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Dockets Management Branch (HFA-305); 1 7 6 '00 APR 28 110 :32
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852



DOCKET No. 00D-0087
Re: Draft Guidance for Industry on
IND Meetings for Human Drugs and
Biologics; Chemistry, Manufacturing
and Controls Information;
Availability

Merck & Co., Inc. is a leading worldwide, human health product company. Merck's corporate strategy-- to discover new medicines through breakthrough research-- encourages us to spend more than \$ 2 Billion annually on worldwide Research and Development (R & D). Through a combination of the best science and state-of-the-art medicine, Merck's R & D pipeline has produced many of the important pharmaceutical products on the market today.

Today's R&D is a highly risk-intensive worldwide business. Commercialization of products in many countries directly depends upon a regulatory climate that foster timely development and government policies that are consistent and socially responsible, but do not add extra uncertainty to the research process. Worldwide R&D programs must also be responsive to international economic and social concerns. Indeed, we are also concerned about inconsistencies among regulatory regimes in different countries that may require unusual or duplicative research testing.

For these reasons, we are very interested in and well qualified to comment on this FDA Draft guidance entitled, "IND Meetings for Human Drugs and Biologics; Chemistry, Manufacturing and Controls Information; Availability.

We have reviewed the document in detail and offer the following comments for consideration as the guidance document evolves.

General Comment:

It should be recognized that agreements as to what constitutes an adequate submission package should be obtained at the End-of-Phase 2 meeting. The Pre-NDA meeting should focus on the content and presentation of data. If additional information is warranted after discussion at the Pre-NDA meeting, the sponsor should be allowed to submit this data within a reasonable time frame after the initial NDA submission within a reasonable time frame.

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Specific Comments:

Page 1, Line 9: Recommend changing “during the course of a clinical investigation” to “during the course of drug development” to more accurately reflect the time frame.

Page 3, Line 56: The guidance states that CMC questions should be presented in the same relative subject matter order as a typical CMC section of an application. A clause should be added to the end of the sentence: “or as otherwise appropriate to aid in the review of the information”.

Page 4, Lines 80-85: If the Agency wishes to raise questions that are outside of the scope of the background package, the sponsor should be informed in advance of the meeting to ensure that the appropriate experts are available.

Page 5, Line 111: Stability data for a Phase I IND will typically be short-term in nature, thus data may not be available for presentation at a meeting prior to IND filing.

Page 7, Line 164: Coordination of activities with contractor and suppliers is an internal sponsor issue. Why does this need to be discussed with the Agency?

Page 7, Lines 171-173: Recommend changing from “coordination between sponsor and Agency chemists and pharmacokinetics to establish proper dissolution test procedures” to “review by Agency chemists and pharmacokinetics of sponsor-developed dissolution test procedures”.

Page 7, Lines 184-185: The guidance states “Appropriateness of the stability protocols to support Phase 3 studies and the planned NDA or BLA”. Recommend changing to “Review of non-standard stability protocols to support Phase 3 studies and the planned NDA or BLA” since review of standard stability protocols are not necessary.

Page 7, Line 186: Why are site changes from Phase 2 through the NDA listed as topic for the End-of-Phase 2 meeting, especially in light of the new agreement for site stability?

Page 8, Line 219-223, 228: Six months prior to NDA filing may be appropriate for discussion of format issues, but inappropriate for most technical issues. These issues should have been resolved at the End-of-Phase II meeting.

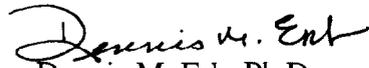
Page 9, Line 239: As noted with regard to page 7, line 164, coordination of activities with contractor and suppliers is an internal sponsor issue. Why does this need to be discussed with the Agency?

Page 9, Lines 243-244: If appropriate bridging studies have not been conducted, it will most likely be too late in the NDA process to generate/review the data and have it included in the filing, maintaining the original target filing date. Comparability or bridging studies should be agreed to at the End-of-Phase 2 meeting.

Page 9, Lines 245-246: Agreement on the adequate amount of stability to be included in the submission should be accomplished at the End-of-Phase 2 meeting. If additional stability data is warranted, the sponsor should be allowed to submit data after the original submission.

We appreciate the opportunity to provide comments which, from our perspective, will clarify some of the outstanding issues. We trust that these comments will be considered in further development of the proposed rule.

Sincerely,


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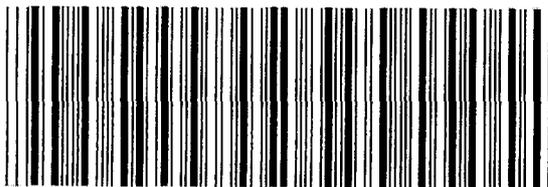
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