1200 G Street NW Suite 400
Washington DC 20005-3814
tel 202 783 8700
fax 202 783 8750
www.AdvaMed.org

0 5 0 2 '03 MAY 30 P3:11

AdvaMed
Advanced Medical Technology Association

May 30, 2003

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

Re: Docket Number 02N-0475; Draft "Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection"

Dear Madam/Sir:

AdvaMed appreciates the opportunity to provide comments on the draft HHS guidance document, "Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection."

AdvaMed, the Advanced Medical Technology Association, represents more than 800 innovators and manufacturers of medical devices, diagnostic products and medical information systems. Our members produce nearly 90 percent of the $68 billion in health care technology products consumed yearly in the United States and nearly 50 percent of the $159 billion purchased around the world annually.

AdvaMed has a number of comments, both general and specific, discussed below:

General Comments
AdvaMed is committed to maintaining the highest standards for human subject protection and supports the Department's efforts to strengthen human subject protection in clinical research and to ensure that investigator conflict of interest does not compromise the rights and welfare of research subjects.

Medical device innovation is unique and different from some other types of product innovations. For example, medical device trials may require surgical skill implanting a particularly complex investigational device – a skill which may only be possessed by the inventor of the technology or a small group of clinicians and which may be essential to the safety of the trial participants. Accordingly, it is important that inventors be allowed to participate as investigators so long as their interests are disclosed and managed. Device trials

02N-0475 C18

also often involve complex procedures, requiring outcome analysis such as imaging and clinical follow-up. This increased time may require reimbursement, and that reimbursement, along with the reimbursement of reasonable costs associated with conducting a trial, does not represent a conflict of interest.

The previous draft interim guidance (January 10, 2001) suggested that *any* financial relationship, no matter how trivial, could affect the conduct of a trial. As such, it suggested a "zero tolerance" for any type of financial relationship. AdvaMed appreciates that the revised draft guidance takes into consideration AdvaMed's previous comments on this topic and recognizes that "not all financial interests cause conflicts of interest or harm to human subjects" and that "financial interests may be managed by eliminating them or mitigating their potentially negative impact."

AdvaMed also supports the draft guidance's implicit acknowledgement of the strength and value of existing human subject and conflict of interest requirements, including those of the FDA. AdvaMed's members must comply with all existing Food and Drug Administration regulations governing human subject protection, financial disclosure and conflict of interest. These regulations, 21 CFR Part 50 – Protection of Human Subjects, 21 CFR Part 56 – Institutional Review Boards, and 21 CFR Part 54 – Financial Disclosure by Clinical Investigators, have all been in place for some time, are well-understood, and offer substantial protections *for* human subjects and *against* conflicts of interests.

Specific Comments

II. Guidance for Institutions, IRBs and Investigators

B. Points for Consideration

This section encourages Institutional Review Boards (IRBs) and institutions engaged in research to consider a series of questions to help in the establishment and implementation of methods to protect human subjects from potential conflicts of interests. In particular, the guidance suggests that individuals or institutions involved in research consider whether "significant payments of other sorts" are being received. Medical device manufacturers are familiar with the definition of "significant payments of other sorts" from 21 CFR Pt. 54.2(f) and understand that it excludes the costs of conducting the clinical trial. However, other entities may not be as familiar with this regulation. AdvaMed recommends that the guidance make clear that legitimate payments to cover clinical trial costs should not be considered in the context of potential conflicts of interests.

C.1. Specific Issues for Consideration Regarding Institutions

This section encourages institutions to consider establishing conflict of interest committees (COICs) or other bodies or persons to deal with potential conflicts of interest. Generally, IRBs are in a good position to evaluate conflicts of interest if they are given sufficient information to do so. AdvaMed supports the establishment of an institutional committee or officer to ensure expeditious consideration of conflicts of interest in those cases where the IRB is overburdened and is unable to review protocols in a timely fashion. However, the

addition of a COIC has the potential to add another layer of review and to slow down protocol reviews. Too many bureaucratic layers and delays can ultimately slow down patient access to new technologies. AdvaMed recommends that the guidance encourage those institutions that establish COICs to conduct the COIC and IRB reviews concurrently to reduce delays and ensure efficient conflict of interest and protocol reviews.

C.3. IRB Review

This section encourages IRBs to carefully consider whether additional actions or activities are needed to adequately protect the rights and welfare of human subjects. As indicated above, in order to ensure the expeditious consideration and review of clinical trial protocols by the IRB, AdvaMed recommends that for those institutions that have established COICs, the guidance make clear that IRBs can defer to the findings of the COIC so that valuable time is not consumed by a de novo collection and review of the facts.

C.4. Investigators

Where there are financial relationships, this section encourages investigators to consider taking additional steps such as including information about the financial relationship or how such relationships are being managed in the consent form, or having a non-biased third party obtain consent. AdvaMed agrees that it is important for human subjects to have access to any information which is necessary to help them understand the potential risks and benefits of participating in a particular clinical trial and to understand any potential conflicts of interest, including financial conflicts.

However, device innovation is complex. Investigator compensation can involve many important variables including the difficulty of the study, the types of procedures and diagnostic tests required and their costs, the time it takes to complete data forms, the timeframe in which the study must be completed, etc. Potential human subjects are not likely to know the market valuation of each of the many and varied components of investigator compensation or to be able to discern payments that go beyond the normal costs of the study. Additionally, reviewing complex financial compensation information could distract potential human subjects from focusing on the important issues involved in understanding the medical benefits and risks of the clinical trial. AdvaMed recommends that potential human subjects should be told that an IRB or COIC has reviewed conflicts of interest and that they may request any additional information they may need.

In addition, this section encourages investigators to consider having a non-biased third party – such as an independent physician – obtain consent. Because the investigator and others involved in the investigation are the most knowledgeable about the investigational product and the study protocol, they are in the best position to explain the risks and benefits of investigational products to potential human subjects. For these reasons, AdvaMed urges the addition of clarifying language to the guidance that makes clear the advantages of informed consent which is obtained by the investigator and individuals trained in the investigational product and study protocol.

Conclusion

In conclusion, AdvaMed supports the Department's efforts to strengthen human subject protection in clinical research. We further commend the Department for crafting a balanced guidance that acknowledges and builds on the strengths of existing FDA regulations that are intended to protect human subjects and protect against conflicts of interest.

Sincerely,

Tara Federici

Tara Federici,
Associate Vice President
Technology and Regulatory Affairs