

**Model Operational Procedures for the Implementation and Review of NIH
Sponsored Multicenter Clinical Trials with Exception from Informed Consent
(EFIC) for Emergency Research**

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Introduction

The purpose of this document is to provide a model process and procedures that can be used as starting point for implementation of clinical trials using Exception from Informed Consent for Emergency Research (EFIC) in NIH funded multicenter clinical trials. The process and procedures described can and must be adapted to the specific needs and details of any future trials. The materials provided were developed and informed by both thorough review of the accumulated scholarship related to EFIC, and other lessons learned through practical shared experiences of prior NIH funded emergency care researchers.

This document is intended to be a useful, practical, and tested peer-to-peer tool for future investigators in this field. It is not intended to be a definitive guideline for application of the EFIC regulations, and should **NOT** be interpreted as any form of regulatory guidance. [Regulatory guidance is available from FDA](#). This document does not represent the only way to implement Exception from Informed Consent, and may not be applicable or optimal for EFIC studies that differ from those for which this document was created. This document is intended to be open access, and shared through a Creative Commons Attribution-NonCommercial (CC BY-NC) license that lets others adapt, and build upon the work non-commercially. New works must acknowledge the source materials and the NIH and be non-commercial. The derivative works do not have to be licensed on the same terms.

Background

Planned emergency research involving clinical trials in which critically ill or injured patients are unable to express a desire to consent to or decline participation are necessary for the advancement of acute life-saving medical care. United States regulations allow an exception from the requirement for informed consent (EFIC) for certain clinical trials. Prior to the passage of these regulations in 1996 (21 CFR 50.24), there was no clear regulatory provision to allow clinical trials in emergency settings where consent is impracticable. The EFIC regulations contain a number of important provisions. Most obviously, they require that it be impracticable to conduct the proposed trial by only enrolling individuals who can provide informed consent or who have a legally authorized representative (LAR). In addition, the regulations require a prospect of direct benefit for enrolled subjects, and limit the use of EFIC to life-threatening conditions for which existing therapy is unsatisfactory or unproven, and in which there is a short therapeutic window for the proposed intervention. They are also notable for requiring two forms of community engagement; community consultation prior to approval and initiation of a study; and public notification or disclosure prior to and after the study.

In the more than 20 years since passage of the EFIC regulations, investigators, IRBs, and regulators have gained substantial experience interpreting and implementing this regulatory structure. Determining precisely which studies qualify for EFIC, what constitutes an “unsatisfactory or unproven” standard of care, and what constitutes impracticability of informed consent can all be difficult. Implementation of EFIC can be especially intimidating for investigators and IRBs who lack experience with this kind of research. The recent single IRB review requirements in NIH clinical trials policy, and in the revised Common Rule, creates additional unprecedented challenges to EFIC trials and review of community engagement. Single IRB review, however, also offers an opportunity to consolidate experience with EFIC and build better, more consistent, and equitable processes.

Organization of this document

This document is organized into three model procedures or process statements. These sub-documents are examples developed for specific prior EFIC clinical trials performed in NIH funded clinical trial networks. The documents contain language and details that may be specific to a single NIH funded clinical trial network, and a sample trial of patients with traumatic brain injury, but that are illustrative of approach and method that can be used for most other types of planned emergency research with EFIC in any NIH funded infrastructure.

For each document, the body of the text (presented in black font) can be considered an example to be modified and individualized for future use. Care should be taken in cutting and pasting. Each EFIC study is unique with particular needs that should be carefully considered. More generalized commentary, explanation, and instruction is provided in blue font in wide margins notes.

The three sub-documents include the following:

A. Investigator's EFIC Implementation Plan

This is the longest part of the document. It describes the plan for a single clinical trial created by investigators and submitted to the single IRB, that describes why the trial meets the criteria for EFIC, lays out the principles that guide the investigators' approach to implementation, and proposes a specific menu for the kinds of community consultation and public disclosure activities that will be conducted. The plan also summarizes how results of those activities will be reported back to the IRB.

B. Standard Operating Procedure for Trial Applications involving Exception from Informed Consent (EFIC) to a Single/Central Institutional Review Board

This SOP describes the general workflow developed by a clinical trial network and a partnering single or central IRB. The strategy is intended to organize and streamline the many steps required in sequence to properly and efficiently review, consider, and approve (or reject) an EFIC protocol application, and subsequent enrollment site applications to the IRB. It can serve as a template for an SOP for either a trial coordinating center or an IRB.

C. Guidelines for Centralized Review of Community Consultation and Public Disclosure

The last document provides a sample of the kind of guidance that an IRB might adopt internally to help a board create a cohesive approach to EFIC reviews. It discusses elements of review, management of deliberations, and types of board actions. It is intended to provide IRB leadership and board members with a common platform from which to work, and around which board education and training might be organized.

Supplemental Material: Sample Site EFIC Activity Reports for IRB Submission

The three subdocuments and the supplemental material are meant to be complementary. They are intended to be useful and practical examples and strategies for implementation. As noted previously, they are not intended to be binding or definitive guidelines or interpretations of the EFIC regulations, and should not be considered as regulatory guidance.

A. Investigator's EFIC Implementation Plan

INTRODUCTION

The goal of this plan is to describe the implementation of the protections associated with 21 CFR 50.24, Exception from Informed Consent (EFIC) Requirements for Emergency Research in a specific clinical trial. Implementation of this plan is the first phase of conducting the proposed trial. The findings acquired from planned activities will be presented to the Central IRB (CIRB) to help the IRB assess community attitudes related to the study.

Research involving the acute care of patients with emergencies such as severe Traumatic Brain Injury (TBI) presents ethical challenges. Respecting participants and their autonomy through the informed consent process is a cornerstone of ethical research, but patients with severe TBI are comatose and unable to participate in an informed consent process. When available a legally authorized representative (LAR) may act as a surrogate decision maker for a comatose patient. The LAR can decide if the patient will participate in the research study, even though the wishes of the patient may not be known. However, for many patients with severe TBI, no LAR is readily available during the patient's resuscitation and emergency care. Excluding patients without capacity or an available LAR from TBI research does not necessarily defend patient autonomy since the patient's actual wishes are unknown. In fact, when they can be asked, patients and their representatives choose to participate more often than not. Excluding patients without capacity, however, limits the ability to ever scientifically improve care, and makes enrollment in the emergency setting impracticable. Therefore, this study will enroll participants for whom an LAR is unavailable with EFIC.

OVERVIEW

All patients meeting eligibility criteria for this trial will be obtunded or comatose and unable to give informed consent to participate. Participants will be enrolled in this trial either with the informed consent of a LAR or with exception from informed consent (EFIC) for emergency research under the conditions established at 21CFR50.24 and pursuant to 45CFR46.101(i) and the HHS Secretarial Waiver at FR Doc. 96-24968.

Upon hospital arrival of a potentially eligible subject, study teams will diligently attempt to determine the patient's identity and the availability

This "Investigator's EFIC Implementation Plan" is a sample procedure based upon a trial enrolling participants with acute severe traumatic brain injury (TBI). This is intended to be used as a model or template for trials involving patients with any qualifying emergency condition. For trials involving patients with other conditions, the elements in this example that refer to TBI must be modified as appropriate to the clinical trial for which this is being adapted. The plan also sometimes refers to specific elements of the sample trial's protocol, which should also be disregarded when adapting this procedure for a future trial.

The implementation plan is where the investigators explain their plan for conducting EFIC. It is part of the proposal reviewed by regulators and is a roadmap to educate participating sites.

The INTRODUCTION and OVERVIEW lay out the anticipated use of EFIC and informed consent in the trial.

of an LAR. If an LAR is available at any time prior to the routine emergent placement of intracranial probes for standard clinical management of severe TBI, the patient may only be enrolled with prospective informed consent from the LAR, as documented by a signed informed consent document. If an LAR is not available prior to the routine emergent placement of intracranial probes, eligible patients will be enrolled with EFIC. When enrolling with EFIC, enrollment and randomization take place immediately after probe placement. Subsequent to an EFIC enrollment, attempts will be made to notify an LAR at the earliest opportunity, and consent to continue in the study will be sought.

Enrollment with Consent

If an LAR is available prior to the routine emergent placement of intracranial probes, the patient will only be enrolled with the prospective informed consent of the LAR. Informed consent is a process involving a meaningful and compassionate exchange of information, questions, and answers between an LAR and a study team member delegated to obtain informed consent. The study team member will discuss the opportunity to participate in a balanced and fair manner and will review the informed consent document with the LAR. The informed consent document provides a record of the informed consent process. The LAR signature on the consent document indicates permission for the patient's participation and acknowledges this consent.

Enrollment with EFIC

Upon hospital arrival of a potentially eligible subject, study teams will diligently try to determine the patient's identity and the availability of an LAR. Both routine hospital and study team resources and processes should contribute to these efforts. The steps undertaken to identify the patient and find the LAR should be documented on the informed consent log case report form. If an LAR is not available prior to the routine emergent placement of intracranial probes, eligible subjects will be enrolled with EFIC. After EFIC enrollment, efforts to contact an LAR will continue. Once the LAR is available and as soon as it is feasible, the LAR will be informed of the subject's enrollment in the study. Details of the study, the potential risks and potential benefits of participating in the study will be explained to the LAR. After discussing the study with the LAR, the LAR will be given the option of allowing the subject to continue study participation, or to withdraw from the study. The LAR will be informed that the decision to continue participation in the study may be withdrawn at any time throughout the

An important element that will differ between EFIC clinical trials is whether the investigators foresee circumstances in the trial in which it may be practicable that some participants could enroll with prospective consent from the subject or LAR.

In some trials the therapeutic window of the investigational therapy may require immediate administration (such as in victims of cardiac arrest or acute seizures) such that all participants are enrolled under EFIC, even if an LAR is present. In other trials, such as the one described in this plan, there may be a narrow window in which consent from an LAR may be sought. If the clinical situation may allow prospective consent from some participants, the plan should accommodate this option.

When a trial will use both prospective consent and EFIC, the EFIC plan should provide clear and rational criteria for when prospective consent becomes impracticable and the EFIC enrollment is allowed.

course of the study. If the LAR wants to continue the subject's participation, the LAR will sign the informed consent form.

An informed consent log is used to document the continuing efforts to locate an LAR, the notification of the LAR, the consent process, and the decision of the LAR. This log will include the types of attempts made, the number and times of those attempts, and the outcome of each attempt. If the subject regains decision-making capacity, the patient will be notified of the study and will be asked if he or she wants to continue the study. If no LAR is found and the subject never regains decision-making capacity, the subject will remain enrolled under EFIC. For subjects who expire prior to identification of an LAR, consent is not obtained. If an LAR is eventually located, they must be notified of the subject's participation. In the rare case where an LAR cannot be found and the subject remains incapable of consent at 6 months, attempts to find an LAR will be discontinued, but documentation of the LAR search process until that time, and the subject's decisional capacity, will be documented.

Withdrawal from Participation

Regardless of whether a subject was initially enrolled with informed consent or EFIC, an LAR may withdraw the subject from further participation at any time and for any reason. If the subject regains consciousness and decision making capacity, subjects may also withdraw from further participation. Whenever possible, the reason for wishing to withdraw should be determined. Those wishing to just withdraw from the intervention (but not the study) should be aware that the intervention can be discontinued (i.e. request that the PbtO2 probe be removed, or that ICU staff be unblinded to PbtO2 values) without withdrawing from the trial and further data collection.

Discontinuation of the intervention itself does not constitute withdrawal from further participation in the study, so the study team needs to determine and accommodate what the participant or the LAR prefer.

After withdrawing from either the intervention or any further participation in the study, the participant's care should revert to usual care based upon patient characteristics, treating physician preference, and institutional practice. Consistent with OHRP and FDA guidance, participant data collected prior to withdrawal from the study is maintained in the study database, but no additional participant data will be collected from the participant or their medical record following withdrawal from the study.

Our experience in trials that will use both prospective consent and EFIC, is that sites should not be activated until they can enroll with EFIC. The short-cut of starting with prospective consent may undermine the rationale and the subsequent implementation of EFIC.

Ideally, the EFIC plan should include a procedure for tracking and documenting efforts made to seek an LAR. Depending on the trial, the search for an LAR may start before or after EFIC enrollment, but in any case there should be clearly documented efforts to find an LAR and notify them of the enrollment as early as possible.

REGULATORY CRITERIA FOR USE OF EFIC

The conditions under which EFIC is allowed are described in FDA regulations for trials conducted under an IND or IDE. These same conditions are specifically referenced in the secretarial waiver and must also be met when an EFIC trial is performed under the secretarial waiver rather than an IND or IDE. This trial fulfills these requirements for emergency research. In the following section. In this section, the components of the regulation are reproduced (in italics), along with an explanation of how this trial will comply with each requirement.

TBI is life-threatening and available treatments are unsatisfactory or unproven.

21 CFR 50.24(a)(1) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

TBI is a major cause of death and disability in modern industrialized societies, the scope of which is described in the study protocol. Despite 52,000 deaths from TBI annually in the US, and years of clinical investigation, there are still no proven specific treatments available. Although both ICP guided and PbtO₂ guided goal-directed therapy are used in the care of patients with severe TBI, neither is proven to be effective. Numerous systematic reviews of various unsuccessful or persistently unproven interventions are [available](#). Further clinical trials are needed. TBI has been recognized as a condition qualifying for EFIC in prior studies.

Obtaining prospective informed consent is often not feasible.

21 CFR 50.24(a)(2) Obtaining informed consent is not feasible because: (i) the subjects will not be able to give their informed consent as a result of their medical condition; (ii) the intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and (iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

Eligible subjects with severe TBI are unconscious and unable to provide informed consent due to their medical condition. The critical care strategies being studied in this trial must be initiated rapidly after hospital arrival to have their intended effect. The hypothesized benefit of reducing tissue hypoxia in this trial relies upon early detection and correction. Prior data demonstrate that brain tissue hypoxia is already present in many patients at the time that their monitoring was initiated.

In a prior trial of 882 participants with moderate to severe TBI within 4 hours of injury, an LAR was not available to provide consent within 6 hours for 52% of participants. When an LAR did not arrive within 6 hours, the time lag until an LAR did become available rapidly increased, with a median value of about 30 hours. In this previous TBI trial, the consent for continued participation after EFIC enrollment and retention rates were very high. Without EFIC, the time and number of sites required to complete the trial would be impracticable. Since TBI is accidental and unpredictable, there is no reasonable way to prospectively identify the individuals who will become eligible for participation in the research.

The REGULATORY CRITERIA FOR USE OF EFIC section explains how the trial qualifies for EFIC by explicitly addressing all criteria of the regulations point-by-point.

The italicized header summarizes the rationale for each regulatory requirement.

This plan is formatted where the complete relevant regulatory requirements are provided verbatim in the indented italicized font.

Investigator rationale for each criterion should be specific to the design of the proposed trial. Eligibility of the subjects in the trial should align with the populations described in these responses.

To the extent possible and practical, these responses should be data driven.

This example was for a trial that was determined not to be FDA regulated. Some of the responses used in this example may be insufficient to satisfy an FDA review.

Participation holds prospect of direct benefit to subjects

21 CFR 50.24(a)(3) Participation in the research holds out the prospect of direct benefit to the subjects because: (i) subjects are facing a life-threatening situation that necessitates intervention; (ii) appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and (iii) risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

Participation in sample TBI trial offers the prospect of direct benefit to subjects. Subjects may directly benefit from participation because TBI is a life-threatening condition and the PbtO2 goal directed interventions used in this study may be more effective than the ICP goal directed therapies alone. In particular, risks associated with the intervention, comparison of two goal-oriented strategies of care, are reasonable in relation to what is known about severe TBI and its treatment. The risks of intervention align with the range of risks of standard care as both strategies themselves are variations of standard care. Some participants report comfort and appreciation from the attention and follow up from the study team that is inherent to their participation.

The trial cannot be practicably carried out without exception from informed consent

21 CFR 50.24(a)(4) The clinical investigation could not practicably be carried out without the waiver.

This research could not be carried out without EFIC because treatment for TBI (including placement of probes and care driven by these measurements) needs to begin rapidly after hospital arrival. Since TBI patients are unable to consent for themselves and there often is no LAR available within the therapeutic window of the proposed intervention, we expect that approximately half of the participants in this trial will be enrolled under EFIC. In TBI, time to treatment is critical. Inability to obtain informed consent in the absence of EFIC can limit the ability to discover better treatments for this critical and life-threatening condition.

Need for rapid treatment of TBI often precludes consent from an LAR

21 CFR 50.24 (a)(5) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

The narrow therapeutic window described above, the inability of patients with TBI to communicate, and the lack of an LAR available to provide surrogate consent in more than half of potential subjects precludes the possibility of obtaining informed consent for many eligible patients in sample TBI trial. Attempts to contact LAR for notification and consent to continue participation will be tracked and summarized at continuing reviews.

The prospect of direct benefit is required to offset risk inherent to EFIC enrollment. It should not be interpreted as requiring a likelihood of direct benefit, which would be in tension with clinical equipoise.

In trials in which an LAR may provide prospective consent for some participants, investigators should explain why it is not practicable to enroll just those subjects. There is no standard threshold, but in this case it would require twice as long or twice as many sites.

These responses should provide specific information about the presumed therapeutic window of the investigational therapy. It should be understood that therapeutic windows are rarely known with confidence and rarely have discrete boundaries. However, the response provided here should be based on a study definition for the therapeutic window that can be justified and that is internally consistent with assumptions and eligibility criteria used elsewhere in the study protocol.

FDA often feels that investigators provide insufficient information to justify an investigational product's therapeutic window.

REGULATORY PROTECTIONS FOR IMPLEMENTING EFIC

The regulations for EFIC research mandate additional requirements for the implementation of this kind of clinical trial. Each of these additional protections and components of the regulation are reproduced (in italics) here, followed by an explanation of how the sample TBI trial will comply with the requirement. Further details about implementation will follow in a subsequent section.

Provision of an informed consent document

21 CFR 50.24(a)(6) The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with Sec. 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph (a)(7)(v) of this section.

A written informed consent document for this study will be reviewed and approved by the study CIRB. Subjects enrolled in this TBI trial, or their LAR, are approached for consent prior to enrollment or are informed of the subject's inclusion in the clinical investigation at the earliest possible opportunity. The study team is immediately notified of the arrival of all potential subjects. An on-call study team member quickly responds to the hospital to enroll subjects or to complete the subject enrollment under EFIC. For the latter, the subject (or LAR or family) is approached, and a notification and/or an informed consent process initiated as soon as feasible. The study team notifies the subject or LAR/family about the subject's enrollment, provides information about the study, the subject's rights, and the responsibilities of the investigators. The study team answers any questions about the study and further participation. A written informed consent document is used to reinforce the information provided in the consent discussion, and to document the decision to continue in the study or to not participate any further. A copy of this form is provided or offered to the LAR or subject and another copy is placed in the research record.

Community Consultation

21 CFR 50.24(a)(7) Additional protections of the rights and welfare of subjects will be provided, including, at least: (i) consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn

The community will be consulted prior to the initiation of research. The community will be asked to give their opinions about the research and the need for EFIC in order to complete this trial. A detailed menu of acceptable options for community consultation is included later in this plan. The site will choose from this menu and perform sufficient consultations to ensure the CIRB that community consultation has been satisfactorily completed at each site. Reporting of community consultation results will be standardized across the sample TBI trial sites.

Public Disclosure

21 CFR 50.24(a)(7) Additional protections of the rights and welfare of subjects will be provided, including, at least:(ii) Public disclosure to

This section on REGULATORY PROTECTIONS FOR IMPLEMENTING EFIC describes in general terms the plans and actions and actions that the investigators will pursue to be compliant with the regulations.

If the study were FDA regulated, an informed consent document would also be included in the IND or IDE application.

Plans and actions related to Community Consultation and Public Disclosure are described here in general terms. More detailed, granular descriptions of possible activities are provided later in the EFIC plan.

the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits; (iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results

Public disclosure is the primary element in making certain that this TBI trial is conducted in an entirely transparent manner. Methods of announcing information about the trial, and the development of advertising and other materials about the trial, will take place both locally and nationally. Public disclosure will be initiated prior to approval of the trial, may continue during enrollment, and will conclude with dissemination of study results after the trial is completed. A menu and discussion of many public disclosure methods and procedures is included later in this plan. The CIRB will approve the types and forms of public disclosure. Reporting of public disclosure efforts will be standardized. Summaries of public disclosure will be reported to the CIRB, and made publically available.

Data Monitoring Committee

21 CFR 50.24(a)(7) Additional protections of the rights and welfare of subjects will be provided, including, at least:(iv) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation;

A Data and Safety Monitoring Board (DSMB) is appointed to provide ongoing evaluation of safety data as well as the overall conduct of the trial, per institute guidelines. The members will meet with the study team prior to study commencement to discuss the protocol as well as content and format of the DSMB reports. The Data Coordinating Center will prepare requested reports at specified time intervals. Data and safety monitoring will be performed consistent with the guidance provided by the NIH notices 98-084 "Policy for data and safety monitoring" and OD-00-038 "Further guidance on data and safety monitoring for phase I and phase II trials".

Contacting Other Family

21 CFR 50.24(a)(7) Additional protections of the rights and welfare of subjects will be provided, including, at least: (v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

Whenever possible, informed consent will be used in lieu of EFIC enrollment. EFIC enrollment will also not proceed if an LAR or any family or other surrogate present either at the bedside or remotely declines participation on behalf of the potential subject. A provision of the protocol has been made to allow subjects who learn of the trial through public disclosure efforts or other means, and who, if treated in the hospital for TBI, would not want to participate, to communicate that decision to the ED without causing any delay in treatment. As part of the primary assessment of any TBI patient, ED providers already check for medical alert jewelry to ascertain emergent medical information about the patient. If the words "<Trial Name> TBI trial

A Data Monitoring Committee or DSMB is required for all EFIC trials.

Unique to the EFIC regulations is a requirement to seek and honor a refusal to participate in the trial, when practicable, from any family member. This is not restricted to an LAR. This objection may variously be anything from a fully informed refusal, to a general objection to research participation without specific knowledge of the particular trial. The distinction between LAR and other family may be moot in most states since all family are usually in the LAR hierarchy and are also legally authorized in emergency situations.

declined,” or similar alternative designation, are listed on the medical alert tag, the patient will not be enrolled in the clinical investigation. A hypoallergenic silicone bracelet may also be provided by the study team to members of the public if requested to indicate their wishes to decline study participation. Use of this enrollment exclusion will be tracked and this information will be provided to the CIRB at the time of continuing review.

Post Enrollment Notification and Consent to Continue

21 CFR 50.24(b) The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

Subjects enrolled in this TBI trial, or their LAR, are informed of the subject's inclusion in the clinical investigation at the earliest possible opportunity as detailed elsewhere. It is anticipated that the notification of subjects, or their families or LAR, will most commonly take place in the ED within hours of subject enrollment. Attempts to notify the subject or an LAR are repeated until successful. All notification attempts for a subject are logged in the subjects' case report form. Summaries of attempts are available for reporting to the CIRB.

Record Keeping

21 CFR 50.24(c) Like other IRB records, records of the determinations above must be kept for a minimum of three years after the completion of the clinical investigation. Again, like other IRB records, these are subject to inspection and copying by FDA.

Records documenting the enrollment of participants using EFIC, procedures for notification of enrollment, and informed consent forms will be kept for a minimum of three years after completion of the clinical investigation.

IND/IDE Requirement

21 CFR 50.24(d) Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under Secs. 312.30 or 812.35 of this chapter.

If a clinical trial is subject to FDA regulations and will be conducted pursuant to 21CFR50.24, then an IND or IDE specific to the EFIC trial is always required. See the [FDA guidance](#) for differences between drugs and devices. FDA guidance recommends contacting FDA for clarification regarding requirements for IDE submission for EFIC trials involving any medical device.

EFIC trials that are not FDA regulated, but are regulated under 45CFR46 are still required under the HHS Secretarial Waiver at FR Doc. 96–24968 to meet the conditions described at 21CFR50.24. However, trials that are not FDA regulated do not have an IND or IDE.

EFIC trials conducted under the HHS Secretarial Waiver at FR Doc. 96–24968 have additional restrictions excluding pregnant women and prisoners from participation.

The sponsor has notified FDA about this trial, provided the study protocol, including intent to enroll with EFIC, and has answered all questions from the Agency. After discussion, the Agency has determined that an IDE is not required for this trial. The Agency has pointed out that this finding is consistent with their latest [guidance on EFIC](#) specifically for device trials.

Communication of IRB Determination

21 CFR 50.24(e) If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (a) of this section or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRBs that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

Pursuant to the NIH single IRB policy for multicenter clinical trials, sample TBI trial will be reviewed and approved by a single CIRB. If the CIRB does not approve the trial, no subjects will be enrolled at any site, and all stakeholders will be informed. Because of a single IRB of record, there will be no opportunity for discordant IRB findings, and no other reporting of disapprovals.

An IND or IDE will almost always be required if there is any interpretation that an investigational drug or device is involved. FDA guidance clearly indicates that any EFIC study involving an FDA regulated product be evaluated by FDA for a determination as to whether an IDE or IND is needed.

The revised Common Rule also requires use of single IRBs.

COMMUNITY CONSULTATION PRINCIPLES

Implementation of community consultation in this trial is based on the applicable regulatory language, applicable FDA guidance documents (from March 2011, updated April 2013), and the investigators own empirical ethics research and experience in developing best network practices.

Goals

The regulatory intent and specific goals of community consultation are not explicit in the regulations, and have been the subject of academic disagreement. As described in the FDA guidance, the goals of community consultation include:

- To **show respect for persons** by informing the community about the study in advance;
- To inform community members about the trial in advance and provide a means for **affected communities to provide meaningful input to the IRB** before its decision to approve, require modifications to, or disapprove the study;
- To show respect for the community by allowing **representatives of the community** to identify potential community-level concerns and effects of the research; and
- To show respect for subjects' autonomy. Respect may be shown by including in community consultation activities **individuals who may have, or be at risk for, the condition under study** (and thereby obtain input from a group that is expected to be similar to the eventual study subjects).

This EFIC plan incorporates and interprets these goals into the following specific actionable elements.

To **show respect for persons**, we require CC events that include going out into the community to talk to people where they already gather, rather than simply asking them to come to us at events that we originate. Showing respect also involves CC events that specifically engage the investigators responsible for the research with the members of the community, rather than only allowing consultations that can be outsourced or delegated.

To create effective opportunities for the **affected communities to provide meaningful input to the IRB**, we train for and promote event

The COMMUNITY CONSULTATION PRINCIPLES section describe the underlying goals and principles upon which the proposed plans for community consultation are based.

Unlike the prior section, these principles are not defined in regulation or guidance. The principles laid out here, however, are general and may be applicable across EFIC trials. The text on this page, therefore, could be reused verbatim for future trials' EFIC plans, if compatible with the investigators' principles and interpretations.

formats that ensure that study teams listen as much as they talk. Simply giving a presentation about the trial and then asking if there are any questions is not effective CC. Deliberately brief descriptions of the trial, preferably with few or no slides, are followed by probing the community members for what additional information is important to them, and by soliciting the values and experiences of the community members that are most relevant to the research and to TBI. Community members are experts about themselves. How their own narratives intersect with the proposed research and the way in which it will be carried out (under EFIC) is the most useful input the community can provide to the IRB.

To show respect for the community, CC activities explicitly reach out both to individuals in the community without specific roles, and to **representatives of the community**. Representative of the community may be religious leaders, community organizers, patient or disease advocates, local political leaders, or others best equipped to identify group-level concerns.

Demonstrating respect for the autonomy of a group of **individuals who may have, or be at risk for, the condition under study** is particularly challenging in TBI research because traumatic injuries can happen to anyone. We meet this goal by asking sites to describe the breadth and depth of the communities they serve, and then asking that they complete CC activities that reflect a sufficient portion of that spectrum. In past TBI trials we have specifically sought out communities that are high risk of TBI, but that may be hard to engage in CC, such as Motorcycle or ATV Clubs and young adult males playing basketball or football. Sites have historically accessed TBI support groups to speak to TBI victims and their caretakers as well. These groups are keenly aware of possible treatments and the cost a traumatic TBI can have on one's quality of life.

It is also important to explicitly reinforce the FDA guidance by stating the goal of CC is **not** intended to represent community consent. Consent to participate in research is meaningful only as an individual decision; community support of the research does not reflect consent for all members of the entire community. Community consultation is therefore not intended to be a form of unbiased voting, deliberative democracy, or other purely quantitative activity, but rather an opportunity for open discussion and commentary. The IRB makes the final determination on study approval based on information obtained from the community consultation.

Here, with regard to the disease-specific or risk-specific community, there may need to be some trial-specific language added as shown here.

Definition of Community

For the purposes of EFIC, the definition of community includes “the community in which research will take place” and the “community from which subjects will be drawn.” In other words, the community includes the geographical area from which patients will be drawn and the group of patients with, or at risk for, the disease of interest. Communities have many subgroups that can be defined by innumerable characteristics such as race, ethnicity, religion, age, gender, wealth, education, employment, neighborhood and other factors. Community consultation should consider the heterogeneity of the community and seek diverse input. It is understood, however, that it is impracticable to reach every possible subgroup, but each site will complete activities that reflect a sufficient portion of the spectrum of their relevant communities.

Content

The content of community consultation will inform the community participants that informed consent will be obtained for any research subjects prior to enrollment whenever possible, and will not be obtained when no LAR is available. Informational materials developed for sample TBI trial CC activities are included in the appendix of this plan and are subject to IRB approval. Additional materials developed later will be submitted to the IRB for approval before being used in any CC/PD activities. Specifically, the content of all CC activities will:

- Tell the community about the most relevant aspects of the trial including its potential risks and potential benefits, and the therapeutic window (based on timing of probe placement, but generally within about 2-10 hours of injury).
- Hear the perspective of the community on the proposed research, elicit values and experiences
- Explain how individuals wishing to be excluded may indicate this preference

Types of Events

Based on our interpretation of the regulations and their proposed ethical basis, we have prepared a menu of the types of events and activities that sample TBI trial sites may use to meet their requirements for CC. Sites will prepare a site plan that lists all the events and activities that they will use to engage the community. Each site plan will:

This section of the plan emphasizes the consideration of diversity within communities. Investigators may ensure representativeness through a combination of activities, some of which are aimed at general community with diverse participants, and other diverse activities that focus specifically on key subgroups. Key subgroups that may benefit in particular from focused efforts at inclusion may be those that are historically underserved, neglected, or vulnerable. IRBs may differ in expectations, but our experience is that IRBs appreciate some focused efforts with regionally prevalent racial and ethnic minorities, the elderly, and perhaps applicable poor or rural communities.

IRBs and regulators have emphasized the importance of acknowledging historical abuses of research without consent in African American and other vulnerable communities in the context of EFIC when planning and performing consultations.

- Provide opportunities for broad community discussion
- Ensure that representatives from relevant communities participate in the consultation process
- Include more than one type of event or activity to provide for effective community consultation
- Consider multiple factors including, but not limited to, the size of the communities, the languages spoken within those communities, the heterogeneity of the population

FDA guidance on the content of community consultation events includes 24 bulleted items. Respectful and effective consultations, however, may involve allowing community members and groups to participate in driving the agenda and content.

COMMUNITY CONSULTATION MENU

A (Interactive - Direct)	B (Asynchronous - Delegated)
A presentation and discussion by an investigator visiting a meeting of an existing group (visits to existing meetings)	Telephone survey (random digit dialing)
Focus group (moderated small group session)	Web-based survey
In-person individual interviews or meetings	Social media messaging
A booth or table at community events involving interactive discussions (not just surveys)	In person solicited survey e.g., waiting room survey, booth survey without other interaction
Meetings convened by the investigators inviting the targeted audience (preferably with RSVP)	

Required mix is at least 6 total CC events or activities. Among these 6 events or activities, at least 2 events or activities must be of a type in column A, and at least 1 event or activity must be of a type in column B. The 2 events of a type in column A may be of the same type, for example, they could both be focus groups or visits to existing groups. Events should include participants representing a sufficient breadth of the diversity of both the geographic community primarily served by the enrolling sites' institution, and the community either at-risk for, or familiar with, TBI. There is no expectation that all of the subgroups of either community can be engaged. However, 6 events is just a minimum, and it is expected that enough events will be completed to reach a meaningfully broad and diverse cross section of community. Quality is just as important as quantity of activities.

Visits to existing meetings or existing groups

In this method of community consultation, members of the study team, sometimes accompanied by representatives of their participating institutional research leadership, ask to present the study and lead a discussion about the study at a regularly scheduled meeting of a relevant community group. Sometimes, the existing group may hold a special meeting for this purpose, but the study team still goes to the group (rather than asking members of the group to come to the study team).

The COMMUNITY CONSULTATION MENU section describes specific menus and descriptions of the types, numbers, and mix of events in which sites are required to engage.

The intention of the community consultation menu of activities is to provide multi-dimensional community engagement while also allowing sufficient flexibility at sites to ensure that sites can adapt the plan to the most effective outreach resources in their specific environment.

FDA stresses that there is no magic number of events required, but rather is whatever is needed to meet the goals of community consultation. This plan agrees, but surmises that these goals can never be accomplished in fewer than what is proposed.

The document here goes on to discuss potential advantages and disadvantages and practical operational suggestions for each type of community consultation activity.

Existing groups that might be consulted using this method may include, but are not limited to: disease-related support or interest groups, civic groups, neighborhood groups, service organizations, athletic groups (inclusive of athletes, coaches, and trainers at any level of competition from high school to professional), parent-teacher associations, faith-based organizations, political or governmental bodies, business groups, social clubs, retiree groups, and college fraternities or others. Examples of disease-related support groups include TBI support networks of parents of children and young adults with TBI. Examples of governmental bodies include law enforcement and fire department groups, city councils, and community boards. This approach may also include study team visits to senior centers or rehabilitation facilities. Participation in an existing meeting shows respect for community by bringing the information to the community, reduces inconvenience to the community and exposes the study to a diverse audience. Community members may be more comfortable expressing their opinions in a known setting. Investigators may have to travel, attend multiple meetings and conform to the community group's schedule. Using this method can encourage more involvement by co-investigators and other members of the study team, which can be advantageous.

Prior to and during the visit, the study team must clearly communicate that being allowed to attend the meeting does not imply any implicit approval or endorsement by the group being visited.

Best Practices:

- An investigator should be present to take and answer questions from the community.
- Presentation should be brief (i.e., 10 to 15 minutes).
- If a presentation is longer than 15 minutes, it should be interactive throughout the presentation.
- The presenter should be knowledgeable about the study and comfortable with the group.
- Allow ample time for community discussion (at least 15-30 minutes).
- Often best to ask for 30 minutes on an existing meeting agenda to allow 10 minutes to present, 15 minutes for discussion, and 5 minutes to hand-out and get back evaluation surveys. Insufficient time for solicitation of feedback greatly reduces the utility of this method.
- Probe for discussion using open-end questions. Ask participants about their experiences and what they care about.
- Ensure that the discussion includes feedback from the participants on EFIC.

Recent community consultation experiences have changed since the onset of social distancing. Restrictions on gathering create challenges for engagement. Attending community events with staffed booths are no longer possible. Visits to existing meetings are still possible, but only when such meetings have been replaced with virtual encounters. Focus groups and individual interviews and meetings, and telephone, web-based, and social-media-based activities have been less affected. Alas, light refreshments are no longer provided. This template EFIC plan remains effective, but requires innovative implementation.

- Light refreshments may be sponsored; direct monetary incentives are uncommon.
- An anonymous survey for group participants to indicate their thoughts, feelings, and opinions about the EFIC regulations and the study is typically collected at the end of the event. The survey template is available on the sample TBI trial website in the toolbox under EFIC.

Focus groups

In this approach, a trained facilitator interviews and moderates a discussion in several small groups (generally about 8 to 12 participants). This method can be conducted with or without an investigator present, but the former is favored. Unlike focus groups designed for other research purposes, these focus groups are performed as community consultations. They are an opportunity for investigators to directly listen to community members, and to show their respect by listening humbly. An investigator may often start the session by briefly presenting information about the trial or may elect to allow the facilitator to proceed, and listen and be available to clarify issues and answer questions. The facilitator runs the discussion using an explicit guide prepared by or reviewed beforehand by the investigative team. The facilitator elicits the group's views, questions, concerns and comments about the study. The interaction is generally audio-taped (and possibly videotaped) for review by the investigative team and the facilitator to allow subsequent analysis and reporting of the session. Focus groups could solicit feedback from any relevant focus of the community, including: the general public, individuals affiliated with particular organizations or subgroups, or specific patient populations.

Recruitment methods for focus group participants will depend on the targeted population. Participants may be recruited by mail or telephone, at random from volunteer banks or public data sets or from special populations (such as patients with prior brain injury or their families, advocacy group representatives or other vested interest groups).

Compared to other methods of community consultation, focus groups may allow for more in-depth discussion of the study because of their small size. They also allow for interaction not only between the facilitator and participant but between participants. For these reasons, focus groups offer a rich set of information and have often been found

Some community consultation activities, such as focus groups, may require more resources than other activities. This example EFIC plan assumes sites can be sufficiently funded to perform the activities suggested by the plan. Individual trials may have to adjust their EFIC plans and expectations to accommodate the available budgets. However, ethical and regulatory obligations are not different for trials with lower budgets.

by investigators and IRB members to be a high-quality source of information.

Best Practices:

- The meeting should be at an accessible location and time for the population included.
- The session should generally be run by a trained facilitator; sometimes it is helpful if it is someone who is also demographically concordant with the focus group participants (experience, race, ethnicity, or gender).
- Sessions should be small, generally including 8 -12 participants.
- Focus groups generally run 1 to 2 hours in length.
- Refreshments should be provided.
- Participants are generally paid for participation in focus group sessions in an amount and form appropriate to the participant population.
- An anonymous written survey for group participants to indicate their thoughts, feelings, and opinions about the study and the focus group session should be conducted at the end of the event.

Convened (invited) meeting

Sometimes called a “Town Hall Meeting”, this type of CC uses the same structure and best practices as visits to regularly scheduled meeting, but invites a target audience to a meeting convened by the study team. The potential advantage of this method is that multiple groups of attendees can be invited to the meeting, and have a chance to interact with each other and the investigator. Because the meetings are typically open to the public, there is the potential to involve everyone. The disadvantage with this method is that organizing such a meeting and attaining adequate attendance can be burdensome and difficult. To be successful, however, an intensive effort to diligently invite several potential attendees and secure their commitment to participate is needed. Merely advertising a public meeting and seeing who shows up leads to events with very few community members. Such low attendance events have been commonly held in prior EFIC trials, but are not acceptable for sample TBI trial. The use of invited meetings, therefore, is discouraged unless the site has a track record of successfully using this method in the past.

Community events - interactive or survey

In this type of event, the study team and investigator typically set up a booth or table at an existing community event and interact with individuals one at a time as they browse or stop by the booth. Events of this kind have occurred at State Fairs, Fire and Emergency Services Open Houses, Farmers Markets, Art Festivals, Music Concerts, Health Fairs, Ice Cream Socials, Disease-related Fundraising Events, Tailgates and other Sporting Events. This kind of event often allows exposure to a large number of community members. Depending on the kind of event it may allow investigators to reach a focused or very diverse group and a large number of participants. Because conversations are typically one on one, this method often allows more intimate and revealing opportunities for the investigator and members of the public to interact. Disadvantages of this approach is that most of the contacts are very brief, usually limiting the opportunity to exchange information. Also, the time commitment from the study team to staff the booth for the duration of the event may be significant, making this potentially inefficient. This type of event can be conducted in a way that is more interactive (a column A event), in which an investigator or other study team member primarily engages participants in conversations, often concluding with having the participant fill out a survey either through an interview or by completing a written tool. The event can also be conducted in a way that is primarily driven by just giving out written information about the study and asking participants to fill out a written survey (a column B event). In this case, the booth can be staffed without an investigator present, which can be more efficient for the study team.

Best Practices:

- Booths should have good signage that attracts passers-by.
- Have small treats or “swag” to attract participants and thank them for taking time to talk to you.
- Have enough staff at the booth to engage with anyone who wants to talk.
- Have enough clipboards and pens to make certain no one has to wait to complete written feedback.
- It is often effective to make this kind of event a fun social team-building exercise for the study team.

Telephone (random digit dialing) survey

Large telephone surveys can provide the most statistically representative description of community responses to questions about

the study and EFIC. This approach also has the potential to access the views of members of the community that are unlikely to attend other types of community consultation activities. This kind of survey is often outsourced to a vendor. Vendors are often costly, but because they can deliver rapid, predictable data, and consume relatively little study team time, this approach can still be efficient. Interviewers should be trained by the study team about sample TBI trial.

Telephone surveyors are trained to read information verbatim provided to them by the study team about the study and EFIC. They then ask close-ended questions and solicit open-ended comments and questions. This information is then summarized and reported back to the investigators and the CIRB. It is important that the survey and accompanying guide used by the interviewers should be carefully written and tested by the study team. Vendors can potentially perform large online surveys that are akin to these large random digit dialing surveys.

There are several limitations to this method. Telephone surveys can be intrusive and unwelcomed. Also, because they are delegated rather than conducted directly by the investigators, they do not allow investigators to demonstrate the same level of interpersonal respect for persons or communities as other methods. Questions are typically narrow and closed ended in this approach. Professional surveyors are also not generally equipped to answer clarifying questions about the trial or EFIC. To achieve a reasonable sample size, telephone surveys have to be short. The presentation of EFIC and BOOST3 is therefore necessarily very limited, so responses may not be as well informed or may be less reflective than responses solicited in more interactive methods. The extent to which this method produces systematically different responses is unknown.

Simple solicited surveys like those performed online, in waiting rooms, or at booths

Simple individual surveys, whether performed on-line or in person, can also be used to solicit community questions and views. This method can be used to reach large numbers and a wide variety of respondents. Online surveys can be linked to social media platforms or can be easily solicited by email. Respondents can also be recruited to complete surveys distributed in-person in relevant clinical settings like emergency department or clinic waiting rooms. These simple survey methods may not be as statistically representative as telephone surveys, but can be potentially provide more background information and are much less expensive. Internet and paper surveys

also allow respondents to see visual aids and diagrams not possible with telephone surveys. Waiting room surveys may allow focus on populations with particular health care or TBI experience. Online and waiting room surveys otherwise have the same limitations as telephone surveys. Careful writing and testing of surveys remains critically important. If surveys are distributed in person, surveyors need to be well trained in the study protocol and in the EFIC regulations.

Best Practices:

Whenever possible, these surveys should be conducted by members of the study team, and or delegated surveyors with medical knowledge and training in the protocol and EFIC. Medical students and residents can sometimes be recruited as surrogates for the investigative team.

Other social media

Social media offers a low cost, potentially far reaching, and potentially interactive method to exchange information with members of a community. Recent data suggest that the penetrance of social media is very high with 80% of adults in the US accessing Facebook, Youtube, Instagram, Pinterest, Snapchat, LinkedIn, Twitter, or WhatsApp daily (while only 29% read print newspapers daily). Social media may also allow messages to be directed to selected subgroups and demographics. However, investigators should still be aware that despite the high prevalence of social media overall, that use is still somewhat weighted toward younger adults, those living in suburbs, those with higher incomes, and those with more education. Also different platforms are favored by different demographics. Social media is a medium that blurs the line between one way communication (as used in public disclosure) and dialog (as used in community consultation). The former type of use is probably more common, but truly interactive social media communications are also possible. If chosen as a CC activity, the content of the presentation, the methods to allow interaction, and gaps in the available population should be clearly described.

REPORTING COMMUNITY CONSULTATION RESULTS

All community consultation activities must be reported to the CCC via the Community Consultation (CC) Form in CTMS. Here, study site personnel will data enter the aggregate data of their community consultation activities, by event. Data captured includes: information about the participants, the presentation, participant questions and

Prevailing culture, access to various platforms, and near-ubiquity of technology is rapidly changing the potential for social media in community engagement. Constant innovation and learning will likely allow this section to expand in the near future to include more suggestions and best practices that are still unclear at present.

The REPORTING COMMUNITY CONSULTATION RESULTS section describes how the results should be reported to the CIRB.

Reporting CC to the public [FDA docket](#) is not required under 21 CFR 50.24 as it is for PD, but including these CC reports with the PD submissions is a good transparent practice.

comments, and responses to closed- and open-ended survey questions. A complete list of CC Form data fields is available on the sample TBI trial website in the toolbox under CTMS. The results will be further collated to produce individual site or trial-level reports.

PUBLIC DISCLOSURE PRINCIPLES

Public disclosure is defined in guidance as the “dissemination of information about the research sufficient to allow a reasonable assumption that communities are aware of the plans for the investigation, its risks and expected benefits and the fact that the study will be conducted”. It also includes “dissemination of information after the investigation is completed so that communities and scientific researchers are aware of the study’s results”.

Goals

The regulatory intent and specific goals of public disclosure are not explicit in the regulations, and have been the subject of academic disagreement. This plan is based on the presumption that the primary goal of public disclosure is transparency.

Transparency is achieved when information about the study is broadly and publicly disseminated through multiple channels. We note that transparency has a protective effect because investigators will not propose anything that they would not be willing to announce and defend openly.

Adequacy of public disclosure and transparency is best measured by the size of the potential audience of the disclosure, rather than by knowledge or recollection of the audience. Awareness is a poor metric because the more benign and acceptable a clinical trial is, the less likely the content of the public disclosure will be internalized and recalled.

Content

The content of public disclosure materials will vary with the media used. Advertisements (whether signs, print media, broadcast, or electronic) may have limited space. These disclosures may convey short messages and how the audience can obtain more detail. Follow up examples may include ways to talk to the study team, or a link to the study website. Short messages should at a minimum emphasize:

- That a research study of patients with traumatic brain injury is being conducted locally.
- That the study will enroll patients with injuries that prevent them from participating in informed consent.
- Who to contact or where to find additional information.

Similar to the prior section on Community Consultation principles and practices, the PUBLIC DISCLOSURE PRINCIPLES section describe the underlying goals and principles upon which the proposed plans for public disclosure are based.

Again, these principles are not defined in regulation or guidance. The principles laid out here are general and may be applicable across EFIC trials. The text on this page, therefore, could be re-used verbatim for future trials’ EFIC plans, if compatible with the investigators’ principles and interpretations.

FDA guidance on the content of public disclosure includes 13 bulleted items. An example of one of these bullets is the study informed consent document. While all the listed content can be public, clearly not every piece of PD material can contain every element of content. A bus ad or 20 second public service announcement is limited. However, all items can say where to learn more.

Other forms of disclosure, such as press releases, websites, or brochures for example, allow for greater detail and should, depending on available space, also include:

- Information about TBI and how it is treated
- The purpose of the research
- Who will be included in the study
- A description of the two treatment strategies being compared
- A balanced description of the potential clinical and research risks and benefits
- Synopsis of the research protocol and study design
- Participating sites/institutions
- Description of the attempts to contact a LAR
- Information about opting out of the study

After the clinical trial is completed, further public disclosure should include:

- The findings of the trial
- Impact of what was learned on patient care
- Where to find resources for further information
- Gratitude and thanks to the study subjects, their families, and their communities.

The primary manuscript, especially in a high profile journal is an important form of post-trial public disclosure. The demographics of those enrolled should be included in the paper, and are included with public disclosure posted to the FDA docket.

PUBLIC DISCLOSURE MENU - PRE-TRIAL

A (networking)	B (paid advertising)	C (conventional outlets)
National or local study website	Newspaper advertisement (and similar print advertising)	Press release
Social media postings	Television and radio ads (broadcast advertising)	News stories, interviews (print, radio, or TV)
Mailings (including email circulars/bursts and direct paper mailings)	Outdoor advertising (placards, bus ads, billboards, etc.)	Newsletters (articles or informational ads, print or electronic)
Booth/Table Community event	Paid online advertisements (banner, block, or video ads purchased from Google, Facebook, Youtube, etc.)	Brochures, flyers, handouts, bulletin boards
		Radio or TV PSA (public service announcements)

Many different channels of public disclosure should be used. This will increase the depth and breadth of market penetration. The required mix is at least 6 total PD activities including at least 2 of a type in column A, and at least 1 of a type in column B or column C.

Distribution of activities should be cognizant of the anticipated audiences, and should include audiences representing a sufficient breadth of the diversity of both the geographic community primarily served by the enrollment site, and the community either at-risk for, or familiar with, TBI. There is no expectation that all potential audiences will be reached. It is expected that PD efforts will represent a good faith effort to provide transparency across the relevant communities.

Networking

Electronic platforms can provide a passive or interactive approach to disseminating information that has benefits and challenges. Measurement of the audience reached by these methods may be elusive. Access may be limited to those segments of the population

The PUBLIC DISCLOSURE MENU section describes specific menus and descriptions of the types, numbers, and mix of activities in which sites are required to engage.

The intention of the public disclosure menu of activities is to provide multi-dimensional community notification and transparency while also allowing sufficient flexibility at sites to ensure that sites can adapt the plan to the most effective outreach resources in their specific environment.

As noted previously, FDA stresses that there is no magic number of events required, but rather is whatever is needed to meet the goals of public disclosure.

with regular computer access, although internet access through cell phones is rapidly becoming common in all parts of society. Despite these minor concerns, electronic social media and other e-platforms are inexpensive to develop, are wide-reaching and can be relatively democratic, and can even permit continuous and anonymous input from the public. Hospitals and community based organizations often host and curate websites, social media accounts (Facebook, Twitter, etc) and listservs, that can be efficiently leveraged to disseminate a message broadly.

Paid advertising

Purchased advertising in broadcast and print media ensures dissemination of accurate materials to a wide audience.

Advertisement of the study may occur on a major news radio station serving the area surrounding the study hospitals. A 30 to 60 second sound bite should include a general description of the study, the website address, and contact information where more information can be provided if desired. Printed materials, including advertisements for publication in newspapers and magazines, brochures, and flyer, are available electronically on the sample TBI website. Advertisements should be placed in both English language and foreign language newspapers as appropriate to the local community. Printed advertisements should provide a general description of the study, the national and/or local website address, as well as site contact information.

Conventional informational outlets

Press releases leading to newspaper and periodical articles are an effective form of public dissemination. Investigator appearances on local news, radio or television call-in talk shows can accomplish both public disclosure and community consultation. In addition to traditional news outlets, it is often possible to obtain coverage in local health focused newsletters, in direct mail advertisements and educational materials sent out by health care organizations and in newsletters of TBI advocacy and support groups. A video on emergency medicine trials and EFIC research in general will be available for use in public service announcements and for dissemination to media outlets. Local community access cable stations may be accessible to investigators. Cable access channels may offer appearances on shows presenting issues of local interest or may offer to broadcast prepared materials.

Brochures and flyers may be disseminated in locations including:

- Medical sites (e.g., emergency department waiting rooms, medical clinics, dentist offices, etc.)
- Health fairs (community, employer, school, etc.)
- Support groups and other existing community groups
- Schools, universities,
- Churches and other religious affiliates
- Grocery & laundry-mat bulletin boards
- Through large employers (i.e., hospitals, universities, etc.)

Local flyers and brochures distributed should reference the trial website as an additional resource for patients, families, and healthcare providers to get information as well as ask questions about the trial.

PUBLIC DISCLOSURE ACTIVITIES - POST-TRIAL

Post-trial public disclosure activities may include any of the methods used pre-trial, especially press releases because results of trials can be especially newsworthy. Post-trial public disclosure also includes a number of more specific additional methods. Post-trial disclosure includes publication of the trial results in a major scientific journal and presentation of the results at scientific meetings. Through these publications and presentations, it is usually possible to leverage the existing public relations machinery of the journals and the meeting to amplify the message through broader media outlets as well. Another specific post-trial public disclosure method is return-of-results to the study participants and their families.

REPORTING PUBLIC DISCLOSURE ACTIVITIES

All public disclosure activities must be reported to the CCC via the sample TBI trial Public Disclosure (PD) Form in CTMS. Study site personnel will enter data on each activity including: name and type of activity, size of anticipated audience, and characteristics of the intended audience, and timing and duration when relevant. A complete list of PD Form data fields is available on the sample TBI trial website in the toolbox under CTMS. Activity data will be further collated to produce individual site or trial-level reports.

The REPORTING PUBLIC DISCLOSURE RESULTS section describes how the results should be reported to the CIRB.

Reporting PD to the public [FDA docket](#) is also an explicit obligation for trials conducted under 21 CFR 50.24. These trial level reports fulfil this requirement most effectively.

CONTACTING A LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The definition and hierarchy of LAR is determined by local state regulations.

When more than one LAR are present, the LAR highest in the local hierarchy should give consent. However, unless otherwise stated in local or state regulations, any LAR may consent if others are not promptly available.

EFIC does not obviate the need to seek an LAR to provide consent prior to enrollment if possible, and to seek patient or LAR consent to continue participation after EFIC enrollment. Potential subjects are also not enrolled under EFIC if any family contacted prior to enrollment objects to enrollment, even if they are not an LAR or are only available by telephone. Subjects enrolled in sample TBI trial, or their LAR or family, are informed of the subject's inclusion in the clinical investigation at the earliest feasible opportunity. The study team is immediately notified of the arrival of potentially eligible patients in the emergency department (ED). An on call study team member quickly responds to the ED to determine eligibility, seek an LAR for consent, and enroll the subject if consent is obtained or enroll under EFIC when appropriate. The subject (or LAR or family) is approached, and an informed consent process initiated as soon as possible.

LAR identification and tracking will typically be a shared responsibility between the onsite social workers (or equivalent) and the study team. Each site PI and team will meet with their social workers (or equivalent) before the trial initiation to inform them of the trial protocol and need for intensive LAR search. The site team should review the local protocol for an LAR search and assure that it is sufficient (multiple methods for locating LAR and multiple attempts), and if not, recommend additional steps be put in place.

Once available after an EFIC enrollment, an LAR will be informed of the patient's enrollment into the study and of the study details and potential risks and potential benefits of study participation. At that time, the LAR will be given the option to continue participation in the study, or to cease participation then or at any time throughout the course of the study. If the LAR wants to continue participation, an informed consent process is performed and an informed consent form signed by the LAR will be obtained. If an established LAR has given consent for the participant to be enrolled, other family members' objections to inclusion will not result in the participant's removal from the study. If the participant regains decision making capacity, the

There is no specific requirement for how soon after an EFIC enrollment an LAR must be sought for consent to continue. Varied urgency may be explained by the extent of ongoing invasiveness of the intervention, by the level of risk, or by how practicable it may be to contact LARs early. In general, notifying as early as possible increases transparency, but may not be appropriate in some trials, such as those of victims of cardiac arrest where most subjects die in the field and no study team is immediately activated at the time of enrollment.

participant will be asked to consent to or decline continued participation in the study. If the participant wishes to continue and an LAR has not already provided consent and signed a consent form, the participant will sign an informed consent form. If the LAR has already signed a consent form, an additional form signed by the participant is not required.

Using the Informed Consent CRF, the study team will document efforts to find an LAR or other family member or surrogate. This will include contact person (Subject, LAR, Other), number of attempts, date and time and outcome of attempts. The tracking process should continue until consent or withdrawal is obtained. The tracking process is complete once the LAR or participant has provided consent or has withdrawn. It is expected that LAR consent or withdrawal be obtained within the first 24 hours, except in rare circumstances (no LAR identified, LAR not available, participant identification is unknown, participant expires prior to consent being obtained, etc.).

For participants who expire prior to identifying an LAR or before LAR consent is obtained, consent should not be pursued further. However, once an LAR or family member is located, they should be informed of the subject's participation. The study team should document the notification conversation. If it is not possible to have this notification conversation with the LAR or family of a deceased subject in the hospital, a "family notification letter for a deceased subject" should be used to notify the LAR or other family. The template for this letter can be found in the "Toolbox" section of the sample TBI trial website. A copy of the family notification letter (with return receipt) should be kept with the study documents.

In the rare case where no LAR consent is obtained, the LAR is never available, and the participant remains incapable of consent at six months, documentation of the attempt process and condition of the participant will be recorded on the Informed Consent Log CRF. In these cases, the final outcome will be discussed and approved by trial leadership.

Tracking attempts to contact LARs is a best practice that promotes timeliness and accountability.

Even after attempts to contact an LAR or family member have ended, a note may be left in the medical record providing study team contact information in the event someone is eventually located.

DESCRIPTION OF REFUSAL OF PARTICIPATION PROCEDURES (OPT-OUT)

Individuals who learn about sample TBI trial and do not wish to participate may contact the trial investigators through the trial website, or by otherwise contacting a site study team or the CCC. At their request, those declining to participate will be provided, prior to study start, an opt-out medical alert silicone bracelet that says “sample TBI trial declined” at no expense. Members of the public may also obtain and may wear this medical alert bracelet, or any other medical alert notification with the same message and be excluded from the trial without providing their name. Wearing the provided bracelet or any other medical alert notification that says the name of the trial and the words “trial declined” is how the individual can communicate to the care team or study team, her/his wishes to opt out of the study in the event of a severe TBI. The presence of a medical alert with the statement “sample TBI trial declined” is the metric for those with prior knowledge of the study to indicate their desire to opt out, which is an enrollment eligibility exclusion.

DATA SAFETY MONITORING BOARD

An independent Data Safety Monitoring Board (DSMB) has been established and has reviewed and approved the trial protocol. The DSMB will oversee the course of the clinical trial. The DSMB will provide ongoing evaluation of safety data as well as the overall conduct of the trial, as per institute guidelines.

Although typical, opt-out mechanisms are not a regulatory requirement for EFIC trials. Whether and how best to implement opt-out is likely to vary by trial and the nature of the enrollment. Medical alert tags, bracelets, wallet cards, online or physical lists, medical record flags, and other options all have advantages and disadvantages to consider. This may include burden on the potential subject, reliability and opportunity for error, protection of privacy and confidentiality, risk of misidentification, potential for stigma, or other complications.

The value of opt-out seems to be primarily as a tool to allow those with objection to be heard and respected. Given the mathematics of populations and study enrollment in most EFIC trials, opt-out may be more about giving these individuals voice, then about preventing the very low likelihood that they might be enrolled.

Depending on the charter, a DSMB may or may not be involved in reviewing elements of EFIC. Some FDA divisions request the charter with an IND/IDE.

APPENDIX

CC Material

[Suggestions for Community Consultation Opportunities](#)

[Meeting recruitment flyer](#)

[Focus group moderator guide](#)

[CC slide set - Full](#)

[CC slide set - Reduced](#)

[Letter to community physicians](#)

[Letter to community members](#)

Survey Instruments

[Self-Administered Survey](#)

[Self-Administered Survey – Additional languages](#)

[Group Evaluation Survey](#)

[Telephone Survey](#)

PD Material

[Suggestions for Public Disclosure Opportunities](#)

Website and Video Content

[Trial-specific Video/Public Service Announcement](#) (6 seconds)

[Trial-specific Video/Public Service Announcement](#) (15 seconds)

[Emergency Research Video Scripts – Non-trial specific](#)

[Emergency Research Video Links - Non-trial specific](#)

Print copy/advertisement

[Brochure](#)

[Brochure – Additional languages](#)

[AD/Flyer/Poster](#)

[AD/Flyer/Poster – Additional languages](#)

Opt-out Material

[Opt-out bracelet request form](#)

[Opt-out bracelet mailing letter](#)

Additional EFIC Material

[Letter to notify families or LAR about EFIC enrollment in subjects who die prior to consent opportunity](#)

This APPENDIX lists the kinds of trial specific community consultation and public disclosure materials that are created and provided as central resources for all participating sites. This would be pre-approved by the CIRB at the time of protocol review, and the unmodified content of these used by sites without further approval. If sites develop additional new and valuable materials, the CCC would send these to the CIRB for review prior to their use by the site. When approved, new materials are added to the list for subsequent use by any site.

Because these materials can be dynamic, the links on this page have been disabled. The list is included here only as an example of the kinds of materials that the study could provide.

B. Standard Operating Procedure for Trial Applications involving Exception from Informed Consent (EFIC) to a Single/Central Institutional Review Board

Purpose

Our goals for this procedure are to protect the interests of human research participants to be enrolled in emergency research trials with EFIC, to respect the communities from which participants will be enrolled, to comply with applicable regulations and their intent, and to create efficiencies for both the IRB and the applicants.

Definitions

The following are operational definitions for the purposes of this procedure

- CC/PD refers to Community Consultation and Public Disclosure activities as described at 21 CFR 50.24
- CCC refers to the investigators' Clinical Coordinating Center for the trial
- IRB-IS refers to the web based IRB information system
- DCC refers to the investigators' Data Coordinating Center for the trial
- DSMB refers to the trial-specific Data Safety Monitoring Board
- EFIC refers to emergency research conducted with exception from informed consent as regulated primarily under FDA regulations 21 CFR 50.24. EFIC also refers to research conducted under 45 CFR 46.101(i) when consistent with the HHS Secretarial Waiver from October 2, 1996 -- Notice, HHS, Informed Consent Exemption for Emergency Research
- CIRB refers to the Central Institutional Review Board reviewing the application
- FDA the United States Food and Drug Administration
- IND Investigational New Drug application
- IDE Investigational Device Exemption application
- CTMS refers to a comprehensive Clinical Trial Management System

Procedures

- A. FDA approval of IND or IDE identifying the plan to conduct a trial using EFIC.

For EFIC research regulated by FDA, the sponsor will obtain approval for an IND or IDE prior to submitting an IRB application. For EFIC research not regulated by FDA, the investigators should typically provide documentation of this, such as a letter from FDA

concordant with this determination. Creation and review of an IRB application may proceed while the IND/IDE is on clinical hold if the reasons for the clinical hold do not contain concerns related to the protection of human research participants.

B. DSMB approval.

The applicants will present the study protocol and consent form to the study DSMB for comment, suggestions, and approval before submission to the ER-CIRB.

C. Protocol (Parent) application submission to ER-CIRB.

The applicant will submit an IRB protocol application that also includes an EFIC plan into IRB-IS. The EFIC plan will be submitted as “Additional Documentation”. The EFIC plan will include the following;

- a. Itemized descriptions of how the trial meets each required qualification for EFIC described at 21 CFR 50.24
- b. Menu of community consultation event types and a plan for a minimum required mix of events
- c. Menu of public disclosure activities and a plan for a minimum required mix of activities
- d. Check off list for disease-based and geographic-based communities of special interest that will be engaged
- e. Templates for materials to be used for community consultation and public disclosure

D. ER-CIRB review of protocol application.

The ER-CIRB will review the study protocol, consent form, and EFIC plan. If the ER-CIRB identifies concerns or requires modifications, the investigators will revise the application as needed. If the protocol, consent form, and EFIC plans are acceptable, the ER-CIRB will approve the protocol application. No CC/PD will be conducted until approval of the protocol application and EFIC plan.

E. Sites prepare individual CC/PD plans.

Sites use the IRB approved menus and the IRB approved required mix of events (from the protocol application) to develop lists of proposed individual CC/PD events and activities. The CCC oversees and assists sites throughout this site development process.

- a. The site plan includes a log of proposed CC/PD events and activities, including planned dates and intended communities to

The FDA “may proceed” determination is required before the study can start.

Site plans include enhanced local context information including local demographics, practice patterns, and relevant aspects of local culture. This should be similar to, but more complete, than the local context form completed for other non-EFIC trials.

be engaged. These events and activities are entered into CTMS. The ER-CIRB will also have access to these event logs in the CTMS.

- b. The site plan includes a supplemental EFIC local context form that will also be completed in the CTMS with additional information about communities served by the institution.
- c. If sites develop new materials for use in CC/PD these must be submitted to the sponsor, via the CCC. The CCC will submit any additional sponsor approved material to the ER-CIRB through IRB-IS via an amendment to the protocol application for review and approval prior to their use.
- d. The ER-CIRB will have continuous access to the site plan (the CC/PD event logs and supplemental EFIC local context form) in CTMS throughout the conduct of CC/PD.

F. Sites perform CC/PD activities and events.

- a. Sites commence the CC/PD activities and events they have listed in the log. As activities and events are completed, event forms are completed in CTMS.
- b. If activities and events are rescheduled or replaced with new events, these changes are immediately logged in CTMS. In this way, site progress may be checked by the CCC or the ER-CIRB at any time.
- c. Representatives of the CCC or the ER-CIRB may also use the log to plan their own visits to site CC/PD activities and events at their discretion.

G. Site application submission to the ER-CIRB.

Sites submit all information for their site CIRB applications in CTMS, including any revisions to the EFIC local context form. After a site has completed its CC/PD and submitted all findings and summaries to CTMS, these are reviewed by the CCC and a report of findings is prepared to include as additional documents with the site ER-CIRB application. The CCC then submits the site application to the ER-CIRB through IRB-IS. [Click for example of a site-specific CCC activities report.](#)

H. ER-CIRB review of site applications.

The ER-CIRB does an explicit review of each site application including discussion of each site-specific CC/PD report. The ER-CIRB may use a checklist to aid in the review of each site. Specifically, the IRB will check if the site's completed activities complied with the menu and requirements in the IRB approved

It is important for the CCC to oversee the site plans to ensure that sites are complying with the overall EFIC plan to maximize the opportunity for site applications to be approvable in a single review by the ER-CIRB.

Through accumulated experience across trials and across sites, the CCC is best situated to help sites benefit from shared resources and peer-to-peer learning.

An alternative strategy is to have the ER-CIRB also review each site plan prior to the site initiating CC/PD. These may help clarify expectations and decrease the risk that the IRB will have to defer a subsequent site application and ask the site for additional activities after the site approval review meeting. The trade-off is that this extra approval step for all sites doubles the number of reviews, potentially decreasing the efficiency of both the IRB and the sites and delaying study start up, even if it does reduce bounce-backs.

EFIC plan in the protocol application, if the completed activities reflect a sufficient portion of the spectrum of community described in the sites local context form, if the CC/PD performed represent sufficient engagement and notification of the communities, and if any of the findings reported indicate a need for additional follow up CC/PD. If the site application and EFIC reports are acceptable, the site may be approved by the ER-CIRB and permitted to begin enrollment. Site applications may be reviewed as rapidly as submitted or may be batched at the discretion of the ER-CIRB.

I. Reporting to the public.

Cumulative reports of CC/PD will be assembled by the CCC and reported to the FDA docket at least annually until all pre-trial CC/PD are completed. An additional report of post-trial public disclosure activities will be assembled by the CCC and to the FDA docket after the trial is completed. If the trial is not FDA regulated, the same materials will be posted on another public facing web-page.

J. Reporting to relying institutions.

Sites will be able to download their own CC/PD findings report from CTMS and may use these to report to their own relying institution if their institution requests to review these internally, but this is not required. Similarly, the ER-CIRB will provide minutes of the review of the site application to the CCC to provide to the relying site if requested. Institutions that wish to share with the CIRB any findings or additional local context beyond that already provided by the investigators are welcome to do so within the site application.

K. Protocol application close out.

At the end of the clinical trial, all sites will report all required post-trial public disclosure activities in CTMS. The CCC will prepare a cumulative report of all post trial public disclosure activities at all sites, which will be submitted to the ER-CIRB with the protocol application's close out.

Post-trial PD reported to the FDA docket must include study results and demographics of the participants.

Although not required, relying institutions may opt for varying levels of internal review by some part of their human research protection program (HRPP), that may or may not involve the IRB itself. Institutional HRPPs may wish to contribute additional local context to the CIRB beyond that already provided by the investigators. This can be provided as a letter or memo supplementing the site application, via the investigators, the sponsor, or by direct communication between the IRBs.

C. Process Guideline for Central IRB Review of Site Applications for EFIC Trials: How to Review Local Community Consultation and Public Disclosure Findings

This document is intended to provide advice to central IRB panels on potential processes they might use to guide and manage deliberations related to local context for site applications of clinical trials involving exception from informed consent (EFIC) for emergency research. The document is informed by observations of IRB deliberations of EFIC-related community consultations and public disclosure and a related stakeholder workshop conducted as part of an empirical ethics grant from the NIH Office of the Director. In addition to this qualitative research, this document is also informed by the cumulative experiences and views of the investigators. The document is meant to suggest a framework to aid in efficiency and effectiveness of the review, but is not intended to constrain IRB consideration or discussion in any way.

Review of the trial EFIC plan in the protocol application

Prior to review of site applications for a trial involving EFIC, the IRB should briefly re-cap the trial-specific EFIC plan proposed with the previously approved protocol application. This allows the panel members to re-familiarize themselves with the quantitative and qualitative expectations of sites. These expectations describe the site self-assessments and reporting of important elements of their own local context, and the number and types of community consultation and public disclosure activities to be completed. The plan also describes the underlying goals of community consultation and public disclosure as contextualized for the application. At the IRB meeting, the IRB chair or other designated reviewer or member should be assigned to present the key elements of the plan to the full board.

Community consultation / public disclosure site report format

Site applications for clinical trials involving EFIC will be accompanied by a consistently formatted report summarizing the community consultation and public disclosure activities performed by the site. The report format presents a brief narrative summary and aggregated data at the front, and then many more pages of granular listings of individual comments in the rest of the report. At the time of the first site application to be reviewed by the panel, prior to deliberation of the reports content and the site application, the IRB chair or other designated reviewer or member should briefly orient the full board to the sections and structure of the report format.

Evaluation of both the aggregate and the source data is helpful. Coding of open-ended comments as indicating 'support' or 'concern' is subjective. The ER-CIRB has noted that sites often designate neutral comments as 'concerns' in an over-abundance of cautious interpretation.

Deliberation - quantitative consideration

During the discussion and deliberation of each site application, a systematic approach to the review of local context requirements may start with quantitative aspects of the site community consultation / public disclosure report. The trial EFIC plan requires a specific number of activities in more than one category of activity types. The IRB should confirm that these requirements have been met. Site applications failing to meet these criteria may be tabled and the site queried prior to further review, or the review may continue but the site application not approved until the deficiency is addressed.

The panel may also want to consider quantitative aspects of the community consultation / public disclosure report that do not have pre-defined requirements, but may be salient. The IRB may wish to consider the number of activities performed at each site, the number of participants in each event, and the number of open-ended comments or closed-ended responses collected and reported. There are no required numerical criteria for these aspects because they are expected to differ from site to site based on the nature of the activities performed. For example, sites performing in depth focus groups may have fewer participants but more feedback, while those hosting a booth at the state fair may have far more participants but briefer contact and fewer recorded responses from each. In the absence of objective criteria, the panel members should evaluate these quantitative aspects subjectively. Panel members may consider these metrics in the context of the numbers they might expect based on the type of activities reported, or in comparison to the numbers reported at other sites. In comparing to other sites, the panel should keep in mind that there will always be a range and that all sites cannot be above average.

Deliberation – qualitative considerations

The panel then should consider qualitative aspects of the community consultation / public disclosure report. First, the panel should consider whether the activities performed by the site are appropriately aligned with, and sufficiently address, the principals and goals established for community consultation and public disclosure in the trial-specific EFIC plan. For example, is there evidence for respect for community, for two-way communication in consultations, for transparency in public disclosures? The site report should be demonstrative of how principals and goals were considered.

Consideration may be given to whether a variety of types of stakeholders participated in the site's activities. Were both geographic and disease-related communities consulted? While it is impracticable

Centralized review of EFIC applications by a single IRB offers a new opportunity to see and compare site CC/PD in ways that local IRBs do not.

The CIRB needs to be aware that sites in the same city or region are encouraged to work together on CC/PD and their applications may include duplicated events and findings. These should be clearly designated in site applications. The IRB may wish to make sure that there is sufficient engagement by both sites to meet the stated principles of CC/PD.

Comparing sites applications can be helpful to the extent that it may provide the IRB a better cumulative understanding of community attitudes that are likely similar between locales. However, the IRB should try to maintain consistent standards for *sufficient* CC/PD, and not allow having seen better and worse prior site applications to raise or lower the bar over time.

to reach all demographics in a representative manner, the panel should consider the diversity achieved in the events conducted. The panel may consider whether any parts of the community with increased stakes or special interest in the research have been adequately consulted. The diversity of community may be considered by the IRB in the context of the site's self-reported local context report, or by comparison with other sites.

Other qualitative assessments of the community consultation / public disclosure findings include consideration of the closed-ended and open-ended feedback from participants in the site's activities. While EFIC is explicitly not a community consent process, the degree of support or concern expressed in these responses can be considered in the context of similar findings from the literature and the FDA EFIC docket for previous EFIC trials, or comparing different communities. The IRB may also consider the nature of specific concerns and any of these should preclude site participation or be otherwise addressed.

Other elements of local context review

Before completing the deliberation of community consultation and public disclosure the panel should review and consider other elements of local context review. Site self-reporting of local context issues related to the community served, past relevant experiences with EFIC or emergency research at the site, local regulations or laws impacting the research, local medical practice patterns intersecting with the trial should all be considered if they may affect the protection of human subjects. Local IRB or other elements of the local institutional research administration also have the option of submitting information relating to local context as well. If submitted, such optional information should be considered and discussed at this point in the site review.

Board actions

These considerations of site applications for clinical trials involving EFIC are supplemental to the standard elements of site application review by the IRB. Approval based on deliberation of community consultation and public disclosure is incorporated into the IRB approval of the site application.

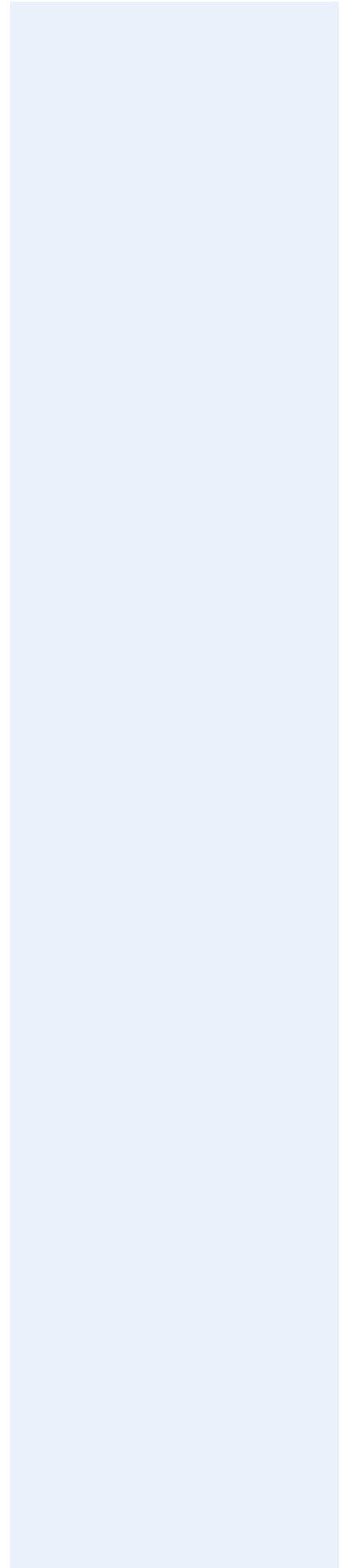
Queries, contingencies, or non-approval based on review of community consultation / public disclosure activities should be reported back to the sites as specifically as possible. Clear and explicit descriptions of any additional activities desired, or modifications of the application required, are necessary to rapidly providing the panel with any necessary corrective actions.

Qualitative evaluations may consider numerous parameters including the numbers of activities, attendees, respondents, or responses.

Diversity can be manifest through events that draw diverse participation. In this case, the narrative description of the activity should indicate whether interactions at the event involved the breadth of their diversity. Alternatively, each event may be focused on a narrow slice of the community, and diversity is obtained by the variety of these focused events. IRBs may wish to emphasize key subgroups including those that are historically underserved, neglected, or vulnerable.

Process refinement

Centralized review of clinical trials involving EFIC is new. It is expected that the IRB and the investigators at both the Clinical Coordinating Center and the sites will identify ways to improve the content and the process over time. Mechanisms for incorporating these lessons back into systematic improvements will be pursued and supported by all parties.,





What we say and do, how we do our job, how we respect, care for, treat, and talk to our research participants matters every day.



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