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Date: OCT 30 2001

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

Re: Docket # 01D-0368

Dear Sir or Madam:

Reference is made to the FDA Guidance entitled, "Guidance for Industry, Submitting Marketing Applications According to the ICH CTD Format—General Considerations," published in the Federal Register on September 5, 2001.

AstraZeneca Pharmaceuticals LP (AstraZeneca) has the following comments:

General Comment

The Guidance is neither complete nor specific enough regarding the FDA's expectations for numbering sections and sub-sections for a CTD. The implication is that this will be clarified in more specific CTD Guidances. AstraZeneca requests that the numbering sequences to be adopted are completely harmonized with the Guidances provided by the EU and Japan. Harmonization cannot be considered to be complete if differences exist in the numbering formats between the three regions.

Specific Comments

- **Page 3, First Paragraph, Last Sentence.** The Guidance states, "The Agency highly recommends that, by 2003, sponsors regularly submit BLAs for specified biotechnological products, NDAs, and ANDAs to the Agency in the CTD format."

The European Union (EU) and Japanese Regulatory Authorities have been more specific about the implementation date for the CTD format in their regions (July 1, 2003). The FDA's statement above implies expected use of the CTD format as of January 2003. We require clarification around the time frame of implementation for the expected use of CTD in the US, since it was understood that the 3 ICH member regions had agreed and harmonized the date of implementation.

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US Regulatory Affairs
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- **Page 5, First Paragraph, First Bullet Point.** This point states that, “letters of authorization for reference to other applications or drug master files (DMF),” should be submitted as part of Module 1.

Please clarify that DMF reference letters are to appear only in Module 1 rather than in Module 1 and in Module 3, Quality, Regional Information, also.

- **Page 7, Last Paragraph.** The paragraph states, “the submission of a separate ISE and/or ISS is not required when the information provided can be incorporated into the CTD summaries and overview...the applicant should raise any questions concerning the ISS and ISE with FDA staff...”

AstraZeneca recognizes that there may be circumstances where a separate ISS/ISE are still required; however, we would welcome introduction of language that specifically states that separate submission of the ISS or ISE would be the exception.

- **Page 9, Last Paragraph, Second Sentence.** The Guidance states, “Occasionally, you may want to use individual pages larger than standard paper size to present a floor plan...these pages should be folded and mounted so they may be opened for review without disassembling the jacket and refolded without damage when the volume is shelved.”

Oversize paper, to be used for floor plans or manufacturing instructions, described above, does not seem compatible with the submission of electronic CTDs. Please clarify.

- **Page 12, Section K, Second Paragraph.** The Guidance states, “If you include a document within a document, such as a protocol within a study report, the document to be included (in this case, the protocol) should be attached as an appendix. You should demarcate each appendix with an appropriately named tab identifier.”

Providing multiple tab identifiers does not seem practical when the appendix contains, for example, the curriculum vita (CVs), which could comprise dozens of documents each with a “page one” and a separate tab identifier. Please provide clarification and/or alternatives on this point.

This submission is being provided in duplicate.

AstraZeneca claims the confidentiality of this submission, and all information contained herein, under all applicable laws and regulations. Disclosure of any such information is not authorized without the prior written authorization of AstraZeneca.

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Please direct any questions or requests for additional information to me, or in my absence, to Robert J. Orzolek, Director of Technical Regulatory Affairs, at (302) 886-4550.

Sincerely,

A handwritten signature in cursive script that reads "Carol Stinson-Fisher".

Carol Stinson-Fisher, Associate Director
Technical Regulatory Affairs
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CSF/jr

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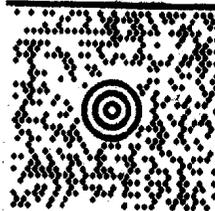
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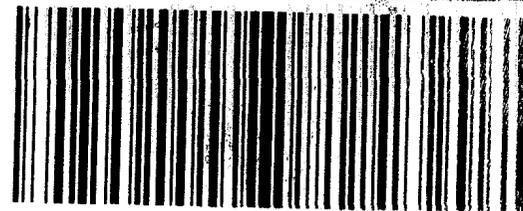


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