DEPARTMENT OF HEALTH & HUMAN SERVICES

DEC 19 1997

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

DEC 16 1997

Herbert J. Nevyas, M.D.
Nevyas Eye Associates
Delaware Valley Laser Surgery Institute
333 City Line Avenue
Bala Cynwyd, PA 19004

Re: G970088/S5
Sullivan Excimer Laser System (Nevyas Model)
Indications for Use: LASIK to correct myopia of -0.5 to -15 Diopters (D) with up to -7 D of astigmatism for protocol NEV-97-001 Myopia; and, LASIK enhancement to correct myopia of eyes previously treated with this laser
Dated: November 12, 1997
Received: November 17, 1997
Annual Report Due: August 7, 1998

Dear Dr. Nevyas:

The Food and Drug Administration (FDA) has reviewed the supplement to your investigational device exemptions (IDE) application. Your application remains conditionally approved because your supplement adequately addressed only deficiency 2 cited in our October 3, 1997 letter. You may continue your investigation at the institution where you have obtained institutional review board (IRB) approval. Your investigation is limited to one institution and 150 subjects: 100 subjects for low myopia (-0.5 to -6.75 D myopia plus up to -7 D astigmatism); 25 subjects for high myopia (-7 to -15 D with up to -7 D astigmatism); and, 25 subjects for enhancements of previously treated subjects (-0.5 to -15 D myopia with up to -7 D astigmatism).

This approval is being granted on the condition that, within 45 days from the date of this letter, you submit information correcting the following deficiencies:

1. You have stated that you currently are working on plans for a fail-safe mechanism for your device. Please submit an engineering plan and time-table for retrofitting your device with an adequate fail-safe mechanism. This mechanism should include a safe means to complete the treatment.

FDA 0 0032

2. Regarding retreatments (enhancements), your data do not appear to support enhancement after 8 weeks postoperatively. It is possible that there is merely a matter of differences in interpreting your data. Please provide your stability data according to the tables enclosed (see enclosure, "Stability of Manifest Refraction"). Also, please submit a retreatment study plan. You may begin retreatment procedures only after FDA has reviewed that data and approved your retreatment study plan.

This information should be identified as an IDE supplement referencing the IDE number above, and must be submitted in triplicate to:

IDE Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, MD 20850

If you do not provide this information within 45 days from the date of this letter, we may take steps to propose withdrawal of approval of your IDE application.

You are reminded that prior to a request for expansion beyond 150 subjects, you should provide adequate responses to deficiencies 5 - 16 in our letter of October 3, 1997.

If you have any questions, please contact Everette T. Beers, Ph.D. at (301) 594-2018.

Sincerely yours,

A. Ralph Rosenthal, M.D.
Director
Division of Ophthalmic Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure:
Tables for Stability of Manifest Refraction

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JAN 2 0 1998

RH

JAN 1 4 1998

Herbert J. Nevyas, M.D.
Nevyas Eye Associates
Delaware Valley Laser Surgery Institute
333 City Line Avenue
Bala Cynwyd, PA 19004

Re: G970088/S6
Sullivan Excimer Laser System (Nevyas Model)
Indications for Use: LASIK to correct myopia of -0.5 to -15 Diopters (D) with up to -7 D of astigmatism for protocol NEV-97-001 Myopia; and, LASIK enhancement to correct myopia of eyes previously treated with this laser
Dated: December 11, 1997
Received: December 15, 1997
Annual Report Due: August 7, 1998

Dear Dr. Nevyas:

The Food and Drug Administration (FDA) has reviewed the supplement to your investigational device exemptions (IDE) application proposing a plan for simultaneous bilateral LASIK. Your supplement is conditionally approved, and you may implement that change at the institution enrolled in your investigation. Your application remains conditionally approved because you have not addressed the deficiencies cited in our December 16, 1997 letter. You may continue your investigation at the institution where you have obtained institutional review board (IRB) approval. Your investigation is limited to 1 institution and 150 subjects: 100 subjects for low myopia (-0.5 to -6.75 D myopia plus up to -7 D astigmatism); 25 subjects for high myopia (- 7 to -15 D with up to -7 D astigmatism); and, 25 subjects for enhancements of previously treated subjects (-0.5 to -15 D myopia with up to -7 D astigmatism).

This approval is being granted on the condition that, within 45 days from the date of this letter, you submit information correcting the following deficiencies:

In your "Substudy for Same-Day Versus Different Day LASIK Treatment for Fellow Eyes":

FDA 0 0034

a. Please revise your informed consent document rider for same day surgery to state that the second eye will be rescheduled if there is a complication or an adverse event with the first eye.

b. Those eyes rescheduled from same day to different day surgery should be accounted for.

c. If the exclusion criteria of the original protocol do not specifically mention the exclusion of patients with anterior segment lid diseases (e.g., blepharitis, etc.), then the substudy protocol should specifically exclude patients with these conditions for same day fellow eye surgery.

d. FDA believes that a one day interval is not sufficient to qualify as a "different day" procedure. It is recommended that the protocol for the substudy be altered to have a minimum 2-week waiting period prior to fellow eye treatment.

e. Your statement in the rider to the informed consent document that "...There have been no failures or malfunctions of the Willis Excimer Laser", should be removed or altered. It may unduly influence potential same day fellow eye surgery candidates into believing that the Nevyas Excimer Laser cannot fail. FDA recommends that you remove this statement or alter it to read: "There have been no failures or malfunctions of the Nevyas Excimer Laser to date."

f. Please specify the minimum time between treatment of same day fellow eyes, in order to evaluate for complications. ½ hr.

g. These same day fellow eye subjects are considered part of your overall total, currently 100 eyes low myopia and 25 eyes high myopia.

This information should be identified as an IDE supplement referencing the IDE number above, and must be submitted in triplicate to:

IDE Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, MD 20850

If you do not provide this information within 45 days from the date of this letter, we may take steps to propose withdrawal of approval of your IDE application.

If you have any questions, please contact Everette T. Beers, Ph.D. at (301) 594-2018.

Sincerely yours,

A. Ralph Rosenthal, M.D.
Director
Division of Ophthalmic Devices
Office of Device Evaluation
Center for Devices and Radiological Health

APR 0 6 1998

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Herbert J. Nevyas, M.D.
Nevyas Eye Associates
Delware Valley Laser Surgery Institute
333 City Line Avenue
Bala Cynwyd, PA 19004

APR - 1 1998

Re: G970088

Dear Dr. Nevyas:

You currently have an investigational device exemption G970088 for your laser. If you should ultimately wish to submit a premarket approval application (PMA) for this laser, please use the following guidance as to the type of information you need to submit to FDA regarding manufacture of your device.

If you do not intend to manufacture additional units of the excimer laser system that is the subject of your PMA, FDA will forego a Good Manufacturing Practices (GMP) inspection, but we will require you to submit manufacturing information in the Manufacturing Section of your PMA. In the past communications with your consultant, Barbara Fant, Pharm.D., we have stated that this information should include:

complete specifications for the laser unit, including operating parameters;

acceptance specifications for raw material and components;

a description of the complaint file procedures; and

procedures for change controls for any changes in the design of the one laser unit.

FDA 0 0037

The above-listed requirements are critical to the submission of your PMA Manufacturing Section, but cannot legally constitute a complete list of the information you will need to submit for this section. Section 515 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) requires that an application for premarket approval for a Class III device, such as yours, shall contain "a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and , when relevant, packing and installation of, such device." 21 U.S.C. 360 (e)(1)(C). Similarly, 21 C.F.R. 814.20(b)(4)(v) requires that unless an applicant

justifies an omission in accordance with 21 C.F.R. 814.20(d), a PMA shall include a complete description of "[t]he methods used in, and the facilities and controls used for, the manufacture, processing, packing, storage, and, where appropriate, installation of the device, in sufficient detail so that a person generally familiar with current good manufacturing practice can make a knowledgeable judgment about the quality control used in the manufacture of the device."

You are responsible for providing all manufacturing information required under the FD&C Act and under FDA's regulations. In order to do so, you should consider in detail each section of FDA's Quality System Regulation, found at 21 C.F.R. Part 820 (reprinted in the Appendix to the Medical Devices Quality Systems Manual located at FDA's website, www.fda.gov/cdrh/dsma/cgmphome.html). If you decide not to manufacture additional units of your device and believe that specific types of manufacturing information are not applicable for your device as a result of this decision, you will be required to identify the omitted information and
justify the omission, in accordance with 21 C.F.R. 814.20(d).

If you have any questions about this letter please call Mary Lou Davis at (301) 594-4613.

Sincerely yours,

A. Ralph Rosenthal, M.D.
Director
Division of Ophthalmic Devices
Office of Device Evaluation
Center for Devices and Radiological Health

MAY 2 0 1998

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

MAY 1 4 1998

Herbert J. Nevyas, M.D.
Nevyas Eye Associates
Delaware Valley Laser Surgery Institute
333 City Line Avenue
Bala Cynwyd, PA 19004

Re: G970088/S8 & S9
Sullivan Excimer Laser System (Nevyas Model)
Indications for Use: LASIK (Laser-Assisted In Situ Keratomileusis) to correct myopia of -0.5 to -15 Diopters (D) with up to -7 D of astigmatism for protocol NEV-97-001 Myopia; and, LASIK enhancement to correct myopia of eyes treated with this laser prior to IDE approval.
Dated: April 12 and 14, 1998
Received: April 14 and May 8, 1998
Annual Report Due: August 7, 1998

Dear Dr. Nevyas:

The Food and Drug Administration (FDA) has reviewed the supplements to your investigational device exemptions (IDE) application. Supplement 8 proposed a plan for a contrast sensitivity substudy and provided a design for a fail-safe mechanism, and Supplement 9 requested additional high myopia subjects. Your plan for a contrast sensitivity substudy is conditionally approved, and you may implement that change at the institution enrolled in your investigation. Your design and time-table for a fail-safe mechanism is approved. Your request for additional high myopia subjects (- 7 to -15 D with up to -7 D astigmatism) is approved for an additional 25 subjects (50 eyes). In addition, your application is approved for an additional 50 subjects (100 eyes) for low myopia (-0.5 to -6.75 D myopia plus up to -7 D astigmatism).

Your application is approved because you have addressed the deficiencies cited in our December 16, 1997 letter. You may continue your investigation at the institution where you have obtained institutional review board (IRB) approval. Your investigation is limited to 1 institution and 225 subjects: 150 subjects (300 eyes) for low myopia (-0.5 to -6.75 D myopia plus up to -7 D astigmatism); 50 subjects (100 eyes) for high myopia (- 7 to -15 D with up to -7 D astigmatism); and, 25 subjects (50 eyes) for enhancements of subjects treated prior to IDE approval (-0.5 to -15 D myopia with up to -7 D astigmatism).

FDA 0 0039

Since FDA believes this change affects the rights, safety or welfare of the subjects, you must

This approval is being granted on the condition that, within 45 days from the date of this letter, you submit information correcting the following deficiency:

Please submit your agreement that you will validate the proposed glare source prior to initiating this substudy. An appropriate validation would be a small control study with 5-10 normal emmetropic subjects. The glare source should just significantly raise contrast thresholds for these subjects. If it does not, the glare is too dim and will not be a sensitive measure of glare effects in LASIK subjects. In that case, the glare source will need to be brightened until it raises normal contrast thresholds.

This information should be identified as an IDE supplement referencing the IDE number above, and must be submitted in triplicate to:

IDE Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, MD 20850

If you do not provide this information within 45 days from the date of this letter, we may take steps to propose withdrawal of approval of your IDE application.

We would like to point out that FDA approval of your IDE supplement does not imply that this investigation will develop sufficient safety and effectiveness data to assure FDA approval of a premarket approval (PMA) application for this device. You may obtain the guideline for the preparation of a PMA application, entitled "Premarket Approval (PMA) Manual," from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597.

You are reminded (see our letter of December 16, 1997) that you may not begin retreatment procedures on subjects treated under this IDE until FDA has reviewed your stability data and approved your retreatment study plan..

FDA 0 0040

We acknowledge your request in your original IDE (dated March 18, 1997) to conduct a study at one site with 400 eyes low myopia and 590 eyes high myopia for each of two investigators (single site total of 1980 eyes or 990 subjects). We believe that adequate safety information has been provided to allow the initiation of your study with a small expansion of an additional 75 subjects (150 eyes). We will allow you to expand to the full number of subjects for this study (990) after you have received approval of supplements addressing the following deficiency from our letter of October 3, 1997 (enclosed). No additional expansions of your IDE will be

Your contrast sensitivity substudy submitted in supplement 8 adequately addresses only deficiency 14.b., in our letter of October 3, 1997. Please submit adequate responses to deficiency 14, page 7, regarding probable multifocal properties of your ablation profiles and the need for procedures for post operative manifest refraction, graphs of dioptric power or radius of curvature as a function of distance from the center of the ablation, preoperative and post operative topographic difference maps, and lensometer measurements of the PMMA profile.

You also may want to consider incorporating into your laser system an additional algorithm to perform spherical ablations, so that you can compare in a clinical substudy your current ablation profile with a spherical ablation profile. We are available to meet with you to discuss our requirements for full approval, if you have any questions or wish further guidance.

You should also give serious consideration to the following items which are considered essential for the analysis of your data for the purposes of determining safety and effectiveness for a future PMA application:

Deficiencies 5 through 16, excluding deficiency 14, in our letter of October 3, 1997.

If you have any questions, please contact Everette T. Beers, Ph.D. at (301) 594-2018.

Sincerely yours,

Nancy C. Brogdon for

A. Ralph Rosenthal, M.D.
Director
Division of Ophthalmic Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure: Letter of October 3, 1997

FDA 0 0041

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUL 7 1998

Herbert J. Nevyas, M.D.
Nevyas Eye Associates
Delaware Valley Laser Surgery Institute
333 City Line Avenue
Bala Cynwyd, PA 19004

Re: G970088/S10
Sullivan Excimer Laser System (Nevyas Model)
Indications for Use: LASIK (Laser-Assisted In Situ Keratomileusis) to correct myopia of -0.5 to -15 Diopters (D) with up to -7 D of astigmatism for protocol NEV-97-001 Myopia; and, LASIK retreatment to correct myopia and myopic astigmatism.
Dated: June 3, 1998
Received: June 8, 1998
Next Annual Report Due: August 7, 1998

Dear Dr. Nevyas:

The Food and Drug Administration (FDA) has reviewed the supplement to your investigational device exemptions (IDE) application addressing glare testing validation and proposing an expansion of your investigation to include both myopic and hyperopic retreatments (enhancements). FDA cannot approve your request as proposed because you have not shown stability of manifest refraction, and you have not presented sufficient detail for your hyperopic retreatment. FDA will conditionally approve, however, an expansion to include myopia and myopic astigmatism retreatments at this time. If you agree to conduct your investigation within the modified limit (myopia and myopic astigmatism retreatments only), you may implement that change at the institution where you have obtained institutional review board (IRB) approval. Your investigation is limited to 1 institution and 225 subjects: 150 subjects (300 eyes) for low myopia (-0.5 to -6.75 D myopia plus up to -7 D astigmatism); 50 subjects (100 eyes) for high myopia (- 7 to -15 D with up to -7 D astigmatism); and, 25 subjects (50 eyes) for enhancements of subjects treated prior to IDE approval (-0.5 to -15 D myopia with up to -7 D astigmatism).

If you do not agree to this modified limit, you should consider this letter as a disapproval of your request for an expansion of the investigation, and you have an opportunity to request a regulatory hearing as described in the enclosure "Procedures to Request a Regulatory Hearing."

FDA 0 0042

Since FDA believes this change affects the rights, safety or welfare of the subjects, you must [illegible] approval before implementing this change

This approval is being granted on the condition that, within 45 days from the date of this letter, you submit your agreement to:

1. conduct the investigation within the modified limit; i.e., retreatment for myopia or myopic astigmatism only;

2. extend the minimum time between the initial operation and the retreatment to 3 months; and,

3. retreat only eyes which are "white and quiet" and in which refractive stability has been documented with two manifest refractions taken at least 30 days apart with less than 1 diopter of change, confirmed by topography.

This information should be identified as an IDE supplement referencing the IDE number above, and must be submitted in triplicate to:

IDE Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, MD 20850

If you do not provide this information within 45 days from the date of this letter, we may take steps to propose withdrawal of approval of your IDE application.

We would like to point out that FDA approval of your IDE supplement does not imply that this investigation will develop sufficient safety and effectiveness data to assure FDA approval of a premarket approval (PMA) application for this device. You may obtain the guideline for the preparation of a PMA application, entitled "Premarket Approval (PMA) Manual," from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597.

You should give serious consideration to the fact that your procedure does not appear to reach stability, as defined by stability of manifest refractions taken 3 months apart: 95% within 1 diopter, mean difference of ≤ 0.1, and a lower confidence limit of 90%. The appearance of instability of manifest refraction may be the result of unreliable or variable refractions having been taken by different persons using different instruments. In addition, you should continue to pursue follow-up on all subjects; it appears that you had 81 subjects eligible for the 3 month visit, yet only 67 were reported to FDA.

Prior to your request to modify your protocol to provide hyperopic retreatments, you should

You indicated that you have performed hyperopic retreatments on your pre-IDE patients. Please provide any information you have on these patients regarding pre-retreatment visual acuity, amount of retreatment required, post-retreatment visual acuity and stability of manifest refraction, and any other information which would be appropriate in demonstrating that this procedure provides a stable retreatment of an overcorrected cornea.

We acknowledge your request in your original IDE (dated March 18, 1997) to conduct a study at one site with 400 eyes low myopia and 590 eyes high myopia for each of two investigators (single site total of 1980 eyes or 990 subjects). We will approve a request to expand to the full number of subjects for this study (990) after you have received approval of supplements addressing the following deficiency from our letter of October 3, 1997. No additional expansions of your IDE will be granted until supplements containing the following information are approved:

Your contrast sensitivity substudy submitted in supplement 8 adequately addresses only deficiency 14.b., in our letter of October 3, 1997. Please submit adequate responses to deficiency 14, page 7, regarding probable multifocal properties of your ablation profiles and the need for procedures for postoperative manifest refraction, graphs of dioptric power or radius of curvature as a function of distance from the center of the ablation, preoperative and postoperative topographic difference maps, and lensometer measurements of the PMMA profile.

You also may want to consider incorporating into your laser system an additional algorithm to perform spherical ablations, so that you can compare in a clinical substudy your current ablation profile with a spherical ablation profile. We are available to meet with you to discuss our requirements for full approval, if you have any questions or wish further guidance.

If you have any questions, please contact Everette T. Beers, Ph.D. at (301) 594-2018.

Sincerely yours,

A. Ralph Rosenthal, M.D.
Director
Division of Ophthalmic Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure:
"Procedures to Request a Regulatory Hearing."

FDA 0 0044

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

SEP 2 8 1998

SEP 2 4 1998

Herbert J. Nevyas, M.D.
Nevyas Eye Associates
Delaware Valley Laser Surgery Institute
333 City Line Avenue
Bala Cynwyd, PA 19004

Re: G970088/S12
Sullivan Excimer Laser System (Nevyas Model)
Indications for Use: LASIK (Laser-Assisted In Situ Keratomileusis) to correct myopia of -0.5 to -15 Diopters (D) with up to -7 D of astigmatism for protocol NEV-97-001 Myopia; and, LASIK retreatment to correct myopia and myopic astigmatism.
Dated: August 24, 1998
Received: August 27, 1998
Next Annual Report Due: August 7, 1998 (Extension granted to September 21, 1998)

Dear Dr. Nevyas:

The Food and Drug Administration (FDA) has reviewed the supplement to your investigational device exemptions (IDE) application addressing deficiencies in our July 7, 1998 letter regarding myopia and myopia plus astigmatism retreatments and addressing the deficiency in our letter of May 14, 1998 regarding validation of your glare source for contrast sensitivity testing. Your supplement proposing an expansion of your study for myopia and myopia plus astigmatism retreatments is approved. Your supplement regarding contrast sensitivity testing is conditionally approved. You may continue your investigation at the institution enrolled in your investigation. Your investigation is limited to 1 institution and 225 subjects: 150 subjects (300 eyes) for low myopia (-0.5 to -6.75 D myopia plus up to -7 D astigmatism); 50 subjects (100 eyes) for high myopia (-7 to -15 D with up to -7 D astigmatism); and, 25 subjects (50 eyes) for enhancements of subjects treated prior to IDE approval (-0.5 to -15 D myopia with up to -7 D astigmatism).

Since FDA believes this change affects the rights, safety or welfare of the subjects, you must also obtain institutional review board (IRB) approval before implementing this change in your investigation (21 CFR 812.35(a)).

This approval is being granted on the condition that, within 45 days from the date of this letter, you submit information correcting the following deficiency: FDA 0 0045

In the validation of your glare source for the contrast sensitivity study, you tested subjects at 2.5 cd without glare and at 2.5 cd with glare of 2 lux. The light level of

cycles per degree (CPD). However, the glare source of 2 lux appears to be too bright, since even the emmetropic subjects have significant reductions (50% to 80%) at all CPD. With this severe degree of impairment in normal subjects, there is very little additional decline, if any, that can be attributed to the study subjects. A small decrease of 10% to 30% with the glare source would show that the glare source was bright enough to affect normals, yet still be able to observe a decrease, if any, in the study subjects. Please re-validate this study using a less intense glare source; perhaps 1.5 lux would be appropriate.

This information should be identified as an IDE supplement referencing the IDE number above, and must be submitted in triplicate to:

IDE Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, MD 20850

If you do not provide this information within 45 days from the date of this letter, we may take steps to propose withdrawal of approval of your IDE application.

We would like to point out that FDA approval of your IDE supplement does not imply that this investigation will develop sufficient safety and effectiveness data to assure FDA approval of a premarket approval (PMA) application for this device. You may obtain the guideline for the preparation of a PMA application, entitled "Premarket Approval (PMA) Manual," from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597.

If you have any questions, please contact Everette T. Beers, Ph.D. at (301) 594-2018.

Sincerely yours,

A. Ralph Rosenthal, M.D.
Director
Division of Ophthalmic Devices
Office of Device Evaluation
Center for Devices and Radiological Health

DEC 07 1998

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administratic
9200 Corporate Boulevard
Rockville MD 20850

DEC 3 - 1998

Herbert J. Nevyas, M.D.
Nevyas Eye Associates
Delaware Valley Laser Surgery Institute
333 City Line Avenue
Bala Cynwyd, PA 19004

Re: G970088/S13
Sullivan Excimer Laser System (Nevyas Model)
Indications for Use: LASIK (Laser-Assisted In Situ Keratomileusis) to correct myopia of -0.5 to -15 Diopters (D) with up to -7 D of astigmatism for protocol NEV-97-001 Myopia; and, LASIK retreatment to correct myopia and myopic astigmatism of eyes treated with this laser prior to IDE approval
Dated: October 30, 1998
Received: November 2, 1998
HCFA Category: A-2
Next Annual Report Due: August 7, 1999

Dear Dr. Nevyas:

The Food and Drug Administration (FDA) has reviewed the supplement to your investigational device exemptions (IDE) application proposing an accommodation substudy to address multifocality of the LASIK ablation. Your supplement is approved, and you may implement that change at the institution enrolled in your investigation. Your investigation is limited to one institution and 225 subjects (450 eyes): 150 subjects (300 eyes) for low myopia (-0.5 to -6.75 D myopia plus up to -7 D astigmatism); 50 subjects (100 eyes) for high myopia (- 7 to -15 D with up to -7 D astigmatism); and, 25 subjects (50 eyes) for enhancements of subjects treated prior to IDE approval (-0.5 to -15 D myopia with up to -7 D astigmatism).

We would like to point out that FDA approval of your IDE supplement does not imply that this investigation will develop sufficient safety and effectiveness data to assure FDA approval of a premarket approval (PMA) application for this device. You may obtain the guideline for the preparation of a PMA application, entitled "Premarket Approval (PMA) Manual," from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597.

Please be aware that we now believe your proposed mesopic contrast sensitivity study will adequately address deficiency 14 of our letter of October 7, 1997, without the need for a test of the multifocal properties of your ablation, such as your proposed test for change in accommodation. The reason for this is that the contrast sensitivity test may

Although it is not required, you may decide to study the change in accommodation anyway; if you do this study, you should use the same subjects as those enrolled in the contrast sensitivity study. You should also keep in mind that in your proposed test, a subject with a multifocal cornea may accommodate, for several reasons: perhaps the infinity point provides more power than the near point, or perhaps the subject is simply accustomed to accommodating under near viewing conditions. Also, you are only proposing to measure two points (infinity and near). A more informative test would be a depth of focus test under cycloplegic conditions, which would measure acuity at many potential planes of focus. This test would have to be performed with an artificial pupil held close to the eye, because the cycloplegic pupil usually would be larger than the diameter ablated.

We continue to be concerned that your ablation is likely to have multifocal properties, which means that some light will be out of focus even at the best focal plane. It is possible that your proposed mesopic contrast sensitivity study will help resolve some of these concerns. Also, any claims you may wish to assert regarding advantages of multifocality may not be supported by your change in accommodation study.

If you have any questions, please contact Everette T. Beers, Ph.D. at (301) 594-2018.

Sincerely yours,

A. Ralph Rosenthal, M.D.
Director
Division of Ophthalmic Devices
Office of Device Evaluation
Center for Devices and Radiological Health

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administrati
2098 Gaither Road
Rockville MD 20850

JAN - 7 1999

Herbert J. Nevyas, M.D.
Nevyas Eye Associates
Delaware Valley Laser Surgery Institute
2 Bala Plaza
333 City Avenue
Bala Cynwyd, Pennsylvania 19004

Dear Dr. Nevyas:

During the period of October 6 through November 2, 1998, Nevyas Eye Associates was visited by Mr. Ronald Stokes, an investigator from the Food and Drug Administration's (FDA) Philadelphia District Office. The purpose of that visit was to inspect your activities as a sponsor and clinical investigator of studies of laser assisted in situ keratomileusis (LASIK) for the treatment of myopia, with or without astigmatism, with the Sullivan Excimer Laser, Nevyas model, to determine if they complied with applicable FDA regulations. Excimer lasers are devices as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval Applications (PMA), and Premarket Notifications [510(k)] are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report submitted by the district revealed deviations from Title 21, Code of Federal Regulations, (21CFR), Part 812 - Investigational Device Exemptions and Part 50 - Protection of Human Subjects and Section 520(g) of the Act. The deviations noted during the inspection were listed on form FDA-483, "Inspectional Observations," which was presented to and discussed with you at the conclusion of the inspection. We acknowledge receipt of a November 30 response to the deviations from your consultant, Barbara S. Fant, Pharm. D.

It was noted on the form FDA-483 that two subjects had undergone simultaneous bilateral LASIK surgery prior to IDE approval for bilateral treatment. The response states that the original conditional approval of your IDE, dated 8/7/98, had included simultaneous bilateral surgery but that this approval had been rescinded for all Sullivan laser users on 10/3/97. Enclosed with the response was a copy of a letter to Dr. Everette Beers, Office of Device Evaluation (ODE), from Dr. Richard H. Sterling dated 10/23/97, which notes that two surgeries had been performed under the IDE study but that no additional bilateral procedures would be performed until specific IDE approval had been received. Dr. Beers confirmed that it had been assumed by Dr. Nevyas and other excimer investigators that IDE approval included bilateral

procedures. This had not been intended by ODE and therefore specific requests for this indication were solicited from those who possessed approved IDEs and wished to continue performing bilateral procedures. The letter from Dr. Sterling reflects Dr. Nevyas' adherence to this request. However, according to Mr. Stokes, he was not shown a copy of this letter during his inspection of your Institute.

Another deviation noted was enhancement of a subject prior to approval of the retreatment supplement to the IDE. Dr. Morris Waxler confirmed that the policy of his division was to allow, upon request, enhancement of small numbers of subjects originally treated with an excimer laser prior to IDE approval. This was with the understanding that an official request for an IDE supplement for this indication would follow shortly. The inspection report notes that you stated that you thought the procedure was approved. It does not include mention of verbal permission from Dr. Waxler, as noted in the response.

With regard to issues related to informed consents, the response states that the subject who had not received a copy of the revision of the informed consent as approved by the Institutional Review Board (IRB) for simultaneous bilateral surgery has since been sent the addendum in question. Moreover, your staff has been instructed to assure that the proper informed consent is used and that each consent form contains a properly executed signature and date in both the subject and witness signature areas. These actions should prevent future problems in this area.

Use of the Summit laser at your Marlton, New Jersey site for off-label procedures is not included in your IDE protocol. Moreover, enhancements approved under your IDE do not include hyperopic procedures. It is therefore considered a protocol violation to retreat subjects of your IDE study using the Summit laser and performing hyperopic LASIK. There is a difference between subjects treated as part of an IDE study and patients treated in the normal course of your practice. It is the responsibility of the clinical investigator to make every effort to assure that the subjects enrolled in a study are aware of the investigational nature of the procedure from the start and the need for specific control of their treatment while they are participants in the study. Treatment of subjects with devices and/or procedures that are not included in the approved IDE are considered protocol violations. The hyperopic enhancement terminates the inclusion of the retreated subjects in the study.

Moreover, according to 21 CFR 812.150(a)(4), an investigator must notify the reviewing IRB of any deviation from the investigational plan in an emergency no later than 5 working days after the emergency occurred. Except in such an emergency, prior approval by the IRB is needed for changes to the protocol.

During the inspection, Mr. Stokes also discussed with you the need to have advertisements related to your IDE study approved by the reviewing IRB. A transcript of a radio advertisement that had aired for several weeks was included with the inspection report (copy enclosed). This advertisement refers to laser vision correction at the Delaware Valley Laser Surgery Institute. According to Mr. Stokes, the only laser at your Bala Cynwyd office used for refractive surgery is your IDE laser. While your Marlton, New Jersey site has a Summit laser, the advertisement does not specify a location. Future advertisements should specify the location(s) of approved lasers, as the enclosed advertisement would not be appropriate for soliciting subjects for your IDE study. All promotional materials designed to solicit participants or to inform subjects about the IDE study need to be approved by the reviewing IRB.

No further response is necessary. For further information concerning the Bioresearch Monitoring program, please visit our internet homepage at http://www.fda.gov/cdrh/comp/bimo.html. Valuable links to related information are included at this site. If you have any questions, feel free to contact Jean Toth-Allen, Ph.D. at (301) 594-4723, ext. 141.

Sincerely yours,

Viola Sellman

Viola Sellman
Chief
Program Enforcement Branch II
Division of Bioresearch Monitoring
Office of Compliance
Center for Devices and
Radiological Health

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administrat
9200 Corporate Boulevard
Rockville MD 20850

JAN 20 1999

Herbert J. Nevyas, M.D.
Nevyas Eye Associates
Delaware Valley Laser Surgery Institute
333 City Line Avenue
Bala Cynwyd, PA 19004

Re: G970088/S15
Sullivan Excimer Laser System (Nevyas Model)
Indications for Use: LASIK (Laser-Assisted In Situ Keratomileusis) to correct myopia of -0.5 to -15 Diopters (D) with up to -7 D of astigmatism for protocol NEV-97-001 Myopia; and, LASIK retreatment to correct myopia and myopic astigmatism of eyes treated with this laser prior to IDE approval
Dated: January 5, 1999
Received: January 6, 1999
HCFA Category: A-2
Next Annual Report Due: August 7, 1999

Dear Dr. Nevyas:

The Food and Drug Administration (FDA) has reviewed the supplement to your investigational device exemptions (IDE) application providing validation data for the contrast sensitivity study. You have corrected the deficiency cited in our September 24, 1998 conditional approval letter. Your application is approved, and you may continue your investigation at the institution enrolled in your investigation where you have obtained institutional review board (IRB) approval. Your investigation is limited to one institution and 1015 subjects (2030 eyes); 990 subjects (1980 eyes) for myopia (- 0.5 to -15 D with up to -7 D astigmatism); and, 25 subjects (50 eyes) for enhancements of subjects treated prior to IDE approval (-0.5 to -15 D myopia with up to -7 D astigmatism).

Please be aware of the following:

In Table 1-1, the data appear to be quite scattered, with some subjects actually increasing in sensitivity during glare (e.g., see BC & CB at 3 cycles per degree (CPD)), while others are severely compromised (see ZM). In order to reduce variability in the data in the contrast sensitivity study, the person administering the test should have experience in this test and the subjects should be well trained prior to testing.