Nevyas Eye Assoc.
333 City Av.
Bala Cynwyd PA 19004
4/19,20,23-30, 5/1-4,7,10/2001 RALS

SUMMARY OF FINDINGS:

The inspection of this Sponsor/Clinical investigator was conducted per assignment from CDRH, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II(HFZ-312)and in accordance with CP 7348.811. Dr. Herbert J. Nevyas is the Medical Director and founder of Nevyas Eye Associates where he performs laser eye surgery on patients. Dr. Nevyas has an excimer laser, [redacted] and is conducting a clinical study, Correction of [redacted] under an approved Investigational Device Exemption (IDE). Dr. Nevyas is a Sponsor/Clinical Investigator and Dr. Anita Nevyas-Wallace is the Co-Investigator.

An inspection conducted on 12/2/96 revealed the firm had assembled a single excimer laser and was using it to perform [redacted] eye surgery on at least [redacted] patients without an approved IDE.

A follow-up inspection on 6/30/97 of this facility revealed the firm continued to use the excimer laser to perform [redacted] eye surgery without an approved IDE, planned to use the excimer laser for new treatment procedures not included in the firms disapproved IDE and verification that the firm had received a disapproval letter from CDRH/ODE notifying them that use of the laser to treat patients was a violation of the law.

The previous inspection conducted 11/2/1998 revealed procedures being performed on IDE patients prior to approval date, missing date on a consent form, consent forms signed after surgery date and procedures done on IDE patients which are outside the IDE with an unidentified laser at an unauthorized location.

The current inspection revealed the firm has corrected the deficiencies noted in the inspection of 11/2/1998 however, the Clinical Investigator did not notify the IRB of all changes or deviations from the protocol. There was an unexplained lapse in IRB approval/coverage for the protocol [redacted] for approximately one month. The inspection is classified [redacted]. An FDA-483 was issued at the conclusion of the inspection.

HISTORY OF BUSINESS:

Dr. Herbert J. Nevyas is the founder, Chief of Staff as well as the most responsible individual of Nevyas Eye Associates/Delaware Valley Laser Surgery Institute, 2 Bala Plaza, 333 City Av., Bala Cynwyd PA 19004. There are six additional physicians and three other locations associated with the practice.

All FDA correspondence should be addressed to Dr. Nevyas at the aforementioned Bala Cynwyd PA address. The firm operates Monday to Friday, 8:00am - 5:00pm.

PERSONS INTERVIEWED AND INDIVIDUAL RESPONSIBILITIES:

On 4/19/01 I presented my credentials and issued a FD-482 to Dr. Richard Sterling, Clinical Coordinator. He is not the most responsible individual at the firm however, Dr. Nevyas, who is the most responsible individual, was unavailable at the time. Dr. Nevyas is the founder and Medical Director of Nevyas Eye Associates. Dr. Nevyas stated Dr. Sterling would be able to answer my questions and be present throughout most of the inspection.

OPERATIONS:

Dr. Herbert J. Nevyas is the Medical Director and founder of Nevyas Eye Associates where he performs laser eye surgery on patients. Dr. Nevyas has an excimer laser and is conducting a clinical study, Correction of [redacted] under an approved Investigational Device Exemption (IDE). Dr. Nevyas is a Sponsor/Clinical Investigator. Dr. Anita Nevyas-Wallace is the Co-Investigator and the only other physician who performs LASIK surgical procedures with an excimer laser at the practice. The laser is identified as a [redacted]. It was built in the fall of 1995 by [redacted] Dr. Nevyas provided [redacted] with the basic specifications for the laser and [redacted] then designed and built the laser indicating to Dr. Nevyas the components that were needed and where to order them. The laser beam generator is a [redacted], serial number [redacted] purchased from [redacted] The housing and electrical/gas delivery system [redacted] source to produce the laser beam] was purchased from [redacted] The other components were ordered from other various manufacturers.

Previously [redacted]. performed all maintenance, repairs and calibrations on the IDE excimer laser. Currently [redacted] a subsidiary of [redacted], performs all maintenance, repairs and calibrations on the IDE excimer laser.

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Dr. Herbert Nevyas performs minor parts replacement and maintenance however, all major work is performed by [redacted] Maintenance records observed during the inspection do indicate that [redacted] is performing maintenance, repairs and calibrations.

The emission from the laser passes through a safety shutter, beam shaping optics, beam modulator, imaging optics and finally is reflected downward into the working region. The operation of the laser, shutter and beam shaping optics is controlled by a computer system. According to Barbara Fant, consultant, validation of the computer system is to be done by an outside firm and will be included with the submission

The desired lens correction information is entered into the computer which controls the laser beam size and delivered energy density during the ablation process. First a very thin corneal flap is created using an instrument called a [redacted]. When the eye is properly positioned, the operator uses a foot pedal to activate the laser and ablate the corneal tissue to achieve the desired lens correction. The corneal flap is then repositioned to heal.

Dr. Nevyas's initial IDE submission was disapproved May 8, 1998. He was granted conditional approval on August 7, 1998. As Dr. Nevyas addressed various issues presented in letters from FDA CDRH/ODE he was granted more uses of the IDE laser. As of 11/2/98 his investigation is limited to **1 institution (333 City Av., Bala Cynwyd PA location)** and [redacted]

IDE approval [redacted].

According to a letter from the FDA to Dr. Nevyas dated 1/20/99 **EXHIBIT #1**, the investigation is still limited to one location, listed in bold above however, the population has grown to [redacted] subjects ([redacted]); and [redacted]

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From the date the first patient was treated under the IDE, August 28, 1997, until 11/2/98 Dr. Nevyas has treated [redacted]

According to Dr. Nevyas' refractive log **EXHIBIT #2**, from December 29, 1999 until April 20, 2001 [redacted] have been treated for [redacted]

Laser Eye surgery is performed at the aforementioned main address and at the office located at 1001-E Lincoln Drive West, Greentree Executive Campus, Marlton NJ 08053.

OBJECTIONABLE CONDITIONS OR PRACTICES:

At the conclusion of the inspection an FD-483 was issued and a discussion with management held. Dr. Herbert J. Nevyas, Clinical Investigator and Dr. Richard Sterling, Clinical Coordinator attended the meeting.

The following observations refer to the Investigational Device Exemption (IDE) Protocol# [redacted] for the indicated study, "[redacted]

1. **There was no documentation to show that the CI notified the IRB about all amendments, changes or significant deviations to the protocol [per IRB requirements] prior to implementation.**

   For example, the FDA granted your firm an increase in the number of subjects you could treat with your investigational device on Jan. 20, 1999. IRB Annual Review dated 7/29/00 does not indicate the IRB knew about population increase. The IRB did not approve the population increase until August 28, 2000, 20 months later.

Dr. Nevyas uses a national IRB, [redacted] for his clinical research study.
EXHIBIT #1 is a letter from the FDA CDRH, Division of Ophthalmic Devices to Dr. Herbert J. Nevyas which among other things granted him an increase in the number of clinical research study subjects to [redacted]

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[redacted] sent Dr. Nevyas a notice dated August 1, 2000, **EXHIBIT #3**, to inform him that the revised protocol dated 7/8/98 in their possession indicated the [redacted] population was limited to [redacted]

Dr. Nevyas reported in a biannual report that was sent to [redacted] the number of [redacted] however, he failed to mention that the patient population had been increased by the FDA in Jan. 1999. Dr. Nevyas drafted a letter to [redacted] **EXHIBIT #4** dated 8/16/2000 explaining the increase in patient population. [redacted] reviewed the information from Dr. Nevyas and responded by letter **EXHIBIT #5** dated August 30, 2000 reapproving Dr. Nevyas' study for another year.

2. The firm is not complying with the Investigator Agreement which was signed and dated by the Clinical Investigator at the beginning of the Clinical Study.

EXHIBIT #6 is an Investor Agreement which was signed by Dr. Herbert Nevyas, Sponsor/Clinical Investigator and Dr. Anita Nevyas-Wallace Co-Investigator. The agreement indicates, among other things, the clinical investigators agree to promptly report to the IRB all changes in the research activity. The clinical investigators failed to report the increase in the number of study patients, granted by the FDA, to the IRB in a prompt manner.

3. There was a lapse of IRB approval for the protocol: [redacted] from 8/3/2000 until 8/29/2000 according to IRB lapse notices and the IRB annual re-approval letter.

EXHIBIT #7 is a reapproval letter from [redacted] dated 8/4/99 for Dr. Nevyas' study with an expiration date of 8/3/00. [redacted] wrote Dr. Nevyas on August 1, 2000, **EXHIBIT #3** indicating they had not received an update in the form of a report from him concerning the study. The letter also stated the IRB approval will lapse on 8/3/00. [redacted] wrote Dr. Nevyas for a second time on 8/7/2000 **EXHIBIT #8** indicating they still had not received any updates concerning the study. The letter also stated Dr. Nevyas should cease enrollment on [redacted] surgeries and if he chose to amend the protocol to request permission to do more [redacted] surgeries he could not begin scheduling the surgeries until the amendment was approved by the IRB. The laser refractive study log **EXHIBIT #2 pgs.12&13** show Dr. Nevyas continued performing [redacted] throughout the month of August 2000.

Finally, the letter stated IRB approval lapsed 8/3/00.

On 8/16/2000 Dr. Nevyas drafted a letter to [redacted] indicating the FDA had granted him an increase in the study patient population **EXHIBIT #4.** [redacted] sent Dr. Nevyas a letter dated August 30, 2000 reapproving the study effective the same date for another year **EXHIBIT #5.**

I explained to Dr. Nevyas that he did not have IRB coverage from 8/3/2000 and until 8/29/00. Dr. Nevyas stated his consultant, Barbara Fant was ill for several months and she normally took care of report submittals and updates which is why the firm was tardy with reporting updates. I indicated to Dr. Nevyas that either he or his consultant should have a back-up plan for such emergencies which could happen at any time. He stated a back-up plan would be drafted and implemented as soon as possible.

VOLUNTARY CORRECTIONS:

1. **[redacted] was performed on IDE patient [redacted] and patient [redacted] on 8/28/97 which was prior to the actual approval date.**

According to Dr. Herbert Nevyas, he was not aware that [redacted] was not approved and could not be performed. He stated this observation represents a misunderstanding between the FDA and him.

Dr. Herbert J. Nevyas stated he had been doing this procedure previously and no one had told him the procedure couldn't be performed as of 8/28/97. There were no violations of this type observed during the current inspection.

2. **IDE Patient [redacted] received [redacted] Enhancement on 9/25/97 OD (right eye) prior to the date approval was given to perform enhancements.**

Dr. Anita Nevyas-Wallace, Co-Investigator performed this procedure and stated her father, Dr. Herbert J. Nevyas, told her it was okay to perform [redacted] enhancements. Both investigators indicated they did not know it was not approved. Dr. Nevyas stated he thought it was okay and remembers getting verbal approval from someone at FDA in Rockville Md. I indicated to Dr. Nevyas that in the future he should obtain documentation for all approvals given. There were no violations of this type observed during the current inspection.

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3. Consent form for patient [redacted] was not signed. There was no way to determining whether consent was obtained before or after [redacted] to the right eye on 12/4/97, due to lack of a date next to patients' signature.

Dr. Nevyas assured me this was merely a mistake and that all patients read and sign consent forms before surgery. He stated he would remind his staff to be more careful when filling out consent forms. There were no incidences of this type observed during the current inspection.

4. Consent forms for patient [redacted] were signed and dated (2/20/98) one day after [redacted] to the right eye was performed (2/19/98).

Dr. Nevyas stated it may appear that patients signed the consent forms one day after surgery however, this is certainly not the case and is not the way things are normally done. He indicated this was a mistake made by someone on his staff. There were no incidences of this type observed during the current inspection.

5. Patient [redacted] had B[redacted] for [redacted] on 8/13/98. However, the patient information and consent form which was approved for use by the IRB on 7/17/98, was not present in the patient file or made available upon request.

Dr. Nevyas indicated this was a mistake and they would have to be more careful in the future. The person who is responsible was new and not aware of the IRB approved consent form to be used. There were no incidences of this type observed during the current inspection.

6. IDE patients, [redacted] had [redacted] performed which is a condition not indicated in the Protocol [redacted] Additionally, the procedures were performed with a laser that is not indicated in the study and the surgery was performed at a location that

is not identified in the protocol.

During the examination of patient records there were no non-indicated procedures performed on IDE patients with a laser that was not indicated in the study at a location which was not identified in the Protocol [redacted].

7. **There was no documentation to show that the CI notified the IRB about all amendments, changes or significant deviations to the protocol [per IRB requirements]**

This observation was carried forth to the current listing of objectionable conditions or practices. **See FDA-483 observation #1 listed above on page #4 of this report.**

Questions from Compliance Program CP 7348.811:

Authority and administration:

1. Barbara Fant, Pharm.D of Clinical Research Consultants, Cincinnati, Ohio 45220 visits the clinical site to monitor the clinical research according to the monitor's log examined during the inspection.

2. Dr. Herbert Nevyas is the principal investigator and Dr. Anita Nevyas-Wallace is the Co-Investigator, they retain control and knowledge of the study.

3. The study was not discontinued before completion and is currently ongoing.

4. A review of file records revealed pre-surgical eye tests for study patients are performed at Nevyas Eye Assoc.

Protocol:

1. Protocol for study is included as **EXHIBIT #9.**

2. There were no major changes to the protocol with reference to subject selection, frequency of subject observations, dosage, route of administration, frequency of dosage and blinding procedures, however there was an increase in the number of subjects.

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3. All changes made to the protocol were documented by the investigator, dated, maintained with the protocol, however all changes were not approved by the IRB **(see FDA-483 observation #1 listed on page 4 of this report)**. Patient files were organized, in good condition, complete and legible.

SUBJECTS' RECORDS:

1. The clinical investigator's raw data files were easy to follow, in good condition, organized complete and legible.

2. According to documents reviewed all audited subjects did exist and were alive and available for the duration of their stated participation in the study.

3. Pre-surgical eye tests, as noted in the case report forms, was documented by the presence of completed test records among the raw data.
   a) Adverse reactions were reported in the case report forms and they were listed in the consent form
   b) All concomitant therapy and/or intercurrent illness was clearly indicated on the patient case report forms.
   c) The number and type of subjects entered into the study were confined to protocol limitations.

4. According to the records I reviewed, I observed each patient record contains:
   a) Observations, information, and data on the condition of the subject at the time the subject was entered into the clinical study;
   b) The identity of all persons and locations obtaining raw data or involved in the collection or analysis of such data.
5. According to records reviewed the clinical investigator did report all dropouts, and the reasons therefore, to the sponsor.

Consent of Human Subjects:

1. According to records reviewed, informed consent was obtained from all subjects prior to their entry into the study.

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Institutional Review Board (IRB):

1. [redacted]

See **EXHIBIT #10** FOR IRB Membership.

According to records reviewed, the investigator maintains copies of all reports submitted to the IRB and reports of all actions by the IRB.

a) The investigator did submit reports of all deaths and adverse reactions to the IRB.

3. According to records reviewed, the investigator did submit and obtain IRB approval of the protocol, modifications to the protocol **(except as noted in FDA-483 OBSERVATION #1)**, report of prior investigations, materials to obtain human subject consent and media ads for patient/subject recruitment before subjects were allowed to participate in the study.

4. There was no indication that the investigator disseminated promotional material or otherwise represent that the device was safe and effective for the purpose for which it is under investigation.

Records Retention:

1. The clinical investigator maintains custody of the clinical study records. Study is ongoing.

ATTACHMENTS:

1. FDA-482, Notice of Inspection dated 4/19/2001
2. FDA-483, Inspectional Observations

EXHIBITS:

1. Letter from the FDA CDRH, Division of Ophthalmic Devices to Dr. Herbert J. Nevyas dated 1/20/99.

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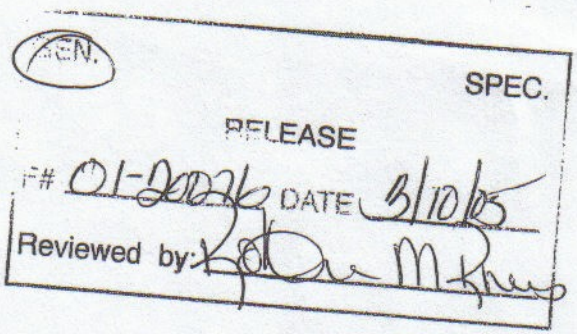
2. Refractive surgery log for Nevyas Eye Assoc.
3. Letter from [redacted] to Dr. Nevyas dated 8/1/2000
4. Letter from Dr. Nevyas to [redacted] dated 8/16/2000
5. Reapproval letter from [redacted] to Dr. Nevyas dated 8/30/2000
6. Nevyas Eye Assoc. Investigator agreement dated 3/18/1997
7. Reapproval letter from [redacted] to Dr. Nevyas dated 8/4/1999
8. Letter from [redacted] to Dr. Nevyas dated 8/7/2000
9. Protocol# [redacted] for the indicated study, [redacted] in the [redacted]
10. [redacted] Board Members

Ronald Stokes

Ronald Stokes, CSO



DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
US Food and Drug Administration Rm. 900 US Customhouse, 2nd and Chestnut Sts. Phila. PA 19106 (215) 597-4390	4/19,20, 23-30, 5/1-4,7, 10/2001
	FEI NUMBER 2531320

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Dr. Herbert J. Nevyas MD

FIRM NAME	STREET ADDRESS
Medical Director	2 Bala Plaza, 333 City Ave
CITY, STATE AND ZIP CODE Bala Cynwyd PA 19004	TYPE OF ESTABLISHMENT INSPECTED Sponsor/Clinical Investigator

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

The following observations refer to the Investigational Device Exemption [redacted] for the indicated study, [redacted]

1. There was no documentation to show that the CI notified the IRB about all amendments, changes or significant deviations to the protocol [per IRB requirements] prior to implementation.

   For example, the FDA granted your firm an increase in the number of subjects you could treat with your investigational device on Jan. 20, 1999. IRB Annual Review dated 7/29/00 does not indicate the IRB knew about population increase. The IRB did not approve the population increase until August 28, 2000, 20 months later

2. The firm is not complying with the Investigator Agreement which was signed and dated by the Clinical Investigator at the beginning of the Clinical Study.

3. There was a lapse of IRB approval for the protocol [redacted] from 8/3/2000 until 8/29/2000 according to IRB lapse notices and the IRB annual re-approval letter.

GEN. SPEC.

RELEASE

F# 01-[illegible] DATE 3/10/05

Reviewed by: [signature]

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE *(Print or Type)*	DATE ISSUED
	Ronald Stokes	Ronald Stokes	May 10, 2001