

**UNIVERSITY OF KENTUCKY
HUMAN RESEARCH PROTECTION PROGRAM
COMPREHENSIVE PLAN**

A1.0100 OVERVIEW OF UK RESEARCH ENVIRONMENT

The University of Kentucky (UK), the Commonwealth of Kentucky's flagship institution of higher education, is a public, research-extensive, land-grant University dedicated to enriching people's lives through excellence in teaching, research and service. The role of the UK research enterprise in developing new knowledge for transfer through teaching and service is critical to the broader institutional mission. Research is conducted in 16 colleges (Agriculture, Food and Environment, Arts and Sciences, Business and Economics, Communication and Information, Dentistry, Design, Education, Engineering, Fine Arts, Health Sciences, Law, Medicine, Nursing, Pharmacy, Public Health, and Social Work) as well as The Graduate School, Lewis Honors College and UK Libraries. In addition, UK's multidisciplinary research focus extends to more than 70 multidisciplinary research centers, institutes and core research facilities. Significant human research at UK is conducted in many of these units and in major research centers.

As a major postsecondary institution with extensive human research activity, UK recognizes its institutional obligation to provide research subjects the highest standards in research protection. The human research protection program (HRPP) at UK is a multi-faceted enterprise designed to protect human subjects across broad-ranging research activities through established institution-wide policies and procedures. The institution's comprehensive plan for human research protection provides a guide to institutional authorizations, ethical principles, accreditation standards, standard operating procedures, responsible units and personnel, and the supporting documents that lay the foundation for the protections provided to research subjects. Essential components of the HRPP include policy, education, procedures, protocol review, conduct of study, study monitoring, and program assessment. All HRPP regulations, policies and operating procedures relevant to these components are incorporated into the comprehensive plan.

A1.0150 Mission Statement

UK is committed to the highest ethical standards in the conduct of research and to ensuring the protection of human subjects involved in research. This commitment governs the structure of the institutional HRPP and forms the basis for the following institutional Administrative Regulations: AR 7:4 (Human Research Subject Protection and Institutional Review Boards); AR 7:2 (Financial Conflicts of Interest in Research); AR 7:9 (Institutional Conflicts of Interest Involving Research); AR 10:1 (Policy Governing Access to and Use of University Information Technology Resource); UK Policy – Due Process (Research Misconduct).

A1.0200 ETHICAL PRINCIPLES AND FEDERAL/STATE REGULATORY GUIDANCE

The conduct of all UK research involving human subjects shall be in accordance with the ethical principles outlined in the Belmont Report, and specifically in accordance with three key concepts: respect for persons (consent, privacy and confidentiality, with additional safeguards for special populations), beneficence (minimize risks and maximize benefits) and justice (fair sharing of benefits and burdens of research). All human research conducted by UK personnel at institutional or non-institutional performance sites for UK, domestic or international, shall also comply with the Department of Health and Human Services (HHS) *Code of Federal Regulations* (CFR) 45 CFR 46 and, as applicable, Food and Drug Administration (FDA) 21 CFR

Parts 50 and 56, and the Health Insurance Portability and Accountability Act of 1996 (HIPAA) 45 CFR 160 and 164 Subparts A and E. In addition, research shall comply with all applicable federal and state laws and regulations. The institution applies additional regulations/policies on a case-by-case basis for projects funded by or covered by federal agencies such as the U.S. Department of Education, U.S. Department of Defense, U.S. National Science Foundation, Department of Justice (DOJ) [Bureau of Prisons and National Institute of Justice], Department of Energy (DOE) or Environmental Protection Agency (EPA), as appropriate to the sponsor. University officials shall develop and implement policies and procedures related to human research protection in alignment with this ethical and regulatory framework.

A1.0225 Accreditation Standards

Following a rigorous, three-year evaluation process, the UK HRPP prepared for and achieved full accreditation by the Association for the Accreditation of Human Research Protection Programs, Inc., (AAHRPP) in June 2007. The UK HRPP was re-accredited and awarded a five-year cycle for reaccreditation in June 2010, June 2015, June 2020 and June 2025. Achieving accreditation demonstrates UK's commitment to the highest ethical standards in conducting human research. This accreditation signals to research volunteers that UK puts their safety first and embraces high standards for participant protections. It also indicates to sponsors and investigators the efficiency and quality of the UK research program. Maintaining the HRPP at this distinguished level involves ongoing evaluation, training, documentation, annual reporting and successful completion of the reaccreditation process every five years.

A1.0250 Activities Covered under the UK HRPP

In accordance with federal and institutional regulations, any undertaking in which any UK faculty, staff or student investigates and/or collects data on human subjects for research purposes is subject to the UK HRPP and review by the appropriate Medical or Nonmedical Institutional Review Board (IRB) regardless of the funding source. Specific institutional procedures which correlate with the assurance and cooperative research guidance of the Office for Human Research Protections (OHRP) govern data collection occurring at "off-site" locations, including criteria for engagement in research by the organization.

Any UK activity that meets either the federal HHS definition of both "research" and "human subjects" or the FDA definition of both "human subject" and "clinical investigation" is subject to all provisions of the institution-wide HRPP. As appropriate, UK applies relevant definitions from other sponsor agencies (e.g., Department of Defense (DoD)).

- Research: "A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge" [45 CFR 46.102 (l)]
- Human Subjects (HHS): "A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information" [45 CFR 46.102 (e)(1)]

- Clinical Investigation (FDA): “Clinical investigation means any experiment that involves a test article and one or more human subjects and that either is subject to the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies.” The terms *research*, *clinical research*, *clinical study*, *study* and *clinical investigation* are deemed to be synonymous for purposes of this part. [21 CFR 56.102(c)]
- Human Subjects (FDA): “An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient.” [21 CFR 56.102(e)] (Drug, Food, Biologic)
- Human Subjects (FDA for medical devices): “A human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or who participates as a control. A subject may be in normal health or may have a medical condition or disease.” [21 CFR 812.3(p)] (Medical Devices)
- In cases in which regulations of any other federal agency apply, institutional oversight of the activity follows the definitions for “research” and “human subjects” as defined by the relevant agency as appropriate.
- For DoD-supported research, institutional oversight of the activity follows the definitions of “research” and “experimental subject” as defined by DoD regulations [DoD Directive 3216.02].

The term *research* encompasses basic and applied investigations such as bench work, clinical research, other work and product development, and other forms of creative activity. *Research involving human subjects* typically applies to behavioral and social sciences research including surveys; interviews; observations; studies of existing records; clinical trials; epidemiological research including surveillance, monitoring, and reporting programs; pilot studies; thesis and dissertation research involving human subjects; repository research including tissue banking and databases from individually identifiable living persons; and human genetic research.

Investigations designed to develop or contribute to *generalizable knowledge* are those designed to draw general conclusions, advance scientific knowledge or generalize findings beyond a single individual or an internal program. Certain quality assurance or quality improvement activities designed to measure the effectiveness of programs or services may constitute human research.

Human subjects typically covered by the UK HRPP include the following categories: normal volunteers, patients, students, employees, children, non-English speaking or non-native volunteers, pregnant women, prisoners, and individuals with limited decision-making or impaired consent capacity, including those who are institutionalized.

The IRB or the designated Office of Research Integrity (ORI) staff determine whether an activity meets the pertinent definitions and, thus, is subject to the HRPP. In the case of class projects involving data collection from human subjects, the instructor is responsible for making the decision whether the activity is subject to the HRPP and is encouraged to contact ORI for assistance in making this determination.

Investigators/researchers may not determine whether research to be conducted is exempt from

the requirement for IRB review and approval. The ORI is responsible for communicating written policies and procedures for the University community to follow in determining whether activities do or do not require IRB review. The IRB Chair and ORI Executive Director make the official determination whether the research is Not Human Research (NHR).

UK policy requires that all investigators/study personnel who conduct research involving human subjects or clinical investigations successfully complete and periodically renew mandatory training in the protection of human subjects. This policy includes research exempt from federal regulations (i.e., those qualifying for Exemption Certification). Exemption reviewers or designated ORI staff may recommend revisions within an exempt protocol to enhance subjects' protection. Investigators conducting Exemption Certification research may also incorporate consent and other procedures covered by human research protections. Finally, a sponsoring agency may require that proposed research receive full or expedited review even when the research activities otherwise qualify for exemption.

A1.0300 ORGANIZATIONAL STRUCTURE FOR HUMAN RESEARCH PROTECTION

Human research protection is a shared institutional responsibility which encompasses diverse units and designated personnel crossing three primary domains: (1) the institution; (2) the Institutional review boards and (3) the investigator/study personnel. Areas of responsibility for each domain with specific reference to the conduct of research are delineated in institutional policies and procedures appropriate to the particular unit mission and/or administrative position of the personnel involved.

A1.0350 INSTITUTIONAL LEADERSHIP AND HUMAN RESEARCH PROTECTION PROGRAM ADMINISTRATION

A1.0400 Vice President for Research

The key institutional leader responsible for oversight and management of all aspects of UK research is the Vice President for Research (VPR), who reports to the University President. The VPR is the designated institutional official for human research protection in UK's Federalwide Assurance (FWA) with the HHS and for all components of the institutional HRPP. The University authorizes the VPR to act on its behalf, specifically committing the University to compliance with all requirements of the *Code of Federal Regulations*, 45 CFR 46, and other applicable federal regulations (e.g., FDA 21 CFR 50 and 56), not only for all federally sponsored research, but for all human research activity regardless of sponsorship. Specific institutional responsibilities in meeting HRPP requirements include: developing policies and procedures that ensure human research protections; establishing an appropriate number of IRBs sufficient to meet institutional research needs and appointing qualified members to serve on the IRBs; ensuring education of IRB members, staff and study personnel; providing sufficient resources and staff support to implement the HRPP and to ensure the effective operation of the IRBs; supporting IRB decisions; implementing mechanisms for institutional oversight; ensuring effective institution-wide communication and access to human research information for all UK entities; ensuring submission of and sign-off on appropriate assurances and certifications for the institution and cooperating performance sites; and overseeing UK reporting to regulatory agencies.

A1.0450 Office of Research Integrity

A1.0500 Coordination and Administration

The Office of Research Integrity (ORI), a research support unit reporting directly to the VPR, plays a significant role in the institutional HRPP, interacting with the IRB and all University constituencies engaged in the HRPP to facilitate effective human research protections. The ORI Executive Director reports directly to the Associate Vice President for Research Integrity. He/she is the designated official responsible for administrative oversight, coordination, implementation and review of all HRPP policies, procedures and functions. This UK official plays a critical leadership role in institutional efforts to remain abreast of current knowledge in the field, including regulatory and other relevant issues. The ORI Executive Director serves as a liaison with federal and other agencies in implementing the UK HRPP and oversees institutional communication and education to ensure that the UK community as a whole and the units specifically responsible for the protection of human subjects are informed of all relevant issues in human research. To maintain a high degree of cross-unit communication, collaboration and interaction, the ORI Executive Director or designee serves as an *ex officio* member of the Medical and Nonmedical IRBs and on other committees with significant roles in protecting human subjects as outlined below.

A1.0550 Program Assessment

The ORI Executive Director, with assistance from the Quality Improvement Program (QIP) Team, the ORI Associate Director, the Research Compliance Officer (RCO), Research Education Specialist, E-IRB Systems Administrator, and the IRB, is responsible for annual and other periodic reports which contain assessments of the scope, volume and nature of human research conducted at UK. These documents serve as the basis for program modifications and are one mechanism for determining the appropriate number of IRBs and for meeting administrative personnel requirements to conduct institutional HRPP functions. The ORI Executive Director makes recommendations to the VPR for additional resources or significant changes in the program.

A1.0575 Post Approval Monitoring

The ORI Quality Improvement Program (QIP) and Reliance teams are responsible for conducting routine (“not-for-cause”) post-approval monitoring visits (“Wellness Checks”) for human research protocols as part of the UK HRPP’s accreditation requirements. The visits serve to evaluate human research protections at varying levels, increase awareness of existing processes, operating procedures, educational programs, and acquire information necessary for enhancing protections. The monitoring provides a means to assess UK’s level of compliance with federal, state and institutional regulations, as well as Good Clinical Practice (GCP) guidelines, which are key elements in meeting the highest standards for human subject protections.

In addition to Wellness Checks, the QIP and Reliance teams also conduct “for-cause” study visits (“Directed Visits”) as needed at the request of the Institutional Review Board (IRB), the Vice President for Research, or ORI Director, due to unusual circumstances, significant risks to subjects, routine failure of an investigator to comply with federal and/or institutional requirements, allegations or concerns about the conduct of the study brought to the IRB’s attention, or any case requiring further scrutiny as deemed appropriate by the IRB.

A1.0600 Human Research Education and Communication

The VPR and the ORI have primary responsibility for establishing and communicating mandatory human research education requirements to all investigators/study personnel,

maintaining current education materials and documenting completion of required investigator/study personnel training. The ORI maintains up-to-date knowledge of federal regulations and issues affecting human research. ORI staff complete mandatory training in human research protections. The ORI also guides the University and the IRB in developing and implementing policies and procedures which ensure compliance with federal requirements for the ethical conduct of research. Responsibilities include facilitating cross-institutional communication and collaboration among the various units and personnel sharing HRPP functions. In addition to providing leadership and assistance to the HRPP, the ORI also assists with the research misconduct policy, data ownership policy and other ethical and regulatory issues related to the conduct of research, as appropriate.

A1.0650 Support Services

ORI administrators support the mission of each Institutional Review Board (IRB), the Institutional Biosafety Committee (IBC) and the Radioactive Drug Research Committee (RDRC) by serving as liaisons with institutional HRPP leadership, the IRB, IBC, Radiation Safety, RDRC, Sponsored Project Services, Clinical Research Support Office (CRSO), Center for Clinical and Translational Science (CCTS) and other administrative units with responsibilities for human research protection. Key responsibilities are as follows: advise investigators and their staff, the RDRC, IRBs and committee chairs/vice chairs, upper-level administration and other institutional administrative units on the review of research protocols and state and federal regulatory requirements; process IRB applications; manage protocol review at regularly scheduled meetings; maintain pertinent records and documentation of protocol review and IRB decisions for mandated periods; complete federally and UK-mandated reports; receive and respond to complaints and allegations of noncompliance; assist in developing HRPP policies and procedures; and manage staff and infrastructure to assist the IRBs in completing their responsibilities. ORI administrators also assist in the development of educational materials, provide and oversee mandated education on the ethical conduct of research, coordinate institutional/IRB/investigator responsibilities, conduct quality assurance and improvement (QA/QI) reviews, assist with IRB review of HIPAA waivers and authorizations and coordinate IRB reliance agreements.

A1.0700 Community Outreach

UK is committed to a policy of providing the public and all individuals participating or considering enrolling in human research information on the rights of research subjects. The ORI maintains a comprehensive set of online outreach materials through the ORI Research Participants webpage. In addition to information regarding clinical trials and the IRBs, the webpage includes materials to assist parents and legally authorized representatives (LARs) in fulfilling their responsibilities. These resources familiarize the broader community and potential human subjects with information on human research participation and protections. Resource videos on this webpage are provided in English and Spanish. The website and IRB-approved informed consent and assent forms provide a means for participants to contact the ORI directly if they have questions, problems or concerns about their rights as research subjects. ORI also maintains a toll-free phone number for questions or concerns from the public or research participants.

A key partner in community outreach, the Participant Recruitment Services core of the Center for Clinical and Translational Science (CCTS) works with UK HealthCare, UK Marketing, the ORI, and clinical investigators to provide education, outreach and research opportunities to the

public. The unit works directly with research investigators in designing ethically appropriate recruitment and advertising materials and requires documentation of IRB approval prior to initiating promotion of the research. The CCTS spearheads community outreach events and delivers patient/subject education via numerous outlets including social media, dedicated research wall mounts and traveling exhibits. The CCTS participates in ResearchMatch, a national recruitment registry which brings together researchers and potential participants who want to learn more about available research studies. The CCTS also offers a variety of secure tools that help match interested participants with health studies, wellness surveys and clinical trials at the University of Kentucky and around the world. The CCTS hosts (and the ORI participates in) an annual UK Research Participants Day to provide outreach and education for UK HealthCare patients, students, faculty, staff and visitors.

A1.0750 Handling Allegations of Regulatory Noncompliance and/or Research Misconduct

The UK Policy - Due Process: Research Misconduct defines and provides direction on the handling of research misconduct. The IRBs/ORI have a standard operating procedure (SOP) for handling allegations of noncompliance. The ORI Research Compliance Officer (Execi) provides critical leadership in handling allegations of noncompliance and any research misconduct which may also have IRB implications. In these cases, the RCO is responsible for identifying the specific allegation of noncompliance or misconduct to ensure coordination among the various components of the HRPP and implementation of the institutional policy. Key areas of responsibility include: developing and implementing policies and procedures for issues related to research misconduct and noncompliance; serving as a liaison with all agencies, organizations, complainants, witnesses and other personnel impacted by allegations of noncompliance; coordinating IRB investigations of allegations; advising senior administration on federal and institutional requirements, proposed changes or actions related to noncompliance; preparing federally mandated reports and correspondence; and assisting in developing and directing the institutional education program and tools to educate the University community on research misconduct and noncompliance. The UK Research website lists the ORI as the designated entity regarding allegations of noncompliance and misconduct and provides a designated toll-free hotline and anonymous online reporting form. Additionally, the ORI Contact Us page identifies the RCO and provides direct access to his/her contact information. The RCO also handles questions about the human subjects outreach process and administrative processes.

A1.0800 INSTITUTIONAL REVIEW BOARD

A1.0825 Institutional Authority and Independence of the IRB

All activities meeting the regulatory definitions of *research involving human subjects* or *clinical investigations involving human subjects* as outlined above is subject to institutional review and approval through the appropriate UK Medical or Nonmedical Institutional Review Board (IRB) committee. The Medical IRB typically reviews research emanating from the colleges of Dentistry, Health Sciences, Medicine, Nursing, Pharmacy and Public Health. The Nonmedical IRB generally reviews research originating from the colleges of Agriculture, Food and Environment, Arts and Sciences, Business and Economics, Communication and Information, Design, Education, Engineering, Fine Arts, Law and Social Work.

UK grants the Medical and Nonmedical IRB committees the authority to act independently to bind all activities falling under their purview to their decisions. No institutional official or committee may approve human research that was disapproved by the IRB.

Individuals with competing business interests or individuals responsible for business development (e.g., Vice President for Research (VPR), director of grants and contracts) may not serve as IRB members or carry out the day-to-day operations of the review process.

Specific authority granted to the IRBs includes: approval, required modifications or disapproval of all human research activities overseen and conducted by the investigators/research team; monitoring the consent process and conduct of the research; and suspension or termination of approval of research that is not conducted in accordance with regulatory or institutional requirements and/or has resulted (or may result) in unexpected serious harm to human subjects. The IRB reviews allegations of noncompliance with human subjects regulations, protocol deviations and violations, and reports of unanticipated problems/adverse events. In cases where corrective action is needed, the IRB issues appropriate sanctions including but not limited to requesting changes, determining data collected cannot be used for analysis/publication, suspending or terminating approval, recommending additional education in the protection of human subjects in research, disqualifying investigators from conducting research involving human subjects at the University, and/or recommending to the University administration that further administrative action be taken.

With applicable approvals and written agreements, the University may also use the IRB of another organization to ensure effective and timely research review.

All UK personnel who become aware of attempts to inappropriately/unduly influence the IRB(s) are to report such incidents to the ORI RCO, who notifies the VPR of all allegations. The VPR, in consultation with the ORI Executive Director, investigates and determines the appropriate response to attempts to unduly influence or undermine the mission of the IRB. Types of responses may include but are not limited to educational intervention, disqualification of the investigator or further administrative action.

A1.0850 Institutional Review Board Responsibilities

The primary responsibility of the UK IRBs is to ensure that the rights and welfare of research subjects at UK are protected. In select circumstances, the UK IRBs may serve as the IRB of Record (reviewing IRB) for other agencies, institutions or facilities. In addition, the UK IRBs may rely on (cede review to) the IRB of another organization in certain circumstances. Policies and procedures include provisions for adjusting the number of reviewing IRB and ceded review agreements (Reliance agreements) that UK enters to ensure that reviews are accomplished in a thorough and timely manner.

Chairs, vice chairs and members are responsible for conducting the ethical review of human research activities; initial, continuation, modification, unanticipated problems/adverse events and protocol deviations/violations — to ensure compliance with all applicable federal and state laws and regulations and with the ethical principles endorsed by the University. The IRB is further responsible for conducting scientific and scholarly review within the context of human subjects protections (i.e., risk/benefit assessment) and for conducting continuation review of relevant approved research at intervals appropriate to the degree of risk, but not less than once per year.

Each regular and alternate IRB member bears the following responsibilities: (1) conducting protocol review (2) applying disciplinary and regulatory knowledge when conducting reviews (3) attending full review meetings as assigned (4) avoiding conflict of interest (COI) in conducting reviews (5) proposing and developing IRB policy (6) completing mandatory education requirements (7) handling/reviewing allegations or reports of noncompliance (8)

maintaining confidentiality and (9) determining whether federal reports are required.

The IRB conducts review and approval operations in accordance with the policies and procedures governing research review at the University. The ORI publishes membership rosters and meeting dates prominently on the ORI website. Meeting dates occur at regular intervals, and ORI administrators provide access to agendas in a timely fashion to allow members sufficient time to review protocols and related information under consideration. The ORI maintains the full set of documents detailing the development, requirements, implementation, review and revision of policies and procedures for the conduct of research review. In addition, the ORI maintains all records of IRB review in accordance with the provisions of all applicable regulations and accreditation guidelines, limiting access to authorized personnel as specified in IRB/ORI operating procedures.

A1.0875 Institutional Review Board Chair/Vice Chair

The designated Medical and Nonmedical IRB chairs are responsible for (1) ensuring that the respective IRB committees carry out their responsibility to review each protocol for compliance with the requirements of 45 CFR 46 and, if applicable, 21 CFR 50 and 56, as well as all other applicable federal, state and institutional regulations and policies (2) conducting exemption certification and expedited review or delegating this authority (through the ORI) to qualified IRB member(s) (3) maintaining communication with the ORI (4) providing oversight and leadership in conducting review of alleged cases of noncompliance and (5) chairing the designated convened Committee meeting(s).

For each IRB, the designated vice chair(s) assist(s) the chair in fulfilling the responsibilities listed above. In addition, as appropriate, the vice chairs serve as primary reviewers in conducting expedited and full annual administrative/continuation review (AAR/CR) and are responsible for reviewing the complete AAR/CR application and making recommendations to the ORI and/or other IRB members. The vice chairs also may delegate (through the ORI) the responsibility of serving as a primary or expedited reviewer for AARs/CRs to qualified IRB members.

A1.0900 Institutional Review Board Membership

IRB membership requirements comply with federal regulations to ensure appropriate and wide-ranging representation from multiple professions, various ethnic/cultural/identity backgrounds and both scientific and non-scientific expertise. Additionally, at least one member must have no affiliation with UK. IRB members serve on the committee for designated terms of service. Select UK administrative units and the ORI nominate individuals for chair, vice chair and regular/alternate member roles on the IRB after review of scholarly, scientific and other credentials. The VPR makes all membership appointments as authorized by the University President. Consideration of the nature and volume of research under review by a specific IRB shall be a factor in the appointment process. The ORI maintains appropriate documentation of professional credentials of each IRB member, and membership rosters contain information on members to ensure appropriate representation at IRB meetings for each protocol under review. Alternate IRB members serve in the absence of regular members.

Non-voting *ex officio* members provide the IRB the expertise from specific units with significant institutional roles for human research protection and ensure coordination among UK administrative units in carrying out all provisions of the HRPP. The membership of the Medical IRBs includes *ex officio* members representing (but not limited to) the following units: UK Office of Legal Counsel, ORI, Investigational Drug Service (IDS), Radiation Safety Committee

(RSC) and Institutional Biosafety Committee (IBC) of UK Environmental Health and Safety. The ORI Executive Director and a representative from the UK Office of Legal Counsel also serve as *ex officio* members on the Nonmedical IRB. Provisions for non-voting ad hoc consultants ensure the availability of special expertise as needed by the IRBs prior to and/or during review.

A1.0925 Institutional Review Board Expertise and Qualifications

The IRB chairs, vice chairs, members and ORI support staff must be familiar with the ethical principles guiding human research, the requirements of applicable federal regulations, state law(s), and institutional policies and procedures established for the protection of human subjects. The IRB must also have effective knowledge of various subject populations and other factors which can potentially contribute to a determination of risks and benefits to subjects, and which can impact subjects' informed consent. Institutional HRPP policies and procedures delineate specific education requirements for IRB members and appropriate tools and educational programs for meeting these requirements.

A1.0950 Conflict of Interest and IRB Members, ORI Staff and Consultants

IRB chairs, members (regular and alternate), ORI staff and contributing consultants may not participate in research review for which a personal conflict of interest (COI) exists. This includes financial COIs. Specific policies and procedures govern the conduct of individuals in these positions and the requirements for recusal from the review process as applicable.

A1.1100 INVESTIGATOR/RESEARCH PERSONNEL

Direct responsibility for ethical conduct of human research and the protection of research subjects lies with each investigator and the study personnel engaged in human research activities. Investigators hold the following key responsibilities: to design and implement ethical research within sound study designs according to the Belmont ethical principles and the standards of the relevant discipline; involve study personnel qualified by training and experience for their research responsibilities; obtain IRB approval prior to initiating any human research activity; comply with federal and state regulations, institutional and IRB requirements and requirements of the Health Insurance Portability and Accountability Act pertaining to research; implement research as approved and in compliance with all IRB decisions, conditions and requirements; maintain appropriate project and personnel oversight and appropriately delegate research responsibilities; conduct recruitment of participants fairly and equitably while assessing the risks/benefits; obtain and document informed consent/assent/authorization when applicable and provide a mechanism for receiving and responding to participant complaints or requests for information; monitor data integrity as well as the rights and welfare of human subjects; submit relevant progress reports; report unanticipated problems/adverse events and protocol deviations/violations; obtain prior approval for modifications to research protocols including promotional materials; maintain written documentation of research activities; and retain relevant records. A detailed list of responsibilities is included in the IRB/ORI SOPs and on the Role & Responsibilities ORI webpage.

In designing human subject protections specific to a project, the principal investigator (PI) shall consider all conflicts of interest (COIs) as defined in AR 7:2 Financial Conflicts of Interest in Research, AR 7:9 Institutional Conflict of Interest Involving Research and, in cooperation with the appropriate associate dean for research or other appropriate University official, identify and develop a plan to manage them.

The PI shall determine that the appropriate resources to protect human subjects are or will be in place (including resources to address adverse events and possible research-related injuries) before initiating the study. For research protocols involving greater than minimal risk, the PI shall specifically detail plans for data safety and monitoring (i.e., for determining harm to research participants and mitigating potential injuries).

The PI and study personnel must also comply with applicable policies, procedures and mandatory education requirements specified by other University administrative units such as, but not limited to, the Institutional Biosafety Committee (IBC), Radiation Safety Committee (RSC), Radioactive Drug Research Committee (RDRC), Markey Cancer Center Protocol Review and Monitoring Committee (PRMC), Corporate Compliance, Clinical Research Support Office (CRSO), Investigational Drug Service (IDS), Sponsored Project Services, and Security, Export, Compliance and University Research Engagement (SECURE).

A1.1125 Investigator Concerns/Appeals of IRB Decisions

The PI communicates with the IRB committee in writing (and may attend a meeting in-person) to resolve any concerns that may arise regarding a specific IRB decision. (See the Initial Full Review SOP, Expedited Review SOP and Exempt Review SOP.)

A1.1200 CROSS-INSTITUTIONAL ROLES AND RESPONSIBILITIES FOR THE UK HRPP

In addition to the institutional official (i.e., the VPR), the IRB, the ORI and investigators, other designated units and personnel share institutional responsibility for human research protection. These include, but are not limited to, the individual unit leaders (i.e., deans, department chairs and departmental administrators); Sponsored Project Services which also administers the Financial Conflicts of Interest in Research policy; Conflict of Interest Committee; Office of Legal Counsel; Committee on Safety and Environmental Health, Institutional Biosafety Committee (IBC), institutional Biological Safety Officer (BSO), Radiation Safety Committee (RSC) and Radiation Safety Officer (RSO); Radioactive Drug Research Committee (RDRC); Investigational Drug Service (IDS); UK Markey Cancer Center; Clinical Research Support Office (CRSO); Security, Export, Compliance and University Research Engagement (SECURE); and the UK Center for Clinical and Translational Science (CCTS). Shared membership on the committees and respective co-signed ORI/IRB SOPs facilitate coordination, communication and implementation of human research in compliance with all provisions of the UK HRPP and ensure that required approvals are in place prior to commencement of research.

A1.1250 College/Department

The colleges and/or departments in which research is to be conducted are responsible for: nominating members to serve on the UK IRBs; assisting investigators in identifying which projects require IRB review and approval; and, in cooperation with the ORI, educating faculty, staff and students about the responsibilities and requirements for human research protections, including compliance with regulatory guidance.

In addition, department chairs (or their authorized designees) conduct preliminary scientific and scholarly review of the human research protocol prior to submission and are responsible for providing the Chairperson's Assurance Statement on all research protocol applications (i.e., full, expedited and exemption certification review). The chair's signature on the protocol application provides a statement of assurance of scientific validity, investigator qualifications, adequate and

appropriate resources, and mentoring to ensure adherence to established standards of scientific integrity.

The Internal Approval Form (IAF), administered by Sponsored Project Services (SPS), is an internal electronic form required prior to submission of a proposal to an external funding agency that provides a summary of pertinent details regarding the proposed research, including the involvement of human subjects. The IAF is signed by department chairs to certify that he/she has reviewed the proposed research and agrees it is consistent with the educational and research objectives of the respective unit.

Department heads, faculty members and supervisors are also directly responsible for maintaining an atmosphere that promotes full compliance with university safety policies and procedures in all facets of university operations, including human research. The mandate places equal responsibility on investigators and administration to handle biohazardous agents and radiation-producing devices safely by following established policies, procedures and regulations, and in accordance with research reviews conducted by the IBC and the RSC.

A1.1300 SPONSORED PROJECT SERVICES

A1.1325 Procurement, Review, Approval, and Submission of Sponsored Projects

Sponsored Project Services (SPS) consists of two units within the Office of the VPR; Office of Sponsored Projects Administration (OSPA) and Collaborative Grant Services (CGS). SPS serves both UK and the University of Kentucky Research Foundation (UKRF) in the review, approval and submission of proposals. The University Administrative Regulation, AR 7:3 (Soliciting, Receiving, Recording, and Administering Grants and Contracts for Sponsored Projects) formalizes unit responsibilities for ensuring compliance with the terms and conditions of grants and contracts and for providing general grant, contract and agreement administration with project sponsors. In addition, SPS is responsible for the following HRPP functions: monitoring funding agency assurance/certification requirements and ensuring compliance; informing the university community about new federal and state regulatory guidelines relevant to sponsored research; coordinating with the IRB to ensure accuracy of completed assurances and certifications; maintaining agency-required documentation; and maintaining a working knowledge of the types of projects needing IRB review.

SPS administers the Internal Approval Form (IAF), which ensures that the proposed project has been reviewed across institutional levels for scientific and sound scholarly design. Department chairs, directors and deans receive a summary of pertinent details of proposed sponsored research projects on or attached to the IAF, including the use of human subjects, hazardous materials or radioactive materials. The IAF contains investigator certifications that he/she will adhere to university policies on conflict of interest, ethical standards in the conduct of research, intellectual properties, and the conduct of human research and that he/she has completed and submitted an online Financial Disclosure Statement. Signatures of chairs, deans and directors certify that the proposed research is consistent with the educational and research objectives of the unit. Investigators certify that their online Financial Disclosure Statement has been completed.

A1.1350 Office of Sponsored Projects Administration (OSPA), a unit within the Office of the Vice President for Research, serves UKRF in the procurement, review, approval and submission of proposals and administration of grants and contracts awarded to the university through UKRF. OSPA also provides general grant, contract and agreement negotiation and

administration with project sponsors. Services to investigators include review and submission of sponsored project proposals to external sponsors and other administrative proposal requirements; review, negotiation and acceptance of awards; provision of information regarding sponsor policies and regulations; and preparation of subcontract documents, including contact and coordination with subrecipient research administrators and grants management staff to establish subawards. OSPA staff ensure compliance with the terms and conditions of grants and contracts, including the submission of progress, final and other appropriate reports and excluding financial reports. OSPA staff also manage research compliance, including financial conflict of interest, clinical trial reporting through ClinicalTrials.gov.

OSPA also prepares subcontracts with collaborators, which include provisions for adherence to human research protections, the research protocol and applicable federal and state regulations. Internal OSPA policy requires that the Research Administrator check for IRB approval prior to establishing an account for a project involving human subjects. If IRB approval is still pending, the account is established with a message to the PI that no human subject activity may take place until IRB approval is finalized. In selected circumstances, OSPA may, however, establish accounts under specific written agreements with the investigator prohibiting contact and enrollment of human subjects prior to obtaining IRB approval.

Every sponsored project must include a written agreement between the sponsor and the institution. OSPA negotiates the terms of the agreements to ensure compliance with federal and state law, University policy and good business practice. Guidance on industry sponsored agreements, available on the SPS website, clearly articulates UK policy regarding agreements with industry. Information on *clinical trial agreements*, posted on the SPS website, outlines administrative and contractual issues applicable to clinical trial agreements. Sample agreements for industry and clinical studies, which include provisions addressing freedom to publish research results, coverage of subject injury expense and adherence to human subject protection regulations, are available from SPS.

A1.1375 Collaborative Grant Services (CGS) is a shared-service unit within the Office of the Vice President for Research. It includes a team of Pre-Award and Post-Award Grant Specialists and Financial Analysts who work with investigators directly on financial and administrative matters related to their sponsored projects proposals and funded activities. Pre-award services to investigators include advice and assistance with sponsor guideline review, budget preparation support, preparation of internal and sponsor administrative forms, facilitation of required internal approvals of college and unit leadership and other administrative proposal requirements. Post-award support includes budgeting, monitoring and analysis, facilitating communication related to award terms and conditions, requesting outgoing subawards, monitoring cost share commitments, advising on appropriate personnel and payroll effort commitments, and regular account reconciliation. In addition to regular meetings with investigators and their business staff, there is close coordination with staff in OSPA and RFS, and regular interaction with an advisory committee comprised of associate deans for research in UK colleges and center and institute directors.

A1.1400 CONFLICT OF INTEREST

A1.1425 Research Conflict of Interest Administration

UK's Administrative Regulation: Financial Conflicts of Interest in Research (AR 7:2) sets forth policies, principles and procedures to ensure that the personal financial interests of university

employees do not compromise the objectivity with which research is designed, conducted and reported or the welfare of research participants. AR 7:2 defines investigators as “the project director or principal investigator/program director, co-investigator, collaborator, senior/key personnel, faculty associate, and any other person, regardless of title or position, who is responsible for the design, conduct, reporting, or proposing of research or other activity that is sponsored by an extramural agency.” AR 7:2 provides for review and management of any relevant significant financial interest that could directly affect the design, conduct, or reporting of research activity.

OSPA administers the Financial Conflicts of Interest in Research policy (AR 7:2), publishes the policy on behalf of the institution and maintains a website of relevant information. OSPA ensures that investigators, co-investigators and other personnel responsible for the design, conduct or reporting of sponsored research activities complete the online Financial Disclosure and required Conflict of Interest training prior to proposal submission to an external funding agency. OSPA is also responsible for coordinating with the ORI on any research project that meets the UK definition of financial conflict of interest and involves human subjects.

A1.1450 Research Conflict of Interest Committee

The VPR and the University Senate Council are responsible for recommending a committee of at least five members for appointment by the University President to a Research Conflict of Interest Committee (RCOIC). Most of the membership consists of faculty members, and the remainder is limited to deans, directors and others employed by the University. In addition, the Directors of OSPA, ORI, UK Innovate Technology Commercialization, and a representative from the Office of Legal Counsel serve as *ex officio* members of the RCOIC.

Investigators or personnel who have an identified potential conflict of interest (COI) propose a plan to eliminate, minimize or manage it. The authorized University official reviews the plan. The investigator and the authorized University official submit the plan to the RCOIC which then may: accept the plan as recommended; add to the plan; or formulate a different course of action to manage, reduce or eliminate the conflict. The RCOIC forwards its recommendations to the VPR for final approval.

The Conflict of Interest Administrator in SECURE notifies the investigator, dean or director, and the RCOIC Committee of the final disposition of the issue. No sponsored project award funds may be disbursed until the final disposition. The Conflict of Interest Administrator in SECURE sends the final management plan to the ORI/IRB. The IRB withholds protocol approval pending receipt and IRB review of the final COI management plan. Noncompliance with or violation of the conflict-of-interest policy is grounds for disciplinary action as specified in AR 7:2.

A1. 1475 Institutional Conflict of Interest

UK Administrative Regulation: AR 7:9 (Institutional Conflicts of Interest Involving Research) identifies areas in which financial dealings of the university could affect research integrity and provides clear guidance on and procedures for the disclosure and management, or elimination, of institutional conflicts of interest, whether real or perceived. The processes cover direct financial holdings of the University or any of its affiliated corporations or personal financial holdings of a University Official who, by virtue of his or her institutional authority, might affect, or reasonably appear to affect, institutional processes for the conduct, review or oversight of research. The VPR serves as the Institutional Conflict of Interest Official with the authority and responsibility for overseeing the implementation of this policy.

A1.1500 OFFICE OF LEGAL COUNSEL

The Office of Legal Counsel provides legal services through an Associate General Counsel who has primary responsibilities to support the UK research enterprise. This position reports to the Office of Legal Counsel but directly supports the Office of the VPR and the units that report to it. Legal counsel serves the IRB and the ORI by advising on legal issues such as informed consent, state law and other research-related areas, including handling of differing state and federal laws. In cases where state law is inconsistent with federal law (i.e., more stringent), policies are developed and implemented which govern the conduct of the research affected by these laws. Legal counsel serves as an *ex officio* member of the Medical and Nonmedical IRB committees and works closely with IRB chairs, ORI staff and the VPR in reviewing legal issues affecting human research, assessing and monitoring UK research practices, and assisting the institution in maintaining compliance with pertinent federal and state legal requirements. Legal counsel also directly supports OSPA, advising on policies and procedures and assisting with review of specific contractual terms related to human subjects research. Legal counsel maintains external professional affiliations to ensure that the University community is apprised of current legal developments.

A1.1600 COMMITTEE ON SAFETY AND ENVIRONMENTAL HEALTH

The Division of Environmental Health and Safety (EHS) has responsibility for assisting the University in achieving overall safety compliance in all operations, including research. EHS staff members assist investigators in assessing environmental, health and safety needs, and compliance requirements of their proposed research through means of a web-based checklist and use the results of the assessment to direct investigators to the appropriate research review. Two specific subcommittees of the Committee on Safety and Environmental Health, the Institutional Biosafety Committee (IBC) and the Radiation Safety Committee (RSC), play important roles in reviewing research protocols involving human subjects, coordinating approvals with the IRBs and providing *ex officio* members to serve on the Medical IRBs during research review. These committees coordinate with the IRBs and ORI through shared membership. The IRB withholds all approvals pending approval from the IBC and RSC, when applicable. The ORI Executive Director serves as an *ex officio* member of the Committee on Safety and Environmental Health.

A1.1700 INSTITUTIONAL BIOSAFETY COMMITTEE

The Institutional Biosafety Committee (IBC) is responsible for advising the institution on all matters related to biological safety and reviewing and approving proposed uses of biohazardous materials in all institutional undertakings. In accordance with the *National Institutes of Health (NIH) Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, UK has established the IBC as the responsible unit for review and approval of recombinant and/or synthetic nucleic acids research. The Biological Safety Officer (BSO) and the IBC must review all research involving infectious agents or recombinant and/or synthetic nucleic acids. All proposals are subject to this review regardless of funding source.

IBC review ensures that such research is conducted in full conformity with the provisions of the *NIH Guidelines* and guidelines from the Centers for Disease Control and Prevention (*Biosafety in Microbiological Biomedical and Biomedical Laboratories, 6th Edition* BMBL). The review includes an independent assessment of the required containment levels and the facilities, procedures, practices, training and expertise of the personnel involved in recombinant and/or

synthetic nucleic acid research. The IBC determines the proper hazard classification. Institutional policy requires IBC review and approval before the IRB may issue initial review approval for protocols.

The IBC is composed of no fewer than five members who are selected to serve so that it collectively has experience and expertise in recombinant and/or synthetic nucleic acid technology and microbiology with the capability to assess research safety and potential risk to public health and/or the environment. At least two members must not be affiliated with the institution apart from their membership on the IBC who represent the interests of the surrounding community with respect to health and the protection of the environment. The IBC must also have people available as consultants who are knowledgeable in institutional commitments and policies, applicable laws, standards of professional conduct and practice, community practice and the environment.

A1.1750 Biological Safety Officer

The Biological Safety Officer (BSO) works closely with the IBC and is responsible for developing, implementing and directing a comprehensive biosafety program throughout all research laboratory and clinical areas that meets NIH, Centers for Disease Control and Prevention, Occupational Health and Safety Administration, and sponsor requirements. The biological safety program covers research on recombinant and/or synthetic nucleic acid and human/plant/animal gene transfer; infectious agents and biologically derived toxins; and human tissues, fluids and cell/cell cultures. As the designated institutional official and administrator for the IBC, the BSO serves as an *ex officio* non-voting member of the Medical IRBs, reviews and approves protocols involving the use of infectious agents and recombinant and/or synthetic nucleic acid, and makes recommendations to the IRB committees in their review of protocols that fall under the purview of the IBC. To maintain optimal compliance, the BSO develops and conducts educational programs for faculty, staff and students to improve institutional biological safety; develops and maintains a database of microorganisms and recombinant and/or synthetic nucleic acid used in research experiments at the University; coordinates the acquisition, transfer and use of “select agents” by UK researchers; performs all required inspections; audits laboratories and work practices and communicates findings to management; develops and maintains a biosafety cabinet certification program database; and investigates accidents and incidents involving biological agents and materials.

A1.1800-RADIATION SAFETY COMMITTEE

The Kentucky Cabinet for Health and Family Services, Radiation Health Branch, authorizes UK to use radiation-producing devices and radioactive material in operations, education, research and development activities. The Radiation Safety Committee (RSC) is appointed by the University President and reports to the Executive Vice President for Finance and Administration. The RSC establishes radiation policies and procedures for the University in accordance with state and federal regulatory requirements governing the procurement, use, storage and disposal of radiation-producing devices and radioactive material. The RSC authorizes individual investigators and study personnel to use these devices in the conduct of their research; however, prospective users must submit proposals to the RSC for review and approval. The RSC coordinates this review with the initial review conducted by the IRBs, which may not approve research requiring RSC review without prior approval from the RSC. The RSC includes individuals experienced in the use of radiation sources in medicine and research at the University, including the Radiation Safety Officer, who serves as an *ex officio* member of the

Medical IRBs.

A1.1850 Radiation Safety Officer

Responsibility for carrying out the policies and procedures of the RSC rests with the Radiation Safety Officer (RSO), who has administrative responsibility for the University's radiation safety program. The RSO reviews all applications for radiation-producing devices and radioactive material use as well as their location, described procedures and disposal. The RSO recommends approval or disapproval of applications for the use of such devices to the RSC, makes recommendations to the IRBs on consent language and/or protocol safety issues for protocols that fall under the purview of the RSC, and may suspend any project or use that is found to be a threat to health or property.

The RSO is responsible for implementing written policies and procedures for comprehensive management of the radiation procurement, use, disposal, documentation and emergency actions and is also responsible for investigating overexposures, accidents and other deviations from approved radiation safety practice and implementing corrective actions, as necessary.

A1.1875 Radioactive Drug Research Committee

Basic research designed to study the metabolism of a radioactive drug or to gain information about human physiology, pathophysiology or biochemistry in response to radioactive drug use is subject to review by the UK Radioactive Drug Research Committee (RDRC), as well as the IRBs. Formed under the authorization of the FDA and the University, the RDRC consists of members appointed by the VPR and is responsible for reviewing and approving all radioactive drug research projects that fall under the purview of FDA regulations as specified in 21 CFR Part 361.1. The RDRC Chair and the UK Radiation Safety Officer are responsible for determining whether a research proposal needs RDRC review in accord with FDA requirements.

Investigators submit research protocols which meet the criteria for review, as outlined in the regulations, to the RDRC for review and approval prior to initiation of the study. The committee is activated upon receipt of a protocol that meets the review criteria. The ORI manages both the IRBs and the RDRC and bears primary responsibility for coordination of the two committee reviews and providing the IRBs with written RDRC recommendations. The IRBs will not approve research without prior approval from the RDRC, if applicable.

A1.1900 INVESTIGATIONAL DRUG SERVICE

The Investigational Drug Service (IDS) offers support for all clinical drug-related research conducted by investigators at the UK HealthCare enterprise. Hospital policy requires IDS support for all in-patient protocols. Outpatient investigational drug studies may opt not to use the IDS for their pharmacy support; however, they are subject to annual audit by the IDS if they do not. The primary activity of the IDS is to ensure the appropriate procurement, storage, distribution and inventory control of investigational and study drugs. Investigational drugs are those drugs which have not received FDA approval for use in humans. Study drugs are those FDA-approved drugs being used under protocol for human research, possibly outside of FDA-approved labeling. The IDS provides the support needed to assure safe and efficient conduct of clinical drug trials including compliance with federal, state and Joint Commission requirements regarding investigational drugs. An IDS pharmacist serves as an *ex officio* or regular member of the Medical IRBs and supplies pharmacy information to the IBC on some protocols such as gene therapy protocols.

Upon initiation of a clinical drug study, the IDS requests a copy of the sponsor's protocol and the investigator's drug brochure (IB). The IDS pharmacist reviews the protocol and meets with sponsor representatives, the investigator, study coordinator and other study personnel to assess the potential IDS requirements. The IDS will not initiate a clinical drug study without documentation of IRB approval.

A1.2000 UK MARKEY CANCER CENTER

The UK Markey Cancer Center (MCC) has a broad mission to reduce the morbidity and mortality of cancer through a comprehensive program of cancer research, education, patient care and community outreach. Markey's research programs span the entire spectrum of cancer epidemiology and etiology, molecular expression and regulation, cancer prevention, early detection and treatment. Associated member scientists include faculty from 28 departments of eight UK colleges. The Markey Cancer Center Clinical Research Organization (CRO) is working to move advanced treatments into mainstream cancer management.

Both the Markey Cancer Center (MCC) and the IRBs are committed to ensuring the protection of human subjects involved in clinical research and have enacted coordination activities in significant areas including protocol review; participant safety, complaints and alleged study team noncompliance; and quality assurance/improvement monitoring and findings. All UK human cancer research is reviewed by the MCC Protocol Review and Monitoring Committee (PRMC). The MCC and the IRBs/ORI outline coordination procedures in joint SOP documents.

In 2013, the UK Markey Cancer Center was recognized as a National Cancer Institute-designated Cancer Center. In 2023, Markey received NCI Comprehensive Cancer Center designation.

A1.2025 Protocol Review and Monitoring Committee

The Protocol Review and Monitoring Committee (PRMC) is charged with overseeing the scientific integrity of clinical cancer trials at the Markey Cancer Center. The PRMC reviews studies for scientific significance, priority and feasibility. Clinical trials will be considered by the PRMC if they are Phase I, II or III NCI cooperative group trials, industry-sponsored or institutional investigator-initiated clinical trials focusing on cancer prevention, cancer control or treatment that has been approved by the appropriate CCART. The PRMC ensures that the study design fulfills study objectives and helps principal investigators of investigator-initiated trials optimize the scientific value of their studies.

The PRMC has the authority to approve protocols for IRB submission, assign risk levels and monitoring schedules, and approve amendments to open protocols. Protocols approved by the PRMC will be reviewed by the PRMC throughout the lifetime of the study to determine whether a study continues to have scientific merit and progress is being made through accruals.

The PRMC also recommends amendments to, or termination of, a protocol. Such reasons include the development of a therapy that is superior to that proposed in the protocol, a change in the standard of care that is no longer reflected in the protocol, poor accrual or other scientific or administrative reasons.

A1.2100 UK CENTER FOR CLINICAL AND TRANSLATIONAL SCIENCE

The UK Center for Clinical and Translational Science (CCTS) was established in 2006 with the

goal of accelerating the translation of basic science discoveries to tangible improvements in public health. The CCTS accomplishes its mission by creating and sustaining an academic home that 1) integrates expertise across the continuum of clinical investigation and translational research to foster collaborative team science 2) provides infrastructure, funding and support services for clinical and translational research 3) develops novel tools, methods and processes to increase the speed and efficiency of research translation and 4) offers training, education, and mentoring to prepare the next generation of clinical and translational investigators. Within UK's role as the flagship university in Kentucky, the CCTS has a specific focus on enhancing and developing outreach pathways and community-participatory research to confront chronic health issues in rural and underserved populations throughout the Commonwealth and the Appalachian region.

The CCTS encompasses a broad-based infrastructure to facilitate sound research design, fiscal and regulatory compliance, research integrity, and regulatory and compliance support. The ORI Executive Director serves as an *ex-officio* member on the CCTS Scientific Advisory Committee and is co-director of the Regulatory Support and Research Ethics Core.

A1.2150 Clinical Services Core

The Clinical Services Core (CSC) includes clinical operations, laboratory services, grants management and participant recruitment services. The CSC Clinical Research Unit (CRU) is a network of resources, facilities and professionally staffed inpatient and outpatient unit for adults and children as well as additional resources and services for conducting CCTS-approved studies. The UK IRBs review and approve all human research conducted in the CSC to ensure protection of the rights and welfare of research subjects.

A1.2200 CLINICAL RESEARCH SUPPORT OFFICE

The Clinical Research Support Office (CRSO) is supported by the UK College of Medicine, UK HealthCare and the Office of the VPR to offer support for the OnCore clinical trial management system, billing integrity and coverage analysis, as well as finance and regulatory assistance in partnership with the CCTS. The mission of the CRSO unit is to facilitate compliance, cost reimbursement, and participant data management by reducing administrative burdens associated with the conduct of clinical trials, enhancing clinical trial efficiency, providing tools to study teams that allow for enterprise-wide automation and gathering of important metrics (e.g., clinical trial accruals), and increasing compliance with federal and state guidelines. The CRSO maintains the UK instance of OnCore and integration with other institutional software. Services include comprehensive clinical trial management infrastructure including OnCore, Advarra Electronic Data Capture system, Advarra electronic regulatory binders (eREG) and financial management support. CRSO services include assistance in using OnCore and providing financial management support. CRSO staff build clinical trial protocols into OnCore for study teams to track subject accrual and project timelines, produce the insurance coverage analysis, provide technical support, software training, budget development, negotiation and post-award management. Regulatory tools include cradle-to-grave management and tracking systems for regulatory requirements for human subjects research; a Quality Assurance/Quality Improvement program with a dedicated auditor to provide audits at project initiation (enrollment of first subject) with a "find it, fix it" approach; random audits for CCTS-supported clinical studies; and for-cause audits requested by Data Safety Monitoring Boards (DSMBs) and/or the ORI. Assistance with regulatory and clinical trials recruitment is also offered.

A1.2225 Regulatory Knowledge and Support

The CCTS Regulatory Knowledge and Support Core integrates faculty, staff and community expertise in bioethics, regulatory knowledge and research integrity to provide investigators, community practitioners and trainees with a single point of access to the spectrum of ethical and regulatory requirements. The core is comprised of highly trained regulatory specialists who can provide support to investigators tailored to their specific needs.

A1.2300 INSTITUTIONAL RESOURCES

Allocation of institutional resources to support effective functioning of the UK HRPP is the responsibility of the VPR. The ORI assesses the needs of the IRBs and its support infrastructure on a continual basis. The ORI submits requests to the VPR for budgetary support and resource allocation to meet the needs identified during regular review of the volume and nature of the research being conducted and the protocols being reviewed by the IRBs.

The VPR receives and processes requests for payments for IRB chairs of the Medical and Nonmedical IRB committees, the costs of meals for IRB members and staff during meetings, travel, professional development costs for IRB members to attend professional meetings, and any additional special project needs.

In addition, various units reporting to the VPR provide the resources necessary to support IRB operations. Research Administrative and Fiscal Affairs (RAFA) provides budget support for ORI personnel salaries and fringe benefits, communications costs, copying and selected office and supply expenses. The Office of Research Information Services (RIS) manages requests for computer and technology resources to support the IRBs and ORI staff. The ORI budget covers additional basic operating costs including education for ORI staff, supplies, office furniture, education materials and selected equipment.

A1.2350 Research Administrative and Fiscal Affairs: Budget Process

Research Administrative and Fiscal Affairs (RAFA), a support unit directly responsible to the VPR, provides executive management and general administrative and support services for all units assigned to the VPR. Specific responsibilities are to initiate, coordinate and manage fiscal activities associated with UK Research including human resource services, budget processes, equipment and resource allocation and inventory, and capital planning and space allocation.

RAFA carries out all UK budgetary policies and procedures following general University procedures with the Board of Trustees having the ultimate and exclusive authority for the approval of all budgets per the Administrative Regulation, AR 1:4 (The Planning, Budgeting, and Assessment Cycle). The ORI and the IRBs (through the ORI) receive budget support primarily from research support funds.

A1.2400 HUMAN RESEARCH PROTECTION PROGRAM COMPLIANCE

A1.2425 Research Information Services

Research Information Services (RIS) supports the computing and networking infrastructure for all units reporting to the VPR, including support of the Medical and Nonmedical IRB committees. The specific responsibility regarding the HRPP compliance is to respond to ORI requests for IRB and ORI computing resources to support the review process. These include E-

IRB application system needs analysis and enhancement, equipment procurement and installation, user support, and communication of institutional policies on information technology use. In addition, the RIS Director or designee works closely with the ORI in ongoing E-IRB systems enhancements to facilitate efficient data management and documentation of all HRPP records. The RIS Director, with input from the IRBs and ORI, makes recommendations to the VPR on systems development, and serves as a liaison between the UK HRPP and any consultants contracted to develop technology infrastructure supporting research review.

A1.2450 Security, Export, Compliance and University Research

The ORI complies with federal sanctions and export laws through UK Security, Export, Compliance and University Research (SECURE). Federal sanctions and export control laws and regulations apply to a broad array of research and academic activities at the University of Kentucky. These activities include conducting restricted sponsored research, engaging in international collaborations, traveling and shipping internationally, and hosting international visitors.

Most UK research is not subject to export controls due to the Fundamental Research Exclusion (FRE), but there may be other limitations imposed that limit activity (e.g., Office of Foreign Assets Control (OFAC) restrictions). There are also several other exclusions from general export control requirements that may apply. Research that is export controlled must work with UK SECURE and OSPA to develop a Technology Control Plan for each export-controlled project.

A1.2500 EDUCATION INITIATIVE

The foundation for the effective implementation of all facets of the HRPP and for efforts to promote compliance with its requirements lies in a comprehensive mandatory education program for investigators/study personnel, IRB members, administrators and research support staff. The ORI, CCTS, SPS and various other units conduct ongoing education programs and maintain training materials on the ethical conduct of human research within federal, state and institutional regulations and requirements. The ORI documents initial and continuing human subject protection (HSP) training for all study personnel conducting human research. Investigators who assume the sponsor role for FDA-regulated research complete mandatory training to ensure they are informed regarding the additional regulatory responsibilities. Various training is offered or mandated based on protocol-specific, institutional or funding agency requirements to contribute to the protection of human subjects and the ethical conduct of research. Examples include conflict of interest (COI) education, responsible conduct of research (RCR) training, good clinical practice (GCP) education, and environmental health and safety courses.

The ORI provides mandatory and continuing education for regular and alternate IRB members. New IRB members complete a comprehensive orientation program including an initial orientation session and subsequent guided instruction by an assigned mentor who is an experienced member. Protocol-specific training materials, webinars, monthly chair meetings, email updates, and brief educational training sessions presented as part of IRB meetings all provide continuing education. Additionally, alternate IRB members also complete an Annual Review Training. The ORI also supports IRB member attendance at the annual Regional Human Subject Protection Conference.

The ORI and CCTS co-host ongoing educational seminars, informed consent workshops, Clinical Research Coordinator 101 course, and regional conferences for researchers aimed at

enhancing human research protection knowledge and practices. In addition, the ORI offers human subject protection (HSP) training, basic IRB information sessions, and customized classroom presentations for undergraduate and graduate researchers. The ORI also offers training for faculty advisors and hosts bi-monthly online Office Hours for faculty, staff and student researchers. The ORI also develops and makes available to the research community human subject protection guidance materials, interactive tools and videos, and training modules.

A1.2600 QUALITY IMPROVEMENT PROGRAM

The ORI and the UK IRBs provide a Quality Improvement Program (QIP) to strengthen human research protections at UK and demonstrate UK's commitment to continuous improvement in compliance. The QIP team evaluates human research protections at varying levels (e.g., federal, state, institutional and Good Clinical Practice); increases awareness of existing processes, operating procedures and educational programs; and acquires information necessary to enhance protections. Components of the program focus on educating UK investigators on the mechanisms by which human subjects are protected and regular assessment of current HRPP practices in relation to AAHRPP accreditation standards. QIP components present the opportunity for researchers, ORI staff and IRB members to continually improve human research protections performance and excel beyond federal and state protections standards.

The QIP provides useful information for identifying educational/training initiatives for researchers and their staff, ORI staff and IRB members. The QIP also plays a significant role in preparing the AAHRPP application and annual reports and in assessment of the UK HRPP as required by AAHRPP accreditation standards.

The QIP consists of three main components which examine the entire research process with focus on the researcher, the IRB's review process, the IRB records maintained by the ORI and/or the HRPP.

Directed on-site reviews are initiated by an IRB or ORI request due to concern with risks to subjects, routine failure of an investigator to comply with federal and/or institutional requirements, allegations or concerns about the conduct of the study brought to the IRB's attention or any case requiring further scrutiny, as deemed appropriate by the IRB.

Principal Investigator Self-assessment reviews are voluntarily performed by the investigator or his/her study personnel. However, the IRB or the ORI may also directly invite an investigator to perform a self-assessment review. The ORI provides a web-based self-assessment form to be completed by the investigator and/or study personnel.

Administrative assessment reviews are conducted at the discretion of the QIP Coordinator, the ORI Director and/or the VPR. The QIP Coordinator shares the results of administrative assessments with the ORI Executive Director. The results may impact current practices and may require additional educational activities for ORI staff and IRB members.

Administrative assessments may include but are not limited to:

- A thorough examination of the IRB records for improvement of management or to evaluate the procedures applied and/or issues addressed by the ORI staff and the IRB for protection of human subjects in research.
- At least annually, dissemination of an IRB Performance Evaluation Questionnaire to select individuals to assess representation of appropriate knowledge, skills, and abilities respective to IRB member, IRB Chair and IRB Vice Chair roles.
- Periodic outreach evaluation concentrating on the quantity and nature of information

available to research subjects through the ORI web site (i.e., enabled by analysis of compiled monthly web page “visitor” reports).

- Program Assessment for Accreditation, a significant component in support of maintaining AAHRPP accreditation, focuses on maintenance of applicable documentation representing current policy and procedures; utilization of the AAHRPP Self-Evaluation Instrument; and evaluation of current HRPP practices to ensure appropriate fulfillment of accreditation standards.

The ORI Research Education Specialist develops educational programs/announcements for investigators, their research staff, ORI staff and IRB members based on the results of QIP reviews. If/when findings from QIP reviews are reported to an IRB, the IRB determines whether to report the findings to the FDA, OHRP, study sponsor, VPR or other internal departmental faculty/staff.

UK’s Markey Cancer Center and the CCTS have Quality Improvement (QI) initiatives to provide continuous quality improvement for the conduct of clinical trials conducted at the University.

A1.2700 INSTITUTIONAL PROGRAM REVIEW AND ASSESSMENT

The IRB, ORI, and OSPA all have roles in conducting ongoing program review and assessment. Information provided in the Strategic Plan Annual Report of unit activity for the fiscal year links closely to the budget process and provides the basis for VPR assessments of HRPP needs to ensure that sufficient resources are available to support effective functioning of the HRPP. The ORI conducts program assessment and review of HRPP administration and communicates new regulatory policy to the University community through formalized programs of education and development of pertinent education materials.

standard operating procedures (SOPs) maintained by the ORI on behalf of the HRPP delineate specific responsibilities for development, review and revision of policies and procedures related to research review and the HRPP.

A1.2725 Plans to Maximize Compliance with the Human Subject Protection Program

UK is committed to continuous improvement in its human research protections and to ensuring compliance with the regulations, policies, procedures and standards that are the foundation for the plan. The UK research enterprise is a dynamic component of the institution. Research growth fluctuations, shifting research focuses and changes in federal regulations are critical factors that mandate provisions to monitor the volume and nature of human research conducted at UK to ensure that the HRPP is functioning effectively. UK has instituted additional provisions to assess and facilitate compliance with the HRPP on an ongoing basis to assist units and personnel engaged in human research protections. These include educational programs, quality assurance/improvement (QA/QI) programs and procedures, and established mechanisms for obtaining feedback from diverse constituents in the HRPP.

A1.2750 Suggestions, Comments, Questions, Complaints, and Concerns with the Human Research Protection Program

The ORI, in accordance with the VPR’s commitment to continuous improvement in institutional HRPP policies, practices and procedures, has established a formal process to register suggestions, questions, comments, problems, concerns, obtain information or offer input regarding the HRPP, the ORI and/or the IRB administrative procedures. Any individual may file

suggestions, questions, complaints or concerns regarding the HRPP, ORI and IRB administrative procedures with the ORI Executive Director, who evaluates and investigates the concerns raised and determines what actions, if any, should be taken by the ORI and/or the IRBs to address the issue. The ORI Executive Director is responsible for resolving issues raised as quickly, fairly and amicably as possible through cooperative exchange of information with pertinent units and personnel involved in the UK HRPP. The ORI Executive Director forwards suggestions or concerns about ORI and IRB administrative procedures that are not resolved at the level of the Executive Director to the VPR, who shall be the final deciding authority.

A1.2800 SUGGESTIONS, CONCERNS, AND QUESTIONS ON RIGHTS, SAFETY, AND WELFARE OF SUBJECTS PARTICIPATING IN SPECIFIC STUDIES AND/OR ALLEGATIONS OF NONCOMPLIANCE

It is ORI and IRB policy to provide a safe, confidential and reliable channel for current, prospective or past research subjects or their designated representatives to discuss problems, concerns and questions; obtain information; or offer input with an informed individual who is unaffiliated with a specific research protocol. Each IRB-approved informed consent document includes the ORI Research Compliance Officer's toll-free phone number (1-866-400-9428) as a subject's primary contact point for this purpose. The ORI and IRBs monitor any concerns/complaints that are received for issues of noncompliance. Issues involving noncompliance are brought to the attention of the relevant IRB Chair, IRB members and the RCO/ORI Executive Director. The procedure for handling noncompliance is outlined in the UK ORI/IRB Noncompliance SOP.

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