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Charles N. Kahn III
President

October 30, 2006

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

Re: Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors; Exception from Informed Consent Requirements for Emergency Research; Docket No. 2006D-0331

Dear Sir/Madam:

The Federation of American Hospitals ("FAH") is the national representative of investor-owned or managed community hospitals and health systems throughout the United States. Our members include teaching and non-teaching hospitals in urban and rural America, and provide a wide range of ambulatory, acute and post-acute services.

The FAH appreciates the opportunity to submit the following comments to the Food and Drug Administration ("FDA") regarding the draft "Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors; Exception from Informed Consent Requirements for Emergency Research" (the "Guidance"), as identified as open for public comment in the August 29, 2006 *Federal Register*. See 71 Fed. Reg. 51,198.

The FAH believes that clinical research can lead to important medical breakthroughs that improve the lives of all Americans. Notwithstanding these benefits, the FAH is generally concerned about the implications of conducting research on human subjects who are not able to provide informed consent (e.g., unconscious) or do not have a legally authorized representative available to provide consent on their behalf. We believe the FDA's regulation at 21 C.F.R. § 50.24, which limits permissible research done on this particularly vulnerable population, strikes an effective, delicate balance to ensure that the best interests of patients are protected while also realizing the benefits of

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such research. In addition to the FDA's work in this area, other federal agencies also have acknowledged the importance of this type of research if conducted properly.¹

For these reasons, we commend the FDA on developing the Guidance as a means of further developing and clarifying these important issues. The Guidance will assist, among others, FAH member hospitals as they endeavor to (1) protect those in their communities who participate in such emergency research, and (2) educate their institutional review boards ("IRBs") and clinical investigators regarding this particular type of research.

The FAH provides the following comments on specific sections in the Guidance, as set forth below.

II. STUDY DESIGN

Practicability

The FAH agrees that a research study should be allowed to take place only in those situations in which a study practicably could not be conducted without waiving informed consent. The FAH appreciates the examples included in the Guidance to illustrate when research may be deemed practicable without waiving informed consent, such that an exception for informed consent for emergency research should not be granted. These examples reinforce the limited circumstances under which this type of research should be pursued, and highlight the preeminent importance of the protection of human subjects.

Subject Exclusion

The FAH agrees that the study protocol should describe situations in which emergency care personnel could reasonably infer that potential subjects may "opt out" of participation in research. For example, the study design may require that emergency personnel examine potential enrollees for obvious signs of indications that the person would choose not to participate in the study.

III. THERAPEUTIC WINDOW

Therapeutic Window Rationale

The FAH agrees that the therapeutic window should be specified in the study protocol and how this relates to the amount of time devoted to seeking informed consent from either the subject or a legally authorized representative, or contacting a family member. While we recognize that the entire window should not be exhausted in search of informed consent or notice to family members for a study that is subject to the

¹ See the Office of the Protection from Research Risks (now referred to as the Office of Human Research Protections) Reports, October 31, 1996.

emergency research exception, all reasonable efforts should be expended for the maximum, appropriate amount of time for the enhanced protection of this vulnerable population.

Contact of Family Members

The FAH agrees that attempts to contact a legally authorized representative or family member must be made, unless the situation is too urgent and requires immediate intervention. Additionally, the FAH agrees with the Guidance's requirement that the IRB review the proposed plan and procedure for attempting to contact the legally authorized representative or family member.

IV. IRB RESPONSIBILITIES

IRB Role in Reviewing Emergency Research

The FAH believes that the IRB should be encouraged to attend at least one public consultation. (This comment also applies to the Guidance's text found in the Community Consultation section below.) As an integral part of the emergency research studies, IRBs should be involved on all levels of the decision making process. We also support an open and transparent process with respect to the family members of the patient.

The FAH commends FDA's clarification of the IRB's responsibilities in reviewing emergency research. The FDA should stress, however, that the order of events listed in the Guidance is just an example of a way in which an IRB may comply with the law, and that this particular approach is not required by the FDA. In other words, the FDA should clarify that an IRB has the flexibility to meet these requirements in the manner best suited to the institution.

IRB Selection

FDA notes in the Guidance that independent IRBs may review emergency research studies involving an exception from the informed consent requirements. With all due respect to the commercial IRBs that furnish valuable review and approval for many of our members, the FAH believes that, in this particular context, the local IRBs are best suited to review and approve these studies. We recognize that an IRB must always consider the community attitudes in which the study will be conducted, and that commercial (or independent) IRBs have developed a process by which this IRB review and approval requirement is generally met. However, given the heightened importance of community involvement, education and consensus building that is required for the conduct of emergency research without informed consent, this task is best left to the local IRBs. Thus, we urge the FDA to stress the importance of local IRB control over these studies and to state its preference for local IRBs.

IRB Documentation

The FAH supports FDA's IRB documentation requirements described in the draft Guidance.

V. LICENSED PHYSICIAN CONCURRENCE REQUIRED FOR IRB APPROVAL OF THE RESEARCH

The FAH supports the requirement that IRBs must have the concurrence of a licensed physician that the criteria of 21 C.F.R. § 50.24 are met.

VI. SPONSOR RESPONSIBILITIES

The FAH supports FDA's clarification of sponsors' responsibilities in the Guidance. We believe that FDA should stress that the order of events required of a sponsor to satisfy their responsibilities is just an example and not an FDA-required route to satisfying the sponsors' responsibilities.

VII. CLINICAL INVESTIGATOR RESPONSIBILITIES

The FAH supports FDA's clarification of the clinical investigator's responsibilities in the Guidance. We believe that FDA should stress that the order of events required of a clinical investigator to satisfy their responsibilities is just an example and not an FDA-required route to satisfying the clinical investigator's responsibilities.

VIII. COMMUNITY CONSULTATION AND PUBLIC DISCLOSURE

The Guidance clarifies the distinction and importance of community consultation vs. public disclosure of the research, (*i.e.*, notice of the research before it is conducted and sharing of results as the research is concluded and analyzed). The FAH appreciates the FDA's general comments in this regard.

A. COMMUNITY CONSULTATION

The Role of the Sponsor, Clinical Investigator, and IRB in Community Consultation

The FDA states that "the investigator, the sponsor, or the IRB" conducts the community consultation activities. We believe that all parties should be involved in the community consultation. This delicate process requires the successful collaboration of multiple interests, and as such, each stakeholder should have an active involvement with the community. Additionally, such tripartite involvement should relieve some pre-existing concerns from members of the community.

With regard to the IRB members' involvement, the FAH strongly encourages the FDA to require IRBs to attend the community consultations. As a key component of this

process, it is imperative that IRBs receive information firsthand, as opposed to analyzing community attitudes, support and/or objects third-hand. In other words, it will be difficult for IRBs to fully assess the community reaction to the proposed study without IRB attendance or representation at the community consultations.

Type & Frequency of Community Consultation

The FAH believes that using a wide variety of community consultation activities will allow for the greatest possible public input. We support the FDA's suggestions regarding the various types of community consultation activities that may be employed to ensure adequate public education. We also believe that information regarding the community consultation process should be made publicly available through the FDA public docket. This will enable future research study proposals to have the benefit of others' past experiences with respect to this important procedural step.

B. PUBLIC DISCLOSURE

The FAH supports the development of sufficient safeguards to ensure public disclosure of data about a study both prior to the initiation of the study and after completion of the study.

1. BEFORE THE STUDY BEGINS

Content

The FAH appreciates the FDA's approach in enumerating what is required in the appropriate disclosure. Specifically, the FAH agrees with beginning this list of required information with "a clear statement that informed consent will not be obtained for most research subjects." A key component to protecting human subjects (which may include entire communities-at-large in this case) is education about the study at issue, and that the subjects may not furnish consent prior to enrollment if the person's condition does not allow for consent.

Moreover, it is important for the disclosure to suggest how individuals may "opt out" of participation. Again, the FAH strongly supports the Guidance's requirement that this information be included in the disclosure plan reviewed by the IRB.

Access to Public Disclosure Information

To ensure maximum flexibility, we suggest the Guidance indicate that a clinical investigator can (and should) be the entity providing the public disclosure materials to the sponsor. As drafted, the Guidance can be interpreted as directing the IRB to make this showing, but we think the more appropriate guidance is to indicate that either the clinical investigator or the IRB can make this disclosure.

The FDA should require the publicly disclosed information to the sponsor to be available through electronic means, such as the internet. It should not take the laborious Freedom of Information Act request process before this information can be viewed by the public.

2. AFTER THE STUDY IS COMPLETED

How

The FAH believes that the study results should be made publicly available through the FDA public docket and/or the same public disclosure mechanism used prior to the start of the study. Where pre-study disclosure methods are inadequate for post-study disclosure, the FDA should encourage sponsors and clinical investigator to utilize additional disclosure methods for the community at large. Members of the community should also be made aware of where to find this information. A primary reason for this position is that FAH firmly believes that one of the greatest barriers to these important studies is public skepticism. A transparent process will help alleviate this skepticism.

The FAH agrees that the information should also be shared with the researchers for a variety of reasons, including the prevention of unnecessary duplication of studies involving vulnerable subjects who are unable to consent.

IX. CONTACT OF LEGALLY AUTHORIZED REPRESENTATIVES OR FAMILY MEMBERS

A. PRIOR TO ADMINISTRATION OF THE TEST ARTICLE

Procedures

The FAH supports the FDA's requirement that the IRB find and document that procedures are in place for contacting and providing information to a subject, a legally authorized representative or family member.

Informed Consent Document

The FAH supports the use of an IRB-approved informed consent document. We believe that this document should contain adequate information to educate and inform subjects, legally authorized representatives and family members about the study, including their right to withdraw from participation in the study.

Opportunity to Object

The FAH supports the FDA's statements in the Guidance.

Summary of Contact Efforts

The FAH supports the FDA's statements in the Guidance.

B. AFTER ADMINISTRATION OF THE TEST ARTICLE

When

The FAH understands the sensitivities involved in informing family members about a subject's participation in a research study if a patient dies, particularly one where there is no informed consent. While families must be able to grieve for a lost loved one, if there is an extended period of time before the family is notified of the study then there may be a layer of suspicion that can only detract from the goals of emergency research. As such, IRBs should be required to develop processes and/or policies addressing the process for informing loved ones when there is an adverse event. Such a disclosure may be more appropriate and meaningful being delivered by the clinical investigator than the IRB.

Conclusion

The FAH appreciates the FDA's efforts in reviewing the Guidance and seeking public input. As highlighted above, it is imperative that this process be open to the public and transparent for all parties involved. The sensitivities involved with conducting research on a patient who cannot provide informed consent must not be taken lightly. It is important that the FDA set forth meaningful requirements to ensure that these studies are conducted in an ethical manner. We believe the Guidance generally achieves that goal.

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On behalf of our members, the FAH appreciates this opportunity to submit comments to the FDA regarding the draft Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors; Exception from Informed Consent Requirements for Emergency Research. If you have any questions about this letter or need further information, please contact Jeff Micklos at (202) 624-1521.

Respectfully submitted,

