Aventis

9615 '03 FEB 28 A10:52

February 25, 2003

Via fax and UPS

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

Re: Docket No. 02D-0509
Draft Guidance for Industry on the M4 Common Technical Document – Quality: Questions and Answers/Location issues [67FR79639, December 30, 2002]

Dear Sir/Madam:

Aventis Pharmaceuticals Inc. appreciates the opportunity to comment on the above-referenced draft guidance entitled "Common Technical Document – Quality: Questions and Answers/Location issues".

This draft guidance provides further clarification for preparing the quality components of an application file in the CTD format (M4Q: The CTD-Quality). The draft guidance addresses the relationship between linked sections for certain parameters, and location issues.

The development of the draft guidance on the Common Technical Document – Quality: Questions and Answers/Location issues is welcomed. The underlying principles are generally sound and acceptable. We offer the following comments/clarification for your consideration.

2. General Issues

Nomenclature used in the guidance should be consistent throughout the document. For example, on page 2, the term "***section***" applies to the third level (e.g. 2.3.S), whereas on page 4, it applies to the fifth level (e.g. 3.2.S.2.3) and to the fourth level (e.g. 3.2.P.2)."

02D-0509

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2.1 Definition of a Quality Document
Module 3
Pages 3 & 4

We propose moving the following items for which a separate document should be provided:

3.2.S.4.4 Batch Analyses
3.2.S.6 Container Closure System
3.2.S.7.2 Post-approval Stability Protocol and Stability Commitment
3.2.S.7.3 Stability Data
3.2.P.5.4 Batch Analyses
3.2.P.7 Container Closure System
3.2.P.8.2 Post-approval Stability Protocol and Stability Commitment
3.2.P.8.3 Stability Data

to the list of sections for which the applicant can submit one document or multiple documents.

2.2 Document Pagination and Segregation
Page 5

Introductory texts are often provided to summarize the content of each section or to include the reference to any other sections of the dossier. We propose that the management of the introductory texts in the dossier be specified at the end of section 2.2 of the guidance.

2.3 Table of Contents Formatting
Module 3
4th paragraph, page 6

All Table of Contents title entries should either correspond to heading names and section numbering as defined in the M4Q guidance or to identifiers appearing on tabs (for a paper-based drug submission only), preferably by their full title, which should easily identify any abbreviated title which might be used on the corresponding tab. The Table of Contents should not specify any page numbers.

It is assumed that page numbers refers to the page numbers on the document level but not to the pages on the dossier level which should be part of the Table of Contents.

2.4 When can separate or repeated sections be appropriate?
Drug Product
1st paragraph, pages 6 & 7

Depending on regional requirements, different product presentations (e.g., strengths, container closure configurations, formulations) and/or manufacturing schemes (e.g., aseptic and terminal sterilization) can be submitted in the same dossier. In general, when a single dossier can be submitted, information for each of the product presentations and manufacturing schemes should be combined and presented together in one P section with information provided in the Appendices, and Regional Information sections for each of the product presentations and manufacturing schemes, as warranted. For example, if 100milligram (mg) tablets will be marketed in a bottle and a unit-dose blister package, the information should be presented in one P section. The majority of the quality information would be identical for the two products. The information that differs between the two would be presented together in the appropriate subsections (e.g., P.7 Container Closure System, P.8 Stability), but would be physically or electronically separated within the subsection.

For more clarity, we suggest that an example be provided of the way the information is given in the appropriate subsections.

For instance:
3.2.P.8 Stability (bottles)
3.2.P.8.1 (bottles)
3.2.P.8.2 (bottles)
3.2.P.8.3 (bottles)

3.2.P.8 Stability (blisters)
3.2.P.8.1 (blisters)
3.2.P.8.2 (blisters)
3.2.P.8.3 (blisters)

4. Location Issues in Drug Substance
P.8.2 No format comments
Page 30

Instead of "*P 8.2 No format comments*", it should be read "**P.8.2. Post-approval Stability Protocol and Stability Commitment**".

On behalf of Aventis Pharmaceuticals Inc. we appreciate the opportunity to comment on the draft guidance for Industry on the Common Technical Document – Quality: Questions and Answers/Location issues and are much obliged for your consideration.

Sincerely,

Steve Caffé, M.D.
Vice President, Head US Regulatory Affairs