# THE RAND CORPORATION

# HUMAN SUBJECTS PROTECTION COMMITTEE

# STANDARD OPERATING POLICIES & PROCEDURES

**November 2020**

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## INTRODUCTION

The RAND Code of Ethical Conduct under **Protection of RAND Research Participants** states**:** RAND is committed to ethical and respectful treatment of RAND research participants, consistent with the Belmont Report. RAND Associates[1] comply with all applicable laws and regulations, including the Federal Policy for the Protection of Human Subjects, also known as the "Common Rule." In addition to RAND's Code of Ethical Conduct, RAND also has a specific policy titled Protection of Human Subjects and Ethical Treatment of Research Participants that describes RAND's requirements for appropriate means for acquiring and safeguarding Human Subjects Information and the role of the Human Subjects Protection Committee in ensuring the ethical treatment of Research Participants.

The Common Rule requires that Institutional Review Boards (IRBs) have written policies and procedures, and that activities at the institution are carried out as described in the written policies and procedures document. As RAND's IRB, the Human Subjects Protection Committee's (HSPC) Standard Operating Policies and Procedures (SOP) are written to enable IRBs to maintain a system of compliance and reflect not only the applicable laws and regulations, but also the underlying ethical principles that are the basis of HSPC's mandate. These policies also reflect RAND's commitment to provide protection for all human subjects involved in research conducted under the direction of RAND Associates. The Common Rule represents a minimum standard of protection for research participants. RAND may require additional protections or protections for research participants who may not be defined as "human subjects" according to the regulations.

The RAND Human Subjects Protection Committee (HSPC) is charged with ensuring the ethical treatment of individuals who are participants in RAND projects through observation, intervention, interaction or use of data about them. The HSPC also serves as RAND's Institutional Review Board (IRB) to review research involving human subjects. RAND's Federalwide Assurance (FWA) for the Protection of Human Subjects (FWA00003425, effective until June 22, 2023) serves as our assurance of compliance with federal regulations. According to this assurance, the HSPC is responsible for review of all research, regardless of the source of funding.

RAND's investigators are expected to advance knowledge that can improve the human condition or generate new knowledge and, at the same time, recognize the absolute imperative to treat research participants with the utmost care and respect.

RAND's HSPC assists investigators in identifying and mitigating risks to research participants and shares the responsibility of protecting the subjects of this research. These SOPs apply to all the day-to-day operations of HSPC. The SOPs apply to HSPC staff, all members who serve on it as part of their overall institutional responsibilities,

[1] All regular and term employees, adjunct, or affiliated adjunct staff member, or any Pardee RAND Graduate School students and sponsored fellows.

and all others who must subscribe to its decisions and its requirements (for example, the Investigators, research managers/coordinators, research staff, support staff, etc.).

These SOPs will be reviewed periodically to ensure that they are up-to-date, that new legislation or regulations are reflected in the policies and that daily activities are being performed as described in the SOPs.

These SOPs are based on current laws, regulations, ethical principles, and guidelines for the protection of the human subjects of social behavioral research. The policies state what this institution requires for the ethical conduct of research. The procedures detail how these policies are carried out.

The policies and procedures are not an end unto themselves. They are the framework upon which research activities at RAND is conducted. Therefore, all members of the research enterprise who are working within RAND are expected to read, understand, and comply with them. This way, the burden of conducting sound, effective and ethical research can be shared.

NOTE:
The revised Common Rule was published on January 19, 2017. The revised rule went into effect on January 19, 2018. The compliance date for the new rule, except for the cooperative research, was January 19, 2018. The compliance date for the cooperative research was January 20, 2020. This SOP reflects relevant revised rule. The details of the revised Common Rule can be found here:
https://www.federalregister.gov/documents/2017/01/19/2017-01058/federal-policy-for-the-protection-of-human-subjects

As noted in the Federal Register, ongoing research studies that were initially approved by an IRB, waived pursuant to § 45 CFR 46.101(i), or determined to be exempt before January 19, 2018 will not be required to comply with the changes reflected in the final rule.

## LIST OF ABBREVIATIONS

| | |
|---|---|
| AE | Adverse Event |
| CFR | Code of Federal Regulations |
| CITI | Collaborative Institutional Training Initiative |
| CRO | Contract Research Organizations |
| DHHS | Department of Health and Human Services (or HHS) |
| DoD | Department of Defense |
| DSMB | Data Safety and Monitoring Board |
| FDA | Food and Drug Administration |
| GCP | Good Clinical Practice |
| HIPAA | Health Insurance Portability and Accountability Act of 1996 |
| HRPO | Human Research Protection Official (of DoD) |
| HSPC | Human Subjects Protection Committee |
| ICF | Informed Consent Form |
| ICH | International Conference on Harmonisation |
| IDMC | Independent Data Monitoring Committee |
| IEC | Independent Ethics Committee |
| IO | Institutional Official |
| IRB | Institutional Review Board |
| NIH | National Institutes of Health |
| OCR | Office for Civil Rights |
| OHRP | Office for Human Research Protections (former OPRR) |
| OPRR | Office for Protection from Research Risks |
| PHI | Protected Health Information |
| PI | Principal Investigator |
| QA | Quality Assurance |
| QC | Quality Control |
| RHINO | RAND HSPC Information Online |
| SAE | Serious Adverse Event |
| SOP | Standard Operating Procedure |
| UPIRTSO | Unanticipated Problems Involving Risks to Subjects or Others |

# STATEMENT OF AUTHORITY AND PURPOSE

## 1. GOVERNING PRINCIPLES

RAND is committed to the ethical and respectful treatment of research participants and compliance with applicable laws and regulations. All research participants deserve to be treated with respect, beneficence, and justice, as described in the Belmont Report. The decision to acquire information from research participants includes taking responsibility for safeguarding the acquired information in ways that respect and protect its confidentiality. RAND Associates must fully carry out our commitment to protecting such information and associated data consistent with the standards of ethical behavior and as required by law, including adherence to each of the following: (1) U.S. federal, state, and local laws, regulations, and requirements that affect the acquisition and safeguarding of information obtained from Human Subjects, (2) any foreign laws applicable to the research, and (3) any requirements from the Human Subjects Protection Committee (HSPC) regarding the ethical treatment of research participants.

Institutional Review Boards (IRBs) are guided by the ethical principles applied to all research involving humans as subjects, as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, titled: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the "Belmont Report"). These principles are defined in the Belmont Report (Appendix A) as follows:

- Beneficence -- The sum of the benefits to the subject and the importance of the knowledge to be gained so outweigh the risks to the subjects as to warrant a decision to allow the subject to accept these risks.
- Autonomy -- Legally effective informed consent is obtained, unless the requirements for waiver of informed consent are met by adequate and appropriate methods in accordance with the provisions of applicable regulations.
- Justice -- The selection of subjects is equitable and is representative of the group that will benefit from the research.

## 2. AUTHORITY

RAND's HSPC is established and empowered under the auspices of that Institution's executive authorities, and, if federal funding is used to support human subject research in whole or in part, by the Institution's Assurance with the federal Office for Human Research Protections (OHRP). RAND requires that all projects be screened for involvement of humans as subjects and all research involving human subjects be reviewed and approved by the Human Subjects Protection Committee (HSPC) prior to initiation of any research related activities. The HSPC does not review any research that is subject to regulation by the Food and Drug Administration (FDA). The HSPC may undertake review of certain minimal risk medical device studies (e.g. pill counter) that are approved devices for use in research. The HSPC has a

mechanism in place to defer certain studies under certain circumstances to other IRBs for a review or vice versa. For example, RAND has a Memorandum of Understanding (MOU) in place with the University of California, Los Angeles (UCLA), where one institution, depending on the scope of the research, will serve as the sole reviewing institution for health services and related research. The RAND HSPC sometimes directs projects to obtain review from another IRB with specific experience not available on the RAND HSPC, such as for approval of medical devices developed with therapeutic intent.

The HSPC reviews all research involving human subjects regardless of the source of funding and location of the study. Except for research in which the only involvement of humans is in one or more of the categories exempted or waived, all research involving human subjects, and all other activities which even in part involve human research activities, regardless of the source of funding, are subject to these policies and procedures if one or more of the following apply:

- The research is sponsored by RAND authorities and/or;
- The research is conducted by or under the direction of any employee, staff, student or agent of RAND in connection with his or her institutional responsibilities; and/or
- The research is conducted by or under the direction of any employee, staff, student or agent of RAND using any property or facility of the RAND; and/or the research involves the use of RAND's nonpublic information to identify or contact human research subjects.

The HSPC has the authority to ensure that research is designed and conducted in such a manner that protects the rights and welfare of participating subjects. Specifically, the HSPC:

- May disapprove, modify or approve studies based upon consideration of human subject protection aspects;
- Reviews, and has the authority to approve, require modification in, or disapprove all research activities that fall within its jurisdiction;
- Conducts continuing review as it deems necessary to protect the rights and welfare of research subjects, including requiring progress reports from the Investigators and auditing the conduct of the study, and observing the informed consent process and/or auditing the progress of any study under its jurisdiction as it deems necessary to protect the rights and welfare of human subjects;
- May suspend or terminate approval of a study; and
- May place restrictions on a study.

The HSPC may, in its discretion, determine that although a particular project does not meet the Common Rule definition of Human Subjects Research, fulfillment of the principles of The Belmont Report (respect, beneficence, and justice) or RAND's Institutional Principles requires implementation of certain protections and procedures associated with Human Subjects Research. All research participants in RAND studies are entitled to ethical treatment as determined by the HSPC.

Regarding federally funded research, if the study is part of an application to a federal sponsoring agency, the human subjects protocol must be reviewed by HSPC before or when the application is processed and prior to expenditure of any grant funds.

Other RAND officials or RAND committees may not approve research if it has been disapproved by the RAND HSPC.

The HSPC recognizes that local laws in the jurisdictions where research is conducted impose additional requirements. To ensure that the applicable requirements are met, the HSPC members and staff will consult with the Office of General Counsel of the RAND Corporation for guidance on additional legal requirements.

The HSPC recognizes that the Department of Defense (DoD) and several of its components have directives and instructions that implement various aspects of the Common Rule. RAND has signed a DoD Addendum to the Federal Wide Assurance (DoD Number F50389) covering all DoD-sponsored research performed at RAND. In the addendum, RAND agrees to abide by the human subjects research requirements set by the DoD as well as those of the following components: 1) Department of the Army; 2) Department of the Navy; 3) Department of the Air Force and 4) Office of the Under Secretary of Defense for Personnel. The RAND Associates will abide by the DoD directives and instructions.

## 3. RESPONSIBILITY

### A. HSPC REVIEW OF RESEARCH

All research involving human subjects (as defined below), and all other activities, which even in part involve such research, regardless of the funding source, must be reviewed and approved by the RAND's HSPC. No intervention or interaction with human subjects in research, including recruitment, may begin until HSPC has reviewed and approved the research protocol. The HSPC applies the definitions of "research" or "human subjects" and the implications for the jurisdiction of HSPC under Institutional policy.

Most projects that involve human subjects that are funded by DoD also require a secondary review by a designated agency of DoD. Unit directors or their designated representatives are responsible for determining whether a secondary review is required and identifying the agency that will conduct the review.

The HSPC's purpose and responsibility is to protect the rights and welfare of human subjects. The HSPC reviews and oversees such research to ensure that it meets well-established ethical principles and that it complies with federal regulations at 45 CFR 46 that pertain to human subjects protection. If the research is exempt from HSPC review per 45 CFR 46 Section 104(d)(1-8) but involves human subjects or materials, the HSPC requires that the research be reviewed in order to ensure that the subjects are appropriately protected.

According to the Common Rule, the activities that require HSPC review include any activities involving the collection of data through intervention or interaction with a living individual or involving identifiable private information regarding a living

individual. Specific activities that may require HSPC review include, but are not necessarily limited to the following:

- Collection of data about a series of standard procedures or interventions for dissemination or generalization.
- Survey studies using online, telephone, in person, or any other modes.
- Interview studies that solicit information about research subjects or their personal opinions on certain topics.
- Focus group studies, "gaming", or workshops where the goal is to collect research data.
- Research use of existing data unless publicly available or use of a limited dataset with a data use agreement.
- Field or cognitive type experiments involving randomization of subjects.
- Emergency and disaster-related studies.
- Oral history projects that involve interviewing individual(s) for a prolonged period or are intended for research purposes as determined by the HSPC.
- Student-conducted research, which includes all activities that meet the definition of research with human subjects and that are conducted by students for a class project or for work toward a degree. These activities include: (i) All doctoral dissertations that involve human subjects; and (ii) all projects that involve human subjects and for which findings may be published or otherwise disseminated.
- Case studies, such as when a series of subject observations are compiled in such a way as to allow possible extrapolation or generalization of the results from the reported cases. Additionally, when there is intent to publish or disseminate the data or findings.

## B. FAILURE TO SUBMIT A PROJECT FOR HSPC REVIEW

The implications of engaging in activities that qualify as research that is subject to HSPC review without obtaining such review are significant. Results from such studies may not be published unless HSPC approval had been obtained prior to collecting the data. If an Investigator begins a project and later finds that the data gathered could contribute to the existing knowledge base or that he or she may wish to publish the results, the Investigator should submit a proposal to the HSPC for review as soon as possible. If the HSPC does not approve the research, data collected cannot be used as part of a thesis or dissertation, and/or the results of the research cannot be published. Furthermore, the journals to which an investigator wishes to publish may reject such data if an HSPC approval is not properly obtained.

## C. ASSURANCE OF INDEPENDENCE

HSPC acts as an independent entity within RAND. All decisions made by the HSPC are binding and cannot be overturned or overruled by any RAND officials.

## APPLICABLE POLICIES AND GUIDELINES

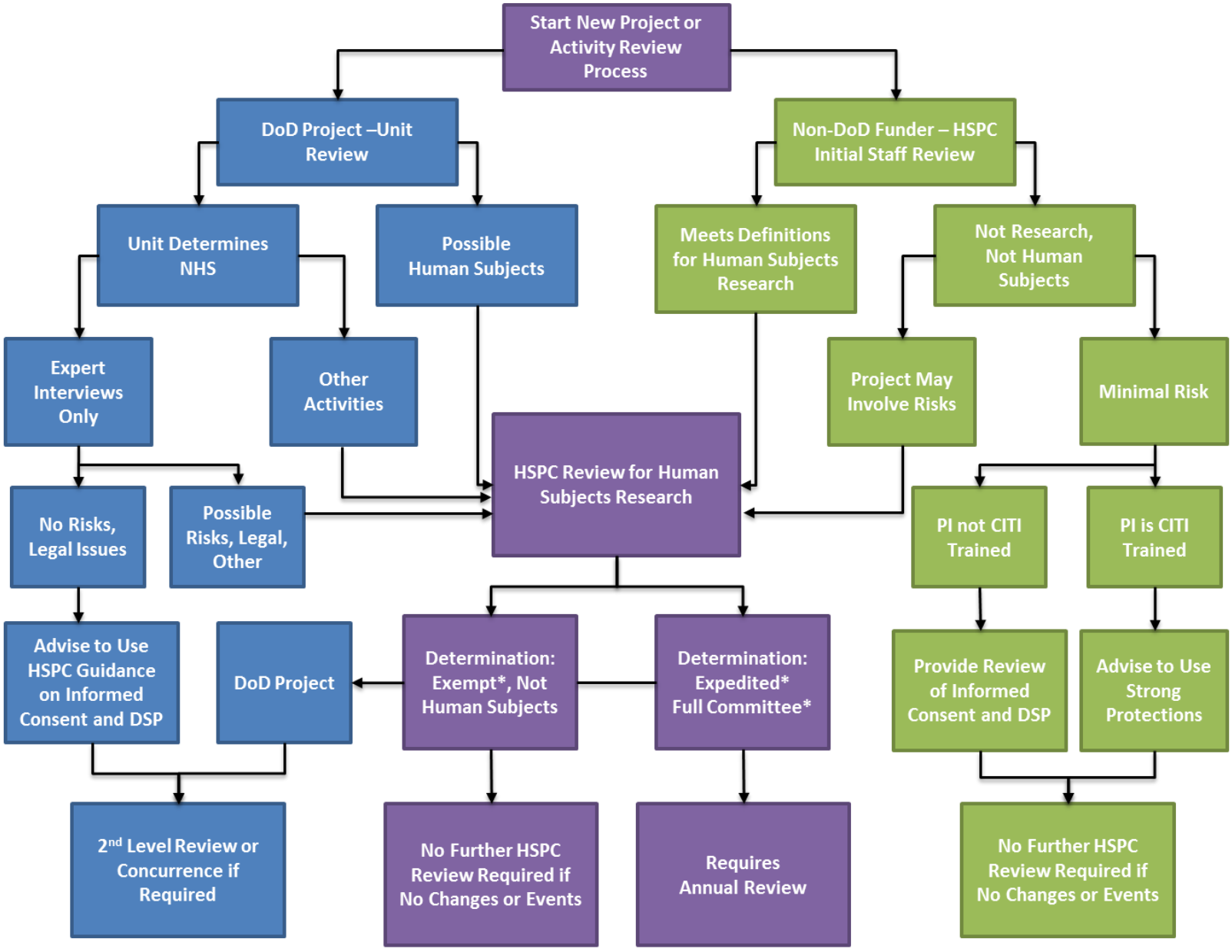
The Belmont Report: http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html

https://randus.sharepoint.com/research/hspc/Pages/home.aspx

https://randus.sharepoint.com/research/hspc/Pages/dod-guidance.aspx

https://randus.sharepoint.com/research/hspc/Pages/responsibilities.aspx

## RAND Research Participant and Human Subjects Review Process




*PI and project staff in contact with human subjects or human subjects data must have CITI training.

## Overview of Research Participant and Human Subjects Review Process

As described in the flowchart above, the HSPC will screen all new projects or activities prior to any researcher undertaking any project activities. The workflow for review differs for projects managed by DoD Federally Funded Research and Development Centers (FFRDC) Units versus all other projects, as shown in the above Decision Chart. Detailed procedures for ensuring projects are screened through each unit are provided on the HSPC website:
https://randus.sharepoint.com/research/hspc/Pages/screening.aspx

## Department of Defense (DoD) Funded Projects Managed Through FFRDCs

Projects managed through the DoD FFRDC Units (Project Air Force, Arroyo, National Defense Research Institute) will obtain an initial screening in their units. The Principal Investigator (PI) is responsible for completing the appropriate Unit Screener form describing the intended purpose of the project, the activities that will be undertaken, and any potential risks or other issues that might apply. This form will be reviewed at the unit level by a unit staff member appointed by the Unit Head who will determine:

- Whether the planned activity appears to fit the definition of DoD Instruction 3216.02 of "not research involving human subjects": Activities, including program evaluation and surveys, user surveys, outcome reviews, and other methods, designed solely to assess the performance of DoD programs where the results are only for the use of government officials responsible for the operation or oversight of the program being evaluated.
- Whether there are any activities that may involve data collection from individuals or use of individually identifiable data, *other than* expert panel/workshop or expert interviews or use of designated datasets provided by the DoD to RAND and maintained and used according to standard procedures.
- Whether there are any more than minimal risks that may be associated with the project, regardless of whether it meets the definition for "not human subjects".
- Whether there are any other issues, such as potential legal liability, expectation of adverse publicity, or other factors meriting additional consideration.

If a project does not involve human subjects or the activity meets the DoD definition above, involves only expert interviews or use of designated dataset, and presents no other concerns the project may be approved at the unit level. The PI is advised to use HSPC-provided guidance on informed consent for expert interviews and guidance on data safeguarding and the project is referred for 2nd Level Review, if required by designated Human Research Protection Official.

The PI is provided with the following determination:

> Planned activity appears to fit the definition of DoD Instruction 3216.02 of not research involving human subjects: Activities, including program evaluation and surveys, user surveys, outcome reviews, and other methods, designed solely to assess the performance of DoD programs where the results are only for the use of government officials responsible for the operation or oversight of the program being evaluated.

PI is responsible for carrying out appropriate consent and data safeguarding procedures, and any changes to the planned activities or uses of the results must be reported to the HSPC. The project may still require DoD 2nd level administrative review as determined by the applicable RAND unit.

PI should follow HSPC guidance on informed consent for expert interviews and use strong data safeguarding procedures.
https://randus.sharepoint.com/research/hspc/Pages/expertiw.aspx

In reporting project findings in briefings and publications project should avoid making statements generalizing results beyond the specific program being studied.

If the Unit reviewer determines that the project may not clearly fit the definition above as "not research involving human subjects" (that is, it may be a human subjects project or activity), if it involves activities other than those specified above, or if it presents any other issues, the Unit reviewer will instruct the PI to obtain HSPC review.

The PI will enter the project in RHINO (The RAND HSPC Information Online submission system and protocol database used at RAND) using standard procedures. The HSPC may determine that the project or activity does meet the DoD definition for "not human subjects" or may elect to review it as "human subjects research". Regardless of the determination, the HSPC may require specific procedures for informed consent or data safeguarding to comply with ethical requirements for protection of research participants. After the project is approved by either the FFRDC Unit or the HSPC, the Unit may determine that the project requires 2nd Level Review and will work with the PI to obtain this.

The Unit review process was developed in coordination with the HSPC and is carried out with approval of the HSPC. The HSPC will have full access to records of this unit review process and may conduct audits of the process for compliance with DoD Instructions and HSPC requirements at any time. This will require the full cooperation of Unit staff, the PI, and project staff as requested by the HSPC.

**All Other Projects, including Non-DoD Funded Projects, DoD-Funded Projects not Managed Through FFRDCs or DoD Funded Projects Requiring Human Subjects Review**

All other projects will be reviewed using standard HSPC procedures. The PI should submit the project in the RHINO system as soon as possible. The PI should allow at least a month for HSPC review and longer if the project is likely to present significant issues, which may require more than one monthly full committee meeting to obtain approval.

To ensure the project is described accurately and completely, the PI (individual listed in RAND information systems as the PI), or someone who is thoroughly familiar with the design and operation of the project and who has a current CITI Training certificate, must accurately and completely fill out the RHINO forms. *If the PI's designee completes the*

*form, the PI is responsible for ensuring the information is current, complete and accurate before submitting the initial form.*

For initial project review, the PI should include all contemplated activities, populations, and procedures, even if some of the contemplated activities are not yet fully developed or funded. The PI can include activities that were not anticipated at the time of submission of the initial RHINO forms as proposed amendments to the existing project.

The PI should not copy and paste the whole proposal into the RHINO form. The PI should summarize the proposal so that HSPC or unit reviewers can review all pertinent information quickly and attach a copy of the proposal for reference. Even if the PI anticipates that the HSPC or unit reviewers will determine that the project is "not research", "not human subjects research", or exempt the project may still be required to follow ethical requirements for informed consent and responsible data protection. Accordingly, the PI should attach all applicable draft data interview guides or questionnaires: draft informed consent forms or guidelines or oral consent and invitation letters, emails, or advertisements, draft data safeguarding plans, and data use agreements or a specific web address where the data are available for download for all datasets. The HSPC requires complete, accurate, and current information to determine the appropriate review of the project.

NOTE: As of 6/29/2020, RHINO 2 is in parallel use with the old RHINO system. Any projects submitted prior to 6/29/2020 will remain and continue to be managed in the old RHINO system whereas any projects submitted on or after 6/29/2020 will be managed in RHINO 2.

**Projects Initially Determined to be "Not Research" or "Not Human Subjects Research"**

The HSPC staff conducts an initial review to determine the appropriate review process for the project. If the project does not meet OHRP criteria for "research" or for "research involving human subjects", the HSPC staff still screens the project to determine if there is a possibility that it might pose more than minimal risks for participants.

Projects that do not meet the above criteria, but may involve more than minimal risk, can be referred to an HSPC subcommittee or to the full committee for further review. If the HSPC staff determines a project involving no more than minimal risk is led by a PI who is current on CITI training, the HSPC staff may advise the PI to use strong protections for participants. If the PI does not have current CITI training, the HSPC staff may require training and/or provide the PI with a review of informed consent and data safeguarding plans and materials. Unless there are subsequent changes or events that need to be reported, the project will not be the subject of further review.

**Human Subjects Research Projects or Projects That May Involve More Than Minimal Risk**

Projects determined by HSPC staff to meet criteria for human subjects research or that may pose greater than minimal risks to participants will be reviewed according to the

requirements of RAND's Federalwide Assurance for the Protection of Human Subjects. https://randus.sharepoint.com/research/hspc/Pages/federal-wide-assurance.aspx

# GA- 100
# GENERAL ADMINISTRATION

| SOP: GA 101 | SOP POLICIES AND PROCEDURES MAINTENANCE | Version No: |
|---|---|---|

## 1. POLICY

Following federal regulations and RAND policies assures that the rights and welfare of participants in human subjects research will be protected in a uniform manner, regardless of changes in RAND personnel. Written procedures ensure the highest quality and integrity of the review, oversight of research involving human subjects and for the adequate documentation of such oversight.

Standard operating policies and procedures (SOPs) provide the framework for the ethical and scientifically sound conduct of human research.

**Specific Policies**

### 1.1 Review, Revision, Approval of Policies & Procedures

1.1.1 Changes to regulations, federal guidelines, or research practice as well as the policies and procedures of the RAND Corporation may require a new SOP or a revision to a previously issued SOP.

1.1.2 Policies will be reviewed by the HSPC Chairperson and any appropriate HSPC staff at least every five years, or as needed.

1.1.3 Approval of new or revised SOPs is required by the HSPC Chairperson.

### 1.2 SOP Dissemination and Training

1.2.1 Any new or revised SOPs will be posted on the HSPC website and highlighted as new information.

1.2.2 Training will be provided to all members of the HSPC and HSPC staff on any new or revised policy and/or procedure.

1.2.3 Each new HSPC member or staff employee must review all applicable SOPs prior to undertaking any responsibilities at the HSPC.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.108

| SOP: GA 102 | TRAINING AND EDUCATION | Version No: |
|---|---|---|

## 1. POLICY

Training of HSPC staff and members is critical if the HSPC is to fulfill its mandate to protect the rights and welfare of research subjects in a consistent manner throughout the RAND research community.

HSPC members, staff and others charged with responsibility for reviewing, approving, and overseeing human subject research should receive detailed training in the regulations, guidelines, ethics and policies applicable to human subjects research.

All RAND researchers and other appropriate personnel will be required to provide evidence of training and qualifications by submitting relevant documentation to the HSPC, sponsor, or regulatory authorities.

### Specific Policies

### 1.1 Training

1.1.1 Management level staff and HSPC members who are overseeing research on human subjects, as defined in 45 CFR 46.102 (e), that is managed, funded, or taking place in an entity under the jurisdiction of RAND are required to have a current certificate of successful Collaborative Institutional Training Initiative (CITI) training and review this SOP before assuming their duties. CITI is a web-based educational program that is designed to fulfill the protection of human research participants training.

RAND Associates are required to take the Social-Behavioral-Educational (SBE) Basic Course unless a staff has taken the course before and the previous certificate has not expired. A PI on a research project funded by the US Department of Defense (including any of its components such as a branch of the military or DMDC) may be required to take the CITI training through the DoD.

CITI training certificates are honored for 3 years and may be renewed within that period by taking “refresher” training. If not renewed within three years, a complete retraining is required to maintain a current certificate.

1.1.2 HSPC Chairperson establishes the educational and training requirements for HSPC members and staff who review research involving human subjects and who perform related administrative duties.

1.1.3 HSPC staff will receive initial and continuing training in the areas germane to their responsibilities, including all Standard Operating Policies and Procedures (SOP).

1.1.4 HSPC members and staff will be encouraged to attend workshops and other educational opportunities focused on HSPC functions. RAND will

support such activities to the extent possible and as appropriate to the responsibilities of members and staff.

### 1.2 Documentation

Training and continuing education shall be documented and added to the records of the HR training tracking and support system, when it is implemented.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.107

OHRP IRB Guidebook

NIH NOTICE: OD-00-039 Required Education in the Protection of Human Research Participants

https://randus.sharepoint.com/research/hspc/Pages/citi.aspx

| SOP: GA 103 | MANAGEMENT OF HSPC PERSONNEL | Version No: |
|---|---|---|

## 1. POLICY

HSPC staff provides consistency, expertise, and administrative support to the HSPC and serve as a link between the HSPC and the research community. Therefore, the highest level of professionalism and integrity on the part of HSPC staff is expected. The HSPC Chairperson manages the day-to-day operations of the HSPC staff and HSPC.

### Specific Policies

### 1.1 Job Descriptions and Performance Evaluations

Members of the HSPC staff should have a description of the responsibilities expected of their positions. The performance of HSPC staff will be reviewed according to current RAND policy.

### 1.2 Staff Positions

Staffing levels and function allocation will be determined according to RAND policy, management assessment of support requirements and budget constraints.

### 1.3 Hiring and Terminating HSPC Staff

RAND's human resource policies for recruiting and hiring staff are applicable.

### 1.4 Delegation of Authority or Responsibility

The HSPC Chairperson may authorize delegation of specific functions, authorities, or responsibilities to an appropriate staff member.

### 1.5 Documentation

RAND's HR policies determine the means of identifying, documenting and retaining formal staff interactions (such as performance reviews, termination procedures).

## 2. APPLICABLE REGULATIONS AND GUIDELINES

https://randus.sharepoint.com/pp/Pages/index_humanresources.aspx

| SOP: GA 104 | CONFLICT OF INTEREST | Version No: |
|---|---|---|

## 1. POLICY

In the environment of research, openness and honesty are indicators of integrity and responsibility, characteristics that promote quality research and can only strengthen the research process. Therefore, conflicts of interest should be eliminated when possible and effectively managed and disclosed when they cannot be eliminated.

### Specific Policies

### 1.1 Definition of a Conflict of Interest (COI)

The definition of a conflict of interest for HSPC members, consultants and staff aligns with the RAND's policies on conflicts of interest for RAND Associates. Questions regarding COI may be referred to the Office of the General Counsel.

### 1.2 Investigator COI

All RAND Associates must disclose conflicts of interest (as defined by the RAND's Conflict of Interest policy) to the HSPC. Each potential conflict will be reviewed on an individual basis. The HSPC may require that conflicts be disclosed in the informed consent or that the investigator recuse him or herself either as the principal investigator or from the project entirely.

### 1.3 HSPC Member COI

It is the responsibility of each HSPC member or alternate member to disclose any COI involving any research project submitted to the HSPC and recuse him or herself from deliberations and voting for all research projects reviewed by the full HSPC committee. The HSPC minutes will include documentation of any HSPC member with a COI on a research project who did not participate in voting on that project. HSPC members with COI on a research project do not count towards any required quorum for voting on that project.

No regular, alternate HSPC member or consultant may participate as a lead reviewer or a subcommittee member in the initial or continuing review of any research project in which the member has a COI, except to provide information as requested.

### 1.4 Education and Training in COI

HSPC members and staff are required to participate in education and training activities related to conflict of interest issues.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.107(e)
https://randus.sharepoint.com/pp/Pages/conflict.interest.aspx

| SOP: GA 105 | SIGNATORY AUTHORITY | Version No: |
|---|---|---|

## 1. POLICY

The HSPC Chairperson and other HSPC designees are authorized to sign documents in connection with the review and approval of research projects involving the use of humans as subjects, which have been reviewed and approved pursuant to RAND policies and procedures. In all cases individuals must sign their own name and indicate their title under their signature.

### Specific Policies

#### 1.1 Authorization for Signatory Authority

Authorization to sign documents not described in this policy may be made in writing by the HSPC Chairperson.

#### 1.2 Results of Reviews, Actions and Decisions

The results of reviews and actions taken by the HSPC, either by the full HSPC or by expedited review, that grant Investigators with initial or continuing approval of research, including reviews that result in exemption and not human subjects research determinations, may be signed by designated HSPC staff members.

#### 1.3 Routine Internal Correspondence

Any action, letters, memos or emails between the HSPC, and/or members of the faculty or staff of RAND that provides information concerning the review of research protocols by the HSPC or staff which do not imply or appear to imply approval of this activity, may be signed by designated staff members.

#### 1.4 Correspondence with External Agencies

Any letters, memos or emails sent to agencies of the federal government, funding agencies (whether private or public) or their agents must be signed by the HSPC Chairperson or a designee.

#### 1.5 Decisions Made by Chairperson

Any letters, memos or email sent representing the decision or opinions of the Chairperson of the HSPC or his/her respective designees, as long as such correspondence does not imply review and approval of research projects, may be signed by designated HSPC staff.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.103, 46.115

# 200- OR
# HSPC ORGANIZATION

| SOP: OR 201 | COMPOSITION OF HSPC | Version No: |
|---|---|---|

## 1. POLICY

The HSPC's role is to review proposed research in accordance with applicable law, RAND policy and standards of professional conduct and practice to ensure ethical treatment of research participants

HSPC will consist of at least five voting members. Qualified persons from multiple professions will be considered for membership. HSPC membership will not consist entirely of men or of women, one race or cultural background or of one profession. RAND will make efforts to have a diverse membership appointed to the HSPC.

### Specific Policies

### 1.1 Membership Selection Criteria

The members of the HSPC will be qualified through experience and expertise, to reviewing research proposals by applying, applicable law, standards of professional conduct and practice, RAND policy and this SOP.

To achieve diversity among HSPC members, selection will include consideration of race, gender, cultural backgrounds, clinical experience, healthcare experience, social-behavioral science experience, including but not limited to fields such as economics, statistics, sociology, politics, and sensitivity to such issues as community attitudes to assess the research submitted for review.

There will be at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. There will be one non-affiliated member who has no personal or family affiliation with RAND.

### 1.2 Composition of the Board

Regular members: Regular members must include:

A. Nonaffiliated member(s): The nonaffiliated member(s), who can be either scientific or nonscientific reviewer(s), should be knowledgeable about the local community and willing to discuss issues and research from that perspective. Consideration should be given to recruiting individuals who represent the communities from which RAND draws its research subjects. The nonaffiliated member(s) should not be vulnerable to intimidation by the professionals on HSPC, and their services should be fully utilized by the HSPC.

B. Scientific member: The HSPC will include at least one member whose primary concerns are scientific. The HSPC may use a consultant to assist in the review of research projects involving science beyond the expertise of the members.

C. Nonscientific member: The HSPC will include at least one member whose primary concerns are not in scientific areas.

D. Representatives of special groups of subjects: When certain types of research are reviewed, members or consultants who are knowledgeable about the concerns of certain groups may be required. For example, if the HSPC reviews research involving prisoners, a member who can represent this group, either an ex-prisoner or an individual with specialized knowledge about this group must be included on the HSPC.

E. Chairperson: The individual HSPC Chairperson will be a highly respected senior staff from RAND, fully capable of managing the HSPC and the matters brought before it with fairness and impartiality.

F. Consultants: The Chairperson may invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the HSPC. Consultants may not vote with the regular and alternate members of the HSPC and their presence or absence will not be used in establishing a quorum for a meeting. Consultants will used at the Chairperson's discretion, or if requested by the full HSPC. All consultants will be required to sign a Conflict of Interest Statement and a Confidentiality Agreement if they have access to confidential information.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.107

| SOP: OR 202 | MANAGEMENT OF HSPC | Version No: |
|---|---|---|

## 1. POLICY

The management of the membership of the HSPC and oversight of member appointments, HSPC related activities, communications, and other administrative details are the responsibility of the HSPC staff.

### Specific Policies

### 1.1 Term

Members will serve on the HSPC for a term of five years and Alternate Members will serve for a term of 3 years. Reappointment for additional terms may occur, by mutual agreement of the HSPC Chairperson and the HSPC member, subject to approval of the Membership and Advisory Committee.

### 1.2 Appointments

The RAND HSPC Membership and Advisory Committee determines the membership of the HSPC, including regular members and alternate members. The Committee Chair of the Membership and Advisory Committee appoints the members of the Membership and Advisory Committee, which includes e representatives of major research programs at RAND that carry out human subjects research, at least one current HSPC member, and the HSPC Chair ex officio (nonvoting). The Committee meets annually (or more often, if needed) to review the HSPC membership status, to assure that the HSPC's collective expertise is aligned with RAND's current and anticipated human subjects research agenda, as well as regulatory requirements, and to fill vacancies left by departing HSPC members.

### 1.3 Resignations and Removals

A member may resign before the conclusion of his/her term. The vacancy will be filled as quickly as possible. A member may be removed by the HSPC Chairperson at any time with the approval of the Membership and Advisory Committee.

### 1.4 Compensation

HSPC service is regarded as a valuable contribution to the RAND community and is recognized in performance reviews. HSPC members receive coverage for participation in training, reviews, and committee meetings. Members not affiliated with RAND are paid a stipend for their work reviewing studies via a letter agreement.

| SOP: OR 203 | DUTIES OF HSPC MEMBERS | Version No: |
|---|---|---|

## 1. POLICY

Each HSPC member's primary duty is the protection of the rights and welfare of the individual human beings who are serving as RAND research participants. The HSPC member must understand that he or she is not serving on the HSPC to expedite the approval of research, but to serve as a link between the Investigator and the research subjects or participants. In order to fulfill their duties, HSPC members are expected to be knowledgeable about regulations governing human subjects protection, research ethics, and the RAND policies concerning human subjects protection.

The HSPC must be fair and impartial, immune from pressure from RAND's administration, the investigators whose projects are brought before it, or other professional and nonprofessional sources.

### Specific Policies

### 1.1 Duty to RAND

The HSPC is RAND's Institutional Review Board. As such, HSPC members serve RAND as a whole rather than a particular department or program. Therefore, members must not allow their own interest or that of their department or program to supersede their duty to protect the rights and welfare of research subjects.

### 1.2 Specific Duties

1.2.1 Regular Members:

- Nonaffiliated member(s): Nonaffiliated members are expected to contribute to the evaluation of research based on their knowledge about the local community.
- Non-scientific members: Nonscientific members are expected to contribute to the evaluation of research based on their knowledge, expertise and experience. Non-scientific members should advise the HSPC if additional expertise in a non-scientific area is required to assess if the project adequately protects the rights and welfare of subjects.
- Scientific members: Scientific members are expected to contribute to the evaluation of a project on its scientific and statistical merits and standards of practice. Scientific members should advise the HSPC if additional expertise in a scientific area is required to assess if the project adequately protects the rights and welfare of subjects.
- Chairperson: In addition to the above responsibilities (germane to the member's capacity), the Chairperson leads meetings of the HSPC. Chairperson performs or delegates to an appropriate voting

HSPC member expedited review when appropriate. The Chairperson has the authority to recommend suspending the conduct of any research deemed to place individuals at unacceptable risk. The Chairperson also has the authority to recommend suspending the conduct of a project if he/she determines that an investigator is not following HSPC's requirements.

- The Chairperson may appoint a Co-chairperson or Associate Chairperson to assist or act on behalf of the Chairperson in particular HSPC matters and at HSPC meetings, either as a general procedure, or on a case-by-case basis. The Chairperson also may delegate any of his/her responsibilities as appropriate to other qualified individual(s).

1.2.2 Primary and Secondary Reviewers:

The Chairperson assigns reviewers to review a research project based on their expertise and availability. In addition to the duties described in section 1.2.1, each regular member will be expected to act as a Primary Reviewer for assigned projects. The assigned Primary Reviewer may also request additional reviewer(s) to be selected to form a Subcommittee. Secondary Reviewers may also be assigned by the Chairperson. The Primary Reviewer communicates as needed with Subcommittee members via email, telephone conference call, or face-to-face meeting. All reviewers are expected to record their review comments and motion in RHINO.

Any member of the Subcommittee can request that the full HSPC review any research project initially considered for an expedited review at the next available HSPC meeting. In that event, the HSPC staff will notify the PI that their research project will be reviewed by the full HSPC.

During meetings of the full HSPC, the Primary Reviewer, or the Secondary Reviewer, in the absence of the Primary Reviewer, presents his or her findings resulting from review of the application materials, provides an assessment of the soundness and safety of the project and recommends specific actions to the HSPC. He or she leads the HSPC discussion of the project. The Primary Reviewer may be required to review additional material requested by the HSPC for the purpose of study approval. The Secondary Reviewer, if assigned, adds to the discussion as necessary. The Chair or other designated member may present information about a project and recommendations on behalf of the subcommittee if subcommittee members are not able to be present at a meeting.

For both expedited and full committee review items, the subcommittee members are expected to record their review comments and motion in RHINO.

1.2.3 Alternate Members:

Alternate members are appointed and function in the same manner as regular members. Alternate members serve as voting members of the HSPC when the regular member is unavailable to attend an HSPC meeting or the alternate member is invited instead of the regular member, such as when a particular kind of expertise is required. When an alternate member substitutes for a regular member, the alternate member will receive and review the same materials prior to the HSPC meeting that the regular member received or would have received. The alternate member will not be counted as a voting member unless the regular member is absent or if the alternate member served as the primary or secondary reviewer, in which case the alternate member's vote will be counted in place of the regular member. The HSPC minutes will document when an alternate member replaces a regular member.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

OHRP IRB Guidebook

# 300- FO
# FUNCTIONS AND OPERATIONS

| SOP: FO 301 | RESEARCH SUBMISSION PROCEDURES | Version No: |
|---|---|---|

## 1. POLICY

RAND requires the HSPC screen all projects for the involvement of human subjects before any contact with human subjects or acquisition of human subjects data begins (including acquisition of data sets), regardless of funding source and regardless of whether the Principal Investigator (PI) believes the project is human subjects research. The HSPC staff will seek out new projects to assist the PIs in referring their projects for screening. However, it is the responsibility of the Principal Investigators to submit all work so that the required determinations can be made. Only the HSPC can make a final determination whether a project involves human subjects, regardless of the designation made by the Principal Investigator at the proposal stage.

HSPC review is generally conducted once a project has been funded and must be completed before any individual-level data collection activities may commence. However, certain RAND clients require HSPC approval before funds will be released (e.g., a National Institutes of Health "Just-In-Time review"). In this case, the PI will submit the full study information insofar as it is available to the HSPC for approval of the overall project plan and identification of any potential issues or concerns. The HSPC may approve the project in Just-In-Time review with the requirement that the PI submit amendments for approval by the HSPC once specific plans and project materials are available and before the human subjects research activity may take place.

PIs must submit all new projects for HSPC screening and review using the RAND HSPC Information Online (RHINO) system. It is the responsibility of the Principal Investigator to ensure that the RHINO submission is complete and accurate: only the PI may formally submit the project in RHINO for approval. These procedures help assure careful attention to potentially high-risk projects, while avoiding prolonged review of low-risk projects. The first step in the review process is to make the distinction between the two.

HSPC members often rely solely on the documentation submitted by investigators for initial and continuing review. Therefore, this material must provide HSPC members with enough information about a study to assess if it adequately meets the HSPC's criteria for approval. However, HSPC members may require additional information and may elect to communicate directly with project staff to clarify information or discuss procedures to meet ethical and regulatory requirements. The project staff is responsible for actual development of any materials or procedures submitted to the HSPC.

A submitted protocol will be scheduled for HSPC review only when the HSPC staff and reviewers have determined that the information and materials submitted present an adequate description of the proposed research.

RAND's DoD Federally Funded Research and Development Centers (FFRDC) have a screening procedure in place where the PIs are required to fill out a unit screening form to determine whether their project would need HSPC review. As of 6/29/2020, the unit screening form and the unit screening process are part of RHINO 2. All research units at RAND have a contact person(s) who functions as a liaison between the unit and the HSPC. Designated personnel at each FFRDC function as screeners to determine whether a project meets the DoD definition of research involving human subjects. If the project does not meet the definition for "not research involving human subjects" according to the DoD Instruction 3216.02, or if the project is identified as possibly presenting more than minimal risk or involves other risk or hazards, such as legal issues, or if the project involves specific procedures requiring HSPC review, the FFRDC screener will notify the PI (with a copy to the HSPC) to complete and submit a RAND HSPC Information Online (RHINO) form, which is a formal online-based application system.

The DoD definition of not research involving human subjects most applicable to RAND research is:

> Activities, including program evaluation and surveys, user surveys, outcome reviews, and other methods, designed solely to assess the performance of DoD programs where the results are only for the use of government officials responsible for the operation or oversight of the program being evaluated.

The designated Unit screeners will make a determination of whether a project meets this definition, subject to approval by the HSPC and concurrence of the DoD representative responsible for monitoring human subjects research for the project. HSPC may audits these determinations.

## Specific Policies

### 1.1 Submission Requirements for Initial Review

1.1.1 Electronic submission requirements via RHINO for initial review are outlined in the HSPC website. PIs applying for initial approval of proposed project must follow the guidance and complete a study application. Unless an FFRDC unit screener has determined that the DoD research managed by an FFRDC is "not human subjects research", a PI or someone who is thoroughly familiar with the design and operation of the project and has a current CITI Training certificate, must accurately and completely fill out the RHINO form. *If someone other than the PI fills out the form, the PI must review all the information to ensure it is current, complete and accurate before submitting the initial form.* The PI has the responsibility for submission of current, complete and accurate information. The information submitted is subject to audit.

## 1.2 Submission Requirements for Ongoing Review

1.2.1 During the approval period, PIs must submit via RHINO documentation of all changes in the project or status of the project including, but not limited to:

- Deviations from the project (project violations)
- Reports of serious or unexpected adverse events
- Changes to the status of Principal or Co-investigators
- Changes to the research activities or study materials, such as purpose, target population, procedures, recruitment materials, or consent forms

1.2.2 Continuing Review

All research that has been approved by the full HSPC will be reviewed in continuing review on an annual basis. Per the 2018 Requirements, continuing review is eliminated for all studies that undergo expedited review, unless the reviewer explicitly justifies why continuing review would enhance protection of research subjects. For studies initially reviewed by the full HSPC, once certain specified procedures are all that remain for the study, continuing review would not be required, unless specifically mandated by the HSPC. These activities include: (1) Research eligible for expedited review in accordance with 45 CFR 46.110; or (2) Research that has progressed to the point that it involves only one or both of the following, which are part of the HSPC-approved study: (a) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or (b) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

The revised rule does not require investigators to provide annual confirmation to the IRB that such research is ongoing and that no changes have been made that would require the IRB to conduct continuing review. Institutions that choose to require some accounting of ongoing research not subject to continuing review have significant flexibility in how they implement their own requirements.

For projects requiring a continuing review, the PI (or designee) must complete the continuing review form so that the HSPC can determine whether to extend approval of the research project. If the PI's designee completes the form, the PI is responsible for reviewing the information to ensure it is current, complete and accurate before submitting the form.

If the research project is not approved prior to the expiration date, all human subjects activity must cease.

If the PI does not supply the HSPC with timely required information, the HSPC staff will report such noncompliance to the applicable research unit. PI's continued noncompliance with HSPC requests for continuing review information will be reported to HR, Contracts, Director of Global Research Talent Operations and the General Counsel's office.

### 1.3 Action Taken If Documentation is Not Adequate or Additional Information is Required

If the HSPC or HSPC staff determines that the submitted documents are not adequate, the HSPC may require PIs to submit additional information, answer questions, or explain the details of the project. The HSPC will not review incomplete submissions.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.115

https://randus.sharepoint.com/research/hspc/Pages/home.aspx

| SOP: FO 302 | HSPC MEETING ADMINISTRATION | Version No: |
|---|---|---|

## 1. POLICY

Except when an expedited review procedure is used, the HSPC will review proposed research project at convened meetings at which a quorum is present. The HSPC will meet monthly, unless there is no item to review. The Chairperson may request an ad hoc committee review if there is an emergency research project that needs to be reviewed as soon as possible.

### Specific Policies

#### 1.1 Quorum

1.1.1 A quorum is defined as one half of the number of regular members plus one.

1.1.2 A quorum consists of regular and/or their alternate members and includes: at least one member whose primary concerns are in scientific areas, and one member whose primary concerns are in nonscientific areas.

1.1.3 An alternate member may attend in the place of an absent regular member in order to meet the quorum requirements outlined above.

1.1.4 A special consultant(s) will not be used to establish a quorum.

1.1.5 A quorum includes a member who abstains from voting.

1.1.6 If a member recuses him/herself from deliberations and voting because of a COI, or for any other reason, the quorum does not include that member for the duration of review of the item from which the member is recused.

#### 1.2 Primary Reviewers

Prior to the meeting, the Chairperson will designate primary reviewers for each research proposal. The primary and secondary reviewers' duties are described in SOP OR 203 above.

#### 1.3 Meeting Materials Sent Prior to HSPC Meetings

The HSPC staff will send all HSPC members project documentation required for review sufficiently in advance of the meeting (e.g. 5 to 7 business days) to allow time for adequate review. These include:

1.3.1 Agenda: A meeting agenda will be prepared by the HSPC Administrator or designee and distributed to HSPC members prior to each meeting. A copy of the agenda and attached materials will be maintained on file with the meeting minutes.

All HSPC members must review the agenda to determine if they have any a potential COI concerning any research project scheduled for review at that meeting, advise the HSPC of their potential COI at the beginning of the meeting and recuse themselves from voting on such research project. The HSPC minutes will specifically reflect COI recusals as they occur during meetings.

1.3.2 Reviewer materials: The HSPC staff will send all HSPC members who have confirmed attendance at a meeting the materials necessary to review the submissions to determine whether the HSPC approval criteria are met. The materials include all submitted project materials including a copy of the RHINO application.

1.3.3 At the invitation of the HSPC, the PI and other project key staff and other interested individuals may attend the portion of the HSPC meeting relating to their research project to answer questions and provide information. Unless otherwise requested to leave prior to voting on their research project, the PI and other key project staff may stay through voting on their project.

1.3.4 With the approval of the HSPC Chair, other RAND staff may occasionally attend HSPC meetings to observe.

### 1.4 Minutes

1.4.1 Recording: The HSPC Administrator attending a meeting will take minutes of each meeting. Minutes will include the following:

- Meeting attendance; including status of each attendee (regular member, alternate member, etc.), and conflicts of interest, if any;
- Actions taken by the HSPC on each agenda item requiring full HSPC action, including the basis for requiring changes in or disapproving the research;
- Summary of the discussion of controverted issues and resolution;
- Any vulnerable population findings and risk determination, if applicable;
- Voting results, including number for, against, abstentions and members who recused themselves and reason for recusal.

1.4.2 The HSPC staff will distribute finalized draft minutes, which have been reviewed and approved by the Primary Reviewers and the HSPC Chair, to HSPC members at the next HSPC meeting for their review and approval.

- The HSPC Administrator or designee will make any corrections to the minutes requested by the HSPC and provide the revised minutes to the HSPC members at the following meeting.
- The HSPC staff will maintain copies of the minutes and the agenda. The finalized minutes will be posted on the RAND internal website for access.

### 1.5 Telephone Use

1.5.1 Convened meeting using speakerphone:

Should a member not be able to be physically present during a convened meeting, but is available by telephone, the meeting can be convened and the member who is not physically present will be connected to the rest of the members via speakerphone. In this manner, all members will be able to discuss the project even though one or more members is not physically present. Members participating by such speakerphone call may vote, provided they have had an opportunity to review all the material the other members have reviewed.

1.5.2 Meetings Conducted Solely Via Telephone Conference Calls:

On occasion, meetings may be convened via a telephone conference call. A quorum (as defined above) must participate for the conference call meeting to be convened. To allow for appropriate discussion to take place, all members must be connected simultaneously for a conference call to take place -- "telephone polling" (where members are contacted individually) will not be accepted as a conference call.

Members neither present at the convened meeting, nor participating in the conference call may not vote on an issue discussed during a convened meeting

### 1.6 Voting

Members of the HSPC vote upon motions as made and seconded according to the criteria for approval (see SOP RR 402 and 404) below. Members also will determine level of risk and the frequency of review for each project An HSPC staff will count the votes and document them in the meeting minutes.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.103, 46.108, 46.109, 46.115

| SOP: FO 303 | ADMINISTRATIVE REVIEW AND DISTRIBUTION OF MATERIALS | Version No: |
|---|---|---|

## 1. POLICY

The efficiency and effectiveness of the HSPC is supported by administrative procedures that ensure that HSPC members not only have adequate time for thorough assessment of each proposed study, but that the documentation they receive is complete and clear enough to allow for an adequate assessment of study design, procedures, and conditions.

### Specific Policies

### 1.1 Exemptions

The HSPC member(s) review(s) the information from the project application, ask(s) for more information as needed, and determine(s) whether the study meets the criteria for exemption. Even if a project is sent through the exemption review procedure the reviewers are free to make any determination including that no human subjects are involved or full committee review is required. The only determination they cannot make is to disapprove the study, which is reserved for the full committee. A motion of “Exempt with conditions” is not available, so any issues raised must be resolved before a determination of exemption can be issued to the PI.

### 1.2 Incomplete Submissions

Incomplete submissions will not be accepted for review. The HSPC staff will notify the submitting PI to obtain any outstanding documentation or additional information before the submission is scheduled for review. For example, the HSPC staff may request draft data collection forms, a Data Safeguarding Plan, changes to Population or Procedures or other pertinent changes.

### 1.3 Scheduling for Review

The HSPC staff will forward complete submissions that appear to meet qualifications for expedited review to the Chairperson or his/her designee. If a submission meets expedited review requirements, the review will be performed as described in SOP RR 401 (Expedited Review) below. All other submissions will be placed on the agenda for the earliest meeting possible for review by the full HSPC.

A list of upcoming meeting dates is provided in the HSPC website along with the dates required for submission of complete materials in advance of the meeting date. Whenever possible, Just-In-Time reviews will be scheduled for the closest available meeting as long as sufficient information is provided in time to circulate it to the HSPC members in advance of the meeting and allow time for adequate consideration of the project.

### 1.4 Distribution of Materials Prior to HSPC Meetings

Copies of submission materials will be distributed to all HSPC members, generally at least five (5) business days prior to the meeting, either via paper and/or electronically in a shared file for the members (RAND SharePoint). Each regular member of the HSPC, and any alternate members attending the meeting in place of a regular member, will receive a copy of the initial submission material. Consultants will only receive copies of material that pertain to those research projects for which they are consulting. The project teams whose submissions will be reviewed will also receive a copy of the agenda and the materials that pertain to their research project that will be reviewed by the HSPC.

### 1.5 Confidentiality

All material received by the HSPC will be considered confidential and will be distributed only to meeting participants (regular members, alternate members, consultants and project teams for the purpose of review). All submission materials will be stored in an HSPC study file with access limited to HSPC members, HSPC staff and project team members.

### 1.6 Ownership of HSPC Materials and Determinations

All materials submitted to the HSPC or provided by the HSPC, such as correspondence and determinations, are the property of RAND and may not be provided to individuals outside RAND or the HSPC except for purposes of HSPC approved review and audit without the permission of the HSPC Chair or the Office of General Counsel.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.108

| SOP: FO 304 | DOCUMENTATION AND DOCUMENT MANAGEMENT | Version No: |
|---|---|---|

## 1. POLICY

The HSPC's files must be maintained in a manner that contains a complete history of all HSPC actions related to review and approval of a project including continuing reviews, amendments and adverse event reports. All records regarding a submitted project (regardless of whether it is approved) must be retained in an appropriate manner as required by regulatory requirements and/or RAND policy.

Records must be accessible for inspection and copying by authorized representatives of the Sponsor, funding department or agency, regulatory agencies, and auditors at reasonable times and in a reasonable manner.

Documents must be submitted to the appropriate funding entity as instructed by the funding entity.

### Specific Policies

### 1.1 Document Retention

The HSPC will retain all records regarding a project submission (regardless of whether it is approved) for at least three (3) years. The HSPC will retain all records regarding approved research projects for at least three (3) years after completion of the research or termination of HSPC approval, whichever shall last occur. All currently active project-related materials are retained in RHINO.

RAND will retain signed consent forms of projects that were approved in full Committee review for seven (7) years after the completion of a project. The HSPC will obtain the signed consent forms, digitize and archive them, then destroy the paper forms. The archived consent forms will be destroyed seven years after the completion of the pertinent research project.

### 1.2 HSPC Administration Documents

The HSPC will maintain and retain all records regarding HSPC administrative activities that affect review activities for at least three (3) years.

1.2.1 The HSPC will maintain rosters of regular and alternate HSPC members identified by name, earned degrees, representative capacity, and indications of experience sufficient to describe each regular and alternate member's chief anticipated contribution to the HSPC's deliberations; and any employment or other relationship between each member and HSPC and/or RAND (e.g., full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant).

In addition to the above information, the roster will indicate the regular member for whom the alternate may substitute.

1.2.2 The HSPC will maintain current and previous versions of the Standard Operating Policies and Procedures.

### 1.3 Destruction of Copies

In accordance with RAND policy, at the end of all HSPC meetings, the HSPC staff will collect and destroy all confidential material received by the HSPC, and in excess of the required original documentation and appropriate controlled forms.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.103,115

# 400- RR
# REVIEW OF RESEARCH

| SOP: RR 401 | EXPEDITED REVIEW | Version No: |
|---|---|---|

## 1. POLICY

An expedited review procedure consists of a review of research by the Chairperson, HSPC staff, or by one or more experienced reviewers designated by the Chairperson or HSPC staff from among members of the HSPC.

The categories of research that may be reviewed by the HSPC through an expedited review procedure include research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the specific categories listed in the regulations at 45 CFR 46.110.

**Specific Policies**

### 1.1 Definition of Minimal Risk

Minimal risk is defined at 45 CFR 46.102(i) as “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.”

The DoD notes the following in their Instruction sheet 3216.02: The phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests” in the definition of minimal risk shall not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

### 1.1 Expedited Review Categories

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

   (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

   or

   (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the

medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

   (a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

   (b) from other adults and children[2] , considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means.
   Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)
   Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring

[2] Children are defined in the DHHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." 45 CFR 46.402(a).

radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt. This category does not apply to previously collected data obtained for research purposes)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt. This category includes previously collected data obtained for research purposes)

8. Continuing review of research previously approved by the convened IRB as follows:

    a. where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

    b. where no subjects have been enrolled and no additional risks have been identified; or

    c. where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

1.2.1 The activities listed should not be deemed to be of minimal risk simply because they are included on the list of eligible research. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

1.2.2 The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. Furthermore, the expedited review procedure may not be used for classified research involving human subjects.

### 1.3 Authority of the Expedited Reviewer

The HSPC Chairperson (or designated reviewer) may exercise all of the authorities of the HSPC, except for disapproving the project, including an amendment. A research project including an amendment, may be disapproved only after review by the full HSPC. An expedited reviewer or subcommittee may decide that expedited review is not appropriate and determine that the review should be conducted in full committee.

### 1.4 Notification of the HSPC

At the next convened meeting, the attending members will be notified of all the new projects approved via the expedited review procedure.

### 1.5 Documentation

If the project qualifies for expedited review, the HSPC Chairperson or designee will document his/her determination of the applicable expedited review category(ies).

The HSPC staff will document in RHINO all projects that were reviewed via expedited review and any issues resolved relating to questions that HSPC members had concerning the research reviewed.

### 1.6 Additional Items That May be Reviewed by the Chairperson or Designee

1.6.1 Conditional approval pending minor revisions, clarification: Revisions to consent documents and other documentation or clarifications submitted as a result of full HSPC review and as a condition to final approval may be reviewed by the HSPC Chairperson or his/her designee. The HSPC Chairperson or designee can issue final approval providing the revisions, documentation or clarifications do not indicate or result in a change to the project or change the risk/benefit ratio.

1.6.2 Continuing review:

HSPC staff may approve a project in continuing review if the project was previously approved in expedited review and if there have been no changes or amendments and no events reported since the last review.

The HSPC Chairperson/designee may use the expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized. Any protocol revision

that entails more than a minimal risk to the subjects must be reviewed by the full HSPC at a convened meeting.

- Revisions to informed consent documents: Minor changes to informed consent documents that do not affect the rights and welfare of study subjects, or do not involve increased risk or significant changes in study procedures may be reviewed and approved by the Chairperson/designee.
- Reportable Event: A reportable event is immediately assigned to the HSPC reviewer(s) of record. Other members may be assigned at the discretion of the Chairperson. The reviewer may request more information or forward recommendations to the Chairperson. The Chairperson makes a determination of whether to suspend the study, require changes, close the event or refer it to the full committee for further consideration

## 2. APPLICABLE REGULATIONS AND GUIDELINES

Minimal Risk: 45 CFR 46.102

Expedited Review: 45 CFR 46.110

OHRP IRB Guidebook

| SOP: RR 402 | RESEARCH EXEMPT FROM FURTHER HSPC REVIEW | Version No: |
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## 1. POLICY

Research activities in which the only involvement of human subjects will be in one or more specific categories (see below) may be exempt from further HSPC review. Exempt status may be only determined by the HSPC Chairperson, HSPC staff or HSPC members who are assigned by the Chairperson to review a submitted project.

Determination of exemption must be based on regulatory criteria, including OHRP guidance or recommendations on the interpretation of the exempt categories. The HSPC will document all determinations that research is exempt from further HSPC review. Research activities in categories listed below will not be deemed to be exempt simply because they are included on the list of eligible research. Research activities in categories listed below merely means that the activity is eligible for consideration for exemption when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

### Specific Policies

### 1.1 Exempt Research Activities

Research activities in which the only involvement of human subjects will be in one or more of the following categories may be exempt from HSPC review if the research presents no more than minimal risk:

(1). Research conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2). Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met: (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §__.111(a)(7).

(3)(i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

(A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(C) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §__.111(a)(7).

(ii) For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

(4) Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of “health care operations” or “research” as those terms are defined at 45 CFR 164.501 or for “public health activities and purposes” as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 *et seq.*

(5) Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

(i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

(6) Taste and food quality evaluation and consumer acceptance studies:

- If wholesome foods without additives are consumed, or
- If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

(7) Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by § __.111(a)(8).

(8) Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

(i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with § __.116(a)(1) through (4), (a)(6), and (d);
(ii) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with § __.117;
(iii) An IRB conducts a limited IRB review and makes the determination required by § __.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and (iv) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

### 1.2 Exempt Research Approval Period

Annual continuing review is not required for research determined to be exempt.

### 1.3 Changes to the Project Made After an Exempt Determination

Investigators are required to report changes that may affect the initial exempt determination and to notify the HSPC of any new procedures so they can be reviewed by the HSPC.

### 1.4 Adverse Events

It is the investigator's responsibility to report any injuries to research participants or other adverse events that occur on a study that is exempt from further review.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.104(d); 45 CFR 46.102

| SOP: RR 403 | INITIAL REVIEW - CRITERIA FOR HSPC APPROVAL | Version No: |
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## 1. POLICY

Research that involve living individuals about whom an investigator conducting research obtains data through intervention or interaction with the individual, or obtains identifiable private information must meet certain criteria before research-related procedures can be initiated. The criteria are based on the principles of justice, beneficence and autonomy as discussed in the Belmont Report and are specified below. In addition, certain other criteria that are unique to RAND may apply and must be met as well.

### Specific Policies

### 1.1 Criteria for Approval of Research

In order for a research project to be approved, the HSPC must find that:

1.1.1. Risks to subjects are minimized:

- By using procedures that are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
- Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

1.1.2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result.

- In evaluating risks and benefits, the HSPC will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies that subjects would receive even if not participating in the research). The HSPC should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

1.1.3. Selection of subjects is equitable.

- In making this assessment the HSPC should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, or individuals with impaired decision-making ability, or economically or educationally disadvantaged persons.

1.1.4. 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 appropriate local, state and federal regulations.

1.1.5. Informed consent will be appropriately documented or appropriately waived as required by local, state and federal regulations.

1.1.6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

1.1.7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

1.1.8. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

### 1.2 Reliance on Other IRBs for Review and Approval of Research Conducted at RAND.

The HSPC may enter into joint review arrangements, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort. For example, RAND has a Memorandum of Understanding (MOU) in place with the University of California, Los Angeles (UCLA), where one institution, depending on the scope of the research, will serve as the sole reviewing institution for health services and related research conducted by both institutions.

The Revised Common Rule requires, with some exceptions, that any institution located in the United States engaged in cooperate research must rely upon approval by a single IRB for that portion of the research that is conducted in the US. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research. The compliance date of this requirement was January 20, 2020. Due to COVID-19, more exceptions to the single IRB requirement were issued on October 8, 2020. The HSPC will take into account the collaborating institutions, the prime funding institution and the human research activities involved to enter into any IRB reliance agreement where either the RAND HSPC will serve as the IRB of record or rely on another institution's IRB to serve as the IRB of record for RAND.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.111

45 CFR 46.114

https://randus.sharepoint.com/research/hspc/Pages/defer.aspx

https://www.hhs.gov/ohrp/regulations-and-policy/single-irb-exception-determinations/november-2019-exception-determination/index.html

https://www.hhs.gov/ohrp/regulations-and-policy/single-irb-exception-determinations/october-2020-exception-determination/index.html

| SOP: RR 404 | ONGOING REVIEW | Version No: |
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## 1. POLICY

The regulations authorize HSPC to establish procedures for the concurrent monitoring of research activities involving human subjects. Periodic review of research activities is necessary to determine whether approval should be continued or withdrawn.

HSPC may withdraw its approval of research at any time if warranted by the conduct of the research. For example, HSPC approval for the conduct of a study may be withdrawn if it determines the risks to the subjects are unreasonably high; more than an expected number of adverse events have occurred; there have been unexpected serious adverse events; or evidence that the investigator is not conducting the investigation in compliance with HSPC or RAND guidelines. HSPC may also require more frequent review of the study to determine if approval should be withdrawn or enrollment stopped until corrective measures can be taken or the study terminated. Ongoing review includes, but may not be limited to the following:

- Site Visits, Observation and Verification
- Review of Adverse Events and other Reportable Events
- Review of Amendments
- Review of Significant New Findings
- Review of Reports from Employees, Staff and Faculty
- Review of Noncompliance
- Review of Complaints from research participants or others

**Specific Policies**

### 1.1 Site Visits, Observation and Verification

HSPC staff or members may perform site visits or use another party, either affiliated or not with the institution, to verify information in the study application, or in any interim or continuing review submissions, observe the informed consent process of research it has approved, and to verify that the study is being conducted as required by the HSPC and within the RAND policies and procedures and site-specific procedures as appropriate.

Other means of verification include questionnaires sent to investigative staff to verify information submitted by the Investigator. Investigators may be asked to submit copies of signed informed consent forms or other documents to ensure their compliance with HSPC requirements. The HSPC may conduct interviews with screened and/or enrolled subjects as deemed necessary

The HSPC will consider the following criteria to determine if a site visit or verification process is required:

- The research involves vulnerable populations or high risk interventions.
- The investigator has a history of serious or continuing non-compliance related to continuing review and the information provided by the investigator is inconsistent with other information known to the HSPC and the inconsistency cannot be resolved through communication with the investigator.
- The HSPC has reason to doubt the veracity of the information provided by the investigator.
- Procedures are particularly complex or may be subject to misinterpretation or error, such as when delegated to individuals who are not RAND staff.
- Any other reason where the HSPC believes observation or verification is appropriate.

## 1.2 Adverse Events and Other Reportable Events

Subject safety is of the greatest importance for both the individual subject and the goals of a research study. The Principal Investigator is responsible for reporting any actual or potential noncompliance with required study procedures such as Data Compromises or Adverse Events to the HSPC within one working day of any such incident.

(a) *Data Compromise* means disclosure of Human Subjects Information to any individual not specifically authorized to receive or possess such information, or any unplanned loss of possession or control of Human Subjects Information.

(b) *Adverse Event* means an incident occurring in the course of research that deviates from the existing approved research plan; that may be unanticipated or surprising; and/or that may have potentially negative consequences for the research subject(s) involved (including consequences associated with intentional or inadvertent breaches of confidentiality).

The PI is expected to submit a report to HSPC by filling out a RHINO Reportable Event form within 24 hours of the data compromise or adverse event. If the PI is unable to do so, the PI is expected to contact the HSPC by phone and/or email immediately and follow up by completing the Reportable Event form as soon as possible.

Submitted Reportable Event forms will be reviewed by the HSPC Chairperson or designee and legal counsel, if necessary. Additional reviewers may be assigned by the Chairperson as needed. Every attempt should be made by the reviewers to respond quickly to the PI to discuss:
• An assessment of the magnitude of the harm,

• A determination of whether the project or any portion should be suspended until the event is resolved,
• Suggestions for ways to mitigate any harm already done, and
• changes in project protocols to help prevent such harm from reoccurring.

When the reviewers agree on what needs to be done, that is communicated to the project, including possible suspension of some activities or of the project as a whole if needed. Should changes in the project protocol be required, they are treated as conditions of approval, and notice of closure of the event is only sent when they have been met. If all or part of the project was suspended, the suspension may be lifted at that time.

### 1.3 Amendments

Changes in approved research, during the period for which approval has already been given, may not be initiated without prior HSPC review (full or expedited review, as appropriate) and approval, except where necessary to eliminate apparent immediate hazards to human subjects.

Investigators or Sponsors must submit requests for changes to the HSPC in writing. Upon receipt of the protocol change, the Chairperson/designee will determine if the revision meets the criteria for minimal risk. If the change represents more than a minimal risk to subjects, it must be reviewed and approved by the full HSPC. Minor changes, involving no more than minimal risk to the subject, will be reviewed by the expedited review procedure.

### 1.4 Significant New Findings

During the course of a study, the HSPC may review reports generated from a Data and Safety Monitoring Board (DSMB), adverse event reports, current literature, and other sources to ascertain the status of the study and assess whether or not the risk/benefit balance is still acceptable. HSPC will determine whether or not new information needs to be conveyed to subjects, or if a segment of the population may be bearing an undue burden of research risk or being denied access to promising intervention.

### 1.5 Reports From Employees, Staff, Research Participants and Others

It is the responsibility of the HSPC staff and members to act on information or reports received from any source that indicate a study being conducted at any facility under the jurisdiction of the HSPC has adversely affected or threatens to adversely affect the rights and welfare of research subjects. The HSPC routinely provides an 800 number for communications with the HSPC which is monitored by an HSPC staff daily during normal work periods. Serious concerns will be reported to the Chair immediately. All calls received will be logged with date, time, phone number and name of caller, the concern or problem that was presented, resolution by the HSPC, and communication back to the caller if required.

### 1.6 Ensuring Prompt Reporting of Any Serious or Continuing Noncompliance with Applicable Regulations or the Requirements or Determinations of the HSPC

All credible reports of inappropriate involvement of human subjects in research must be investigated by the HSPC staff and referred to the HSPC. The results of the investigation will be reported to the appropriate RAND official(s). Regulatory authorities or Sponsors may also be notified. Such reports of noncompliance may come from any source including HSPC members, investigators, subjects, institutional personnel, the media, anonymous sources or the public.

The HSPC has the authority to suspend or terminate approval of research that is not being conducted in accordance with the HSPC policies, is not in compliance with federal regulations, or has been associated with unexpected actual or potential harm to subjects. All such suspensions and or terminations will be reported to the OHRP or DoD as appropriate.

Enrolled subjects will be notified if a protocol in which they are enrolled is suspended or terminated by HSPC. The HSPC will determine at a convened meeting how and when the notification will take place. The HSPC will consider whether to notify any former subjects.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.103, 46.109, 46.115

https://randus.sharepoint.com/research/hspc/Pages/home.aspx

| SOP: RR 405 | CONTINUING REVIEW – CRITERIA FOR RENEWAL | Version No: |
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## 1. POLICY

The HSPC conducts continuing review of research taking place within its jurisdiction at intervals appropriate to the degree of risk, but not less than once per year, except as described below in section 1.5. If an investigator decides to modify an exempt human subjects research project, the investigator must submit the modified research protocol to the HSPC for review prior to implementation of the modified research project to ensure the changes do not affect the initial exempt determination.

### Specific Policies

### 1.1 Interval for Review for Purposes of Renewal

The HSPC must conduct continuing review of protocols for purposes of renewal of the HSPC approval period, at intervals appropriate to the degree of risk, which is determined at the initial review, but not less than once per year. “Not less than once per year" means that the research must be reviewed on or before the one-year anniversary of the previous HSPC review date, even though the research activity may not have begun until some time after the approval date.

The HSPC follows the procedure for maintaining a fixed anniversary date as long as the subsequent continuing reviews, whether via a full committee or an expedited review, are conducted within the 30-day period from the expiration date. For example, if the HSPC conducts initial review of a research project and approves it without conditions on May 1, 2016 for one year, the HSPC may conduct its first continuing review anytime between April 1 and May 1, 2017 and re-approve the research for another one-year period that expires on May 1, 2017. If there are conditions, the approval date will fall on the date the conditions are satisfied.

Investigators or qualified designees are required to submit a periodic report prior to the expiration of the study or as specified by the HSPC, but at least annually. The report should be filed 60 days before the study approval period ends for a study that requires convened review. The PIs are ultimately responsible for keeping track of the expiration dates of their studies.

### 1.2 Extensions of Approval Period

There is no grace period extending the conduct of the research beyond the expiration date of HSPC approval. Extensions beyond the expiration date will not be granted. If Continuing Review Report forms and other requested progress reports are not received as required, the investigator must suspend the study and study enrollment until HSPC reviews and approves continuation of the research.

The HSPC will address on a case-by-case basis those rare instances where failure to enroll new subjects would jeopardize the safety or well-being of an individual.

### 1.3 Criteria for Renewal

Continuing review must be substantive and meaningful. When considering whether or not to renew approval for a study, the HSPC revisits the same criteria used to grant initial approval. Therefore, the HSPC (or the reviewers for protocols reviewed under an expedited procedure) must determine that:

- The risks to subjects continue to be minimized and reasonable in relation to the anticipated benefits;
- The selection of subjects continues to be reasonable in relation to anticipated benefits;
- Informed consent continues to be appropriately documented;
- Additionally, there are:
    - Provisions for safety monitoring of the data,
    - Protections to ensure the privacy of subjects and confidentiality of data, and
    - Appropriate safeguards for vulnerable populations.

Because it may be only after research has begun that the real risks can be evaluated and the preliminary results used to determine the actual risk/benefit ratio, HSPC will consider whether approval of the study can be renewed at the same risk/benefit ratio as the previous approval, or if new information has changed that determination.

In order to determine whether to renew approval of a study, HSPC will review the following:

1) Continuing review form: All HSPC members participating in the meeting shall receive the continuing review form prepared and submitted by the Investigator including the number of subjects entered to date and since the last review. The progress report shall summarize adverse event experiences and amendments.
2) Currently approved consent document to ensure that the information is still accurate and complete. Any significant new findings that may relate to the subject's willingness to continue participation should be provided to the subject in an updated consent document after review and approval by HSPC as an amendment.
3) Other materials – The primary reviewer may require that the continuing review packet distributed to members include additional materials relevant to review, such as event reports, amendments, or other materials.

### 1.4 Possible Outcomes of Continuing Review

As an outcome of continuing review, the HSPC may approve the research or require that the research be modified or halted altogether. The HSPC may

need to impose special precautions or relax special requirements it had previously imposed on the research protocol.

### 1.5 Circumstances Not Requiring Continuing Review

Unless the HSPC determines otherwise, continuing review of research is not required in the following circumstances:

- Research eligible for expedited review in accordance with § 45 CFR 46.110;
- Research reviewed by the IRB in accordance with the limited IRB review described in § 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8);
- Research that has progressed to the point that it involves only one or both of the following, which are part of the HSPC-approved study:

  (A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

  (B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

### 1.6 Failure to Submit for Renewal

The HSPC makes reasonable efforts to obtain PI's cooperation with continuing review requirements. Failure by a PI to submit required information in a timely manner may result in termination or suspension of study approval, reports to unit and RAND management staff and, where required, to clients.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.111, 45 CFR 46.103(b) and 46.109(e)

OPRR Reports 95-01

http://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html

http://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-continuing-review-2010/index.html

| SOP: RR 406 | STUDY COMPLETION | Version No: |
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## 1. POLICY

The completion or termination of the study is a change in activity and must be reported to the HSPC. Although subjects will no longer be "at risk" under the study, a final report via a continuing review form to the HSPC allows it to close its files as well as provide information that may be used by the HSPC in the evaluation and approval of related studies. Per the RAND policy, when the study ends, the identifiable data must be destroyed or the PI must provide justification for retention of identifiable data. The PI must notify the HSPC when all identifying information has been destroyed.

### Specific Policies

When a project has ended or is being moved to another institution by a researcher leaving RAND, it may be possible for the HPSC to close its files. The information gathered by a Continuing Review Form is also designed to determine whether the project can be closed or needs continuing monitoring.

If a project is being moved to another institution, it can be closed at RAND once the new institution provides documentation of ownership and approval from the institution to which the research is being transferred.

If a project is retaining identifiable data, the HSPC files cannot be closed unless identifiable data are being kept solely for the purpose of possible future funding for other projects. Project participants must have granted permission for their identifiers to be kept beyond project completion. For all other projects, monitoring of the data will continue annually with a Continuing Review Form until the identifiers are destroyed. Once identifiers have been destroyed the HSPC can close its files, although RAND will keep signed consent forms for seven years after the project’s end for full committee projects.

If all planned data collection activities have ended but analysis is continuing, the project will be asked to continue adhering to the approved Data Safeguarding Plan. Determination of whether to approve a project in continuing review or close it can sometimes be made by one of the HSPC administrators.

If an expired study is identified, the HSPC staff will attempt to reach out to the PI and/or the main study contact of the expired protocol directly or via their unit liaisons if the PI is no longer at RAND to request the PI submit a final continuing review form to close out the study. If the PI is no longer at RAND, the HSPC may accept an email from the PI affirming that the identifiable data has been destroyed.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.103, 46.109

| SOP: RR 407 | CATEGORIES OF ACTION | Version No: |
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## 1. POLICY

As a result of its review, the HSPC may approve, require modifications in (to secure approval), or disapprove the proposed research activity, or table review until additional information is received. Except when the expedited review procedure is used, these actions will be taken by a vote of a majority of the regular and alternate members present at a full committee meeting, except for those members who recuse themselves from voting present but unable to vote in accordance with HSPC's conflict of interest policies described in section G104 above. When reviewed via expedited review, the Chairperson or designee can approve or conditionally approve a study.

### Specific Policies

### 1.1 Determinations

The HSPC may make one of the following determinations as a result of its review of research submitted for initial review or continuing review:

A. Approval: The protocol and accompanying documents are approved as submitted. Approval is effective on the day the study is approved by an action of the convened HSPC or Chairperson or designee. Approval expires one year from the effective date, unless otherwise noted.

B. Conditional (Contingent) Approval: Minor modification of, or addition to, a protocol or accompanying document(s) is required. Changes will be voted upon during HSPC's meeting, as well as the terms of approval. The investigator will be informed in writing of the required changes and requested information and must provide the HSPC with the changes or information.

The HSPC Chairperson or his/her designee has the authority to review the information via expedited review unless the HSPC requires that the material or information be reviewed by the full HSPC, the primary reviewer or another individual delegated by the HSPC to review the response. Upon satisfactory review, approval will be issued as of the date that the requested information or materials are approved. However, the expiration date of HSPC approval will be based on the anniversary date of the initial HSPC review. Subjects must not be recruited into the study until final approval has been issued.

C. Tabled: The full HSPC determines that the project raises significant questions (e.g. open-ended questions to the study design, procedures, risks, etc.) that require its reconsideration after additional information is received from the Sponsor and/or investigator. The additional information will need to be re-reviewed by the full HSPC. The expiration date of HSPC approval will be based on the anniversary date of the latest full HSPC review date.

D. Disapproval: The project is disapproved by the full HSPC because it fails to meet one or more criteria used by the HSPC for approval of research.

Disapproval cannot be given through the expedited review mechanism and may only be given at a convened HSPC meeting. The investigator will be notified in writing of the reasons for the determination and will be given an opportunity to respond in person or in writing.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.109

# 500- CO
# HSPC COMMUNICATION AND NOTIFICATION

| SOP: CO 501 | INVESTIGATIVE STAFF | Version No: |
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## 1. POLICY

It is important that staff, subjects, and other interested parties have a means of communicating information about the conduct of a research project directly to the appropriate institutional officials. It is vital that HSPC members, department heads, and other officials with responsibility for oversight of research have open and ready access to the highest levels of authority within the institution. The researcher and his/her research staff interact with subjects; therefore, it is vital that open and frequent communication with the investigative team be maintained.

### Specific Policies

### 1.1 Investigator Notifications

1.1.1 Initial submission: The Investigator will be notified in writing of the HSPC's decision as soon as possible after the meeting or after the expedited review is conducted by HSPC staff or designated reviewer(s). If the approval is pending upon receipt and review of requested materials or responses from the Investigator or Sponsor, the HSPC must receive the response within a reasonable timeframe of the date of notification. No activities involving research participants can be undertaken until approval or determination that review is not required is obtained.

1.1.2 Renewals and revisions (amendments): Investigators will be notified in writing as soon as possible as to action taken by the HSPC for any continuing reviews or revisions.

1.1.3 Notification of final approval: Investigators will be notified in writing of the final approval.

1.1.4 Disapproval: Correspondence will provide the reason(s) for disapproval and will give the investigator an opportunity to respond in person and in writing to the HSPC.

### 1.2 Investigator Appeal of HSPC Action

If an investigator disagrees with a determination of the HSPC expedited review or with the conditions of the expedited review, the investigator may request reconsideration by a full Committee by writing to the HSPC Chairperson. Investigators may also respond to an HSPC decision to disapprove a study. Any such response may be in writing or in person and must be reviewed by the full HSPC at a convened meeting. If the appeal is denied and the study disapproved, the Investigator's institution cannot override the HSPC's decision.

### 1.3 Noncompliance

Investigator noncompliance may often be the result of communication difficulties, therefore the HSPC will attempt to resolve apparent instances of

noncompliance without interrupting the conduct of the study, especially if the rights and welfare of subjects may be jeopardized by the interruption.

However, if it appears that an Investigator is intentionally in noncompliance, the HSPC, through the HSPC Chairperson will notify the Investigator in writing, detailing the alleged noncompliance, specifying corrective action, and stating the consequences. Copies of such correspondence may also be sent to the Sponsor, the individual's supervisor, and any relevant oversight agencies (e.g. OHRP, DoD) based on contractual or other requirements.

Should noncompliance continue, appropriate action will be determined at a convened meeting. Action by the HSPC can include but is not limited to:

- Halting the research until the Investigator is in compliance. If the research is halted, OHRP or DoD will be notified if the research is funded by a government agency, and any other entities that are sponsoring the research.
- Requiring the Investigator to complete a training program.
- Barring the Investigator from conducting further research.
- Any other action deemed appropriate by the HSPC.

When unapproved research is discovered, the HSPC will act promptly to halt the research, ensure remedial action regarding any breach of regulatory or institutional human subject protection requirements, and address the question of the Investigator's fitness to conduct future human subject research. In rare instance where the HSPC chooses to approve the research retrospectively the PI will be required to submit an event report explaining why the research was conducted without approval and providing a plan for preventing a similar occurrence in the future. This will only apply to minimal risk research where noncompliance appears to be the result of miscommunication or misunderstanding. Retrospective approval is at the discretion of the HSPC.

Serious or continuing noncompliance with federal policies on the protection of human subjects or the policies, procedures or determinations of the HSPC must be reported promptly to the HSPC Chairperson as well as the appropriate department or agency head for funded projects, Sponsors if appropriate, and to OHRP and/or DoD as appropriate.

### 1.4 Research Misconduct

The HSPC's responsibility is to protect the rights and welfare of research subjects, who could be placed at risk if there is research misconduct on the part of an Investigator or any member of the investigative team. It is, therefore, the duty of the HSPC to be receptive to and act on credible allegations of misconduct. Allegations of misconduct in research should be referred to the General Counsel, for handling under RAND's Policy on Research Misconduct.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.109, 46.113

https://randus.sharepoint.com/pp/Pages/research.mis.aspx

| SOP: CO 502 | REPORTING REQUIREMENTS | Version No: |
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## 1. POLICY

The HSPC is required by federal regulation and institutional policy to communicate certain actions to entities that may have an interest in the status of the research being conducted.

### Specific Policies

### 1.1 Communications to Institutional Officials and Others

The purpose of this policy is to ensure prompt reporting to appropriate RAND Officials, funding sources, agency heads, regulatory agencies and any other appropriate entity of:

- Any unanticipated problems involving risks to human subjects or others
- Any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the HSPC
- Any suspension or termination of HSPC approval

### 1.2 Department of Defense (DoD) Requirements:

The following items need to be forwarded by the RAND researchers to the DoD HRPO (Human Research Protection Official):

- Initial study approval or determination: HRPO will then review the research protocol and the HSPC determination of level of risk and approval of the study for compliance with this Instruction. This includes HSPC determination that the activity is not research involving human subjects or is exempt involving human subjects.

- Amendment approvals: HRPO will then review HSPC-approved substantive changes to an approved research protocol before they are implemented. DoD does not define what “substantive changes” are but the USAMRMC defines it as “Substantive modifications to the research protocol and any modifications that could potentially increase risk to subjects.” RAND defines this as amendments to the HSPC-approved study that the HSPC determines meet the USAMRMC criteria.

- Continuing review approvals: HRPO requires that the HSPC conducts an appropriate continuing review at least annually. The Air Force instruction states that they must provide a copy of all continuing review reports (in addition to the approval letters) submitted to the HSPC. The same condition is stated in the US Army Medical Research and Material Command.

In addition, **UPIRTSO** (Unanticipated Problems Involving Risk to Subjects or Others) must be reported to the DoD HRPO. UPIRTSO are any incident, experience, or outcome that meets ALL three of the following conditions:

1) Is **unexpected** (in terms of nature, severity, or frequency) given the procedures described in the research protocol documents (e.g., the HSPC-approved research protocol and informed consent document) and the characteristics of the human subject population being studied.
2) Is **related or possibly related to participation in the research** (in this Instruction, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).
3) **Suggests that the research places human subjects or others at a greater risk of harm** (including physical, psychological, economic, or social harm) than was previously known or recognized, even if no harm has actually occurred.

The PI must report any event or problem on any project, including those that were determined to be Not Human Subjects according to the DoD regulations, to HSPC. The HSPC will consult with the Unit and project to determine whether the event or problem is an UPIRTSO that must be reported to DoD. The DoD Instruction also contains the following reporting requirements that are directed to the HSPC:

- If the HSPC used to review and approve the research changes to a different HSPC (for example, from the RAND HSPC to the UCLA IRB)
- When the institution is notified by any Federal department/agency or national organization that any part of its Human Research Protection Program is under investigation for cause involving a DoD-supported research protocol
- Suspensions, termination and serious and continuing noncompliance regarding DoD-supported research involving human subjects

The DoD Instruction defines **serious noncompliance** as: “Failure of a person, group, or institution to act in accordance with this Instruction and its references such that the failure could adversely affect the rights, safety, or welfare of a human subject; place a human subject at increased risk of harm; cause harm to a human subject; affect a human subject’s willingness to participate in research; or damage or compromise the scientific integrity of research data.”

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46. 113
Department of Defense Instruction Number 3216.02

Air Force Instruction 40-402

United States Army Medical Research and Materiel Command, Office of Research Protections (ORP), Human Research Protection Office (HRPO), Human Subjects Research Review Board (HSRRB) Policies and Procedures, Version 2, 25 January 2010

# 600- IC
# INFORMED CONSENT

| SOP: IC 601 | GENERAL REQUIREMENTS AND DOCUMENTATION | Version No: |
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## 1. POLICY

Informed consent must be legally effective and prospectively obtained. Consent shall be sought only under circumstances that provide the prospective research participant or the legally authorized representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

### Specific Policies

**1.1** The Consent Form is a written consent document that embodies the elements of informed consent described in 45 CFR 46.116(a). This form may be read to the subject or the subject's legally authorized representative, but, in any event, the Investigator shall give either the subject or the representative adequate opportunity to read it before it is signed. The subject must also be given a copy of the form.

### 1.2 Basic Elements of Informed Consent

A. A statement that the study involves research, an explanation of the purposes of the research, the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are investigational.

B. A description of any reasonably foreseeable risks or discomforts to the subject.

C. A description of any benefits to the subject or to others that may reasonably be expected from the research.

D. A disclosure of appropriate alternative procedures or courses of treatment, if any, which might be advantageous to the subject.

E. A statement describing the extent to which, if any, confidentiality of records identifying the subject will be maintained.

F. For research involving more than minimal risk, an explanation as to whether any compensation is provided 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.

G. 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.

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

I. One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

(i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or

(ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

### 1.3 Additional Elements

When appropriate, one or more of the following elements of information shall also be provided to each subject or legally authorized representative:

A. 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.

B. Anticipated circumstances under which the subject's participation may be terminated by the Investigator without regard to the subject's consent.

C. Any additional costs to the subject that may result from participation in the research.

D. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

E. 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.

F. The approximate number of subjects involved in the study.

G. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;

H. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and

I. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (*i.e.,* sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

### 1.4 Other Requirements

A. Second person: The language of the consent document should be in the second-person style so the consent form conveys a dialogue with information being provided and that there is a choice to be made by the subject rather than presumption of the subject’s consent with the use of the first person style.

B. Language should be simple: The information provided in the informed consent documents must be in language understandable to the subject or legally authorized representative. The informed consent document should not include complex language that would not be understandable to subjects or legally authorized representative. Technical and scientific terms should be adequately explained using common or lay terminology.

C. Exculpatory language: Informed consent documents may not contain any exculpatory language through which the subject is made to waive or appears to waive legal rights, or releases or appears to release the Investigator, the Sponsor, or RAND from liability for negligence.

### 1.5 Documentation of Informed Consent

Each subject or his/her legally authorized representative must sign a copy of the current HSPC-approved consent form prior to enrollment or any participation in any phase of the study, unless the requirement is waived by the HSPC. The subject must also be given a copy of the document.

The HSPC may approve procedures for documentation of informed consent that involve (a) a written consent form signed by the subject; (b) a short form written consent form with oral presentation; or (c) in limited circumstances, waiver of signed written consent form. Each of these three options is described in detail below. It is the responsibility of the HSPC to determine which of the procedures described below is appropriate for documenting informed consent in protocols that it reviews.

1.5.1 Written consent form signed by subject or legally authorized representative. In most circumstances, the HSPC should require that informed consent is documented by the use of a written consent form approved by the HSPC and signed by the subject or the subject's legally authorized representative. The Investigator should allow the subject or the legally authorized representative adequate opportunity to read the consent document before it is signed. A copy of the document must be given to the person signing the form.

1.5.2 The written informed consent document should embody, in language understandable to the subject, all the elements necessary for legally effective informed consent (see above).

1.5.3 Subjects who do not understand English should be presented with an informed consent document written in a language understandable to them. In most cases this should be a standardized written translation rather than an ad hoc translation. If ad hoc translation is necessary (for example, for dialects used by a few participants) the translators must be supplied by the project team.

1.5.4 If a witness signature line is included on the informed consent, the witness signature line must include a description of what is being witnessed. Examples of the description may include but are not limited to: a statement that the witness is observing the entire consent process, or a statement that the witness is only observing the study participant’s signing of the informed consent form.

## 1.6 Oral Presentation Using Short Form

As an alternative to standard written informed consent documents, oral presentation of informed consent information may be used in circumstances approved by the HSPC.

In such cases, the subject must be provided with both:

- A short form written informed consent document stating that the elements of informed consent have been presented orally to the subject or the subject's legally authorized representative; and
- A written summary of the information that is presented orally.

1.6.1 A witness to the oral presentation is required. The witness must sign both the short form written informed consent document and a copy of the written summary.

1.6.2 The subject or the legally authorized representative must sign the short form written consent document.

1.6.3 The person obtaining consent (*e.g.*, the Investigator) must sign a copy of the written summary of the information that is presented orally. The person obtaining consent may not be the witness to the consent.

1.6.4 Subjects who do not speak English: Where informed consent is documented using this short form procedure for non-English speaking subjects, the written informed consent document should embody, in language understandable to the subject, all the elements necessary for legally effective informed consent. When this procedure is used with subjects who do not speak English, (i) the oral presentation and the short form written informed consent document should be in a language understandable to the subject; (ii) the HSPC-approved English language informed consent document may serve as the summary; and (iii) the witness should be fluent in both English and the language of the subject.

1.6.5 The HSPC must receive all foreign language versions of the short form document as a condition of approval.

Expedited review of these foreign language versions is acceptable if the convened full HSPC has already approved the protocol, the full English language informed consent document, and the English version of the short form document.

## 1.7 Observation and Monitoring of the Informed Consent Process

The HSPC foresees circumstances that may arise under which the HSPC may want to observe the consent process. For example, at the time of initial protocol review, the Committee may determine that although the risk/benefit determination allows for consenting of potentially cognitively impaired adults, additional safeguards may be instituted to protect the rights and welfare of subjects. In this situation, the HSPC may delegate the administration or observation of the consent process to a qualified third party.

Studies involving subjects who are cognitively impaired may take place over extended periods. The HSPC may consider whether periodic re-consenting of individuals should be required to ensure that a subject's continued involvement is voluntary. The HSPC may require that Investigators re-consent subjects after taking into account the study's anticipated length and the condition of the individuals to be included (e.g., subjects with progressive neurological disorders). Additionally, the HSPC may consider whether, and when, it should require a reassessment of decision-making capacity.

### 1.8 Use of Facsimile or Mail to Document Informed Consent

The HSPC may approve a process that allows the informed consent document to be delivered by mail or facsimile to the potential subject or the potential subject's legally authorized representative and to obtain consent by telephone when the subject or the legally authorized representative can read the consent document as it is discussed. All other applicable conditions for documentation of informed consent must also be met when using this procedure.

### 1.9 Exempt Studies and Studies Determined to be Not Human Subjects Research

Projects that are determined to be exempt from specific regulatory requirements or from further HSPC review are not exempt from ethical requirements of informed consent and responsible data protection. If the project does not meet OHRP criteria for "research" or for "research involving human subjects" it will still be screened for the possibility that it might pose more than minimal risks for participants. Projects do not meet the above criteria but may involve more than minimal risk can be referred for further review. Projects that involve no more than minimal risk led by a PI who is current on CITI training will receive advice to use strong protections for participants and will receive no further review, unless there are changes or events that need to be reported. If the PI does not have current CITI training the HSPC staff may provide a review of informed consent and data safeguarding plans and materials.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.116, 46.117

https://randus.sharepoint.com/research/hspc/Pages/consent.aspx

| SOP: IC 602 | CONSENT WAIVERS | Version No: |
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**1. POLICY**

The HSPC recognizes that there may be exceptions to requirements for informed consent and/or documentation as follows:

## A. WAIVER OR ALTERATION OF INFORMED CONSENT

In certain circumstances, the HSPC may waive the requirement to obtain informed consent if the HSPC finds that the research meets specific criteria that is in accord with the provisions at 45 CFR 46.116(c).

### Alteration of Elements of Informed Consent

The HSPC may approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent (such as written documentation).

### Specific Policies

**1. Waiver of Informed Consent**

1.1 The HSPC may waive the requirement to obtain informed consent provided the HSPC finds and documents that:

1.1.1 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:

- Public benefit or service programs;
- Procedures for obtaining benefits or services under those programs;
- Possible changes in or alternatives to those programs or procedures; or
- Possible changes in methods or levels of payment for benefits or services under those programs; and
- The research could not practicably be carried out without the waiver or alteration.

1.1.2 In order for the HSPC to waive consent, the HSPC must find and document that:

- The research involves no more than minimal risk to the subjects;
- The research could not practicably be carried out without the requested waiver or alteration;
- If the research involves using identifiable private information or identifiable biospecimens, the research could not

practicably be carried out without using such information or biospecimens in an identifiable format;

- The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

**2. Alteration or waiver of one or more elements of informed consent**

2.1 The HSPC may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent described in SOP IC 601 above as follows.

2.1.1 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:

- Public benefit or service programs;
- Procedures for obtaining benefits or services under those programs;
- Possible changes in or alternatives to those programs or procedures; or
- Possible changes in methods or levels of payment for benefits or services under those programs; and
- The research could not practicably be carried out without the waiver or alteration.

2.1.2 In order for the HSPC to alter consent, the HSPC must find and document that:

- The research involves no more than minimal risk to the subjects;
- The research could not practicably be carried out without the requested waiver or alteration;
- If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

**B. WAIVER OF DOCUMENTATION OF INFORMED CONSENT**

The HSPC may Waive Documentation of Informed Consent for some or all subjects if it finds any of the following:

1. That the only record linking the subject and the research would be the

informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern;
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; or
3. If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

In cases in which the documentation requirement is waived, the HSPC may require the Investigator to provide subjects with a written statement regarding the research.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 116; 45 CFR 117

| SOP: IC 603 | ASSENT | Version No: |
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## 1. POLICY

The principle of respect for persons requires that the choice of an autonomous person be respected. Under the usual conditions of human research, this is accomplished by soliciting the informed consent of the prospective research subject. When prospective participants have diminished capacity to consent, such as a child (generally younger than seven years old), the consent of either the parent or legally authorized representative is required. However, any individual capable of some degree of understanding (generally, a child of seven or older) should participate in research only if they assent. When assent is required, however, the decision of the individual assenting should be binding.

### Specific Policies

### 1.1 Use of Assent

In instances where the subject may not be capable of giving informed consent or where the subject is cognitively impaired, the HSPC must find that adequate provisions are made for soliciting the assent of the subject when in the judgment of the HSPC, the subject is capable of providing assent.

1.1.1 Assent means a subject's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

1.1.2 In determining whether subjects are capable of assenting, the Investigator and the HSPC shall take into account the age, maturity, and psychological state of the subject involved. This judgment may be made for all subjects to be involved in research under a particular protocol, or for each subject, as the HSPC deems appropriate. If the HSPC determines that the capability of some or all of the subjects is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the subject and is available only in the context of the research, the assent of the subject is not a necessary condition for proceeding with the research. Even where the HSPC determines that the subjects are capable of assenting, the HSPC may still waive the assent requirement under circumstances in which consent may be waived as stated in section 1 of SOP IC 602.

1.1.3. When the HSPC determines that assent is required, it shall also determine whether and how assent must be documented.

## 4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46 Subpart D

# 700 - RI
# RESPONSIBILITIES OF INVESTIGATORS

701 HSPC- Required Investigator Actions

| SOP: RI 701 | HSPC-REQUIRED INVESTIGATOR ACTIONS | Version No: |
|---|---|---|

## 1. POLICY

It is the investigator's responsibility to keep the HSPC informed of unexpected non-serious and serious adverse events and other unexpected findings that could affect the risk/benefit ratio of the research. An Investigator is responsible for the accurate documentation, investigation and follow-up of all possible study-related adverse events. Investigators are also responsible for informing government and other Sponsors of any unanticipated or serious adverse events, as appropriate.

In addition, the Principal Investigator retains responsibility for any activities delegated to other RAND Associates and third parties, including contractors and other investigators who have agreed to be screened by RAND HSPC and have signed an Individual Investigator Agreement under this policy. Therefore, the Principal Investigator is responsible for ensuring that the individual assigned any such activity has sufficient training, knowledge, experience, resources, and judgment to successfully undertake such activities in compliance with RAND policies and HSPC directives. No Principal Investigator responsibilities may be delegated to any individual other than a qualified RAND Associate without prior HSPC approval.

### Specific Policies

### 1.1 HSPC Review of Research

All human subjects research that is conducted by or under the direction of any employee, faculty, staff, student or agent of RAND in connection with his or her institutional responsibilities must be reviewed by the HSPC.

### 1.2 Informed Consent

The Investigator must obtain informed consent from subjects prior to their enrollment into the research unless the HSPC has waived this requirement. The Investigator must use the informed consent document approved by the HSPC. Investigators must follow RAND guidelines for obtaining informed consent. The consent form should include the HSPC number for the project.

### 1.3 Adverse Event Reporting

The HSPC must be informed of any serious, unexpected adverse events or other reportable events as defined by SOP RR 403. Study staff needs to submit an Event Report via RHINO as soon as they learn that: 1) there is more potential for harm to subjects than was originally thought; 2) one or more subjects has actually been harmed; or 3) other unanticipated human subjects incidents have occurred.

A report is expected within 24 hours of the event, but should it not be possible for staff to fill out an Adverse Event form within that time, they should attempt to contact the HSPC by phone and/or email immediately and follow up with the completed form as soon as possible. When the report is received,

administrative staff will forward it to the reviewer(s) of record and if appropriate to the HSPC chair and legal counsel. Additional reviewers may be assigned by the chair as needed.

### 1.4 Changes in Approved Research

Changes in approved research, during the period for which approval has already been given, may not be initiated without HSPC review (or expedited review, where appropriate) and approval, except where necessary to eliminate apparent immediate hazards to human subjects. Investigators must submit requests for changes to the HSPC via RHINO. Upon receipt of the protocol change request, the HSPC staff or HSPC member will determine if the revision meets the criteria for expedited review. If the change represents more than a minimal risk to subjects, it must be reviewed and approved by the HSPC. Minor changes involving no more than minimal risk to the subject will be reviewed by the expedited review process.

### 1.5 Unanticipated Problems

All unanticipated problems must be reported promptly to the HSPC. An unanticipated problem is defined as any unforeseen event or events that may involve risks or affect the safety or welfare of subjects or others, or that may affect the integrity of the research. Examples of an unanticipated problem include, but are not limited to: difficulty recruiting subjects, higher than expected adverse events, higher than expected subject drop-out rate, higher than expected protocol deviation rate, loss of multiple staff members, injury to a staff member while conducting study-related procedures, or subject difficulty understanding the informed consent.

### 1.6 Continuing Reviews

The length of time approval is given to a research protocol will be no more than one year and is dependent on the risk involved with the research. Investigators are responsible for requesting renewal in anticipation of the expiration of the approval period. Investigators or their designees are required to provide a periodic report regarding their investigation prior to the end of the approval period, or upon completion of the study.

### 1.7 Student-Conducted Research

All activities that meet the definition of research with human subjects and that are conducted by students for a class project or for work toward a degree must be reviewed by the HSPC. For example, activities that must be reviewed and approved by the HSPC include: (i) All doctoral dissertations that involve human subjects; and (ii) All projects that involve human subjects and for which findings may be published or otherwise disseminated.

### 1.8 Conflict of Interest

The protection of human subjects requires objectivity in communicating risks, selecting subjects, promoting informed consent, and gathering, analyzing and

reporting data. Therefore, the HSPC should consider conflict of interest issues in its deliberations of applications.

All Investigators must reveal on their application to the HSPC whether they or any other person responsible for the design, conduct, or reporting of the research has an economic interest in or acts as an officer or a director of any outside entity whose financial interests would reasonably appear to be affected by the research. It is the Investigator's obligation to also report such conflicts to the appropriate institutional official as outlined in the RAND Policies and Procedures.

### 1.9 Responsibility of Terminating Associates

When terminating from RAND, Principal Investigators/Project Directors, and all other Associates who are custodians of Human Subjects Information must consult with the appropriate unit liaisons to HSPC to determine whether the Human Subjects Information for which they are responsible should be archived for future use or designated for disposal. If identifiable data are to be retained, the HSPC will determine the manner in which they must be archived. The HSPC Chair can offer guidance on this procedure. Terminating Associates will be required to acknowledge that they have met these requirements in the sign-out process with RAND's Human Resources Department. Information that is designated for disposal must be handled in in accordance with the procedures outlined on the Data Protection website.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.109, 46.111

OHRP COI Policy Draft

https://randus.sharepoint.com/pp/Pages/conflict.interest.aspx

https://randus.sharepoint.com/research/hspc/Pages/home.aspx

# 800- SC
# REVIEWS REQUIRING SPECIAL CONSIDERATION

801 Special Populations

- Prisoners
- Children
- Pregnant Women and Fetuses
- Individuals with Impaired Decision-Making Ability
- Other Vulnerable Groups

| SOP: SC 801 | SPECIAL POPULATIONS | Version No: |
|---|---|---|

## 1. POLICY

Not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Some persons are in need of extensive protection, even to the point of excluding them from activities that may harm them. Other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequence. Indeed, some types of research may, in and of themselves, create a vulnerable group – that is, the subjects lose their autonomy or are exposed to unknown risks. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

- Groups that require additional protection considerations include:
  - Prisoners
  - Children
  - Pregnant women and fetuses
  - Individuals with impaired decision-making ability
  - Other vulnerable groups, such as those vulnerable to coercion

### Mandated Reporting in Relation to RAND Studies

The HSPC review of a study will include consideration of a plan to address potential issues of abuse or neglect that may arise. Occasionally, such issues may arise for the first time after the research has commenced. Although RAND researchers may be faced with situations where they might consider themselves mandated reporters of abuse and neglect, they may not fall within the definition of a mandated reporter under the applicable local law for a number of reasons, including their role as a researcher. Unless it is an emergency, the PI should include the information in an event report to HSPC and consult with HSPC before making a report to authorities. HSPC may consult with counsel and others to determine whether any report to authorities is required.

### Specific Policies

#### 1.1 Prisoners

1.1.1 Federal regulations define “prisoner” as any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending

arraignment, trial, or sentencing.

Individuals detained under house arrest are considered to be incarcerated.

If an Investigator indicates in the study submission that prisoners will participate in the research, or that subjects may reasonably be expected to be incarcerated at some time point during the study, the following additional requirements will apply to HSPC review of the project:

- A. Local regulations: In addition to meeting federal regulations, the project must comply with local and state requirements for inclusion of prisoners as subjects.
- B. HSPC composition: A majority of HSPC members will have no association with the prison(s) involved; and at least one member shall be a prisoner or prisoner advocate with appropriate background and experience to serve in that capacity.
- C. Additional duties where prisoners are involved: The HSPC may review research involving prisoners only if it finds that the following conditions are met:

  1. The research falls into one of the following categories:

     i. The research under review involves solely research on the practices both innovative and accepted, which has the intent and reasonable probability of improving the health and well-being of the subjects. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups, which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice in the FEDERAL REGISTER of the intent to approve such research.

     ii. Research on conditions particularly affecting prisoners as a class (e.g., vaccine trials on hepatitis) provided that the Secretary, HHS, or designee has published notice in the Federal Register of its intent to approve such research.

  2. Any possible advantages accruing to the prisoner through participation in the research, when compared to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in prison, are not of such a magnitude that the prisoner's ability to weigh the risks and benefits of the research in the limited-choice environment of the prison is impaired.

  3. The risks involved in the research are commensurate with risks that would be accepted by non-prison volunteers.

  4. Selection procedures within the prison are fair to all prisoners and immune from arbitrary intervention by prison authority or prisoners. Unless the Investigator provides the HSPC justification in writing for following some other procedures, control subjects must

be selected randomly from the group of eligible prisoners for the research project.

5. Any information given to subjects is presented in language that is appropriate for the subject population.

6. Adequate assurance exists that parole board(s) will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the clinical investigation will have no effect on his/her parole.

7. Where there is need for follow-up examination or care of subjects after the end of their participation in the research, adequate provision has been made for such examination or care, taking into account the varying lengths of prisoner sentences, and for informing subjects of this fact.

1.1.2. If the HSPC makes a determination that the study meets the criteria discussed in section 1.1.1., the determination will be documented as required, and a copy of the research proposal will be sent to the Prisoner Research Contact Person at OHRP.

The study cannot be initiated unless OHRP determines that the proposed research involves at least one of the categories of research permissible under 45 CFR 46.306(a)(2), and if so, which one.

1.1.3 When Subjects Become Prisoners During a Research Protocol

This policy applies whenever any human subject in a research protocol becomes a prisoner at any time during the protocol, *e.g.,* after the research has commenced. This is necessary because it is unlikely that review of the research and the consent document contemplated the constraints imposed by the possible future incarceration of the subject.

- If a subject becomes a prisoner after enrollment in research, all research interactions and interventions with, and obtaining identifiable private information about the subject must cease. The Principal Investigator is responsible for reporting this situation in writing to the HSPC immediately.
- At the earliest opportunity after receiving the Investigator's notice or otherwise becoming aware of the prisoner status of a subject, the HSPC should review the protocol again with a prisoner representative as a member of the HSPC. The HSPC should take special consideration of the conditions of being a prisoner.
- Upon this review, the HSPC can either (a) approve the involvement of the prisoner-subject in the research in accordance with this policy, (b) determine that no further data collection may take place until the subject is no longer incarcerated or (c) determine that the subject must be withdrawn from the research.
- Additionally, the HSPC should confirm that, when appropriate, the informed consent process includes information regarding when subsequent incarceration may result in termination of the subject's

participation by the Investigator without regard to the subject's consent.

- In special circumstances in which the principal investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated, the HSPC Chairperson may determine that the subject may continue to participate in the research until the requirements of subpart C are satisfied.

1.1.4 Application of Subpart C Regulations at RAND

The following three cases will guide the application of Subpart C:

1. The findings will always be made for all situations where subjects are physically detained involuntarily, including cases where research projects planned to "follow" subjects who were free when enrolled in research but incarcerated during the course of a study.
2. The *potential presence* of probationers or parolees in studies in community or other situations – where there is no reason to believe the individual's ability to freely agree or refuse participation is impaired – will no longer be viewed as a rationale for application of the Subpart C regulations.
3. In studies where individuals who are on probation, parole, or have been ordered by the court to participate in – non-residential and non-confining – treatment or counseling programs are *intentionally and purposefully included* in research, judgements will be made on a case-by-case basis. The judgment regarding whether the subjects should be treated as prisoners will be based on whether or not the circumstances and process of data collection raises questions about the ability of the individuals to freely decline participation. For example, data collection in a police setting or at the location of individual's court-mandated counseling program might be viewed as research involving prisoners while collecting data from those same individuals about the same topics individually in varied location of their choosing might not be.

1.1.5 **Detainees**

The Department of Defense prohibits involvement of detainees as a human subject in DoD-funded projects.

**1.1.6 Type of Review**

Research involving interaction with prisoners may be reviewed by the expedited procedure if a determination is made that the research involves no greater than minimal risk for the prison population being studied. The Prisoner Representative must concur with the determination that the research involves no greater than minimal risk. The Prisoner Representative must review the research as a reviewer, designated by the Chair or as a consultant. This may be as the sole reviewer or in addition to another reviewer, as appropriate. Review of modifications and continuing review must use the same procedures for

initial review using this expedited procedure including the responsibility of the Prisoner Representative.

For research that does not involve interaction with prisoners (e.g., existing data, record reviews), this research may be reviewed by the expedited procedure if a determination is made that the research involves no greater than minimal risk for the prison population being studied. Review by a Prisoner Representative is not required. The Prisoner Representative may review the research as a reviewer or consultant if designated by the IRB Chair. Review of modifications and continuing review must use the same procedures as initial review.

Minor modifications to research may be reviewed using the expedited procedure. Modifications involving more than a minor change reviewed by the convened IRB must use the same procedures for initial review, including the responsibility of the Prisoner Representative to review the modification and participate in the meeting.

Continuing review must use the same procedures as for initial review, including the responsibility of the Prisoner Representative to review the continuing review materials and to participate in the meeting as described above. If no participants have been enrolled, the research may receive continuing review using the expedited procedure under expedited Category 8.

***Exempt*** review procedures may not be used for research involving prisoners.

## 1.2 Children

1.2.1 Federal regulations define “children” as persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

Under California law, persons under the age of eighteen (18) generally meet this definition of “children.”

If the research includes enrollment of participants in other states or countries, the principal investigator is responsible for providing the HSPC with sufficient information to verify the age at which participants in such jurisdictions have the ability to consent to participation in research.

Exemptions at §46.104(d)(1) and (d)(4) through (d)(8) are applicable to this subpart. The exemption at §46.104(d)(2) regarding educational tests is also applicable to this subpart. However, the exemption at §46.104(d)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior

when the investigator(s) do not participate in the activities being observed.

1.2.2 Research with children requires that the HSPC consider the following:

Determination of probable risks and associated discomforts: Procedures that usually present no more than minimal risk to a healthy child include: urinalyses, obtaining small blood samples, EEGs, allergy scratch tests, minor changes in diet or daily routine, and/or the use of standard psychological or educational tests. The assessment of the probability and magnitude of the risk, however, may be different in sick children and may vary depending on the diseases or conditions the subjects may have. For example, obtaining blood samples from a hemophiliac child may present more than minimal risk to the child. On the other hand, HSPC may consider that children suffering from chronic illnesses who are accustomed to invasive procedures are placed at minimal risk by involvement in similar research procedures, in contrast to children who have not had such experiences. The HSPC must also consider the extent to which research procedures would be a burden to any child, regardless of whether the child is accustomed to the proposed procedures.

Riskier procedures might include biopsy of internal organs, spinal taps, or the use of drugs whose risks to children have not yet been established. Behavioral interventions likely to cause psychological stress may also exceed minimal risk.

Determination of possible benefits: In assessing the possible benefits of research intervention, the HSPC should consider the variability in health statuses among potential subjects. For example, a potential subject might be a normal, healthy child, or a child who has been exposed to a disease or a toxin (*e.g.*, meningococcus or lead) where it is known that a percentage of the children exposed will actually experience untoward consequences. A child may also be in an early state of disease, *e.g.*, an HIV-infected child, or may actually suffer from disease or other significant medical condition. Thus, the HSPC must take into account the current health status of a child and the likelihood of progression to a worsened state without research intervention.

1.2.3. Determination of Risk: HSPC is required by Federal regulations to classify research involving children into one of four categories and to document its discussions of the risks and benefits of the research study. The Minutes will document how the research protocol meets the required criterion.

The four categories of research involving children based on degree of risk and benefit to individual subjects are as follows:

1. **Research not involving greater than minimal risk (45 CFR 46.404).**

Research in this category is approvable provided the HSPC finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

2. **Research involving greater than minimal risk, but presenting the prospect of direct benefit to an individual subject (45 CFR 46.405).**

   Research in this category is approvable provided: (a) the risk is justified by the anticipated benefit to the subject; and (b) the relationship of risk to benefit is at least as favorable as any available alternative approaches; and (c) adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

3. **Research involving greater than minimal risk with no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition (45CFR 46.406).**

   Research in this category is approvable provided: (a) the risk represents a minor increase over minimal risk; (b) the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational settings; and (c) the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition that is of vital importance for the understanding or amelioration of the subject's disorder or condition; and (d) adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

4. **Research that is not otherwise approvable, but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (45 CFR 46.407)**.

   - Research that is not approvable under 45 CFR 46.404, 46.405, or 46.406 may be conducted or funded by DHHS provided: (a) The HSPC finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
   - (b) The Secretary of HHS, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, determines either:

     (1) That the research in fact satisfies the conditions of §46.404, §46.405, or §46.406, as applicable, or

     (2) That the following conditions are met:

(i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

(ii) The research will be conducted in accordance with sound ethical principles; and

(iii) Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in §46.408.

1.2.4 Parental Permission: Children may be subjects of research only if informed consent is obtained from the parents or legal guardian. The HSPC will determine whether the permission of both parents is necessary, and the conditions under which one parent may be considered not reasonably available.

The regulations provide that the HSPC may find that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404 (minimal risk research) or 45 CFR 46.405 (research involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects) [45 CFR 46.408(b)]. Where research is covered by 45 CFR 46.406 and 45 CFR 46.407, and permission is to be obtained from parents, both parents must give their permission, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child [45 CFR 46.408(b)].

The regulations define “permission” at 46.402(c) as the “agreement of parent(s) or guardian to the participation of their child or ward in research.” The term “parent” means a “child's biological or adoptive parent.” The term “guardian” means “an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.”

1.2.5 Waiver of Parental Consent: HSPC may waive the requirements for obtaining parental or guardian permission if it makes and documents the findings under either 45 CFR 46.116(c) or (d). In addition to the provisions for waiver contained in 46.116(c) and (d), if the HSPC determines that a research protocol is designed to study conditions in children or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the parental permission requirements provided that an appropriate mechanism is in place to protect the children, and provided that the waiver is not inconsistent with federal, state, or local law (45 CFR 46.408(c)). The choice of an appropriate substitute mechanism (for example, appointing a child advocate or an assent monitor) for protecting children participating in research would depend on the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the

research subjects, and the child's age, maturity, status, and condition (45 CFR 46.408(c)).

1.2.6 Assent of Children: The HSPC must determine that adequate provisions are made for soliciting the assent of the children when in the judgment of the HSPC the children are capable of providing assent. In determining whether children are capable of providing assent, the HSPC must take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research activities under a particular protocol, or for each child, as the HSPC deems appropriate. When the HSPC determines that assent is required, it must also determine whether and how assent must be documented.

"Assent" means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

1.2.7 Waiver of Assent: The assent of the child is not a necessary condition for proceeding with the research if the HSPC determines:

- (1) That the capability of some or all of the children is so limited that they cannot reasonably be consulted, or
- (2) That the intervention or procedure involved in research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the clinical investigation.

Even where the HSPC determines that the subjects are capable of assenting, the HSPC may still waive the assent requirement if it finds and documents that:

- (1) The research involves no more than minimal risk to the subjects;
- (2) The waiver will not adversely affect the rights and welfare of the subjects;
- (3) The research could not practicably be carried out without the waiver; and
- (4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

## 1.3 Pregnant Women and Fetuses

1.3.1 Pregnant women or fetuses prior to delivery may be involved in research if all of the following conditions are met:

A. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

B. The risk to the fetus is not greater than minimal, or any risk to the fetus, which is greater than minimal, is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus;

C. Any risk is the least possible for achieving the objectives of the research;

D. The woman's consent or the consent of her legally authorized representative is obtained in accord with the informed consent provisions of subpart A of 45 CFR 46, unless altered or waived in accord with Sec. 46.101(i) or Sec. 46.116(c) or (d);

E. The woman or her legally authorized representative, as appropriate, is fully informed regarding the reasonably foreseeable impact of the research on the fetus or resultant child;

F. For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46 subpart D;

G. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

H. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

I. Individuals engaged in the research will have no part in determining the viability of a fetus.

1.3.2 Research involving fetuses after delivery:

A. After delivery, fetuses may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to fetuses;

2. The individual(s) providing consent under the applicable regulations is/are fully informed regarding the reasonably foreseeable impact of the research on the fetus or resultant child;

3. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

4. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy;

5. Individuals engaged in the research will have no part in determining the viability of a fetus; and

6. The regulatory requirements have been met as applicable.

B. Viable fetuses. A fetus, after delivery, that has been determined to be viable is a child as defined by 45 CFR 46.402(a) and may be included

in research only to the extent permitted by and in accord with the requirements of 45 CFR 46 subparts A and D.

### 1.4 Individuals with Impaired Decision-Making Ability

Although there are no federal regulations specifically written to address the needs of this vulnerable group, the HSPC will generally follow the recommendations governing the conduct of research in children and of specific recommendations made by the National Commission.

1.4.1 Selection of Subjects. Research involving individuals with impaired ability to consent should have a direct relationship to their illness or condition. Particular attention should be paid to institutionalized individuals, as issues of dependence and coercion may be factors that may compromise the voluntary nature of their participation in research. For this reason, subjects should be recruited from among noninstitutionalized populations whenever possible.

1.4.2 Risk Determination: Generally, the HSPC will follow the recommendations of the National Commission when determining the degree of risk and its impact on the approvability of a research protocol in cognitively impaired subjects as follows:

- a minor increase over minimal risk may be permitted in research involving those institutionalized as mentally disabled, but only where the research is designed to evaluate an intervention of foreseeable benefit to their care.
- for research that does not involve beneficial interventions and that presents more than minimal risk, the anticipated knowledge sought should be of vital importance for understanding or eventually alleviating the subject's disorder or condition.

1.4.3 Limiting Risks. The following measures should be addressed in the protocol to limit a subject’s exposure to risk:

- Description of appropriate psychological or medical screening criteria to prevent or reduce the chances of adverse reactions to the therapeutic and research procedures
- Specific diagnostic, symptomatic, and demographic criteria for subject recruitment
- Description of methods for assuring adequate protections for the privacy of the subjects and the confidentiality of the information gathered
- Justification of plans to hospitalize subjects or extend hospitalization for research purposes
- Measures to protect Individually identifiable information
- Measures to ensure that proposed research procedures will not be detrimental to ongoing therapeutic regimens.

1.4.4 Informed Consent: Generally, mentally impaired adults should be presumed competent to understand the issues of being a research subject and either refuse or consent to participate in a research study. Mental disability alone should not disqualify a person from consenting to participate in research; rather, there needs to be specific evidence of incapacity to understand and to make an informed voluntary choice before they are deemed unable to consent for themselves.

The HSPC follows the National Commission's recommendation that "despite the fact that consent may be obtained from a legally authorized representative or guardian, the feelings and expressed wishes of an incompetent person should still be respected".

If a cognitively impaired adult subject objects to participate in a research study, that decision should be binding, except when the individual's participation is specifically authorized by a court of law, the intervention is expected to provide a direct health benefit to the subject, and the intervention is available only in the context of the research. The HSPC will seek legal counsel to assess applicable laws that might affect the participation of legally incompetent persons and/or the role of guardians in the consenting process.

Studies involving subjects who have impaired decision-making ability may take place over extended periods. The HSPC should consider whether periodic re-consenting of individuals should be required to ensure that a subject's continued involvement is voluntary. The HSPC may require that Investigators re-consent subjects after taking into account the study's anticipated length and the condition of the individuals to be included (e.g., subjects with progressive neurological disorders). Additionally, the HSPC should consider whether, and when, it should require a reassessment of decision-making capacity.

### 1.5 Other Vulnerable Groups

Although federal regulations specifically list children, prisoners, pregnant women and fetuses as groups that require additional protections, other groups may include employees of the Sponsor or Investigator, terminally ill patients, and the very elderly. The HSPC will determine special protections for these groups on a case-by-case basis, taking into account the risks and benefits and other protections afforded by RAND policies and state and federal law. Consideration of special issues of groups that require additional protections may also be extended to individuals subject to coercion or perceptions of coercion in relation to the context of the study – for example, students in a classroom, patients in a medical practice, or members of the military.

## 4. APPLICABLE REGULATIONS AND GUIDELINES

The Belmont Report

45 CFR 46: Subparts A, B, C, D

45 CFR 46.101, 46.115(B), 46.116, 46.122, 46.303(c)

OHRP IRB Guidebook

OHRP Guidance on the Involvement of Prisoners in Research Dated May 23, 2003

https://randus.sharepoint.com/research/hspc/Documents/prisoners.pdf

http://www.hhs.gov/ohrp/policy/faq/children-research/exemptions-research-involving-children.html

http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.402

Department of Defense Instruction Number 3216.02

# 900- AU
# AUDITING

901 AUDITING

| SOP: AU 901 | AUDITING | Version No: |
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## 1. POLICY

The HSPC and other entities designated by RAND may conduct periodic audits of compliance with Human Subjects protection procedures such as administration of informed consent, storage and retention of consent materials and other required records, and data safeguarding procedures.

Outside agencies, such as DoD or the Office for Human Research Protections ("OHRP"), an office of the United States Department of Health and Human Services, may also audit RAND from time-to-time for compliance with Human Subjects regulations. The Principal Investigator is responsible for facilitating compliance with any such audits in cooperation with the HSPC.

### Specific Policies

#### 1.1 Internal Audit

1.1.1 Ongoing assessment of HSPC operations and outputs is conducted through Quality Control monitoring and Quality Assurance auditing. QC monitoring involves periodic, real time checks of specific HSPC operations, documents and records. The HSPC Chairperson has the authority to implement these QC steps on a routine basis.

1.2.1 Internal auditing is a retrospective assessment of HSPC operations through document and record review. Internal audits may be horizontal, where a particular function is assessed across several studies (e.g., minute-taking); or they may be vertical, where a particular study is audited in whole or in part (e.g., high-risk research). An independent auditor performs internal auditing generally on an annual basis.

1.3.1 HSPC staff discusses the results of QC, internal/external QA audits and regulatory inspections. The consideration of adverse findings derived from these activities results in a determination of the root cause(s) of the adverse findings and the development and implementation of a corrective and preventive action (CAPA) plan to improve the effectiveness of the HSPC human research protection program. The HSPC Chairperson or a designee will lead the meetings, monitor the implementation of CAPA plans and provide status reports.

### 2.1 External Audit

2.1.1 For external audits involving OHRP or DoD, the following must be notified immediately:

- RAND President (Designated Official for FWA)
- RAND General Counsel
- HSPC Chairperson
- HSPC staff designated to participate in the audit are required to follow the steps outlined by this institution for preparing the site for an audit.

### 2.2 Participating in an Audit

2.2.1 HSPC staff and researchers are expected to know and follow the procedures outlined by this Institution for the conduct of a regulatory audit.

2.2.2 Prior to being granted access to HSPC documentation, inspectors or auditors must exhibit proof of their authority or authorization to conduct the audit and to access HSPC documents, and no entity other than those listed on the consent forms may have access to any document that includes subject identifiers.

2.2.3 Auditors will be provided with adequate working area to conduct an audit and HSPC staff and members must make every reasonable effort to be available and to accommodate and expedite the requests of such auditors.

2.2.4 Documents may be copied and taken off-site only by individuals authorized in writing by the HSPC Chairperson and the Office of General Counsel to do so.

### 2.3 Follow-up After an Audit

Reports of the audit, either verbal or written, should be addressed by the HSPC staff as soon as possible after the audit.

## 2. APPLICABLE REGULATIONS AND GUIDELINES

https://randus.sharepoint.com/research/hspc/Pages/home.aspx

## GLOSSARY

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| 1. | **ASSOCIATE** | All RAND U.S. Regular and Term Employees, Adjunct or Affiliated Adjunct staff, Pardee RAND Graduate School students, and Sponsored Fellows, and RAND Europe and RAND Australia Associates when they are working on RAND U.S. research projects. |
| 2. | **ADVERSE EVENT** | An undesirable and unintended, although not necessarily unexpected, result of therapy or other intervention (*e.g.*, headache following spinal tap or intestinal bleeding associated with aspirin therapy). |
| 3. | **ANONYMITY** | The condition that exists when there are no identifiers on research materials that could link or identify the data to an individual subject even to the research investigators. |
| 4. | **ASSENT** | Agreement by an individual not competent to give legally valid informed consent (*e.g.*, a child or cognitively impaired person) to participate in research. |
| 5. | **ASSURANCE** | A formal written, binding commitment that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved. |
| 6. | **AUTHORIZED INSTITUTIONAL OFFICIAL** | An officer of an institution with the authority to speak for and legally commit the institution to adherence to the requirements of the federal regulations regarding the involvement of human subjects in biomedical and behavioral research. The AIO at RAND is Michael Rich. |
| 7. | **AUTONOMY** | Personal capacity to consider alternatives, make choices, and act without undue influence or interference of others. |
| 8. | **BELMONT REPORT** | A statement of basic ethical principles governing research involving human subjects issued by the National Commission for the Protection of Human Subjects in 1978. |
| 9. | **BENEFICENCE** | An ethical principle discussed in the Belmont Report that entails an obligation to protect persons from harm. The principle of beneficence can be expressed in two general rules: (1) do not harm; and (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm. |
| 10. | **BENEFIT** | A valued or desired outcome; an advantage. |

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| 11. | **BLIND STUDY DESIGNS** | *See: Masked Study Designs; Double-Masked Design; and Single-Masked Design*. |
| 12. | **BOARD** | *See: Institutional Review Board* |
| 13. | **CASE-CONTROL STUDY** | A study comparing persons with a given condition or disease (the cases) and persons without the condition or disease (the controls) with respect to antecedent factors. (*See also: Retrospective Studies*.) |
| 14. | **CDC** | Centers for Disease Control and Prevention; an agency within the Public Health Service, Department of Health and Human Services. |
| 15. | **CHILDREN** | Persons who have not attained the legal age for consent to treatment or procedures involved in the research, as determined under the applicable law of the jurisdiction in which the research will be conducted. In most cases this means individuals who are under age 18. |
| 16. | **CERTIFICATE OF CONFIDENTIALITY** | An authorization from the Department of Health and Human Services (DHHS) that helps researchers and their institutions safeguard the privacy of research participants enrolled in sensitive biomedical and behavioral research by protecting against compulsory legal or administrative demands such as requests or subpoenas for identifying information. |
| 17. | **CLASSIFIED** | Research involving human subjects where the protocol or other information required by the IRB for review and oversight or required or provided by the research subjects includes classified information. "Classified information" means information that has been determined pursuant to an Executive Order or any predecessor order to require protection against unauthorized disclosure and is marked to indicate its classified status when in documentary form. |
| 18. | **CLINICAL TRIAL** | A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. |
| 19. | **CODE OF FEDERAL REGULATIONS (CFR)** | The federal compendium of regulations on numerous topics related to compliance with federal laws. Title 45, Part 46, of the Code of Federal Regulations (45 CFR 46), which outlines the basic provisions for Internal Review Boards (such as RAND's HSPC), informed consent, and Assurances of Compliance is known as the Common Rule. |
| 20. | **COHORT** | A group of subjects initially identified as having one or more characteristics in common who are followed over time. In social science research, this term may refer to any group of persons who are born at about the same time and share common historical or cultural experiences. |
| 21. | **COMMON RULE** | The Federal Policy for the Protection of Human Subjects, codified at Title 45, Part 46, of the Code of Federal Regulations (45 CFR 46), which outlines the basic provisions for Institutional Review Boards (such as RAND's HSPC), informed consent, and Assurances of Compliance. |
| 22. | **COMPENSATION** | Payment or medical care provided to subjects injured in research; does not refer to payment (remuneration) for participation in research. |

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| | | (*Compare: Remuneration*.) |
| 23. | **COMPETENCE** | Technically, a legal term, used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. (*See also: Incompetence, Incapacity*.) |
| 24. | **CONFIDENTIALITY** | Pertains to privacy and non-disclosure of personal information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure. |
| 25. | **CONFLICT OF INTEREST** | A conflict of interest is defined as: a close personal or professional association with the submitting Investigator(s), direct participation in the research (e.g., protocol development, Principal or Sub-investigator), or any significant financial interest in the sponsoring company defined as $10,000 or 5% ownership by the Investigators or their immediate family. |
| 26. | **CONSENT** | *See: Informed Consent*. |
| 27. | **CONTRACT** | An agreement; as used here, an agreement that a specific research activity will be performed at the request, and under the direction of, the agency providing the funds. Research performed under contract is more closely controlled by the agency than research performed under a grant. (*Compare: Grant*.) |
| 28. | **CONTRAINDICATED** | Pertains to the use of a treatment that should not be used in certain individuals or conditions due to risks of disadvantageous, perhaps dangerous results (*e.g.*, a drug may be contraindicated for pregnant women and persons with high blood pressure). |
| 29. | **CONTROL (SUBJECTS) OR CONTROLS** | Subject(s) used for comparison who are not given a treatment under study or who do not have a given condition, background, or risk factor that is the object of study. Control conditions may be concurrent (occurring more or less simultaneously with the condition under study) or historical (preceding the condition under study). When the present condition of subjects is compared with their own condition on a prior regimen or treatment, the study is considered historically controlled. |
| 30. | **CROSS-OVER DESIGN** | A type of clinical trial in which each subject experiences, at different times, both the experimental and control therapy. For example, half of the subjects might be randomly assigned first to the control group and then to the experimental intervention, while the other half would have the sequence reversed. |
| 31. | **DATA SAFEGUARDING PLAN (DSP)** | The document approved by the HSPC for a specific project that outlines what Human Subjects Information will be obtained and defines the ways specific projects will safeguard it, from initial acquisition through publication to final data destruction. |
| 32. | **DEBRIEFING** | Giving subjects previously undisclosed information about the research project following completion of their participation in research. (Note that this usage, which occurs within the behavioral sciences, departs from standard English, in which debriefing is obtaining rather than imparting |

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| | | information.) |
| 33. | **DECLARATION OF HELSINKI** | A code of ethics for clinical research approved by the World Medical Association in 1964 and widely adopted by medical associations in various countries. It has been revised several times, most recently in October 2000. |
| 34. | **DETAINEE** | Any person captured, detained, held, or otherwise under the control of DoD personnel (military, civilian, or contractor employee). It does not include persons being held primarily for law enforcement purposes, except where the United States is the occupying power. |
| 35. | **DEPENDENT VARIABLES** | The outcomes that are measured in an experiment. Dependent variables are expected to change as a result of an experimental manipulation of the independent variable(s). |
| 36. | **DHHS** | Abbreviation for U.S. Department of Health and Human Services. |
| 37. | **DIAGNOSTIC (PROCEDURE)** | Tests used to identify a disorder or disease in a living person. |
| 38. | **DOUBLE-MASKED DESIGN** | A study design in which neither the Investigators nor the subjects know the treatment group assignments of individual subjects. Sometimes referred to as "double-blind." |
| 39. | **DRUG** | Any chemical compound that may be used on or administered to humans as an aid in the diagnosis, treatment, cure, mitigation, or prevention of disease or other abnormal conditions. |
| 40. | **EMANCIPATED MINOR** | A legal status conferred upon persons who have not yet attained the age of legal competency law (for such purposes as consenting to medical care), but who are entitled to treatment as if they had by virtue of assuming adult responsibilities such as being self-supporting and not living at home, marriage, or procreation. (*See also: Mature Minor*.) |
| 41. | **EMBRYO** | Early stages of a developing organism, broadly used to refer to stages immediately following fertilization of an egg through implantation and very early pregnancy (*i.e.*, from conception to the eighth week of pregnancy). (*See also: Fetus*.) |
| 42. | **EMERGENCY USE** | Use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain HSPC approval. |
| 43. | **EPIDEMIOLOGY** | A scientific discipline that studies the factors determining the causes, frequency, and distribution of diseases in a community or given population. |
| 44. | **EQUITABLE** | Fair or just; used in the context of selection of subjects to indicate that the benefits and burdens of research are fairly distributed. |
| 45. | **ETHICS ADVISORY BOARD** | An interdisciplinary group that advises the Secretary, HHS, on general policy matters and on research proposals (or classes of proposals) that pose ethical problems. |
| 46. | **ETHNOGRAPHIC** | Ethnography is the study of people and their culture. Ethnographic |

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| | **RESEARCH** | research, also called fieldwork, involves observation of and interaction with the persons or group being studied in the group's own environment, often for long periods of time. (*See also: Fieldwork*.) |
| 47. | **EXCULPATORY** | Pertaining to that which relieves of a responsibility, obligation, or hardship; clearing from accusation or blame. |
| 48. | **EXPEDITED REVIEW** | Review of proposed research by HSPC Chairperson or a designated voting member or group of voting members rather than by the entire HSPC. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research. |
| 49. | **EXPERIMENTAL STUDY** | A true experimental study is one in which subjects are randomly assigned to groups that experience carefully controlled interventions manipulated by the experimenter according to a strict logic allowing causal inference about the effects of the interventions under investigation. (*See also: Quasi-Experimental Study*). |
| 50. | **EXPERIMENTAL** | Term often used to denote a therapy (drug, device, procedure) that is unproven or not yet scientifically validated with respect to safety and efficacy. A procedure may be considered "experimental" without necessarily being part of a formal study (research) to evaluate its usefulness. (*See also: Research*.) |
| 51. | **FAMILY MEMBER** | One who is part of the basic unit in society traditionally consisting of two parents rearing their own or adopted children; *also***:** any of various social units differing from but regarded as equivalent to the traditional family |
| 52. | **FEDERAL POLICY (THE)** | The federal policy that provides regulations for the involvement of human subjects in research. The policy applies to all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency that takes appropriate administrative action to make the policy applicable to such research. Currently, sixteen federal agencies have adopted the Federal Policy. (Also known as the "Common Rule.") |
| 53. | **FIELDWORK** | Behavioral, social, or anthropological research involving the study of persons or groups in their own environment and without manipulation for research purposes (distinguished from laboratory or controlled settings). (*See also: Ethnographic Research*.) |
| 54. | **FOOD AND DRUG ADMINISTRATION (FDA)** | An agency of the federal government established by Congress in 1912 and presently part of the Department of Health and Human Services. |
| 55. | **FULL HSPC REVIEW** | Review of proposed research at a convened meeting at which a majority of the membership of HSPC are present, including at least one member whose primary concerns are in nonscientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting. Also referred to as Full Committee Review. Full HSPC review is also required to disapprove or suspend approval of a project or an amendment to an approved project. |
| 56. | **GENE THERAPY** | The treatment of genetic disease accomplished by altering the genetic |

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| | | structure of either somatic (nonreproductive) or germline (reproductive) cells. |
| 57. | **GENETIC SCREENING** | Tests to identify persons who have an inherited predisposition to a certain phenotype or who are at risk of producing offspring with inherited diseases or disorders. |
| 58. | **GENOTYPE** | The genetic constitution of an individual. |
| 59. | **GRANT** | Financial support provided for research study designed and proposed by the Principal Investigator(s). The granting agency exercises no direct control over the conduct of approved research supported by a grant. (*Compare: Contract*.) |
| 60. | **GUARDIAN (LEGAL GUARDIAN)** | An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care. |
| 61. | **HELSINKI DECLARATION** | *See: Declaration of Helsinki*. |
| 62. | **HHS** | *See: DHHS.* |
| 63. | **HISTORICAL CONTROLS** | Control subjects (followed at some time in the past or for whom data are available through records) who are used for comparison with subjects being treated concurrently. The study is considered historically controlled when the present condition of subjects is compared with their own condition on a prior regimen or treatment. |
| 64. | **HUMAN RESEARCH PROTECTION OFFICIAL (HRPO)** | An individual designated by the head of the applicable DoD component and identified in the component's Human Research Protection Management Plan as the official who is responsible for the oversight and execution of the requirements of this clause, although some DoD components may use a different title for this position. |
| 65. | **HUMAN SUBJECTS** | A living individual about whom an investigator (whether professional or student) conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. NOTE: FDA's regulations define human subject as an individual and do not use the adjective "living." |
| 66. | **HUMAN SUBJECTS INFORMATION** | Any data obtained through intervention or interaction with a Human Subject and/or any identifiable private information of a Human Subject. |
| 67. | **HUMAN SUBJECTS PROTECTION COMMITTEE (HSPC)** | RAND's institutional review board for Human Subjects research, authorized by RAND's Federalwide Assurance (FWA) for the Protection of Human Subjects. The HSPC is concerned with both ethical and regulatory issues associated with the acquisition and protection of Human Subjects Information. |
| 68. | **IN VITRO** | Literally, "in glass" or "test tube;" used to refer to processes that are carried out outside the living body, usually in the laboratory, as distinguished from in vivo. |
| 69. | **IN VIVO** | Literally, "in the living body;" processes, such as the absorption of a drug |

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| | | by the human body, carried out in the living body rather than in a laboratory (in vitro). |
| 70. | **INCAPACITY** | Refers to a person's mental status and means inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Often used as a synonym for incompetence. (*See also: Incompetence*.) |
| 71. | **INCOMPETENCE** | Technically, a legal term meaning inability to manage one's own affairs. Often used as a synonym for incapacity. (*See also: Incapacity*.) |
| 72. | **INFORMATION, PRIVATE** | Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).<br><br>*Identifiable private information* is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.<br><br>*An identifiable biospecimen* is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen. |
| 73. | **INFORMED CONSENT** | A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. The Common Rule specifies requirements for required elements of informed consent. |
| 74. | **INSTITUTION** | (1): Any public or private entity or department or agency (including federal, state, and other agencies). |
| 75. | **INSTITUTION** | (2): A residential facility that provides food, shelter, and professional services (including treatment, skilled nursing, intermediate or long-term care, and custodial or residential care). Examples include general, mental, or chronic disease hospitals; inpatient community mental health centers; halfway houses and nursing homes; alcohol and drug addiction treatment centers; homes for the aged or dependent, residential schools for the mentally or physically handicapped; and homes for dependent and neglected children. |
| 76. | **INSTITUTIONAL REVIEW BOARD** | A specially constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research. At RAND the HSPC serves this function. |
| 77. | **INSTITUTIONALIZED COGNITIVELY IMPAIRED** | Persons who are confined, either voluntarily or involuntarily, in a facility for the care of the mentally or otherwise disabled (*e.g.*, a psychiatric hospital, home, or school for the retarded). |
| 78. | **INSTITUTIONALIZED** | Confined, either voluntarily or involuntarily (*e.g.*, a hospital, prison, or nursing home). |

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| 79. | **INTERACTION** | In the context of research, interaction includes communication (including conversations, monitoring, gathering, or recording of data, that occurs via telephone, e-mail, or other electronic device) or interpersonal contact between the Investigator, or member of the research staff, or other individual who is gathering and recording data for a research study and the research participant. |
| 80. | **INTERVENTION** | In research, intervention includes both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. |
| 81. | **HSPC** | *See: Institutional Review Board*. |
| 82. | **JUSTICE** | An ethical principle discussed in the Belmont Report requiring fairness in distribution of burdens and benefits; often expressed in terms of treating persons of similar circumstances or characteristics similarly. |
| 83. | **LEGALLY AUTHORIZED REPRESENTATIVE** | An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. If there is no applicable law addressing this issue, *legally authorized representative* means an individual recognized by institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research. |
| 84. | **LONGITUDINAL STUDY** | A study designed to follow subjects forward through time. |
| 85. | **MASKED STUDY DESIGNS** | Study designs comparing two or more interventions in which either the Investigators, the subjects, or some combination thereof do not know the treatment group assignments of individual subjects. Sometimes called "blind" study designs. (*See also: Double-Masked Design; Single-Masked Design*.) |
| 86. | **MATURE MINOR** | Someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain purposes (*e.g*., consenting to medical care). Note that a mature minor is not necessarily an emancipated minor. (*See also: Emancipated Minor*.) |
| 87. | **MEDICAL DEVICE** | A diagnostic or therapeutic article that does not achieve any of its principal intended purpose through chemical action within or on the body. Such devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intraocular lenses, and orthopedic pins or other orthopedic equipment. |
| 88. | **MENTALLY DISABLED** | *See: Cognitively Impaired*. |
| 89. | **MINIMAL RISK** | A risk is considered minimal where the probability and magnitude of harm or discomfort anticipated in the proposed 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. For example, the risk of drawing a small amount of blood from a healthy |

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| | | individual for research purposes is no greater than the risk of doing so as part of routine physical examination.*<br><br>The definition of minimal risk for research involving prisoners differs somewhat from that given for noninstitutionalized adults. *See: Prisoner*<br><br>*DoD Instruction states: The phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests" in the definition of minimal risk (section 219.102(i) of Reference (c)) shall not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain). |
| 90. | **MONITORING** | The collection and analysis of data as the project progresses to assure the appropriateness of the research, its design and subject protections. |
| 91. . | **NATIONAL COMMISSION** | National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. An interdisciplinary advisory body, established by Congressional legislation in 1974, which was in existence until 1978, and which issued a series of reports and recommendations on ethical issues in research and medicine, many of which are now embodied in federal regulations. |
| 92. | **NIAAA** | National Institute on Alcohol Abuse and Alcoholism; an institute in NIH. |
| 93. | **NIDA** | National Institute on Drug Abuse; an institute in NIH. |
| 94. | **NIH** | National Institutes of Health: a federal agency within the Public Health Service, DHHS, comprising 21 institutes and centers. It is responsible for carrying out and supporting biomedical and behavioral research. |
| 95. | **NIMH** | National Institute of Mental Health; an institute in NIH. |
| 96. | **NONAFFILIATED MEMBER** | Member of an Institutional Review Board who has no ties to the parent institution, its staff, or faculty. This individual is usually from the local community (*e.g.*, minister, business person, attorney, teacher, homemaker). |
| 97. | **NONSIGNIFICANT RISK DEVICE** | An investigational medical device that does not present significant risk to the patient. (*See also: Significant Risk Device*.) |
| 98. | **NONTHERAPEUTIC RESEARCH** | Research that has no likelihood or intent of producing a diagnostic, preventive, or therapeutic benefit to the current subjects, although it may benefit subjects with a similar condition in the future. |
| 99. | **NONVIABLE FETUS** | An expelled or delivered fetus which, although it is living, cannot possibly survive to the point of sustaining life independently, even with the support of available medical therapy. Although it may be presumed that an expelled or delivered fetus is nonviable at a gestational age less than 20 weeks and weight less than 500 grams, a specific determination as to viability must be made by a physician in each instance. (*See also: Viable* |

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| | | *Infant*.) |
| 100. | **NORMAL VOLUNTEERS** | Volunteer subjects used to study normal physiology and behavior or who do not have the condition under study in a particular protocol, used as comparisons with subjects who do have the condition. "Normal" may not mean normal in all respects. For example, patients with broken legs (if not on medication that will affect the results) may serve as normal volunteers in studies of metabolism, cognitive development, and the like. Similarly, patients with heart disease but without diabetes may be the "normals" in a study of diabetes complicated by heart disease. |
| 101. | **NULL HYPOTHESIS** | The proposition, to be tested statistically, that the experimental intervention has "no effect," meaning that the treatment and control groups will not differ as a result of the intervention. Investigators usually hope that the data will demonstrate some effect from the intervention, thereby allowing the Investigator to reject the null hypothesis. |
| 102. | **NUREMBERG CODE** | A code of research ethics developed during the trials of Nazi war criminals following World War II and widely adopted as a standard during the 1950s and 1960s for protecting human subjects. |
| 103. | **OFFICE FOR HUMAN RESEARCH PROTECTIONS (OHRP)** | The office within the Department of Health and Human Services, responsible for implementing DHHS regulations (45 CFR Part 46) governing research involving human subjects. |
| 104. | **OPEN DESIGN** | An experimental design in which both the Investigator(s) and the subjects know the treatment group(s) to which subjects are assigned. |
| 105. | **PATERNALISM** | Making decisions for others against or apart from their wishes with the intent of doing them good. |
| 106. | **PERMISSION** | The agreement of parent(s) or guardian to the participation of their child or ward in research. |
| 107. | **PHARMACOLOGY** | The scientific discipline that studies the action of drugs on living systems (animals or human beings). |
| 108. | **PHENOTYPE** | The physical manifestation of a gene function. |
| 109. | **PHS** | Public Health Service. Part of the U.S. Department of Health and Human Services, it includes FDA, NIH, CDC, SAMHSA, and HRSA. |
| 110. | **PLACEBO** | An inert substance or sham activity used in the guise of treatment; used in controlled clinical trials as a comparator to determine if an investigational therapy is more effective than no treatment. |
| 111. | **PREGNANCY** | The period of time from confirmation of implantation of a fertilized egg within the uterus until the fetus has entirely left the uterus (*i.e*., has been delivered). Implantation is confirmed through a presumptive sign of pregnancy such as missed menses or a positive pregnancy test. |
| 112. | **PREMARKET APPROVAL** | Process of scientific and regulatory review by the FDA to ensure the safety and effectiveness of Class III devices. |

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| 113. | **PRESIDENT'S COMMISSION** | President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. An interdisciplinary advisory group, established by congressional legislation in 1978, which was in existence until 1983, and which issued reports on ethical problems in health care and in research involving human subjects. |
| 114. | **PRINCIPAL INVESTIGATOR** | RAND Associate identified as having primary responsibility for the design and conduct of a specific RAND research project or task. The Principal Investigator/Project Director for a research project is generally the Associate identified in RAND's financial information system "Oasis" as the "Project Leader." |
| 115. | **PRISONER** | An individual involuntarily confined in a penal institution, including persons: (1) sentenced under a criminal or civil statue; (2) detained pending arraignment, trial, or sentencing; and (3) detained in other facilities (*e.g.*, for drug detoxification or treatment of alcoholism) under statutes or commitment procedures providing such alternatives to criminal prosecution or incarceration in a penal institution.<br><br>The definition of minimal risk for research involving prisoners differs somewhat from that given for non-institutionalized adults. |
| 116. | **PRIVACY** | Control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. |
| 117. | **PROBAND** | The person whose case serves as the stimulus for the study of other members of the family to identify the possible genetic factors involved in a given disease, condition, or characteristic. |
| 118. | **PROPHYLACTIC** | Preventive or protective; a drug, vaccine, regimen, or device designed to prevent, or provide protection against, a given disease or disorder. |
| 119. | **PROSPECTIVE STUDIES** | Studies designed to observe outcomes or events that occur subsequent to the identification of the group of subjects to be studied. Prospective studies need not involve manipulation or intervention but may be purely observational or involve only the collection of data. |
| 120. | **PROTOCOL** | The formal design or plan of an experiment or research activity; specifically, the plan submitted to an HSPC for review and to an agency for research support. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data. |
| 121. | **QUASI-EXPERIMENTAL STUDY** | A study that is similar to a true experimental study except that it lacks random assignments of subjects to treatment groups. (*See also: Experimental Study*.) |
| 122. | **RANDOM**<br><br>**RANDOM ASSIGNMENT** | Assignment of subjects to different treatments, interventions, or conditions according to chance rather than systematically (*e.g.*, as dictated by the standard or usual response to their condition, history, or prognosis, or according to demographic characteristics). Random assignment of subjects to conditions is an essential element of |

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| | **RANDOMIZATION**<br>**RANDOMIZED** | experimental research because it makes more likely the probability that differences observed between subject groups are the result of the experimental intervention. (Random assignment to treatment or control groups should not be confused with random or probability sampling of research subjects.) |
| 123. | **RECOMBINANT DNA TECHNOLOGY** | DNA resulting from the insertion into the chain, by chemical or biological means, of a sequence (a whole or partial chain of DNA) not originally (biologically) present in that chain. Recombinant DNA technology is also used to develop diagnostic screens and tests, as well as drugs and biologics for treating diseases with genetic components. |
| 124. | **RECUSE** | To disqualify (oneself) as judge in a particular case; *broadly*: to remove (oneself) from participation to avoid a conflict of interest. |
| 125. | **REMUNERATION** | Payment for participation in research, also referred to as “incentive”. (NOTE: It is wise to confine use of the term "compensation" to payment or provision of care for research-related injuries.) (*Compare: Compensation*.) |
| 126. | **RESEARCH** | A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:<br>(1) Scholarly and journalistic activities (*e.g.,* oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.<br>(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).<br>(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.<br>(4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions. |

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| 127. | **RESEARCH PARTICIPANT** | An individual about whom, or from whom, RAND, or persons acting on behalf of RAND, obtains data for use in a RAND project. Such data may include factual information, opinions, and attitudes, whether or not Human Subjects Information. |
| 128. | **RESPECT FOR PERSONS** | An ethical principle discussed in the Belmont Report requiring that individual autonomy be respected and that persons with diminished autonomy be protected. |
| 129. | **RETROSPECTIVE STUDIES** | Research conducted by reviewing records from the past (*e.g.*, birth and death certificates, medical records, school records, or employment records) or by obtaining information about past events elicited through interviews or surveys. Case control studies are an example of this type of research. |
| 130. | **REVIEW (OF RESEARCH)** | The concurrent oversight of research on a periodic basis by an HSPC. In addition to the at least annual reviews mandated by the federal regulations, reviews may, if deemed appropriate, also be conducted on a continuous or periodic basis. |
| 131. | **RHINO** | The RAND HSPC Information Online submission system and protocol database used at RAND which was introduced in 2008. |
| 132. | **RISK** | The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only "minimal risk." (*See also: Minimal Risk*.) |
| 133. | **SCIENTIFIC REVIEW GROUP** | A group of highly regarded experts in a given field, convened by NIH to advise NIH on the scientific merit of applications for research grants and contracts. Scientific review groups are also required to review the ethical aspects of proposed involvement of human subjects. Various kinds of scientific review groups exist and are known by different names in different institutes of the NIH (*e.g.*, Study Sections, Initial Review Groups, Contract Review Committees, or Technical Evaluation Committees). |
| 134. | **SIGNIFICANT RISK DEVICE** | An investigational medical device that presents a potential for serious risk to the health, safety, or welfare of the subject. |
| 135. | **SINGLE-MASKED DESIGN** | Typically, a study design in which the Investigator, but not the subject, knows the identity of the treatment assignment. Occasionally the subject, but not the Investigator, knows the assignment. Sometimes called "single-blind design." |
| 136. | **SITE VISIT** | A visit by agency officials, representatives, or consultants to the location of a research activity to assess the adequacy of HSPC protection of human subjects or the capability of personnel to conduct the research. |
| 137. | **SOCIAL EXPERIMENTATION** | Systematic manipulation of, or experimentation in, social or economic systems; used in planning public policy. |
| 138. | **STATISTICAL SIGNIFICANCE** | A determination of the probability of obtaining the particular distribution of the data on the assumption that the null hypothesis is true. Or, more simply put, the probability of coming to a false positive conclusion. If the |

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| | | probability is less than or equal to a predetermined value (*e.g.*, 0.05 or 0.01), then the null hypothesis is rejected at that significance level (0.05 or 0.01). |
| 139. | **STUDY SECTION** | *See: Scientific Review Group*. |
| 140. | **SUBJECTS (HUMAN)** | *See: Human Subjects*. |
| 141. | **SURVEYS** | Studies designed to obtain information from a large number of respondents through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures. |
| 142. | **THERAPEUTIC INTENT** | The research physician's intent to provide some benefit to improving a subject's condition (*e.g.*, prolongation of life, shrinkage of tumor, or improved quality of life, even though cure or dramatic improvement cannot necessarily be effected.) |
| 143. | **THERAPY** | Treatment intended and expected to alleviate a disease or disorder. |
| 144. | **UNANTICIPATED PROBLEM** | Any unforeseen event or events that may involve risks or affect the safety or welfare of subjects or others, or that may affect the integrity of the research. |
| 145. | **UNANTICIPATED PROBLEMS INVOLVING RISK TO SUBJECTS OR OTHERS (UPIRTSO)** | Any incident, experience, or outcome that is unexpected, is related or possibly related to participation in the research and suggests that the research places human subjects or others at a greater risk of harm that was previously known or recognized, even if no harm has actually occurred. |
| 146. | **UNIFORM ANATOMICAL GIFT ACT** | Legislation adopted by all 50 States and the District of Columbia that indicates procedures for donation of all or part of a decedent's body for such activities as medical education, scientific research, and organ transplantation. |
| 147. | **VACCINE** | A biologic product generally made from an infectious agent or its components — a virus, bacterium, or other microorganism — that is killed (inactive) or live-attenuated (active, although weakened). Vaccines may also be biochemically synthesized or made through recombinant DNA techniques. |
| 148. | **VARIABLE (NOUN)** | An element or factor that the research is designed to study, either as an experimental intervention or a possible outcome (or factor affecting the outcome) of that intervention. |
| 149. | **VIABLE INFANT** | When referring to a delivered or expelled fetus, the term "viable infant" means likely to survive to the point of sustaining life independently, given the benefit of available medical therapy. This judgment is made by a physician. In accordance with DHHS regulations, the Secretary, HHS, may publish guidelines to assist in the determination of viability. Such guidelines were published in 1975 and specify an estimated gestational age of 20 weeks or more and a body weight of 500 grams or more as indices of fetal viability. These indices depend on the state of present |

technology and may be revised periodically. (*See also: Nonviable Fetus*.)

150. **VOLUNTARY** Free of coercion, duress, or undue inducement. Used in the research context to refer to a subject's decision to participate (or to continue to participate) in a research activity.