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## Framework for Analyzing the Ethics of a Human Subjects Research Study (for IRB Members)<sup>1</sup>

- I. **FACTS:** Review the facts – who, what, why, where, when, and how.
- II. **IDENTIFY ETHICAL/MORAL CONCERNS:** What moral issues or challenges are raised by the proposal?
- III. **ETHICAL PRINCIPLES ASSOCIATED WITH MORAL ISSUES/CHALLENGES:** Separate out each moral issue or challenge you have identified and consider the ethical principle which will assist you in its analysis.
  - a. **Beneficence**
    - i. **Scientific Validity:** The background and rationale, aims, hypothesis, and methodology to achieve the scientific objectives must be sound because it is not ethical to involve a participant in a study which cannot yield an answer. Is the science sound? The sample size justified? The statistical methodology likely to yield a result? *45 CFR 46.111(a)(1)(i); 21 CFR 56.116(a)(1)(i).*
    - ii. **Professional competence and financial support:** It is not ethical to involve participants in a study which cannot be completed as planned. The study must have trained leadership and staff who can successfully execute the research plan, and the financial support to complete the study. *45 CFR 46.107(a); 21 CFR 56.107(a); (Drug Study) 21 CFR 312.53(a); (Device) 21 CFR 812.43(a)*
      1. **Professional Responsibility and Data Integrity :**
        - a. **Accountability and Transparency:** Data are not reliable if they are not objective, protected, and subject to good management.
        - b. **Organizational structure of the research collaborators and team:** Need clarity as to who is responsible for which aspects of the study. PI oversight of the study is essential.
        - c. **Monitoring:** verification that study proceeds as approved.
    - iii. **Social value/essentiality:** The value of the answer to the scientific question posed by the study must be worth the risk, inconvenience, and resources committed to it. That value may be direct to the participant, to the community from which the participants come,

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<sup>1</sup> Adaptation of Nancy Kass, Holly Taylor, Joseph Ali, and Anant Bhan's "Framework for Analyzing a Case"



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and/or to the body of scientific knowledge about the topic. *45 CFR 46.111(a)(2); 21 CFR 56.111(a)(2)*

- iv. Precaution and risk minimization: The study procedures and the management of the data/specimens collected must adhere to practices which protect the participants against unnecessary risk. Risk minimization includes, but is not limited to, anticipating protections to personal privacy, data confidentiality, and future specimen use, as well as eliminating redundant procedures which pose physical risk to participants, and providing extra protections to vulnerable participants. *45 CFR 46.111(a)(1), (6), (7), 46.111(b); 21 CFR 56.111(a)(1), (6), (7), 56.111(b)*
1. Privacy: *45 CFR 46.111(a)(7); 21 CFR 56.111(a)(7)*
    - a. Physical privacy: A person's expectation of personal privacy in spatial terms varies from place to place, and from community to community. Consider what protections are needed to protect unnecessary intrusion into a person's personal space.
    - b. Mental/Emotional privacy: A research activity may expose personal aspects of an individual's health, personal behavioral choices, or consequences of other personal decisions. The risks of these exposures must be minimized.
  2. Data Safety Monitoring: To verify that anticipated risks remain within expected bounds and to ensure that unanticipated benefits or harms are detected early; stopping rules should be specified, if appropriate. *45 CFR 46.111(a)(6); 21 CFR 56.111(a)(6)*
  3. Data Confidentiality: Requires data security protections to prevent unintended disclosure of personal information. These protections include process for training study personnel, data coding, storage, management, access, and transfer. Certificates of Confidentiality may also be needed to protect highly sensitive data which, if released could cause harm to participants. *45 CFR 46.111(a)(7); 21 CFR 56.111(a)(7)*
- v. Risk-Benefit ratio: The balance of the potential risk to the participant and to the participant's community against the potential benefit must be AT LEAST *reasonable*. The potential value of the research, as analyzed in iv, above, must be feasible under the study design and worth exposing participants to the risk, even if minimized under v, above. *45 CFR 46.111(a)(2); 21 CFR 56.111(a)(2)*
- vi. Compensation for research-related injury or access to clinical care: It isn't ethical to subject a research participant to medical injury without considering access to care in the event of that – or other – research related injury. In resource poor areas, the research



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enterprise tends to have more capacity to provide care than is available locally. As part of the informed consent process, participants be told what will happen if they are hurt. *45 CFR 46.116(a)(6); 21 CFR 50.25(a)(6)*

- vii. Post-trial access to study interventions proven beneficial (most likely to occur in drug/device studies).

b. Justice

- i. Fair selection of study population: Why this group? It's important to evaluate whether the selection of this group will lead to an answer to the research question, but also to consider whether the selection either unfairly excludes other populations, or unfairly exploits this one. *45 CFR 46.111(a)(3); 21 CFR 56.111(a)(3)*
  - 1. If the selection is fair, then one must ask whether this population is vulnerable and whether it requires additional protections.
  - 2. Determination of exploitation involves an analysis of the burdens and benefits of research borne/enjoyed by the selected population.
  - 3. "Fair" also requires inquiry into the relevance of the study objective to the community from which participants will be drawn.

c. Respect for Persons/Study Communities

- i. Definition of "human subject": This concept is evolving to expand beyond the individual to include the community from which the individual participant comes. Risks and benefits, informed consent, communication of results and other research related analyses should consider both the individual and the community. *45 CFR 46.102(f); 21 CFR 50.3(g)*
- ii. Informed Consent: *45 CFR 46.116 (general requirements), 46.117 (documentation); 21 CFR 50.20-21 CFR 50.27 (general requirements, exceptions, emergency research, elements required, documentation)*
  - 1. Community Engagement: The involvement of a community is part of the overall "presentation" of a study and consideration about whether or not it is "appropriate" to a locale. Sometimes the participation of the REC/IRB's non-affiliated (community) member in the discussion is adequate, but particularly for international studies, more is required.
  - 2. Comprehension: Each individual and community should have the opportunity to understand what the study involves prior to deciding whether or not to participate.



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The information should be presented in the language, and at a level, that the individual may comprehend. There should be enough time for the participant to ask questions, and when appropriate, consult family or community members.

3. Voluntariness: The decision to participate should be made free of undue influence or coercion.
- iii. Dissemination of results: The results achieved under the activity must be disseminated; otherwise the value projected in a. iii, above, will not be achieved. Those results, whether positive, negative, or uncertain, contribute to the advancement of knowledge about the research topic, and may also advance knowledge about the conduct of research itself. The kind of dissemination appropriate to the particular activity should consider the value of the information to the participants and the participants' community, and how participants may access the information. *45 CFR 46.102(d)*
- iv. Local capacity building: Collaborative and non-exploitive partnerships among investigators, and negotiated and equitable ownership of research findings, help improve the ability of the local community to become peers in research. This objective goes beyond the parameters of any one study and looks to the future of a community's ability to address its own research needs.

#### IV. Analysis:

- a. Do you have all the facts you need? If not, ask for more information.
- b. Has the PI addressed all the issues required?
- c. Is there conflict among the principles presented? Can they be resolved?
- d. Are there other options the PI could consider to resolve the conflicts? (Don't try to solve the problems; ask the PI to do so. The PI must write the research plan, not the IRB.)