Minerva Human Subjects Documentation Discussion for Air Force (AF) Proposals

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Attendees:

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Disclaimer: This discussion is applicable to only the Air Force human subject documentation compliance procedures; researchers conducting research for the other Services should consult their Program Officers for the appropriate processes for their Service.

Notes:

For the Minerva proposals, proposers do not need to provide their Institutional Review Board (IRB) office's approval or full protocols while in the proposal stage, though they can be appended to the proposal as available. What the evaluation team will be looking for is an understanding of the Air Force (AF) requirements and the associated ethics review in general. For the international proposals this will include understanding how to establish local research context as described below.

Ms. Bruce provided a broad overview of the human subjects compliance oversight process for the Air Force Office of Scientific Research. The Air Force compliance process seeks to provide concurrence with the investigators' IRB procedures while reviewing adherence to additional agency, state and local regulations. Early involvement of your agency in the human subjects documentation submittal process is strongly recommended, including before you submit your materials to your institution's IRB.

Material Discussed:

Two most common levels of determination for social science are:

- Exempt – lowest threshold of compliance. Categories of exemption are described in federal regulations, 45 CFR 46.101(b)
- Minimal risk – these protocols are not exempt but represent the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

Key Aspects of Procedures for Air Force Concurrence Review:

<u>Submit materials to your prospective AFOSR Program Officer before they go to your institution's Institutional Review Board (IRB).</u>

- **Subject Recruitment**

  - Recruitment is viewed as part of the informed consent process, and details must be sufficient to ensure compliance with the requirements of 32 CFR 219.116 (e.g., that no subjects are coerced or subject to undue influence).

  i. Please ensure the protocol clarifies who will do what, when, to whom, and how.

  ii. Will lists of potential subjects be obtained from somewhere, and, if so, what are the subjects' expectations of privacy, and how might they respond to a cold-contact from the investigators?

  iii. Submit copies of all recruitment materials (i.e., copies of all advertisements) sufficient to show compliance with the requirements of 32 CFR 219.116/45 CFR 46.116.

  - Identify procedures to protect against coercion/undue influence to participate/continue participation in the portion of the study to be performed by the investigators [e.g., as part of subjects' daily workplace environment, or due to the fact that investigators seek to enroll their own students in this research during class time, etc.]. If the research will take place during class/work time, alternate plans must be made to accommodate students who may not want to participate in the research.
  - AF generally does not support cold calling of subjects who are unfamiliar with the investigator, as this can be, or may merely concern subject by giving the appearance of being, an improper release of protected personal information. Any plans to cold-call potential subjects must be clearly described for consideration of human research protection issues related thereto.
  - While it is not prohibited, we recommend that compensation is not stressed in advertisements for research, e.g., via bold or larger print, in order to avoid the appearance of coercion in recruitment of subjects.

- **Informed Consent Documents**

  Discussion Points:

- Translations required to be submitted to the IRB office in order to make its determination of a protocol.
    - Please forward translations of all submitted documents that are not in English, along with the CV/resume or other statement of qualifications of the translator.
- DoD statements required for some sections – inquire with AFOSR Program Officer for appropriate language.
- DoD should be identified as sponsor and access to research records.
- Method for data protection needs to be documented as well as full understanding of participant risks.

- Additional guidance referred to during discussion regarding informed consent documents is below. Please note that 32 § 219.116 outlines the basic, therefore necessary, elements of what must be in the ICD:

32 § 219.116:

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(a) **Basic elements of informed consent**. Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research; ***AFOSR Note for this part of the ICD: Compensation is not considered a "benefit" of human research for the purposes of meeting the requirement.**
(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;
(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and ***AFOSR Note for this part of the ICD:** The AF strongly recommends that the informed consent document include an alternate contact than the investigator(s) for questions

about subject rights. While the investigator(s) may be knowledgeable about human research protection, subjects may feel uncomfortable asking the investigator questions of a sensitive nature and may desire a more neutral point of contact.

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
(3) Any additional costs to the subject that may result from participation in the research;
(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and
(6) The approximate number of subjects involved in the study.

(c) 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 above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

(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:

- (i) Public benefit of service programs;
- (ii) Procedures for obtaining benefits or services under those programs;
- (iii) Possible changes in or alternatives to those programs or procedures; or
- (iv) Possible changes in methods or levels of payment for benefits or services under those programs; and

(2) The research could not practicably be carried out without the waiver or alteration.

(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.

(e) The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

(f) Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

End citation of 32 § 219.116

Additional Notes Regarding ICDs:
a. Reference the sponsor (such as U.S. federal government, DoD, or AFOSR) will have access research records per 32 CFR 219.116(a) (5).
b. Comply with the Common Rule (32 CFR 219.116).
c. Not be revised and used without new IRB approval.

International Protocols:

- Early discussion with AFOSR PM is essential.
- When research is conducted in one or more foreign countries whose laws and regulations are applicable to that research, per DoDI 3216.02, the requirements of each foreign country must be met before the IRB approves research involving human subjects per the requirements of sections 219.103, 219.107, and 219.111 of Reference (c). Please submit documentation that this was done.
    - There are many acceptable means to ensure the requirements of this paragraph have been met. For example:
      a. Obtain approval from a local human research protection expert (e.g., IRB or ethics review board) within each country where the research will take place;
      b. Obtain approval from a government official with knowledge of human research protection (e.g., a local Ministry of Health) or other point of contact provided via the Office for Human Research Protections International Compilation of Human Research Standards guidance (http://www.hhs.gov/ohrp/international/intlcompilation/intlcompilation.html) for each location;
      c. A U.S. IRB could demonstrate it has obtained necessary information about the foreign research context through written materials and/or discussions with appropriate consultants, who may participate in convened IRB meetings

- To ensure documentation of foreign research context consideration is acceptable to AF, it is recommended that, at a minimum, written documentation provided pursuant to this paragraph should include the following statement, **"The research is acceptable in light of institutional commitments, regulations, applicable law, standards of professional conduct, standards of practice, cultural backgrounds, and community attitudes of the proposed subject population and/or research location. Provisions to protect the privacy of subjects and maintain the confidentiality of data are adequate."**

- Identification of **U.S. DoD as a sponsor is critical in the informed consent document**.

The Air Force generally requires ICDs to identify DoD as a sponsor. This is a material issue that must be disclosed to subjects in order to ensure informed consent per 32 CFR 219.116. However, the **AF Surgeon General's Human and Animal Research Panel (SGHARP)** has allowed an **exception** to the requirement above on certain conditions:

i. The ICD must state the "government" will use study results, and
ii. The IRB must provide documentation justifying how the omission of a statement that DoD is a sponsor meets each element required for alteration of

consent elements under 32 CFR 219.116(d). When performing this analysis, it is important to address the loss of subject autonomy that may occur due to the omission per 32 CFR 219.116(d) (2). While we realize 32 CFR 219.116(a) does not literally require the ICD to identify sponsors, the AF SGHARP has determined that analysis of the regulatory requirements for alteration of consent elements is necessary to meet the spirit of the regulation with respect to the material issue of DoD sponsorship.

- Please include in all ICDs a statement that, "Federal government offices that oversee human research protection may review identifiable subject records to ensure compliance." Note this includes the AF Human Research Protections Official as well as OHRP. See 32 CFR 219.116(a) (5).
- If this research will target international subjects outside of the US, we strongly recommend investigators provide in the informed consent document an e-mail address, international phone number, and/or contact information for persons local to subjects whom they can contact with questions per 32 CFR 219.116(a).

Specific Remarks Made About Local Research Context in International Locales:

Demonstration of local research context is necessary. Establishing local research context can be achieved through a local IRB review, ethics panel, or expert/consultant attesting that the methods associated with the protocol do not violate the cultural norms, country and local laws, or cultural values of the local participants desired for the study. There are three main approaches to establish local research context:

- Locate an IRB in-country
  - Institution such as a University
  - Companies may offer this service as well
  - Utilize OHRP website to locate IRBs
  - IRB must have a CURRENT registration with OHRP and CURRENT Federal Wide Assurance - these can be ascertained on the OHRP website
- Utilize an expert/consultant who is not involved in the proposed research but is an expert on that locale
  - Familiar with the locale, with laws, and cultural values; they attest to the fact that the protocol will cause no harm in the proposed research participant pool
  - Cannot have a conflict of interest – i.e., cannot be affiliated with the proposed work
    - CV/resume determines their expertise/depth of knowledge
    - They will write a memo as a part of the materials submitted for the for the IRB of record's review or join the IRB when they have convened as a non-voting consultant to the IRB
  - Common mistakes –
    - Using someone who is affiliated with the proposed work
    - Sending in memo that does not include the following text:

"The research is acceptable in light of institutional commitments, regulations, applicable law, standards of professional conduct, standards of practice, cultural backgrounds, and community attitudes of the proposed subject population and/or research location. Provisions to protect the privacy of subjects and maintain the confidentiality of data are adequate."

- Ethics Review Panel
  - Much like a single expert; their determination of the protocol and its materials will be considered by the IRB whose assurance covers the investigators
  - They too must write a memo of determination which includes the specific text regarding their depth of knowledge:
    "The research is acceptable in light of institutional commitments, regulations, applicable law, standards of professional conduct, standards of practice, cultural backgrounds, and community attitudes of the proposed subject population and/or research location. Provisions to protect the privacy of subjects and maintain the confidentiality of data are adequate."

Q&A Portion of Discussion:

What about utilizing subjects in other countries recruited by a shared data pool?

- Would depend on how they are recruited – will vary by case-by-case
- Depends on exact procedures for enrollment

What about multi-year research – do we need to have an IRB approval and AF concurrence in place if the research involving human subjects will not come until later?

- IRB approval and AF concurrence are required before you engage in any human subjects research
  - If you specify that human subjects research will be in the first year then we cannot issue a grant without an IRB approval and AF concurrence in place
  - Often investigators in this situation should plan a pilot study; subsequent human subjects work will need a revised IRB approval and AF concurrence

Confidentiality in relation to anonymity

- Discussion would be regarding specific protocol

Will the government require access to research records?

- Traditionally, government access to research records is only required for investigational purposes or site visits. Records should be maintained as outlined by your institution's Human Research Protections Plan (HRPP)

What about waver of written consent? Is this possible?

- This is determined during the review of the IRB office at your institution

Training:

Each engaged investigator must complete appropriate human research protection (HRP) training per DoDI 3216.02, Enclosure 3, Paragraph 5. Please provide either:

a. Documentation of completion of HRP training by each investigator to be engaged in this research or

b. A copy of the section of the institution's HRP Protection policy regarding HRP training.

Materials Required for AF Review:

i. Documentation of appropriate Assurance coverage for the non-DoD institution;

ii. The IRB approval letter or Optional Form 310;

iii. The IRB approved protocol;

iv. The IRB approved informed consent document (and/or documentation of justification, with appropriate facts, for IRB approval of any waiver of consent or consent elements)), per 32 CFR 219.116;

v. Documentation of justification, with appropriate facts, for IRB approval of any waiver of consent signature per 32 CFR 219.117;

vi. Other IRB approved documents, e.g., advertisements, letters to subjects, drug brochures, surveys, and data collection tools;

vii. Documentation of any special determinations made by the IRB (e.g., regarding vulnerable populations);

viii. Approved IRB minutes endorsed by the IO and/or IRB chair. Alternately, IRBs may document their determinations in writing via letter.

ix. For collaborations, submit the IRB review agreements that allow reliance upon a single IRB. Alternately, if no such agreement exists, a separate HRPO review and approval will be required, in accordance with this section, for each collaborating institution engaged in the non-exempt research involving human subjects.

Elements which should be in the IRB Determination Letter:

Please submit IRB approval documentation from every IRB to oversee activities of engaged persons (i.e., X and Y (if engaged), unless an Institutional Agreement for IRB Review has been executed to allow reliance upon either one of the IRBs alone). Ensure the IRB approval documentation shows:

a. The determinations were made by an IRB

b. The IRB's risk determination (greater than minimal, minimal)

c. Approval date

d. Timing of continuing review (must be no later than the one year anniversary of the protocol's initial approval per 32 CFR 219.109(e)/45 CFR 46.109(e))

e. Documentation of any special regulatory determinations made by the IRB (e.g., waiver of informed consent per 32 CFR 219.116(d))

f. If the determination is Exempt, paragraph of exemption should be included 45 CFR 46.101(b)