



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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JAN 14 1999

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

WARNING LETTER

VIA FACSIMILE
VIA FEDERAL EXPRESS

Tim Sear
President and Chief Executive Officer
Alcon Laboratories
6201 South Freeway
Fort Worth, Texas 76134

Dear Mr. Sear:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has reviewed some recent promotional material distributed by an Alcon Laboratories (Alcon) sales representative. The material makes inappropriate claims for Alcon's Acrysof intraocular lenses. The lenses are devices within the meaning of section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act).

The promotional material consists of a letter, signed by [redacted], and some graphs. The materials were distributed to at least one physician in the Buffalo, New York area. It is possible that others of your sales force are distributing similar materials. The letter specifically at issue says, "We at Alcon Laboratories are very excited and pleased that The FDA [sic] has given us permission to change our labeling on our Acrysof Lens Package Insert. We have been able to demonstrate over a three-year period, [sic] scientifically that Acrysof lenses do reduce posterior capsular opacification "

The letter continues, "We have anecdotally discussed this, however the enclosed study and package insert demonstrates [sic] this outcome. . . This is a milestone for Alcon as this is the very first claim that any manufacturer can make towards PCO."

These statements have misbranded and adulterated your lenses within the meanings of sections 502(o) and 501(f)(1)(B), respectively, of the Act. The lenses are misbranded because the company did not submit to FDA a notice or other information respecting the device as required by section 510(k) of the Act. The company did not submit data to support the claims made in the promotional material.

The device is adulterated because it is a class III device without either an approved premarket approval application (PMA) in effect as required by section 515 of the Act or an approved investigational device exemption as required by section 520(g) of the Act.

We have been advised by CDRH's Office of Device Evaluation (ODE) that in Alcon's discussions with the agency about the approval of additional claims for the Acrysof lens

labeling, ODE explicitly advised Alcon that the additions were limited to claims regarding the utility of the lens in reducing lens epithelial cells. ODE advised the company that a claim for reduction of posterior capsule opacification (PCO) exceeded what the company had studied and that FDA would want any claim of reduction in PCO to be evaluated by the Ophthalmic Devices Panel. The company committed to making claims only for the reduction in lens epithelial cells.

There are several pages of promotional material that include graphs and bibliographic references. These materials are entitled, "New ACRYSOF Labeling Claims Approved by FDA" and are dated November 2, 1998. These materials also contain numerous inappropriate claims. The first is the following: "Area of Opacification significantly lower than silicone and PMMA lenses" followed immediately by "Posterior capsular opacification is one of the last obstacles to truly successful cataract surgery." The juxtaposition of these implies that the area of opacification is the area of posterior capsule opacification, not the area of lens epithelial cells. As noted above, Alcon's studies showed a reduction in the area of lens epithelial cells, not a reduction of PCO.

In addition, ODE asked Alcon to include the *n* numbers in the company's data presentation to show the relatively small number of patients for whom statistical significance was obtained and that number is not present in the promotional material. ODE also asked the company to include in its labeling the range of values obtained, but this information is also not in the materials.

The promotional materials also include a statement that, "LEC regression occurred significantly more frequently in patients implanted with polyacrylic (Acrysof) than those with PMMA or silicone IOLs ($p < 0.0001$)." This statement and the data tables that follow it are inappropriate because data on LEC progression and regression were not reviewed or approved by FDA.

The promotional materials include a statement that, "studies show Silicone and PMMA result in higher YAG rates than ACRYSOF IOLs." ODE required Alcon to state in its labeling that there was not a statistically significant difference in YAG rates between Acrysof and silicone IOLs. ODE required that the company not say that there was a higher rate of YAG for silicone compared with the rate for Acrysof.

Finally, the promotional piece contains claims for "reduced risk of IOL decentration and capsular phimosis." These claims were not included in the approved labeling. ODE allowed a statement that, "...the reduced area of lens epithelial cells observed in this study was associated with decreased... anterior capsule movement for ACRYSOF lenses as compared to models of similarly designed silicone and PMMA lenses." Alcon did not demonstrate the relationship between reduced anterior capsule movement and IOL decentration and capsular phimosis.

As provided at 21 CFR 814.39, after FDA approval of a PMA, an applicant shall submit a PMA supplement for review and approval by FDA before making a change affecting the safety or effectiveness of the device for which the applicant has an approved PMA,

unless the change is of a type for which FDA allows an alternative submission. Changes requiring a PMA supplement include new indications for use and labeling changes. The claims made in this promotional piece require labeling changes.

This letter is not intended to be an all-inclusive list of deficiencies associated with your device. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter may also be reflected in other promotion and advertising materials used by your company. You are responsible for investigating and reviewing all materials to ensure compliance with applicable regulations.

You should take prompt action to correct these violations. Failure to promptly correct these violations may result in FDA's initiating regulatory action without further notice. These actions include, but are not limited to, seizure, injunction and/or civil money penalties

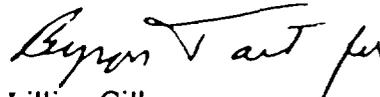
Please notify this office in writing, within 15 working days of your receipt of this letter, of the specific steps you have taken to correct the noted violations. Your response should include steps being taken to address any misleading information currently in the marketplace and to prevent similar violations in the future. If corrective actions cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

In addition to the violations described above, Alcon has made other violative promotional claims. On October 28, 1998, our office issued a letter to Alcon discussing violative claims on the company's website. We received a United States Postal Service return receipt card notifying us that the letter was received at Alcon on November 2. The company has, to date, failed to respond to that letter and the website continues to make the inappropriate claims. Please include in your response to the warning letter a discussion of how you intend to address the issues raised in the October 28 letter.

Direct your response to Deborah Wolf, Regulatory Counsel, Promotion and Advertising Policy Staff (HFZ-302), Office of Compliance, Center for Devices and Radiological Health, 2098 Gaither Road, Rockville, Maryland 20850

A copy of this letter is being sent to FDA's Dallas District Office. Please send a copy of your response to the District Director, Dallas District Office, Food and Drug Administration (HFR-SW140), 3310 Live Oak Street, Dallas, Texas 75204.

Sincerely yours,

A handwritten signature in cursive script, appearing to read "Lillian Gill".

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