

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

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I. GENERAL INFORMATION

Device Generic Name: Ophthalmic Excimer Laser System

Device Trade Name: SVS Apex Plus Excimer Laser Workstation, emphasis® discs (K and L), and axicon

Applicant's Name and Address: Summit Technology, Inc.
21 Hickory Drive
Waltham, MA 02154 USA

Premarket Approval Application (PMA) Supplement Number: P930034/S12

Date of Notice of Approval to Applicant: October 21, 1999

The SVS Apex Plus Excimer Laser Workstation was approved on February 7, 1997 for both phototherapeutic keratectomy (P910067/S1) and myopic photorefractive keratectomy using a 6.0 mm ablation zone in patients 21 years of age or older with myopia 1.5 to 7.0 D and concomitant astigmatism ≤ 1.5 D and for whom the refractive change for the one year prior to the laser treatment is within ± 1.0 D (P930034/S2). On March 11, 1998 (P930034/S9), the indication for the laser, with the addition of emphasis® discs M, was expanded to include toric photorefractive keratectomy for the reduction or elimination of mild to moderate myopia (-1.00 to < -6.00 D) and concomitant reduction or elimination of mild to moderate astigmatism (-1.00 to < -4.00 D), in which the combined attempted correction must be < -6.00 D spherical equivalent at the spectacle plane. The sponsor submitted the current supplement to further expand the indication statement. The updated pre-clinical and clinical work to support this expanded indication is provided in this summary. For more information on the data that supported the approved indications, the Summaries of Safety and Effectiveness Data to the respective PMA applications should be requested from the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20857. Please identify Docket # 95M-0179 for phototherapeutic keratectomy, #96M-0274 for myopic photorefractive keratectomy, or #98M-0329 for toric photorefractive keratectomy. The summaries can also be found on the FDA CDRH Internet Home Page located at <http://www.fda.gov/cdrh/pmapage.html>.

II. INDICATIONS FOR USE

The SVS Apex Plus Excimer Laser Workstation, emphasis® discs K and L, and axicon are indicated to perform hyperopic photorefractive keratectomy (PRK):

- for the reduction or elimination of mild to moderate hyperopia (+1.5 to + 4.0 D) with low astigmatism (<-1.00D) at the spectacle plane;
- in patients with documentation of a stable manifest refraction ($\pm 0.5D$) over the past year; and,
- in patients who are 21 years of age or older.

III. CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS

A. CONTRAINDICATIONS:

Hyperopic PRK treatment should not be performed in:

1. patients with uncontrolled vascular disease or auto-immune diseases because it is well known that these patients have difficulty in corneal healing and are more susceptible to corneal melting;
2. women who are pregnant and/or nursing, due to the potential for temporary fluctuation in refraction during this time;
3. patients with signs of keratoconus since eyes with this condition may have unstable corneas;
4. patients known to have a previous history of keloid formation because their corneal healing response is less predictable; or,
5. patients taking Accutane (isotretinoin) or Cordarone (amiodarone hydrochloride)

B. WARNINGS:

1. Hyperopic PRK should not be performed in patients whose refractive history is unstable since an accurate pretreatment baseline refraction for the calculation of the desired correction can not be obtained.
2. Hyperopic PRK is not recommended in patients with Herpes Simplex Virus or Herpes Zoster since cases of herpes reactivation have been

reported after use of the excimer laser. Further clinical experience is necessary regarding the use of the 193 nanometer excimer laser wavelength in patients with these conditions.

C. PRECAUTIONS:

1. Hyperopic PRK should not be performed in patients who are unable to cooperate during the treatment because of the potential difficulty in aligning the laser beam and keeping the eye steady during the treatment.
2. Prior to removing the epithelium, the practitioners should arm and test the laser to ensure that it is ready to deliver laser energy.
3. The long term safety and effectiveness of Hyperopic PRK has not been established.
4. The safety and effectiveness of Hyperopic PRK in patients who are under 21 years of age have not been established.
5. The safety and effectiveness of Hyperopic PRK in patients taking Immitrex (sumatriptan succinate) have not been studied.
6. Although the effects of Hyperopic PRK on visual performance under poor lighting conditions have not been determined, it is possible that post-procedure patients will find it more difficult than usual to see in conditions such as very dim light, rain, snow, fog, or glare from bright lights at night.
7. Patients with known sensitivity to any of the treatment medications
8. Patients with a history of glaucoma because of the potential for a strong response to postoperative steroids.

IV. DEVICE DESCRIPTION

The Apex Plus, emphasis® discs (K and L), and axicon constitute the device that is the subject of this PMA supplement. Hyperopic correction is delivered by the laser and disc within the central 6.5 mm diameter, and by the laser and axicon from 6.5 to 9.5 mm. The optical zone or the area that provides the actual refractive correction is within the central 5.0 mm diameter.

The excimer laser is the same one previously approved for Toric PRK, but with the addition of the software for hyperopic correction. The emphasis® discs for hyperopic correction are models K and L. Ten discs are made available for corrections from +1.5 to

+ 4.0 D. The axicon is an optical lens that converts the round shape of the excimer beam into a ring shape

V. ALTERNATE PRACTICES AND PROCEDURES

There are currently three other alternatives for the correction of mild to moderate hyperopia:

- Contact Lenses
- Hexagonal Keratotomy
- Spectacles

Each alternative has its own advantages and disadvantages. A prospective patient should fully discuss with his/her care provider these alternatives in order to select the correction method that best meets his/her expectation and lifestyle.

VI. MARKETING HISTORY

Since 1995, Summit Technology, Inc. has sold or distributed over 300 Apex Plus worldwide. The Summit 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

During the immediate/early postoperative period, reported problems include: postoperative pain (first 24 to 48 hours), discomfort, double vision, foreign body sensation, ghost images, and peripheral corneal epithelial defect. These signs and symptoms appear to subside several months after surgery.

The adverse reactions reported at the postoperative examinations include: anterior stromal reticular haze, loss of best spectacle near or distance acuity, undercorrection, overcorrection, glare, halo, foreign body sensation, patient discomfort, ghost images, double images, light sensitivity, ptosis, dryness/night driving difficulties, persistent central corneal epithelial defect, peripheral corneal epithelial defect, and recurrent corneal erosion.

A rates of these adverse reactions at the 6 month visit, 12 month stability time point, and 18 month visit are found in the Summary of Clinical Study of this document (section IX.F.2.d).

VIII. SUMMARY OF PRECLINICAL STUDIES

Each disc was individually verified with a lensometer. In addition, nonclinical laboratory studies were performed to evaluate the achieved profiles (depth, width, and radius of curvature) in polymethylmethacrylate (PMMA). Sets of K and L discs were tested in PMMA to verify that their profiles follow an expected linear relationship of curvature (inverse radius) versus diopter.

A hazard analysis was performed to evaluate the effect of the hardware and software modifications for hyperopia correction. The safety or effectiveness of the device was not determined to be affected by the change.

IX. SUMMARY OF CLINICAL STUDY

The sponsor performed a clinical study of the K discs in the US and England under the auspices of an IDE G900142. The data from this study served as the basis for the approval decision. Specifically, safety and effectiveness outcomes at 12 months postoperative were assessed as stability is reached by that time. Outcomes at 18 months postoperatively and data from another site in England were also evaluated for confirmation. The IDE study is described in detail as follows.

A. STUDY OBJECTIVES

The overall reason for the Hyperopic PRK procedure was defined by two main treatment goals: improving uncorrected near vision or improving uncorrected distance vision. Since safety from this type of procedure has been demonstrated previously, the effectiveness of the device for the proposed indication was the primary objective of the study.

B. STUDY DESIGN

The study was a prospective, multi-center, two-arm cohort study where the primary control was the preoperative state of the treated eye (*i.e.*, comparison of pretreatment and post-treatment visual parameters in the same eye).

C. INCLUSION AND EXCLUSION CRITERIA

Enrollment in the Hyperopic PRK study was limited to patients in need of mild to moderate spherical corrections of +1.00 to +4.00 D; preoperative distance best spectacle corrected visual acuity (BSCVA) of 20/32 or better; preoperative near BSCVA of 20/30 or better; preoperative best contact lens over refraction corrected visual acuity ("BCCVA") that did not differ more than 11 letters from the BSCVA; and refractive stability within ± 1.00 D for a period of at least one year.

Subjects entering the near vision treatment group were required to have a preoperative near uncorrected visual acuity (UCVA) of worse than 20/40. Subjects entering the distance vision treatment group were required to have distance UCVA of worse than 20/40.

Patients were not permitted to enroll in the Hyperopic Study if they met any of the following exclusion criteria: functionally monocular (i.e., BSCVA of fellow eye worse than 20/40); difference of more than 1.00 D between preoperative MRSE and cycloplegic refraction spherical equivalent; more than 1.00 D of corneal astigmatism, history of glaucoma or a preoperative intraocular pressure of 21 mm Hg or greater; irregular astigmatism; progressive retinal pathology, such as diabetic retinopathy; clinically significant cataract; signs of keratoconus; previous intraocular or corneal surgery; any systemic autoimmune disease or disseminated vasculopathies; herpes simplex or herpes zoster; or are pregnant or nursing.

D. STUDY PLAN, PATIENT ASSESSMENTS, AND EFFICACY CRITERIA

All subjects were expected to return for follow-up examinations at 1, 3, and 7 days (only required at 7 days if not re-epithelialized at 3 days), and 1, 3, 6, 9, 12, 18 and 24 months postoperatively.

Subjects were permitted to have second eyes (fellow eyes) treated a minimum of three months after treatment of the first eye. In addition, subjects were eligible for retreatment if they had a stable UCVA of worse than 20/40 and a stable MRSE greater than +1.00 D. Retreatment was not permitted until at least six months after the initial treatment.

Preoperatively, the subject's medical and ocular histories were recorded. Immediately postoperative, re-epithelialization data were collected. The objective parameters measured during the study included best spectacle corrected visual acuity (near, distance, with and without glare), uncorrected visual acuity (near and distance), manifest and cycloplegic refraction, intraocular pressure, pupil size and status of the cornea, conjunctiva, anterior chamber, lens, vitreous, retina, and externals. Corneal topography was performed on all subjects preoperatively, and postoperatively in subjects with certain adverse reactions. Specular microscopy was performed on the first 50 subjects. A patient questionnaire was to be administered to all subjects preoperatively and postoperatively at 6, 12, 18 and 24 months.

The primary efficacy variables for this study were: improvement of near or distance UCVA based on the per eye treatment goal of the procedure, and predictability of manifest refraction spherical equivalent (MRSE).

E. STUDY PERIOD, INVESTIGATIONAL SITES, AND DEMOGRAPHICS

1. STUDY PERIOD AND INVESTIGATIONAL SITES

Subjects were treated between January 31, 1997 and September 29, 1998. The database for this PMA supplement reflected data collected through March 31, 1999 and included 201 eyes: 119 first eyes and 82 second eyes. There were eight investigational sites.

TABLE 1: INVESTIGATION SITES	
Principal Investigator/Co-Investigator and Site	Number of eyes treated
Peter Hersh, MD The Cornea and Laser Vision Institute Teaneck, NJ	17
Steven Wilson, MD Cleveland Clinic Cleveland, OH	20
Jonathan Rubenstein, MD/ Robert Mack, MD Rush Presbyterian-St. Luke's Eye Center Physicians Ltd. Chicago, IL	3
Michael Gordon, MD/Perry Binder, MD Vision Surgery and Laser Center San Diego, CA	49
Vance Thompson, MD Ophthalmology, Ltd Sioux Empire Medical Center Sioux Falls, SD	43
Helen Wu, MD/Roger Steinert, MD Lawrence Memorial Eye Clinic Medford, MA	31
Edward Manche, MD Stanford University Medical Center Stanford, CA	18
Prof. John Marshall/ Christopher G. Stephenson, MD United Medical and Dental Schools Department of Ophthalmology St. Thomas' Hospital London, England	20
TOTAL	201

2. DEMOGRAPHICS

The demographics of this study were predominantly female (66%) and Caucasians (94%). The mean age of the subjects treated was 55 ± 7 years with a range from 35 to 71. The majority of patients (53%) fell in the 50-

59 age decade. Preoperative patient characteristics that were found to associate with outcomes are discussed in section IX.F.2.f.

No patient in this study was younger than 35. The sponsor provided literature references for hyperopia in the younger population. The FDA Ophthalmic Devices Advisory Panel (the Panel) has previously recommended an age limit as low as 21 for this group of patients. Younger than 21 was not deemed acceptable because stability of refraction may not be reached in young patients. Based on the available data, the approved indication was limited to 21 years of age and older.

Table 2: Preoperative Characteristics															
Distance															
UCVA 20/40 or better*	24/168 (14.3%)														
UCVA 20/50 to 20/80	66/168 (39.3%)														
UCVA 20/100 or worse	78/168 (46.4%)														
*protocol deviation; to be excluded from PMA cohort															
Near															
UCVA 20/40 or better*	0														
UCVA 20/50 to 20/80	1/26 (3.8%)														
UCVA 20/100 or worse	25/26 (96.2%)														
*protocol deviation; to be excluded from PMA cohort															
Manifest refraction sphere (D)	<table> <tr> <td>>0.0 to <=1.0</td> <td>8/194 (4.1%)</td> </tr> <tr> <td>>1.0 to <=2.0</td> <td>89/194 (45.9%)</td> </tr> <tr> <td>>2.0 to <=3.0</td> <td>56/194 (28.9%)</td> </tr> <tr> <td>>3.0 to <=4.0</td> <td>28/194 (14.4%)</td> </tr> <tr> <td>>4.0 to <=5.0</td> <td>12/194 (6.2%)</td> </tr> <tr> <td>>6.0 to <=7.0</td> <td>1/194 (0.5%)</td> </tr> <tr> <td>Mean</td> <td>2.33 Std. Dev. 1.02</td> </tr> </table>	>0.0 to <=1.0	8/194 (4.1%)	>1.0 to <=2.0	89/194 (45.9%)	>2.0 to <=3.0	56/194 (28.9%)	>3.0 to <=4.0	28/194 (14.4%)	>4.0 to <=5.0	12/194 (6.2%)	>6.0 to <=7.0	1/194 (0.5%)	Mean	2.33 Std. Dev. 1.02
>0.0 to <=1.0	8/194 (4.1%)														
>1.0 to <=2.0	89/194 (45.9%)														
>2.0 to <=3.0	56/194 (28.9%)														
>3.0 to <=4.0	28/194 (14.4%)														
>4.0 to <=5.0	12/194 (6.2%)														
>6.0 to <=7.0	1/194 (0.5%)														
Mean	2.33 Std. Dev. 1.02														
Attempted Spherical Correction (D)	<table> <tr> <td>+1.6D (disc K102)</td> <td>70/194 (36.1%)</td> </tr> <tr> <td>+2.3D (disc K104)</td> <td>36/194 (18.6%)</td> </tr> <tr> <td>+3.1D (disc K106)</td> <td>35/194 (18.0%)</td> </tr> <tr> <td>+3.9D (disc K108)</td> <td>53/194 (27.3%)</td> </tr> </table>	+1.6D (disc K102)	70/194 (36.1%)	+2.3D (disc K104)	36/194 (18.6%)	+3.1D (disc K106)	35/194 (18.0%)	+3.9D (disc K108)	53/194 (27.3%)						
+1.6D (disc K102)	70/194 (36.1%)														
+2.3D (disc K104)	36/194 (18.6%)														
+3.1D (disc K106)	35/194 (18.0%)														
+3.9D (disc K108)	53/194 (27.3%)														
Cylinder (D)	<table> <tr> <td>0.00</td> <td>60/194 (30.9%)</td> </tr> <tr> <td>-0.25</td> <td>33/194 (17.0%)</td> </tr> <tr> <td>-0.5</td> <td>59/194 (30.4%)</td> </tr> <tr> <td>-0.75</td> <td>28/194 (14.4%)</td> </tr> </table>	0.00	60/194 (30.9%)	-0.25	33/194 (17.0%)	-0.5	59/194 (30.4%)	-0.75	28/194 (14.4%)						
0.00	60/194 (30.9%)														
-0.25	33/194 (17.0%)														
-0.5	59/194 (30.4%)														
-0.75	28/194 (14.4%)														

F. DATA ANALYSIS AND RESULTS

1. PREOPERATIVE CHARACTERISTICS

Table 2 contains a summary of the preoperative acuity and refraction. Note that per protocol, subjects with preoperative refractive error greater than that specified in the inclusion criteria can be enrolled in the study as long as the correction that was being sought fell within the range specified for the study. The attempted correction is therefore not indicative of a subject's preoperative refractive error, but rather dependent on the treatment goal for each eye: to improve near or distance vision.

2. POSTOPERATIVE RESULTS

a. Accountability and definition of the PMA cohort

At the 12 month visit, 178 eyes were available for analysis, yielding an accountability rate of 92% (table 3). The 178 eyes represented the cohort available for safety analysis at twelve months.

At twelve months, the PMA cohort or the cohort available for the effectiveness analysis consisted of 165 eyes. Six protocol deviated and seven retreated eyes were excluded from this PMA cohort.

Status	1 months	3 months	6 months	9months	12 months	18 months
Discontinued (Death)	0	0	0	1	2	2
Not Eligible for Interval	0	0	0	4	5	137
Unavailable for Visit						
Overdue	0	2	1	21	1	3
Missed Visit	2	5	7	14	11	1
Lost to Follow-up	1	1	3	4	4	4
Available for Analysis	198	193	190	157	178	54
Evaluable = Avail- retreated - protocol deviations	191	186	183	148	165	51
% Accountability = Avail/(201-discont.- not eligible)	99	96	95	80	92	87

b. Stability of outcome

In the 9-12 months window, greater than 95% of eyes experienced a change of MRSE not exceeding $\pm 1.0D$. Furthermore, the mean of the pair-difference of MRSE progressively decreased over time, and reached a change of about 0.1 D in the 9-12 months window (tables 4 and 5). The changes in the 12-18 months window for the entire cohort were smaller than those observed in the previous time window; thus, stability was demonstrated by 12 months postoperative. The assessment of the efficacy was therefore performed using the outcomes of the 165 eyes evaluable at 12 months.

It was however noted that when the data are stratified by discs, the amount of change for disc K108 in the 12-18 months window was slightly higher than that observed in the previous time window. This observation was a reason behind the post approval requirement of continued monitoring of the eyes treated with this disc.

Table 4: Stability Analyses (change in MRSE over time for eyes that had every exam, through 12 months)				
Analysis	1 to 3 Months	3 to 6 Months	6 to 9 Months	9 to 12 Months
Change $\leq 1 D$ N/N (%) (95% CI)	102/131 (77.9%) (69.8,84.6)	116/131 (88.5%) (81.8,93.4)	119/131 (90.8%) (84.5,95.2)	126/131 (96.2%) (91.3,98.7)
Change (Pair-Differences)				
Mean	0.48	0.233	0.145	0.094
Std.Dev.	0.746	0.635	0.576	0.481
(95% CI)	(0.35,0.61)	(0.12,0.34)	(0.05,0.24)	(0.01,0.18)

Table 5: Stability Analyses (change in MRSE over time for eyes that had 2 consecutive exams, through 12 months)				
Analysis	1 to 3 Months	3 to 6 Months	6 to 9 Months	9 to 12 Months
Change $\leq 1 D$ n/N (%) (95% CI)	141/184 (76.6%) (69.8,82.5)	160/177 (90.4%) (85.1,94.3)	129/142 (90.8%) (84.9,95)	131/137 (95.6%) (90.7,98.4)
Change (Pair-Differences)				
Mean	0.525	0.243	0.147	0.08
Std.Dev.	0.74	0.608	0.572	0.492
(95% CI)	(0.42,0.63)	(0.15,0.33)	(0.05,0.24)	(0,0.16)

c. Effectiveness Outcomes

The analysis of effectiveness was based on the 165 eyes evaluable at the 12 months stability time point. Of the 165 eyes, there were 21 in which treatment was for near vision; hence, these 21 eyes were excluded from the presented UCVA data in table 6 since they pertained to distance vision. The near UCVA outcomes of these 23 eyes at 12 months were: 5/21 (23.8%) with 20/20 or better, 10/21 (47.6%) with 20/25 or better, and 17/21 (81.0%) with 20/40 or better.

To simplify the effectiveness analysis, the intended versus the achieved correction (predictability) of each disc was evaluated in table 6. Effectiveness by treatment goal was not scrutinized, because the sponsor was not pursuing this claim given the small number (23 eyes) treated for near vision. Effectiveness by preoperative refraction was not deemed appropriate because the amount of correction does not necessarily correlate with the patient's preoperative refraction.

Table 6 revealed better performance with lower levels of correction. MRSE \pm 1.0 D followed the same trend but remained above 75% for all discs. Overall, the effectiveness of the device was deemed acceptable.

Table 6: Summary of Key Effectiveness Variables at 12 Months by Disc					
Efficacy Variables	Disc				Cumulative n/N (%) (95%CI)
	K102: 1.6D	K104: 2.3D	K106: 3.1D	K108: 3.9D	
UCVA 20/20 or better	32/56 (57.1%) (43.2,70.3)	17/34 (50.0%) (32.4,67.6)	8/24 (33.3%) (15.6,55.3)	9/30 (30.0%) (14.7,49.4)	66/144 (45.8%) (37.5,54.3)
UCVA 20/25 or better	44/56 (78.6%) (65.6,88.4)	25/34 (73.5%) (55.6,87.1)	12/24 (50.0%) (29.1,70.9)	17/30 (56.7%) (37.4,74.5)	98/144 (68.1%) (59.8,75.6)
UCVA 20/40 or better	54/56 (96.4%) (87.7,99.6)	33/34 (97.1%) (84.7,99.9)	21/24 (87.5%) (67.6,97.3)	24/30 (80.0%) (61.4,92.3)	132/144 (91.7%) (85.9,95.6)
MRSE +/- 0.50 D	42/56 (75.0%) (61.6,85.6)	17/34 (50.0%) (32.4,67.6)	13/30 (43.3%) (25.5,62.6)	20/45 (44.4%) (29.6,60)	92/165 (55.8%) (47.8,63.5)
MRSE +/- 1.00 D	54/56 (96.4%) (87.7,99.6)	28/34 (82.4%) (65.5,93.2)	23/30 (76.7%) (57.7,90.1)	34/45 (75.6%) (60.5,87.1)	139/165 (84.2%) (77.8,89.4)
MRSE +/-	56/56	33/34	28/30	43/45	160/165

Table 6: Summary of Key Effectiveness Variables at 12 Months by Disc					
2.00 D	(100.0%) (93.6,100)	(97.1%) (84.7,99.9)	(93.3%) (77.9,99.2)	(95.6%) (84.9,99.5)	(97.0%) (93.1,99)

d. Safety Outcomes

The analysis of safety was based on the entire 178 eyes that have had the 12 months exam. The key safety outcomes for this study are presented in table 7, with all the adverse reactions reported in tables 8 and 9. It should be noted that the safety of the device for PRK was not based on this small sample size alone, but rather on all the available data for the device for this type of procedure to date. The safety data from this study were for confirmatory purposes. Overall, the device was deemed reasonably safe.

It was observed that the loss of BSCVA ≥ 2 lines appeared to be higher in eyes treated with K108 than with the other discs, which may be due to the low N. A closer look at the 3 affected eyes revealed that none had the 18 months follow-up exam; only one had 20/40 or worse BSCVA, and, none had undergone re-treatment prior to the loss of BSCVA. Longer follow-up of these eyes was needed to determine their natural course of progression. This was the second reason behind the post approval requirement of continued monitoring of the eyes treated with the K108 disc.

Table 7: Summary of Key Safety Variables at 12 Months by Disc					
Efficacy Variables	Disc				Cumulative n/N (%) (95%CI)
	n/N (%) (95%CI)				
	K102: 1.6D N=61	K104: 2.3D N=34	K106: 3.1D N=34	K108: 3.9D N=49	
Loss of > 2 Lines Distance BSCVA	1/61 (1.6%) (0,8.8)	0 (0,10.3)	0 (0,10.3)	1/49 (2.0%) (0.1,10.9)	2/178 (1.1%) (0.1,4)
Loss of 2 Lines Distance BSCVA	0 (0, 5.9)	1/34 (2.9%) (0.1, 15.3)	0	2/49 (4.1%) (0.5,14.0)	3/178 (1.7%) (0.3,4.8)
Increase of >2.0D Cylinder	0	0	0	0 (0,7.3)	0 (0, 2.1)
Distance BSCVA worse than 20/40	0	0	0	0	0 (0, 2.1)
Distance BSCVA	1/61	0	0	0	1/178

Table 7: Summary of Key Safety Variables at 12 Months by Disc					
worse than 20/25 if 20/20 or better preoperatively	(1.6%)				(0.6%) (0,3.1)

Table 8 presents a summary of the FDA defined adverse events. The benchmark for each adverse event is a rate of less than 1 % per event. For the PMA cohort which has a sample size of 178 eyes, a 0 observed rate means that the true rate can be as high as 2.1% (in simple terms, if this study of 178 eyes were to be repeated over and over again, the observed adverse event rate for each study may be different each time but it will not be higher than 2.1%). Obviously, a rate of 2.1% is higher than the 1.0% benchmark. As previously explained, FDA's assessment of the safety of the PRK procedure with this laser was not limited to the data from this one study since there are prior PRK safety data for this laser. Rather, the data from this specific study were assessed for confirmation. The observed adverse events and complications from this specific study did not appear to be different from those noted previously.

Table 8: FDA defined Adverse Events at 12 months	
Adverse Event	PMA cohort
Corneal infiltrate or ulcer	0
Persistent central corneal epithelial defect at 1 month or later	1 month: 1 (0.5%) 3 months: 1 (0.5%) 6 and later: 0
Corneal edema at 1 month or later	0
Uncontrolled IOP with increase of > 10 mm Hg above baseline, or any reading above 25 mm Hg	0
Late onset of haze beyond 6 months with loss of 2 lines (10 letters) or more BSCVA	0
Decrease in BSCVA of > 10 letters not due to irregular astigmatism as shown by hard contact lens refraction, at 6 months or later	0
Retinal detachment	0

All adverse reactions, measured or reported by patients, are presented in table 9. Events observed at the 12 months stability time point and at the two adjacent visits are included for comparison. In general, the rate of an adverse reaction tends to be highest immediately postoperative and tapers down over time. The reverse was noted for moderate "2" and marked "3" haze which seemed to occur after the one month visit and peak by the six month visit. The rate of moderate and marked haze at one month is 4.5% (9/198) and at three months was 12.4%

(24/193). An analysis of the 19 eyes at twelve months indicated that the location of haze was at the periphery and only 1 eye lost more than 2 lines of near BSCVA while none lost more than 2 lines of distance BSCVA.

Adverse Reaction	6 months N=190	12 months N=178	18 months N=54
Anterior Stromal Reticular Haze	12.6%	10.7%	5.6%
Double images in the operative eye	2.6%	1.7%	1.9%
Double vision	0.6%	0.6%	0
Foreign body sensation	2.1%	1.7%	1.9%
Ghost images in the operative eye	2.6%	2.2%	1.9%
Glare	2.8%	2.8%	1.9%
Halo	0.6%	0.6%	3.7%
Light sensitivity	0.6%	0.6%	0
Loss of near or distance BSCVA	5.8%	4.5%	5.6%
Overcorrection of hyperopia by > 2.0 D	0.5%	0.6%	0
Patient discomfort	0.5%	3.4%	1.9%
Ptosis	0.6%	0.6%	0
Recurrent corneal erosion	0.5%	0.6%	0
Undercorrection of hyperopia by > 2.0 D	0.5%	2.4%	0
Other: dryness/night driving difficulties	0.6%	0.6%	0

e. Retreatment

All retreatment procedures were performed at least 6 months after the initial treatment date with written approval from Summit. There were a total of 12 retreatments on the 201 eyes: 7 after six months, 2 after nine months, and 3 after twelve months. The type of retreatment varied: 6 astigmatic keratotomy, 2 myopic PRK, and 4 hyperopic PRK. There were no major safety concerns for these retreated eyes. Since there were only 4 hyperopic retreatments performed in this trial, we do not have enough data to form any definitive conclusions regarding retreatment outcomes with this device.

It was noted that six of the 12 retreatments were for eyes treated with the K108 disc. They included hyperopic, myopic and AK corrections of residual refractive errors. Such high rate of re-

treatment could partially be due to the wide range of pre-operative refractive errors in eyes treated with K108. Nevertheless, this was the third reason for the post approval requirement of continued monitoring of the eyes treated with the K108 discs.

f. Factors associated with outcomes

These preoperative characteristics were evaluated for potential association with outcomes: gender, site, age, preoperative MRSE, and attempted MRSE.

Gender was not found to be associated with any of the safety or efficacy variables. Site was found to be statistically significant with stability of MRSE and re-epithelialization within 7 days. Age was found to be associated with re-epithelialization within 7 days. Preoperative MRSE was found to be associated with predictability within $\pm 0.5D$. Attempted MRSE was found to be associated with predictability within $\pm 0.5D$, with fewer eyes came to within $\pm 0.5D$ of the intended level in the higher attempted MRSE groups. Similar results were seen with MRSE predictability within $\pm 1.0 D$.

g. Patient Satisfaction

Patient surveys were completed on an eye-by eye basis. Information at 12 months was presented in the PMA.

Ninety percent (146/162) were either 'satisfied' or 'very satisfied' with the results of their treatment. Three did not respond. The primary reason for dissatisfaction in the 16 'not satisfied' eyes was with one's near uncorrected vision.

Ninety five percent (156/162) of patients would recommend the procedure to a friend at the time of the 12 month visit for each eye treated. Three did not respond. Six patients reported that they would not recommend the treatment to a friend.

h. Device failure

None occurred during the course of the study.

i. Confirmatory 18 months and international data

The limited safety and effectiveness data at 18 months postoperative follow the same trends observed for the earlier time

point. The key safety and effectiveness variables are presented in tables 10 and 11.

Table 10: Summary of Key Effectiveness Variables at 18 Months by Disc					
Efficacy Variables	Disc n/N (%) (95% CI)				Cumulative n/N (%) (95%CI)
	K102: 1.6D	K104: 2.3D	K106: 3.1D	K108: 3.9D	
UCVA 20/20 or better	9/14 (64.3%) (35.1,87.2)	2/8 (25.0%) (3.2,65.1)	3/10 (30.0%) (6.7,65.2)	2/10 (20.0%) (2.5,55.6)	16/42 (38.1%) (23.6,54.4)
UCVA 20/25 or better	11/14 (78.6%) (49.2,95.3)	6/8 (75.0%) (34.9,96.8)	5/10 (50.0%) (18.7,81.3)	54/10 (40.0%) (12.2,73.8)	26/42 (61.9%) (45.6,76.4)
UCVA 20/40 or better	14/14 (100.0%) (76.8,100)	8/8 (100.0%) (63.1,100)	8/10 (80.0%) (44.4,97.5)	9/10 (90.0%) (55.5,99.7)	39/42 (92.9%) (80.5,98.5)
MRSE +/- 0.50 D	10/14 (71.4%) (41.9,91.6)	4/8 (50.0%) (15.7,84.3)	4/12 (33.3%) (9.9,65.1)	5/17 (29.4%) (10.3,56)	23/51 (45.1%) (31.1,59.7)
MRSE +/- 1.00 D	13/14 (92.9%) (66.1,99.8)	6/8 (75.0%) (34.9,96.8)	9/12 (75.0%) (42.8,94.5)	10/17 (58.8%) (32.9,81.6)	38/51 (74.5%) (60.4,85.7)
MRSE +/- 2.00 D	14/14 (100.0%) (76.8,100)	8/8 (100.0%) (63.1,100)	12/12 (100.0%) (73.5,100)	17/17 (100.0%) (80.5,100)	51/51 (100.0%) (93,100)

Table 11: Summary of Key Safety Variables at 18 Months by Disc					
Efficacy Variables	Disc				Cumulative n/N (%) (95%CI)
	n/N (%) (95% CI)				
	K102: 1.6D	K104: 2.3D	K106: 3.1D	K108: 3.9D	
Loss of > 2 Lines Distance BSCVA	0	0	0	0	0 (0,6.6)
Loss of 2 Lines Distance BSCVA	0	0	0	1/19 (5.3%) (0.1, 26)	1/54 (1.9%) (0,9.9)
Increase of >2.0D Cylinder	0	0	0	0	0 (0,6.6)
Distance BSCVA worse than 20/40	0	0	0	1/19 (5.3%) (0.1, 26)	1/54 (1.9%) (0,9.9)
Distance BSCVA worse than 20/25 if 20/20 or better preoperatively	0	0	0	0	0 (0,6.6)

International data from Dr. David O'Brart at St. Thomas' Hospital, London, UK was provided in this PMA as confirmatory in support of the safety and effectiveness of the device. This confirmatory data included 24 months data from a study of 43 eyes. The St. Thomas study had similar inclusion criteria as the US IDE study, except in the following areas: +1.75 to +7.50 D preoperative refraction and an age limit of 21 years minimum. Treatment was with these three discs: K106 (3.1D), K110 (4.7D) and K114. St. Thomas' patients were not given the option of retreatment until the third postoperative year had passed.

The stability of the St. Thomas' cohort was reached by 12 months postoperative and confirmed with the 24 months results (table 12). Even though the range of correction in the St. Thomas data did not correspond exactly with the PMA Cohort, the observed stability was reassuring given that stability usually decreases with increasing magnitude of correction. Thus, adequate stability with the higher corrections most probably indicates adequate stability with the lower range of corrections as well.

Table 12: Stability Analyses of St. Thomas Data (change in MRSE over time for eyes that had every exam, through 24 months)					
Analysis	1 to 3 Months	3 to 6 Months	6 to 9 Months	9 to 12 Months	12 to 24 months
Change \leq 1 D n/N (%) (95% CI)	23/42 (54.8%) (38.7, 70.2)	30/42 (71.4%) (55.4, 84.3)	37/42 (88.1%) (74.4, 96.0)	40/42 (95.2%) (83.8, 99.4)	39/42 (92.9%) (80.5, 98.5)
Change (Pair-Differences) Mean Std.Dev. (95% CI)	1.006 1.336 (0.6, 1.41)	0.372 1.378 (-0.04, 0.79)	0.351 0.643 (0.16, 0.55)	0.098 0.468 (-0.04, 0.24)	-0.09 0.526 (-0.25, 0.07)

The following safety profiles were noted for the St. Thomas' eyes. Twelve eyes (28%) lost lines of Snellen BSCVA. Only 2 eyes (5%) lost 2 lines of BSCVA with none losing greater than 2 lines of BSCVA. No change or an improvement in BSCVA was seen in 31 eyes (72%). Distance BSCVA was worse than 20/40 in 2 eyes (5%) at the 6 month postoperative examination. By the 2 year postoperative examination, 3 eyes (7%) had a distance BSCVA worse than 20/40.

Under slit lamp examination at 6 months postoperatively, 34 eyes (79%) showed clear central corneas with no evidence of central anterior stromal reticular haze. In 9 eyes (21%), slight subepithelial haze less than or equal to grade 1 was present.

One eye (2%) experienced recurrent corneal erosion presenting at 2 months postoperatively and resolving at 3 months postoperatively with subsequent management with lubricating ointment. There was no recurrence after 3 months postoperatively. Two eyes (5%) experienced irregular epithelial healing during the first month after treatment which was attributed to the age of the patients. Both were among the oldest treated and were in their seventies. Two eyes (5%) had peripheral subepithelial haze which was associated with regression.

The safety outcomes of the O'Brart data do not raise any concern for the PMA data.

X. EMPHASIS DISCS L

The L discs were introduced to fill in the gaps of the K discs. The L discs covered the treatment range of 1.0 to 4.0 D in 0.5 increments. Their names are indicative of their corrective power: L10 for 1.0D, L15 for 1.5 D, etc.

The L discs were not used in the studies summarized herein; nevertheless, they were approved with the K discs. For this approval, the sponsor must first demonstrate that all discs are manufactured with consistency, precision and accuracy, and then generate a statistical model to predict the clinical outcomes of the L discs using the results of the K discs. Since outcomes with each individual K disc were deemed acceptable and the various discs can be properly manufactured, interpolation between K discs was deemed acceptable for the purpose of predicting L discs' outcomes. Only limited extrapolation of the K disc data was allowed.

The predicted outcomes of the L discs are provided in table 13.

Probability	L10	L15	L20	L25	L30	L35	L40
Within + 0.5 D	0.76 (0.62, 0.86)	0.70 (0.59, 0.80)	0.65 (0.55, 0.73)	0.58 (0.50, 0.66)	0.50 (0.43, 0.60)	0.44 (0.34, 0.55)	0.38 (0.26, 0.51)
Within ± 1.0 D	0.95 (0.87, 0.98)	0.93 (0.85, 0.97)	0.91 (0.83, 0.95)	0.87 (0.80, 0.92)	0.83 (0.76, 0.88)	0.77 (0.68, 0.85)	0.70 (0.56, 0.82)

XI. CONCLUSIONS DRAWN FROM THE CLINICAL STUDY

The data in this application supports reasonable assurance of safety and efficacy of this device for the treatment of hyperopia from +1.5 to +4.0 D sphere.

XII. PANEL RECOMMENDATION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. FDA DECISION

On October 21, 1999, FDA issued an approval order to Summit Technology, Inc.

XIII. APPROVAL SPECIFICATIONS

- Post approval requirements and restrictions: see approval order.
- Hazards to health from use of device: see indications, contraindications, warnings, precautions, and adverse events in the labeling.
- Directions for use: see the labeling.