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Subject: UAB Policy on the Protection of Human Subjects in Research

introduction

As part of its mission, the University of Alabama at Birmingham (UAB) performs research to advance knowledge. A significant portion of UAB’s research involves clinical research in humans. This policy establishes UAB’s program for the protection of human subjects and describes the ethical standards and institutional commitments applicable to the conduct of human subjects research at UAB.

MISSION STATEMENT

The mission of the human research protection program is to protect the rights and welfare of human subjects involved in research.

Definitions

The definitions in this policy apply to all other policies established for the Protection of Human Subjects in Research.

*Agent* – Person authorized to act on behalf of UAB. This includes an individual performing UAB designated activities or exercising UAB-delegated authority or responsibility.

*Clinical Trial (as defined by DHHS regulations)* – 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.

*Clinical Investigation* – See definition for Research (as defined by FDA regulations).

*Code of Federal Regulations (CFR)* – A codification of federal agency regulations which has the force and effect of law.

*Federal Guidance* – Information published by federal agencies on the topic that represents the agency’s current thinking or view but does not have the effect or force of law.

*Federalwide Assurance (FWA)* – A document filed with the Office for Human Research Protections (OHRP) of the Department of Health and Human Services expressing an institution‘s commitment to comply with the department’s regulations for the protection of human subjects.

*FTE* – Full-time equivalent appointment.

*Generalizable Knowledge* – Information derived from a systematic investigation that can be applied to: other facilities or institutions; existing body of knowledge on a topic, disease or disorder disseminated through publication or scientific meeting; or a change in the standard of care.

*Human Subject (as defined by DHHS regulations)* – 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; (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

*Intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes.

*Interaction* includes communication or interpersonal contact between investigator and subject.

*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 that the individual can reasonably expect will not be made public (for example, a medical record).

*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.

*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 information.

*Human Subject (as defined by FDA regulations)* – An individual who becomes a participant in research regulated by the Food and Drug Administration (FDA), either as a recipient of a test article or as a control. A subject may be either a healthy human or a patient. In the case of research involving medical devices, a human subject includes an individual on whose specimen a medical device is used.

*Human Subjects Research* - Any activity that is either (a) “research” as defined by DHHS regulations that involves “human subjects” as defined by DHHS regulations or (b) "research” as defined by FDA regulations that involves “human subjects” as defined by FDA regulations.

*Human Subjects Research* (as defined by DOE 443.1A )- Any systematic investigation (including research development, testing, and evaluation) utilizing living individuals or personally identifiable information or materials, designed to develop or contribute to generalizable knowledge. (See DOE P 443.1A for examples and exclusions.)

*Research Involving a Human Being as an Experimental Subject* (as defined by DoDD 3216.02) *–* an activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction.(32CFR219.102(f).

*IRB* – Institutional Review Board established in accord with and for the purposes expressed in federal regulations to protect the rights and welfare of human research subjects.

*Research (as defined by DHHS regulations)* – A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. The following activities are deemed not to be research:

*(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.*

*(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 disease, 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).*

*(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.*

*(4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.*

*Research (as defined by FDA regulations*) (synonymous with the term *Clinical Investigation*) – Any experiment that involves a test article and one or more human subjects that is subject to the IND or IDE regulations or that is not subject to the IND or IDE regulations but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

*An experiment subject to the IND regulations* is defined as any use of a drug other than the use of a marketed drug in the course of medical practice.

*An experiment subject to the IDE regulations* is defined as any evaluation of the safety or efficacy of a medical device.

*Research (as defined by DoDD 3216.02) –* Any systematic investigation, including research, development, testing, and evaluation (RDT&E), designed to develop or contribute to generalizable knowledge.

*Systematic Investigation -* an orderly collection to obtain information about which conclusions can be drawn and so that others can review those conclusions.

*UAB Facilities* – Facilities owned and operated by UAB; does not include facilities leased by the Board of Trustees of the University of Alabama to private entities.

*UAB Institutional Official* – Individual authorized to act for UAB and, on its behalf, obligates UAB to the Terms of its Federalwide Assurance with the Department of Health and Human Services and OHRP.

*UAB-Affiliated Entities* –UAB Hospital; UAB Hospital-Highlands, UAB Women & Infants Center, Spain Rehabilitation Center, Hazelrig-Salter Radiation Oncology Center, The Kirklin Clinic of UAB Hospital, 1917 Clinic, and Civitan Sparks Clinic and their wholly or majority owned subsidiaries.

POLICY statement

1. Guiding Principles

When UAB performs research using human subjects, the ethical principles expressed in the Belmont Report shall apply, unless other appropriate ethical standards are called for by properly authorized federal departments, agencies, or foreign states that have controlling jurisdiction over the research.

2. Scope of Authority

This policy applies whenever UAB engages in human subjects research as described by the Federal Policy for the Protection of Research Subjects (the “Common Rule”). UAB holds a Federalwide Assurance (FWA) with the Department of Health and Human Services. Under its FWA, UAB extends the applicable regulations of the Department of Health and Human Services in Title 45 Part 46 of the Code of Federal Regulations to all federally-funded research involving human subjects as defined by DHHS regulations. UAB applies these ethical principles to all research involving human subjects being conducted by investigators acting as agents of UAB regardless of the site of the activity; to all human research involving any UAB personnel, patients, students, or facilities owned and operated by UAB or UAB affiliated entities; research that is supported by extramural funds granted to (or applied for through) UAB; or for research conducted using UAB funding at non-UAB sites. Under this FWA, UAB extends the regulations of the Department of Defense in Title 32 Part 219 of the Code of Federal Regulations to all applicable research involving a human being as an experimental subject.

In addition this policy applies to clinical investigations and other clinical activities requiring IRB review under FDA regulations, and to human subjects research regulated by other federal agencies. Research studies involving humans not covered by UAB’s FWA will be conducted according to the guiding ethical principles above.

3. Jurisdiction

A. Activities Involving UAB Investigators. All faculty and staff paid by UAB or UAB affiliated entities equal to or greater than a cumulative total of 0.5 FTE or any agents of UAB, who are conducting studies involving human subjects within the course and scope of their duties, regardless of the source or amount of funding, are required without exception to have prior approval from the UAB IRB before research is initiated. All UAB students, including post-graduate trainees, conducting research involving human subjects research as part of their educational training at UAB must have prior approval from the UAB IRB before research is initiated.

Regardless of the fraction of FTE for faculty or staff appointment, prior approval of the UAB IRB is required, without exception, when studies conducted by UAB faculty or staff access any UAB patients, personnel, students, or facilities owned and operated by UAB or UAB affiliated entities; or when the human subjects research is supported either by extramural funds granted to (or applied for through) UAB, or for research conducted with UAB funding at non-UAB sites, or when UAB has a written agreement to provide IRB review for research studies.

Prior approval of the UAB IRB is not required when part-time (< 0.5 cumulative FTE) or unpaid faculty are not acting as staff members, employees, or agents of UAB, when no UAB patients, personnel, students or facilities owned and operated by UAB or UAB affiliated entities are used, and when the activity is not represented to subjects as being conducted under the aegis of UAB. However, in such cases investigators holding UAB appointments must nevertheless obtain approval for the use of human subjects from a duly constituted IRB, not necessarily at UAB.

B. Activities Accessing UAB Facilities, Patients, Staff, or Students Not Being Conducted by a UAB Principal Investigator. All non-UAB investigators involving human subjects in research projects that access any UAB facilities, patients, staff, or students in a manner engaging UAB in research must either identify a UAB faculty member to serve as a UAB Principal Investigator for the project or submit their research proposal to the IRB administrative unit for an administrative review. The administrative review will determine the following:

1. Whether the study must have a UAB faculty member serve as a Principal Investigator, or
2. Whether the study can be certified as exempt or otherwise not fall under human subjects regulation, and/or
3. Whether the study will require additional institutional review and approval.

Determinations of whether or not UAB is engaged in research for any study will be made by the Institutional Official for UAB’s FWA or the IO’s delegates (OIRB Senior Staff) and may be done in conjunction with the IRB Chair and an attorney from UAB’s Office of Legal Counsel using OHRP regulations and guidance for engagement in research as the standard for decision. In debatable situations referral for determination will be made to the appropriate federal agency, when applicable, in accordance with federal regulations.

C. Activities Involving Research Conducted by BVAMC Investigators: UAB has agreed to provide human subjects protection program services by the IRB and Office of the IRB through a memorandum of understanding (MOU) with the Birmingham Veterans Administration Medical Center (BVAMC). The UAB IRB agrees to comply with the federal regulations under 38 CFR 16 as well as the applicable VA policies for review and conduct of exempt and non-exempt human subjects research, including, but not limited to, the VA policies in VHA Handbook 1200.05 (Requirements for Protection of Human Subject Research in Department of Veterans Affairs (VA) Research) and VHA Handbook 1058.01 (Research Compliance Reporting Requirements).BVAMC Investigators must follow the UAB IRB Human Research Protection Program policies (HRPP) regarding submission, review, reporting, and oversight of VA research under the oversight of the UAB IRB.

4. Institutional Review Board

UAB hereby establishes and designates its institutional review board as the UAB IRB. The UAB IRB may consist of one or more committees as is necessary to properly review and approve human subjects research for UAB. The UAB IRB shall review all research covered under this plan and is granted authority to approve, make modifications in, or disapprove human subjects research; decisions of the UAB IRB on individual research protocols are final. UAB may not approve research lacking approval by a designated IRB. Implementation of UAB IRB approved research protocols may be prevented or terminated by decision at any other level of the institution, although the UAB IRB approval will not be voided by such action. In reviewing research protocols the UAB IRB shall take into account all applicable federal and state laws and regulations and federal guidance including but not limited to, the regulations of the Department of Health and Human Services at 45 CFR Part 46, the FDA at 21 CFR Parts 50, 56, Department of Defense Directive (DoDD) 3216.2, Secretary of the Navy (SECNAVINST) 3900.39D, Department of Justice (DOJ) 28 CFR Part 28, Department of Energy (DOE) 10 CFR Part 745, and Department of Education (DE) 34 CFR 97 pertaining to human subjects research, the Veterans Administration (VA) under 38 CFR 16 as well as the applicable VA and VHA policies related to review and conduct of exempt and non-exempt human subjects research., the applicable regulations pertaining to privacy in research under the Health Information Portability and Accountability Act at 45 CFR Parts 160 and 164, and state laws regarding legal authorization to consent. The UAB IRB will establish procedures to determine when proposed research may be expedited under or exempted from federal regulations and guidance. The UAB IRB shall establish written policies and procedures in conjunction with the Institutional Official, as appropriate, in accordance with federal and state laws and regulations and UAB policies to implement this policy. UAB may utilize additional external IRBs to act in the capacity of a UAB IRB as circumstances require, external IRBs will be specified in writing. The IRB will not issue approval of human subjects research until all other applicable institutional approvals are attained.

UAB IRBs will conduct reviews of clinical trials involving drugs, devices, or biologics in accordance with ICH-GCP to the extent adopted by the FDA. If a sponsor requires the additional requirements in the ICH-GCP (E6) guidance be followed, then the clinical trial involving drugs, devices, or biologics will be submitted to the Western IRB for review (unless it is a VA study) or proceed internally following that guidance.

The IRB will conduct a review in accordance with ICH-GCP guidelines when OSP and/or the investigator informs the OIRB that a sponsor requires it or it is noted in a communication to the IRB with the application submitted for review. When these studies are reviewed, the IRB minutes will reflect that they were reviewed according to ICH-GCP (E6) guidelines.

If required by Federal regulation; funding agency; Cooperative Group; or Consortium, UAB will allow review by an external IRB or EC if the investigator wants to participate in a multi-site research study. The reviewing IRB must be accredited and there must be a reliance agreement in place prior to the conduct of the research. This does not apply to VA research overseen by the UAB IRB.

In instances where the external IRB or EC is not accredited, the UAB Office of the IRB, IRB Chair and Institutional Official will make a determination as to whether UAB will rely upon the non-accredited IRB/EC. These determinations will be made on a protocol-by-protocol basis taking into account the level of research risk and oversight measures to ensure human participants are protected. A reliance agreement must be in place prior to the conduct of the research. This does not apply to VA research overseen by the UAB IRB.

A. Undue Influence or Coercion upon the IRB. IRB proceedings and implementation of policies and procedures must be free of undue influence or coercion to maintain the integrity and fairness of the IRB review process. IRB members, OIRB staff, investigators, research staff, or participants who have concerns about events or actions covering undue influence or coercion should report those concerns either to the OIRB Director or IRB Chair in accordance with the University Compliance Office. The OIRB Director or IRB Chair should document and report the concerns to the UAB Institutional Official, who will evaluate the report, develop findings, and take remedial actions based on those findings. If the concern is related to the IRB Chair or OIRB Director reports should go to the Institutional Official. If the concern is related to the Institutional Official, the reports should go to the Provost or University Compliance Office. Concerns related to the Research Compliance Office should be reported to the UAB General Counsel. UAB maintains a Research Compliance Hotline for anonymous and confidential communication with the university to promote reporting of concerns about noncompliance with research regulations and UAB policies.

B. Resource Allocation for Human Research Protection Program. UAB will maintain a separate designated budget for the OIRB and the IRBs. Proposed budgets will be submitted annually through the Office of the Vice President for Research and Economic Development after consultation with the IRB Chair and the OIRB Director. The submitted IRB budget will be forwarded to the UAB Office of the Vice President for Financial Affairs and Administration, where it will be finalized following review and adjustment consistent with the overall institutional budget.

5. Responsibility

The responsibility for the protection of human subjects at UAB is a shared responsibility between the Vice President for Research as the institutional representative, the UAB IRB, UAB academic departments, UAB administrative departments and the investigators including their research teams. These responsible parties will maximize compliance with this policy through coordination of activities among regulatory and academic units within UAB and provision for appropriate training programs in human subjects research to all stakeholders.

A. Vice President for Research

1. The Vice President for Research is responsible for implementation of this policy.
2. The Vice President for Research serves as UAB Institutional Official under its FWA and exercises overall responsibility for the human research protection program.
3. The Institutional Official has the authority to develop policies and procedures, which are binding on the institution; to allocate resources to the human research protection program; to designate one or more IRB committees and appoint the Chair(s) and Vice-Chair (with the advice and consent of the UAB President and Provost) and individual members of the on-campus IRBs; to suspend human subjects research activity; to exercise overall supervision of the human research protections program including IRB communication, education, record keeping, reporting, monitoring and oversight, and to develop procedures to determine when research activities are exempt or otherwise do not fall under UAB’s FWA or other regulations.
4. The Institutional Official may delegate the authorities in Section 5.A.iii. for the Program to the IRB Chair and OIRB Director, or other individuals as appropriate.

B. UAB-Designated IRBs.UAB-designated IRBs are obligated and/or authorized to:

1. Act knowledgeably in review of human subjects research in accordance with federal law and/or regulations including DoD, DoE, DE, DOJ, and VA, state/local laws and/or regulations, ICH-GCP (E6) guidance when required by the sponsor and UAB policy.
2. Approve, disapprove, or require modifications for approval for all human subjects research activities.
3. Determine that risks to subjects are minimized by using procedures 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 therapeutic purposes; that risks to subjects are reasonable in relation to anticipated benefits, if any, to the subjects and the importance of the knowledge that may be expected to result; that selection of subjects is equitable; and that informed consent will be sought and documented from each subject unless waiver of informed consent process or its documentation is proper under federal regulations.
4. When appropriate, determine that the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects; that there are adequate provisions to protect the privacy of subjects and the confidentiality of the data; also, when subjects likely to be vulnerable to coercion or undue influence are involved, determine that additional safeguards have been included in the research to protect the rights and welfare of these subjects.
5. Observe or have a third party observe the consent process or the research (45 CFR 46.109, 21 CFR 56.109). This includes review of research records as well as research activity.
6. Suspend or terminate approval of ongoing research that violates the IRB’s requirements or that has been associated with unexpected serious harm to subjects.
7. Notify parties in writing of its decisions to approve, disapprove, or require modifications to approve research.
8. Have written policies and procedures to ensure prompt reporting to the IRBs, regulatory agencies, and institutional officials of unanticipated problems involving risks to subjects or others, and serious or continuing noncompliance with this policy, federal regulations, or the requirements or determinations of the IRB.
9. Use applicable federal, state, and local laws and regulations pertaining to human subjects research, as substantive standards for decision making; treat applicable federal guidance in the same manner as a regulation unless permission to act otherwise is granted by the UAB Institutional Official; and render decisions and determinations that are not arbitrary or capricious.

C. Investigators.Under UAB’s FWA investigators have the primary responsibility for protecting the rights and welfare of human research subjects and complying with all applicable provisions of UAB’s FWA and laws and regulations governing their research activities. Investigators should be knowledgeable about federal laws and/or regulations including those of the DoD, DOE, DE, DOJ, and VA, as well as state laws and/or regulations pertaining to human subjects and UAB policies for the protection of human subjects. If investigators are conducting research at the VA they must have a VA appointment. Principal investigators are responsible for:

1. Ensuring no trial activity is initiated without formal written approval having been obtained from the IRB for the protocol and any written information being provided to participants;
2. Ensuring research staff are knowledgeable about and follow all legal and regulatory requirements and the Organization’s policies and procedures that pertain to their research;
3. Ensuring that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions;
4. Performing research studies in accordance with generally accepted scientific principles, the ethical principles adopted by this policy, and with sufficient resources to protect human research subjects.
5. Conducting research according to the UAB IRB–approved protocol and complying with all IRB determinations.
6. Obtaining and documenting the informed consent of each subject or the subject’s legally authorized representative, using an IRB validated and approved informed consent document unless the IRB has waived these requirements.
7. Giving a copy of the informed consent document to each subject or the subject’s legally authorized representative, when applicable.
8. Promptly reporting to the IRB all unanticipated and reportable events as defined in written policies and procedures.
9. Promptly reporting to the IRB all allegations or findings of non-compliance with federal regulations on human subjects or determinations or requirements of a UAB-designated IRB.
10. Maintaining documents and providing reports to the IRB in accordance with federal regulations, UAB, and IRB requirements;
11. Adhering to industry-sponsored trial contract requirements and, if applicable, to follow ICH-GCP standards.

D. Departmental Chairs. The departmental chairs or their designee are responsible for reviewing the research activities within their department to determine that:

1. Proper scientific review and approval (e.g. oversight committee) have been obtained;
2. The Principal Investigator is qualified to conduct the research;
3. The hypothesis and procedures of any research study are consistent with generally accepted scientific principles in the discipline; and
4. Appropriate resources including facilities are available to conduct the research.
5. BVAMC research activities are reviewed by a scientific/scholarly supervisor to assure the obligations of i.-iv. are met.

The obligations in clauses i-iv above may be delegated by the Chair; however, the Chair maintains ultimate responsibility for these obligations.

E. University.

1. UAB under its FWA assures the federal government that it will comply with federal research regulations and no research involving human subjects will be conducted without appropriate prior review and approval.
2. UAB provides treatment for research related injury, but not free of charge. Patients and third parties will be billed for treatment, when appropriate.
3. UAB, as a state entity, is not ordinarily legally responsible for the acts and omissions of its employees and agents. However, UAB has agreed to provide for legal representation and indemnification for judgments rendered against its employees and agents acting in the course and scope of their duties. UAB considers an individual acting in the capacity of an IRB member to be its agent.
4. UAB will develop additional policies and procedures and other materials, as necessary, to implement this policy and a human subjects protection program generally.

APPROVED:

Ray L. Watts, MD, UAB President