

February 13, 2004



Division of Dockets Management  
HFA-305  
Food and Drug Administration  
5630 Fishers Lane  
Room 1061  
Rockville, Maryland 20852

6201 South Freeway  
Fort Worth, Texas 76134-2099  
(817) 293-0450

Re: Docket No. 2000N-1449

Dear Sir or Madam:

Provided herewith are two (2) copies of Alcon's comments regarding FDA's "Guidance for Industry - Changes to an Approved New Drug Application or Abbreviated New Drug Application".

If you have any questions regarding these comments, please contact me via e-mail at [garry.heidel@alconlabs.com](mailto:garry.heidel@alconlabs.com) or via telephone at (817) 551-6813.

Sincerely,

A handwritten signature in cursive script that reads "Garry G. Heidel".

Garry G. Heidel  
Associate Director  
Regulatory Compliance  
Alcon Research, Ltd.

Attachment

00N-1449

C 2

**Alcon Comments to  
Guidance for Industry  
Changes to an Approved NDA or ANDA  
[Docket No. 2000N-1449]**

The following are comments and proposed revisions to the FDA Guidance for Industry – Changes to an Approved NDA or ANDA. Alcon’s Comments are presented in two (2) categories: General Comments and Specific Comments. General comments related to the guidance document are followed by specific section comments presented in a tabular format.

I. General Comments are as follows:

1. The FDA insights such as those included in the “Changes to an Approved NDA or ANDA Questions and Answers” should be incorporated into the new guidance to provide better explanation and clarity.
2. In some circumstances, the guidance document allows for reducing the reporting category if the change is equivalent to a condition or process that has already received CDER approval for another related drug substance or drug product. We would like for the Agency to consider expanding this type of approach to encompass most of the post-approval changes.
3. For major changes to ANDAs (i.e., currently Prior Approval Supplement) that do not require submission of clinical study data, we would like the Agency to consider adding the reporting category, Changes Being Effectuated – 180 Days.
4. Changes that FDA has termed “Changes Being Effectuated” can be implemented as soon as received by FDA. These changes are considered low risk and prior review by FDA is not required prior to implementation. We recommend that the Agency change the requirements for reporting in sections VI.C.2.a; VII.C.2.a. and b.; VIII.C.2.a and b.; and IX.C.a and b. from Changes Being Effectuated to Annual Report.

II. Specific Comments are listed in the table below:

<b>Section</b>	<b>Proposed Revision</b>	<b>Comments</b>
VI.B.4	Delete “and sizes” from the first sentence. Delete “and/or sizes” from the next sentence.	A transfer to an approved existing area that is simply a new size, but not a new type of container, should be a CBE-30 supplement.
VI.C.1.b	Replace “...a move to an aseptic processing facility or area at the same or different manufacturing site...” with “...a move to an aseptic processing facility or area at a different manufacturing site...”	If the change is a move at the same manufacturing site to an area that is already CDER approved for the same type of product, then the filing should be an Annual Report.

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Section	Proposed Revision	Comments
VI.D	Add “For aseptically processed sterile drug substance or aseptically processed sterile drug product, a move to an aseptic processing facility or area at the same manufacturing site that manufactures similar (including container and size) approved products.”	See comment above.
VII.B.2	Replace “Addition, deletion, or substitution of sterilization steps...” with “Deletion or substitution of sterilization steps...”.	Addition of sterilization steps should be a CBE, since it provides increased assurance of sterility (see VII.C.2.a).
VII.B.2	Replace “...that will come in contact with sterilized bulk solution or sterile drug components, or deletion of equipment from an aseptic processing line” with “...that will come in direct or indirect contact with sterilized bulk solution”.	A change in a material that does not come in direct or indirect product contact has no impact on the drug product. Deletion of equipment is more suitably addressed by changes in processing methods.
VII.B.2	Replace “Changes in sterilizer load configurations that are outside the range of previously validated loads” with “Changes in sterilizer load configurations that are outside the range of previously validated loads, if there is a change in the validation approach”.	If the change in sterilizer load is validated using the approved validation approach, then the change should be a CBE-30 like a change to another sterilization chamber (see VII.C.1.d).
VIII.B.3	Delete VIII.B.3	Establishing a new regulatory analytical procedure that provides the same or increased assurance of the identity, strength, quality, purity, or potency of the material being tested as the approved analytical procedure should be a CBE (see VIII.C.2.b). A new regulatory analytical procedure that does not provide the same or increased assurance is already addressed by VIII.B.4.

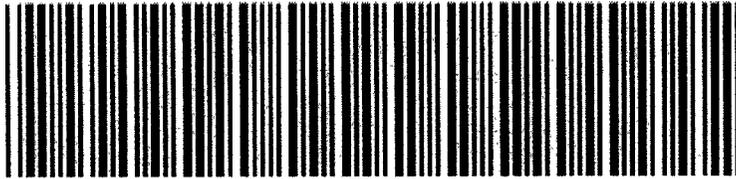
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<b>Section</b>	<b>Proposed Revision</b>	<b>Comments</b>
VIII.C.2.b	Replace “A change in an analytical procedure used for testing components, packaging components, the final intermediate, in-process materials after the final intermediate, or starting materials introduced after the final intermediate that provides the same or increased assurance...” with “A change in an analytical procedure that provides the same or increased assurance...”	Expand the scope to include drug product.
IX.B.4	Replace “Changes in the size and/or shape of a container for a sterile drug product” with “Changes in the size and/or shape of a container for a sterile drug product that are not bracketed by approved smaller and larger containers”.	A change to a container that is bracketed by approved smaller and larger containers should be a CBE-30.
XI.C	Add “A change from previously approved stability storage container orientation to the most stressful orientation (i.e., change from upright to inverted orientation).”	A change to an identified worst case condition should be an Annual Report.

**END**

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