AstraZeneca

Date: JUN 16 2003

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

RE: Docket Number 03D-0061
Response to FDA Call for Comments
Draft Guidance for Industry on Comparability Protocols – Chemistry, Manufacturing, and Controls Information

Dear Sir/Madam:

Reference is made to the Federal Register availability notice issued on February 25, 2003 for the Draft Guidance for Industry on Comparability Protocols – Chemistry, Manufacturing, and Controls Information.

AstraZeneca has reviewed this draft guidance and our comments are as follows:

Line(s)	Comment
86 - 91	For consistency AstraZeneca (AZ) suggests putting the listed changes in the same order as in the SUPAC guidance whenever possible.
86 - 91	AZ suggests adding "specifications", "stability protocols", "expiration period extensions" and "other changes".
89	AZ suggests changing "manufacturing facilities" to "manufacturing sites" in order to remain consistent with SUPAC.
101	AZ recommends inserting "(for example, a stability study)" after the word "study" in order to give an example.
130 -132	AZ recommends inserting a statement that this guidance may supersede other FDA guidance documents for filing strategy.
150	AZ suggests inserting "future" before "CMC changes".
156 - 157	Please provide examples of a potential 2 step change, for example, a container/closure change.
164	Please add: "...of a repetitive nature, for example, container/closure."
170 - 171	AZ recommends replacing this sentence with "We recommend that comparability protocols be considered only for CMC changes that applicants anticipate will be made that may qualify for reduced filing burden.
190 - 192	AZ suggests that FDA should refer to the Acceptance Criteria (starting line 416) in order to allow for changes that result in adjustments to the specifications.

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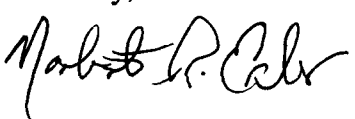
192 - 194	Please clarify what level of validation is required and state if analytical validation data is expected to be submitted with the validation protocol.
244 - 250	AZ recommends inserting a second bullet – "A prior approval supplement that contains data obtained from a small-scale process or other studies incorporating the proposed change to provide preliminary evidence that the change is feasible, as well as preliminary information on the effect of the change on the product.
246 - 250	This description seems indistinguishable from a standard prior approval supplement. Can a sponsor submit a comparability protocol and sNDA simultaneously?
294 - 296	Please consider allowing the modification of an existing (approved) protocol via an annual report.
300	AZ recommends inserting "unless otherwise provided for in this guidance" after the word "application".
315 - 316	AZ recommends the following first sentence: "Editorial or minor changes (i.e. alternate methods) can also be made."
425 - 436	This paragraph is confusing. If a PAS is required for a specification change as per "Changes to approved ANDA or NDA" guidance, the draft guidance indicates the firm should file as a PAS. If "Changes to approved ANDA or NDA" says that a lesser filing category is required, a firm can use the comparability protocol (which is a PAS) to get approval of a specification change that could otherwise be approved without the submission of a PAS. AZ suggests that FDA may want to clarify the intent of this paragraph.
439 - 443	AZ suggests that this paragraph/sentence should end at "...is reported to FDA."

This submission is being provided in duplicate.

Please direct any questions or requests for additional information to me, or in my absence, to Ms. Lora Love, Manager – Technical Regulatory Affairs, at (302) 886-8501.

Sincerely,



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