Review of Exception from Informed Consent applications by the Emergency Research Central Institutional Review Board

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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.

This procedure will help harmonize processes, but implementation is ultimately contingent and subordinate to any procedures and requirements of the ER-CIRB for these reviews.

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 SIREN Clinical Coordinating Center at the University of Michigan.
CIRBI	refers to the Advarra web based platform for application submissions.
DCC	refers to the SIREN Data Coordinating Center at the Medical University of South Carolina
DSMB	refers to the SIREN or 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.
ER-CIRB	refers to the Emergency Research Central Institutional Review Board run by Advarra for the SIREN Emergency Clinical Trials Network.
FDA	the United States Food and Drug Administration
IND	Investigational New Drug application
IDE	Investigational Device Exemption application
WebDCU	refers to the web-based comprehensive Clinical Trial Management System run by the SIREN DCC.

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

b. The site plan includes a supplemental EFIC local context form that will also be completed in WebDCU 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 CIRBI 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 WebDCU 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 WebDCU.

b. If activities and events are rescheduled or replaced with new events, these changes are immediately logged in WebDCU. 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 WebDCU, including any revisions to the EFIC local context form. After a site has completed its CC/PD and submitted all findings and summaries to WebDCU, 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 CIRBI. 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 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 WebDCU 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.

K. Protocol application close out.
At the end of the clinical trial, all sites will report all required post-trial public disclosure activities in WebDCU. The CCC will prepare a cumulative 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.

L. Co-enrollment in more than one EFIC trial.
Co-enrollment in two trials that are both enrolling with EFIC should be considered a special case in which extraordinary efforts at coordination between the clinical trial teams are required and the ER-CIRB should be informed. See the SIREN SOP - Competing Enrollment and Co-enrollment

M. Conduct of EFIC with more than one enrollment site in a community.
Sometimes a clinical trial to be conducted with Exception from Informed Consent for emergency research (EFIC) involves multiple enrollment sites serving a single geographic community. Under these circumstances, the SIREN network considers a coordinated and collaborative approach to community consultation and public disclosure to be the most respectful and most understandable for members of that geographic community. Sites with similar or overlapping catchments are encouraged to work together to provide consistent messaging and branding so that members of the community are aware of all the institutions in their area that are participating in the trial. Coordinated efforts are more respectful because they prevent the same community groups from being repeatedly approached for the same trial by different sites, and are less confusing because community members are not presented with similar ads and disclosures providing inconsistent information about which local sites are participating.

SIREN provides sites with the following guidance on when and how to collaborate on CC and PD within a shared community.

a. CC and PD efforts should be coordinated when sites are sufficiently co-located that they serve overlapping patient populations and communities. EFIC efforts are combined to benefit the communities served. The primary purpose of combined efforts is not for efficiency or the convenience of the site study teams, but efficiency is an anticipated secondary benefit..

b. Sites collaborating on coordinated CC and PD efforts all need to be meaningfully engaged in combined CC efforts. Investigators and study team members from all sites are expected to participate in focus groups and required in-person CC activities.

c. Sites may share all or only some CC and PD efforts with the other sites serving their communities, but all efforts should be coordinated. Sites may, for example, pursue separate events for some portion of the community that they uniquely serve, if that portion of the community was not included in the shared efforts. Sites should avoid redundant efforts to individually approach parts of the community that have already been engaged in shared efforts. All collaborations on CC and PD are tracked in WebDCU, the SIREN clinical trial management system.

d. Individual CIRB applications and approval are required for each site. Specific EFIC reports will be prepared for each site. Shared events will be included in each site's report, but will be clearly identified as shared events and will specifically designate the other site or sites with whom they collaborated. The report will describe the engagement of that site's investigator and study team in the shared events. Reports will describe the counties and zip codes reached through collaborative efforts.

e. The scope, reach, and the minimum number of activities required for communities with multiple collaborating sites are the same as for communities with single sites rather than cumulative. These are inclusive of local and EFIC Core supported efforts. Although collaborative efforts are not pursued for purposes of efficiency, efficiency in collaboration is also encouraged.

N. New site within a community previously consulted in which the trial is already enrolling.
As previously noted, whenever possible, all sites that will enroll in an EFIC trial within the same or overlapping communities should be identified ahead of time and should work collaboratively on CC and PD activities prior to the start of enrollment in that community. However, situations may arise where an additional enrollment site is proposed to be added within a community that has already been consulted, where public disclosure has already been performed, and where enrollment is already ongoing. With appropriate planning these situations are anticipated to be uncommon.

SIREN provides sites with the following guidance to address this situation.

a. Determination should be made as to whether the new site serves substantially the same community as other already enrolling sites in the trial and in which CC and PD has already been conducted. Any parts of the community served that differ from those already consulted should be identified.

b. New sites being added within shared communities are expected to perform a limited number of additional CC activities. Additional limited CC activities should generally have two goals: (1) consultation of any parts of the community served by the new site but not previously consulted or with lesser representation in the previous CC efforts, and (2) to provide the investigators and

research staff exposure to, and the opportunity to directly interact with, community members and stakeholders, such as occurs with direct or in-person activities. Ideally both of these goals can be achieved by the same 1-2 additional events, as appropriate based on a given trial's EFIC plan. Additional CC activities are generally not expected to include indirect CC activities such as redundant surveys of the community, where previously conducted efforts should still be sufficient.

c. New sites being added within shared communities are expected to perform a limited amount of additional PD activities. Additional limited PD activities should generally focus primarily on informing the community that the new site has joined the existing sites in this on-going trial within the community. This limited additional PD is anticipated to be less extensive than that initially performed but may include brief updates through the same channels used initially in the community.

d. A new individual CIRB application and approval is required for new sites being added within a previously consulted community. The EFIC report for the new site should explain the overlap with the previously consulted community and any parts of the community that differs. The report should include both the elements of the previously conducted CC and PD shared with the existing sites in the community, and the new limited CC and PD conducted by the new PI and site. Shared events will be clearly identified as shared events and will specifically designate the other site or sites providing those events. The report should indicate when the previous shared events were conducted, but there is no established interval over which any previously conducted shared CC and PD should be considered to be too old or "expired"; we have previously found attitudes and findings to vary little over time. The report should also describe the engagement of that site's investigator and study team in the new CC events.

SIREN CCC PI Sign-off: Robert Silbergleit 2025.12.16 15:40:54 -05'00'

SIREN DCC PI Sign-off: Valerie Durkalski-Mauldin Digitally signed by Valerie Durkalski-Mauldin Date: 2025.12.16 15:49:43 -05'00'

NIH Administrative PO Sign-off: JEREMY BROWN -S Digitally signed by JEREMY BROWN -S Date: 2025.12.16 11:37:04 -05'00'