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June 2, 2009

Julie Kaneshiro

Office for Human Research Protections

Department of Health and Human Services

1101 Wootton Parkway

Suite 200

Rockville, MD 20852

IRBaccountability@hhs.gov

Subject: IRB Accountability RFI

Dear Ms. Kaneshiro:

With more than 27,000 members, the American Society of Clinical Oncology (ASCO) is the leading medical society for physicians involved in cancer treatment and research. One of ASCO's core missions is to improve clinical outcomes for individuals with cancer through clinical research, and ASCO has a longstanding interest in helping to promote the effectiveness and efficiency of the clinical trials process in the United States.

We commend the Office for Human Research Protections (OHRP) for seeking ways to encourage institutions to rely on institutional review boards (IRBs) that are operated by another institution or organization. Promotion of collaborative IRB arrangements will serve to protect the interests of patients while also removing unnecessary and duplicative inefficiencies to important research efforts. In particular, holding external IRBs directly accountable for meeting certain regulatory requirements, coupled with additional safeguards, would have a positive impact on the ability of individual institutions to rely upon the unique expertise and perspectives that centralized IRBs can provide in evaluating and monitoring oncology trials.

ASCO has formally supported efforts to promote the use of robust centralized review of human subjects protections in multi-center clinical trials since 2003.¹ Multi-center trials are critical to modern cancer clinical research because our growing knowledge of the molecular origins and mechanisms of cancer is increasingly leading toward treatments focused on

¹ ASCO Special Article: "American Society of Clinical Oncology Policy Statement: Oversight of Clinical Research," *Journal of Clinical Oncology*, Vol. 21, No. 12 (June 15, 2003).



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smaller subpopulations of cancer patients. Therefore, it is more important than ever to conduct trials across multiple research settings (including academic institutions, community hospitals and community-based physician practices) to enroll sufficient numbers of trial participants. ASCO supports centralized review to “provide for greater consistency across the trial sites to enable review boards and investigators to implement more quickly and consistently protocol and informed consent amendments.”¹

Centralizing more IRB reviews and functions would help improve the effectiveness of human subjects protection. It can be difficult for individual institutions, particularly community hospitals not affiliated with academic institutions, to assemble an IRB that includes members with oncology expertise, particularly patient advocates and other non-scientists. Regional or national review panels are able to draw from larger pools of qualified individuals. Regional or national panels also can conduct more effective consideration of adverse events (AEs) because an individual AE can be viewed in the context of the entire study population. In addition, a local IRB that uses an external IRB is able to devote more attention to review of trials occurring only at its institution, as well as conducting continuing review.

ASCO offers the following responses to selected questions posed in Section VII of OHRP’s request for comments:

1. Is there sufficient need for HHS to pursue a regulatory change to enable OHRP to hold IRBs and IORGs directly accountable for meeting certain requirements of the HHS regulations at 45 CFR part 46? Please explain your response.

Yes. OHRP correctly notes that participants in the November 2005 and November 2006 meetings identified regulatory liability as a significant institutional concern associated with whether to pursue an alternative to a local IRB.

The Report of the 2006 conference summarizes the issue and need for a regulatory solution:

Participants believed that regulatory agencies could do much to encourage institutions to use external IRBs when appropriate. They recommended that regulatory agencies give clear signals that alternative forms of review are acceptable. In addition, because of concerns about the potential for



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regulatory liability resulting from the actions of an external IRB, participants asked HHS to revise its policies regarding the responsibility of institutions for all work conducted under their FWAs. They suggested that HHS consider policies similar to those of the FDA, which ties regulatory liability to the organization responsible for the alleged problem.

Especially in this time of economic uncertainty, we can anticipate that many institutions will remain hesitant to rely on external IRBs if such reliance could jeopardize their ability to receive federal funds for research. We believe that the use of centralized review has the potential to improve the quality of ethical reviews, particularly for specialized forms of research.

Under the current regulations, it seems likely that institutions with large research programs would remain hesitant to rely upon external IRBs because the institution's federalwide assurance (FWA) could be placed in jeopardy through no fault of the local institution. The regulatory change that OHRP is contemplating would ensure that OHRP has the ability to enforce regulatory requirements directly with the organization responsible for carrying out those activities. OHRP must provide sufficient safeguards that permit institutions to reasonably rely on determinations arising from centralized IRBs.

2. Would the proposed regulatory change reduce concerns about regulatory liability as a barrier to the use of external IRBs and contribute to an increase in collaborative IRB review arrangements?

Yes. Based on comments made by participants at the 2005 and 2006 meetings, the proposed regulatory change would reduce concerns about regulatory liability. As noted previously, the need for conducting collaborative research is greater than ever. Collaborative IRB review arrangements have the real potential to reduce duplication, increase efficiency and improve the quality of ethical review.

3. Are there other approaches and strategies that would decrease concern about regulatory liability and increase collaborative IRB review arrangements?

Yes. In addition to pursuing this regulatory change, ASCO recommends that OHRP and Department of Health and Human Services' (HHS) agencies that fund research strongly encourage use of collaborative IRB review



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arrangements for federally funded research. The National Institutes of Health's Clinical and Translational Science Award Program has laid important groundwork for identifying and addressing barriers to collaboration among institutions. The NIH is encouraging institutions to examine models for IRB review. In addition, several extramural research sites use the National Cancer Institute's Central Institutional Review Board (CIRB) Initiative's facilitated review process, and the pediatric CIRB has been well received by the Children's Oncology Group sites. The CIRB Initiative is undergoing a thorough evaluation that will provide important information to the regulatory and cancer communities. Clear expressions of encouragement from HHS agencies to use collaborative IRB review arrangements would help in providing institutions with sufficient protections to participate in collaborative review for federally funded projects (without the need to duplicate centralized review efforts). To achieve the desired outcome, OHRP must provide adequate safeguards that permit institutions to rely reasonably on the reviews conducted by centralized IRBs.

In addition to the regulatory change, ASCO recommends that OHRP facilitate a process that allows institutions to learn from each other about effective approaches to collaborative IRB review arrangements. Several institutions already have charted this course and may be willing to not only share experiences but also provide the model agreements they have negotiated. This type of opportunity was created with OHRP's assistance at the widely-attended 2006 workshop. We urge OHRP to help foster ongoing exchanges of information, perhaps via its website and listserv.

We appreciate OHRP's thoughtful approach to this important issue. ASCO strongly urges OHRP to proceed with rulemaking in this area to help encourage greater use of collaborative IRB review.

Sincerely,

Douglas W. Blayney, MD
ASCO President