

# SCHERING CORPORATION

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February 15, 2002

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

Re: Docket No. 01D-0489

Dear Sir or Madam:

Reference is made to docket No. 01D-0489 and the draft document "Guidance for Clinical Trial Sponsors on the Establishment and Operation of Clinical Trial Data Monitoring Committees" dated November 2001. I am submitting the following comments on behalf of Schering-Plough Research Institute to be considered prior to preparation of the final document.

## **I. Determining Need for a DMC**

The guidance recommends that a DMC be established for controlled trials with mortality or major morbidity as a primary or secondary endpoint and those for drugs for which safety may be an issue. However, there is no guidance as to the definition of "major" morbidity or criteria that may necessitate a DMC. In addition, the guidance focuses on individual studies; however, the use of a DMC may be practical in the case of sequential short-term studies that make up a clinical program. For these studies it may be desirable for the DMC to review the full body of available data for the product to provide an overview of the safety profile for making decisions for ongoing or future studies. Based on the above comments, it is our opinion that a process should be identified that involves both the Sponsor and the Agency to identify the criteria used to define the need for a DMC. This determination should be made at the time of the pre-IND meeting for a program oriented DMC and at the end of phase 2 for a study specific DMC.

## **II. Role of DMC**

The guidance documents suggests that in addition to the DMCs role in reviewing safety, including review of effectiveness relative to safety, that the DMC may take on tasks such as review of protocol design and study monitoring. We feel that a DMC does not have the resources, tools, or capacity to adequately take on these types of responsibilities and that to do so would result in duplication of effort with other entities (e.g., Sponsor, FDA, IRB, Steering Committee, etc.). In particular, we do not believe that a DMC should take on the task of monitoring a clinical trial.

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### III. Interim Data and Analyses

The guidance proposes that all evaluation of unblinded data (both safety and efficacy) be conducted by the DMC statistician with the sponsor providing the database and random code to the DMC with no access to the unblinded results. It is our opinion that this proposal is unrealistic and would result in duplication of a significant amount of resources and potentially make the sponsor liable for errors made by the "independent DMC" analyses. The sponsor as part of its organization will have in place all of the components to conduct accurate and timely analyses. In addition, as the sponsor is responsible for the conduct and reporting of the study it is our opinion that the sponsor should not delegate this responsibility to the DMC. As part of the sponsor's analysis plan there must be documentation that the availability of the unblinded results submitted to the DMC will be restricted to a limited number of individuals in the sponsor's organization who have no direct contact with the conduct of the study but need to review the deliberations and conclusions of the DMC since the sponsor is ultimately responsible and liable for the drug under investigation.

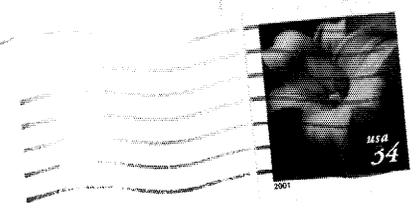
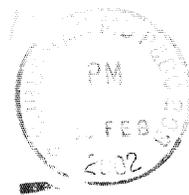
We appreciate your review and consideration of these comments.

Sincerely yours,



Gretchen Trout  
Director  
Regulatory Relations and Policy  
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