

Aventis Pharmaceuticals



November 2, 2001

0932 '01 NOV -2 07:15

Via fax and UPS

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

Re: Docket No. 01D-0368

Draft Guidance for Industry: Submitting Marketing Applications According to the ICH/CTD Format; General Considerations [66FR 46464, September 5, 2001]

Dear Sir/Madam:

Aventis Pharmaceuticals and Aventis Behring together would like to thank you for the opportunity to comment on the above-referenced Draft Guidance for Industry entitled "Submitting Marketing Applications According to the ICH/CTD Format; General Considerations". The document provides some general information on the organization and format of the Common Technical Document (CTD) as well as recommendations for completing module 1, which contains administrative and prescribing information specific to each regulatory authority. We offer the following comments/clarification for your consideration.

III. CTD FORMAT FOR EACH SUBMISSION

A. Module 1 - Administrative and Prescribing Information

3. Administrative documents

c. Annotated labeling text

Page 5 - 1st sentence

"For the NDA, you should provide a copy of the proposed labeling text with annotations directing reviewers to the information in the summaries and other modules that support each statement in the labeling, as described in 21 CFR 314.50(c)(2)(i). The annotated labeling text should include the content of the labeling described under 21 CFR 201.57 and all text, tables, and figures used in the package insert."

Since this guidance document applies to applications for drug and biological pharmaceuticals, we would suggest to specify "For the NDA and the BLA."

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C2

E. Module 5 – Clinical Study Reports

2. Study reports and related information

Page 7 - 1st paragraph, 2nd sentence

"We recommend that tab identifiers be provided for each appendix in a study report."

Are tab identifiers required for Appendix 1 and all sub appendices, i.e. Appendix 1.1, Appendix 1.2, or are they required just for the high level, i.e. Appendix 1, Appendix 2?

Page 7 - 2nd paragraph

"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. When the ISS or ISE is submitted, it should be included in Module 5.3.5.3, Meta-Analyses. The applicant should raise any questions concerning the ISS and ISE with FDA staff prior to submission of the application."

We support the streamlining of ISE and/or ISS information into the CTD summaries and overview. As mentioned in the draft guidance, the general rule should be that a separate ISE and/or ISS may not be needed since all the information can be incorporated into the CTD summaries and overview. However, the inclusion of ISE and/or ISS in Module 5.3.5.3 introduces a regionalization in Module 5. It would also introduce a summary-level documentation in Module 5, which is clearly not the intention of the CTD structure. We would like to stress that any regional specific information i.e. the ISS and/or ISE, should be included in Module 1 and not in Module 5.

Page 8 - 3rd paragraph

"You should include any case report forms (CRF) as separate documents. The case report forms should be organized by study."

As it is mentioned in the draft guidance that any CRF should be included as separate documents, we understand that in the paper paradigm it should be separated by tab identifiers.

Page 8 - 4th paragraph, 3rd sentence

"As with the CRFs, the CRTs should be organized by study."

As with the CRFs, we understand that in the paper paradigm the CRTs will be separated by tab identifiers.

IV. GENERAL ISSUES FOR SUBMISSIONS

B. Organizing Documents

Page 8 - 1st paragraph, 1st sentence

"You should bind all documents in separate volumes, or documents can be combined in volume as long as they are separated by appropriately named tab identifiers."

It would be helpful, for all literature references, to describe how the tab identifier should be named, e.g. by author names, abbreviated title, reference number based on the table of content.

V. ELECTRONIC SUBMISSION

Page 13- 3rd paragraph

Since this guidance refers to the current CDER and CBER guidances on applications in electronic format, we would suggest the following bullet point on review aids that may accompany an electronic submission:

- For paper review aids that accompany an electronic submission, tab identifiers should be provided as specified elsewhere in this guidance.

Finally, with regard to the terminology, several terms are used interchangeably throughout this document for tab identifiers (i.e. tab identifiers, tab dividers). It would be helpful if terms could be used consistently.

On behalf of Aventis Pharmaceuticals and Aventis Behring we appreciate the opportunity to comment on "Submitting Marketing Applications According to the ICH/CTD Format; General Considerations" and thank you for your consideration.

Sincerely,



Steve Caffè, MD
Vice President, Head GRAMS – North America
Global Regulatory Approvals and Marketing Support



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FAX

Date: November 2, 2001

Number of pages including cover sheet: 4

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REMARKS: Urgent For your review Reply ASAP Please comment

Dear Sir/Madam:

Attached please find comments regarding "Guidance for Industry: Submitting Marketing Applications According to the ICH/CTD Format; General Considerations [66FR 46464, September 5, 2001].

Should you have any questions, please call me at your convenience.

Regards,

Jackie Knoble