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May 29, 2003

Glen Drew
Public Health Analyst
Office for Human Research Protections
Office of Public Health and Science
C/o Dockets Management Branch (HFA-305)
Docket Number 02N-0475
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Dear Mr. Drew:

The University of Kentucky welcomes this opportunity to provide comments on the Draft "Financial Relationships and Interests in Research Involving Human Subjects; Guidance for Human Subject Protection" (68 Federal Register, 15456, March 31, 2003). The University of Kentucky is a comprehensive public land grant institution with an active extramurally supported research base. In FY 2002, UK researchers brought in a record $212 million in extramural funding for grants and contracts. The current level of extramural activity includes more than 1,700 active sponsored projects, 463 of which involve human subjects.

The University of Kentucky is generally pleased with the new draft guidance issued by the Department of Health and Human Services. The suggested points and actions to consider provide institutions with flexible guidance for strengthening human research protections through elimination, management, reduction and oversight of financial conflicts of interests. There are numerous strengths of the proposed guidance that deserve comment.

The University appreciates that the Department has responded to the research community's concerns regarding the unnecessarily prescriptive nature of the 2001 interim guidelines. To develop effective human research protection programs, institutions need to be able to develop policies and procedures that fit within the local organizational structure and meet the needs of the local subject population. The draft document provides appropriate guidance without being overly prescriptive.

The University is pleased that the Department's guidance includes options for dealing with individual financial interests in research, and is not limited to creating a conflict of interest

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committee. Committee review may or may not be the appropriate model for managing, eliminating, reducing or overseeing financial conflicts of interests. It is important that institutions be given the option to consider other models.

The University of Kentucky is committed to maintaining a strong web of protections for its human research studies. Human research protection requires the integrated efforts of variety of constituencies. The University agrees with the Department's approach in providing guidance for the institution, Institutional Review Board (IRB), and investigators.

Although the University supports the guidance, we also believe several issues need to be addressed and improved. Set forth below are our general concerns and specific suggestions for strengthening the draft guidance.

General Concerns

- The University appreciates the Department's inclusion of comments in the preamble which attempt to make it clear that the document is for guidance, is non-binding, and should not be interpreted as a list of non-negotiable requirements. However, we are concerned with how third parties may seek to utilize the guidance in a variety of judicial or administrative hearings, turning what is intended to be helpful guidance into a comprehensive list of mandates. Consequently, we suggest adding the following clarification in the supplementary information: "This guidance document is not drafted nor intended to be used as evidence of required management activities."

- The University shares the expressed interest in the concept of institutional conflict of interest. This is an evolving area and one that requires continued discussion within the scientific community as to how institutions may best address this complex topic. For example, what are conditions where firewalls within an institution constitute effective strategies for dealing with potential conflicts? How can the concept of a *de minimus* (from the individual conflict of interest guidance) be applied to an institution? Are all financial holdings to be considered or only those with a direct tie to research? There is reference to an institutional conflict of interest committee, but it is not clear what the best strategy would be and therefore we would request that this be made less specific. It is quite likely that whatever the entity addressing institutional conflict of interest would be different from the one addressing individual CoI and it would be helpful if this document reflected that expectation.

Specific Suggestions

<u>B. Points for Consideration</u>

- We recommend that the first sentence of this section "Financial interests may be managed by eliminating them or mitigating their potentially negative impact" be revised to read as follows: "Financial interests determined to create a conflict of interest may be managed by ....."

The statement as currently written implies that all financial interests need to be eliminated or mitigated. The University agrees with the Department's following statement included in I.A.D; "Financial interests are not prohibited and not all financial interests cause conflicts of interest or harm to human subjects." Consequently, the statement listed above should be revised to make it clear that financial interests that have been determined to potentially cause conflict of interests or harm to human subjects are the ones that should be mitigated or eliminated.

C.1 Specific Issues for Consideration Regarding Institutions

- The University recommends that under the first sentence that the word "federally" be replaced with Department of Health and Human Services.

  The Department's authority does not extend to all federal agencies. Institutions may choose to apply the guidance to all research including industry as well as federal, but that is a policy decision to be made by the institution.

- We recommend that the following statement be deleted: "Include IRB members and staff and appropriate officials of the institution, along with investigators, among the individuals who report financial interests to COICs."

  There are several reasons why we think this statement is unnecessary and too prescriptive. The area of institutional conflict of interest is one about which there is no consensus in the community. It is not clear who would meet the "appropriate officials" criterion. It is not clear whether an institutional official who has nothing to do with specific project or has no decision making authority regarding the project should be disclosing to the COIC. Also, it is not clear whether disclosure by institutional officials should be managed by the same body that is charged with handling individual conflicts of interests. Potential IRB member conflicts should be handled using the other methods as outlined in the section on IRB operations. Including IRB member disclosure to COIC is redundant and unnecessary. Also, it implies that the IRB reports to the COIC, which we do not think is an appropriate model.

C.2 Special Considerations Regarding IRB Operations

- We recommend deleting the first bullet point: "Reminding members of conflict of interest policies at the start of each meeting"

  This item is rather bureaucratic, and we do not think would do much to address potential or actual conflicts of interests on the part of IRB members. Also, the other suggested methods included in this section are more effective in ensuring IRB members do not vote in a case where they have a conflict of interest.

C.3 Special Considerations Regarding IRB Review

- We recommend combining the first point ("Determining whether methods being considered or used for management of financial interests of parties adequately protect the rights and welfare of subjects") with the second bullet point ("Determine when an IRB needs additional information to decide whether financial interests could affect subjects"). We support replacing the two bullets with a statement developed by the Association of American Medical Colleges: "Determine whether the analysis and recommendations of the COIC for management of the financial interests of investigators and the institution adequately protect the rights and welfare of human research subjects."

It is important that redundancy between IRB and COIC roles be reduced to the extent possible and that the roles of the two bodies be clearly delineated. Combining the first two bullets and using the foregoing language would clarify these roles. Also, the University believes that the function of the COIC should be to evaluate financial interest but that the ultimate decision making authority for human research protections should rest with the IRB. Combining the two points and using the language recommended above supports this view.

C.4 Special Considerations Regarding Investigators

- We request clarification regarding the statement "having a non-biased third party obtain consent".

  We have assumed that the intent is not to suggest that the individual obtaining consent be someone independent from the institution. Individuals obtaining consent should be qualified to do so and should have adequate expertise with respect research procedures and experience with the subject population. However, other individuals within the institution should, in most cases, be able to fill this role.

The University of Kentucky thanks you for giving us this opportunity to comment on your draft guidance.

Sincerely,

Wendy Baldwin, Ph.D.
Vice President for Research

Cc
Katherine Adams, Legal Counsel
Deborah Davis, Office of Sponsored Projects Administration
Ada Sue Selwitz, Office of Research Integrity