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Division of Dockets and Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Regarding: Draft Guidance for industry on "Using a Centralized IRB Process
in Multicenter Clinical Trials" [Docket No. 2005D-0103]

Dear Sir or Madam:

With more than 21,000 members worldwide, the American Society of Clinical Oncology (ASCO) is the leading medical society for physicians involved in cancer treatment and research. As such, ASCO has a longstanding interest in the efficiency of the clinical trials process, as reflected in its 2003 Policy Statement on Oversight of Clinical Research.¹ Specifically, the ASCO Policy Statement advocates measures to facilitate the use of a Central Review Board (CRB) mechanism in the large multi-center trials that are a staple of cancer clinical research, in part by limiting local Institutional Review Board (IRB) reviews that are frequently duplicative. As noted in the 2003 Policy Statement, "centralized review would 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."² More efficiently conducted clinical trials will give answers to important research questions in a more timely fashion and ultimately enhance the quality of cancer care.

Following publication of the Policy Statement, ASCO has engaged in outreach to federal authorities and other interested parties in an effort to move this initiative forward. Among those with whom ASCO has met are representatives of the Food and Drug Administration (FDA), the Office for Human Research Protection (OHRP), and the Secretary's Advisory Committee on Human Research Protections (SACHRP). Almost without exception, those with whom ASCO met have expressed concerns with the burdens and inefficiencies of the current system, which seems to encourage duplicative reviews by local IRBs despite the fact that scientific and ethical issues have already been considered by a qualified CRB. Indeed, a significant source of dissatisfaction with the current CRB demonstration project conducted by the National Cancer Institute (NCI) has been the inability to avoid the delays caused by numerous reviews undertaken by local IRBs, notwithstanding the existence of CRB review.

ASCO commends FDA for seeking to clarify the variety of ways in which local IRBs might discharge their responsibilities under the regulations set forth in Part 56. These include:

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).

² *Id.* At 6.

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- Provision of relevant local information to the central IRB in writing by individuals or organizations familiar with the local community, institution, and clinical research;
- Participation of consultants with relevant expertise, or IRB members from the institution's own IRB, in the deliberations of the central IRB; and
- Limited review of a central IRB-reviewed study by the institution's own IRB, with that limited review focusing on issues that are of concern to the local community.

FDA added that “[o]ther mechanisms may also be appropriate” to address “local” aspects of IRB review.

While flexibility is typically a welcome response from FDA and other federal agencies, ASCO questions its utility here. The most frequently voiced concern about streamlining local IRB functions relates to perceived threats of liability should local IRB review be less rigorous or comprehensive than the federal standard, which is poorly defined. ASCO is concerned that giving a menu of possible ways of satisfying the requirement of local review will not achieve the desired result of clarifying definitively how the local responsibility can be addressed. Thus, while the Draft Guidance represents an important step in the right direction, ASCO believes the guidance could be more directive, resulting in greater predictability with respect to review of local issues.

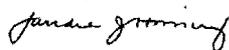
ASCO recommends that there be one and only one method of satisfying the local review requirement in cases where a qualified CRB is employed and the institution in question wishes to defer to the CRB on scientific and ethical issues. In such circumstances, the local IRB could be asked to provide an initial review of the protocol with the purpose of identifying local issues, if any, that require further review at the local level. Examples of such issues might be language or cultural questions or religious matters specific to the community that are not addressed by the protocol. After this relatively minimal review conducted solely for the purpose of identifying unaddressed local issues, the local IRB could certify to the CRB that there were no such issues. To the extent that such issues are identified, it would be the responsibility of the local IRB to bring them to the attention of the CRB, which would then consider and resolve them pursuant to the advice provided by the local IRB.

ASCO believes that this more definitive and straightforward process will help to dispel the uncertainty in the current system that drives excess fears of liability. Ultimately, as ASCO has previously advised SACHRP, the role given to “community attitudes” in the review process should be revisited in the applicable regulations in Part 56 and elsewhere. When the regulations were first promulgated, clinical research was in its infancy, and many communities no doubt had individualized concerns about such activities. With widespread public knowledge of clinical trials and the information power of the internet and other communication advances, the significance of local community attitudes is now much less clear and indeed deserves a reconsideration.

In addition, ASCO strongly advocates that the FDA work with OHRP to encourage uniform guidance on this issue across federally regulated and funded clinical trials. Harmonization of federal guidance will demonstrate consistency among federal agencies in approach to this issue and increase the likelihood that institutions will adopt this approach.

Thank you for addressing this important issue in the Draft Guidance and for considering ASCO's suggested revisions.

Sincerely,



Sandra J. Horning, MD
ASCO President

Cc: Bernard Schwetz, DVM, PhD, Director, HHS Office for Human Research Protections