

Presentation Abstract; Docket No 2006D-0331;  
Conduct of Emergency Clinical Research; Public Hearing

Submitted by Michelle H. Biros, MD, MS on behalf of the  
Society for Academic Emergency Medicine and  
The Coalition of Acute Resuscitation Researchers.

The Society for Academic Emergency Medicine ( SAEM ) is grateful for the opportunity to provide comments from its membership to the FDA related to Exception from Informed Consent in Emergency Research Circumstances. The Coalition of Acute Resuscitation Researchers ( the Coalition) joins SAEM in this oral presentation.

In 1994, SAEM took the lead in discussions related to issues of consent in emergency research circumstances. The Coalition was developed at the request of SAEM to broaden these discussions and include thought leaders from throughout the research community. The Coalition developed a Consensus Document that was subsequently endorsed by over 25 professional organizations, and presented concepts that were eventually incorporated into the FDA's Final Rule ( 21CFR 50.24 ). Since the advancement of the Final Rule, SAEM has continued to discuss , educate its members on, and monitor the use of the Final Rule. In May, 2005, the Society's journal, *Academic Emergency Medicine*, sponsored a consensus conference entitled: " The Ethical Conduct of Resuscitation Research; Exception from Informed Consent." The proceedings of the conference were published in the November 2005 issue of *AEM* and widely disseminated.

With this history in mind, we feel well qualified to offer these comments related to specific issues raised by the FDA, and offer a few additional questions of our own.

A. Scientific aspects

FDA # 1, 2 and 4) We believe there are many challenges to successful implementation of the regulations that have not yet been addressed. While some relate to specific patient populations, other challenges relate to inconsistent interpretations by IRBs and investigators, or lack of meaningful definitions of criteria set forth in the regulations. We will provide specific examples and discussion.

B. Additional human subjects protection

FDA #5,6 and 11) Community consultation has been problematic, and we suspect that methods used to achieve this have not resulted in broad representation of the community of potential subjects or the community in which the research is to be conducted. Few people attend public meetings and those who do are likely to be non-representative. Who then in the community is giving feedback and how does it reflect the general concerns? In order to provide useful discussion, the community should understand the protocols under consideration. Data suggest that even members of focus groups, with multiple educational sessions, do not generally understand the actual study goals and protocol. How do we make sure the community understands? If understanding is lacking, and involvement is non

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representative, the goals of community consultation are not met and it becomes a cumbersome exercise. What was the actual intent of community consultation and is this purpose still meaningful, based on experience with the regulations?

FDA # 12 and 13) Disclosure of the full protocol or certain scientific information to the public causes concerns similar to that outlined above. If we include protocols or specific scientific information in the public notification, how can we be sure the public understands the information or the protocol? If no assessment of understanding is included, has the purpose of the notification been met?

### C. Additional challenges

FDA #20 ) Many additional challenges exist related to the use of the Exception from Informed consent. Some of these are listed here;

1) The IOM's recently released report on the Future of Emergency Care describes a paucity of clinical effectiveness trials for the treatment of critically ill or injured patients in the out of hospital setting. Are the requirements of the regulations too stringent in the pre-hospital setting? What prospective interventional methods would work in EMS research? Have unanticipated problems or unique circumstances arisen that have negatively affected the out of hospital implementation of exception from informed consent research?

2) Many special vulnerable populations, such as children, merit special consideration and have not been separately considered in the existing regulations. Should the same set of regulations always apply?

3) Resuscitation research includes studies of varying complexity, across a wide spectrum of topics, with different risks and different benefits. Is one set of regulations appropriate for all studies, or should incremental risk assessment be considered?

4) The translational emphasis of the NIH has led to the development of at least three emergency based research networks ( PECARNS, Neuro-NETT, and ROC). All aim to discover new treatments for critical illness or injury. This will require research using the Exception. New challenges are present when trying to successfully and consistently implement a protocol at several sites. Since there are variable levels of comfort among IRBs regarding the use of the Exception, how can we ensure a consistent protocol review at all sites? Will reluctance of some sites to allow research using the Exception result in a demographic bias in patients' enrollment? Should a central IRB be established for network studies?

**Tinch, Latroy D**

**From:** Michelle Biros [michelle.biros@gmail.com]  
**Sent:** Friday, September 15, 2006 11:59 AM  
**To:** Crescenzi, Terrie  
**Cc:** Mary Ann Schropp; Lewis, Roger J.; Baren, Jill; Barb Mulder  
**Subject:** Oct 11 meeting  
**Attachments:** FDA Abstract.doc

Hi Terrie,

Thanks for talking to me this AM. I have attached the abstract, and appreciate your offer to be sure it gets on the public docket, and that I will be considered for oral presentation at the Oct. 11 meeting.

I am representing the Society for Academic Emergency Medicine, and the Coalition of Acute Resuscitation Researchers.

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