

I believe that the present regulations providing an exception from informed consent for emergency research require major revisions. The regulations pose a major barrier to the conduct of ethically appropriate and scientifically sound research in emergency situations. The requirement for community consultation and disclosure imposes an unfunded mandate that neither informs the community nor assures that the potential subjects of the research have substantive input into the research.

The regulations have created several ethically problematic outcomes. The burden and cost required to implement research in emergency situations has led to the fact that many recent advances, especially in resuscitation research, are conducted outside the United States. In this situation the community (United States) benefits from the research, but does not equitably participate in the risks. This is a direct violation of the Belmont principles. Among such examples is the demonstration of the benefits of hypothermia in cardiac resuscitation (Austria, Australia) and the lack of benefit of a CPR device (Canada). 21CFR50.24 poses a major impediment to research in areas where clinical research is clearly indicated in order to provide an evidence base for treatment.

Perhaps more problematic is the observation that with a mobile population, "community" concept is not a meaningful concept. Recent experience regarding research with an artificial blood substitute illustrated the limitations of the "community" concept. An interesting paradox was created whereby a member of the local IRB which rejected the research as failing to meet the regulatory requirements of 21CFR50.24 could fly to a city where the protocol was approved and could become a subject in a study which the Board (or the member) had determined was unethical! In a situation where potential subjects could be recruited from a broad geographic area covered by helicopter transport the actual participants would probably be those traveling on interstate highways who have nothing to do with the communities within a given geographic area. Does "consultation" with the communities actually have any meaning for these potential subjects?

I believe that there should be either national or regional panels that review and approve research in defined areas of emergency research. These should include resuscitation research, acute neurology, trauma, pulmonary and critical care research. Centralized review panels should be able to weigh the risks and benefits of the research in the context of the clinical condition. In this sense, the "waiver" requirements would be broadened to include research posing greater than minimal risk, but where the risk is acceptable in the context of the clinical condition. Informed consent could be modified as appropriate to the emergent condition. For example, no consent for cardiac arrest and abbreviated "consent for research participation" for a subject in shock or unstable with a myocardial infarction (heart attack).

Specific issues from the regulations:

1. The human subjects are in a life-threatening situation

This is not adequately defined. Is any illness or condition with mortality a possible outcome life threatening under this definition? The guidance document indicates that head injury or stroke would be examples of diseases and conditions that could be included stating "patients with head injury or stroke are at risk of both death and severe disability." The observed mortality even in severe stroke or head injury is low. There are many diseases where death is a possible outcome and research should be appropriately permitted in an emergency situation.

2. available treatments are unproven or unsatisfactory.

The use of "or" is conceptually problematic and "unsatisfactory" undefined. I would suggest either making the requirement "unproven and unsatisfactory" or providing reasonable examples as to what kinds of treatments could be considered "unsatisfactory." Is a treatment "unsatisfactory" because it is costly, has side effects, is not readily available or has less than ideal efficacy?

3. Community consultation and disclosure

As noted previously, this requirement is burdensome, costly and ineffective. The

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actual potential subjects may not have meaningful input into the decision as to whether the research is acceptable. If panels (national or regional panels) had open or televised reviews of emergency research proposals and there was an avenue for public comment, wouldn't this be preferable to the present requirements?