

October 18, 2000

**Alcon**  
**RESEARCH, Ltd.**

8676 '00 OCT 20 AM 11:48  
Federal Express # **8203 1519 7191**

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, rm. 1061  
Rockville, MD 20852

6201 South Freeway  
Fort Worth, Texas  
76134  
817.551.8388  
817.551.4630 (fax)

**RE: [Docket No. 00D - 1385] Draft Guidance for Industry on Refractive Implants: Investigational Device Exemptions (IDE's) and Premarket Approval Applications (PMA's); Draft**

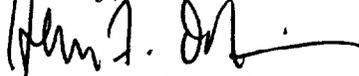
Dear Sir or Madam:

As described in Federal Register Vol. 65, No 148 / Tuesday, August 1, 2000 / Notices / page 46938, Alcon Research, LTD. is taking this opportunity to submit comments for your consideration.

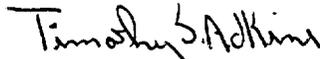
Reference the attached table "**Comprehensive Alcon Comments on Proposed Standards As of 25 September 2000 - FDA-RI-Comments-08012000.doc.**"

Alcon Research, LTD. appreciates the opportunity to provide input into the development of this guidance document. The final document will provide an excellent base of knowledge for Intraocular Lens Manufacturers and Distributors.

Sincerely,



John O'Riordan, Ph.D.  
Associate Director  
Surgical IOL / R&D



Timothy S. Adkins  
Sr. Manager, Regulatory Affairs

PC: Rebecca Walker  
Mary Pencis  
Daniel Stanley

/TSA  
D:FDAREfractive08.00.doc

00D-1385

C1

**Comprehensive Alcon Comments on Proposed Standards  
As of 25 September 2000**

<b>Standards Reviewed</b>	<b>Title</b>	<b>Version</b>
<b>Proposed FDA Guidance Document</b>	Refractive Implants: Guidance for Investigational Device Exemptions (IDE) and Premarket Approval (PMA) Applications; Draft	draft dated 1 August 2000

<b>Standard/Section</b>	<b>Proposed Change</b>	<b>Technical Rationale Supporting Proposed Change</b>
I.A.Scope	Remove the last sentence and the "Note" paragraph. These refer to clear lens exchanges which are not within the scope of this document.	Not within the scope of this document.
I.B. Definitions General Refractive Implant (RI)	Remove the last phrase that refers to clear lens exchange.	Not within the scope of this document.
I.B. Definitions Biocompatibility Test Material	Change to read: ... processed using the same contact materials and a procedure equivalent to that used for the RI.	The requirement that the full process be validated prior to collecting the Biocompatibility data is an unreasonable constraint to the development process. Once the process has been defined and contact materials finalized, the material should be useful for biocompatibility testing. Data on biocompatibility are needed as early in the development process as is reasonable without the time constraints of a formal process validation.
II. Biocompatibility Testing B. Extracts	The last sentence in the first paragraph of this section refers to the ISO/FDIS 11979-5, etc. Change to ISO 11979-5.	The final edition of this document was published on 11-15-99 and should no longer be referred to as a "FDIS".

Standard/Section	Proposed Change	Technical Rationale Supporting Proposed Change
II.C.3. Maximization Sensitization Test	Change the sentence to read: "Testing for sensitization potential is to be conducted using two extractants as outlined....."	Correct grammar so the sentence reads better.
II.C.4. Non-Ocular Animal Implantation Test	Change the second sentence to read: "The results should demonstrate tolerance of the material in the tissue."	Correct grammar.
II.C.8. Test for Photostability	Include reference for change to light intensity value from 0.5 to 0.75 mW/cm <sup>2</sup> .	There are many publications regarding the amount of light energy that enters the eye. It would be helpful to know the specific reference that was used.
IV.A. General	Replace the paragraph with: The properties of refractive implants should be determined at in-situ conditions with the temperature tolerance of ± 2°C. The precise composition of the solution used should be reported in all cases.	Realistic behavior can only be obtained by performing the tests at in-situ conditions.
IV.D.6. Out-of-Optic Plane Bending Strength	Change Out-of-Optic Plane Bending Strength to Out-of-Optic Plane Bending Stiffness.	Based on the description, the intent is to determine the bending stiffness of the supports not the strength. A schematic and a recommended test method would be helpful.
V.B2 (2 <sup>nd</sup> bullet) Sterility Testing.	Change to read: Documentation of the successful end product BI testing; validation of pyrogen testing and EO residual testing, then monitored. Delete "on all lots produced over one calender year"	Documentation of the successful completion of end product sterility testing, pyrogen testing and EO residual testing on all lots produced over one calender year.

Standard/Section	Proposed Change	Technical Rationale Supporting Proposed Change
V.C. Product Release Testing.	Remove "should be performed on each manufacturing lot." Should state: ...the testing shall be validated, then monitored. ETO residual is validated and controlled through aeration. Bacterial Endotoxin is a result of the process on proven materials and a single acceptable process may produce multiple lots.	ETO residual is validated and controlled through aeration. Bacterial Endotoxin is a result of the process on proven materials and a single acceptable process may produce multiple lots
V.C3 Product Release Testing.	Change the first sentence to read: ...carried out in accordance with ISO 10993-7 (1995) and AAMI TIR-19:1998 Guidance for ANSI/AAMI/ISO 10993-7:1995.	Draft has been published.
VI.D. Accelerated Shelf-Life Studies	In the first paragraph, last sentence, change to read: ...T <sub>0</sub> is the typical storage temperature (usually room temperature, 25°C).	Need to explicitly define room temperature in order to standardize the length of time to age the test samples.
VII.B.4.f. Bilateral Implantation	At the time of expansion to Phase II is approved....	The document discusses bilateral implantation for phase I and phase III, but does not discuss phase II. Bilateral implantation should be allowed for phase II, as most patients will not be contact lens wearers willing to have only one eye operated on. There is currently no FDA approved refractive implant for the fellow eye.
VII.B.7.b. Reporting Periods and Evaluations	Assessment of the natural lens for cataractogenesis should not be a requirement for intracorneal refractive implants	Intracorneal refractive implants should have no effect on cataract formation in the natural lens. Requiring 3 year follow-up for all subjects for assessment of cataractogenesis is over-burdensome.

Standard/Section	Proposed Change	Technical Rationale Supporting Proposed Change
VII.B.7.b. Reporting Periods and Evaluations	Pachymetry should only be done for refractive implants that alter the cornea.	Phakic intraocular lenses do not alter the cornea, therefore, pachymetry readings are not necessary.
Annex C Section C.2 "Note"	Change to read: "ISO 10993-6...., e.g. in subcutaneous or muscle tissue, which...."	Correct grammar
Annex D (normative) Shelf-Life Test Table	Instead of identifying particular materials generically as in the current Table, define test requirements on the basis of five years on-the-market experience with any RI material and packaging.	This will give fair consideration to any future RIs comprised of proven materials and packaging.
No specific location	Add allowances for Level A and Level B children models of clinically evaluated parent models.	Although FDA and others thought there was too little data to establish criteria for Level A and Level B changes at this time (Therefore, all new models will require a clinical study), this ability is still desired. Certainly, there is great experience with AC lenses, at least.