

Division of Drug Information (HFD-240)  
Center for Drug Evaluation and Research  
Food and Drug Administration,  
5600 Fishers Lane,  
Rockville, MD 20857

## **2005D-0103 - Guidance for Industry: Using a Centralized IRB Process in Multi-Center Clinical Trials**

Novartis supports the development of a guidance to encourage the efficient use of a centralized process for IRB review/approval of clinical research. Novartis has experience with centralized IRB reviews conducted on multi-center studies for sites that are not otherwise affiliated with an institution that has an IRB. It has been our experience that, these central IRBs are extremely diligent in their reviews and therefore provide adequate resource to perform a full and comprehensive review of the proposed research. We see no differences in the depth and issues that result from the review when compared to individual IRBs.

Our experience is that these centralized reviews are efficient and provide effective protection for the subjects enrolled in the trials they cover and we feel it is an appropriate time to consider promoting this greater efficiency than the current duplicative and inefficient process which exists today by which much research is currently reviewed. The implementation of a centralized process would not only reduce the review load on each participating IRB but allow it to more effectively and thoroughly review research. If you realize the number of redundant submissions/reviews and resources that result from IRB activities associated with a large multi-center trial when individual IRBs are used, one can begin to understand the significant efficiencies to be gained with a central review IRB review process, while not comprising the safety and rights of the subjects participating in the trials.

In addition, we recognize that FDA has never prohibited the use of a centralized IRB review; however, the concept has never been adopted within institutions that have their own IRBs. These institutions appear reluctant to give up local control of studies performed at their institutions. Aside from giving up local control, one of the reasons may also reside in their concern over liability if they delegated the study to an outside IRB.

Comments on specific sections of the guidance follow.

### **Apportioned Responsibility between Central and Local IRBs**

Although it is the prerogative of the Institution to decide whether to use centralized or local IRB, we do not find it pragmatic or effective for an Institution to apportion IRB review responsibilities between the central and its own IRB because there are a wide variety of Institutional requirements for waiving local IRB jurisdiction in order to allow Central IRB review. For example, some Institutions require the Central IRB to report safety information from the research project, and some require other periodic reporting about the Central IRB and how it manages IRB members. Either of these approaches introduces a duplication of time and effort, given that the FDA already oversees Central IRBs, and has regulations in place that define its responsibilities, and require

compliance. In addition, to require the Central IRB to assume varying portions of responsibility across all participating sites in a single research study, and negotiate cooperative agreements with each site, risks shifting energy from review and oversight of human subjects to compliance with hundreds of individual cooperative agreements – each with different terms.

### **How does a Central IRB Address Local concerns During IRB Review?**

The guidance requires the central review process include a means to ensure any local issues are taken into consideration during the review process. To remove any confusion or misinterpretation, it is recommended that the guidance should identify a list of items FDA would consider a local issue.

In addition, we agree and fully recognize that IRB review, through diversity of IRB membership, is intended to provide meaningful consideration of various local factors in assessing research activities and that a centralized IRB review process should include mechanisms to ensure significant consideration of important and relevant local factors. However, the guidance is written in a manner that regardless if a central IRB were used to review studies for an institution that already has an IRB there is the possibility of having two review/approvals.

We would strongly recommend that there should be one review/approval rather than have the possibility and the problems that could be posed by having a local and central IRB review. Therefore we would like to suggest several mechanisms to address local issues. One mechanism would be to allow ad hoc participation by the a local IRB at the Central IRB meeting to address issues on local medical practice, prevailing community attitudes on research and cultural issues. Another method to ensure local issues are considered would be to include in the IRB's membership roster key community contacts across different areas of the country that could provide expertise in reviewing relevant local factors. We would also like to suggest that Central IRBs document their methods for considering these important local factors during review in its Standard Operating Procedures. Since the Central IRB can review many hundreds of sites in a multicenter study, the methods are likely to be standardized, and it would not be realistic to document the methods on an ad hoc basis with each site's review.

### **Additional Suggestions – IRB Submissions**

We would like to suggest that since a central IRB would be handling multiple sites for a study, it would be beneficial from resource perspective to allow a sponsor to make single submission by the sponsor of information that affects all sites rather than have each individual investigator be required to submit the protocols, any amendments and or safety reports. These submissions would indicate all covered investigators. Any submission letters would be provided to each investigator as well as any approvals from the central IRB.

If you have any questions please contact Wayne Sadowski at (862)778-8995.

Wayne Sadowski  
CQA Head Country Management