| DEPARTMENT OF HEALTH AND HUMAN SERVICES<br>PUBLIC HEALTH SERVICE<br>FOOD AND DRUG ADMINISTRATION | DISTRICT ADDRESS AND PHONE NUMBER<br>US Food and Drug Administration<br>900 US Customhouse<br>2nd & Chesenut Sts.<br>Phila PA 19106<br>(215) 597-4390 |
|---|---|
| NAME OF INDIVIDUAL TO WHOM REPORT ISSUED<br>TO: [redacted] | PERIOD OF INSPECTION<br>10/6,7,8,13,14,15,20,22,23,26,<br>27,30 - 11/2/98 |
| TITLE OF INDIVIDUAL<br>Medical Director | TYPE ESTABLISHMENT INSPECTED<br>Clinical Investigator |
| FIRM NAME<br>[redacted] | NAME OF FIRM, BRANCH OR UNIT INSPECTED<br>SAME |
| STREET ADDRESS<br>[redacted] | STREET ADDRESS OF PREMISES INSPECTED<br>SAME |
| CITY AND STATE *(Zip Code)*<br>[redacted] | CITY AND STATE *(Zip Code)*<br>SAME |

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

The following observations refer to the Investigational Device Exemption [redacted] for the indicated study, "[redacted] with a [redacted] in the Surgical Treatment of Refractive errors: Myopia with and without Astigmatism"

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

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

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

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

5. [redacted] had [redacted] for Myopia 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.

6. [redacted] had [redacted] performed for a condition that is not indicated in 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.

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].

SEE REVERSE OF THIS PAGE [redacted]

DATE ISSUED 11/2/98

DATE ASSIGND: 10/98 [redacted]

CENTRAL FILE NO.: [redacted]

CITY: [redacted]

PRIORITY: 1

JD/TA: 11

STATE: [redacted]

DATE INSP: 27,30-11/2/98 1,6,7,8,12,14,17,20,22,25,26, GRP: 5

CNTY: [redacted] PHONE: [redacted]

STREET: [redacted]

ZIP: [redacted] DISTRICT: E

## ENDORSEMENT

The routine inspection of this Sponsor/Clinical investigator was conducted per assignment from CDRH, Office of Compliance, Division of Bioresearch Monitoring, (HFZ-312) and in accordance with CP 7348.811. [redacted] is the Medical Director and founder of [redacted] where he performs laser eye surgery on patients. [redacted] has an excimer laser and is conducting a clinical study, Correction of Myopia with and without astigmatism Protocol #[redacted] under an approved Investigational Device Exemption (IDE). [redacted] is a Sponsor/Clinical Investigator and this is the initial inspection for the firm in that capacity. [redacted] 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 120 patients

Previous inspection on 6/30/97 of this facility revealed the firm continued to use the [redacted] laser to perform [redacted] eye surgery without an approved IDE, planned to use the [redacted] laser for new treatment procedures not included in the firms disapproved IDE and verified 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 current inspection revealed the firm now does Myopic [redacted] surgical procedures under an approved IDE however, procedures are being performed on IDE patients prior to approval date, the date is missing on a consent form, consent forms were signed by patients after surgery date and procedures were performed on IDE patients which are outside the IDE with an unidentified laser at an unauthorized location.

Forward to CDRH HFZ-312 with Warning Letter Recommendation
Reinspect upon assignment from CDRH HFZ-312

### VOLUNTARY CORRECTION DATA

| PAC | PROBLEM TYPE | CORRECTIVE ACTION | EST. COST OF ACTION | DATE ACTION VERIFIED | CORRECTING UNIT | REPORTING DISTRICT |
|---|---|---|---|---|---|---|
| [redacted] | | | | | | |

SIGNATURE: [redacted] DATE: 11/19/98

DISTRIBUTION: ORIG + EXH - [redacted]
CC ORIG + EXH - [redacted]
CC -

[redacted]

NOV 24 1998

FORM FDA 481(E)-CG (09/83)

DATE ASSIGND: 10/98 [redacted] PRIORITY: 1 DATE INSP: 10/6,7,8,13,14,15,20,21,22,23,27,28-11/2/98 GRP: 5

CENTRAL FILE NO.: 2531320 JD/TA: 11 CNTY: 091 PHONE: [redacted]

NAME: [redacted] STREET: [redacted]

CITY: [redacted] STATE: [redacted] ZIP: [redacted] DISTRICT: [redacted]

RELATED FIRMS: **NONE** ST-ASSGN: **NO** ITS:

REGISTRTN:

| REG TYP | MNTH/YR | MNTH/YR | MNTH/YR | REG TYP | MNTH/YR | MNTH/YR | MNTH/YR | REG TYP | MNTH/YR | MNTH/YR | MNTH/YR |
|---|---|---|---|---|---|---|---|---|---|---|---|
| F | | | | D | | | | V | | | |
| M | | | | R | | | | B | | | |

| ESTAB-TYPES/ IN-CODES ON OEI: | 1: 7 86, 95 | 2: 5 86, 95 | 3: |
|---|---|---|---|

| TOTAL ESTAB SIZE | INTERSTATE BUSINESS RECEIVED | SOLD | DISTRICT USE #1 #2 #3 | RECALL NUMBER | REFUSAL CODE | PROFILE | PASS FAIL |
|---|---|---|---|---|---|---|---|
| 5 | yes | no | | | 0 | no | |

ESTABLISHMENT CHANGES: NEW FIRM NONE NAME ADDRESS OWNERSHIP SIZE PROD-CODE OTHER EST-TYPE O/B INACTIVE NOT-OEI AUX-FIRM REGISTRATION

| PAC | PROCESS (PRODUCT) CODE | EST TYP | INSP BASIS | EMPL1 PC: 2 NO: 784 HD: E | EMPL2 PC: NO: HD: | EMPL3 PC: NO: HD: | PRODUCT | PR IT Y | RESC HED DATE | INSP CONC | DIST DCSN |
|---|---|---|---|---|---|---|---|---|---|---|---|
| [redacted] | 86——— | 7 | 1 | 145 | | | [redacted] | 1 | 10/01 | A | A |
| | | | | | | | | | | | |
| | | | | | | | | | | | |
| | | | | | | | | | | | |
| | | | | | | | | | | | |
| | | | | | | | | | | | |

SAMPLES COLLECTED: **NONE**

SAMPLE#: **N/A** PRODUCT: [redacted]

HEADQUARTERS UNIT REFERRED: **HFZ-312** FD 483 ISSUED: YES

REASON REFERRED: **As per attached assignment** OTHER FED GOVT INSP OR GRADING: **NO**

INSPECTOR'S NAME/SIGNATURE: [redacted] SUPERVISOR'S NAME/SIGNATURE: [redacted]

11/19/98 DAW OK

DATE ASSIGND: 10/98 CS#: 83562 PRIORITY: 1 DATE INSP: 27,30 – 11/2/98 GRP: 5

CENTRAL FILE NO.: [redacted] JD/TA: 11 CNTY: [redacted] PHONE: (610) 668-2777

NAME: [redacted] STREET: [redacted]

CITY: [redacted] STATE: [redacted] ZIP: [redacted] DISTRICT: [redacted]

PRODUCTS COVERED

| DATE COVERED | PRODUCT CODE | EST TYP | EST TYP | EST TYP | PRODUCT DESCRIPTION |
|---|---|---|---|---|---|
| 11/2/98 | 86---- | 7 | | | [redacted] |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |

[redacted]

10/6,7,8,13,14,15,20
22,23,26,27,30-
11/2/98 RALS

**SUMMARY OF FINDINGS:**

The routine inspection of this Sponsor/Clinical investigator was conducted per assignment from CDRH, Office of Compliance, Division of Bioresearch Monitoring, (HFZ-312) and in accordance with CP 7348.811. [redacted] is the Medical Director and founder of [redacted] where he performs laser eye surgery on patients. [redacted] has an [redacted] and is conducting a clinical study, Correction of Myopia with and without astigmatism Protocol [redacted] under an approved Investigational Device Exemption (IDE). [redacted] is a Sponsor/Clinical Investigator and this is the initial inspection for the firm in that capacity. [redacted] is the named Co-Investigator.

An inspection conducted on 12/2/96 revealed the firm had assembled a single [redacted] and was using it to perform [redacted] eye surgery on at least 120 patients

Previous inspection on 6/30/97 of this facility revealed the firm continued to use the [redacted] laser to perform [redacted] eye surgery without an approved IDE, planned to use the [redacted] laser for new treatment procedures not included in the firms disapproved IDE and verified 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 current inspection revealed the Clinical Investigator currently performs Myopic [redacted] procedures under an approved IDE however, procedures are being performed on IDE patients prior to approval date, the date is missing on a consent form, consent forms were signed by patients after surgery date and procedures were performed on IDE patients which are outside the IDE with an unidentified laser at an unauthorized location.

**HISTORY OF BUSINESS:**

[redacted] is the founder and Chief of Staff of [redacted] There are six additional physicians and three other locations associated with the practice which are identified along the left and bottom border of **EXHIBIT #1**. All FDA correspondence should be addressed to [redacted] at the aforementioned address. The firm operates Monday to Friday, 8:00am - 5:00pm.

[redacted]

10/6,7,8,13,14,15,20
22,23,26,27,30-
11/2/98 RALS

**PERSONS INTERVIEWED AND INDIVIDUAL RESPONSIBILITIES:**

On 10/6/98 I presented my credentials and issued a FD-482 to [redacted] Clinical Coordinator. He is not the most responsible individual at the firm however, [redacted], who is the most responsible individual, was unavailable at the time. [redacted] is the founder and Medical Director of [redacted] stated [redacted] would be able to answer my questions and would be present throughout most of the inspection.

**OPERATIONS:**

[redacted] is the Medical Director and founder of [redacted] where he performs laser eye surgery on patients. [redacted] has an [redacted] and is conducting a clinical study, Correction of Myopia with and without astigmatism Protocol [redacted] under an approved Investigational Device Exemption (IDE). [redacted] is a Sponsor/Clinical Investigator and this is the initial inspection for the firm in that capacity. [redacted] is the named Sub-Investigator and the only other physician at the firm who performs [redacted] surgical procedures with an [redacted] laser. The IDE laser is identified as a [redacted] It was built in the fall of 1995 by [redacted] a laser scientist and President of [redacted] provided [redacted] with the basic specifications for the laser and [redacted] then designed and built the laser indicating to [redacted] the components that were needed and where to order them. The laser system consists of a Laser beam generator, optical lens system, beam shaping apparatus, computer control system and patient treatment chair.

The laser beam generator is a [redacted] as halogen source to produce the laser beam; serial number [redacted] purchased from [redacted], [redacted] The housing and electrical/gas delivery system was purchased from [redacted], [redacted] The other components were ordered from other various manufacturers. [redacted] of [redacted] performs all maintenance, repairs and calibrations.

Prior to Myopic [redacted] surgery the patient is given a patient information and consent form, **EXHIBIT #2**, to read and sign.

[redacted]
10/6,7,8,13,14,15,20
22,23,26,27,30-
11/2/98 RALS

It also serves as an enrollment form for the clinical study. According to [redacted] they always ensure the patient understands the form before proceeding. The patient is then either scheduled for surgery at a later date or it is performed the same day the form is signed.

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.

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 microkeratome (provides suction to eye to flatten it and a blade to cut the cornea). 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.

The surgical procedure with associated pertinent information is recorded on an Excimer Laser Log/Intra-Operative form **EXHIBIT #18**. A copy of the form is filed in a logbook and another copy is placed in the patients' file.

[redacted] initial IDE submission was disapproved May 8, 1998. He was granted conditional approval on August 7, 1998. As [redacted] addressed various issues presented in letters from FDA CDRH/ODE he was granted more uses of the IDE laser. To date his investigation is limited to 1 institution [redacted] location) and 225 subjects: 150 subjects (300 eyes) for low myopia (-0.5 to -6.75 diopters myopia plus up to -7 diopters astigmatism); 50 subjects (100 eyes) for high myopia (-7 to -15 diopters with up to -7 diopters astigmatism); and 25 subjects (50 eyes) for enhancements/retreatments of subjects treated prior to IDE approval (-0.5 to -15 diopters myopia with up to -7 diopters astigmatism). From the date the first patient was treated under the IDE, August 28, 1997, until this inspection [redacted] has treated 154 subjects (276 eyes) for high and low myopia and 24 subjects (23 eyes) for myopic enhancements. The figures were retrieved from the [redacted] Log which according to [redacted] represents all IDE patients treated to date.

[redacted]

10/6,7,8,13,14,15,20
22,23,26,27,30-
11/2/98 RALS

[redacted], built the [redacted] for [redacted] however, [redacted] owns it. He was responsible for submitting the information for the IDE, in conjunction with [redacted] and eventually Pre-Market Approval for the device. He is therefore a Sponsor/Clinical Investigator.

[redacted] has retained the services of [redacted] Pharm D., President of [redacted] as a monitor and consultant for his clinical research, **EXHIBIT #3.** She has made a site visit which is reflected on the Monitor's Log, **EXHIBIT #4,** and also prepared a Monitoring Report, **EXHIBIT #5.** Ms Fant is responsible for ensuring that [redacted] and [redacted] did read, understand, sign and adhere to the Investigator Agreement forms, **EXHIBITS 6&7.**

[redacted] is the Institutional Review Board [redacted] IRB) that is used by [redacted] to oversee the IDE clinical study, Protocol [redacted] beginning 8/20/97, **EXHIBIT #8.** A list of the IRB members is included, **EXHIBIT #9 and** it should be noted that [redacted] is listed as an alternate member.

**[redacted] is performed at the [redacted] location and at the office located at [redacted] and [redacted]**

**OBJECTIONABLE CONDITIONS OR PRACTICES/DISCUSSION WITH MANAGEMENT:**

At the conclusion of the inspection a F[redacted] was issued and a discussion with management held. [redacted], Clinical Investigator, [redacted], Co-Investigator [redacted] Clinical Coordinator attended the meeting.

The following observations refer to the Investigational Device Exemption (IDE) [redacted] for the indicated study, [redacted] with [redacted] n the Surgical Treatment of Refractive errors: Myopia with and without Astigmatism"

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

[redacted]
22,23,26,27,30-
11/2/98 RALS

[redacted] for treatment of Myopia was not approved until January 14, 1998 according to a letter to [redacted] from the FDA dated the same **EXHIBIT #10.**

**EXHIBIT #11** indicates [redacted] had [redacted] on 8/28/97. **EXHIBIT #12** shows [redacted] also had [redacted] on 8/28/98. These procedures were performed well before approval was granted.

[redacted] 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.

I indicated to [redacted] that [redacted] dated March 18, 1997 was part of his initial IDE submission and did include provisions for simultaneous bilateral [redacted] on page 24 of **EXHIBIT #13.** However, the entire IDE submission was disapproved as per a letter dated 5/18/97 from the FDA to [redacted], **EXHIBIT #14** . Conditional approval was not granted until 8/7/97, **EXHIBIT #15,** and did not specify simultaneous bilateral [redacted] could be done. That procedure was specifically approved in a letter January 14, 1998.

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

Myopic [redacted] enhancements/retreatments was not approved under the IDE until October 3, 1997 according to a letter from the FDA to [redacted] dated the same **EXHIBIT #16.** [redacted] received [redacted] on 9/25/97 OD (right eye) **EXHIBIT #17.** [redacted] Co-Investigator performed this procedure and stated [redacted] told her it was okay to perform myopic [redacted] enhancements and did not know it was not approved. [redacted] stated he thought it was okay because he thought the procedure was approved.

[redacted]

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

According to the [redacted]/intra-operative form **EXHIBIT#18** [redacted] had right eye myopic [redacted] surgery on 12/4/97.

Page 9 of the patient information and consent form **EXHIBIT #19** indicates the patient signed the form however, the date is missing. Therefore, it is not certain what date the patient actually signed the consent form. [redacted] assured me this was merely a mistake and that all patients read and sign consent forms before surgery.

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

The [redacted]/intra-operative form for [redacted] **EXHIBIT #20** and [redacted] **EXHIBIT #22 verify** both had [redacted] surgery on their right eyes for myopia on 2/19/98.

However, page 9 of the patient information and consent forms, **EXHIBIT #21, EXHIBIT #23,** respectively show a date next to the patients signature of 2/20/98. This indicates the patients signed the consent forms one day after they had surgery.

[redacted] stated it might appear the patients signed the consent forms one day after surgery however, this was a mistake made by someone on his staff.

**5 P[redacted] had [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.**