DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

MAR 4 1997

Robert E. Roehrs, Ph.D.
Senior Director, Regulatory Affairs
Alcon Laboratories, Inc.
6201 South Freeway
Fort Worth, TX 76134-2099

RE: **NDA 19-992**
Ciloxan (ciprofloxacin HCl) 0.3% as Base Sterile Ophthalmic Solution
MACMIS # 5197

Dear Dr. Roehrs:

This letter is in reference to Alcon Laboratories, Inc.'s (Alcon) submission, dated December 11, 1996, of promotional materials under cover of Form FDA 2253 for Ciloxan (ciprofloxacin HCl) 0.3% as Base Sterile Ophthalmic Solution. This submission included a sales aid identified as CN96605VS. The Division of Drug Marketing, Advertising and Communications (DDMAC) regards the sales aid to be false and/or misleading under the Federal Food, Drug, and Cosmetic Act and its implementing regulations. Our specific objections follow:

Misleading graphic

In the sales aid, Alcon presents a color representation of an eye segment that includes the claim that Ciloxan has rapid tissue loading. The eye representation has labeled areas of tear, cornea, and aqueous with corresponding concentrations values. These values may correspond to Ciloxan concentration at some time after drug instillation although they are not identified as such. DDMAC considers this presentation to be misleading because Alcon implies that this rapid (undefined time) penetration of Ciloxan has some relation to clinical effectiveness (see next comment regarding "IQ"). However, Alcon has not submitted evidence to support this clinical effectiveness claim. As an additional example that these data do not relate to clinical effectiveness, close examination of the eye representation shows that two of the "tissue" values are related to human data and the aqueous "tissue" value is from **rabbit data.** Thus, this presentation is misleading and its clinical significance is unknown.

"Inhibitory Quotient (IQ)"

In the sales aid, Alcon claims that it has defined a new method for evaluating ocular anti-infective drug products by relating statistical outcome to tissue penetration divided

by MIC_{90} (ug/mL) values. Some "statistical outcome" numbers are presented in an Inhibitory Quotient "IQ" column of two tables, one for tear concentrations and one for cornea concentrations [DDMAC notes that the reference to support the cornea concentrations show values of 5.8 ± 3.4]. In smaller print under the tables, Alcon states that "penetration divided by potency equals IQ." Alcon also qualifies this statement by stating that there is not necessarily a correlation between in vitro activity (MIC_{90} data) and in vivo results (the clinical effectiveness of Ciloxan). Because Alcon's claim of clinical effectiveness relies on in vitro data, and because Alcon has not submitted adequate supporting clinical data, DDMAC considers that the theme of "IQ" is an unsubstantiated clinical effectiveness claim for Ciloxan, is false and/or misleading, and should be discontinued.

Alcon should cease immediately using this sales aid and all other materials that make the above described false and/or misleading claims. Alcon should respond to DDMAC regarding this issue by March 18, 1997, detailing its disposition of these promotional materials.

If you have any questions, please contact me by telephone at (301) 827-2831, by facsimile at (301) 594-6771, or by written communication at the Division of Drug Marketing, Advertising, and Communications, HFD-40; Room 17B-20; 5600 Fishers Lane; Rockville, MD 20857.

In all future correspondence regarding this matter, please refer to MACMIS # 5197 and NDA 19-992.

Sincerely,

Warren Rumble

Warren F. Rumble
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications

ciloxan9.nov

Drafted:	Rumble	02-25-97
Comments:	Sherman	02-26-97
Comments and discussion:	Abrams	02-27-97
Revised:	Rumble	03-03-97

WR 3/4/97

cc. HFD-40 NDA 19-992
HFD-40 chron/Rumble/Abrams
HFD-550 19-992
HFD-550 Div Dir-Chambers/ CSO-Holmes

MACMIS ID#	5197
MACMIS Type Code:	LTTR
MACMIS Action Code:	VIOL
2253 ID#:	47464
Material ID#:	CN96605VS
Close Out:	NO
Due Date:	March 18, 1997

FOI Status- Releasable