



Hemostatic Medical Device Meeting For Trauma Use

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Overview

- General overview of regulatory requirements related to conducting research in the emergency setting when obtaining informed consent is not feasible (21 CFR 50.24)
- General considerations about obtaining an IND or IDE for exception from informed consent for emergency research under § 50.24

Exception From Informed Consent Requirements For Emergency Research (EFIC)

- 21 CFR 50.24
- Effective November 1, 1996
- Federal Register Notice
 - 61 FR 51528 October 2, 1996

What is required for EFIC emergency research? (21 CFR 50.24)

- A separate IND/IDE that is clearly marked as such.
- Not permitted to proceed without the prior written authorization (FDA given 30 days)
- IRB must include a licensed physician (member or consultant) who is not o/w participating in the research
- Sponsor must report IRB non-approvals to FDA and other participating IRBs
- IRB finds and documents the following.....

IRB Determinations

1. Subjects are in a life-threatening situation
2. Available treatment is unproven or unsatisfactory
3. Valid scientific evidence is necessary to determine the safety and effectiveness of the intervention

IRB Determinations

4. Obtaining IC is not feasible because:
 - Subject unable to give IC as a result of their medical condition
 - Intervention must be given before consent can be obtained from the LAR
 - No reasonable way to prospectively identify individuals likely to become eligible

IRB Determinations

5. Research holds out the prospect of direct benefit to the subject:
 - Subject facing a life-threatening situation
 - Preclinical studies support the prospect of direct benefit
 - Risks of research are reasonable in relation to what is known about the condition, the risks and benefits of standard therapy (if any), and the risks and benefits of the proposed intervention

IRB Determinations

6. Research could not practicably be carried out without the waiver
7. The protocol defines the length of the potential therapeutic window based on scientific evidence
8. PI committed to attempting to contact LAR within that window (if feasible).
 - PI must summarize these effort and provide to the IRB at continuing review

IRB Determinations

9. IRB approves ICD and procedures c/w 50.25
 - To be used when feasible
10. IRB approves procedures and information to be used when providing family members an opportunity to object to the participation

IRB Determinations

11. Assures the following additional protections:

- CC consultation with representatives of the community
- PD of the study plans and the risks and benefits prior to starting the study
- PD of the study results after the study is completed
- Establishment of an Independent Data Monitoring Committee
- PI commitment to attempting to contact the subjects family within the therapeutic window (if feasible and LAR not available).

IRB Determinations

12. Assures procedures are in place to inform, as soon as feasible, subjects, LAR, or Family member about the subjects' participation in research. Information provided should include:
- Details found in the ICD
 - Assurance subject may withdrawn at any time without penalty
 - To include a plan to inform LAR or Family of the research in the event of death

What needs to be submitted to FDA

- A separate IND/IDE
 - May reference previously submitted data
- Address the specific 50.24 requirements. For example:
 - Plans for CC and PD
 - Justification for conducting the study in subjects who cannot consent
 - A description as to why existing available treatments are unproven or unsatisfactory and why the investigational product may be better
 - A rationale for the therapeutic window
 - A description of the investigator's commitment to attempting to contact a LAR for each subject within the therapeutic window
 - A copy of the informed consent document (s)

When is an IND needed for EFIC emergency research?

- Exemptions...
 5. The investigation is conducted in compliance with the requirements for review by IRB (§ 56) and with the requirements for informed consent (§ 50).
- i.e., IND is required for all drug/biologic studies being conducted under EFIC for an investigational US

When is an IDE needed for EFIC emergency research?

- IDE is required for nearly all device study being conducted under EFIC
- If device is cleared or approved for marketing and is being used c/w labeling an IDE may not be needed
- Contact CDRH IDE@fda.hhs.gov

FDA recommendations

- Work closely with the IRB(s) and provide them all the details they need to make their determinations
- IRB review should occur after FDA review, particularly for multi-site studies
- IRBs should get a copy of FDA's written determination prior to approving the research

Guiding Principles From Belmont Report

- Respect for Person's
 - Informed consent
- Beneficence
 - Risk to benefit assessment
- Justice
 - Equitable selection of subjects

Principles continued

- State of Clinical Equipoise Required
 - current unresolved dispute in the expert clinical community as to whether the relative benefits/risks of the research intervention are equivalent, or better than, standard therapy
 - the purpose of the trial is to resolve the dispute
 - the research intervention must be promising, not a project only for pure science, future generations or the community

Resources

- FDA guidance: “Exception from Informed Consent Requirements for Emergency Research”
 - <http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm249673.pdf>
- EFIC Dockets (examples of Public Disclosures)
 - <http://www.regulations.gov/#!home>
 - Enter 1995-S-0036
- FDA Review Division



Thank You

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