AdventHealth Orlando

CHECKLIST: Waiver of Consent

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Notes:	

Can non-exempt research involving a waiver or alteration of the consent process be approved? One of the following categories must be met:

1. ☐ Planned Emergency Research[1,2]

1.1. ☐ The subjects are in a life-threatening situation

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1.2. ☐ Available treatments[3] are unproven[4] or unsatisfactory[5]

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1.3. ☐ 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

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1.4. ☐ Obtaining informed consent is NOT feasible because The following are true:
- The subjects will NOT be able to give their informed consent as a result of their medical condition
- The intervention must be administered before consent from the subjects' LARs is feasible
- There is NO reasonable way to identify prospectively the individuals likely to become eligible for participation

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1.5. ☐ Participation in the research holds out the prospect of direct benefit to the subjects because The following are true:[6]
- Subjects are facing a life-threatening situation that necessitates intervention
- 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
- Risks 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

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1.6. ☐ The research could NOT practicably be carried out without the waiver[7]

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1.7. ☐ An independent data monitoring committee will oversee the research

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1.8. ☐ Additional protections of the rights and welfare of the subjects will be provided, including:
- Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research will be conducted and from which the subjects will be drawn[8,9]
- Public disclosure to the communities in which the research will be conducted and from which the subjects will be drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits[10]
- Public disclosure of sufficient information following completion of the research to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results[11]

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1.9. ☐ The IRB has considered the concerns and objections raised during community consultation activities[12]

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1.10. ☐ The proposed research defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact an LAR for each subject within that window of time and, if feasible, to asking the LAR contacted for consent within that window rather than proceeding without consent

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1.11. ☐ The investigator will summarize efforts made to contact LARs and make this information available to the IRB at the time of continuing review

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1.12. ☐ When feasible, consent of subjects or LARs will be obtained and documented in accordance with "WORKSHEET: Criteria for Approval (HRP-400)"

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1.13. ☐ If obtaining informed consent is NOT feasible and an LAR is NOT reasonably available, the investigator has committed, if feasible, to attempt to contact within the therapeutic window the subject's family member[13] who is NOT an LAR, and asking whether he or she objects to the subject's participation in the research

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1.14. ☐ The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review

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1.15. ☐ Procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, LAR of the subject, or if such LAR is NOT reasonably available, a family member, of the subject's inclusion in the research, the details of the research and other information contained in the informed consent document

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1.16. ☐ There is a procedure to inform the subject, or if the subject remains incapacitated, LAR of the subject, or if such LAR 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

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1.17. ☐ If an LAR or family member is told about the research and the subject's condition improves, the subject is also to be informed as soon as feasible

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1.18. ☐ If a subject is entered into research with waived consent and the subject dies before an LAR or family member can be contacted, information about the research is to be provided to the subject's LAR or family member, if feasible

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1.19. ☐ A licensed physician who is a member of or consultant to the IRB and who is NOT otherwise participating in the clinical investigation concurs with the above findings

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1.20. ☐ The research does NOT involve <Prisoners>, <Fetuses>, or <Pregnant Women>, or human *in vitro* fertilization

1.21. ☐ One of the following is true:

1.21.1. ○ The research is NOT FDA-regulated

1.21.2. ○ The protocol is performed under a separate IND or IDE that clearly identifies such protocols as protocols that may include subjects who are unable to consent[14]

1.22. ☐ One of the following is true:

1.22.1. ○ The research is NOT subject to regulation by a federal department or agency other than HHS or FDA

1.22.2. ○ The applicable department or agency Secretary has issued a waiver

2. ☐ Public Benefit or Service Programs[15,16,17,18]

2.1. ☐ The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine one or more of the following:
- Public benefit or service programs
- Procedures for obtaining benefits or services under those programs
- Possible changes in or alternatives to those programs or procedures
- Possible changes in methods or levels of payment for benefits or services under those programs

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2.2. ☐ The research could NOT practicably be carried out without the requested waiver or alteration

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2.3. ☐ The research is NOT FDA-regulated

2.4. ☐ One of the following is true:

2.4.1. ○ The research has to follow the <Revised Rule>

2.4.2. ○ The research does NOT have to follow the <Revised Rule>

2.5. ☐ The research does not involve subjects who previously refused to provide broad consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

2.6. ☐ The waiver or alteration is not for broad consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

3. ☐ Impracticable Minimal Risk Research[1,19,20]

3.1. ☐ The research involves NO more than <Minimal Risk> to subjects

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3.2. ☐ The research could NOT practicably be carried out without the requested waiver or alteration

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3.3. ☐ The waiver or alteration will NOT adversely affect the rights and welfare of the subjects

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3.4. ☐ One of the following is true:

3.4.1. ○ Providing the subjects or LARs with additional pertinent information after participation is NOT appropriate

3.4.2. ○ The subjects or LARs will be provided with additional pertinent information after participation

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3.5. ☐ One of the following is true:

3.5.1. ○ The research has to follow the <Revised Rule>

3.5.2. ○ The research does NOT have to follow the <Revised Rule>

3.6. ☐ One of the following is true (2018):

3.6.1. ○ The research does NOT involve using <Identifiable Private Information> or <Identifiable Biospecimens>

3.6.2. ○ The research could NOT practicably be carried out without using <Identifiable Private Information> or <Identifiable Biospecimens>

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3.7. ☐ The research does not involve subjects who previously refused to provide broad consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

3.8. ☐ The waiver or alteration is not for broad consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

Footnotes

1. In this category, "research" means <Human Research> and "subject" means <Human Subject as Defined by HHS> or <Human Subject as Defined by FDA>.
2. 21 CFR §50.24, 45 CFR §46 Waiver of informed consent requirements in certain emergency research, Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research and FDA Guidance for Sponsors, Investigators, and Institutional Review Boards: IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects
3. FDA has interpreted the term “available therapy” to mean therapy that is specified in the approved labeling of regulated products, with only rare exceptions. For example, a treatment that is not FDA-regulated (e.g., surgery) or a drug that is not labeled for a specific use but which is nevertheless supported by compelling evidence in the medical literature may be considered an “available treatment.” The IRB should consider: What is the current “standard of care”? What treatments are available? Are available treatments (including standard of care treatments) “unproven”? If a product is not approved, but widely used, could a study be done to support approval? Are available treatments unsatisfactory, and if so, how?
4. In general, “unproven” means that there is not substantial evidence that a treatment is effective for the condition of interest. This may reflect the absence of any data or the absence of studies of acceptable quality. The term “unproven therapy” includes: Treatment that is considered “standard of care” but which has never been subjected to rigorous scientific testing or submitted to FDA for approval; Treatment for which there are or insufficient clinical or pre-clinical data to support safety or efficacy of the product; Treatment for which existing studies and data are insufficient to serve as the basis of approval even if the data were submitted to FDA; A product that is not approved for, nor does the labeling for the product contain, the specific indication under study; and an available product or therapy that is not labeled for use in a specific patient population (e.g., pediatric use).
5. Although a treatment may be “approved” and “available,” it may be unsatisfactory. “Unsatisfactory” includes situations in which the available product or therapy is effective, but there are other drawbacks to its use, such as: Safety issues (e.g., high incidence of adverse effects; exacerbation of an adverse effect for the relevant subject population); Efficacy issues, including: Poor survival rate; The treatment is only partially effective; The treatment fails to prevent a significant permanent disability; Established efficacy is low; The time for the treatment to be effective is too long (e.g., time to cessation of seizures); The treatment has limitations related to the setting in which it is needed (e.g., should be administered in the field but needs refrigeration; is not portable; may be difficult to use (must be administered intravenously, requires surgical intervention))
6. The information from animal and preclinical studies, other clinical data (e.g., use of the product in another setting or for another diagnosis or in a different study population) or other evidence should support the potential for the investigational product to provide a direct benefit to the individual subjects.
7. If the results obtained in consenting subjects could be generalized to subjects who are unable to provide consent, or the research would not be unduly delayed by restricting it to consenting subjects, then FDA would expect the research to be performed in consenting subjects.
8. The IRB must review the plans for community consultation and public disclosure before the plans are implemented. The IRB should assess whether the community consultation plans adequately provide for reaching the community from which subjects will be drawn.
9. At a minimum, the content of community consultation should include:
   - A summary of the research protocol, study design, and a description of the procedures to be followed, including the identification of any procedures which are experimental;
   - A summary of other available treatment options and what is known about their risks and benefits;
   - An estimate of how long the study will last and expected duration of the subject’s participation;
   - How potential study subjects will be identified;
   - Information about the test article’s use, including a balanced description of the risks and expected benefits and any relevant information that is known about adverse events;
   - A clear statement that informed consent will not be obtained for most research subjects;
   - The rationale as to why the study must be conducted using an exception from informed consent;
   - A copy of the informed consent document;
   - Relevant information that would be part of the informed consent process, e.g., available treatments for the condition under study; risks/potential benefits of participating in the research; possibility that FDA might inspect the subject’s records;
   - A description of the therapeutic window, during which the test article must administered, and the portion of that window that will be used to contact the subject's LAR;
   - A description of the attempts that will be made to contact the subject's LAR to obtain consent, or, if no LAR is available, a family member to provide an opportunity to object to the subject’s enrollment in the study, both before and after the test article is administered;
   - A description of the way(s) in which an individual may express his/her desire not to participate and avoid involvement as a subject in the research (e.g., opt-out mechanisms), if any will be made available;
   - Reasons why community input is important;
   - Known community perceptions/concerns associated with the study, product, and/or standard of care; and
   - Identification of individuals to contact for more information about the study.

10. FDA interprets the term “public disclosure” to mean dissemination of information (i.e., one-way communication) to the community(ies), the public, and researchers about the emergency research. Appropriate disclosure includes:
    - A summary of the research protocol, study design and a description of the procedures to be followed, including identification of any procedures which are experimental;
    - A summary of other available treatment options and what is known about their risks and benefits;
    - An estimate of how long the study will last and expected duration of the subject’s participation;
    - How potential study subjects will be identified;
    - Information about the test article’s use, including a balanced description of the risks and expected benefits and any relevant information that is known about adverse events;
    - A clear statement that informed consent will not be obtained for most research subjects;
    - The rationale as to why the study must be conducted using an exception from informed consent;
    - A copy of the informed consent document;
    - A description of the attempts that will be made to contact the LAR to obtain consent, or, if no LAR is available, a family member to provide an opportunity to object to the subject’s enrollment in the study, both before and after the test article is administered;
    - If the IRB determines that an opt-out mechanism is appropriate and feasible, a description of the way(s) in which members of the community may communicate a decision not to participate in the study (e.g., use of medical identification bracelets or wallet cards, annotation on driver’s license);
    - The sites or institutions that will be participating in the research;
    - Community perceptions/concerns with the study, product, and/or standard of care that were raised during community consultation and any associated modifications that were made to the research; and
    - Identification of individuals to contact for more information about the study.
11. The information disclosed should provide sufficient detail to allow a clear understanding of the study design and its results, both positive and negative, including:
    - Information about the primary outcome(s) of the study
    - The number and nature of adverse events associated with the test article
    - Whether the study was terminated, and the basis for that decision
12. Before making this determination the IRB should defer the research to allow the plans for community consultation and public disclosure to take place. The IRB should then determine whether meaningful feedback was secured from the community(ies) and consider the concerns and objections raised. Guidance for Institutional Review
13. “Family member” means any one of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.
14. If an IRB determines that it cannot approve FDA-regulated research because the research does not meet the above criteria or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the investigator and to the sponsor.
15. In this category, "research" means <Research as Defined by HHS> involving <Human Subjects as Defined by HHS>, and "subject" means <Human Subject as Defined by HHS>.
16. Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal website or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.
17. 45 CFR §46.116(e) (Revised Rule)
18. 45 CFR §46.116(c) (Original Rule)
19. 45 CFR §46.116(f) (Revised Rule)
20. 45 CFR §46.116(d) (Original Rule)