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

**Re: Docket No. 00D-0186; Draft Guidance on M4 Common Technical Document;
The Common Technical Document for the Registration of Pharmaceuticals for
Human Use – Quality**

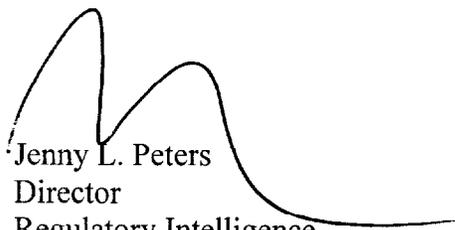
Dear Sir or Madam:

Thank you for this opportunity to review the draft guidance for *The Common Technical Document for the Registration of Pharmaceuticals for Human Use – Quality*. Our comments are attached. These remarks, together with our docket submission of September 26, 2000, complete our inputs regarding the draft guidance on the *M4 Common Technical Document*.

Should any clarification of our input be required, please don't hesitate to contact me at (616)-833-8141.

Sincerely,

Pharmacia Corporation


Jenny L. Peters
Director
Regulatory Intelligence
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00D-1335

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THE COMMON TECHNICAL DOCUMENT FOR THE REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE – QUALITY

General Comments – Module III

- The intent with the guideline is, as appropriately stated in the introduction of the scope, to provide guidance for the format of the dossier. The type of data to include in each section should be as advised by applicable ICH guidelines. We believe that regional requirements regarding section titles should be all inclusive with respect to the ICH regions (as opposed to the guidance noting that all required regional sectional titles may not have been included). Including all regional section titles would significantly strengthen the usefulness of the guidance.

Specific Comments – Module III

- Page 1: We propose to delete the three notes and to add the following to the end of “Scope”:

“The text following the section titles is intended to be explanatory and illustrative only. The content requirements are defined by ICH guidelines. In sections where guidelines cannot be applied, regional requirements for the content may apply.”

- Section S 2.3: We find this section up to “Biotech” to be confusing and feel the text could be better organized. Additionally, the meaning of the term “raw material” is not clear. We propose that this term refers to all ingredients used in the production of drug substance. In summary, the following text is proposed for section S 2.3, up to “Biotech”:

“Starting materials, solvents, reagents, catalysts, and any other materials used in the manufacture of the drug substance (raw materials) should be listed and it should be indicated where each material is used in the process.

Information on the quality and control of raw materials used in the manufacturing process should be provided. Tests and acceptance criteria should be provided.

Information necessary to demonstrate that raw materials meet standards appropriate for their intended use, including the clearance or control of adventitious agents, should be provided. For biologically-sourced materials this may include detailed information regarding the source, manufacture (e.g., preparation, validation of monoclonal antibody production), characterization and control.”

- Section S 4.4: Please refer to “Description (including size, origin, and use) and test results of all relevant batches...” It is not clear what is meant by “all relevant batches.” We suggest deleting the word “all” in this sentence.

- Section S 6: Please refer to the second paragraph:

“For non-functional secondary packaging components (e.g., those that do not provide additional protection), only a brief description should be provided. For functional secondary packaging components, additional information should be provided.”

We propose to delete this text. Secondary packaging information is not relevant for the CMC section.

For clarity reasons, please add “, S 6” to the last sentence omitting the word “this.” Text would now read, “References to any other suitability information should be placed in section S 6.”

- Section P 3.3: Please refer to the last sentence of the second paragraph:

“Equipment should, at least, be identified by type (e.g., tumble blender, in-line homogeniser) and working capacity.”

We believe it would be more appropriate to indicate the working range of the equipment rather than the working capacity. Please replace “working capacity” with “working range.”

- Section P 4.3 (“Validation of Analytical Procedures”): We suggest the guidance note that reference to a major compendia is sufficient for validation of analytical methods for compendial excipients.
- Section P 6: As for Section S 6, we propose to delete the paragraph about secondary packaging. Secondary packaging information is not relevant for the CMC section.