U.S. Code of Federal Regulations

U.S. Code of Federal Regulations
TITLE 21 C.F.R. [Food and Drugs]
CHAPTER I FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER H MEDICAL DEVICES
PART 812 INVESTIGATIONAL DEVICE EXEMPTIONS
Subpart A General Provisions

[Previous Document in Book] [Next Document in Book]

21 C.F.R. § 812.7 **Prohibition of promotion and other practices.**

A sponsor, investigator, or any person acting for or on behalf of a sponsor or investigator **shall not:**

(a) **Promote** or test market an investigational device, until after FDA has approved the device for commercial distribution.

(b) **Commercialize** an investigational device by charging the subjects or investigators for a device a price larger than that necessary to recover costs of manufacture, research, development, and handling.

(c) Unduly **prolong** an investigation. If data developed by the investigation indicate in the case of a class III device that premarket approval cannot be justified or in the case of a class II device that it will not comply with an applicable performance standard or an amendment to that standard, the sponsor shall promptly terminate the investigation.

(d) **Represent** that an investigational device is safe or effective for the purposes for which it is being investigated.

[Previous Document in Book] [Next Document in Book]

b. Best uncorrected (near and distance)

3. Manifest refraction
4. Corneal topography
5. Slit lamp examination of the cornea, anterior chamber and lens
6. Measurement of intraocular pressure
7. Fundoscopic examination.
8. Cycloplegic refraction
9. Corneal pachymetry
10. Measurement of pupil size

The investigator will again review the available refractive surgery options, including LASIK when it is appropriate. The investigator or his/her staff will review the study and informed consent with patients who are interested in undergoing LASIK to treat their refractive error(s), and confirm that they are eligible for LASIK and participation in the study. The patient will be instructed to contact the clinic to be scheduled for refractive surgery when he/she makes the final decision to have LASIK or another refractive surgical procedure.

C. CONTACT LENS WEARERS: Contact lens wearers should discontinue soft lenses for at least 1 day prior to examination and before surgery. Gas permeable ~~and hard contact lens wearers~~ should discontinue wear for at least 2 weeks before examination and surgery *and hard contact lens wearers should discontinue use for at least 3 weeks prior to examination and the hard lenses* should remain out until the investigator has determined refractive stability *based on keratometry and manifest refractions.*

VIII. STUDY PROCEDURES

Patients who elect to participate in this study and have LASIK performed will complete the study as outlined below. Since refractive surgery is an elective procedure, and the same screening procedures are completed regardless of the type of surgery the patient selects, the informed consent for LASIK and study participation will be signed by the patient before the surgical procedure. A flow chart of study procedures is provided in Appendix C.

A. SUBJECT IDENTIFICATION: Each patient treated in the study will be uniquely identified by a sequentially assigned case I.D. number. Case I.D. numbers will be assigned in the order eyes are treated in the study and will appear on all study documents

be determined by the number of patients who have one or both eyes treated. For eyes that are enhanced, the primary procedure but not the enhancement is included in the enrollment count.

B INCLUSION CRITERIA: Patients meeting all of the following criteria will be considered candidates for this study:

1. Male or female of any race.
2. At least 15 years of age.
3. Desire to be less dependent on glasses and have surgical correction of his/her refractive error(s).
4. Having an uncorrected refractive error that can be surgically treated by LASIK and consists of myopia between -0.5 and -22 diopters, with or without accompanying astigmatism of -7 diopters or less.
5. Able to understand and provide signed informed consent. Consent must also be obtained from a legally authorized representative for patients under 18 years of age.
6. *Best corrected visual acuity of 20/40 or better in both eyes.*
7. *Willing and capable of returning for follow-up examinations for the duration of the study.*
8. *Normal videokeratography.*
9. *Stable manifest refraction, defined as < 0.5D change in sphere or cylinder during the year prior to the screening examination.*

C. EXCLUSION CRITERIA: All patients meeting any of the following criteria will be excluded from this study:

1. History or current evidence of an infection in the eye or other systemic infection, including herpes simplex keratitis.
2. Pupil size which, in the investigator's opinion, is excessively large and would predispose the patient to a higher incidence of evening halos.
3. Keratoconus (conical cornea).
4. Patient age or any finding on ophthalmic examination that indicates that cataract surgery is necessary, or may be necessary in the near future.
5. Presence of any clinically significant abnormality or finding on physical or ophthalmic examination that would contraindicate outpatient refractive surgery.
6. History or current evidence of any other physical condition or illness which would contraindicate outpatient refractive surgery or preclude the patient's participation in this study.

FDA'S QUESTION:

9. *Please clarify why you have omitted or modified the following inclusion criteria (Section 3.2.4.1):*

   a. *BCVA should be 20/40 or better in both eyes.*

   b. *Contact lens wearers should:*

      i. *Remove soft or gas permeable contact lenses two weeks prior to baseline measurements*

      ii. *Remove hard contact lenses three weeks prior to baseline measurements, and have two central keratometry readings and two manifest refractions taken at least one week apart that do not differ by more than 0.50 diopters in either meridian; mires should be regular.*

   c. *The spherical or cylindrical portion of manifest refractions should progress 0.50 diopter or less during the year prior to the baseline exam.*

   d. *Subjects should be willing and capable of returning for follow-up examinations for the duration of the study.*

   e. *Videokeratography should be normal.*

DR. NEVYAS' RESPONSE:

8.a Having a BCVA of 20/40 or better in both eyes is consistent with the screening criteria we currently use for evaluating LASIK candidates. This inclusion criterion has been added to Protocol NEV-97-001.

8.b Contact lens criteria are provided in the protocol in Section VII.C, entitled "Contact Lens Wearers." The protocol specifies that soft lenses be discontinued for at least 1 day prior to examination and surgery. Gas permeable lenses and hard contact lenses should be discontinued at least 2 weeks prior to examination and surgery and remain out until the investigator has determined refractive stability.

Our usual standard is to leave soft contact lenses out for three days prior to the screening examination and prior to the surgical procedure; thus, we have revised the requirement for

X. ETHICAL AND REGULATORY CONSIDERATIONS

A. INVESTIGATOR/SPONSOR: In accordance with 21 CFR 812.3(o), Dr. Herbert Nevyas and Dr. Anita Nevyas-Wallace are the "Sponsor-Investigators," for the Nevyas Excimer Laser, meaning they are the individuals who both initiate and actually conduct, alone or with others, an investigation; and that the investigational device is administered, dispensed, or used under his/her immediate direction. The regulatory obligations of a "sponsor-investigator" include those of an investigator as well as those of a sponsor.

B. INFORMED CONSENT: In accordance with the provision of 21 CFR Part 50, each patient will give written informed consent for participation in this study prior to the use of the investigational device. A copy of the basic elements of informed consent is attached (Appendix E). The study will be explained to the prospective patient by the investigator or his designee. The nature of the investigational device will be explained together with potential hazards of the surgical procedure, including any possible adverse reactions. The patient will be informed that he/she is free to terminate participation in the study for any reason. One copy of the consent form will be given to the subject and a copy of the signed consent form will be kept on file by the investigator. A copy of the IRB-approved informed consent form will be retained in the investigator's files prior to initiating the study.

C. INSTITUTIONAL REVIEW BOARD: This protocol, and the informed consent form, will be approved initially and reviewed annually by an Institutional Review Board constituted according to FDA regulations. The Institutional Review Board granting initial approval shall be responsible for continuing review and approval of this study including the informed consent form. A copy of the Committee's dated approval and a list of the members of the Institutional Review Board, or its DHHS approval number, will be given to the investigator for the investigator's files. Progress reports will be submitted at the completion of the study or at least once yearly, whichever comes first, to the Institutional Review Board (IRB). Serious and unanticipated adverse device effects will be reported to the IRB and the FDA.

D. COMPLICATIONS & ADVERSE EVENTS: Complications or adverse events that are observed by the investigator or reported by the subject should be recorded on the data collection sheets or in the computerized database. For all adverse events, a description

the event, date first observed, any action taken, and ultimate outcome will be recorded.

1. Complications: Postoperative events that are anticipated, occur at an expected rate, and are manageable with usual standard of care should be recorded as complications. LASIK complications could include, but are not limited to:
   - Corneal edema between one week and one month after the procedure
   - Peripheral corneal epithelial defect at 1 month or later (location of the defect to be identified as on, off, or across the flap)
   - Epithelium in the interface (with or without scraping of epithelial cells)
   - Foreign body sensation at 1 month or later
   - Pain at 1 month or later
   - Ghost or double images in the operative eye
   - Central islands, glare or other postoperative visual events at 1 month or later
   - Flap is not of the size and shape as initially intended or microtome stopped in mid-cut

2. Adverse Events: Postoperative complications that are serious in nature, are vision-or-life-threatening, and all unanticipated adverse device effects should be recorded as adverse events. LASIK adverse events could include, but are not limited to:
   - Corneal infiltrate or ulcer
   - Any corneal epithelial defect involving the keratectomy at one month or later
   - Lost, misplaced, or misaligned flap
   - Melting of the flap
   - Uncontrolled intraocular pressure with increase of >10 mm Hg above baseline and any reading above 25 mm Hg
   - Late onset of haze beyond 6 months with loss of 2 lines (10 letters) or more BSCVA
   - Decrease in BSCVA of more than 10 letters not due to irregular astigmatism as shown by hard contact lens refraction at 6 months or later
   - Retinal detachment
   - Retinal vascular accidents

3. Serious and Unanticipated Adverse Device Effects: An unanticipated adverse device effect is defined as "any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device if that

surgically treated as primary procedures with LASIK to provide 339 low myopic eyes and 500 high myopic eyes that are fully evaluable. The final number of patients enrolled will be determined by the number of patients who have one or both eyes treated. For eyes that are enhanced, the primary procedure but not the enhancement is included in the enrollment count.

B. INCLUSION CRITERIA: Patients meeting all of the following criteria will be considered candidates for this study:

1. Male or female of any race.
2. At least 15 years of age.
3. Desire to be less dependent on glasses and have surgical correction of his/her refractive error(s).
4. Having an uncorrected refractive error that can be surgically treated by LASIK and consists of myopia between -0.5 and -22 diopters, with or without accompanying astigmatism of -7 diopters or less.
5. Able to understand and provide signed informed consent. Consent must also be obtained from a legally authorized representative for patients under 18 years of age.
6. *Best corrected visual acuity of 20/40 or better in both eyes.*
7. *Willing and capable of returning for follow-up examinations for the duration of the study.*
8. *Normal videokeratography.*
9. *Stable manifest refraction, defined as < 0.5D change in sphere or cylinder during the year prior to the screening examination.*

C. EXCLUSION CRITERIA: All patients meeting any of the following criteria will be excluded from this study:

1. History or current evidence of an infection in the eye or other systemic infection, including herpes simplex keratitis.
2. Pupil size which, in the investigator's opinion, is excessively large and would predispose the patient to a higher incidence of evening halos.
3. Keratoconus (conical cornea).
4. Patient age or any finding on ophthalmic examination that indicates that cataract surgery is necessary, or may be necessary in the near future.
5. Presence of any clinically significant abnormality or finding on physical or ophthalmic examination that would contraindicate outpatient refractive surgery.
6. History or current evidence of any other physical condition or illness which would

contraindicate outpatient refractive surgery or preclude the patient's participation in this study.

7. History of allergic response or known intolerance to any of the medications used in the surgical procedure or postoperatively, unless an alternate medication can be substituted to which the patient has no known allergy or intolerance.
8. Participation in a previous ophthalmic clinical trial within the 30 days prior to the start of the study.
9. Female patients (by history) who are pregnant.
10. *Taking systemic medications likely to affect wound healing, such as corticosteroids or antimetabolites.*
11. *Immunocompromised patients (e.g. AIDS, autoimmune disease).*
12. *Unstable central keratometry readings with irregular mires.*

VII. SCREENING FOR REFRACTIVE SURGERY ELIGIBILITY

The investigator and his staff will evaluate and screen patients in their usual fashion for refractive surgery. The usual procedures include conducting a refractive consultation, followed by a complete eye examination in interested patients. The patient then determines that he/she wants to have refractive surgery and schedules for the desired procedure. The refractive consultation and complete eye examination are routine screening procedures to determine if the patient is an eligible candidate for refractive surgery of any type.

A. REFRACTIVE CONSULTATION: During the refractive consultation, the patient will meet an ophthalmic technician who will take an ocular history, measure the subject's refractive error, and perform corneal topography to measure the corneal curvature. The investigator will then meet with the patient to discuss whether or not the patient is a refractive surgery candidate. If the patient is a candidate, the investigator will discuss the available refractive surgery options, including LASIK when it is an appropriate procedure.

B. COMPLETE EYE EXAMINATION: Patients who wish to further pursue the option of refractive surgery, will undergo a complete eye examination to determine their eligibility for refractive surgery. The complete eye examination will include:

1. Obtaining a detailed medical history, and ocular history

Contrast sensitivity results have not been evaluated yet. LASIK results are included in the NEV-97-001 summary tables.

G. PROTOCOL DEVIATIONS

Some patients failed to return for the postoperative evaluation. These dropouts were replaced to provide 75 low myopia subjects with preoperative and postoperative evaluations. These substudy patients were all enrolled in NEV-97-001.

H. SUMMARY OF COMPLICATIONS AND ADVERSE EVENTS:

Included with the NEV-97-001 complication and adverse event tables.

1374

2.0 RISK ANALYISIS

The risk analysis remains unchanged from that submitted with the original IDE. There are no emerging complications or adverse events that alter the risk analysis. The adverse event and complication rates remain low.

3.0 DEVICE CHANGES

The following device changes have occured since the last annual report:

- Sculpting device upgrade: The sculpting device component was replaced as a preventative measure. The sculpting device (manufactored by Skepsis) was upgraded to the latest model since the current model was no longer available. The software interface calls in the Nevyas treatment algorithm; hence, no changes have been made to the treatment algorithm.

4.0 CHANGES IN INVESTIGATIONAL PLAN

All reportable changes to the investigational plan have been previously submitted to the FDA for review and approval via amendments, revised versions of the protocol(s), or substudies.

5.0 PROGRESS TOWARDS PMA APPROVAL

It was previously recommended by FDA that only subjects treated with the new contration technique (as previously described) be included in the PMA. We have preliminarily selected the eyes treated between 2/19/98 through 1/22/99 as the cohort of eyes that will be used to support the safety and effectiveness of the device in the PMA submission. This group of eyes is comprised of:

- 125 eyes treated for low spherical myopia only (< -7.0 D MRSE);
- 346 eyes treated for low myopic astigmatism (< -7.0 D MRSE);
- 10 eyes treated for high spherical myopia only (≥ -7.0 D MRSE); and,
- 82 eyes treated for high myopic astigmatism (≥ -7.0 D MRSE).

Since there are less than 125 eyes in the high myopia subset, the initial PMA submission will only include data to support the indications of low spherical myopia and low myopic

eyes even though topical steroids were administered postoperatively. Corneal haze was more severe in patients treated with 9 to 12 diopters of attempted refractive change.[4]

There has been renewed interest in modifying an older refractive surgical procedure, keratomileusis, in an effort to find an effective treatment that minimizes the incidence of postoperative visual events and visual acuity changes that have recently been reported with radial keratotomy and photorefractive keratectomy. Laser in situ keratomileusis (LASIK), as described by Slade[9], involves using a microkeratome to create a corneal flap. The corneal flap is laid back and the laser ablation is applied to the corneal stroma rather than the corneal surface. Ablation with the excimer laser preserves Bowman's membrane and reduces surgical trauma to the corneal tissue, providing more consistent wound healing and more predictable dioptric correction. The ablation is accurate for the amount of corneal tissue removed and the treatment site and its surrounding area (optical zone) can be varied to provide optimal dioptric correction with minimal tissue ablation.

LASIK can effectively treat both low and high degrees of myopia, hyperopia, and astigmatism. Since LASIK does not disrupt the epithelial structure, postoperative healing occurs rapidly and refractive stability occurs as early as one month in many patients. Anecdotal reports of visual adverse events appear to be much lower than those reported with PRK and RK. For these reasons, ophthalmic surgeons are turning their attention to LASIK as an alternative to RK and PRK.

B. PRIOR CLINICAL STUDIES

The investigators (Dr. Herbert J. Nevyas and Dr. Anita Nevyas-Wallace) began treating patients with Laser Intrastromal Keratomileusis (LASIK) in January 1996. As of February 27, 1997, they have performed 147 LASIK myopia procedures in 70 patients. Seventeen of the patients were treated by Dr. Anita Nevyas-Wallace and 53 patients were treated by Dr. Herbert Nevyas.

Informed consent was obtained from all patients prior to the surgical procedure. Patients were considered eligible for LASIK treatment if they were at least 18 years of age and not more than 64 years of age; generally had a preoperative best spectacle corrected visual acuity (BSCVA) of 20/40 in the operated eye; had a stable refraction with a refractive error consisting of myopia between -0.0 and -25.00 diopters with or without astigmatism. Patients

had no current or significant previous history of ocular diseases or conditions or other systemic disease that prohibited the patients from having refractive surgery; and, were taking no medications that would interfere with postoperative wound healing. Patients who had a visually impaired fellow eye (20/50 or worse BSCVA) were also ineligible for LASIK surgery. The current postoperative visit schedule is 1 Day, 4 Days, 2 Weeks, 1 Month, 3 Months, 6 Months and 12 Months after LASIK surgery.

Efficacy data for 66 eyes in 53 patients whose refractive error consisted of myopia with or without astigmatism and have at least a 1 month or 3 month postoperative examination are summarized below in Section B. Safety data for all 147 procedures are provided in Section C. All reported data are for primary procedures. Data for 27 eyes treated in the past three months are not included in the outcome analyses since they have not yet completed a 3-month postoperative visit.

Primary procedures for 66 myopic eyes in 53 patients with or without astigmatism that were treated with LASIK and have at least a 1 month postoperative visit are summarized below. Patients ranged in age from 21 to 64 years at the time of LASIK surgery. All eyes had a BSCVA of 20/40 or less in the operated eye. Dr. Herbert Nevyas treated 36 of the patients and Dr. Anita Nevyas-Wallace treated 17 patients. The degree of preoperative myopia treated by Dr. Herbert Nevyas ranged between -0.75 and -11.25 diopters with accompanying cylinder ranging between 0.0 and -4.25 diopters. Dr. Anita Nevyas-Wallace treated preoperative myopia ranging from -2.0 diopters to -14.0 diopters with an accompanying cylinder of 0.0 to 1.75 diopters. Algorithm 17R was used to treat myopia of less than -7.0 diopters; and, Algorithm 17H was used for myopia of -7.0 diopters or greater. The number of patients with low and high preoperative myopia that have at least a 1 month follow-up visit are summarized in Table 1 below.

TABLE 1: Range of Preoperative Myopia with or without Astigmatism

PREOP MYOPIA (diopters)	DR. HERBERT NEVYAS		DR. ANN NEVYAS		TOTAL	
	(n)	%	(n)	%	(n)	%
-0.75 to -6.75	23	46.0	9	56.3	32	48.5
-7.00 to 14.00	27	54.0	7	43.7	34	51.5
TOTAL	50	100.0	16	100.0	66	100.0

Table 1.1.E-4: Patient Accountability for Eyes Treated for Low Myopia (with or without astigmatism)

Status	1 Month		3 Months		6 Months		12 Months		18 Months		24 Months	
N (Enrolled)	817		817		817		817		817		817	
	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%
Available for Analysis	686	84.0	572	70.0	451	55.2	215	26.3	59	7.2	39	4.8
visit)	8	1.0	35	4.3	86	10.5	226	27.7	348	42.6	535	65.5
Missed Visit	121	14.8	196	24.0	219	26.8	220	26.9	170	20.8	0	0.0
Retreated)	0	0.0	0	0.0	7	0.9	18	2.2	18	2.2	18	2.2
Lost to Follow-up	2	0.2	14	1.7	54	6.6	138	16.9	222	27.2	245	30.0
% Accountability		84.8%		73.1%		62.3%		37.5%		13.1%		10.7%

Table 1.1.E-5: Patient Accountability for Eyes Treated for High Myopia (with or without astigmatism)

Status	1 Month		3 Months		6 Months		12 Months		18 Months		24 Months	
N (Enrolled)	194		194		194		194		194		194	
	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%
Available for Analysis	163	84.0	154	79.4	120	61.9	56	28.9	19	9.8	13	6.7
visit)	2	1.0	5	2.6	22	11.3	56	28.9	79	40.7	111	57.2
Missed Visit	29	14.9	35	18.0	39	20.1	35	19.6	34	17.5	0	0.0
Retreated)	0	0.0	0	0.0	7	3.6	11	5.7	12	6.2	12	6.2
Lost to Follow-up	0	0.0	0	0.0	6	3.1	32	17.0	50	25.8	58	29.9
% Accountability		84.9%		81.5%		72.7%		44.1%		18.4%		18.3%

Table 1.1.E.1-9: Key Safety and Efficacy Variables for Eyes Treated for Low Myopia

	1 Month		3 Months		6 Months		12 Months		18 Months		24 Months	
N	686		572		451		215		59		39	
	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%
EFFICACY VARIABLES												
MRSE ± 0.50 D	408	59.5	359	62.8	278	61.6	144	67.0	39	66.1	28	71.8
MRSE ± 1.00 D	160	23.3	122	21.3	93	20.6	37	17.2	10	16.9	5	12.8
MRSE ± 2.00 D	63	9.2	51	8.9	34	7.5	14	6.5	4	6.8	2	5.1
MRSE ± 1.00 D (cumulative)	568	82.8	481	84.1	371	82.3	181	84.2	49	83.1	33	84.6
MRSE ± 2.00 D (cumulative)	631	92.0	532	93.0	405	89.8	195	90.7	53	89.8	35	89.7
Eyes Without Monovision												
# Non-Monovision (N)	314		260		202		99		23		13	
UCVA 20/20 or better	142	45.2	150	57.7	123	60.9	64	64.6	11	47.8	9	69.2
UCVA 20/25 to 20/40	153	48.7	99	38.1	74	36.6	33	33.3	12	52.2	3	23.1
(cumulative)	295	93.9	249	95.8	197	97.5	97	98.0	23	100.0	12	92.3
SAFETY VARIABLES												
Loss of > 2 lines BSCVA	6	0.9	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
BSCVA worse than 20/40	3	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Increase > 2 D cylinder	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
BSCVA worse than 20/25 if 20/20 or better preop	21	3.1	3	0.5	3	0.7	4	1.9	0	0.0	0	0.0

Table 4-21: NEV-97-002 Adverse Event Summary for All Eyes Treated

	Intraop		1 Month		3 Months		6 Months		9 Months		12 Month		18 Months		24 Months	
N	1013		849		326		571		149		231		73		52	
	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%
ADVERSE EVENTS																
Corneal infiltrate or ulcer		0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Corneal epithelial defect involving keratectomy site at 1 month or later			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Epithelium in interface		0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Lost, misplaced, or misaligned flap	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Melting of the flap		0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Uncontrolled IOP with increase of > 5 mm Hg above baseline or any reading above 25 mm Hg		0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Late onset of haze beyond 6 mos. with loss of 2 lines or more BSCVA							0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Decrease in BSCVA of ≥ 10 letters not due to irregular astigmatism as shown by hard contact lens refraction at 6 months or later							0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Retinal detachment	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Retinal vascular accidents	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Intraop		1 Month		3 Months		6 Months		9 Months		12 Month		18 Months		24 Months	
N	1011		849		326		571		149		231		73		52	
COMPLICATIONS																
Corneal edema between 1 week and 1 month after procedure			0	0.0												
Peripheral corneal defect at 1 month or later			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Epithelium in interface			0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Recurrent corneal erosion at 1 month or later			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Foreign body sensation at 1 month or later			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Pain at 1 month or later			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Ghost/double images in the operative eye			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Flap is not of the size and shape as initially intended or microkeratome stopped mid-cut	5	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Central island			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Posterior vitreous detachment			1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Ghost images			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Sterile keratitis			0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
Foreign body under flap			0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	2	3.8
Diplopia			1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Interface haze			0	0.0	2	0.3	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0
SPE (location not specified)			7	0.8	1	1.0	2	0.4	0	0.0	2	0.9	0	0.0	0	0.0
SPE (inferior)			0	0.0	3	0.4	3	0.5	0	0.0	4	1.5	0	0.0	0	0.0
SPE (epithelium)			15	1.6	7	1.0	9	1.6	5	3.4	2	0.7	0	0.0	2	3.8

Table 1.1.E.1-1: Key Safety and Efficacy Variables for All Eyes Treated

	1 Month		3 Months		6 Months		12 Months	
N	589		451		253		89	
	n/N	%	n/N	%	n/N	%	n/N	%
EFFICACY VARIABLES								
UCVA 20/20 or better	162	27.5	135	29.9	74	29.2	35	39.3
UCVA 20/25 to 20/40	288	48.9	210	46.6	119	47.0	38	42.7
(cumulative)	450	76.4	345	76.5	193	76.3	73	82.0
MRSE ± 0.50 D	261	44.3	200	44.3	125	49.4	53	59.6
MRSE ± 1.00 D	158	26.8	110	24.4	64	25.3	22	24.7
MRSE ± 2.00 D	123	20.9	98	21.7	48	19.0	10	11.2
MRSE ± 1.00 D (cumulative)	419	71.1	310	68.7	189	74.7	75	84.3
MRSE ± 2.00 D (cumulative)	542	92.0	408	90.5	237	93.7	85	95.5
Eyes Without Monovision								
# Non-Monovision (N)	339		260		140		51	
UCVA 20/20 or better	120	35.4	106	40.8	64	45.7	29	56.9
UCVA 20/25 to 20/40	163	48.1	116	44.6	55	39.3	17	33.3
(cumulative)	283	83.5	222	85.4	119	85.0	46	90.2
SAFETY VARIABLES								
Lost of > 2 lines BSCVA	0	0.0	0	0.0	0	0.0	0	0.0
BSCVA worse than 20/40	2	0.3	0	0.0	0	0.0	0	0.0
Increase > 2 D cylinder	5	0.8	3	0.7	1	0.4	0	0.0
BSCVA worse than 20/25 if 20/20 or better preop	7	1.2	3	0.7	0	0.0	0	0.0

G. SUMMARY OF COMPLICATIONS AND ADVERSE EVENTS:

Complications and adverse events that occurred in the study are summarized in the tables below for the pre-IDE and IDE subjects combined. The only reported complications were related to the microkeratome and creation of the corneal flap during the LASIK procedure.

Table 1.1.G-1: Complications Summary Table

COMPLICATION	Intra-operative n/N (%) N = 844	1 Month n/N (%) N = 579	3 Months n/N (%) N = 451	6 Months n/N (%) N = 253	12 Months n/N (%) N = 89
Corneal edema between 1 week and 1 month after the procedure	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Peripheral corneal epithelial defect at 1 month or later	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Epithelium in interface	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Foreign body sensation at 1 month or later	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pain at 1 month or later	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ghost/double images in the operative eye	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Flap is not of the size and shape as initially intended or microkeratome stopped in mid-cut.	5 (1.2)%	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TOTAL	5 (1.2)%	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

N = number of eyes completing the postoperative visit

Table 1.1.G-2: MICROKERATOME RELATED COMPLICATIONS SUMMARY TABLE

COMPLICATION	Intraoperative n/N (%) N = 875	Comment
Incomplete reverse of keratome	2 (0.2%)	Resulted in induced astigmatism (n=1); no effect on visual outcome (n=1).
Flap is not of the size and shape as initially intended	5 (0.5%)	Irregular keratectomy with thin central flap and case aborted (n=1).
Torn flap	12 (1.4%)	Torn flap resulted in wrinkling/ghosting (n=1), holes (n=1), decreased BCVA (n = 5), overcorrection or undercorrection (n=5).

Table 1.1.G-2: Adverse Events Summary Table

ADVERSE EVENT	1 Month n/N (%) N=155	3 Months n/N (%) N=156	6 Months n/N (%) N = 80	12 Months n/N (%) N=7
Corneal infiltrate or ulcer	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Any corneal epithelial defect involving the keratectomy site at ≥1 mo.	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Corneal edema at 1 month or later (specify flap or bed)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Epithelium in the interface	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lost, misplaced, or misaligned flap	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Melting of the flap	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Uncontrolled IOP with increase of >5 mm Hg above baseline and any reading >25 mm Hg	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Late onset of haze beyond 6 months with loss of 2 lines (10 letters) or more BSCVA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Decrease in BSCVA of > 10 letters not due to irregular astigmatism	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Retinal detachment	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Retinal vascular accidents	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TOTAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

N = number of eyes completing the postoperative visit

IDE Supplement No. 13

ANNUAL REPORT

IDE NUMBER: G970088

DEVICE: Nevyas Excimer Laser

INVESTIGATOR/ SPONSOR:

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INDICATIONS: LASIK for Myopia with or without Astigmatism
(-0.5 to -22 Diopters Sphere with up to -7 Diopters Astigmatism)

DATE SUBMITTED: November 4, 1998

PURPOSE: Supplement #13 is being filed as the annual report.

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TABLE OF CONTENTS

1.0 Study Progress 3
1.1 PROTOCOL NEV-97-002 3
1.2 Substudy NEV-97-002 10

2.0 Risk Analysis 11

3.0 Device Changes 12
3.1 Attenuator Plate 12
3.2 Fixation System for Optimal Centration 12

4.0 Changes in Investigational Plan 15

5.0 Progress towards PMA Approval 16

ATTACHMENTS:
1.1.E-1 Protocol NEV-97-001 Key Safety and Efficacy Variables 17