



JUL 30 1997

Food and Drug Administration
Rockville MD 20857Via Federal Express
WARNING LETTER

Ralph G. Berkeley, M.D.
Director
Mann Berkeley Eye Center
1200 Binz, Suite 1000
Houston, Texas 77004

Dear Dr. Berkeley:

The purpose of this letter is to warn you that your [REDACTED] located at the Mann Berkeley Eye Center in Houston, Texas, may not be used to treat patients beyond the conditions of approval of your investigational device exemption (IDE). Any use of the [REDACTED] beyond the terms of the conditional approval of the IDE is in violation of federal law. 21 U.S.C. § 351(f)(1)(B). As discussed further below, inspection of your facility by the United States Food and Drug Administration (FDA) reveals that you have used the [REDACTED] in a manner that does not comply with the Federal Food, Drug, and Cosmetic Act (the FD&C Act) and FDA's IDE regulations.

Background

On December 27, 1996, you submitted an IDE application ([REDACTED]) to FDA for the [REDACTED]. On February 13, 1997, FDA sent you a letter identifying numerous deficiencies in your IDE application, which were to be corrected within 45 days from the date of the letter. In spite of these deficiencies, FDA's letter notified you that your application was conditionally approved and that, "after you have received institutional review board (IRB) approval and submitted certification of IRB approval to FDA," you could begin your investigation. FDA's conditional approval limited use of the [REDACTED] to performing [REDACTED] on a total of [REDACTED] patients at [REDACTED]. FDA's letter expressly stated, "It is expected that you will not treat subjects outside these approved limits."

On March 28, 1997, on behalf of the Mann Berkeley Eye Center, [REDACTED] M.D. submitted a supplement to [REDACTED]. The supplement stated that because you were "still establishing the format, it has been decided to delay beginning the study until final approval is obtained." You further stated that FDA's conditional approval "has been taken under advisement, and the study has not yet been started." The supplement stated, however, that the Mann Berkeley Eye Center intended to continue using the [REDACTED] to treat patients with the [REDACTED] "during the interim," but that such patients "will not be considered part of the IDE cohort."

By letter dated April 30, 1997, FDA notified you that your supplement did not address all of the deficiencies in your IDE application and again requested that the deficiencies be corrected within 45 days. FDA explained that your IDE remained approved on a conditional basis and reiterated that the approval is "limited to [REDACTED] and [REDACTED] subjects." Moreover, FDA again stated that before your conditionally approved study could commence, you must obtain IRB approval and

submit certification of IRB approval to FDA. FDA also warned you that you could not use the [REDACTED] outside of the conditions of approval of your IDE.

On May 28, 1997, you requested an additional 45 days to respond to FDA's April 30 letter and that request was granted on June 10, 1997.

FDA's Inspection of the Mann Berkeley Eye Center

In May 1997, FDA inspected the Mann Berkeley Eye Center in Houston, Texas, and reviewed records of patients treated with the laser. The FDA inspection revealed the following:

1. Between March 7, 1997 and May 12, 1997, you treated at least [REDACTED] patients with the [REDACTED] even though the approved limit under the IDE was [REDACTED] patients. During the FDA inspection, members of your staff stated that these patients were not treated under your IDE.
2. You failed to obtain Institutional Review Board (IRB) approval of your IDE clinical studies and to submit certification of the IRB approval to FDA, as required under IDE regulations. See, e.g., 21 C.F.R. §§ 812.40, 812.42, 812.62, and 812.110.
3. You continue to use an unacceptable version of the informed consent form, even though you submitted an acceptable revision to that form in your March 28 supplement to your IDE. Your use of an unacceptable informed consent form violates FDA's regulations. See, e.g., 21 C.F.R. §§ 50.20 and 50.25.
4. Review of approximately [REDACTED] patient records revealed that at least 5 subjects should have been excluded based on exclusion criteria of the IDE.

The above-listed violations are not necessarily all-inclusive. Moreover, the violations are based on observations made during FDA's inspection of your facility, and the concerns they raise are separate from and in addition to the deficiencies in your IDE application that were identified in FDA's February 13 and April 30 letters.

Violations of the FD&C Act and FDA's Regulations

The Mann Berkeley Eye Center's continuing treatment of patients with the [REDACTED] is in violation of federal law. The [REDACTED] that you are using to treat patients is an unapproved Class III device under Section 513 of the FD&C Act. Your treatment of patients with this unapproved device violates the FD&C Act.

As FDA explained in the February 13, 1997 letter, contrary to your assertions, your [REDACTED] is not a custom device as that term is defined in the FD&C Act. Among other conditions, a custom device must be intended for use by an individual patient and must be made specifically for that patient, or must be intended to meet the special needs of an individual practitioner. These special needs may be either an individual

anatomical need or a special practice need that is not shared by other physicians. The laser does not meet these conditions.

Because the [REDACTED] is not a custom device and does not have an approved premarket approval application (PMA), it may be used to treat patients only in strict compliance with the conditions of an IDE and FDA's IDE regulations. Although the Mann Berkeley Eye Center has received conditional approval from FDA on IDE [REDACTED] you have claimed that the patients who have been treated with the [REDACTED] were not treated under your IDE. FDA explicitly rejected this contention in our April 30 letter, paragraph 2:

Your stated intent to treat subjects with your device outside an FDA approved IDE is not in compliance with Federal medical device regulations. You may correct this deficiency by providing a written statement signed by all prospective investigators in your IDE that no subjects will be treated with your device outside your IDE, and that treatments will be limited to the indications and numbers of subjects approved for the IDE by FDA, and that all investigators will comply with all applicable regulations. If the requested statement is not provided, FDA will consider taking steps to propose withdrawal of approval of your IDE.

If, as you claim, your use of the [REDACTED] has in fact been outside your conditionally approved IDE, then, despite clear warnings from FDA, you have treated patients with an unapproved Class III device in violation of the FD&C Act.

Alternatively, even if you treated your patients with the [REDACTED] pursuant to your IDE, you have violated the FD&C Act because you have violated the conditions of approval of your IDE and FDA's IDE regulations. As discussed above, FDA's inspection of your facilities has revealed that you (1) treated [REDACTED] patients between March 7, 1997 and May 12, 1997, despite FDA's limiting your study to [REDACTED] patients and twice warning you to adhere to that limit; (2) commenced using the [REDACTED] on patients even though you failed to obtain IRB approval of your study; (3) used an informed consent form that FDA had notified you was unacceptable; and (4) treated patients who should have been excluded from the study.

Thus, whether your treatment of patients with your [REDACTED] has been conducted outside of or pursuant to your conditionally approved IDE, you have violated the FD&C Act and FDA's IDE regulations. You must immediately cease all treatment of patients that does not conform to FDA's conditional approval of your investigation and FDA's regulations. Please note that where, as here, a device has been conditionally approved for treatment of a limited number of patients, all treatments of all patients with that device count against the number of patients that may be included in the study. Therefore, because you have already exceeded the limited number of patients [REDACTED] specified in FDA's conditional approval of your investigation -- whether or not you believe those patients were treated under the IDE -- you may not resume your investigation unless and until you have received IRB approval and submitted certification of IRB approval to FDA, corrected all deficiencies identified in FDA's conditional approval letters, and obtained FDA approval to treat additional patients under your IDE.

Page 4 - Ralph G. Berkeley, M.D.

Within 15 working days of your receipt of this letter, please notify this office of what actions you are taking to bring your device into compliance with the requirements of the FD&C Act. Please send your response to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II, 2098 Gaither Road, Rockville, MD 20850, Attention: Jean Toth-Allen, Ph.D.

A copy of this letter has been forwarded to our Dallas District Office, 3310 Live Oak, Dallas, Texas 75204. We request that a copy of your response be sent to that office.

We want you to be aware that failure to comply with the law may result in further regulatory action against you or the device by FDA without further notice. These actions include, but are not limited to, seizure, injunction, and civil money penalties.

If you have any questions, you may contact Jean Toth-Allen at (301) 594 - 4723, ext. 141.

Sincerely yours,



Lillian J. Gill
Director
Office of Compliance
Center for Devices and Radiological
Health