University of Virginia IRB for Health Sciences Research

# **Full Board Modification Scientific Reviewer Checklist**

**RB-HSR# or UVA Study Tracking       PI:**

**Reviewer:       Meeting Date:**

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| **CHANGE IN PRINCIPAL INVESTIGATOR (PI)  N/A**  **Instructions**: Complete the following questions when the Full Board Modification involves a change in the PI at UVA: | |
| The reason for the Change in PI is provided: | **YES  NO**  Reason: |
| The proposed PI’s professional and education experience is appropriate to become the PI of the study:   * The new PI’s investigator experience is provided in the IRB application? | **YES  NO**  **YES  NO**  Comments: |
| Has the NEW PI confirmed they have the adequate resources (including space, equipment, and personnel) for conducting the study? Comments:  Does the NEW PI have adequate financial resources (funding) to conduct this study?  If yes, provide details of current funding source(s): | **YES  NO**  Comments:  **YES  NO**  If yes, provide details of current funding source(s): |
| CITI and if applicable GCP training are complete:  *Note: Full Board Study Requires GCP training* | **YES  NO**  Comments: |
| Documents have been revised to include the NEW PI contact information (consent, assent, recruitment materials) | **YES  NO**  List documents revised: |

*If the modification ONLY includes PI change,* ***STOP HERE---Complete Motion p.10----***

***\*\*\*\*\*\*\*\*\*\*\*\* OTHERWISE, CONTINUE with the MEMBER REVIEW ON PAGE 2\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\****

Scientific Reviewer's Oral Presentation

*The reviewer should state the following during their oral presentation to the IRB. Planned responses need to also be written below.*

1. **Background**

**What does the modification involve in 2-3 sentences?**

**Does the modification change the target group? YES  NO**

**If YES, state if this is an appropriate group for this study.**

**If YES, add your thoughts here about the potential usefulness of the protocol to present and future patients in the newly targeted group.**

1. **Would the information included in the modification affect a subjects’ willingness to participate in the study? YES  NO** 
   * **If YES, is the study teams plan to inform current or potential subjects adequate?**

**YES  NO If No- provide required changes:**

1. **Vulnerable Populations**
   * **Does the study currently enroll or does the modification add any subjects likely to be vulnerable to coercion or undue influence? YES  NO** 
     + **If YES, Which ones?**

**YES  NO Children**

**YES  NO Pregnant Women, Fetuses,**

**YES  NO Neonates**

**YES  NO Prisoners**

**YES  NO Cognitively Impaired**

* **What safeguards are in place to protect vulnerable populations from undue influence?**
* **Are the safeguards adequate given the changes in this study? YES  NO** 
  + - **If NO, what additional safeguards should be added?**

*NEW VULNERABLE POPULATION ADDED:*

*Complete the applicable checklist from the list below if a new vulnerable population is being added with this modification.*

*STUDY CURRENTLY ENROLLS A VULNERABLE POPULATION:*

*Refer to the applicable checklist below to determine if the current protections in place continue to be appropriate. You are not required to complete the checklist.*

**Vulnerable Population Checklists**

* + - **[Children](https://research.virginia.edu/sites/vpr/files/2019-08/Vulnerable_Population_checklist_CHILDREN.doc)**
    - **[Pregnant Women, Fetuses, Neonates](https://research.virginia.edu/sites/vpr/files/2020-10/IRB%20Member%20Populations%20Requiring%20Additional%20Protections%20Checklist%20-%20Pregnant%20Women%20Fetuses%20Neonates%201-21-19.doc)**
    - [**Prisoners**](https://research.virginia.edu/sites/vpr/files/2020-11/IRB%20Member%20Populations%20Requiring%20Additional%20Protections%20Checklist%20-%20Prisoners%2011-2-20.doc)
    - [**Adults with Impaired Decision Making Capacity**](https://research.virginia.edu/sites/vpr/files/2021-05/IRB%20Member%20Populations%20Requiring%20Additional%20Protections%20Checklist%20-%20Adults%20with%20Impaired%20Decision%20Making%20Capacity_10%2009%2020.doc%22)

**4. Does the modification add Community Engaged Research? YES  NO**

*If YES, complete Appendix A.*

1. **Regulatory Issues**

Risk Assessment

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| **With the implementation of this modification what do you consider the risk level of this study to be?**  Minimal Risk  Greater than Minimal Risk  *“Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.* |

Children

Does this modification add a request for inclusion of children or change the additional protections? YES  NO *If YES, answer the following:*

Children: Part A: Parental Permission (Check one)

*See Vulnerable Population Checklist for Children for additional information.*

One parent signature required

Two parents signature required

Children: Part B: Assent of Child (Check one)

*See Vulnerable Population Checklist for Children for additional information.*

Assent not required

Assent required (*If checked, check one option below*)

Verbal Assent

Written Assent

Surrogate Consent (One adult giving consent for another adult)

**Does this modification add a request for surrogate consent**? **YES  NO**

*Things to consider:*

* *Is it clear that individuals cannot give informed consent for themselves?*
* *Where appropriate, have animal and other pre-clinical studies been conducted which suggest a potential for therapeutic benefit?*
* *Has standard wording been added to consent?*

If YES, Check one:

Surrogate consent/ Use of Legally Authorized Representative approved

Surrogate consent Use of Legally Authorized Representative NOT approved

Surrogate consent Use of Legally Authorized Representative NOT approve

Drugs/IND

Does this modification ADD research on a drug, biologic, supplement, or food additive?

**YES  NO**

If yes, do the following criteria from ***21CFR312.2***apply?

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| **YES  NO** | The investigation is intended to be reported to FDA as a well-controlled study in support of a new indication for use or intended to be used to support any other significant change in the labeling for the drug; |
| **YES  NO** | If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is intended to support a significant change in the advertising for the product; |
| **YES  NO** | The investigation does involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product. |
| *IRB Guidance* | *If any of the criteria listed above are answered Yes, an IND # from the FDA is required. Withhold approval to enroll subjects until IND # is received.* |

Devices /IDE

Does this modification ADD research on a medical device? **YES  NO**

*If YES, answer the following:*

Exempt from IDE regulations

*According to 21CFR812.2 (b)(3) a diagnostic device is exempt if it:*

1. *Is non-invasive*
2. *Does not require an invasive sampling procedure that presents significant risk*
3. *Does not by design or intention introduce energy into a subject, and*
4. *Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.*

*Additional exempt criteria may be found in 21CFR812.2(c )*

NOT Exempt from IDE regulations: *check one below:*

Significant Risk: *if SR- requires IDE from FDA.*

Non-significant Risk

*According to 21CFR812.3(m) a Significant Risk (SR) device study is one that presents a potential for serious risk to the health, safety, or welfare of a subject and*

* *is intended as an implant; or*
* *is used in supporting or sustaining human life; or*
* *is for use of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or*
* *otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.*

*Note: If the participant must undergo a procedure as part of the investigational study, e.g., a surgical procedure to implant the device, the IRB-HSR must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.*

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| Waiver of Consent (No Consent)  NA- Verbal or written consent will be obtained.  Also check NA if EFIC Study (Emergency Research and see checklist for EFIC Studies) | |
| **CRITERIA (All 3 must apply)** | **PROVIDE STUDY SPECIFIC JUSTIFICATION BELOW** |
| The research involves no more than minimal risk to the subjects **because:** |  |
| The waiver or alternations will not adversely affect the rights and welfare of the subjects because |  |
| The research could not practicably be carried out without the waiver or alteration because |  |

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| Waiver of Documentation of Consent/HIPAA Authorization (Verbal Consent)  NA- Written consent will be obtained. | |
| **CRITERIA (**CHOOSE ONE**)** | **PROVIDE STUDY SPECIFIC JUSTIFICATION BELOW** |
| That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern; | **OTHER:** |
| That the research presents no more than minimal risk of harm to subjects because and involves no procedures for which written consent is normally required outside of the research context. |  |

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| Mandatory Banking of Specimens for Future Research in a Study with a Potential for Therapeutic Benefit  NA- Study does not include Mandatory Banking. OR  NA- Study does not have a potential for therapeutic benefit. | |
|  | **PROVIDE STUDY SPECIFIC JUSTIFICATION BELOW** |
| **Mandatory Banking is justified because:** | Future research will be related to disease process under study  Other: |

1. **With the incorporation of this modification, does the protocol continue to meet the approval criteria?**

Answer questions below

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| **INSTRUCTIONS:(*45CFR46.116/21CFR56.111)***   * *If any of the questions below are answered NO, the modification cannot be approved.* * *See references in Appendix B to assist in addressing the criteria below.* * *These points must be discussed during the oral presentation at the IRB meeting.* | | | | | | | | |
| 1. **Risks to participants are minimized by using procedures which are consistent with sound research design and do not unnecessarily expose participants to risk AND**   **whenever appropriate, that are already being performed for diagnostic or treatment procedures.** | | **YES** | | **NO** | |  | | |
| Points to Consider:   * Consider physical, psychological, social, legal and economic risks. * Can less risky procedures answer the question? * Can few procedures answer the question? Are the procedures needed at all? * Are the hypothesis and objectives clear? * Are there adequate preliminary data and is there appropriate justification for the research? * Are there qualified staff and resources to conduct the research? * Are all services/specialties involved in the research represented in the personnel? * Can different exclusion criteria reduce risk? * Is there a plan in place to manage any potential conflict of interest? * Are procedures that will answer the scientific question being performed for non- research purposes?   1. If so, can the data from these procedures be used to reduce the likelihood or magnitude of harm? * Is there a clear differentiation between research and usual practice? * Does the protocol present no more than minimal risk to subjects? If yes, continuations may be expedited | | | | | | | | |
| *If NO, list conditions that must be met to meet this criterion:*   * + **Required Conditions** | | | | | | | | |
| 1. **Risks to participants are reasonable in relation to anticipated benefits to participants directly or society in knowledge that may be expected to result.** | | **YES** | | **NO** | |  | | |
| ***CHECK AT LEAST ONE***  Potential benefit to subjects  No potential benefit to subjects  Societal benefit | | | | | | | | |
| Points to Consider:   * Does the research have scientific merit? * Will the research achieve the proposed aims? * Does the investigator have access to a population that will allow recruitment of the necessary number of subjects? * Are both risks and anticipated benefits accurately identified, described, and evaluated?   Do the aims outweigh the risks and burdens to the subject? | | | | | | | | |
| *If NO, list conditions that must be met to meet this criterion:*   * + **Required Conditions** | | | | | | | | |
| 1. **Selection of subjects is equitable, taking into account the purposes of the research, the setting in which the research will be conducted, the special problems of research involving vulnerable populations, the selection criteria and the recruitment process.** | | **YES** | | **NO** | |  | | |
| Points to Consider:  *NOTE: If study is funded by Department of Defense see Appendix C for additional requirements.*  Take into account the purposes of the research and the setting in which the research will be conducted. Be particularly cognizant of the special problems of research involving vulnerable populations.   * Are burdens and benefits are distributed fairly? Will any group be unfairly burdened or unfairly benefited? * Does the nature of the research justify using the proposed subject population? * Are the methods of recruitment appropriate? * Does the amount of compensation and the proposed timing of disbursement present the potential for undue influence? * Are the inclusion and exclusion criteria justified by science, adequately defined and equitable? * If there is exclusion of women, minorities, and other vulnerable populations are they justified? * Is the setting, location and timing of recruitment appropriate for this study? * Are recruitment methods well described and appropriate for this study? | | | | | | | | |
| *If NO, list conditions that must be met to meet this criterion:*   * + **Required Conditions** | | | | | | | | |
| 1. **Informed consent will be sought from each prospective subject or the subject’s legally authorized representative, in accordance with, and to the extent required by the regulations and the applicable elements of the consent form are included.**   ***NA* Consent will not be obtained.** | | **YES** | | **NO** | |  | | |
| Points to Consider:   * Is the information given to the subject or the representative in a language that is understandable to them? If not, have procedures been implemented? (e.g. use of translators, use of consent in a language, use of short forms) * Is adequate time devoted to the consent discussion and decision-making process? * Do the circumstances of consent minimize the possibility of coercion or undue influence? * Have all issues regarding the capacity to make a decision been addressed appropriately? * Does the consent form include an exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject’s legal rights? * Are steps taken to help the subjects or representatives understand the facts? * Does the investigator adequately address how he/she will determine that a subject understands the research prior to providing consent/assent? * Are the appropriate persons being asked for consent/assent? * Is the timing, location and setting of obtaining consent acceptable? * Are payment arrangements acceptable? * Will parents and children be compensated and if so, is the amount fair and distributed appropriately between parent and child? * If study procedures are not complete or a subject withdraws is there any pro-rating of compensation? * Is the written consent form accurate, complete, and consistent with the protocol? * If written consent will be obtained does the consent form include the required elements ( see Appendix C 4a) and additional elements if applicable ( see Appendix C4b) * If consent to be waived see regulations in Appendix C4c) * If verbal consent will be obtained see regulations in Appendix C 4d) | | | | | | | | |
| *If NO, list conditions that must be met to meet this criterion:*   * + **Required Conditions** | | | | | | | | |
| 1. **Informed consent will be appropriately documented per 45CFR46.117.**   ***NA* Consent will be waived ( no consent to be obtained) .** | | **YES** | | **NO** | |  | | |
| Points to Consider:   * Will the participant or the participant’s legally authorized representative sign and date the consent document? * Will a copy of the consent document be given to the person signing the consent document? * If documentation of consent will not be required, are all criteria met per 45CFR46.117/21CFR56.109 | | | | | | | | |
| *If NO, list conditions that must be met to meet this criterion:*   * + **Required Conditions** | | | | | | | | |
| 1. **hen appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants.** | | **YES** | | **NO** | |  | | |
| Points to Consider:   * Does the protocol adequately specify:   + Who will monitor the data?   + What data will be monitored?   + How frequently will data be monitored?   + What analysis will be performed on the data?   + What decision rules (e.g., stopping rules) will be considered? * Is there appropriate monitoring of the subject during and after the research (e.g. safety tests, stopping rules, follow up visits etc.)? * Is there a plan to promptly detect unexpected harms or an increase in frequency or severity of harms? * Is there an adequate plan to stop the protocol if benefits are proven to outweigh harms or harms are proven to outweigh benefits? | | | | | | | | |
| * + If NO, list conditions that must be met to meet this criterion:   **Required Conditions** | | | | | | | |
| **7A. When appropriate, there are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data.** | **YES** | | **NO** | | **N/A** | | |
| Points to Consider:  *For Resources see Appendix B 7A*  *Privacy refers to persons and their interest in controlling access of others to themselves. How the potential subject is identified*   * Where consent is negotiated * Consideration of the time and place where subjects are recruited or given information about the study * Should a parent be present for the discussion of the study with a young child vs an adolescent?   *Confidentiality refers to maintenance of the Researcher’s agreement with the participant about how the participant’s identifiable private information will be handled, managed, and disseminated. Some of the info needed to review this criterion may be found in the Data Security Plan*   * How data will be secured * Who will have access to data * When will data be discarded and how? * Are there adequate provisions to assure the privacy of the subject? * Does the investigator accurately disclose how their data will be protected? * Are confidentiality procedures being made to subjects? If so, are the protocol procedures sufficient to meet their promises? | | | | | | | |
| *If NO, list conditions that must be met to meet this criterion:*   * + **Required Conditions** | | | | | | | |
| 7B. When some or all the participants are likely to be vulnerable to coercion or undue influence, such as **children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons,** additional safeguards are included in the study to protect the rights and welfare of these participants. | **YES** | | **NO** | | **N/A** | |
| Points to Consider: *For Resources see Appendix B 7B*  **For all vulnerable populations included in this study (may or may not have a separate checklist noted above) consider the following:**   * Is inclusion of the vulnerable population warranted? * Is the research of importance to this vulnerable population? * Can the research question be answered by using a non- vulnerable population? * Are additional measures needed to protect these subjects in terms of the recruitment process, payment, informed consent process, where the research occurs, how information is managed and protected and who conducts study procedures? * Is consent monitoring required or the presence of a subject advocate or witness during the consent procedure?   + *May be warranted if:*  1. High risk studies; 2. Studies that involve particularly complicated procedures or interventions; 3. Studies involving highly vulnerable populations (e.g., ICU patients, children who are wards); 4. Studies involving study staff with minimal experience in administering consent to potential study participants; or 5. Other situations when the IRB has concerns that consent process may not be/is not being conducted appropriately (e.g., prior investigator non-compliance, etc.).  * IRB’s should not overprotect vulnerable populations so that they are excluded from participating in beneficial research, or so that important research information is never gathered in a way that applies to them. | | | | | | |
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| * + If NO, list conditions that must be met to meet this criterion:   **Required Conditions** | | | | | | |

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| **List any suggestions:**  *Suggestions are items that do not affect the ability of the study to meet the approval criteria and are not required but may improve the protocol/ consent.* |
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**Motion:**

**Approve modification**

**Approvable with Conditions**

*PI will need to submit one copy revised protocol and two copies of revised consent. Consents will be provided after all conditions submitted and accepted. Examples of items which are considered minor: grammatical, spelling errors, template issues, providing investigator specific wording to insert.*

**Deferred**

*PI will need to re-submit the protocol and consent at future IRB-HSR Meeting.*

*PI may be asked to attend future meeting to answer questions.*

*Examples of items that may require a deferral:*

* *the investigator has not answered all the questions in the protocol*
* *investigator has not provided adequate background information including previous animal/ human data,*
* *procedures to be done are unclear- making it impossible to determine risk level.*

**Disapproved**

*The investigator may attend a future IRB-HSR meeting to defend the modification if he/she wishes to pursue the modification.*

**By entering my name below, I confirm I had no conflicts with this protocol.**

**(Scientific Reviewer) Date**

Appendix A: Community Engaged Research Review Checklist

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| Was the community appropriately involved or consulted in defining the need for the proposed research (i.e., getting the community’s agreement to conduct the research)? | YES NO |
| Was the community appropriately involved or consulted in generating the study research plan? | YES NO |
| Do the research procedures, including recruitment strategies and consent processes be ensure sensitivity and appropriateness to various communities (e.g., literacy issues, language barriers, cultural sensitivities, etc.)? | YES NO |
| Will the community be appropriately involved in the conduct of the proposed research? | YES NO |
| Will the community members who participate in the implementation of the research be appropriately trained and supervised? | YES NO |
| Have “power” relationships between investigators and community members on the research team, and in subject recruitment strategies been considered to minimize coercion and undue influence? | YES NO |
| Will the boundaries between multiple roles (e.g., investigator, counselor, peer) be maintained appropriately, i.e., what happens when the investigator/research staff is the friend, peer, service provider, doctor, nurse, social worker, educator, funder, etc.) | YES NO |
| Will the research outcomes be disseminated appropriately to the community? | YES NO |
| If there is a signed partnership agreement or memorandum of understanding between the University of Virginia investigator and community partners that describes how they will work together? | NO  YES NA |

**Appendix B: Approval Criteria References**

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| **1. Risks to subjects are minimized (i) by using procedures which are consistent with sound research design and do not unnecessarily expose subjects to risk, and (ii)whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.**  Regulations and Guidance:   * DHHS: 45 CFR 46.111(a)(1), 45 CFR 46.111(a)(2), 45 CFR 46.111(a)(6) * FDA: 21 CFR 56.111(a)(1), 21 CFR 56.111(a)(2), 21CFR 56.111(a)(6); * Guidance for IRBs, Clinical Investigators, and Sponsors: IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed * DoD: Instruction 3216.02 6.b. * ICH-GCP: 2.2, 2.3, 3.13,4.2.1, 4.2.2, 4.2.3 * [AAHRPP Tip Sheet 1](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_1_Criteria_for_Approval_of_Research.PDF) * [AAHRPP Tip Sheet 20](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_20_Sufficient_Information_to_Determine_Whether_the_Criteria_for_Approval_are_Met.PDF) |

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| **2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.**  Regulations and Guidance:   * DHHS: 45 CFR 46.111(a)(1), 45 CFR 46.111(a)(2), 45 CFR 46.111(a)(6) * FDA: 21 CFR 56.111(a)(1), 21 CFR 56.111(a)(2), 21CFR 56.111(a)(6); * Guidance for IRBs, Clinical Investigators, and Sponsors: IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed * DoD: Instruction 3216.02 6.b. * ICH-GCP: 2.2, 2.3, 3.13,4.2.1, 4.2.2, 4.2.3 * [AAHRPP Tip Sheet 1](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_1_Criteria_for_Approval_of_Research.PDF) * [AAHRPP Tip Sheet 20](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_20_Sufficient_Information_to_Determine_Whether_the_Criteria_for_Approval_are_Met.PDF) |

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| **3. Selection of subjects’ is equitable, taking into account the purposes of the research, the setting in which the research will be conducted, the special problems of research involving vulnerable populations, the selection criteria and the recruitment process.**  Regulations and Guidance   * DHHS: 45 CFR 17.92, 45 CFR 46.111(a)(3), 45 CFR 46.116; OHRP Guidance on Written Institutional Review Board (IRB) Procedures * FDA: 21 CFR 56.111(a)(3), 21 CFR 50.20, 21 CFR 56.111(a)(3); FDA Information Sheets: Frequently Asked Questions: Informed Consent Document Content, Frequently Asked Questions: IRB Organization, A Guide to Informed Consent, Recruiting Study Subjects, Payment to Research Subjects * DoD: Instruction 3216.02 11; Dual Compensation Act, 24 U.S.C 301; DoD 3216.2, para. 4.4.4; SECNAVINST 3900.39D, para. 6a(6) * ICH-GCP: 3.1.8 * [AAHRPP Tip Sheet 1](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_1_Criteria_for_Approval_of_Research.PDF) * [AAHRPP Tip Sheet 20](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_20_Sufficient_Information_to_Determine_Whether_the_Criteria_for_Approval_are_Met.PDF) |

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| **4. Informed consent will be sought from each prospective subject or the subject’s legally authorized representative.**  **Regulations and Guidance**   * DHHS: 45 CFR 46.109(b), 45 CFR 46.109I, 45CFR 46.111(a)(4), 45 CFR 46.116, 45 CFR 46.117; * OHRP Guidance on Exculpatory Language in Informed Consent; * OHRP Guidance on Obtaining and Documenting Informed Consent of Subjects Who Do Not Speak English * FDA: 21 CFR 50.20, 21 CFR 56.109(b), 21 CFR 56.109(f), 21 CFR 56.111(a)(4), 21 CFR 50.25(a),21 CFR 50.25(b), 21 CFR 50.27(a), 21 CFR50.27(b), 21 CFR 56.111(a)(5); * FDA Information Sheets: A Guide to Informed Consent, Frequently Asked Questions: Informed Consent Document Content, Recruiting Study Subjects, IRB Procedures; FDA Information Sheets: Frequently Asked Questions: Informed Consent Process, Data Retention When Subjects Withdraw from FDA- Regulated Clinical Trials * DoD: Instruction 3216.2, para. 5.3.4; SECNAVINST 3900.39D, para. 6a(5) * ICH-GCP: 2.9, 3.1.5, 3.1.9, 4.3.4, 4.8.1-4.8.9, * 4.8.11 * [AAHRPP Tip Sheet 19.](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_19_State_and_Local_Law.PDF) * [AAHRPP Tip Sheet 20.](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_20_Sufficient_Information_to_Determine_Whether_the_Criteria_for_Approval_are_Met.PDF) |

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| **4a. The basic elements of the consent form per are included.**  Regulations and Guidance   * DHHS 45CFR46.116(a), .45CFR46.116(a)(5). * FDA...21CFR50.25(a), .21CFR50.25(a)(5)   Basic Elements  (1)Research: purpose, duration, procedures  (2)Risks/ Discomforts  (3)Benefits  (4)Alternatives  (5)Confidentiality  (6)Compensation for Injury  (7)Whom to contact  (8)Right to refuse, or withdraw without penalty |

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| **4b**. **The additional elements of the consent form are included when appropriate.**  Regulations and Guidance  DHHS45CFR46.116(b)  FDA 21CFR50.25(b)  Additional Elements   * + Unforeseeable Risks   + Termination Language   + Costs   + Consequences of withdrawing   + New Findings   + The approximate number of subjects involved in the study   + Compensation |

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| **4c. If consent/HIPAA authorization to be waived the following criteria are met**  Regulations and Guidance   * DHHS: 45 CFR 46.116I, 45 CFR 46.116(d),45CFR46.117I   + OHRP Guidance on Informed Consent-Legally Effective and Prospectively Obtained * FDA: 21 CFR 56.109I(1), 21 CFR 56.109(d) * HIPAA: 45CFR164.512(i)(2) * DoD: Instruction 3216.02 9. (2.1.1); 10 USC 980(a,b) * [AAHRPP Tip Sheet 1.](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_1_Criteria_for_Approval_of_Research.PDF) * [AAHRPP Tip Sheet 20.](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_20_Sufficient_Information_to_Determine_Whether_the_Criteria_for_Approval_are_Met.PDF)   Waiver of Consent/Parental Permission- DHHS Criteria:  *Must meet the criteria below if no consent to be obtained unless study is regulated by the Department of Defense.*  **DHHS: 45 CFR 46.116**  (d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:   1. The research involves no more than minimal risk to the subjects; 2. The waiver or alterations will not adversely affect the rights and welfare of the subjects; 3. The research could not practicably be carried out without the waiver or alteration; and 4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.   Waiver of Consent/Parental Permission- Department of Defense Criteria:  *Must meet the criteria below if no consent to be obtained and study is regulated by the Department of Defense.*  **DoD: Instruction 3216.02 9. (2.1.1); 10 USC 980(a,b)**  (d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the  elements of informed consent set forth in this section, or waive the requirements to obtain informed  consent provided the IRB finds and documents that:  (1) The research involves no more than minimal risk to the subjects;  (2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;  (3) The research could not practicably be carried out without the waiver or alteration; and  (4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.  Waiver of HIPAA Authorization Criteria:  *Must meet the criteria below if no HIPAA Authorization to be obtained and study involves collection of identifiable health information.*  **HIPAA 45CFR164.512(i)(2)**  (ii) Waiver criteria A statement that the IRB or privacy board has determined that the alteration or waiver, in whole or in part, of authorization satisfies the following criteria:   1. The use or disclosure of protected health information involves no more than minimal risk to the privacy of individuals, based in, at least, the presence of the following elements; 2. An adequate plan to protect the identifiers from improper use and disclosure; 3. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and 4. Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted by this subpart. 5. The research could not practicably be conducted without the waiver or alteration and 6. The research could not practicably be conducted without access to and use of the protected health information.   Waiver of Consent/Parental Permission: FDA Criteria  *Must meet the criteria below if no consent to be obtained on an individual subject basis and study is regulated by the FDA (requires and IND or IDE).* 21CFR50.23 (FDA)  * + - 1. The obtaining of informed consent shall be deemed feasible unless, before use of the test article (except as provided in paragraph (b) of this section), both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:  1. The human subject is confronted by a life-threatening situation necessitating the use of the test article. 2. Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from the subject. 3. Time is not sufficient to obtain consent from the subject’s legal representative. 4. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject. 5. If immediate use of the test article is, in the investigator’s opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent determination required in paragraph (a) of this section in advance of using the test article, the determinations of the clinical investigator shall be made and within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. 6. The documentation required in paragraph (a) or (b) of this section shall be submitted to the IRB within 5 working days after the use of the test article.   **OR**  *Must meet the criteria below if the study is regulated by the FDA (requires and IND or IDE) and if more than 1 subject will need to be enrolled with no consent. (e.g. EFIC study)*  **21CFR50.24 (FDA)**  (a) The IRB responsible for the review, approval, and continuing approve that investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:  (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.  (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.  (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 pre clinical 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.  (4) The clinical investigation could not practicably be carried out without the waiver.  (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.  (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.  (7) Additional protections of the rights and welfare of the 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;  (ii) Public disclosure to 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;  (iv) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and  (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.  (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.  I The IRB determinations required by paragraph (a) of this section and the documentation required by paragraph I of this section are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with Sec. 56.115(b) of this chapter.  (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 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. |

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| **4d. Waiver of Documentation of Consent** (e.g. verbal consent ) FDA Regulations:***The criteria below must be met if requesting “verbal consent” and study is regulated by the FDA (has an IND/IDE).*** The IRB may, for some or all subjects, waive the requirement that the subject, or the subject’s legally authorized representative, sign a written consent form if it finds:   * That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context  OR  * Find that the requirements in 21CFR50.24 for an exception from informed consent for emergency research are met.   **DoD Regulations*:*** ***The criteria below must be met if requesting “verbal consent”,*** **32CFR219.117I**  An IRB may waive the requirement for the investigator to obtain a signed consent form for some or  all subjects if it finds either:  (1)That the only record linking the subject and the research would be the consent document and the  principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be  asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern;  **OR**  (2) That the research presents no more than minimal risk of harm to subjects and involves no procedures  for which written consent is normally required outside of the research context. In cases in which the  documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.  **HIPAA 45CFR164.512(i)(2)**  (ii) Waiver criteria A statement that the IRB or privacy board has determined that the alteration or waiver, in whole or in part, of authorization satisfies the following criteria:   1. The use or disclosure of protected health information involves no more than minimal risk to the privacy of individuals, based in, at least, the presence of the following elements; 2. An adequate plan to protect the identifiers from improper use and disclosure; 3. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and 4. Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted by this subpart. 5. The research could not practicably be conducted without the waiver or alteration and 6. The research could not practicably be conducted without access to and use of the protected health information. |

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| 5. **Informed consent will be appropriately documented in accordance with and to the extent required.**  **NA-Consent will not be obtained.**  **Regulations and Guidance**   * DHHS: 45 CFR 46.109(b), 45 CFR 46.109(e), 45CFR 46.111(a)(4), 45 CFR 46.116, 45 CFR 46.117; * OHRP Guidance on Exculpatory Language in Informed Consent; * OHRP Guidance on Obtaining and Documenting Informed Consent of Subjects Who Do Not Speak English * FDA: 21 CFR 50.20, 21 CFR 56.109(b), 21 CFR 56.109(f), 21 CFR 56.111(a)(4), 21 CFR 50.25(a),21 CFR 50.25(b), 21 CFR 50.27(a), 21 CFR50.27(b), 21 CFR 56.111(a)(5); * FDA Information Sheets: A Guide to Informed Consent, Frequently Asked Questions: Informed Consent Document Content, Recruiting Study Subjects, IRB Procedures; FDA Information Sheets: Frequently Asked Questions: Informed Consent Process, Data Retention When Subjects Withdraw from FDA- Regulated Clinical Trials * DoD: Instruction 3216.2, para. 5.3.4; SECNAVINST 3900.39D, para. 6a(5) * ICH-GCP: 2.9, 3.1.5, 3.1.9, 4.3.4, 4.8.1-4.8.9, * 4.8.11 * [AAHRPP Tip Sheet 19.](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_19_State_and_Local_Law.PDF) * [AAHRPP Tip Sheet 20.](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_20_Sufficient_Information_to_Determine_Whether_the_Criteria_for_Approval_are_Met.PDF) |

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| **6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.**  Regulations and Guidance   * DHHS: 45 CFR 46.111(a)(6) * FDA: 21 CFR 56.111(a)(6) * DoD: Instruction 3216.02 8; SECNAVINST 3900.39D, para. 6c * ICH-GCP: 5.1.6 * [AAHRPP Tip Sheet 1](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_1_Criteria_for_Approval_of_Research.PDF) * AAHRPP Tip Sheet 6. * [AAHRPP Tip Sheet 20](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_20_Sufficient_Information_to_Determine_Whether_the_Criteria_for_Approval_are_Met.PDF) |

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| **7a.When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.**  Regulations and Guidance   * DHHS: 45 CFR 46.111(a)(7) * FDA: 21 CFR 56.111(a)(7) * ICH-GCP: 2.11 * AAHRPP Tip Sheet 1. * [AAHRPP Tip Sheet 4.](https://admin.share.aahrpp.org/Website%20Documents/Tip_Sheet_4_Evaluating_the_Maintenance_of_Confidentiality_of_Data_in_Proposed_Research.PDF) * AAHRPP Tip Sheet 5. * AAHRPP Tip Sheet 20. |

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| **7b.** When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as **children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, students, employees, paroles, terminally ill etc.** additional safeguards continue to be included in the study to protect the rights and welfare of these subjects.  Points to Consider:  **For all vulnerable populations included in this study ( may or may not have a separate checklist noted above) consider the following:**   * Is inclusion of the vulnerable population warranted? * Is the research of importance to this vulnerable population? * Can the research question be answered by using a non- vulnerable population? * Are additional measures needed to protect these subjects in terms of the recruitment process, payment, informed consent process, where the research occurs, how information is managed and protected and who conducts study procedures? * Is consent monitoring required or the presence of a subject advocate or witness during the consent procedure?   + *May be warranted if:*  1. High risk studies; 2. Studies that involve particularly complicated procedures or interventions; 3. Studies involving highly vulnerable populations (e.g., ICU patients, children who are wards); 4. Studies involving study staff with minimal experience in administering consent to potential study participants; or 5. Other situations when the IRB has concerns that consent process may not be/is not being conducted appropriately (e.g., prior investigator non-compliance, etc.).  * IRB’s should not overprotect vulnerable populations so that they are excluded from participating in beneficial research, or so that important research information is never gathered in a way that applies to them. |