University of Maryland Baltimore
School of Medicine

Human Research Protections Program

Research Administrators Committee

April 8, 2010

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Assistant Dean
Human Research Integrity and Compliance

UMB Human Research Protections Program (HRPP)

(UMB Policy I.1.A)

- Oversees research in humans
- Campus-wide: all schools
- Includes other organizations: HRPO, IRB, ACHRP, ORD, EHS, RIO, CCT, GCRC, COI, University Counsel, etc
- Institutional Official- Dr. Bruce Jarrell
- Shared responsibility
  - Institution
  - Institutional Review Board (IRB)
  - Investigator and Research Team
  - Sponsor
- AAHRPP accredited

UMB HRPP Mission

To cultivate a culture of conscience in the research community to ensure the highest levels of protections and advocacy for research participants by:

- actively engaging and working cooperatively with the Institutional Official, Institutional leaders, and all components of the HRPP
- facilitating ethical and scientifically sound research institutional oversight and IRB review processes
- contributing to the knowledge of investigators and research personnel through education and training programs
- communicating with sponsors, ***and***
- serving as a consistent resource for all current, past, and prospective participants

UMB HRPP Components

- Human Research Protections Office (HRPO)
- Institutional Review Board (IRB)
- IRB Executive Committee (EC)
- Research Subject Advocate and Safety Specialist
- Environmental Health and Safety (EHS) Office
- Investigational Drug Service (IDS)
- Baltimore Veterans Administration Maryland Health Care System (VAMHCS) and Research and Development (R & D) Committee
- Division/Departmental/Entity Signatories
- University Counsel

UMB HRPP Components, cont

- Advisory Committee for Human Research Protection (ACHRP)
- Office of Research and Development (ORD)
- Center for Clinical Trials (CCT)
- General Clinical Research Center (GCRC)
- Conflict of Interest Officer
- Conflict of Interest Committee
- Office of Research Integrity
- HIPAA Privacy Officer
- SOM Information Systems Liaison

Institutional Official (IO)

- President Ramsay has delegated this responsibility to Bruce E. Jarrell, MD, FACS
- Signatory to the UMB Federal-Wide Assurance (Required for Federal Funding)
- Ultimate responsibility for UMB HRPP and ensuring UMB compliance with federal requirements
  - $350M Research Funding
  - Violation of Assurance jeopardizes **all** research
- Designates Human Protections Administrator (HPA)
  - Susan C. Buskirk, MS, Assistant Dean, Human Research Integrity and Compliance
- Special category review:
  - Children- No direct benefit to individual child
  - Prisoners
  - FDA 50.24 –(waiver of informed consent for emergency research)
  - Humanitarian Use Devices

Federalwide Assurance (FWA)

- The University of Maryland, Baltimore Human Research Protections Program (HRPP) maintains a current Federalwide Assurance (FWA, 00007145)
  - Before a federal grant or contract can be awarded, the institution must file for an Assurance of Compliance with the government 45 CFR 46.103(a)
  - In the Assurance the Institution (and its investigators) agrees to comply with federal regulations, monitor research, and to report instances of serious non-compliance
  - Applies to all research at this institution regardless of funding

- University of Maryland, Baltimore's faculty, staff, and students, which comprise its seven schools and their departments, divisions, and facilities, are subject to the Assurance and this policy. This includes any research for which an Assurance or another formal agreement (e.g., MOU, IRB Authorization Agreement) identifies the UMB Institutional Review Board (IRB) as the IRB of Record.

  » UMB HRPP SOP I.3.K: University of Maryland, Baltimore's Federalwide Assurance

Federalwide Assurance (FWA)

- Failure to comply with the assurance can result in an institution's research being suspended or restricted

- The IRB is required to promptly report the following to OHRP:
  - unanticipated problems involving risks to subjects or others
  - serious or continuing noncompliance with the federal regulations or the requirements or determinations of the IRB
  - suspension or termination of IRB approval

Advisory Committee for Human Research Protections (ACHRP)

- Multi-disciplinary support from entire UMB campus community
  - All Schools, Institutional Official, IRB Chair, HRPP Executive Director, Investigators, University Counsel

UMB President and Deans:

- Strong Leadership
- Actively engaged
- Positive interactions
- Accessibility
- Open communication
- Mutual respect

- UMB's HRPP is robust, efficient, and effective

Association for the Accreditation of Human Research Protection Programs

- AAHRPP is a nonprofit organization founded in 2001 under the auspices of PRIM&R, the Association of American Medical Colleges (AAMC), AAU and several other national organizations.
- “AAHRPP seeks not only to ensure compliance, but to raise the bar in human research protection by helping institutions reach performance standards that surpass the threshold of state and federal requirements” (from AAHRPP website www.aahrpp.org).

AAHRPP Accreditation December 2005

Areas of Distinction:

- Resources to the UMB HRPP from the Organization (I.2.A)
- Quality Improvement Program (I.3.L)
- Data Safety Monitoring Plan - IRB Review (II.4.B)
- Fair and Equitable Recruitment Plans (III.1.D)
- Departmental Review Process (I.1.B)

Area of Concern:

- Inconsistencies in written UMB HRPP SOPs

Re-Accreditation December 2008

Strengths

- Strong organizational leadership (Institutional Official, HRPP Assistant Dean for Human Research Integrity and Compliance, IRB chairs, members, analysts) and high level of resources, budget, and personnel (I.1.C., I.2.A.)
- Data and safety monitoring plans and IRB review (II.4.B.)
- Investigator evaluation of decisional capacity for decisionally impaired participants at the time of enrollment and throughout the study (II.4.C.4)
- Investigational Drug Pharmacists: dedicated, resourceful, and attendance at each IRB meeting as a member

Re-Accreditation December 2008

Areas of Concern:

- Inconsistent Department Scientific and Feasibility Review (I.1.B.)
- Lack of familiarity with the terminology and reporting requirements for “Unanticipated Problems Involving Risk to Research Participants or Others” across all UMB personnel (I.3.J., III.2.B)
- IRB Member and Vice Chair evaluation and feedback process II.1.G.)
- Contracts did not include specific language regarding provision medical care for research-related injury, obligation of sponsor to promptly report findings that may affect the ongoing oversight of the study by the IRB, & communication of results to participants when safety or medical care could be affected (IV)

Human Research Protections Office (HRPO)

UMB Policy I.2.G

- Coordinating office for the Human Research Protections Program
- Support for the Institutional Review Board (IRB)
- Support for the Embryonic Stem Cell Research Oversight (ESCRO) Committee
- Support for the UMSOM Conflict of Interest (COI) Committee (future)
- Provides research support to the UMB community
  - Oversight of > 1,500 clinical research protocols.
  - 2 million dollar budget
  - Education in human research protections and Good Clinical Practices
    - > 2000 investigators and research staff
    - ~ 130 IRB members
    - Train International IRB Administrators

School of Medicine Financial Investment

FY'03

- $470,000
- 7 FTE
- 1700 Protocols
- Paper IRB System
- Electronic protocol management system implemented – BRAAN

FY'10

- $2.0 M
- 24 FTE
- 1500 Protocols
- CICERO replaces BRAAN

IRB Leadership

- 1 Chair: Dr. Robert Edelman
  - Assures the IRB operates in full compliance with federal regulatory requirements governing IRB functions
  - 35 % FTE

- 5 Vice-Chairs:

  Dr. Christopher DeFilippi
  Dr. Lisa Dixon
  Dr. Robert Rosenthal
  Dr. Stephen Seliger
  Dr. Ann Zimrin

  ALL:
- Chair IRB meetings once/month
- On Duty 1 day/wk (6-8 hrs) to review:
  - Expedited protocols – 35/day
  - Reportable Events – 20/day

UMB HRPO/HRPP Milestones

- **2003**
  - Established the Human Research Protections Office (HRPO)
  - Electronic Protocol Management System – BRAAN
- **2004**
  - Expanded to a comprehensive, integrated Human Research Protections Program
  - Developed HRPO Business Plan
    - comprehensive Quality Improvement Program
- **2005**
  - AAHRPP Accreditation (5 Areas of Distinction)
  - Implemented Deferral Prevention Program
- **2006**
  - International Activities- Education, Organizational Assessment, Audit

UMB HRPP/HRPO Milestones (cont)

- **2007**
  - Added IRB Panel #5
  - FDA Inspection of UMB IRB May 7-14; No Form 483 issued

    Two findings:
    - BRAAN allowed Investigators to “cut and paste” between protocols resulting in incorrect transfer of IRB review history
    - **Reporting of Expedited reviews to fully convened IRB was not compliant in BRAAN**
- **2008**
  - New Electronic Protocol Management System- CICERO
    - Go live September 8, 2008
  - AAHRPP Re-Accreditation through 2011
  - Education on Unanticipated Problems for over 1500 individuals

UMB HRPP/HRPO Milestones (cont)

- **2009**
  - Established Embryonic Stem Cell Research Oversight (ECSRO) Committee
  - Implemented Project Plan for developing COI modules in CICERO
  - New IRB Vice Chair - Dr. Stephen Seliger
  - Added IRB Panel # 6

HRPO/IRB Customer Evaluation and Feedback

- **2002**: **Investigators Education Needs Assessment**

- **2004**: **IRB Member Knowledge Quiz**
  - All panel to assess members knowledge of required elements of criteria for approval and ICD; special requirements for children;
    - Scores were presented 8/28/04-throu 9/04 as pp presentation to all committee
    - OUTCOME: Developed targeted education program for IRB members

- **2005: BRAAN Satisfaction Survey**

- **2006**: **Research Community Education Needs Assessment and HRPO Quality & Effectiveness Survey**

HRPO/IRB Customer Evaluation and Feedback

- **2007:**
  - **Research Community Survey on HRPO Quality and Effectiveness**
  - **IRB member survey for IRB Chairs**

- **2008: Research Community Survey on HRPO Quality and Effectiveness**

- **2009: Research Community Survey on HRPO Quality and Effectiveness**

Levels of Protections for Research Participants

There are three levels of protection

- Regulatory Oversight
- IRB
- Informed Consent

UMB Institutional Review Board

UMB HRPP I.3.B

- Functions independently, but in coordination with other entities
- Led by a Chair and six Vice-Chairs
  - experienced researchers
  - former IRB Members
  - respected among the research community
- Comprised of five panels, plus an ad hoc panel
  - meet every Thursday

Authority and Independence of the IRB

- The IRB is charged with protecting the rights and welfare of research participants
  - Protecting participants is ***not just*** the IRBs responsibility

- It is a ***shared*** responsibility for the protection of participants
  - Investigator
  - Institution (EHS, University Counsel)
  - Research Team Members
  - IRB

Authority and Independence of the IRB

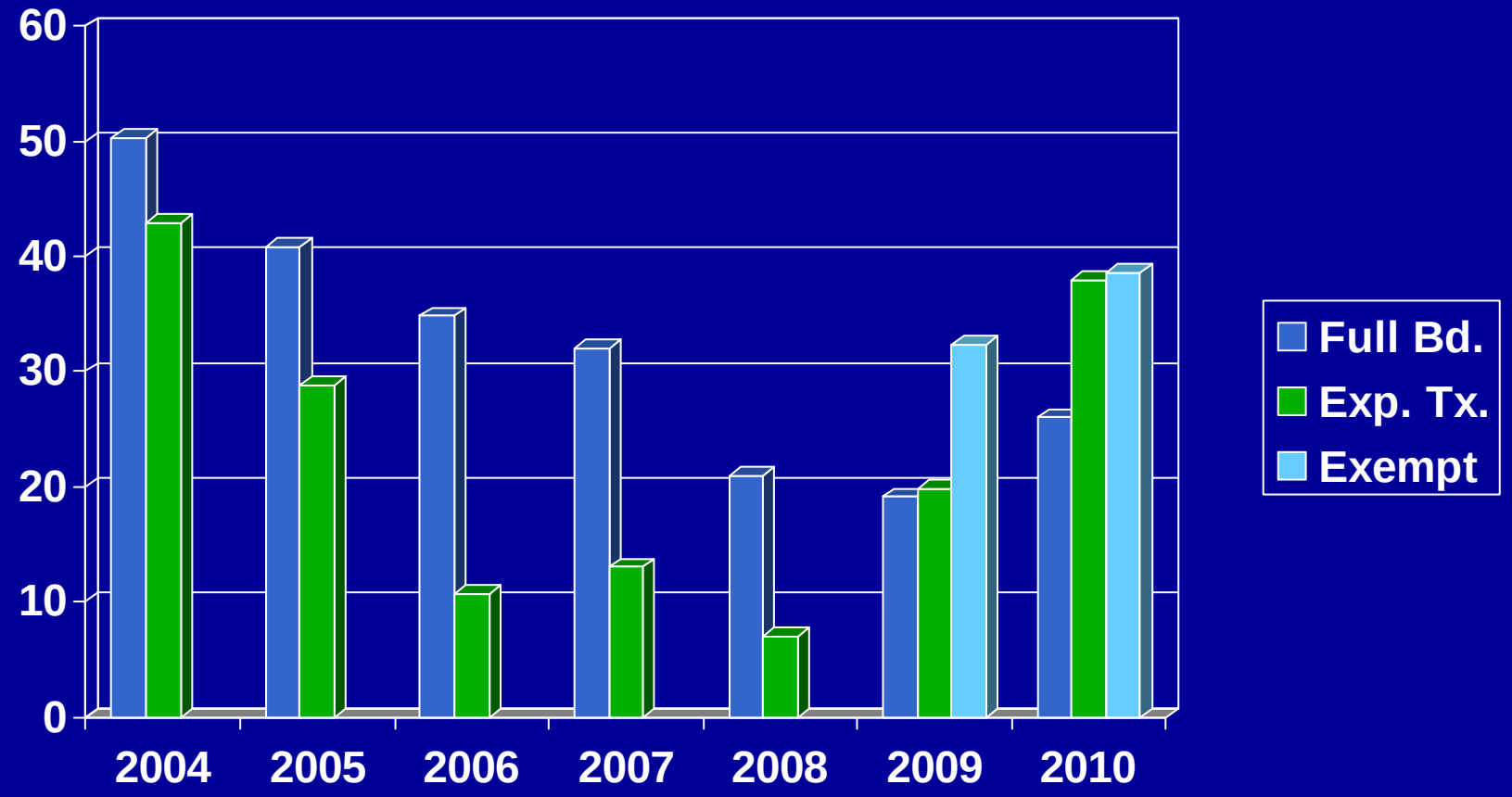
- The IRB has the authority to approve, require modifications to secure approval (approve with contingencies or defer), or disapprove all research activities that fall within its jurisdiction.
- The IRB has the authority to suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that had been associated with unexpected serious harm to participants.
- The IRB has the authority to observe or have a third party observe the informed consent process or conduct of the research.
- The IRB has the authority to appoint an ombudsman, a neutral third party also known as a participant advocate, to advocate for the participant, their family, or legally authorized representative. The role of the ombudsman may be served by a member of the HRPO, IRB, General Clinical Research Center (GCRC), VAMHCS representative, or may be an impartial third party.

UMB HRPP SOP I.3.B: Authority and Independence of the Institutional Review Board (IRB)

UMB IRB Oversight

- > 1400 human participant protocols
- Target turnaround times for submissions:
  - Full board review 3-4 weeks
  - Expedited transactions 2 weeks
- > 2000 investigators and research staff

Turnaround Time
FY 2004 - 2010



Full Board & Expedited

Requirements for Conducting Research at UMB

UMB HRPP Policy III.2.A

Principal Investigator (PI)

- Full-time (>51% effort) faculty member
- Holding one of the following titles at UMB:
  - Professor
  - Associate Professor
  - Assistant Professor
  - Or has been granted approval by the Institutional Official

- The IRB recognizes only one PI for each project

PI Responsibilities

UMB HRPP Policy III.2.A

- Principal Investigator bears ultimate responsibility for assuring that the conduct of the study complies with all UMB HRPP policies and procedures for the protection of human subjects.
- The Principal investigator is the critical component in the conduct of high quality research and in the assurance of human research participants' safety.

Principal Investigator Responsibilities

UMB HRPP Policy III

- Appropriate expertise
- Adequate resources
- Assure oversight of research
- Respond to participant concerns
- Provide adequate Data & Safety Monitoring
- Provide appropriate care to the participants
- Scientific validity/appropriate design
- Ethical principles upheld
- Compliant with federal, state, institutional requirements including Good Clinical Practices (GCP's)

Basic Training Requirements for Investigators and Research Staff

UMB HRPP Policy III.2.A

- ***Human Subjects Protections Training-*** (online)
  - All individuals engaged in human participant research at UMB are required to completed CITI training ***bi-annually***
    - www.citiprogram.org

- ***HIPAA Training*** (online)
  - UMB policy requires that all individuals employed at UMB must take HIPAA 125
  - All individuals engaged in research at UMB are also required to complete HIPAA 201.
    - http://medschool.umaryland.edu/orags/hrpo/education_hipaa.asp

Engaged in Research?

UMB HRPP Policies I.1.A, II.13

- Individuals
  - Persons who interact with living individual specifically for research purposes, including but not limited to performing procedures and manipulating the environment
  - Persons who interact with individually identifiable information for research purposes
- Performance sites
  - Engaged or Not Engaged in Research
  - Must have IRB approval or documentation of site IRB approval or letter of cooperation

Is it Human Subjects Research?

- Definition of Research
  - DHHS: 45 CFR 46.102(d)
  - FDA: 21 CFR 56.102.(c)
  - VA: 38 CFR 16
- Definition of Human Subject
  - DHHS: 45 CFR 46.102
  - FDA: 21CFR56.102(e)
- Identifying Research Intent: UMB HRPP Policy I.3.C
  - HRPO/IRB decision
  - Must speak to an IRB analyst for guidance

Department or Entity Scientific and Feasibility Review

UMB HRPP Policy I.1.B:

All new research applications must be reviewed by the primary campus entity for scientific merit, available resources, and feasibility prior to submission to the UMB IRB for review and determination.

- Only those protocols that pass entity-level review will be considered by the IRB.

Purpose of Scientific and Feasibility Review

At a minimum, the review should address the following questions:

1. Is the research question meritorious?
2. Is the study design valid?
3. Is the study design likely to result in significant new information for the field?
4. Is the sample size adequate to answer the major scientific questions in the project?

Purpose, cont.

5. Have all potential risks been identified?
6. Does the protocol incorporate all possible mechanisms for reducing risks?
7. Are there adequate resources (space, personnel, and patients/participants) to carry out the study and ensure the safety and welfare of all participants?
8. Are all investigators aware of their individual responsibilities with respect to this study?

Purpose, cont.

9. Does the principal investigator have adequate time and expertise to supervise the study appropriately?
10. Have the financial implications of the research been considered and deemed acceptable to the department?
11. Have ethical principles AND CONFLICT OF INTEREST ISSUES been appropriately addressed?

IRB Review Process

UMB Electronic Protocol Management System

- **CICERO**: Comprehensive, Institutional Collaborative Evaluation of Research On-line
  - www.medschool.umaryland.edu/ORAGS/hrpo/cicero.asp
  - COI statement
  - Industry-sponsored Fees

Minimal & Greater Than Minimal Risk

- *Minimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

  - » 45 CFR 46.102(i)
  - » 21 CFR 50.3(k)
  - » The FDA and HHS share the same definition for minimal risk

Minimal & Greater Than Minimal Risk

- Examples of Minimal Risk Research
  - Chart review
  - Survey
  - Physical exam
  - Drawing blood
    - limited by volume and frequency

Minimal & Greater Than Minimal Risk

- **Protocols that do not meet the definition of minimal risk are considered <u>Greater Than Minimal Risk</u>**

- When the IRB Analysts triage new IRB applications the first criteria they ascertain is the risk level to ensure the appropriate level of review
  - Only the risks of the research are taken into consideration when evaluating the risk level of an application. The risks associated with standard of care are not factored into the determination

Full Board & Expedited Reviews

Once the risk level of an application has been established the application is reviewed under one the two review levels

- **Full Board Review**
  - All Greater than minimal risk applications (initial and continuing review) are reviewed by a fully convened IRB panel
  - Modifications that affect safety and risks
- **Expedited Review**
  - Minimal risk applications are reviewed by the Chair and/or Vice Chair(s) individually
    - Exempt applications are also reviewed by the Chair and/or Vice Chair(s)
    - Modifications that involve minor changes (ex., adding research team members)

Full Board & Expedited Reviews

- If an application is reviewed under the Expedited process the appropriate category must be determined to ensure it qualifies
- There are 9 categories of Expedited review
- Expedited categories apply to **both** initial and continuing review

» 45 CFR 46.110 & 21 CFR 56.110

Full Board & Expedited Reviews

Expedited Review Categories - 45 CFR 46.110 & 21 CFR 56.110

- (1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met. (a - IND not required or b - IDE not required)
- (2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows (a – healthy non pregnant adults b – other adults and children
- (3) Prospective collection of biological specimens for research purposes by noninvasive means
- (4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing.
- (5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes
- (6) Collection of data from voice, video, digital, or image recordings made for research purposes.
- (7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.
- (8) Continuing review of research previously approved by the convened IRB as follows: (a) - permanently closed to the enrollment, completed all research-related interventions and active only for long-term follow-up, (b) - no subjects have been enrolled and no additional risks have been identified, (c) - data analysis
- (9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified

Full Board & Expedited Reviews

- **Exempt Research**
  - Certain minimal risk research activities are “exempt” (45 CFR 46.101b)
    - » For example, does not expire or require a continue review however any changes must be submitted to the IRB via modification
  - The IRB, not the investigator, determines if the research is “exempt”
  - Six exempt categories
    - The most common exempt category at UMB is Category #4
      - » Example: Retrospective chart/database review
    - Research involving prisoners, survey research involving children are not permitted to be Exempt

Full Board & Expedited Reviews

Exempt Categories - 45 CFR 46.101(b)(1-6)

- (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
- (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:(i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
- (3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:
(i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
- (4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
- (5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:
(i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.
- (6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Types of IRB Submissions:

New
Continuing Review
Modification
Reportable Events
Final Report

Sponsored Research

UMB HRPP Policy Section IV

- UMB applies its HRPP to all sponsored research by ensuring that written agreements with sponsors document that both parties bear responsibility for complying with applicable law and adhering to ethical standards.
- It is the responsibility of the investigator to assure that the IRB application is consistent with the proposal for funding for extramural and intramural support. (UMB HRPP SOP III)
- The investigator should act as liaison between the IRB and the research sponsor.

IRB Fees for Industry-Sponsored Applications

UMB HRPP Policy IV.1

- The UMB IRB will assess a fee for all industry-supported initial and continuing renewal applications IRB submitted to the IRB for review.
  - Studies that receive less that $10,000 are exempt from this policy.
- Complete appropriate the IRB Industry-Sponsored Billing information in CICERO

HRPO Research Support Services

The HRPO team that provides research support services includes:

- IRB Analysts
- Research Subject Advocate & Safety Specialist
- Compliance Specialists
- Quality Improvement Specialists
- Education and Investigator Support staff
- Administrative Support staff

HRPO Services

IRB Analysts	*Research Compliance Specialists*	*Quality Improvement / Investigator Support*
•Support 6 IRB Panels •Support ESCRO Committee •Education regarding IRB submission process •Liaison with investigators & IRB members	•Monitoring •Investigator Self Assessments •Auditing • For cause • Routine • Random **Research Subject Advocate and Safety Specialist**	•Consultation prior to IRB Review •Assist with study set-up •Training for investigators and research personnel •CICERO support

UMB HRPO Contact Information

UMB Human Research Protections Office

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