Chesapeake Research Review, Inc.

Biomedical and Healthcare Research
Consultation • IRB Services • Development Services

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

Re: Response to Draft "Financial Relationships and Interests in Research involving Human Subjects: Guidance for Human Subject Protection" [Docket No. 02N-0475] 68 FR 15456, March 31, 2003.

Chesapeake Research Review, Inc. (CRRI) agrees with, and supports in principle, the concept of the draft guidance document. We have the following comments and suggestions.

The 2003 Draft Guidance keeps all of the categories that were included in the 2001 Draft Interim Guidance but eliminates much of the guidance and discussion. So IRBs, investigators and institutions are left with what will likely be construed as requirements without the current best thinking of the government that was included in the 2001 document. The guidance and discussion is important for two reasons: (1) it sets the minimum standards for meeting the guidance; and, (2) it sets an upper limit to the meeting the guidance. IRBs, investigators, and institutions rely on such upper limits to be able to say when enough is enough. They need positive goals to be able resist efforts to go far beyond what is reasonable.

The "points to consider" asks the right questions but neither the points nor other parts of the Guidance document sets a minimum performance requirement. The guidance enables IRBs, investigators, and institutions to meet the recommendations outlined in the guidance by considering each of these points and determining that no oversight or action is required. Documentation of a no-action decision could be held out as meeting the letter of the Guidance, while providing no additional protection.

The present financial disclosure practice is very wide-ranging. For example, the conflict of interest requirements for FDA employees are very strict, essentially banning any financial interest in any entity that is involved in producing or marketing FDA regulated products. The minimum dollar amount is $1,000, not $10,000, $25,000 or $50,000. If FDA employees can be influenced by such a small amount of financial conflict of interest, how come those actively conducting a study are considered to be not influenced by a much more substantial ownership stake in a company?

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Independent monitoring of the research is a worthy goal. However, the suggestion that a Data Safety Monitoring Board (DSMB) is the appropriate body may be erroneous as current regulatory interpretation holds IRBs responsible for maintaining such oversight, with current guidance remaining silent in the delegation/sharing or communications of information between the DSMB and the IRB. DSMBs review the scientific progress of the research, not the financial conflicts of interest. The DSMB reviews take place at specified points after the research project has been started, reviewing study data after the fact. In the recent high profile cases of research gone bad, active involvement of any DSMB would have come too late to prevent the deaths of the research subjects.

The focus of the Guidance is on the IRB members and staff, the principal investigators and the institution. No mention is made of the study staff working with the principal investigators. As experience has suggested, the study staff could have more direct and significant influence on the subject's participation and/or data generation than the IRB staff.

It is our observation that the first two suggestions under item 4, "Investigators," provide little if any additional protection for study subjects. Including information in the informed consent document about the source of funding, funding arrangements, or financial information about an institution or investigator empowers only the most emboldened prospective subjects. The information that is provided will at best be minimal and at worst confusing or incomprehensible if not properly explained. As we have experienced all to many times, obtaining informed consent is a process which requires simply more than including information in an informed consent document. As such, the significance of the financial arrangements will not be apparent to, or understandable by, the subjects. It is our concern that the information will not convince anyone to rethink a decision to enter the study.

Having the informed consent process conducted by an impartial third party could, in some situations, provide greater protection for the study subjects. A caveat: If the research project is to be conducted by a "powerful" researcher, such as a department head, delegating the informed consent process to a person lower in the hierarchy will accomplish little. The subordinate could be more conflicted than the researcher, as he could perceive his future career to depend on the positive results of the consent process. Also, the principal investigator is the most knowledgeable person about the study, and is in the best position to explain complex concepts. If the principal investigator cannot be trusted to conduct the informed consent interview, should he be trusted to conduct the study and make study related decisions?

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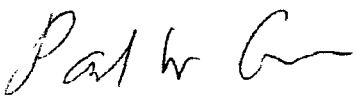
Finally, we wish to address the need to define "institution" as written in the Draft Guidance. It has been our experience that interpretation of "institution" is commonly thought of as a university or hospital campus, and usually as the site at which the research project is being conducted – with the IRB serving under the institutional umbrella. In fact, other entities meet the definition of institution. For example, the entity managing an independent IRB may meet the definition of an institution.

On behalf of Chesapeake Research Review, Inc., I would like to express our appreciation for the opportunity to comment on this very worthwhile initiative and would welcome adding further contributions. I hope these comments contribute to meaningful and effective management of financial conflicts of interest.

Sincerely,



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