



June 28, 2004

Ernest D. Prentice, Ph.D.
Chair, SACHRP
Associate Vice Chancellor for Academic Affairs
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University of Nebraska Medical Center
Omaha, NE 68198

Dear Dr. Prentice:

On behalf of the American Society of Clinical Oncology (ASCO), I am seeking review by the Secretary's Advisory Committee on Human Research Protections (SACHRP) of an issue that is increasingly demanding the attention of clinical research scientists, at least in cancer, and we believe in other disciplines, as well. The issue on which ASCO seeks guidance from SACHRP is the ability of clinical research sponsors to rely on a centralized, or cooperative, review process to avoid duplication of review by the local institutional review board (IRB).

ASCO's Interest

With more than 20,000 members worldwide, ASCO is the leading medical society for physicians involved in cancer treatment and research. An overarching mission of ASCO is to enhance prevention, diagnosis, and treatment of cancer through clinical cancer research. In recent years, ASCO has undertaken extensive review of the clinical trials enterprise, considering ways in which the process might be made more efficient and effective, with a goal of enhancing the unfortunately low rate of participation in cancer clinical research. Among the concerns repeatedly identified during this review has been the frustration of those who seek to streamline the scientific and ethical review by relying on a centralized review authority and avoiding needless duplicative review by local IRBs.

Such frustration was no doubt fueled by the experience of cancer clinical trials cooperative groups as they sought to initiate multi-site trials under a mandatory National Cancer Institute (NCI) central IRB (CIRB). The anticipated efficiencies of centralized review dissipated in the face of continued insistence by IRBs at local institutions on conducting their own reviews. Thus, rather than eliminating duplication, the NCI CIRB seemed to add another layer of review, making the process more – not less – protracted. As a result of that experience, centralized review has developed a somewhat negative image in the cancer community, but ASCO believes the concept deserves further consideration, with a targeted approach to removing the duplication and inefficiencies in the current system.



ASCO CIRB Roundtable

Given ASCO's interest in the efficiency of the cancer clinical trials process, the Society convened on May 24, 2004, a meeting of thought-leaders in clinical research, including representatives of cancer centers, cooperative groups, patient advocates, and federal government agencies. The ASCO meeting on May 24 was attended by the Director of the Office for Human Research Protection (OHRP), Dr. Bernard Schwetz, and by Dr. Joanne Rhoads, from the Office of Scientific Investigations at the Food and Drug Administration (FDA). These government officials made clear that the guidance from their agencies permitted local IRBs to defer to a CIRB on matters properly within the purview of both, but they also acknowledged that, for a variety of reasons, local IRBs were unlikely to do so.

The discussion at the May 24 meeting was significantly informed by the contribution from the president of the leading privately-operated IRB, the Western IRB, or WIRB. Her description of the potential efficiencies flowing from a more rational review process was both instructive and inspirational. Notably, the patient advocates in attendance voiced no concerns about the prospects of streamlining IRB review, encouraging us to explore incorporating such efficiencies into the context of federally sponsored clinical research in cancer and other diseases.

The May 24 meeting confirmed ASCO's conviction that the current system of scientific and ethical review for clinical research is burdened by needless duplication of effort that not only wastes scarce resources but also contributes substantially to the delay in discovery and reporting of medical advances. We are bringing this matter to the attention of the SACHRP in the hope that it will become an integral part of the Committee's agenda for reform of clinical research.

Issues for Consideration

It is clear from the available guidance of both OHRP and FDA that federal agencies do not require duplication of CIRB review by local IRBs. But it is also clear that local IRBs are free to engage in such duplicative review, and there is nothing in federal policy to deter them from it. This situation wastes both public and private resources, contributes to delay in clinical research findings, and is a worthy target for government reform efforts.

We understand that there is a complex of factors impelling local IRBs to conduct reviews that may not, according to federal guidance, be necessary. Foremost among these is concern about prospective liability should litigation ensue from injury suffered in a clinical trial. This, we believe, could be addressed by federal directives encouraging local IRBs, as a matter of good government, not to conduct unnecessary duplicative reviews. It is possible that greatly enhanced education about the lack of necessity for duplicative local review would suffice to change the attitude of local IRBs, but, if that fails, we believe federal authorities should be prepared to go further and consider proscribing, or at least strongly discouraging, unnecessary duplicative reviews.

We further understand that federal authorities have no authority to indemnify or otherwise protect local IRBs from tort liability in connection with their review responsibilities. However, federal regulations and guidance could be more specific in delineating review responsibilities in a manner that might help to alleviate concerns of local IRBs and even provide some degree of insulation against liability in the event of litigation. We urge the Committee to undertake a review of such options to consider



whether they might enhance the efficiency of scientific and ethical review in circumstances where centralized review is available.

Should the Committee see fit to consider these questions, we believe that it would also be useful to review the continued utility of the emphasis on “community attitudes.” At the time the regulations for protection of human research subjects were first promulgated, the solicitude for “community attitudes” was certainly understandable, as clinical research was a new undertaking, and there might have been widely divergent views on sensitive issues related to research activities. Now, however, in the age of the internet and other widespread communication opportunities, it is less certain that individual community differences within the United States are significant. It would appear that the emphasis on autonomy of local IRBs—and the corresponding tendency to duplicate reviews—may be related to the perception that local review is necessary to vindicate the requisite sensitivity to “community attitudes.”

The FDA representative at the May 24 meeting noted that a CIRB was certainly capable of reviewing community attitudes through consultation with local sources, but formalization of this advice would be welcome. Even more welcome would be guidance that consideration of community attitudes may not be required in the absence of reason to believe that such attitudes would be implicated by the proposed research.

ASCO is well aware of this Committee’s dedication to protection of special populations—children, the disabled, prisoners and more—but we do not see that local community attitudes necessarily inform protection for those special populations. If the mandate for sensitivity to community attitudes supports, directly or indirectly, continued insistence of local IRBs to pursue unnecessary duplicative reviews of clinical trials, then that mandate should be re-examined.

Conclusion

Clinical research, in cancer and other diseases, is the engine for medical progress that has enabled major decreases in morbidity and mortality in the United States and throughout the world. We should be doing everything possible to maximize the efficiency and effectiveness of clinical research, particularly that funded by federal tax dollars. All of us in the clinical research enterprise have an obligation to achieve optimal research results with minimal resource investment. Our hope is that the Committee will welcome the opportunity to explore ways in which to optimize the results of federal funding for clinical research in cancer and other important diseases, and we look forward to working with the Committee in this effort.

Sincerely,

A handwritten signature in black ink, appearing to read "David H. Johnson".

David H. Johnson, MD
ASCO President

A handwritten signature in black ink, appearing to read "Margaret Tempero".

Margaret Tempero, MD
ASCO Immediate Past-President

Cc: Bernard Schwetz, DVM, PhD
Executive Secretary, SACHRP