

**Recommendations for Implementation of Community Consultation and Public Disclosure under the FDA "Exception from Informed Consent Requirements for Emergency Research"**

**American Heart Association**

**Emergency Cardiovascular Care Committee**

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On behalf of the American Heart Association (AHA) and over 22.5 million AHA volunteers and supporters, we would like to offer the following comments at the Food and Drug Administration's Hearing on Conduct of Emergency Clinical Research.

Since 1924, the American Heart Association has dedicated itself to reducing disability and death from cardiovascular disease and stroke — the #1 and #3 leading causes of death in the United States — through research, education, community based programs and advocacy. AHA's efforts include, but are not limited to the following:

- The development of evidence-based clinical practice guidelines designed to help advise physicians and other providers on the prevention, treatment and chronic management of cardiovascular disease and stroke;
- the development of international guidelines for emergency cardiovascular care (ECC), in collaboration with the international liaison committee on resuscitation (ILCOR)<sup>1</sup>; and the development of a series of high-quality courses and training materials that serve to educate the public on how to recognize the signs of heart attack and stroke, how to administer cardiopulmonary resuscitation (CPR) and instruction on proper operation of an automated external defibrillator.<sup>2</sup>

Approximately 250,000 people die annually from sudden cardiac arrest outside of the hospital. Central to our efforts in improving the outcomes of sudden cardiac arrest is our commitment to ensuring that clinical research in this critical area proceeds and that research findings are translated into practice in an appropriate and timely manner. There are a number of barriers to the conduct of this research, and that is the reason for our presence here today.

I would like to comment specifically about the issue of informed consent in resuscitation research, and have submitted a draft document that is in development by the American Heart

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<sup>1</sup> To see the AHA Guidelines on CPR and Emergency Cardiac Care go to <http://www.americanheart.org/presenter.jhtml?identifier=3035517>

<sup>2</sup> See [http://www.americanheart.org/downloadable/heart/1053032137284healthsafety\\_courses.pdf](http://www.americanheart.org/downloadable/heart/1053032137284healthsafety_courses.pdf)

Association. This document is not yet in final form and it may be modified before publication, but there are a number of concepts included within it about which there is general agreement within the resuscitation research community, and it is these that are the substance of my testimony today.

### **Community Consultation and Public Disclosure Template**

We propose to provide guidance for implementation of community consultation and public disclosure. A template is presented which (1) provides for quantification of the minimum requirements that an IRB might adopt, (2) gives examples to help IRBs quickly become familiar with the process of implementing and reviewing studies proposed with Exception to Informed Consent, and (3) proposes that trials of interventions approved by the FDA for the indication being studied should require different levels of community consultation and public disclosure than studies of unapproved interventions. The template gives a common interpretation of the requirements, and provides a list of actions acceptable for the implementation of community consultation and public disclosure.

#### **Ethics**

The guiding ethical principle for the template is that there is a range of actions that are acceptable to protect subjects' autonomy, dependent on the risk of the study. The risk referred to here is the incremental risk of participation in the proposed study, over and above the risks of having sustained a life threatening emergency and being treated with standard interventions. The higher the risk of the study, the more stringent are the actions that are required to protect subjects' autonomy. Since there is a range of risk associated with different study interventions, different levels of community consultation and public disclosure can be used to balance appropriately subjects' autonomy with the public good.

A trial of an approved therapy should not require the same level of community notification and consultation as one where non-approved or not-generally-accepted interventions are being introduced for the first time. For interventions that were not approved by the FDA, the risk of the therapy could be

incrementally higher, and the level of community consultation and public disclosure for the study should similarly be higher.

### Stratification of Risk

This template breaks studies into categories of minimal, low, intermediate, and high incremental risk. Any sudden, catastrophic, life threatening condition places patients at high risk for substantial morbidity and mortality. Instead of considering only the inherent risk of the underlying disease, which is present whether the patient is enrolled in the study or not, we recommend evaluating the incremental risk from participating in the proposed study. That evaluation can then be used to determine the degree of community consultation and public disclosure appropriate for the proposed study.

Certain studies are justifiable without documented consent under minimal risk criteria. Consider the study of a therapy approved by the FDA for the indications being studied being compared to another therapy that was approved or did not need approval (e.g.: manual CPR). The study likely would carry a risk that was minimally above the risk of being treated with either approved therapy. In the absence of a research protocol, physicians could ethically and legally choose to treat patients with a life-threatening condition with either of these interventions. The only additional factors introduced by a research study of these interventions are 1) that the patients are being randomized to one of the approved interventions, and 2) the loss of privacy and confidentiality during review of the clinical record after the intervention has been applied. Therefore, if the randomization procedure does not introduce any significant delay in applying the approved therapies, such a study is justifiable without documented consent under minimal risk criteria. The rationale for not having an informed consent document is described in the preamble to the final rule for 21 CFR 50.

During the comment period for these regulations, the agency received feedback that the subject should be able to choose to continue to participate fully in a study, to continue the intervention but not

have their data included in the research database or results, or to discontinue the intervention and use of the subject's data. This was rejected by the agency, however.

The factors that can help decide the degree of incremental risk added by a particular study are shown in Table 1. We propose that IRBs use the following criteria to determine incremental risk:

- (1) FDA labeling status of the investigational therapeutic drug or device, for studies of interventions;
- (2) an evaluation of whether the study introduces any additional risk of harm over that of simply using the investigational therapeutic drug or device (such as any delays in applying therapy that may be introduced by the randomization process);
- (3) the degree of invasiveness and need for real-time clinical decisions, for studies of diagnostics; and
- (4) the potential sensitive nature of the study from the community(ies)' perspective, including political cultural and religious considerations.

For a therapeutic intervention, therefore, the study would have minimal, low, intermediate, or high incremental risk based on the FDA labeling status of the therapy and the assessment of whether there was minimal risk of being in the study (Table 1, "Intervention" row), unless it were placed in a higher risk category based on the community(ies)' sensitivity (Table 1, bottom row). The same would be true for the study of a diagnostic, where the type of diagnostic would place it in minimal, intermediate or high risk categories based on the degree of invasiveness, the need for real-time decision making, and whether the diagnostic is FDA approved (Table 1, "Diagnostic" row), unless it were placed in a higher risk category by the perceived community(ies)' sensitivity (Table 1, bottom row).

#### Levels of Community Consultation and Public Disclosure

Once the degree of incremental risk is determined, we propose that the amount and types of community consultation and public disclosure be guided by Table 2. For minimal risk studies, no community consultation or public disclosure is required, although minimal community consultation should be considered. For low incremental risk studies, minimal community consultation would be needed. For example, review and feedback from an appropriate group, committee, panel or

organization representative of the study community could allow appropriate community consultation without excessive time being needed to wait for public comment from a published advertisement.

Alternatively, there could be solicitation through a website or public notices (such as through the mass media), with a call-in number and/or web address provided for feedback. For a high incremental risk study, however, more community consultation would be required, including an appropriate number of mass media solicitations, community meetings, and contact with prominent community organizations.

Specific examples of community consultations and public disclosures are available at:

[www.americanheart.org/emergencyexception](http://www.americanheart.org/emergencyexception). We emphasize that the recommendations of Table 2 are simply guidelines. Individual IRBs will set their own standards based on their individual considerations. We also emphasize that involvement of the community should include attempts to consult with targeted, at-risk, or interested, populations.

Table 1. Assessment of Incremental Risk of Research Studies.

| Study Type  | Potential incremental risk added by study   |   |  |   |
|---|---|---|--|---|
|   | Minimal   | Low   | Intermediate   | High  |
| Intervention<br>(Device/ drug)  | 1) FDA approved for proposed study indication<br>2) and/or already in clinical use for study indication<br>3) and have minimal risk of harm from being in the study.<br>(e.g.: Approved mechanical CPR device vs standard CPR; amiodarone vs lidocaine) | 1) FDA approved for proposed study indication<br>2) and/or already in clinical use for study indication<br>3) and have higher than minimal risk of harm from being in the study | 1) FDA approved for clinical use,<br>2) but not for the study indication.  | Not FDA approved for any indication yet.  |
| Diagnostic<br>(Test/device/feature)                                   | 1) Non-invasive,<br>2) and not used for real-time clinical decisions.<br>(e.g.: non-invasive monitor, low volume blood drawing)   |   | 1) Minimally invasive,<br>2) and not used for real-time clinical decisions.<br>(e.g.: transconjunctival oxygen saturation) | 1) More than minimally invasive,<br>2) or used for real-time clinical decisions,<br>3) or not FDA approved.<br>(e.g.: intracranial pressure monitor), |
| Community's potential sensitivity<br>(Political, cultural, religious) | Very unlikely to have community sensitivity   | Very unlikely to have community sensitivity   | Possibly to have community sensitivity   | Likely to have community sensitivity  |

For a therapy, the study would have minimal, low, intermediate, or high incremental risk based on the FDA labeling status of the therapy, and the assessment of whether there was minimal risk from being in the study (“Intervention” row), unless it were placed in a higher risk category based on the community(ies)’ sensitivity (bottom row). For a diagnostic: the study would have minimal, intermediate or high risk categories based on the degree of invasiveness and the need for real-time decision making (“Diagnostic” row), unless it were placed in a higher risk category by the perceived community(ies)’ sensitivity (bottom row).

Table 2: Levels of Community Consultation and Public Disclosure suggested at different degrees of incremental risk.

|  | Potential incremental risk added by study  |   |  |
|--|--|---|--|
|  | Low  | Intermediate  | High   |
| Community Consultation Options                 | Review and feedback from an appropriate group, committee, panel or organization representative of the study community.<br><br>Alternatively, consider solicitation through website or public notices (such as through a mass media piece), with a call-in number and/or web address provided for feedback      | 1) As in Low,<br>2) Plus consider solicitation through website or public notices (such as through a few mass media pieces).<br>3) Call-in number and/or web address provided for feedback | 1) Review and feedback from at least one group, committee, panel or organization representative of the study community,<br>2) Public forum(s) or presentation at municipal government meeting(s) in the study community.<br>3) Solicitation via a number of mass media pieces.<br>4) Call-in number and/or web address provided for feedback |
| Public Disclosure Options                      | Single targeted effort deemed most likely to reach study community: This could be through a mass media piece or distribution of information in more focused manner to likely subjects.<br><br>(e.g.: targeted: poster, brochure or newsletter article in senior citizen center where study will be conducted.) | At least one targeted effort and a mass media piece. Consider website.  | Multiple efforts, including both targeted efforts and mass media pieces, as deemed necessary to reach the community adequately. Website recommended.   |
| Patient / family notification of participation | Reasonable attempts required for written communication regardless of patient survival status<br>(e.g.: letter, including invitation to meet with investigator or study coordinator to discuss)   |   |  |

For minimal risk, no community consultation or public disclosure is needed, although a single announcement could be considered. A mass media piece refers to a newspaper article or advertisement, or a radio announcement, or a television spot.