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May 30, 2003

Dockets Management Branch (HFA-305)
Docket Number 02N-0475
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. 02N-0475, Draft "Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection"

Dear Madam/Sir:

As Director of the Research Conduct and Compliance Office of the University of Pittsburgh I am submitting, on behalf of the University of Pittsburgh, comments regarding the above-named draft guidance document. The University of Pittsburgh and University of Pittsburgh Institutional Review Board (IRB) are committed to the protection of individuals who are asked to participate and who agree to participate in research studies. We are well aware that certain financial relationships of the institution, research investigators, and/or IRB members have the potential to create conflicts-of-interest in the conduct of research that may adversely affect the rights and welfare of research subjects. We are also well aware that this is an extremely complex issue which is convoluted by many competing agendas including the Bayh-Doyle Act, competition for research funding, industry recognition of technology innovators, tenure stream requirements, etc. Thus, this issue demands deliberate and extensive consideration by each institution involved in the conduct of human subject research; such consideration taking into account not only the institution's ethical obligations and mandate to protect human research subjects but also the specific nature (i.e, public or private), governance structure and objectives of the institution and the interests of its faculty.

It is felt that this draft guidance document appropriately recognizes the complexity of this issue. As correctly stated in the document:

> "Financial interests are not prohibited, and not all financial interests cause conflicts of interest or harm to human subjects. HHS recognizes the complexity of the relationships between government, academia, industry and others, and recognizes that these financial relationships often legitimately include financial relationships."

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It is also felt that the document appropriately recognizes that there must be some flexibility in the manner by which institutions can address this issue and achieve a high level of confidence that the financial interests of the institution and/or its research investigators will not adversely impact human subject protections. The document's approach of asking thought provoking questions and identifying points for consideration will serve to stimulate each institution's deliberation of this issue while permitting the flexibility necessary to address the varied interests and scope of different institutions. This approach also permits the consideration of multiple different solutions and/or mechanisms to address this issue, which is felt to be extremely important in recognition of the complexity of the issue and the constantly changing environment surrounding the conduct of human subject research. As such, the document truly provides guidance to institutions rather than prescribing certain specific actions. While certain specific regulations to address potential conflict-of-interest in the conduct of human subject research may be warranted in the future, it is felt that it may be more productive at this stage to allow well-intentioned institutions the flexibility to develop appropriate institutional policies to address this issue. Such will likely lead rapidly to standards-of-practice related to the institutional management of financial interests which can and should form the basis for subsequent future regulations.

As stated above, the document's approach of asking thought provoking questions and identifying general points for consideration is felt to be appropriate in consideration of the fact that this is a guidance document. There is a concern, however, that the specific bulleted points that appear under part II.C., Specific Issues for Consideration, will be interpreted as de-facto requirements by the various federal regulatory agencies that oversee human subject research. This situation has been observed with other guidance documents issued by these agencies and should be avoided with this document in order to permit the flexibility necessary, at this point in time, for institutions to appropriately address the issue. Thus it is recommended that these specific issues for consideration be reworded in a manner consistent with the question and general points for consideration format that appears in parts A.and B. of section II.

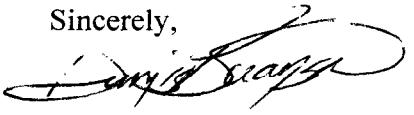
It is noted that section II. C., item 1. of the draft document promotes the establishment of institutional conflict-of-interest committees (COICs) to serve as the primary entity for, among other responsibilities, the development of institutional policies and procedures related to the disclosure of institutional and investigator financial interests and the evaluation of these interests against pre-defined criteria for what constitutes a conflict-of-interest. The section of the document further specifies that there should be separate responsibilities for financial decisions and research decisions within the institution, and that the institution should establish measures to foster the independence of IRBs and these COICs. It is felt that these recommendations are not only appropriate and important, but that the role of the COICs should be further expanded to include certain of the responsibilities of IRB Review as listed under item 3. of this section of the document. It is commonplace for institutions to make their IRBs responsible for overseeing all federal and institutional polices associated with human subject research even though such policies may not be related directly to human subject protections. As a result, IRBs are distracted from their primary responsibility of ensuring that the rights and welfare of individuals asked to participate or who agree to participate in research studies are adequately and appropriately protected and conveyed to these individuals. While determinations listed under bullet points 3 and 4 under item 3. of this section are appropriate responsibilities of the IRB, it is felt that the

determinations listed under bullets 1 and 2 should be assumed by the institutional COIC (i.e., assuming that the IRB operates within an institutional environment). Once these latter determinations have been made by the COIC, it should submit a copy of its decisions regarding an appropriate plan for managing institutional and/or investigator financial interests to the IRB. The management plan approved by the COIC should include recommendations as to whether the financial interests should be disclosed to potential research subjects. In summary, the IRB should be removed, to the extent possible, from direct involvement in establishing plans for the management of institutional and investigator financial interests so as to permit its focus on issues related directly to human subject protections.

In this Notice of the draft document, the Secretary asks for views and ideas as to how to assess any impacts of this guidance, as well as related non-Federal recommendations on enhancing the protection of human subjects. It is generally recognized that there have been a limited number of certain highly publicized misadventures involving human subject research wherein the investigators have held financial interests which may or may not have contributed to the misadventures; and, as a result, it is felt that there is a need for guidance or policies to address potential conflicts-of-interest in research. It is also generally recognized that financial interests of research investigators or the institution may or may not constitute a conflict-of-interest in research, depending upon how these financial interests are managed. In addition, it must be emphasized that there are interests (e.g., desire for academic promotion, tenure stream requirements, public recognition), other than financial interests, that may also potentially create conflicts-of-interest in the conduct of research. Also, many institutions, including the University of Pittsburgh, have had policies in place for several years to address potential conflicts of interest in research associated with the financial interests of investigators. Thus, it is felt that an accurate and meaningful assessment of the impact of this guidance will be very difficult to achieve. It is suggested that the corresponding time commitments and resources devoted to such an assessment might be better expended in addressing other matters related to enhancing the ethical conduct of human subject research; including, but not limited to, mandating investigator training in good clinical research practices; increasing institutional commitments related to the auditing of ongoing research studies; establishing Federal regulations mandating investigator and research coordinator reports of non-compliance with IRB-approved research protocols and informed consent requirements; reducing the medico-legal complexities of informed consent documents and improving the informed consent process; and educating the public regarding clinical research, the differing roles of a physician versus a research investigator, and their rights as research subjects.

In conclusion, we thank you for the opportunity to comment on this draft guidance document which we feel is much improved over the previous version.

Sincerely,



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Director