DoW Supported Extramural Research: Submission Instructions

General Submission Information

711 HPW/IR serves as the designated office of the AFRL Human Research Protections Official (HRPO), appointed by the AFRL/CC, who is the AFRL Institutional Official (IO) for human research protections. For more information about requirements of DoW Supported research, visit the 711 HPW – Institutional Review website.

- All submission questions, requests, and related correspondence must be sent directly to the AFRL HRPO group inbox: AFRL.IR.HRPO@us.af.mil
- Human Research Protection Official (HRPO) review will not begin until the non-DoW submission is complete.
- Submissions are reviewed in order of receipt unless a timeline with mission priority is provided to the HRPO office.

Submissions

- HRPO review and approval is for individual studies and not for the whole Award. There may be multiple studies/protocols under one award; each study/protocol must be submitted for HRPO concurrence.
- Submit all documentation in Microsoft Word or PDF. Do not combine PDF documents into a single file; it will delay your review significantly.
- Label each document to facilitate quick content identification. This should include version date and/or page number.
- Only provide final approved Institutional Review Board (IRB) / Ethics Committee (EC) approved documents (no drafts or documents with tracked changes will be accepted for initial submission).
- Submit the complete package to the HRPO group box (noted above); copy the DAF Program Manager/Program Officer (PM/PO) and other relevant support staff.
  - E-mail is the preferred route of submission.
  - Contact the AFRL HRPO office for a DoW SAFE submission upload link for secure transmission of very large submissions (up to 8 GB). DoW SAFE also supports zip files. Submissions with greater than 25 documents must be zipped or will require additional DoW SAFE links.
- After the review is complete, a HRPO letter will be issued to the DAF PM/PO and Principal Investigator (PI). Contact the HRPO via the AFRL HRPO group box with any questions, as needed. If an AFRL FWR ID number has been assigned to your protocol, include the AFRL FWR ID in the subject line of the email correspondence. AFRL HRPO group inbox: AFRL.IR.HRPO@us.af.mil

Note: If the activity has an existing HRPO review from another DoW Component (e.g. Army or Navy), contact the HRPO office before completing any AFRL checklists. Duplicate reviews may not be required.

Initial Review

Regulatory Basis: Per DoWI 3216.02_DAFI 40-402: The non-DoW institution must obtain HRPO concurrence prior to the start of human subjects research.

Submission Requirements: Investigators must submit their IRB/EC submission and approval of the described activity that was proposed in the award for review.

- Complete the AFRL Extramural Research Initial Submission Checklist and submit it with your study documents.
- If there are personnel from other institutions that are 'engaged' in the research, there may be additional follow-up questions or required documentation.
- Ensure that all documents submitted to the IRB/EC are also submitted to the AFRL HRPO office, except for CV/biosketch and CITI certificates. AFRL HRPO office only requires the PI's CV and CITI certificate.

DoW Supported Extramural Research: Submission Instructions

Required Documentation:

1. DoW Supported Extramural Research: Initial Submission Checklist
2. A copy of the executed Award; this can be a Contract, Grant, Cooperative Agreement or any other type of Award. Contact your PM/PO for assistance as needed. The Contract must contain the Human Subjects Research (HSR) DFARS clause 252.235-7004; other types of Awards must contain similar HSR language. Sub-awards with HSR must also contain this information. (For AFWERX/SpaceWERX projects your Award has already been provided to AFRL HRPO.) Sub-award agreements must also contain this language.
3. The Statement of Work (SOW)/Proposal/Work plan/Task order: a copy of the SOW that describes the component approved research activity for both the Prime and any sub-awards.
4. A copy of the IRB/EC Submission package.
    a. All the forms and documents that were submitted to the IRB/EC.
    b. If the IRB/EC determined the study to be HSR, provide a copy of the PI's biosketch/CV and CITI or other human subjects protection training.
5. The IRB/EC Approval letter. The following are common best practice items in a letter (as applicable):
    a. Correct Protocol Title
    b. IRB/EC's determination and justification of determination as applicable (not research or not research involving human subjects, expedited review category and subcategories, exempt determination category and subcategories), if a limited IRB was conducted the IRB must provide an analysis as to how the requirements of the privacy and confidentiality provisions have been met
    c. Approval Date & Expiration (if applicable)
    d. Written documentation from the IRB/EC that Scientific Merit was considered during review of all non-exempt research
    e. Risk Determination (Minimal or Greater than Minimal Risk)
    f. Language granting any waiver request, such as waivers of documentation of informed consent
    g. Documentation of applicable regulatory requirements were used (such as FDA and HIPAA regulations)
    h. Whether the IRB documented that the DoW Ethical Principles for Artificial Intelligence were considered and appropriately provided for in the protocol
6. All documents the IRB/EC provided back to you, such as recruitment material, consents, etc.
7. Studies conducted internationally must include consideration of local research context and cultural sensitivities review along with abiding by the applicable laws of the country and region.

HRPO Response: Written letter of 'Concurrence' or determination provided to the Awardee and PM/PO via email.

Modifications / Amendments

Regulatory Basis: Per DoWI 3216.02_DAFI 40-402: The non-DoW institution must obtain HRPO approval prior to implementation of modifications with substantive changes.

Instruction: Investigators must submit <u>any modification</u> for the previously approved research to their IRB/EC; follow your institutional guidelines for submission. Changes may not be instituted without IRB/EC review and approval except when necessary to eliminate apparent immediate hazards to participants.

The HRPO must <u>review and approve</u> 'substantive changes' to the study <u>prior to implementation,</u> these include but are not limited to:

- Any modifications that could potentially increase risk to subjects
- Change in Principal Investigator
- Change or addition of an Institution
- Elimination or alteration of the consent process

DoW Supported Extramural Research: Submission Instructions

- Change in the IRB of Record
- Change to the study population that has regulatory implications (e.g. adding children, adding active-duty population, etc.)
- Significant change in study design (i.e. would prompt additional scientific review)

Required Documentation:

1. IRB/EC modification/amendment submission
2. Track change versions of any modified documents (so HRPO can readily identify changes)
3. Corresponding IRB/EC approval letter that specifies the new approval date
4. All other IRB/EC approved modified materials

HRPO Response: Email verification that all requirements are complete and the changes are 'Approved.' You must receive HRPO Approval prior to implementation of substantive amendments.

Continuing Review / Re-Approval

Regulatory Basis: Per DoWI 3216.02_DAFI 40-402, the non-DoW institution must promptly notify HRPO of the results of the IRB/EC's continuing review, if required. Continuing Review (CR) is a periodic review of a research protocol by the IRB. The review must be substantive and meaningful.

Instruction: The non-DoW IRB protocol renewal documentation is due within 2 weeks of the IRB/EC expiration date. At the time of CR the supporting DAF institution (PM/PO) is responsible for verifying the award remains active and for conveying this to HRPO.

As a courtesy, the PM/POs and PIs will be notified when the study they oversee approaches expiration; notices are sent via email 30 days prior to expiration and on the expiration date.

At the time of Continuing Review/Re-Approval, routine file audits are conducted and there may be additional information requested.

IMPORTANT: Approval periods expire at 11:59 pm on the expiration date issued by the IRB/EC. If the study expires, the PI must cease **all** research activities, including enrollment and data analysis. Any continuation of research activity is a violation of DoW and Federal regulations. PIs who want to continue research activities must submit a renewal request to their IRB/EC in accordance with their IRB/EC policy. Research activities may not resume until a new IRB/EC approval has been issued.

Required Documentation:

1. A copy of the IRB/EC continuing review/renewal or progress report form and any additional documents submitted
2. The IRB/EC's approval letter
3. Any new approved documents received from the IRB/EC

HRPO Response: Email verification that all requirements are complete and the submission is 'Acknowledged.'

DoW Supported Extramural Research: Submission Instructions

End of DoW Support

- **Regulatory Basis:** Per DoWI 3216.02_DAFI 40-402: The non-DoW institution must promptly notify HRPO "of a DoW supported study's closure."

Instructions: Closing HRPO oversight can be accomplished at the end of DoW support through the following:

- The study/protocol can be closed with the IRB/EC, OR
- Investigators may continue the research by amending the study to remove the DoW funding and required support statements. If the project receives additional support by the DoW in the future, it will require re-submission for HRPO review through the new supporting agency.

Note: If the study/protocol was considered "Not Research," "Not Human Subjects Research," or "Exempt Human Subjects Research," then the DAF PM/PO can confirm the end of DoW support to the HRPO office, and this suffices as closure documentation. (This procedure does not apply to "Non-exempt HSR" and "Exempt HSR with Limited IRB review.")

Closure Required Documents:

1. A copy of the IRB/EC closure form and any additional documents
2. The IRB/EC's acknowledgement of the study closure

Modification Required Documents:

1. A copy of the IRB/EC modification showing the supporting has ended and the required statements in the informed consent and recruitment statements have been removed
2. The IRB/EC's approval letter
3. All the approved documents showing DoW references are removed

HRPO Response: Email verification that all requirements are complete and AFRL HRPO oversight has ended.

General Guidance

Extramural Research

- Extramural research is research supported by the DoW / Department of the Air Force but conducted by a non-DoW institution and reviewed and approved by a non-DoW IRB/EC. 'Support' includes, but is not limited to, funding (i.e. grants, contracts, and cooperative agreements), use of DoW facilities or equipment, program management and award management performed by DoW personnel, access to or information about DoW personnel for recruitment, including data and/or specimens.
- If DoW-affiliated personnel are engaged, the study may be subject to a DoW IRB review.

Assurances and Addendums

- An Assurance is required by any institution (including international institutions) performing non-exempt HSR supported by any U.S. Federal department/agency that has adopted the Common Rule (45CFR46 or 32CFR219). A Federalwide Assurance (FWA) is acquired through the U.S. Department of Health and Human Services Office for Human Research Protections (OHRP).
- For individuals without a specific institutional affiliation (e.g. an independent contractor), an Individual Investigator Agreement (IIA) is a specific assurance used to cover one person by another assured institution. The agreement can be limited to a specific study or set of studies.

DoW Supported Extramural Research: Submission Instructions

Human Subject Protection Training

- Human Subject Protections (HSP) training is required for any individual 'engaged' in a human subjects research project. Engaged means that the individual will have direct interaction with subjects or their identifiable data. HSP training must be completed within three years to be considered valid and must remain current during the person's engagement in the research. A popular service for HSP training is the CITIprogram, but HRPO will accept the HSP training documentation from your institution.

Research Records/Audits

Records maintained by non-DoW institutions that document compliance or noncompliance in accordance with DoWI 3216.02 must be accessible for inspection and copying by authorized representatives of the DoW. Representatives of the Department of the Air Force (DAF) Component Office of Human Research Protections (COHRP) have authority, and the AFRL HRPO may perform periodic Post Approval Compliance Monitor (PACM) or for-cause audits of the non-DoW institution's supporting HSR. Quality assurance visits may consist of the following: one-on-one interviews with the investigator and/or research staff, observation of the informed consent process and data collection, or viewing of data files at the discretion of the HRPO/COHRP. The HRPO will notify the supporting AF office (via the PM/PO/Component POC) in writing of the results, any deficiencies, and any corrective actions that may be required.

Recruitment of DoW-Affiliated Personnel or any other DoW support

1. If DAF-affiliated personnel (active duty, civilian or contractors) will be recruited to participate in HSR or are providing any other support for research, and the supporting DAF institution does not have a human research protection program (HRPP), it must establish a "Limited HRPP." A specific template to facilitate this requirement is available from the AFRL HRPO office.
2. For other DoW Components, if the recruitment of DoW-affiliated personnel (active duty, civilian or contractors), the key investigator must receive a command or component letter of support from the DoW-affiliated personnel's command to conduct the research and before they can be recruited.
3. If the DoW supported HSR is conducted on a DoW facility, the key investigator must receive approval from the command or component responsible for the facility.
4. HRPOs must receive written documentation of permission from the DoW institution(s) providing support for the activity.

The key investigator must provide command or component copies of the IRB approved protocol and informed consent documents for review when requesting approval.

Large Scale Genomic Data (LSGD)

Instruction: Contact the HRPO office if the research involves LSGD of DoW-affiliated personnel. DoW supported research involving LSGD collected on DoW-affiliated personnel, or for which research the DoW provides assistance, is subject to additional requirements per DoWI 3216.02_DAFI 40-402:

1. Since disclosure of DoW-affiliated personnel's genomic data may pose a risk to national security; accordingly, such research requires administrative, technical, and physical safeguards commensurate with risk, including the secondary use or sharing of de-identified data or specimens.
2. All research involving LSGD collected from DoW-affiliated personnel will apply a Health and Human Services Certificate of Confidentiality pursuant to Title 42, U.S.C., and Public Law 114-255.
3. Research involving LSGD collected from DoW-affiliated personnel is subject to DoW Component security review to ensure the adequacy of the proposed administrative, technical, and physical safeguards, including the secondary use or sharing of de-identified data or specimens.

DoW Supported Extramural Research: Submission Instructions

Compensating DoW-Affiliated Personnel in Research Studies

Investigators who plan to compensate DoW-affiliated personnel must comply with regulations and requirements specific to each DoW Component (e.g., Army or Air Force). Each DoW Component may have additional specific requirements regarding compensation paid to DoW-affiliated personnel. Investigators must describe their plan for any compensation of DoW-affiliated personnel, including the military status of potential subjects targeted for enrollment in the IRB application. A summary of current compensation plan for DoW-affiliated personnel is listed below.

On-duty DoW-affiliated personnel, including military members:

- Compensation is not allowed for general research participation.
- Up to $50 for blood draws, if Statute 24 USC 30 is met in conjunction with clinical care or during donation of blood.

Off-duty DoW-affiliated personnel including military members:

- For research participation beyond blood draws, compensation is allowed in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research, so long as the personnel are off-duty.
- Off-duty employment can be verified many ways, including through an AF Form 3902.
- Payment may not come directly from a federal source. Payment from a federal contractor or non-federal source is permissible.

Reminders

1. **This list is not meant to be all inclusive.** Some protocols may be more complex than others and may have additional documentation requirements. You will be advised either by the DAF Program Officer/Manager or HRPO if additional documents are needed.

2. **HRPO review will not begin until the package is complete.** If items are missing from the initial submission, the protocol will be held in a 'pending' status until all items are received and the submission is added to the HRPO queue. Be aware that 90 days without a response/update will automatically withdraw the submission.

3. **Each submission stands alone**. Please do not assume that previously submitted documents (e.g., addendums and awards) from a prior study proposal will be cross referenced to the new protocol. Each new submission is viewed as distinct and therefore must include all required documentation.

4. **Care should be given to ensure all study titles match**. The IRB/EC approved protocol title should match the IRB/EC approval documentation (letter) and the titles on the informed consent documents and recruitment information. For document control, each document should include a version number and date, although we understand some IRBs/ECs do not include this step. This is considered good document practice. Please do not use the title of a program/project or grant as the protocol title, unless it is the award's only associated protocol, as most awards have multiple associated protocols.