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Mr. David Lepay
Division of Dockets Management (HFA)
Food and Drug Administration
5630 Fishers Lane.
Room 1061
Rockville, Maryland 20852

SUBJECT: Docket No. 2005D-0103
Draft Guidance on Using a Centralized Institutional
Review Board In Multicenter Clinical Trials

Dear Mr. Lepay:

The Council on Governmental Relations (COGR) is an association of 160 research intensive universities, affiliated hospitals and research institutes in the United States. COGR works with federal agencies to develop a common understanding of the impact that federal policies, regulations and practices may have on the research conducted by the membership. Strengthening and streamlining the review and approval of human subject's research to ensure the protection and enhance the participation of the subjects are critical to the conduct of biomedical research. We share the Food and Drug Administration's (FDA) interest in improving the efficiency of trials without compromising protections afforded the participants.

A key feature of the proposed guidance is the reaffirmation that the use of a centralized institutional review board (IRB) process is consistent with the current regulations. As research institutions consider the opportunities and challenges of participating in a centralized review, FDA's outline of responsibilities and reminders of record keeping and procedural requirements is useful. The use of central IRBs is an evolving process and the proposed guidance will be helpful in understanding the agency's expectations.

We share the FDA's interest a centralized IRB process but are cautiously weighing the impact of using a central IRB on the broad management of research at our institutions. Establishing criteria for when to participate in a centralized process versus an institutional review; ensuring a thorough airing of local concerns; coordinating IRB review with other oversight activities; and maintaining the currency of our Federal-wide assurance are areas that require careful consideration before the implementation of a central review.

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The FDA's focus in this guidance is on multicenter clinical trials and the use of a centralized IRB review for cooperative research. As such, the guidance highlights mechanisms to manage shared or joint review. However, the guidance notes, in passing, that permitting a central IRB to be entirely responsible for the initial and continuing review of a study is consistent with current regulations. This is a very different approach for which the FDA needs to describe its expectations in much greater detail. The option is briefly noted in section III.A. as one institutional approach for ensuring IRB review and described in slightly greater detail in section VII for unaffiliated sites. We assume that when a central IRB assumes full responsibility, the central IRB's procedures and minutes will document how it considered relevant local factors. So far, only a few research institutions with fully functioning IRBs have elected to use a central IRB to conduct the complete review, including continuing review, for certain types of research or for specific studies often to bring greater scientific expertise to the review or to avoid an appearance of conflicts of interest.

The FDA acknowledges that one of the principal areas of concern for institutions considering participation in a centralized process is the obligation to address local community issues. The FDA suggests three possible approaches and recognizes that "other mechanisms may also be appropriate." The use of other mechanisms that achieve the same purpose – consideration of local community concerns – must continue to be recognized as meeting the regulatory requirements. We would be very concerned if the three mechanisms proposed by the FDA became de facto standards.

Institutions need flexibility in participating in a centralized IRB processes primarily because IRB review and approval is one step in a complex web of regulatory reviews. Depending on the nature of the clinical study proposed, the traditional IRB review is often supplemented with other related processes like pharmacy, radiation, or biosafety reviews. The most expeditious approach is to have these reviews conducted simultaneously and contributing to the consideration of risks and benefits to the human subjects. Continuing reviews and adverse event reporting and analysis must be considered within this regulatory matrix as well. Thus, local concerns take on a broader meaning.

We are also concerned about the requirement to amend our Federal-wide assurance (FWA) whenever institutions engage in collaborations or participate in a centralized IRB process. Except in cases when the central IRB is entirely responsible for the initial and continuing review, the overall responsibility for the protection of human subjects remains with the institution. If the institution chooses central review as the review mechanism in a specific case, it does not seem necessary or appropriate to amend the FWA for a specific study.

We suggest that one might consider a different, more expeditious approach. OHRP could design an online database that permits institutions using a central IRB for a specific study to post that information for the duration of the study. The data could include the research institution, the central IRB (and its assurance number), the study name, sponsor, and its duration. This type of database would be easier and more current than the process of amending the FWA.

Finally, the FDA offers other examples of a centralized approach, including the National Cancer Institute's (NCI) Central IRB (CIRB) which provides a "facilitated," centralized review of

David Lepay

Guidance on Using a Centralized IRB in Multicenter Clinical Trials

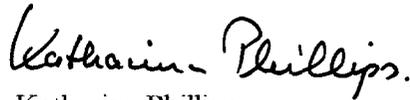
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NCI-sponsored clinical trials. Research institutions have begun to participate in the CIRB because the responsibilities of the partners are clearly defined; significant communication resources are available to participants; and the coordinated continuing review and management of adverse event reporting and evaluation contribute to greater effectiveness and efficiencies. Unfortunately, research institutions have had varying experiences with commercial and private-sponsor supported efforts. The CIRB demonstrates that when it works well, a centralized IRB process holds great potential for streamlining the process to the benefit of the subjects. If other federal institutes or agencies consider supporting a similar effort, we believe the NCI CIRB might be used as a model to avoid the proliferation of a variety of processes and approaches. A single model would indicate the government's efforts to streamline and simplify research management.

In conclusion, we encourage the FDA to emphasize that the possible mechanisms included in the proposed guidance are suggestions and that other arrangements that meet the requirements for consideration of local concerns will be appropriate. To enhance the FDA's efforts to streamline the review of clinical trials, we encourage FDA and OHRP to consider an online, simplified notification process. As the research community gains confidence in the use of centralized IRB processes, everyone will benefit.

Sincerely,



Katharina Phillips
President