The Research on Community Consultation: An Annotated Bibliography

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Abstract

Community consultation is a required element of research studies that use a waiver of or exception from informed consent. Its intent is to provide an additional patient safeguard in emergency research circumstances when prospective informed consent is not possible. Investigators have reported that community consultation may be the most difficult aspect in implementing research trials using a waiver of or exception from informed consent. This article presents a brief overview of the sparse literature available on the process of community consultation since the inception of the current emergency research regulations. To determine if the process is meeting its goals, more research will be required.


Keywords: community consultation, exception from informed consent, waiver of informed consent

COMMUNITY CONSULTATION

Community consultation is a required element of the federal regulations 45 CFR 46 and 21 CFR 50.24 that govern emergency research studies using a waiver of informed consent or exception from informed consent (EFIC). Community consultation was envisioned as a patient safeguard in emergency research circumstances when prospective informed consent is not possible. It was believed that consultation with the community of potential research subjects, and the community in which the research would be performed, would provide investigators and institutional review boards (IRBs) insight into aspects of the study, such as cultural concerns, that may not have been considered by the investigators. While community consultation was not designed to provide surrogate consent or to allow a community to veto proposed projects, issues arising during community consultation require consideration before the project can be approved by the local IRB.

Investigators have reported that community consultation may be the most difficult aspect in implementing research trials using a waiver of informed consent or EFIC. The regulations were codified more than a decade ago, but since that time, very little has appeared in the medical literature to study the process and effectiveness of this regulatory requirement. This article presents a brief overview and critical appraisal of the currently available literature on community consultation since the inception of the current emergency research regulations. This article is also intended to illustrate the overall lack of published information on experience with the community consultation process and an even greater lack of analytical information examining the effectiveness and adequacy of the process. Without studying the process of community consultation itself, we may never be sure that it meets its intended objectives.

UNANSWERED QUESTIONS

In 2006, the Food and Drug Administration (FDA) advanced a draft guidance document to assist investigators and IRBs in appropriately fulfilling the requirements of 21 CFR 50.24. Comments on the draft document were solicited from interested stakeholders, and public testimony was provided at a meeting held in October 2006. In the 2006 draft guidance, the FDA asks several questions:

1. What are the costs, benefits, and feasibility of community consultation as currently required under CFR 50.24?
2. What aspects of community consultation as currently practiced are effective mechanisms for human subject protection?
3. Are there additional practices that could enhance human subjects’ protection?
4. Are there elements of community consultation, both procedural and substantive, that should, at a minimum, be required?
5. Would opt-out mechanisms to identify individuals who do not wish to be included as subjects, in particular emergency research studies, provide a necessary protection for human subjects? If so, are they feasible?

6. Who should use the information obtained from the community consultation process and how should they use it? Should the regulation be more specific on this point, and if so, what should it provide?

7. Are there others beside the IRB who should play a role in determining the adequacy of the plan for community consultation and the material to be publicly disclosed?

8. Should the regulation require documentation of meeting activities and discussions in sufficient detail to show the information that was disclosed and the community reaction to the clinical investigation? If so, who should be responsible for such documentation?

9. Should the regulation also require that documentation of community consultation activities be submitted to FDA, for example by being placed in the public docket? If so, who should be responsible for doing this?

10. Should this information also be available elsewhere such as on clinicaltrials.gov?4

These are just a few of the unanswered questions related to the goal and success of community consultation. While the regulations were developed in good faith, it was not until the process was attempted that these unanticipated and difficult-to-answer questions arose. Many, if not most, of these questions cannot be answered without research on the regulation itself, focusing on community consultation activity both within the context of the trial and as a theoretical construct for obtaining needed information.

Because of the relative paucity of information on the community consultation process since the implementation of 21 CFR 50.24, any change in the regulations will not be evidence based. Therefore, rigorous scientific inquiry on the application of the special protections of CFR 50.24, particularly the required elements of community consultation and public disclosure, must occur.

THE EXISTING LITERATURE

To date, there are eight published articles that describe community consultation activities.5–12 Six of these were conducted within the context of a clinical trial using an EFIC under 21 CFR 50.24.5–10 The predominant method used was the hosting of public meetings where presentations were made about the study and participants were provided an opportunity to ask questions. Other methods that were found to be feasible were random digit dialing telephone interviews, face-to-face interviews, and focus groups.9 Communities were defined both broadly and specifically, with activities targeting both types. The remaining two studies offered suggestions for community consultation methods, although they did not take place concomitantly with a trial using EFIC. One of these conducted a survey of a proxy population for the population “at risk” in a hypothetical trial using EFIC.11 and the other used focus groups and telephone surveys to obtain the needed information for a future planned trial.12 The study by Baren et al. informally consulted with ethicists and IRB chairpersons who endorsed this particular method,11 whereas the Morris study ultimately did receive IRB approval to use the information as the community consultation in preparation for the actual trial, which currently remains in the protocol-design stage.12 Two additional studies have examined the attitudes of individuals toward the process of community consultation by conducting surveys and focus groups. One study performed a content analysis of the FDA docket in 1999, when only four studies had been approved for use of EFIC.15 Community consultation performed for one additional study has been described for only one site in a multicenter trial.16 There may be additional experiences with community consultation that are not published and therefore are not included in this analysis.

Information from these studies is presented in the following text. Additional unpublished data and expert opinion are presented afterward. This material is primarily directed at the specific questions posed by the FDA that cannot be answered by the review of the available literature.

Diaspirin Cross-linked Hemoglobin Study
This study involved the use of a blood substitute in the resuscitation of trauma patients with hemorrhagic shock.5 To fulfill the community consultation requirements, the community relations staff at the hospitals involved assisted in identifying key members of the high-volume trauma communities around the hospital. These individuals were invited to participate in a community council where they received a presentation from the researchers. Other key individuals and members of the community were invited to public meetings. To provide public disclosure, information was disseminated via flyers, in-house publications, and newspapers, and there were also radio public service announcements and a 24-hour hotline set up to facilitate feedback.

Presentations to community councils were advertised to hospital personnel and the local and regional community three weeks before four scheduled public meetings. The research team, an IRB member, a hospital public relations coordinator, and a community relations coordinator were in attendance. An overview of the study was presented and general information was distributed, followed by time for questions. As an additional activity, a talk radio program was arranged with a local station highlighting the research project.

Attendance was documented at all meetings. There were 12 individuals present at the hospital community council meetings and 83 at public meetings. Only five calls were made to the live radio program and 16 to the 24-hour hotline. Feedback from the community indicated general acknowledgment of the need for study but also general skepticism about risks, motives, and potential profit. The African American community in particular was very sensitive to the issue of “shouldering a large proportion of the research burden,” and this concern was highlighted by concurrent media coverage of President Clinton’s apology to the victims the 1932 Public Health Service study on syphilis. There were isolated
concerns regarding the loss of decision-making liberties, but this was seen as little deviation from the norm during any presentation for emergency care. Initial skepticism was believed to be reduced by frank discussion and clarification of medical terminology.

These activities required 80 person–hours, but no direct cost estimates were provided in the report and there was no discussion of IRB concerns. Only a small portion of the community actively participated, as indicated by these data. A number of important feelings surfaced. It is reasonable to assume that this was costly in terms of human resources. No measure of the adequacy of these activities was provided. This was the first research study to publish an experience related to the community consultation requirement.

**Multicenter Vest Cardiopulmonary Resuscitation Study**

This was a randomized protocol investigating the benefit of circumferential chest compression provided by a pneumatically inflated vest compared with standard manual cardiopulmonary resuscitation. It was performed on hospitalized patients who experienced cardiac arrest refractory to an initial defibrillation. The study was first attempted in 1995 with prospective informed consent from inpatients but abandoned due to low numbers of actual patients enrolled. Only 18 of 2,131 individuals approached gave consent, and 7,100 were screened for eligibility, with considerable resources expended.

The investigators then attempted to conduct the study under 21 CFR 50.24. Their initial plan for community consultation was to advertise the study in the newspaper without any plans for community input. This initial plan, therefore, did not meet the definition of community consultation and was not approved by the IRB.

The investigators revamped their proposal, offering these subsequent methods: a call-in telephone line, hospital presentations, posting large posters on hospital units, placing brochures in patient rooms, and having one-on-one nurse–patient discussions about the study. They held a single public forum with the chair of the IRB in attendance, offered free parking, and demonstrated the use of the vest device. This was then followed by time for questions and answers.

Twelve individuals called the hotline and 25 attended the public forum, with all 25 indicating “approval” of the study. The IRB granted approval of the protocol after four months but first requested a revision of patient-oriented brochures. However, no patient asked for information based on contact with the brochure. The estimated direct cost for the community consultation activities was $5,600. This protocol was ultimately performed on only four patients in four months and then abandoned due to escalating cost, despite 1,750 potentially eligible patients admitted over that period.

The community consultation activities were poorly attended and poorly utilized at a significant expense. More than 1,750 patients were admitted to the hospital during this time, and only one requested to be exempted from the study. Enrollment was slow, and the trial was terminated due to escalating costs. Notification of the study termination and results were published in a local newspaper in compliance with 21 CFR 50.24.

**Feasibility of a Proposed Method of Performing Community Consultation**

A randomized controlled trial of phenytoin versus placebo for posttraumatic seizures in children with head injury using the “deferred consent” mechanism was placed on hold in 1996 during development and discussion of the federal regulations governing research without consent. In response to the regulations, and before resumption of the trial, the investigators designed a separate study to determine the feasibility and utility of a particular method of community consultation. They conducted a survey of parents of children seen in three emergency departments for minor head injury, in an attempt to approximate the potential community from which subjects would be drawn. The investigator described a hypothetical scenario (the actual randomized trial) and asked whether parents would agree to allow their child to participate if the situation were real. They were also asked about their reasons for their responses.

A total of 227 interviews were conducted, and 61% of the parents indicated that they would give consent had the situation been real. Parents who would have agreed to give consent cited benefit to their child, benefit to future children with injury, and a contribution to medical knowledge as reasons for their consent decision. Parents who would not have consented cited fear of an adverse event, that they did not want their child to be a research subject, that they needed to consult with other family members, or that they could not decide unless they were in a real situation. Parental ethnicity (white and Hispanic) and household income (<$50,000/year) were associated with the decision to consent, but child’s age, child’s gender, parent’s age and gender, parent’s religious affiliation, level of education, language, and number of children in the family were not.

Before publication, the investigators discussed the results with selected ethicists and IRB chairpersons. Although the study results and discussion do not reflect the views of these individuals, the surrogate method of a survey of representatives of potential patients was found to be quite acceptable as a method of community consultation and was believed to be able to be performed at a low cost, on a targeted population, yielding specific and important information about this community.

**The Prehospital Treatment of Status Epilepticus Trial**

This trial compared the use of lorazepam and diazepam in the prehospital control of status epilepticus in patients older than 18 years. The study was conducted from 1994 to 1999, thus spanning the period when the EFIC regulations were being discussed and finalized. The investigators published the details of the study design and methodology distinct from the results. The study was approved under the Department of Health and Human Services regulations for waiver of informed consent (45 CFR 46). Because both drugs were approved for this indication, the risk of the study was believed to be no more than minimal and related primarily to randomization. There was no request to obtain an Investigational New Device Application at that time either by the approving IRB or after November 1996 (when 21 CFR 50.24 and 45 CFR 46 went into effect).
To target the population of potential subjects with neurologic disease or preexisting seizure disorders, the investigators posted announcements in the neurology and epilepsy clinics describing the study and included information on how to contact the investigators. The article describes this as "community consultation," but there was no evidence of the two-way communication required by the regulations. They also "targeted the community at large" by posting an announcement in an edition of the local newspaper and had one investigator provide study information to a local community representative of the Epilepsy Foundation of Northern California. These activities are consistent with public disclosure, but not with community consultation, and illustrate the confusion and misinterpretation that can occur both on the part of the investigator and the IRB.

Content Analysis of the FDA Docket
This study was an attempt to see how this aspect of the regulation was being documented and if it seemed to be effective. Because the sponsor is only required to report information about public disclosure to the FDA docket, there was no focus on obtaining information particular to community consultation. Four trials had been reported to the FDA docket at the time of this study and were analyzed. Two studies reported both their community consultation and public disclosure activities in the literature. Two additional studies operating under 21 CFR 50.24 did not publish any information related to informed consent, community consultation, or public disclosure (a monoclonal antibody trial in patients with hemorrhagic shock, and a randomized double-blind study of magnesium sulfate, diazepam, both, or neither for out-of-hospital cardiac arrest) and only published the results of the trial itself.

Information contained in the docket showed that most communications with communities were "one way" in the sense that they were directed toward getting information to the community and not back from the community. Many two-way communications that appeared in relation to these trials were not directed toward laypersons, and many involved fewer than 15 persons. Some of the issues raised by communities were the inability to refuse study participation, potential racial biases affecting study design and execution, and ambiguity regarding how the community input would be used. Investigators concluded that much could be learned from creative approaches to meet the community consultation requirements but that it is imperative to continue to monitor the suitability and appropriateness of different measures that are used in obtaining waiver of consent.

Attitudes of Emergency Department Patients and Visitors toward EFIC
This survey was conducted on a population of emergency department patients and visitors and asked about their attitudes toward EFIC. The survey obtained a high response rate and was conducted by trained research assistants using a convenience sample in the waiting room of three geographically diverse Level 1 trauma center emergency departments.

A total of 530 surveys were completed (82% response rate); 49% of respondents believed that enrolling subjects without prior consent in an emergency situation would be acceptable to them and 70% would not object to being entered. Informing and consulting the community as a substitute for patient consent in emergency research was believed to be reasonable by 45% of respondents, and most indicated that they would prefer to be informed by radio and television (42%) or by attending a community meeting (49%).

Although these data validate the preferences of community members and the methods that have already been used to perform community consultation, the study was not linked to a particular trial and the inferences that can be drawn regarding these preferences are limited. This study is one of only two to provide a broad understanding of the attitudes toward the regulations. Of interest is that the study was conducted in communities that actually had an ongoing study using EFIC—the Public Access Defibrillation (PAD) Trial—but only 5% of those surveyed were aware of this, raising further questions about the effectiveness of public disclosure in the existing trial.

PAD Trial
The PAD Trial was a prospective, multicenter, randomized clinical trial comparing two out-of-hospital resuscitation strategies (on-site layperson cardiopulmonary resuscitation, and 9-1-1 activation with and without deployment of automated external defibrillators for patients with out-of-hospital cardiac arrest). The aim of this study was to describe the IRB approval process and the number and type of community consultation and public disclosure activities associated with the trial. It was the largest-scale effort to date on a trial using EFIC.

There were 24 primary sites that conducted the trial, and all 101 IRBs involved approved the study. Overall, the investigators conducted about 12,000 activities to achieve community consultation and public disclosure, and these activities varied greatly from site to site in type and quantity. These included 1,030 meetings attended by 8,169 individuals (mean attendance was 88 per meeting); 475 press releases; distribution of 9,270 letters, brochures, newsletters, or e-mails; 231 radio, television, or print advertisements; 286 feature news stories; and 75 radio or television appearances.

A total of 1,502 comments were received by investigators, of which 96% were interpreted as "positive." The study failed to document additional costs associated with these activities, but personnel time, print, and media accounted for most of the estimated cost. The length of time to obtain IRB approval and the extent of the other activities suggest that more specific guidance on adequate community consultation activities may be useful. It also suggests that the determination of effective strategies is needed, because these large-scale and impressive efforts to conduct community consultation were accepted without any independent evaluation process. Any trial of similar scope and expense would likely use this information to design community consultation and public disclosure activities without the benefit of knowing the effectiveness and true costs associated with them.
Brain Cooling after In-hospital Pediatric Cardiac Arrest

The objectives of this study were to perform a community consultation and public disclosure activity that was specific to a trial of induced hypothermia in children who were just resuscitated from cardiac arrest and to determine whether EFIC was applicable to trials that examined interventions after in-hospital pediatric cardiac arrest.12

Investigators used focus groups, information notices, e-mails, and telephone conversations to gather data from several groups of individuals: parents of critically ill children, hospital staff, and hospital administrators. In focus groups, parents and hospital staff both acknowledged that prospective informed consent was not feasible for such a trial. Parents endorsed EFIC as long as study information was prospectively accessible and there was an opportunity to decline participation with a verbal conversation before enrollment. One hundred percent of parents and 50% of hospital staff who provided written opinions endorsed the use of EFIC for the study, while 12% of the hospital staff disapproved and 38% were neutral.

The trial remains in the protocol-planning phase, but the information from community consultation activities has been found to be acceptable to the IRB if the trial proceeds with a request to operate under EFIC.

Effectiveness of an Innovative Emergency Department Procedure for the Initial Management of Brain Trauma Compared with Standard Procedure

This trial compared an “innovative” emergency department procedure for the initial management of traumatic brain injury with a standard protocol.9 A waiver of informed consent was sought under the Department of Health and Human Services regulations (45 CFR 46). In preparation for community consultation, the IRB assigned a “community liaison” to work with the research team. This individual attended all public community presentations and administered postpresentation questionnaires. The investigators updated each subsequent presentation based on feedback from the previous meeting. These techniques were aimed toward both the broad and the more narrowly targeted communities in which the trial was taking place.

Presentations were made statewide at regularly scheduled meetings of civic organizations (broad community) and also at targeted; strategic meetings in areas where trauma frequently occurred. Presentations lasted 20–45 minutes, followed by questions. Postpresentation surveys assessed knowledge of study methodology and willingness to participate. There were five initial meetings; the IRB subsequently asked for two more targeted to a specific group.

Postpresentation survey results showed a high level of understanding of the study methodology except for the concept of random assignment to a treatment group. When asked if they wanted to be enrolled in the study if they suffered brain trauma, 93% of participants were in agreement, 95% were willing to have a family member participate in the study, and 100% were willing to have the study performed in their community. One year after its initial review, the IRB approved the study to enroll patients and requested quarterly reports of ongoing community consultation efforts in an attempt to verify continued community support. Although not part of the current regulations, this request for ongoing information may be of interest to the regulatory community and also warrants further exploration. This is the only study to mention such activity extending beyond the pretrial phase, but no information is given beyond that.

Views on Informed Consent in Emergency Situations (VOICES) Study

In association with the PAD Trial, focus group participants were recruited from residential sites in New York City and were asked about the ethical issues raised by the conduct of research without consent.14 The information obtained in this study was not collected as part of the community consultation process for the PAD Trial; rather, it was an exploration of community attitudes following the conduct of this trial. Its intent was to examine the appropriate and relevant definition of the community, as well as effective methods of communication for purposes of consultation and public disclosure related to EFIC studies.

There were 42 bilingual participants who provided wide definitions of community and had no overall consensus regarding the definition of community. The most frequently cited definitions of community were references to a common geography but also “belonging to a group” with a common interest, such as religion.

No strategy for community consultation was consistently endorsed. No particular leaders or individuals were thought to be authoritative in terms of whom the participants believed the investigators could consult with before the start of a research study, although healthcare workers and clergy were most frequently suggested. There was a tendency to trust deliberative group processes rather than individuals, for example, community boards rather than a single elected official.

No participant spontaneously suggested consulting individuals with the disease being studied or their family members, but when asked specifically about this, some thought it was essential while others continued to believe that the community should be viewed more broadly.

The only consistent predictor of views associated with the acceptability of performed research without consent was personal experiences (both good and bad) with researchers or health care professionals. These preliminary qualitative findings, based on a small sample, suggest that more research needs to be conducted to understand whom to speak with during community consultation. This may differ for each study conducted, and these responses may be uniquely related to where a trial is conducted and the composition of the focus groups providing input.

L-Arginine Trial

This trial of the use of L-arginine for treatment of reduced cerebral blood flow following traumatic brain injury used three methods of community consultation designed to target three different definitions of community.10 To date, this was the most systematic approach to community consultation and the most well designed of the studies on this topic.
Community was defined in three ways, and the investigative team developed methods to correspond to each. For population-based assessment, random digit dialing survey of county residents was used. To assess the at-risk population of those who were likely to present to the hospital conducting the study, interviews in hospital waiting and treatment areas were conducted. Finally, individuals responding to an invitation to attend a series of public meetings were thought to represent self-selected, highly interested individuals. Sampling techniques were designed to match the demographics of the study location, and the same evaluation instruments were used to assess all of the techniques.

Each of the methods was determined to be feasible for community consultation because they had a large number of attendees, but telephone surveys were deemed the most efficient and guaranteed that the desired geographic distribution was represented. The cost per respondent was estimated at $55 for the telephone survey and $63 for a community meeting, but this did not account for staff time (30 minutes per interview). The time to completion for consultation activities was two weeks for the telephone survey and nine weeks to one year for the meetings and interviews.

This is the only study with the size and diversity to answer questions about the effect of the method, framing, and demographics on the rate of agreement between respondents. Overall, 80% approved of the research, 68% agreed that the benefits justified the risks, 54% agreed that randomization was justified, and 58% agreed that waiver was justified.

There remained a substantial level of concern among participants even when the risks of the study were low. The investigators also expressed concern about lack of guidance related to these issues. Their overall conclusion was that community consultation activities are feasible but that the results depend heavily on the method of consultation.

The PolyHeme® Trial
PolyHeme® (Northfield Laboratories, Inc., Evanston, IL) is a hemoglobin-based product developed for use in acute resuscitation in the face of blood loss due to injury. Many of its properties, such as its long shelf life and no requirement for blood typing before use, make it particularly attractive for out-of-hospital or battlefield administration. A recently conducted clinical trial randomized patients to treatment with PolyHeme® or normal saline fluid infusions, starting in the field and continuing into the inpatient setting. This study has become the focus of ethical controversy for a number of reasons. Randomization continued up to 12 hours after study entry, even after the patient was admitted to the hospital, when blood would be available. The 12-hour time frame included a phase during which legally authorized representatives might become available, and some ethicists suggested that the trial could be designed to seek consent once the out-of-hospital phase using EFIC was completed. Additional concern relates to the consistencies of local IRB reviews of the protocol; some IRBs found serious concerns and disapproved it, while others approved the same protocols with no recognition or, at least, little discussion on the problematic areas. There was a delay in reporting of a number of potential adverse events that occurred in patients who received the product, and investigators were not informed of adverse events that were reported by other sites.

Although a detailed examination of the community consultation processes for the included sites has not yet been published, public concerns about the adequacy of the process at one site were brought to the attention of local county commissioners who had been asked to approve the involvement of emergency medical services in the protocol. Community consultation at the site had included four information sessions (that were reported to have been poorly attended): once at a Rotary club meeting, twice at a shopping mall, and once at a baseball game. Of note, requests to perform community consultation at two African American churches were declined.

Two relevant observations arise from these descriptions of community consultation at this single site. First, a private citizen brought forward concerns regarding the adequacy of consultation to the county commissioners, who subsequently approved the study and appear not to have addressed these concerns. In addition, because community consultation was not allowed at the African American churches, an important minority population did not weigh into the protocol, despite the fact that the population served by the study site includes many African Americans who would be potential study subjects. Both observations raise even more questions about the process of community consultation, how it is monitored, what determines its effectiveness, and what defines community.

Supplemental Information
Jason Karlawish, an expert on medical decision making in cognitively impaired individuals, has conducted focus groups with community members to better understand their attitudes toward community leaders and how trusted they are to speak for community members. His work showed that people identify with communities in different ways and that they often identify with multiple communities (J. Karlawish, personal communication, June 2006). His results indicate that people can identify community leaders that can represent their views. It is possible that consulting with local government, medical, neighborhood, and religious leaders may be a viable way to perform community consultation for EFIC. He also found that information about the research should be disseminated through media channels most accessible to the community, such as local health care providers, basic cable, radio, and free periodicals.

This work has some important implications. It suggests that these methods may be a more viable and cost-effective way to conduct community consultation.

CONCLUSIONS

Since the regulations were finalized in 1996, there have been few studies using EFIC and even fewer reports on the conduct of community consultation and public disclosure activities associated with implementing EFIC. The available small body of literature on this topic shows that the scope and breadth of these activities are wide and that the effectiveness of these activities has not been adequately evaluated. Future versions of the FDA
guidance should incorporate any available existing data on the process of community consultation and public disclosure. Community consultation activities should be mandated to appear in the FDA docket in association with a trial using EFIC, and methodologies should be made available to other investigators through clinicaltrials.gov.

In addition, the FDA should consider independently developing an assessment tool or evaluation procedure that assures the adequacy of the community consultation process. This tool should be developed by an expert panel of thought leaders and researchers that have proposed, performed, and researched the community consultation aspect of 21 CFR 50.24 and 45 CFR 46. Such a tool has great potential for facilitating the IRB approval process of studies using EFIC.

References