence the ablation rate of the excimer laser energy and could lead to poor procedural result.

   b. The HeNe aiming beams mark the image plane of the excimer beam. The desired vertical area of effect is located where the two HeNe beams appear as one spot. In order to assure that the patient is not exposed to hazardous levels of laser energy, the HeNe beams should not be fired at the patient continuously for longer than 390 seconds.

   c. Do not lean on the surgical microscope or the Excimer Laser System during laser energy delivery.

IV. DEVICE DESCRIPTION

The Excimer Laser System is a self-contained ophthalmic laser workstation. The ExciMed UV200LA Excimer System contains only an excimer laser, while the SVS Apex (formerly the OmniMed) Excimer System may share its chassis with a holmium laser. The excimer laser is the subject of this PMA; hence, it will be described in detail as follows.

A. The excimer laser

There are three models of excimer lasers: The model names are ExciMed UV200LA, SVS Apex/OmniMed (configuration 1) and SVS Apex/OmniMed (configuration 2). The excimer lasers in the ExciMed® UV200LA and the SVS Apex/OmniMed (configuration 1) are identical. The SVS Apex/OmniMed (configuration 2) has a different laser head and iris diaphragm from the other two, so that its maximum ablation zone can be 6.5 mm (instead of 5 mm) while its fluence remains the same as the other two.

The excimer laser system operates based on the principle that radiation at 193 nm wavelength is highly absorbed by the cornea (Srinivasan et al[1]). The delivered 193 nm radiation or photon energy disrupts the intramolecular collagen bonds of the corneal tissue vaporizing the irradiated area (Aron Rosa et al[2]). Furthermore, the disruption is so precise that 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 laser beam (Marshall et al[3] and Trokel et al[4]). Another advantage of this wavelength is that there is minimal damage to the surrounding tissue (Marshall et al[3], Trokel et al[4], Courant et al[5], and Puliafito et al[6]).

The delivery of the laser beam to the eye involves 13 primary subsystems, as described below:

1. Excimer laser subsystem:

Laser wavelength:	193 nanometers
Laser pulse duration:	14 nanoseconds
Repetition rate:	10 Hertz
Fluence (at the eye):	180 mJ/cm2
Ablation zone diameter:	0.5 mm to 5.0/6.5 mm in 0.1 mm increments
Laser head output:	< 400 mJ*
Composition of gases:	< 1.0% Fluorine < 10.0% Argon < 60.0% Neon Balance Helium

*Maximum energy assumes a 17% end of life efficiency delivery system and a 6.5 mm ablation diameter.

2. Excimer beam delivery subsystem

The raw laser beam produced by the excimer laser is shaped by the Excimer Beam Delivery Subsystem into a uniform intensity circular shaped beam of 0.5 to 5.0/6.5 mm in diameter. This transformation is accomplished by an array of mirrors and lenses. The approximately square beam exiting the excimer laser head is used to illuminate the iris, which is a set of metal leaves like a camera iris arranged to form a circular aperture.

3. Patient fixation subsystem

The Patient Fixation Subsystem is designed to assist the physician in: (1) properly positioning the patient's eye in the appropriate vertical plane for laser energy delivery, and (2) providing a target for the patient to fixate on during the PTK. To position the patient's eye at exactly 180 mm from the laser, a class I aiming Helium-Neon (HeNe) laser is used. The fixation target consists of a single green light surrounded by 6 red LED's positioned in an outer ring.

4. Microscope subsystem

The laser system comes equipped with a coaxial Zeiss Operating Microscope. The excimer laser procedure may be viewed safely through the microscope because the glass used to form the image in the microscope is opaque to the 193 nanometer laser wavelength.

5. Interlock and safety subsystem

There are ten electromechanical interlocks on the Excimer Laser System to prevent unintentional exposure to excimer radiation and high voltage: 2 on the Secondary Containment Device (SCD), 2 on the rear holmium laser optics cover, 1 on the rear cover, 2 on the optical rail, and 2 on the holmium laser fiber optic. The tenth interlock, a remote (external) interlock, can be used at the physician's discretion.

6. SCD subsystem

The Secondary Containment Device (SCD) is a complete, welded, steel enclosure (0.25" thick) which has a 5 sided front section and a back door (0.25" thick) that is attached to the front section by a vertical hinge on one side. The SCD is patented by Summit. It houses the entire Excimer Laser Subsystem which includes all high voltage components in the excimer laser and all pressurized gases (except for the external N_2 purge gas cylinder).

7. EMI shield subsystem

This subsystem consists of a set of sheet metal covers to block radiated EM fields from getting out of the laser system. The excimer laser system has been tested for radiated and conducted EMI, and found to meet the Radiated and Conducted Emission Standards for medical devices.

8. Power distribution subsystem

The electrical requirements from the wall plug are 110 V +/- 10%, 60 Hz and 15 Amps.

9. Control subsystem

The Control Subsystem monitors all subsystems. The Control Subsystem has a user interface at the Keypad or Control Pad for entry of the number of laser pulses and outer beam diameters to be used for a PTK procedure. All buttons are labeled and the software prompts the user through each step of a PTK procedure.

10. Gas handling subsystem

There are two components in the Gas Handling System:

a. External gas component

Dry N_2 is used in conjunction with the laser system to protect the excimer laser optics from damage due to the formation of trace O_3 from the energetic 193 nm photons, and to reduce the attenuation throughout the beam path due to exposure to air. The regulated N_2 gas cylinder is external to the laser system and is supplied by the user in accordance with the specifications outlined in the User's Manual. The N_2 is not for blowing over the patient's cornea during laser energy delivery.

b. Internal gas component

The excimer laser gas system includes a cylinder of compressed gas which is pre-mixed to a precise balance of Argon, Fluorine, Helium and Neon to achieve the correct lasing conditions in the laser cavity in order to produce the 193 nanometer laser wavelength. All these pressurized components are contained within the SCD as a general safety precaution.

11. Cooling (temperature controlling) subsystem

The Cooling Subsystem is a self contained unit and the laser system requires no external cooling.

12. Patient chair and physician stool

The patient chair allows for both coarse and fine position control in three axes. The headrest is capable of very fine vertical control movements. The physician stool was selected based on the height of the microscope system for physician comfort during the ophthalmic laser procedures.

13. System software

The system software controls the laser operation and provides an interface to the user. The major subsystems controlled or monitored by software are the Gas Handling Subsystem, the Laser Subsystems, the Beam Delivery Subsystems, the Cooling (Temperature Controlling) Subsystem, the Safety and Interlock Subsystem, and the User Interface or Control Panel (Key Pad).

B. Regulation

The excimer laser system is a Class IV laser system and conforms to the regulation outlined in Title 21 CFR Chapter 1 Subchapter J CFR 1040.10 and 1040.11 for Class IV Laser Products. Retlif Testing Laboratories tested the excimer laser system and found it be in compliance with the *1046/1984 General Permit, Limit Class B and VDE 0871/6.78 Limit Class B standards for radiated and conducted electromagnetic emissions. Technischer Überwachungs Verein (TÜV) Rheinland of Germany issued a Geprüfte Sicherheit (GS) Mark for the OmniMed Laser System in 1993 confirming that this laser design complies with:

*IEC 601-1/1	Edition 1977
*IEC 601-1/2	Edition 1988
*IEC 601-Z-22	Edition 1991
*IEC 825	Edition 1984

*IEC 825 amendments to IEC 825 (1984) August 10, 1987

V. ALTERNATIVE PRACTICES OR PROCEDURES

Conventional procedures used in the treatment or mitigation of the signs and symptoms of Superficial Corneal Dystrophies; Epithelial Basement Membrane Dystrophy; Irregular corneal surfaces; and Corneal Scars and Opacities include penetrating keratoplasty, lamellar keratoplasty, stromal micropuncture, superficial keratectomy, chemical chelation, contact lens therapy, patching and medical therapy. Of the 398 eyes treated in this study, 149 (37.4%) were candidates for the most invasive alternative of penetrating keratoplasty.

VI. MARKETING HISTORY

Summit has over 250 laser systems located in approximately 40 countries. The Excimer Laser System has not been withdrawn from any country or market for reasons of safety or effectiveness.

VII. ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Adverse reactions/complications associated with the PTK clinical procedures include corneal scarring, glare, decrease of best corrected visual acuity, induced astigmatism, foreign body sensations, patient discomfort, corneal epithelial defect, corneal infection/ulceration, and persistent corneal edema, bacterial keratitis (attributed to contact lens wear), cataract, delayed re-epithelialization, epiphoria, graft rejection episodes (reversed with steroids), recurrence of herpes simplex virus, hyphema, iritis, keratitis attributed to antibiotics, neovascularization and recurrence of pterygium. Adverse events were analyzed for the 3, 6, 12, and 12 or longer examination postoperative examinations (also noted as 12 month aggregate; see Clinical Studies, Section D Study Plan, Patient Assessments, and Efficacy criteria section for further explanation). A discussion of these adverse events is found in the clinical summary section of this document.

VIII. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

1. Performance evaluation of the iris

Testing was performed to evaluate the performance characteristics of the Excimer Laser Iris System. An optical comparator and a digital micrometer were used to measure the aperture size in 2 orthogonal axes for all conceivable outer beam diameter or outer diameter selections. Measurements were collected starting at the smallest outer beam diameter and moving to the largest possible outer beam diameter at the intervals allowable by the excimer laser system. The difference between the predicted outer beam diameter and the actual outer beam diameter measured was quantified at the image plane on the eye.

Conclusions:

The outer beam diameter selected across the range of possible outer beam diameter selections closely matched the actual outer beam diameters measured by the optical comparator and digital micrometer.

2. Pulse width and stability

Testing was performed to measure the pulse width and pulse to pulse stability of the excimer laser. A storage oscilloscope connected with a photodiode was used to collect a series of laser pulses delivered from the laser system.

Conclusions:

The photograph of one laser pulse was examined and the full width half maximum measured to be 7 nanoseconds. The pulse width and pulse to pulse stability are well within the accepted tolerances for medical laser systems.

3. Beam divergence measurements

Testing was conducted to measure the divergence of the excimer laser beam in the near and far field. These two measurements were used to calculate the beam divergence both in the horizontal and vertical directions.

Conclusions:

The beam divergence was calculated to be:

Horizontal	0.39 Milliradians
Vertical	0.42 Milliradians.

4. Effect of laser electrode voltage on beam homogeneity

Testing was performed to determine the effects of varying the electrode voltage, (kilovolts: "kv") on the homogeneity of the excimer laser beam in the image plane. The excimer laser system was set to run at an electrode potential of 27 "kv" and 250 laser pulses were delivered to a piece of polymethylmethacrylate (PMMA). This test was repeated at 32 "kv". 27 and 32 "kv" represent the range of electrode potentials normally encountered during the routine operation of the excimer laser system. Upon completion of the laser energy delivery, a light section microscope was then used to measure the ablation depth of the laser cuts in the two pieces of PMMA. Four depth measurements were made for each "kv" setting.

Conclusions:

The excimer laser system is designed to operate at electrode voltages ("kv") that will vary from approximately 27 to 32 kilovolts. This change in electrode voltage does not affect the homogeneity of the laser output as demonstrated in the similarity in the flatness of the beams and the resulting laser cuts. For both ablations at the range of the electrode voltage operating parameters, the surface quality and flatness were similar.

5. Beam homogeneity testing

The objective of the study was to measure the energy profile of the excimer laser beam output homogeneity of the excimer laser beam. A commercially available laser beam profiling system capable of analyzing the excimer laser beam exiting the excimer laser system was used to evaluate the homogeneity of the beam. The beam profiling system is capable of providing cross sectional and 3-D plots of the laser output beam.

Conclusions:

The excimer laser system delivers a homogeneous or flat beam which is the optimum beam for corneal surgical applications.

6. Power monitor assembly testing

Testing was conducted to evaluate the reliability and linearity of the power monitor calibration. An initial stability test was performed involving over 5,000 shots. After the initial stability testing, the diffuser and power monitor board were removed and the diffuser was exposed to 20,000 shots of the high reflector of a laser cavity. After 20,000 shots the diffusers were replaced in the power monitor fixture and recalibrated as necessary. Long term testing was also conducted where the testing consisted of 100,000 shots out of the high reflector in 20,000 shot intervals. After each 20,000 shot interval, the diffuser was replaced in the power monitor fixture and its calibration was recorded.

Conclusions:

The power monitor showed excellent stability after an initial break in period of approximately 20,000 shots. The normal final testing alignment procedure during the manufacturing of the laser system is comparable to the 20,000 shot break in period after which power monitor calibration remains constant within normal fluctuation.

7. Shutter life cycle testing

Testing was conducted to confirm that the two mechanical shutter mechanisms are capable of performing their required function. These shutters are controlled by the microprocessor and have a pair of photodiode/detectors that monitor the opened or closed status. The shutter units were cycled through their operating parameters to a total of 50,000 cycles.

Conclusions:

All of the shutter units tested passed the 50,000 cycle test; there were no cycle failures. The shutter mechanism is capable of performing its required functions: (1) remaining closed to prevent the emission of laser light, and (2) opening when instructed by the microprocessor.

8. Gelatin perforation data

A retrospective review of the effect of environmental factors (i.e.. humidity, temperature) on the gelatin wratten filter used in conjunction with the Excimer Laser Beam Profile Test and Alignment Procedure was conducted.

Conclusions:

The effects of temperature and humidity differences that occur with the seasonal changes did not effect the gelatin wratten filter used in conjunction with the Excimer Beam Profile and Alignment Tests.

9. Output energy over the course of a gas fill

Testing was conducted to confirm that the output energy of the excimer laser remains constant over the course of a gas fill. Testing was conducted from the start of a gas fill procedure until another gas fill was required by the system. The test was concluded when the laser would no longer come out of the test mode.

Conclusions:

The study results demonstrated that the mean pulse (delivered energy) remained constant over the course of the gas fill ranging from 8.48 to 9.34 (10.1%). The data verified that the feedback loop between the laser system's two power monitors was able to effectively control the high voltage power supply in order to compensate for the normal depletion of the gas fill and therefore keep the output energy constant.

10. Beam homogeneity over the course of a gas fill

Testing was conducted to evaluate the excimer beam homogeneity or beam profile over the course of a gas fill for the excimer laser. The beam was sampled at intervals over the life of the gas fill. At each interval, a PMMA disk was subjected to 200 pulses. When the laser would no longer come out of the test mode this signaled the need for a new gas fill and testing was concluded. The uniformity which is a measure of the ratio of the maximum and minimum ablation depths of the PMMA (uniformity = maximum ablation depth - minimum ablation depth/maximum ablation depth) was determined for the PMMA samples.

Conclusions:

Over the course of the gas fill the beam homogeneity varied in uniformity by a maximum of 2%. The study results confirm that the excimer laser system beam homogeneity remains constant over the course of a gas fill.

B. Animal/Enucleated Human Eye Studies

1. Calculation of normal bovine thickness

This study was performed to determine the natural thickness of the bovine cornea in vivo as a baseline for future in vitro studies. An ultrasonic pachymeter was used to measure the corneal thickness in a series of bovine eyes within 1 minute post mortem.

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Conclusions:

Ablation rate calculations performed using eyes in the range of 581 to 671 microns represent an acceptable model for the extrapolation of this data for future research purposes. The data collected during this testing provided the necessary information to develop an in vitro model to begin a series of bovine ocular experiments to determine the optimal parameters for excimer laser corneal applications.

2. In-vitro energy density/repetition rate studies

Testing was performed to identify the appropriate energy density range in conjunction with the usage of the excimer laser system for corneal surgical applications. Energy density is defined as: Energy Density at the Image Plane (i.e., at the eye) or the Fluence. Testing was performed on both freshly enucleated bovine eyes with intact epithelium and a second group of eyes with the epithelium removed and hydration controlled.

Conclusions:

An evaluation of the Scanning Electron Micrographs demonstrated that the 193 nanometer laser wavelength could create smooth surface cuts in corneal tissue as seen in the surface quality of the ablated tissue at a range of fluences around 180 mJ/cm^2. No discernible damage to the tissue surrounding the ablated area could be detected. A smooth surface cut was possible with the 193 nanometer wavelength even at both repetition rates and no deleterious effects were noticed at the upper repetition rate limit (20 Hertz) indicating that a range of repetition rates would be appropriate in the clinical setting. Based on this testing, an intermediate repetition rate of 10 Hertz was chosen as a suitable repetition rate for the excimer laser system.

3. Calculation of the ablation rate in bovine eyes at low energy densities

Testing was conducted to measure the ablation rate of the 193 nanometer wavelength of the Summit Technology excimer laser beam in bovine eyes. The energy density for these studies was varied using a range of energy densities, 124 to 205 mJ/cm^2. The study involved the use of freshly enucleated bovine corneas with the epithelium removed. Laser energy was delivered to produce a large area ablation and the laser cut depth was measured using a light section microscope.

Conclusions:

These initial ablation rate studies reported ablation rates between 0.013 at 137 mJ/cm^2 to 0.24 at 205 mJ/cm^2 which were comparable to ablation rates reported by other researchers.

4. Calculation of the ablation rate in enucleated human cornea

Studies were performed to measure the ablation rate of the 193 nanometer laser wavelength Summit Technology excimer laser beam in human corneal tissue. The study involved the use of 20 hour old enucleated human eyes with the epithelium removed. An ultrasonic pachymeter was used to determine the corneal thickness of the human corneal specimens. Laser energy was delivered until the initial perforation of the cornea was achieved and number of laser pulses required for perforation recorded.

Conclusions:

This study confirmed previously reported information that the ablation rate in human corneal tissue fell somewhere in the range of 0.20 to 0.25 microns per pulse for the 193 nanometer laser wavelength produced by the excimer laser system.

C. Additional Studies

1. Radiated & Conducted Emissions testing

Retlif Laboratories, an independent testing house, conducted tests to evaluate the radiated and conducted electromagnetic emissions from the excimer laser system. The testing was conducted to determine if the laser conforms to accepted standards for the safety of electrical medical devices. The testing involved the measurement of all electric and magnetic fields and conducted electrical interference produced by the Summit Technology excimer laser system.

Conclusions:

Retlif Testing Laboratories concluded that the Summit Technology excimer laser system fulfills the conditions for the GENERAL PERMIT according to the "High Frequency Equipment Law" of August 9, 1949. The excimer laser system was found to be in compliance with the *1046/1984 General Permit, Limit Class B and VDE 0871/6.78 Limit Class B standards. Therefore, the radiated and conducted emissions levels for the excimer laser system are within the conventional standards for electronic equipment indicating that the operation of the device does not pose a safety risk in terms of radiated and conducted emissions.

2. TÜV Rheinland electrical & radiation safety testing

TÜV Rheinland, an independent testing house in Germany granted TÜV approval (issuing the GS Mark for the OmniMed Laser System) in 1993 based on its evaluation of the device's electrical and radiation safety. TÜV Rheinland's testing of the excimer laser system involved extensive testing of the Company's excimer laser system by TÜV Rheinland personnel during several visits to Summit Technology's facilities. Supplementing this first hand testing by the TÜV personnel was the submission of detailed documentation concerning the OmniMed Laser System by Summit Technology's Research and Development Engineering Department. The Company previously received the GS Mark for the ExciMed UV200LA Laser System in 1991.

The TÜV Approval GS Mark for the ExciMed/OmniMed Laser System confirms that the ExciMed/OmniMed Laser System conforms to the following electrical/radiation safety standards:

*IEC 601-1/1	Edition 1977
*IEC 601-1/2	Edition 1988
*IEC 601-Z-22	Edition 1991
*IEC 825	Edition 1984

*IEC 825 amendments to IEC 825 (1984) August 10, 1987

Conclusions:

This independent testing supports the safety aspects of the ExciMed/OmniMed Laser System which have been incorporated into the system to ensure that the operation of the ExciMed/OmniMed is safe for the personnel operating the equipment in addition to the patient undergoing a clinical procedure. Receipt of the GS Mark verifies that system's conformance with the previously mentioned electrical radiation standards.

IX. SUMMARY OF CLINICAL STUDIES

A. Study Objectives

The objectives of the multicenter clinical investigation of Summit Technology's Excimer Laser System for PTK conducted under IDE G880234 included the treatment or mitigation of signs and symptoms in the following 3 groups:

Corneal Dystrophies
Recurrent Erosion Syndrome
Corneal Scars, Opacities and Other Irregular Surfaces.

The Excimer Laser System was intended for use in PTK procedures for the treatment of patients with the above pathologic superficial corneal conditions sufficiently severe to have adversely affected their visual acuity or caused the patient significant pain or discomfort.

The goal in the treatment of the corneal dystrophy cases was to improve vision and/or symptoms of pain or discomfort. The goal in the treatment of the recurrent erosion syndrome cases was to improve symptoms of pain or discomfort by improving epithelial adhesion and producing a smoother underlying surface. The goal in the treatment of the corneal scars, opacities and other irregular surface cases was to improve vision and/or symptoms of pain or discomfort by smoothing the corneal surface, improving corneal transparency and topography. Patients were also assessed preoperatively as to whether they were candidates for penetrating keratoplasty no matter what category they were designated, the goal in treatment being to avoid or postpone penetrating keratoplasty.

All patients treated in this clinical investigation of PTK were categorized by the investigator based on the condition being treated and the primary reason for treatment. Individual charts for patients were submitted in conjunction with this Premarket Approval Application and reflect these categorizations as well as the diagnosis for each patient. Some patients had more than one diagnosis so the investigator made an attempt to classify the patient's into one primary category.

The following classifications were made:

Dystrophy	103 (25.9%)
Recurrent Erosion	64 (16.1%)
Scars, Opacity or Other Irregular Surface	231 (58.0%)

A subset assessment of dystrophies for superficial corneal dystrophies and epithelial basement membrane dystrophies was also assessed to look for differences in these two groups. Although success rates were similar the primary treatment goal was more commonly to improve vision for superficial dystrophy cases while the primary treatment goal was more commonly to decrease pain and discomfort in the epithelial basement membrane cases.

B. Study Design

This was a prospective, nonrandomized, uncontrolled, unmasked multicenter clinical study.

C. Inclusion and Exclusion Criteria

Subjects were at least 21 years of age and were enrolled in the study if they had one of the following pathologic conditions: superficial corneal dystrophies such as granular, lattice, and Reis-Buckler's; epithelial basement membrane dystrophy; recurrent erosion due to trauma, non-traumatic, and post-infectious; irregular corneal surfaces and opacities including Salzmann's degeneration, post-surgical scars, keratoconus nodules and other irregular surfaces or scars due to trauma, infection and pathology. The condition must have been located in the anterior 100 microns of the cornea and the treatment area must have been at least 400 microns thick.

Subjects not meeting the above enrollment criteria were excluded from the study. In addition, anyone with an uncontrolled vascular disease or autoimmune disease which could affect corneal wound healing or could cause corneal melting were excluded from the study.

Subjects were assessed as possible penetrating keratoplasty candidates if: their best corrected visual acuity was 20/50 or worse and they had one of the following ocular conditions: anterior stromal dystrophies, corneal scars, and keratoconus nodules. A subject was included as a candidate for penetrating keratoplasty if they had a previous penetrating keratoplasty in the eye. In addition, the physician's subjective evaluation that the patient was a candidate was required.

D. Study Plan, Patient Assessments, and Efficacy Criteria

Subjects were evaluated preoperatively, and at 1 day, 3 days, 1 week, 1 month, 3 months, 6 months, and 12 months postoperatively. For those patients who may have missed their actual 12 month follow up exam but were seen at a later date (e.g. 15 months or 18 months etc.) a 12 month or longer (aggregate) examination, was included in the analysis of safety and efficacy. Some subjects were followed and data collected beyond the 12 month study period, though this was not a study requirement.

Preoperatively, the subjects medical and ocular history including prior ocular surgery were recorded. During the study, symptoms of pain and discomfort were the primary criteria recorded. Glare and distorted vision were also assessed. Objective parameters measured included manifest refraction, best spectacle corrected visual acuity, best spectacle visual acuity with glare (added in March 1991), uncorrected visual acuity, conjunctival status, corneal status by slit lamp examination including assessment of the smoothness of the cornea, keratometry readings, corneal thickness by pachymetry, intraocular pressure, anterior chamber and lens status.

Success or failure of the clinical procedure was determined based upon the preoperative goal of the case and the postoperative result at the 3, 6, 12 and 12 plus beyond (12 month aggregate) follow up examinations. The primary goal was determined by the investigator preoperatively. The goals of the majority of procedures performed were to improve vision, defined as at least a 2 or more line increase in best spectacle visual acuity; or decrease in pain or discomfort symptoms as determined by the physician and patient as well as by objective scale rating of 0 to 5 (0 being none, 5 being severe).

E. Study Period, Investigational Sites and Demographic Data

1. Study Period

The PTK study was conducted under an approved investigational device exemptions application G880234. A total of 398 eyes were treated across 15 participating clinical centers. During all three phases of the clinical investigation the same follow up and operative technique was used. The testing performed throughout the clinical investigation was also standardized. Some objective testing was added after phase 1 and this is noted in the preoperative characteristics section of this document. The standardization of the clinical technique and testing throughout all phases of the clinical investigation was provided to ensure that pooling of all study patients would be justified. In addition, the Summit Laser Systems utilized during all phases of this clinical investigation are comparable in delivering an excimer laser beam with the identical clinical laser parameters again justifying the pooling of the clinical results across centers and phases of this study.

Phase	Treatment Dates	Number of eyes
1	9/9/89 to 3/6/90	25
2	5/19/90 to 2/8/93	288
3	2/28/93 to present	85
	TOTAL EYES*	398

* Note: An FDA audit of the data established that at one clinical site the data were not collected properly and were disqualified. This accounted for four patients in the original application. All data from that site is excluded from data analysis.

A total of 398 study case eyes were treated in 358 patients. Forty patients had both eyes treated. This included 424 procedures; 24 eyes had one additional treatment session while 2 eyes had 2 additional treatment sessions. The primary goal of the PTK procedure was to improve vision in 231 cases (58.0%) and to decrease pain and discomfort in 162 cases (40.7%) Five patients (1.3%) were protocol violations and were excluded from the efficacy assessment. The goal was to allow visualization for cataract surgery to avoid a penetrating keratoplasty in 2 cases. In 3 cases the goal was to prevent recurrence of pterygium and were performed early in the clinical investigation. One hundred forty-nine eyes (37.4%) were candidates for penetrating keratoplasty prior to the PTK clinical procedure. Two hundred forty-nine eyes (62.6%) were not considered candidates for penetrating keratoplasty prior to the PTK clinical procedure.

2. Investigational Sites

The following roster is the 15 sites that participated in the clinical investigation:

SITE	NUMBER OF EYES
D. Chase Center - VT	38
Hunkeler Eye Clinic - MO	123
Vision Surgery & Laser Center - CA	9
Pacific Cataract and Laser Institute - WA	8
Montefiore Hospital - NY	29
Eye Physicians Omaha - NE	28
John Eye Clinic - IN	14
Jones Eye Clinic - IA	2
Western Pennsylvania Eye Center - PA	21
Jules Stein Eye Institute - CA	8
Washington University Hospital - MO	13
Houston Eye Clinic - TX	15
New England Eye Center - MA	33
Sioux Empire Medical Center - SD	6
Emory University School of Medicine - GA	51
TOTAL EYES	398

3. Demographics

For demographic characteristics (i.e. age, sex, race), binocular patients are counted twice; each eye is considered a separate case.

The mean age of the subjects treated was 57.7 years with a range from 21 to 90 years. The majority of cases reported were white, 377 cases (94.7%). There were 234 cases (58.8%) that were female while 164 (41.2%) were male.

There is no evidence that gender is related to the efficacy outcomes. Age greater than 50 is associated with a greater likelihood of being in the "no change" category. Increasing age is not associated with a greater likelihood of failure. There is no evidence that gender or age are related to the presence of complications.

F. Data Analysis and Results

1. Preoperative Ocular Characteristics

A number of baseline characteristics were measured. The results of these measurements included:

a. Best Spectacle Corrected Visual Acuity (BCVA)

One hundred twenty nine eyes (33.3%) had a preoperative best corrected visual acuity of better than 20/40. The majority of these patients underwent excimer laser PTK, despite their good best corrected visual acuity, in order to improve comfort and/or to improve the quality of their vision. An additional 164 eyes (42.4%) had a preoperative best corrected visual acuity between 20/40 and 20/80, while 67 eyes (17.3%) had a baseline visual acuity between 20/100 and 20/400. Twenty seven eyes (7.0%) had a best corrected visual acuity worse than 20/400. Best corrected visual acuity was not reported in 11 eyes.

b. Uncorrected Visual Acuity

Thirty eight eyes (10.4%) had a preoperative uncorrected visual acuity of better than 20/40. These patients underwent excimer laser PTK, despite their good uncorrected visual acuity, in order to improve comfort. An additional 106 eyes (29.0%) had a preoperative uncorrected visual acuity between 20/40 and 20/80, while 153 eyes (41.7%) had a baseline uncorrected visual acuity between 20/100 and 20/400. Sixty nine eyes (18.9%) had an uncorrected visual acuity worse than 20/400. Uncorrected visual acuity was not available on 32 eyes preoperatively. This information was not collected during Phase 1 of this clinical investigation. It was not an efficacy variable.

c. Best Corrected Visual Acuity with Glare

Seventy one eyes (24.1%) had a preoperative best corrected visual acuity with glare of better than 20/40. An additional 100 eyes (33.9%) had a preoperative best corrected visual acuity with glare between 20/40 and 20/80, while 95 eyes (32.2%) had a baseline best corrected visual acuity with glare between 20/100 and 20/400. Twenty nine eyes (9.8%) had a best corrected visual acuity with glare worse than 20/400. Best corrected visual acuity with glare was collected on a subgroup of patients and therefore was not reported on 103 eyes.

d. Smoothness of the Corneal Surface

The investigator classified the corneal surface as very smooth, moderately smooth, moderately rough or highly rough. Forty eight eyes (17.5%) had a very smooth corneal surface preoperatively, while 98 eyes (35.6%) were reported with a moderately smooth corneal surface. Ninety five eyes (34.5%) reported a moderately rough corneal surface while 34 eyes (12.4%) had a highly rough corneal surface. In 123 cases this information was not reported since this information was only collected on cases treated after March, 1991.

e. Conjunctival Status

Three hundred sixty one eyes (90.7%) had a normal conjunctival status while 37 eyes (9.3%) had an abnormal conjunctiva. Abnormalities included pterygium related changes, injection and conjunctivitis.

f. Corneal Status

All conditions were graded on a scale of Clear, Trace, Mild, Moderate or Marked. All cases were reported as Clear with the following exceptions:

Corneal Condition	# of eyes	% of eyes
Edema	51	12.8%
Haze	151	37.9%
Corneal Thinning	60	15.1%
Diffuse Nebulae	113	28.4%
Diffuse Superficial Punctate Keratitis	76	19.1%
Epithelial Defects	49	12.3%
Guttata	34	8.5%
Hudson Stahli Lines	29	7.3%
Iritis	5	1.3%
Keratitis	16	4.0%
Vascularization	60	15.1%
Other Irregularities in Epithelium	169	42.5%
Other Irregularities in Bowman	165	41.5%
Other Irregularities in Stroma	98	24.6%
Other Irregularities	15	3.8%

g. Anterior Chamber Status

The anterior chamber depth was graded by the investigator as deep, normal or shallow. Deep was defined as greater than 3.5 mm, normal was defined as 2.5 to 3.5 mm and shallow was defined as less than 2.5 mm. 114 eyes (36.0%) had a deep anterior chamber, 202 eyes (63.7%) had a normal anterior chamber and 1 eye (0.3%) was graded as having a shallow anterior chamber preoperatively. Anterior chamber depth was not available on 81 eyes since this information was not collected on cases before August, 1990.

The following anterior chamber conditions were present preoperatively: cells in 8 (2.0%) eyes, flare in 10 (2.5%) eyes, iritis in 5 (1.3%) eyes, particulate matter & debris in 2 (0.5%) eyes, and other irregularities in 5 (1.3%) eyes.

h. Lens Status

One hundred fifteen eyes (28.9%) reported a lens opacity preoperatively.

i. Prior Surgery/Treatment

The majority of eyes enrolled in this clinical investigation had previously undergone ocular surgery/treatment as follows:

Corneal Transplant (one):	22 eyes	5.5%
Corneal Transplant (multi):	7 eyes	1.8%
Mechanical Superficial Keratectomy (one):	38 eyes	9.6%
Mechanical Superficial Keratectomy (multi):	11 eyes	2.8%
Epithelial Debridement	16 eyes	4.0%
Pterygium Removal:	37 eyes	9.3%
Cataract Surgery:	84 eyes	21.1%
EDTA/Chemical Scraping:	10 eyes	2.5%
Medical Therapy for Recurrent Erosion:	117 eyes	29.4%
Glaucoma Surgery:	7 eyes	1.8%
Micropuncture:	22 eyes	5.5%
Punctal Occlusion	6 eyes	1.5%
Bandage Lens/Patching:	48 eyes	12.1%
Refractive Surgery:	3 eyes	0.8%
Vitrectomy:	4 eyes	1.0%
Tarsorrhaphy:	3 eyes	0.8%
Retinal Surgery:	6 eyes	1.5%
Other Surgery:	24 eyes	6.0%

Many of these eyes had undergone multiple previous treatments/surgery so that the percentages do not equal 100%.

2. Operative Characteristics

The mean number of laser pulses used for the PTK procedure was 414.2 pulses. The beam diameter selected for treatment ranged from 1.0 to 5.0 mm. For all procedures, the energy density at the eye (fluence) was fixed at 180 mJ/cm² and the repetition rate was fixed at 10 Hertz.

Three hundred and ten (77.9%) of the cases treated were laser only treatments while 88 (22.1%) of the cases included a mechanical treatment in addition to the laser. A mechanical treatment was defined as any mechanical or surgical intervention beyond epithelium removal.

Topical anesthetic was used preoperatively in all cases, (100.0%).

The laser performed as expected and the procedure was completed in all 398 (100.0%) cases attempted where laser energy delivery was initiated. Damage beyond the treatment area was not reported.

3. Postoperative Characteristics and results

a. Patient Accountability

	Preop	3 M	6 M	12 M	24 M	1 Yr aggregate
# eyes evaluable (%)	398	368 (92.5%)	334 (83.9%)	293 (73.6%)	196 (49.3%)	317 (79.7%)
# eyes evaluated (%)	398 (100%)	325 (88.3%)	270 (80.8%)	221 (75.4%)	108 (55.1%)	255 (80.4%)

The 1 year aggregate is defined as all follow-up examinations that occurred at 1 year or longer. As can be seen in the table above, 293 patients were eligible for the one year follow-up, and 221 patients actually had the follow-up. The one year aggregate examination includes patients who may have missed their actual 12 month follow up exam but were seen at a later time date (e.g. 15 months or 18 months etc.) Some subjects were followed and data collected beyond the 12 month study period, though this was not a study requirement.

b. Re-epithelialization

A total of 398 clinical procedures were performed in this clinical investigation. Re-epithelialization occurred by:

1 day: 13 (3.3%) eyes;
3 days: 243 (61.1%) eyes;
1 week: 342 (85.9%) eyes; and,
1 month: 384 (96.5%) eyes.

Of the 14 eyes which had not re-epithelialized by the one month examination, 4 re-epithelialized by the three month examination. In 10 cases information regarding re-epithelialization is not known either because the patients did not return for follow up at a time period that allowed this information to be collected or the information was not recorded by the clinical center.

c. Best Spectacle Corrected Visual Acuity (BCVA)

	Preop (n=387)[1]	3 M (n=315)[2]	6 M (n=263)[3]	12 M (n=217)[4]	1 Yr Aggregate (n=250)[5]
20/40 or better	176 (45.5%)	189 (60.0%)	170 (64.7%)	144 (66.3%)	160 (64.0%)
20/50 to 20/80	117 (30.2%)	69 (21.9%)	50 (19.0%)	42 (19.4%)	55 (22.0%)
20/100 to 20/400	67 (17.3%)	33 (10.5%)	25 (9.5%)	16 (7.4%)	18 (7.2%)
less than 20/400	27 (7.0%)	24 (7.6%)	18 (6.8%)	15 (6.9%)	17 (6.8%)

Legends:	BCVA ≡	BCVA was measured
	total ≡	number of eyes examined at that follow-up
	not tested ≡	those not tested for BCVA due to the underlying disease; in most cases, the uncorrected visual acuity was reported and was 20/200 or worse
	error ≡	not tested due to error

[1]BCVA = 387; total = 398; not tested = 10; and, error = 1 eyes

[2]BCVA = 315; total = 325; not tested = 10; and, error = 0 eyes

[3]BCVA = 263; total = 270; not tested = 7; and, error = 0 eyes

[4]BCVA = 217; total = 221; not tested = 4; and, error = 0 eyes

[5]BCVA = 250; total = 255; not tested = 5; and, error = 0 eyes

The distribution of best corrected visual acuities is significantly different at 3, 6 and 12 months when compared against preop using a Chi-square test performed with SAS System 6.07. The significance values are 16.714 ($p<.001$) for 3 M versus preop, 24.842 ($p<.001$) for 6 M versus preop, and 24.484 ($p<.001$) for 12 M versus preop.

i. BCVA by Goal to Improve Vision

	Preop (n=228)	3 M (n=192)	6 M (n=164)	12 M (n=139)	1 Yr Aggregate (n=162)
20/40 or better	67 (29.4%)	100 (52.1%)	95 (57.9%)	86 (61.9%)	95 (58.7%)
20/50 to 20/80	96 (42.1%)	61 (31.8%)	44 (26.8%)	36 (25.9%)	48 (29.6%)
20/100 to 20/400	55 (24.1%)	24 (12.5%)	19 (11.6%)	12 (8.6%)	13 (8.0%)
less than 20/400	10 (4.4%)	7 (3.6%)	6 (3.7%)	5 (3.6%)	6 (3.7%)

ii. BCVA by Goal to Improve Comfort

	Preop (n=154)	3 M (n=119)	6 M (n=95)	12 M (n=75)	1 Yr Aggregate (n=84)
20/40 or better	106 (68.9%)	86 (72.3%)	72 (75.8%)	56 (74.7%)	63 (75.0%)
20/50 to 20/80	21 (13.6%)	8 (6.7%)	6 (6.3%)	6 (8.0%)	7 (8.3%)
20/100 to 20/400	11 (7.1%)	8 (6.7%)	5 (5.3%)	3 (4.0%)	4 (4.8%)
less than 20/400	16 (10.4%)	17 (14.3%)	12 (12.6%)	10 (13.3%)	10 (11.9%)

As can be determined from the above two tables, when assessing best corrected visual acuity outcomes, the goal in treatment should be considered. For those eyes treated with the goal of improving vision, the number of eyes with visual acuity of 20/40 or better significantly increased from preoperative to each postoperative period. For those eyes treated with the goal of improving comfort, the number of eyes with visual acuity of 20/40 or better did not significantly change.

d. Best Corrected Visual Acuity Changes from Pre-op

Lines	3 M n = 307[6]	6 M n = 256[7]	12 M n = 213[8]	1 Yr Aggregate n = 245[9]
No Change* ± 1	139 (45.3%)	120 (46.9%)	107 (50.2%)	120 (49.0%)
Increase 2	42 (13.6%)	37 (14.3%)	20 (9.4%)	22 (9.0%)
3	29 (9.4%)	23 (9.0%)	27 (12.6%)	29 (11.8%)
4	15 (4.9%)	15 (5.9%)	17 (8.0%)	21 (8.6%)
5	11 (3.6%)	7 (2.7%)	6 (2.8%)	8 (3.3%)
6	14 (4.6%)	8 (3.1%)	7 (3.3%)	9 (3.7%)
7	10 (3.3%)	5 (2.0%)	4 (1.9%)	4 (1.6%)
8	1 (0.3%)	4 (1.6%)	0	0
9	2 (0.7%)	1 (0.4%)	4 (1.9%)	4 (1.6%)
10	1 (0.3%)	2 (0.8%)	1 (0.5%)	3 (1.2%)
11	1 (0.3%)	0	0	1 (0.4%)
15	0	1 (0.4%)	0	0
total increase	126 (41.0%)	103 (40.2%)	86 (40.4%)	101 (41.2%)

Decrease 2	18 (5.7%)	19 (7.3%)	10 (4.8%)	14 (5.7%)
3	7 (2.3%)	5 (2.0%)	2 (0.9%)	2 (0.8%)
4	7 (2.3%)	2 (0.8%)	6 (2.8%)	6 (2.5%)
5	4 (1.3%)	0	0	0
6	2 (0.7%)	3 (1.2%)	2 (0.9%)	2 (0.8%)
7	2 (0.7%)	2 (0.8%)	0	0
8	0	1 (0.4%)	0	0
9	2 (0.7%)	1 (0.4%)	0	0
total decrease	42 (13.7%)	33 (12.9%)	20 (9.4%)	24 (9.8%)

*"No change" of vision includes one line gain or one line loss on the visual acuity chart and is considered to be within the measurement testing error for visual acuity testing. Per Nizam et al. (The PERK Study Group), "Stability of Refraction and Visual Acuity During 5 Years in Eyes with Simple Myopia" in Refractive and Corneal Surgery, "We concluded that a change of one Snellen line in the spectacle-corrected visual acuity is within the bounds of normal biologic variation and, therefore, can be included in the criteria for stability". In addition, per this article, "Studies that report a one line loss in spectacle-corrected visual acuity as a "complication" are in danger of confusing complications with normal variability."

Legends:

cBCVA ≡	a change in BCVA was observed
total ≡	number of eyes examined for BCVA
not tested ≡	those not tested for BCVA due to the underlying disease

[6]cBCVA = 307; total = 315; and not tested = 8 eyes

[7]cBCVA = 256; total = 263; and not tested = 7 eyes

[8]cBCVA = 213; total = 217; and not tested = 4 eyes

[9]cBCVA = 245; total = 250; and not tested = 5 eyes

Underlying conditions were contributing factors in those patients with large changes in BCVA over time. These confounding conditions included: advancing cataract, recurrence of lattice dystrophy in graft, recurrence of corneal scar, traumatic corneal abrasion between exams, recurrence of pterygium with conjunctival transplant, and cataract surgery between exams.

These results represent reasonable assurance of the stability of BCVA beyond the three month postoperative period for the PTK procedure. Underlying pathologies must be considered when estimating the long term stability.

e. BCVA with Glare

	Preop (n=301)[10]	3 M (n=212)[11]	6 M (n=177)[12]	12 M (n=157)[13]	1 Yr Aggregate(n =174)[14]
20/40 or better	95 (31.6%)	112 (52.8%)	98 (55.3%)	85 (54.1%)	95 (54.5%)
20/50 to 20/80	80 (26.6%)	50 (23.6%)	40 (22.6%)	49 (31.2%)	53 (30.5%)
20/100 to 20/400	96 (31.8%)	35 (16.5%)	27 (15.3%)	15 (9.6%)	17 (9.8%)
less than 20/400	30 (10/0%)	15 (7.1%)	12 (6.8%)	8 (5.1%)	9 (5.2%)

Legends:		
	BCVAg ≡	BCVA with glare was measured
	total ≡	number of eyes examined at that follow-up
	prior ≡	those enrolled before this test was introduced in the study (in March, 1991)
	not tested ≡	those not tested for BCVA with glare due to the underlying disease
	error ≡	not tested due to error

[10]BCVAg = 301; total = 398; prior = 63; not tested = 8; and error = 26 eyes

[11]BCVAg = 212; total = 325; prior = 68; not tested = 3; and error = 42 eyes

[12]BCVAg = 177; total = 270; prior = 61; not tested = 10; and error = 22 eyes

[13]BCVAg = 157; total = 221; prior = 33; not tested = 12; and error = 19 eyes

[14]BCVAg = 174; total = 255; prior = 54; not tested = 9; and error = 18 eyes

The distribution of best corrected visual acuities with glare is significantly different at 3, 6 and 12 months compared with preop using a Chi-square test performed with SAS System 6.07. The significance values are 27.1 ($p<.001$) for 3 M versus preop, 29.6 ($p<.001$) for 6 M versus preop, and 38.4 ($p<.001$) for 12 M versus preop.

f. Changes in BCVA with Glare from Preop

Lines	3M n = 180[15]	6M n = 145[16]	12M n = 123[17]	1 Yr Aggregate n = 134[18]
No Change ± 1	86 (47.8%)	58 (40.0%)	40 (32.5%)	45 (33.6%)
Increase 2	12 (6.7%)	16 (11.0%)	11 (8.9%)	11 (8.2%)
3	18 (9.9%)	9 (6.2%)	10 (8.1%)	11 (8.2%)
4	9 (5.0%)	10 (6.9%)	9 (7.3%)	11 (8.2%)
5	9 (5.0%)	6 (4.1%)	6 (4.9%)	6 (4.5%)
6	11 (6.1%)	12 (8.3%)	7 (5.7%)	7 (5.2%)
7	6 (3.3%)	3 (2.1%)	5 (4.1%)	6 (4.5%)
8	5 (2.8%)	6 (4.1%)	7 (5.7%)	7 (5.2%)
9	3 (1.7%)	2 (1.4%)	7 (5.7%)	7 (5.2%)
10	2 (1.1%)	5 (3.5%)	5 (4.1%)	5 (3.7%)
11	1 (0.6%)	1 (0.7%)	0	0

12	2 (1.1%)	0	0	0
13	1 (0.6%)	0	1 (0.8%)	1 (0.8%)
14	0	0	1 (0.8%)	1 (0.8%)
total increase	79 43.9%	70 (48.3%)	69 (56.1%)	73 (54.5%)

Decrease 2	6 (3.2%)	10 (6.8%)	6 (4.9%)	7 (5.0%)
3	5 (2.8%)	2 (1.4%)	4 (3.3%)	4 (3.0%)
4	2 (1.1%)	2 (1.4%)	1 (0.8%)	1 (0.8%)
5	1 (0.6%)	1 (0.7%)	2 (1.6%)	2 (1.5%)
6	0	1 (0.7%)	0	0
7	0	1 (0.7%)	0	1 (0.8%)
8	1 (0.6%	0	1 (0.8%)	1 (0.8%)
total decrease	15 (8.3%)	17 (11.7%)	14 (11.4%)	16 (11.9%)

Legends:	cBCVAg ≡	a change in BCVA with glare was observed
	total ≡	number of eyes examined for BCVA with glare
	not tested ≡	those not tested at preop

[15]cBCVAg = 180; total = 212; and not tested = 32 eyes

[16]cBCVAg = 145; total = 177; and not tested = 32 eyes

[17]cBCVAg = 123; total = 157; and not tested = 34 eyes

[18]cBCVAg = 134; total = 174; and not tested = 40 eyes

Glare in these pathological conditions can be disabling, even when objective measurements for best corrected visual acuity are excellent. Giving consideration to initial best corrected visual acuity, these data represent that PTK may decrease symptoms associated with glare. Improvement but not full resolution of these symptoms occurred often. These improvements are best seen in the previous table which illustrates that these changes are stable over time.

g. Manifest Refraction (spherical equivalent)

The mean manifest refraction spherical equivalent shows a hyperopic shift of 0.86 diopters from preoperative to the 12 months postoperative examination. The ranges of manifest refraction spherical equivalents are similar pre- and post- operatively.

	Mean ± Std Dev.	Range
Preop (n=344)[19]	-0.70 D ± 3.83	-18.00 to +14.88 D
3 M (n=274)[20]	+0.42 D ± 4.09	-19.50 to +18.00 D
6 M (n=237)[21]	+0.31 D ± 4.12	-21.00 to +17.50 D
12 M (n=198)[22]	+0.16 D ± 3.50	-20.00 to +14.75 D
1 Yr Aggregate (n=227)[23]	+0.12 D ± 3.79	-20.00 to +17.13 D

Legends:
refrac ≡ manifest refraction was measured
total ≡ number of eyes examined at that follow-up
prior ≡ those enrolled before this test was introduced in the study (in March, 1990)
no improvement ≡ testing was performed but the uncorrected visual acuity could not be improved upon
not tested ≡ testing could not be performed due to the underlying pathology
error ≡ not tested due to error

[19]refrac = 344; total = 398; prior = 25; no improvement = 14; not tested = 10, and error = 5 eyes

[20]refrac = 274; total = 325; prior = 23; no improvement = 7; not tested = 14, and error = 7 eyes

[21]refrac = 237; total = 270; prior = 8; no improvement = 6; not tested = 11, and error = 8 eyes

[22]refrac = 198; total = 221; prior = 8; no improvement = 4; not tested = 8, and error = 3 eyes

[23]refrac = 227; total = 255; prior = 8; no improvement = 4; not tested = 10, and error = 6 eyes

h. Change in Manifest Refraction (spherical equivalent) from Preop

(Diopter)	3M n = 257[24]	6M n = 211[25]	12M n = 173[26]	1 Yr Aggregate n = 199[27]
No Change ± 1.0	114 (44.2%)	100 (47.5%)	84 (48.6%)	94 (47.4%)
Towards Myopia 1.1 - 2.0	15 (5.8%)	13 (6.2%)	13 (7.5%)	14 (7.0%)
2.1 - 3.0	10 (3.9%)	6 (2.8%)	3 (1.7%)	3 (1.5%)
3.1 - 4.0	5 (2.0%)	5 (2.4%)	3 (1.7%)	4 (2.0%)
4.1 - 5.0	2 (0.8%)	3 (1.4%)	4 (2.3%)	5 (2.5%)
5.1 - 6.0	2 (0.8%)	3 (1.4%)	1 (0.6%)	2 (1.0%)
6.1 - 7.0	0	0	1 (0.6%)	1 (0.5%)
11.25 - 15.5	0	0	0	2 (1.0%)
total toward myopia	34 (13.2%)	30 (14.2%)	25 (14.5%)	31 (15.6%)

Toward hyperopia 1.1 - 2.0	32 (12.5%)	26 (12.3%)	21 (12.1%)	23 (11.6%)
2.1 - 3.0	23 (8.9%)	20 (9.5%)	15 (8.7%)	16 (8.0%)
3.1 - 4.0	15 (5.8%)	10 (4.7%)	14 (8.1%)	14 (7.0%)
4.1 - 5.0	10 (3.9%)	7 (3.3%)	2 (1.2%)	5 (2.5%)
5.1 - 6.0	12 (4.7%)	6 (2.8%)	3 (1.7%)	5 (2.5%)
6.1 - 7.0	9 (3.5%)	5 (2.4%)	6 (3.5%)	6 (3.0%)
7.1 - 8.0	2 (0.8%)	1 (0.5%)	0	1 (0.5%)
8.1 - 9.0	3 (1.2%)	3 (1.4%)	3 (1.7%)	3 (1.5%)
9.1 - 10.0	2 (0.8%)	2 (0.9%)	0	1 (0.5%)
11.1 - 11.25	0	1 (0.5%)	0	0
12.1 - 12.5	1 (0.4%)	0	0	0
total toward hyperopia	109 (42.4%)	81 (38.4%)	64 (37.0%)	74 (37.2%)

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Legends:		
	crefrac ≡	a change in manifest refraction was observed
	total ≡	number of eyes examined for manifest refraction
	not tested ≡	those not tested at preop

[24]crefrac = 257; total = 274; and not tested = 17 eyes

[25]crefrac = 211; total = 237; and not tested = 26 eyes

[26]crefrac = 173; total = 198; and not tested = 25 eyes

[27]crefrac = 199; total = 227; and not tested = 28 eyes

Manifest refraction was within ± 3.0 D from preop in 150/199 (75.4%) of patients at the 1 yr aggregate exam. Only 14/199 (7.0%) had a greater than 3.0 D shift towards myopia; and 35/199 (17.6%) had a greater than 3.0 D shift toward hyperopia. At the 1 yr aggregate exam the best corrected visual acuity did not change or improved in the majority of eyes treated with change in sphere of greater than 3.00 diopters 42/49 (85.7%). Best corrected visual acuity improved significantly in these patients. The possibility of significant anisometropia should be considered in the evaluation of patients for treatment with the PTK procedure. The ability to tolerate correction of anisometropia should be considered during the evaluation. This represents a low rate of anisometropia compared to other alternative procedures and devices. Operative techniques as described in the physician's guidelines should be carefully followed to maximally decrease significant anisometropia.

i. Postoperative Stability (with consideration of both BCVA and Manifest Refraction)

To determine postoperative stability of eyes that have undergone a PTK, we evaluated changes in BCVA and manifest refraction between the 3 and 6 month examinations and between the 6 and 12 month examinations.

i. BCVA Changes between follow-ups

BCVA Changes (lines)	3 M to 6 M n=239[28]	6 M to 12 M n=191[29]
No Change ±1	184 (77%)	135 (70.8%)
gain 2	18 (7.5%)	10 (10.5%)
3	6 (2.5%)	6 (3.1%)
4	3 (1.3%)	3 (1.6%)
5	1 (0.4%)	2 (1.0%)
> 5	5 (2.1%)	4 (2.1%)
total gain	33 (13.8%)	35 (18.3%)
loss 2	14 (5.9%)	9 (4.7%)
3	3 (1.3%)	8 (4.2%)
4	2 (0.8%)	1 (0.5%)
5	1 (0.4%)	1 (0.5%)
> 5	2 (0.8%)	2 (1.0%)
total loss	22 (9.2%)	20 (10.5%)

[28]Changes between 3 and 6 months observed in 239 eyes, although BCVA was measured on 263 eyes at 6M: eighteen eyes were checked for BCVA at 6M but did not have a 3M follow-up; and, six eyes were checked for BCVA at 6M and had the 3M exam, but did not have BCVA measured at 3M.

[29]Changes between 6 and 12 months observed in 191 eyes, although BCVA was measured on 217 eyes at 12M: twenty-two eyes were checked for BCVA at 12M but did not have a 6M follow-up; and, four eyes had data available at 12M and had the 6M exam, but did not have BCVA measured at 6M.

ii. Changes in Postoperative Manifest Refraction (spherical equivalent) Between Follow-ups

Changes (Diopters)	3M to 6M n = 204[30]	6M to 12 M n = 172[31]
No Change ±1	154 (75.4%)	119 (69.3%)
1.1 to 2.0	30 (14.7%)	31 (18.0%)
2.1 to 3.0	13 (6.4%)	9 (5.2%)
3.1 to 4.0	2 (1.0%)	4 (2.3%)
4.1 to 5.0	2 (1.0%)	5 (2.9%)
5.1 to 6.0	1 (0.5%)	1 (0.6%)
6.1 to 7.0	2 (1.0%)	0
7.1 to 8.0	0	3 (1.7%)

[30]Manifest refraction changes between 3 and 6 months observed in 204 eyes, although manifest refraction was measured on 237 eyes at 6M: eighteen eyes were measured at 6M, but did not have the 3M follow-up; and, fifteen eyes were measured at 6M and had the 3M exam, but did not have manifest refraction done.

[31]Manifest refraction changes between 6 and 12 months observed in 172 eyes, although manifest refraction was measured on 198 eyes at 12M: nineteen were measured at 12M, but did not have the 6M follow-up; six eyes were measured at 12M and had the 6M exam, but did not have manifest refraction done; and, one eye had manifest refraction recorded as "no improvement".

Based on manifest refraction spherical equivalent and best corrected visual acuity, stability after PTK was demonstrated in this study. 154/204 (75.4%) had no change in manifest refraction spherical equivalent between the 3 and 6 months examinations. 184/239 (77.0%) had no change in best corrected visual acuity between the 3 and 6 months examinations. 119/172 (69.3%) had no change in manifest refraction spherical equivalent between the 6 and 12 month examinations.

135/191 (70.8%) had no change in best corrected visual acuity between the 6 and 12 months examinations. Most patients who had a change in best corrected vision and manifest refraction were retreated with PTK, had additional surgical intervention including cataract surgery and penetrating keratoplasty, and had progressive underlying disease.

j. Irregular Astigmatism

The presence of irregular astigmatism throughout the postoperative period was 189/398 (47.5%) preoperatively, 107/261 (41.0%) at 3 M, 95/218 (43.6%) at 6 M, and 74/184 (40.2%) at 12 M.

k. Keratometry Readings

Preoperatively, the mean keratometry reading was 44.33 diopters (D). At 3 M, it was 43.37 D and remained stable throughout the postoperative period. The mean at 6 M and 12 M were 43.18 and 43.49 D, respectively. The mean keratometric astigmatism was 2.37 D preoperatively. This was essentially unchanged at 3 M -- 2.23 D. At 12 M, it was 2.12 D.

l. Intraocular Pressure

The intraocular pressure remained stable within 0.4 mmHg throughout the clinical investigation. Preoperatively, the mean intraocular pressure was 15.2 mmHg with a standard deviation of 4.2 mmHg.

m. Smoothness of the Corneal Surface

	Preop N = 275	3 M N = 203	6 M N = 169	12 M N = 161
very smooth	48 (17.5%)	110 (54.1%)	94 (55.6%)	93 (57.8%)
moderately smooth	98 (35.6%)	75 (37.0%)	56 (33.1%)	52 (32.3%)
moderately rough	95 (34.5%)	17 (8.4%)	15 (8.9%)	14 (8.7%)
highly rough	34 (12.4%)	1 (0.5%)	4 (2.4%)	2 (1.2%)

From the above table, it is observed that the corneal surface became smoother after the PTK clinical procedure. (Note that this information was collected beginning in March, 1991, and is not available in all cases.)

n. Corneal Thickness

The corneal thickness decreased after the PTK procedure and gradually thickened over time. Preoperatively, the mean corneal thickness was 570.7 microns with a standard deviation of 93.3 microns. At 3 M, the mean was 529.3 microns with a standard deviation of 86.2 microns. At 6 M, the mean corneal thickness was 532.6 microns with a standard deviation of 74.1 microns. At 12 M, the mean was 537.2 microns with a standard deviation of 72.0 microns.

o. Conjunctival Status

Preoperatively, 361/398 (90.7%) had a normal conjunctival status while 37/398 (9.3%) had an abnormal conjunctiva. Postoperatively, the percent of eyes with an abnormal conjunctiva decreased to 20/325 (6.2%) at the 3 M, 14/270 (5.2%) at the 6 M, and 11/221 (4.9%) at the 12 M. Abnormalities pre- and post-operatively included pterygium related changes, injection, conjunctivitis, pinguecula, and symblepharon.

p. Corneal Status

All conditions were graded on a scale of Clear, Trace, Mild, Moderate or Marked. All cases were reported as Clear with the following exceptions:

Corneal Condition	Preop (n=398)	3 M (n=325)	6 M (n=270)	12 M (n=221)	12M Aggre (n=255)
Edema	51 (12.8%)	28 (8.6%)	10 (3.7%)	12 (5.4%)	14 (5.5%)
Haze	151(37.9%)	172 (52.9%)	139(51.5%)	126 (57%)	144(56.5%)
Thinning	60 (15.1%)	43 (13.2%)	28 (10.4%)	29(13.1%)	32(12.6%)
Diffuse Nebulae	113(28.4%)	28(8.6%)	20(7.4%)	23(10.4%)	26(10.2%)
Superficial Punctate Keratitis	76 (19.1%)	27 (8.3%)	20 (7.4%)	16 (7.2%)	16(6.3%)
Epithelial Defects	49 (12.3%)	14 (4.3%)	4 (1.5%)	7 (3.2%)	8(3.1%)
Guttata	34 (8.5%)	25 (7.7%)	29 (10.7%)	26(11.8%)	27(10.6%)
Hudson Stahli Lines	29 (7.3%)	2 (0.6%)	7 (2.6%)	5 (2.3%)	7(2.8%)
Iritis	5 (1.3%)	3 (0.9%)	2 (0.7%)	1 (0.5%)	1(0.4%)
Keratitis	16 (4.0%)	6 (1.9%)	4 (1.5%)	0	0
Vascularization	60 (15.1%)	33 (10.2%)	22 (8.2%)	16 (7.2%)	18 (7.1%)
Irregularities in Epithelium	169(42.5%)	32 (9.9%)	27 (10.0%)	17 (7.7%)	19(7.5%)
Irregularities in Bowman's	165(41.5%)	31 (9.5%)	26(9.6%)	23(10.4%)	25(9.8%)
Irregularities in Stroma	98 (24.6%)	21 (6.5%)	17 (6.3%)	18 (8.1%)	20(7.8%)

The incidence of the majority of corneal irregularities decreased post-PTK including edema, thinning, diffuse nebulae, diffuse superficial punctate keratitis, epithelial defects, Hudson-Stahli lines, iritis, keratitis, vascularization, other irregularities in epithelium, Bowman's and stroma. This table represents any report of the above phenomenon during the study. See adverse events section for calculations of occurrences.

q. Anterior Chamber Status

Anterior Chamber Condition	Preop (n=398)	3 M (n=325)	6 M (n=270)	12 M (n=221)	12 M Aggregate (n=255)
Deep (>3.5mm)	114(36.0%)	74(34.7%)	81(44.0%)	73(40.1%)	93(43.9%)
Normal (2.5 - 3.5 mm)	202(63.7%)	138(64.8%)	102(55.5%)	108(59.3%)	118(55.6%)
Shallow (<2.5 mm)	1 (0.3%)	1 (0.5%)	1 (0.5%)	1 (0.6%)	1(0.5%)
Not Reported	81 (20.3%)	112(34.5%)	86(31.9%)	39(17.6%)	43(16.9%)
Cells	8 (2.0%)	4 (1.2%)	2 (0.7%)	1 (0.5%)	1 (0.4%)
Flare	10 (2.5%)	5 (1.5%)	3 (1.1%)	2 (0.9%)	2 (0.8%)
Iritis	5 (1.3%)	1 (0.3%)	1 (0.4%)	1 (0.5%)	1 (0.4%)
Particulate matter & debris	2 (0.5%)	0	0	0	0
Other Irregularities	5 (1.3%)	2 (0.6%)	3 (1.1%)	1 (0.5%)	1 (0.4%)

Anterior chamber depth and status pre- and post-op were unchanged, and irregularities occurred less frequently after the PTK procedure.

r. Lens Status

Lens opacity was reported in 115/398 eyes (28.9%) preoperatively, 85/325 (26.2%) at 3 M, 83/270 (30.7%) at 6 M, 60/221 (27.1%) at 12 M postoperatively. Only 4 patients were reported to develop new cataracts postoperatively during this clinical investigation. Also it should be noted that not all patients with lens opacity returned at each visit.

3. Additional Treatments

A total of 24 (6.0%) eyes underwent an additional PTK procedure during the follow up period. Two of these eyes had a third PTK procedure.

Eyes, with additional PTK treatments, re-epithelialized similarly to eyes treated for the first time with PTK: 14 (60.9%) by 3 day, 20 (87.0%) eyes by 1 week. Two additional eyes re-epithelialized by 1 month, while 1 eye re-epithelialized by 2 months postop. Re-epithelialization information was not available on 1 eye.

The 24 eyes requiring an additional treatment session had the following preoperative diagnosis:

Band keratopathy	1 eye
Lattice dystrophy	7 eyes
Keratoconus nodule	1 eye
Pterygium	1 eye
Salzmann's	2 eyes
Scars	7 eyes
Recurrent Erosions	5 eyes

Seventy five percent of the additional treatment sessions were performed by one clinical center, while the remaining procedures were performed by 5 other clinical centers.

Fourteen retreatments occurred in Phase II-extension (14 eyes). For the remaining: 3 occurred in Phase I, 6 in Phase II, and 1 eye in Phase III.

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The preoperative treatment goal of the patients with an additional treatment session was to improve vision in 14 (58.3%) cases and to improve comfort in 10 (41.7%) cases.

The additional treatment was received at the following time periods following the initial treatment:

prior to the 3 month exam	4 eyes
between the 3 and 6 month	4 eyes
between the 6 and 12 month	7 eyes
after the 12 month	9 eyes.

The additional treatments were given for two primary reasons: recurrence of the initial condition or the initial treatment was too conservative. Ten (41.7%) eyes were treated due to recurrence of the underlying disease process, and 14 (58.3%) eyes were treated because the initial PTK treatment was incomplete.

The success rates in the group of patients that was treated an additional time were lower than that seen in the total population. Not all patients returned or had reached the follow-up period by the specified close of the database. Therefore the following results are only on patients who returned or had reached the follow up time observed at these time periods after the additional treatment:

	3 M after (n=18)	6 M after (n=17)	12 M after (n=10)
Success	10 eyes (55.5%)	10 (58.8%)	4 (40.0%)
No Change	3 eyes (16.7%)	4 (23.5%)	3 (30.0%)
Failure	5 eyes (27.8%)	3 (17.7%)	3 (30.0%)

4. Additional Surgical Intervention

A total of 15 (4.0%) eyes underwent a penetrating keratoplasty during the postoperative period. Four of these 15 eyes already had a penetrating keratoplasty prior to the PTK procedure. One underwent enucleation after the PTK procedure.

5. Device failures

The following represents a summary of device failures reported to date on a worldwide basis for the Summit excimer laser equipment. No permanent injury has been reported from any of these failures.

a. Failure of the laser to come out of the test mode occurred twice.
b. System shutter failure occurred in three instances. Twice it was replaced and did not reoccur. The other required an engineering service visit.
c. Iris diaphragm failure during a photorefractive procedure in two instances. The iris system was replaced. The failure could not be replicated by the company.
d. During in vitro research, the laser was missing pulses that the software counted but in actuality the pulses were not being delivered. The High Voltage Power Cable was not fully seated in the High Voltage Power Supply which was corrected. The problem did not recur.

X. CONCLUSIONS DRAWN FROM THE CLINICAL STUDIES

A. SAFETY

Adverse reactions were calculated up to the 12 month or later evaluation. Adverse reactions reported here are based upon new events which occurred postoperatively (such as cataract or infection); or where the complication continued to interfere with the patient's vision or comfort (such as glare, corneal scarring, foreign body sensation, or patient discomfort). No immediate operative complications were reported. No damage to the area surrounding the treatment area were reported.

Adverse events in this clinical investigation were:

Corneal scarring	35/255 (13.7%)
Glare	31/255 (12.2%)
Decrease of best corrected visual acuity	24/245 (9.8%)
Induced astigmatism	23/255 (9.0%)
Foreign body sensations	15/255 (5.9%)
Patient discomfort	12/255 (4.7%)
Corneal epithelial defect	9/255 (3.5%)
Corneal infection/ulceration	5/255 (2.0%)
Persistent corneal edema	5/255 (2.0%)

The following complications occurred at a rate less than 2.0%:

Bacterial keratitis (attributed to contact lens wear)
Cataract
Delayed re-epithelialization
Epiphora
Graft rejection episodes (reversed with steroids)
Reactivation of herpes simplex virus
Hyphema
Iritis
Keratitis attributed to antibiotics
Neovascularization
Recurrence of pterygium.

Reactivation of herpes simplex virus occurred in two patients in this clinical investigation and has been known to occur in other studies of excimer lasers. Therefore, it has been placed in the warning section for the excimer laser. Patients with active infection should not be treated with the excimer laser. Consideration of reactivation of latent disease and severity of the existing condition should be considered when contemplating the PTK procedure in these patients.

B. EFFECTIVENESS

Success/failure of the clinical procedure was determined based on the preoperative goal of the case and the postoperative result at the 3, 6, 12 and 12 month or longer follow up examinations. The goals of the majority of procedures performed were to improve vision and/or decrease pain or discomfort. In cases where the goal was to improve vision, a minimum of two lines of improvement in best corrected vision was required in order to be considered a success. In cases where the goal was to decrease pain or discomfort, the determination of success was based upon an evaluation by the physician and the patient. The patient's subjective evaluation along with the rating of pain based upon a postoperative survey with a scale of 0 to 5 (0 being none and 5 being severe) was used in the evaluation.

1. Overall Success/Failure

	3 M (n=325)	6 M (n=270)	12 M (n=221)	1 Yr Aggregate (n=255)
Success	237 (72.9%)	201 (74.4%)	161 (72.9%)	185 (72.6%)
No Change	34 (10.5%)	25 (9.3%)	25 (11.3%)	37 (14.5%)
Failure	54 (16.6%)	44 (16.3%)	35 (15.8%)	33 (12.9%)

The overall success rate was stable throughout the long term postoperative follow up period. In addition, a last observed analysis performed comparing the above per protocol analysis at the 1 year aggregate examination to a last observed analysis reveals no significant difference in success or failure outcomes. Of the 62 eyes not evaluated at the 12 month aggregate examination, 31 eyes were seen at 6 months, 17 eyes were seen at 3 months, 9 eyes were seen at 1 month and 5 eyes were seen in the period less than one month. The following outcomes are found when using these last observed values: 222/317 (70.0%) were a success, 43/317 (13.6%) were a failure; and 52/317 (16.4%) exhibited no change.

2. Success/Failure by Treatment Goals

a. To Improve Comfort

	3 M (n=121)	6 M (n=98)	12 M (n=77)	1 Yr Aggregate (n=87)
Success	105 (86.8%)	85 (86.7%)	67 (87.0%)	77 (88.5%)
Failure	16 (13.2%)	13 (13.3%)	10 (13.0%)	10 (11.5%)

b. To Improve Vision

	3 M (n=199)	6 M (n=167)	12 M (n=141)	1 Yr Aggregate (n=164)
Success	127 (63.8%)	112 (67.0%)	91 (64.6%)	104 (63.4%)
No Change	34 (17.1%)	25 (15.0%)	25 (17.7%)	33 (20.1%)
Failure	38 (19.1%)	30 (18.0%)	25 (17.7%)	27 (16.5%)

The clinical results for the patients treated for the two primary goals, of improving comfort and improving vision, demonstrated a sustainable success rate throughout the follow up period.

3. Success/Failure by Treatment Category

a. Corneal Dystrophies

	3 M (n=80)	6 M (n=68)	12 M (n=58)	1 Yr Aggregate (n=68)
Success	63 (78.7%)	59 (86.8%)	46 (79.4%)	52 (76.4%)
No Change	8 (10.0%)	3 (4.4%)	6 (10.3%)	8 (11.8%)
Failure	9 (11.3%)	6 (8.8%)	6 (10.3%)	8 (11.8%)

b. Scars/Other Irregular Surfaces

	3 M (n=199)	6 M (n=166)	12 M (n=138)	1 Yr Aggregate (n=160)
Success	130 (65.3%)	109 (65.6%)	94 (68.1%)	109 (68.1%)
No Change	26 (13.1%)	22 (13.3%)	19 (13.8%)	25 (15.6%)
Failure	43 (21.6%)	35 (21.1%)	25 (18.1%)	26 (16.3%)

The success rates after the PTK clinical investigation vary depending on the condition being treated. 76.4% of dystrophy patients treated were a success at the 1 yr aggregate, while 68.1% of scar patients were a success at this time period.

c. Recurrent Erosion Syndrome

The success rate after the PTK procedure at 3 months was 44/46 (95.7%); at 6 months 33/36 (91.7%); at 12 months 21/25 (84.0%) and at the 1 yr aggregate examination 24/27 (88.9%). Because of the limited numbers of patients, this category was subsequently excluded from the indication for approval.

4. Success/Failure for Penetrating Keratoplasty Candidates

	3 M (n=128)	6 M (n=106)	12 M (n=85)	1 Yr Aggregate (n=102)
Success	90 (70.3%)	76 (71.7%)	61 (71.8%)	72 (70.6%)
No Change	10 (7.8%)	9 (8.5%)	9 (10.6%)	14 (13.7%)
Failure	28 (21.9%)	21 (19.8%)	15 (17.6%)	16 (15.7%)

Of the 149 patients designated preoperatively as penetrating keratoplasty candidates, 15 (10.1%) of eyes subsequently underwent penetrating keratoplasty during this clinical trial. Patients who otherwise may have undergone penetrating keratoplasty, had a success rate of 70.6% one year or longer after PTK in the clinical investigation study period.

C. Conclusion

The clinical data provide reasonable assurance that the Summit Technology's Excimer Laser Systems are safe and effective for the treatment of signs and symptoms of corneal dystrophies, corneal scars, opacities, and irregular surfaces.

XI. Panel Recommendations

On March 21, 1994, a majority of the Ophthalmic Devices Panel recommended that the premarket approval for the excimer laser be conditionally approved, with the conditions that one year or more of follow-up data be submitted for review by the Panel and the FDA, and that the recurrent erosion indication be removed at this time. The Panel suggested that a prospective randomized trial to alternative therapy for recurrent erosion syndrome should be considered. The Panel subsequently received and reviewed the requested information. An approval recommendation was received from a majority of the Panel.

XII. FDA Decision

On June 7, 1994, FDA issued an approvable letter to Summit Technology which requested an update of the clinical data to include one year or more of follow-up results. Labeling changes, including removing the recurrent erosion syndrome indication, to concur with the panel's recommendations and FDA's recommendations were requested. In an amendment received by FDA on July 20, 1994, Summit submitted the requisite material and revisions to the device's labeling. Further modifications to the Operating Manual and the Physician Guidelines were requested. Summit submitted the revisions in January, February and March of 1995. FDA found the submitted data adequately addressed the issues raised by the Agency and the Panel, and FDA issued an approval order to Summit Technology, Inc. on March 10, 1995. Good Manufacturing Practices (GMP) inspections, performed on July 11-14, 1994 and January 18-26, 1995, showed that the company was in compliance with the GMP regulations.

XIII. Approval Specifications

Continued approval of the device is contingent upon the submission of postapproval reports to the Food and Drug Administration as described in the conditions of approval enclosed in the approval letter (Attachment A), and the conditions that Summit must also report to the Agency the following information as they become available to Summit:

1. any instances of device tampering (such as the removal of the PRK lockout mechanisms) or device usage outside of the approved indications;

2. any excimer systems that were exported under the 801(e) order, but are now back in use in the U.S.; and,

3. all complications to be included in the annual reporting.

A copy of the Physician Guidelines for Phototherapeutic Keratectomy is attached (Attachment B).

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For a more complete listing of the publications on the excimer laser, please refer to the appendix in the Physician Guidelines (in attachment B).

SUMMIT TECHNOLOGY®, INC.
EXCIMED®/OMNIMED/SVS APEX
EXCIMER LASER SYSTEM
PHYSICIAN GUIDELINES

PHOTOTHERAPEUTIC KERATECTOMY

CAUTION: RESTRICTED DEVICE: U.S. Federal law restricts this device to sale, distribution, and use by or on the order of a physician. U.S. Federal law restricts the use of this device to physicians who have been trained in its calibration and operation. U.S. Federal law restricts the use of this device to physicians with experience in the medical and surgical management and treatment of corneal pathology. This device is not for use in mobile clinics.

A. BACKGROUND:

Summit Technology's ExciMed/OmniMed/Apex Excimer Laser System has been designed to perform Phototherapeutic Keratectomy (PTK) clinical procedures. The following physician guidelines have been developed based on the multicenter clinical study conducted in the United States to provide you, the physician, with recommendations concerning the use of the Summit Technology Excimer Laser System for the Phototherapeutic Keratectomy technique.

A Summit Technology training program should be completed by the physician **prior** to performing their first PTK clinical procedures. This training program will include (1) attendance of the physician and staff at an inservice program conducted by Summit regarding the recommended operation of the Company's Excimer Laser System, (2) completion of a series of in vitro training exercises developed by Summit Technology's Clinical Department intended to familiarize the physician and staff with the recommended Phototherapeutic Keratectomy clinical technique and (3) the performance of a center's initial patients in conjunction with the presence of a Summit Technology Clinical Specialist.

The physician and staff should read the User's Manual and the following Phototherapeutic Keratectomy Physician Guidelines thoroughly in preparation for the first clinical procedures. In addition, Summit Technology strongly recommends that new physicians visit an active center experienced in Phototherapeutic Keratectomy using the Summit Excimer Laser System as well as review the bibliography of peer review journal publications regarding this corneal surgical technique.

B. INDICATIONS FOR USE:

The Summit Technology ExciMed/OmniMed/Apex Excimer Laser System is indicated for use in Phototherapeutic Keratectomy (PTK) procedures which treat superficial pathology located in the anterior 100 microns of the cornea, where the proposed treatment area is at least 400 microns in thickness, and where other less invasive treatments have failed or are not possible, such as contact lens intolerance. This indication is limited to patients with decreased visual acuity or symptoms of pain and discomfort of sufficient severity to cause disability for the patients with any of the following conditions:

1. Superficial Corneal Dystrophies (granular, lattice, and Reis-Buckler's)

2. Epithelial Basement Membrane Dystrophy

3. Irregular corneal surfaces (secondary to Salzmann's degeneration, keratoconus nodules and other irregular surfaces)

4. Corneal Scars and Opacities (post-traumatic, post-surgical, post-infectious and secondary to pathology).

C. CONTRAINDICATIONS FOR USE:

1. The Phototherapeutic Keratectomy procedure should **not** be performed in patients with uncontrolled vascular disease or autoimmune disease which is known to affect corneal healing or cause corneal melting.

2. The Phototherapeutic Keratectomy procedure should **not** be performed in patients who are immunocompromised or on drugs or therapy which suppress the immune system.

D. WARNINGS:

Reactivation of herpes simplex virus has occurred after the Phototherapeutic Keratectomy procedure and is **not** recommended in patients with a history of herpes simplex virus corneal infection. However, if a patient's only alternative therapy is a penetrating keratoplasty and the patient is informed regarding the possibility of

reactivation of the virus after the PTK procedure, PTK may be considered in these patients.

E. PRECAUTIONS:

1. The safety and effectiveness of the ExciMed/OmniMed/Apex Excimer Laser System has not been established in:

   a. The treatment of superficial corneal erosion syndrome;

   b. Patients under 21 years of age;

   c. Pregnant women;

   d. Patients whose pathologic condition would require the area of ablation to be deeper than 100 microns;

   e. Patients whose proposed treatment area of the cornea is less than 400 microns thick.

2. Consideration should be given to the following in determining appropriate patients for Phototherapeutic Keratectomy procedures:

   a. The potential induced refractive error would include significant uncorrectable anisometropia and/or induced astigmatism; or

   b. The patient is unable to cooperate during the procedure because of the potential difficulty aligning the laser beam and keeping the eye steady during the procedure.

3. During the Phototherapeutic Keratectomy Procedure:

   a. Do not use alcohol, cocaine or any other substances to remove the epithelium. Application of these substances may influence the ablation rate of the excimer laser energy and could lead to a poor procedural result.

   b. The HeNe aiming beams mark the image plane of the excimer beam. The desired vertical area of effect is located where the two HeNe beams appear as one spot. In order to assure that the patient is not exposed to hazardous levels of laser energy, the HeNe beams should not be fired at the patient continuously for longer than 6.5 minutes.

   c. Do not lean on the surgical microscope or the Excimer Laser System during laser energy delivery.

F. ADVERSE REACTIONS:

Adverse reactions were calculated up to the 12 month or later evaluation. Adverse reactions reported here are based upon new events which occurred postoperatively (such as cataract or infection); or where the complication continued to interfere with the patient's vision or comfort (such as glare, corneal scarring, foreign body sensation, or patient discomfort).

The following adverse reactions have been reported in clinical studies with the use of the ExciMed/OmniMed/Apex Laser System for the performance of Phototherapeutic Keratectomy clinical procedures: corneal scarring (35/255, 13.7%); glare (31/255, 12.2%); decrease of best corrected visual acuity (24/245, 9.8%); induced astigmatism (23/255, 9.0%); foreign body sensations (15/255, 5.9%); patient discomfort (12/255, 4.7%); corneal epithelial defect (9/255, 3.5%); corneal infection/ulceration (5/255, 2.0%); and persistent corneal edema (5/255, 2.0%). The following complications occurred at a rate less than 2.0%: bacterial keratitis (attributed to contact lens wear), cataract, delayed re-epithelialization, epiphora, graft rejection episodes (reversed with steroids), reactivation of herpes simplex, hyphema, iritis, keratitis attributed to antibiotics, neovascularization, and recurrence of pterygium.

G. CLINICAL EXPERIENCE:

Success/failure of the clinical procedure was determined based on the preoperative goal of the case and the postoperative result at the 3, 6, 12 and 12 month or longer follow up examinations. The preoperative goal was determined by the investigator and the postoperative result (i.e. success/failure determination) was also determined by the investigator based upon the achievement of the preoperative goal.

The goals of the majority of procedures performed were to improve vision and/or comfort. In cases where the goal was to improve vsion, a minimum of two lines of improvement in best corrected vision was required in order to be considered a success. In cases where the goal was to decrease pain or discomfort, the determination of success was based upon an evaluation by the physician and the patient. The patient's subjective evaluation of pain was rated by a survey with a scale of 0 to 5 (0 being none, 5 being severe).

Procedural Success was demonstrated at the 3 month postoperative examination in 237/325 (72.9%) of eyes; at the 6 month postoperative examination in 201/270 (74.4%) of eyes; at the 12 month postoperative examination in 161/221 (72.9%) of eyes; at the 12 month or later examination in 185/255 (72.6%) of eyes. The overall procedural success rate was stable throughout the postoperative follow up period.

In the subset of patients treated with the primary goal of improved comfort, Procedural Success was demonstrated at the 3 month postoperative examination in 105/121 (86.8%) of eyes; at the 6 month postoperative examination in 85/98 (86.7%) of eyes; at the 12 month postoperative examination in 67/77 (87.0%) of eyes; at the 12 month or later examination in 77/87 (88.5%) of eyes.

In the subset of patients treated with the primary goal of improved vision, Procedural Success was demonstrated at the 3 month postoperative examination in 127/199 (63.8%) of eyes; at the 6 month postoperative examination in 112/167 (67.0%) of eyes; at the 12 month postoperative examination in 91/141 (64.5%) of eyes; at the 12 month or later examination in 104/164 (63.4%) of eyes.

In the subset of patients who were classified prior to PTK as Penetrating Keratoplasty candidates, Procedural Success was demonstrated at the 3 month postoperative examination in 90/128 (70.3%) of eyes; at the 6 month postoperative examination in 76/106 (71.7%) of eyes; at the 12 month postoperative examination in 61/85 (71.8%) of eyes; at the 12 month or later examination in 72/102 (70.6%) of eyes. A total of 149 of the 398 eyes enrolled in the PTK clinical trial were classified prior to PTK as Penetrating Keratoplasty candidates. Of the 149 Penetrating Keratoplasty candidates enrolled in the PTK clinical trial, 15 (10.1%) eyes underwent a Penetrating Keratoplasty during this clinical trial. In the other 134 eyes (89.9%) who may have undergone a Penetrating Keratoplasty, that procedure was avoided during the duration of this clinical trial because of a PTK procedure.

H. INFORMATION FOR USE:

1. Ancillary Equipment:

The following items will be needed when performing Phototherapeutic Keratectomy procedures with the Summit ExciMed/OmniMed/SVS Apex Excimer Laser System:

a. Materials to perform Excimer Laser System PTK Beam Profile Test
b. Patient Bed or Chair capable of performing fine movements (comparable to Dexta chair supplied by Summit Technology)
c. Sterile eye speculum
d. Gauze pads and tape
e. Hydroxypropyl Methylcellulose (optional, depending on the procedure to be performed)
f. Agent to constrict the pupil
g. Weck-cel® or similar sponges

h. Topical anesthetics
i. Slit Lamp available near the Excimer Laser System
j. Standard instrument used for epithelium removal (optional, depending upon procedure to be performed)
k. Fine forceps (optional, depending upon procedure to be performed).

2. Excimer Laser System Parameters:

Repetition Rate:	System set at 10 Hz
Pulse Energy Density:	System set at 180 mJ/cm^2
Zone Diameter:	1.0 mm to 6.5 mm in 0.1 mm increments
Number of Pulses:	The system allows the physician to select the number of pulses from 1 to 5,000. The procedure should be performed with the minimum number of pulses required to treat the condition.

3. Directions: Phototherapeutic Clinical Procedure
Phototherapeutic Keratectomy clinical procedures may involve the use of the Summit Technology Excimer Laser System as the sole therapeutic modality or it may be used in conjunction with another mechanical therapeutic procedure where the role of the laser is to smooth an irregular corneal surface after the non-laser portion of the procedure has been completed.

Conventional mechanical tissue removal methods should be used to remove as much of the area of pathology as possible. Once the mechanical tissue removal is completed, the ExciMed/OmniMed/ Apex Excimer Laser System can then be used to create a smooth surface over the area of pathology.

PRE-PROCEDURE: (All Cases)

a. Turn on the Excimer Laser System and allow the system to warm up. Refer to the ExciMed/ OmniMed/Apex Excimer Laser System User's Manual for start up and operating instructions regarding your laser system.

b. If it is the first procedure of the day, the PTK Beam Profile Test should be performed in accordance with Summit Technology's Beam Profile Test Instructions. There is no need to perform the Beam Profile Test between procedures if more than one procedure is performed on the same day.

If your test results meet the criteria specified in the Beam Profile Test Instructions, proceed with the Phototherapeutic Keratectomy clinical procedure. If your test results do **not** meet the test criteria; (1) contact Summit's Customer Service Department or your Summit Service Representative immediately and (2) do **not** use the laser on patients because of the potential for improper results.

c. Apply topical anesthetic to the operative eye.

d. Constrict the patient's pupil. Sufficient time should be allowed to ensure for pupil constriction before the start of the procedure (i.e. 30 minutes).

e. Place the patient on a chair with the operative eye centered under the Excimer Laser delivery system.

f. If the eye to be treated is sighted, patch the patient's eye **not** scheduled for treatment. A patch may also be placed on the side of the head next to the treated eye to collect excess fluid from the eye undergoing the laser procedure. Topical anesthetic may be given to relax the reflexes of the untreated eye.

   If the eye to be treated is **not** sighted, the patient's other eye may be used to assist in fixation and should not be patched. A clear plastic eye shield may be used to prevent reflected 193 nm excimer beam from striking the untreated eye.

g. Apply topical anesthetic to the operative eye. Place the speculum in the eye. Reapply anesthetic drops to the eye to be treated throughout the procedure to ensure adequate anesthesia.

h. Turn on the helium-neon aiming beams.

i. Prior to laser delivery, the physician should explain to the patient in detail what will occur during laser energy delivery in terms of the patient's need to fixate their eye, and the light, noise and smell produced by the laser system. The patient should be made aware that there is no pain associated with the laser beam striking the cornea but that the initial sound may be startling.

OPERATIVE TECHNIQUE-Polish Only:
(Relatively smooth surface-i.e. Dystrophies, Scars)

a. Select the Phototherapeutic Keratectomy procedure and enter the desired number of pulses and zone diameter of the treatment area into the Control Pad. Refer to the User's Manual for details on how to enter this information.

b. Arm and test the laser prior to beginning any mechanical portion of the treatment including epithelium removal to ensure that the laser will come out of the test mode allowing delivery of laser energy.

If the laser remains armed for more than 10 minutes without firing, the system will automatically disarm and you will need to clear the laser and rearm and retest the system.

NOTE: When epithelium removal is required, do **not** use alcohol, cocaine or any other substances to remove the epithelium. Application of these substances may influence the ablation rate of the excimer laser energy and could lead to a poor procedural result.

c. The goal of the procedure should be to perform the procedure with the **minimum number** of pulses with which the area of pathology can be feasibly treated.

NOTE: The Phototherapeutic Keratectomy procedure is intended for treatment of pathologic conditions in the anterior portion of the cornea. Areas of treatment should be located within the anterior 100 microns of the cornea. However, the physician should closely monitor the number of pulses being delivered and have a slit lamp available in order to closely monitor the amount of tissue being removed. The amount of tissue removed in each case should be carefully monitored with the goal of removing the minimum amount of tissue possible.

d. The appropriate zone diameter should be selected based on the characteristics of the pathology to be treated.

e. Ask the patient to keep their operative eye focused on the fixation target inside the laser downtube if a central treatment is to be performed. For a peripheral treatment the patient should find a point in the room and fixate on it.

f. Prepare the eye for treatment. The manner in which the Hydroxypropyl Methylcellulose is applied to the eye is dictated by the condition to be treated. In the case that the corneal surface is smooth, it may not be necessary to begin the procedure using Methylcellulose.

Role of Methylcellulose:
The role of the Methylcellulose is to inhibit laser ablation to healthy, uninfected areas of the cornea. Applying too much

Methylcellulose will completely inhibit ablation of the cornea, including the pathologic condition which is to be removed.

As noted during the in vitro exercises, areas of the cornea where Methylcellulose has been applied and those areas where it has not been applied will appear differently during laser energy delivery. The cornea appears darker than the Methylcellulose during laser energy delivery. Also the sound of tissue ablation will differ from the sound of Methylcellulose ablation. Tissue being ablated has a loud, high frequency sound. When the laser strikes Methylcellulose the sound is a lower frequency and softer. Do not confuse the sound of a small spot ablating tissue with the sound of a large spot striking Methylcellulose. The physician should become familiar with these differences during the in vitro exercises.

g. The patient should be aligned so that the helium neon aiming beams appear as one spot on the anterior surface of the cornea in the center of the area to be treated.

NOTE: The HeNe aiming beams mark the image plane of the excimer beam. The desired vertical area of effect is located where the two HeNe beams appear as one spot. In order to assure that the patient is not exposed to hazardous levels of laser energy, the HeNe beams should not be fired at the patient continuously for longer than 6.5 minutes.

NOTE: Do **not** lean on the surgical microscope or the Laser System during laser energy delivery.

h. Press the Footswitch to begin firing the laser.

i. The physician should observe the procedure through the operating microscope.

During this procedure it may be advantageous to move the patient's eye while the laser is firing. This movement of the eye under the laser results in a polishing effect and can be accomplished either by moving the eye directly with forceps or in some cases moving the patient's head, having the patient continue to fixate at one point. The number of laser pulses should be closely monitored during laser energy delivery to meet the objective of delivering the minimum number of pulses necessary.

Once the procedure begins, it is not critical that the Helium Neon beams are exactly coincident.

To determine the endpoint of the procedure, move the patient to the slit lamp. Examine how much of the desired tissue has been removed and remember it is always possible to return and remove more tissue if necessary, but it is impossible to replace tissue.

It is not always necessary to remove all of an opacity to get a good visual result.

j. If the patient is moved to the slit lamp during the procedure and the procedure is to be continued, the physician should realign the patient with the HeNe beams prior to re-initiating laser energy delivery.

k. If Methylcellulose is not used at the beginning of the procedure, it may be necessary to add it as the procedure progresses to ensure that the resulting corneal surface will be as smooth as possible.

OPERATIVE TECHNIQUE-Debride and Polish:
(Highly irregular surfaces and elevated scars, to be smoothed)

a. Select a Phototherapeutic Keratectomy procedure and enter the desired number of pulses and zone diameter of the treatment area into the Control Pad. Refer to the User's Manual for details on how to enter this information.

b. Arm and test the laser prior to beginning any mechanical portion of the treatment to ensure that the laser will come out of the test mode allowing delivery of laser energy.

If the laser remains armed for more than 10 minutes without firing, the system will automatically disarm and you will need to clear the laser and rearm and retest the system.

NOTE: When epithelium removal is required, do **not** use alcohol, cocaine or any other substances to remove the epithelium. Application of these substances may influence the ablation rate of the excimer laser energy and could lead to a poor procedural result.

c. Mechanically remove any tissue peaks in the area to be treated. For example, for nodular conditions attempt to remove high nodules mechanically prior to lasing.

d. The goal of the procedure should be to perform the procedure with the **minimum number** of pulses with which the area of pathology can be feasibly treated.

NOTE: The Phototherapeutic Keratectomy procedure is intended for treatment of pathologic conditions in the anterior portion of the cornea. Areas of treatment should be located within the anterior 100 microns of the cornea. However, the physician should closely monitor the number of pulses being delivered and have a slit lamp available in order to closely monitor the amount of tissue being removed. The amount of tissue removed in each case should be carefully monitored with the goal of removing the minimum amount of tissue possible.

The appropriate zone diameter should be selected based on the characteristics of the pathology to be treated.

NOTE: If there is a High Degree of Surface Irregularity (High Peaks and Valleys) in Treatment Area:

i. Use a small zone diameter to first smooth off the high peaks which could not be mechanically removed in the treatment area.

ii. Change to a larger zone diameter for valleys/low areas of pathology to be treated.

For example, nodules should be treated by first attempting to mechanically debride the nodule. If this is not successful, select a spot smaller than the nodule for initial ablation and a spot just larger for final ablation. If the nodule is successfully removed mechanically use the larger spot for polishing the area.

e. Ask the patient to keep their operative eye focused on the fixation target inside the laser downtube if a central treatment is to be performed. For a peripheral treatment the patient should find a point in the room and fixate on it.

f. Prepare the eye for treatment. The manner in which the Hydroxypropyl Methylcellulose is applied to the eye is dictated by the condition to be treated.

Role of Methylcellulose:
The role of the Methylcellulose is to inhibit laser ablation to healthy, uninfected areas of the cornea. Applying too much Methylcellulose will completely inhibit ablation of the cornea, including the pathologic condition which is to be removed.

As noted during the in vitro exercises, areas of the cornea where Methylcellulose has been applied and those areas where it has not been applied will appear differently during laser energy delivery. The cornea appears darker than the Methylcellulose during laser energy delivery. Also the sound of tissue ablation will differ from the

sound of Methylcellulose ablation. Tissue being ablated has a loud high frequency sound. When the laser strikes Methylcellulose the sound is a lower frequency sound and softer. Do not confuse the sound of a small spot ablating tissue with the sound of a large spot striking Methylcellulose. The physician should become familiar with these differences during the in vitro exercises.

When treating an irregular surface with high/low areas (i.e. Salzmann's), discrete nodules can be surrounded with Methylcellulose. When the nodule has been leveled the area can be blended into the surrounding stroma with additional Methylcellulose.

In the case of an extremely rough cornea, the entire cornea should be covered with Methylcellulose. The Methylcellulose should be replenished frequently. If excess Methylcellulose gets onto the nodule when it is being applied, it can be wiped off with a Weck-cel.

g. Position the patient so that the red Helium Neon aiming beams are coincident on the area to be treated.

NOTE: The HeNe aiming beams mark the image plane of the excimer beam. The desired vertical area of effect is located where the two HeNe beams appear as one spot. In order to assure that the patient is not exposed to hazardous levels of laser energy, the HeNe beams should not be fired at the patient continuously for longer than 6.5 minutes.

NOTE: Do **not** lean on the surgical microscope or the Excimer Laser System during laser energy delivery.

h. Press the Footswitch to begin firing the laser.

i. The physician should observe the procedure through the operating microscope.

If nodules or highly uneven tissue is present, the physician should begin firing the laser at the highest points of the pathology replenishing the Methylcellulose as needed. During this procedure it may be advantageous to move the patient's eye while the laser is firing. This movement of the eye under the laser results in a polishing effect and can be accomplished either by moving the eye directly with forceps or in some cases moving the patient's head, having the patient continue to fixate at one point. The number of laser pulses should be closely monitored during laser energy delivery to meet the objective of delivering the minimum number of pulses necessary.

Once the procedure begins, it is not critical that the Helium Neon beams are exactly coincident.

j. To determine the endpoint of this procedure, move the patient to the slit lamp. Examine how much of the desired tissue has been removed and remember it is always possible to return and remove more tissue if necessary, but it is impossible to replace tissue.

   It is not always necessary to remove all of a scar or pathology to get a good visual result.

k. If the patient is moved to the slit lamp during the procedure and the procedure is to be continued, the physician should realign the patient with the HeNe beams prior to re-initiating laser energy delivery.

OPERATIVE TECHNIQUE-Epithelial Basement Dystrophy:

a. Select a Phototherapeutic Keratectomy procedure and enter between 15 and 40 pulses. The number of pulses to be entered is dependent upon the size of the area to be treated. If only one area is present enter 15 pulses. If more than one area is present, estimate how many seconds it would take to "spray paint" the entire area and multiply that by 10. This is the number of pulses to enter. This should be no greater than 40 pulses. Enter the desired zone diameter, based on the area of the epithelial basement dystrophy, into the Control Pad. Refer to the User's Manual for details on how to enter this information.

b. Arm and test the laser prior to beginning epithelium removal to ensure that the laser will come out of the test mode allowing delivery of laser energy.

   If the laser remains armed for more than 10 minutes without firing, the system will automatically disarm and you will need to clear the laser and rearm and retest the system.

NOTE: When epithelium removal is required, do **not** use alcohol, cocaine or any other substances to remove the epithelium. Application of these substances may influence the ablation rate of the excimer laser energy and could lead to a poor procedural result.

c. Mechanically remove the epithelium in the area to be treated. Thoroughly clean the surface with a Weck-cel. Be sure the epithelium is completely removed in the area to be treated.

d. Ask the patient to keep their operative eye focused on the fixation target inside the laser downtube if a central treatment is to be performed. For a peripheral treatment the patient should find a point in the room and fixate on it.

e. The patient should be aligned so that the helium neon aiming beams appear as one spot on the anterior surface of the cornea in the center of the area to be treated. If the cornea is clear and the procedure is being performed in the center of the cornea, two HeNe beams will appear at 3 and 9 o'clock on the iris. It is the one central HeNe spot on the cornea that the physician should concentrate on.

NOTE: The HeNe aiming beams mark the image plane of the excimer beam. The desired vertical area of effect is located where the two HeNe beams appear as one spot. In order to assure that the patient is not exposed to hazardous levels of laser energy, the HeNe beams should not be fired at the patient continuously for longer than 6.5 minutes.

NOTE: Do **not** lean on the surgical microscope or the Excimer Laser System during laser energy delivery.

f. Press the Footswitch to begin firing the laser.

g. The physician should observe the procedure through the operating microscope.

If the eye moves during the procedure, the physician should stop firing the laser, ask the patient to re-fixate and begin firing again.

Once the procedure begins, it is not critical that the Helium Neon beams are exactly coincident.

h. The endpoint of epithelial basement dystrophy treatment is when up to 40 laser pulses have been fired.

POSTOPERATIVE TECHNIQUE: (All Cases)

a. The patient should be moved to the slit lamp to allow the physician to examine the operative eye after the laser procedure. If the epithelium was removed during the procedure and the edges of remaining epithelium surrounding the laser ablation have been folded back or are overlapping they should be smoothed back into their original position to facilitate re-epithelialization.

b. Remove the eyelid speculum.

c. In reference to postoperative medications during both the immediate postoperative period and for the first several months after the procedure, the physician should refer to the existing peer review literature to determine the appropriate course of action.

d. Patching the eye is recommended for the first 24 hours, after that patching is at the discretion of the physician.

e. Certain patients may experience postoperative pain for the first 24 hours after the PTK procedure. Systemic postoperative pain medication may be prescribed at the physician's discretion.

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