Summary of Major Changes Since 07/2016 Version

Manual Sections

Q. Noncompliance Policy and Procedures added
R. Electronic Signatures Policy added
S. Research Tissue Acquisition Policy added

Other changes include:
1. References to separate HIPAA authorizations (when applicable) were removed as it’s now being embedded into consent forms
2. References to the old human subjects training tutorial were removed and replaced with “UVM and UVM Medical Center approved training” and links provided to resources and FAQs
3. The term blood collection replaced blood drawing
INTRODUCTION

The University of Vermont (UVM) and UVM Medical Center have made a firm commitment to protect human research subjects. The US Department of Health and Human Service regulations require each institution that conducts research involving human subjects to describe, in detail, the procedures it will use to protect the rights and welfare of the human subjects. Each institution prepares a document that describes these procedures. The document is called a “Federalwide Assurance” (FWA).

The FWAs of UVM and UVM Medical Center have identical written statements regarding our program of protections for human subjects in research. These include our adherence to the ethical standards as well as our policies and procedures for the conduct of research involving human subjects. Our guidelines cover all internal and external funded research, as well as unfunded projects and are applicable to faculty, fellow, resident, and student-initiated projects.

Research with human subjects is considered any systematic investigation in which an investigator (student or professional) obtains data through intervention or interaction with an individual or identifiable private information. This not only applies to physical interventions but to such activities as mail, telephone, web-based surveys, questionnaires or tests, interviews and observational research. Review of records, especially those containing information individuals expect will not be made public (a medical or school record, for example) is also considered to be research.

As indicated in this Manual, different review procedures may be applied to research projects depending on the degree of risk presented to the subject and the nature of the procedures. In addition to the medical sciences, these guidelines cover behavioral, social science, and educational research, however benign, and must be submitted to the administrative office of the Committees on Human Research for certification of exemption.

Throughout this manual, all references to Committees on Human Research is interchangeable with the term Institutional Review Boards (IRBs).

The need for faculty attention to the conduct of human research projects by fellows, residents, and students is essential as well as an understanding of their responsibilities for the project. These projects are covered by University review requirements. Some departments that have students conducting research with human subjects appoint a department representative to advise students on the conduct of such research projects and to act as a liaison between the student/department and the Committee office. If there are any questions about students conducting research, they may be directed either to the department representative or the Committee office.

The Committees on Human Research Office is not the only entity responsible for oversight of human subject research. The Office for Clinical Trials Research (OCTR), the The University of Vermont Cancer Center (UVMCC) and the Clinical Research Center (CRC) are entities across UVM and UVM Medical Center that play a role in protecting human subjects in research including information collected about subjects. Unique requirements may be in place if your research activity is performed with the support of one of these units. If so, you should contact the administrative staff for the appropriate unit to determine what, if any, additional responsibilities may be active during the conduct of your research. In addition, these entities share the protocol status, correspondence related to the protocol, adverse events, and monitoring information. This sharing avoids duplication of efforts and also affords a higher level of protection for the subjects.
INTRODUCTION .................................................................................................................. 3

1. COMMITTEE’S MISSION .............................................................................................. 7

2. COMMITTEE’S RESPONSIBILITIES/AUTHORITY ................................................. 7

3. CONTACTS ................................................................................................................... 8

4. DETERMINATION IF THE INSTITUTION(S) IS ENGAGED, WHETHER THE PROJECT IS CONSIDERED RESEARCH AND IF THE RESEARCH INVOLVES HUMAN SUBJECTS ........................................ 4

5. TRAINING REQUIREMENTS ...................................................................................... 13

6. NON-FACULTY RESEARCHERS WHO CONDUCT HUMAN SUBJECT RESEARCH .......................................................................................................................... 14

6.A. USE OF HUMAN SUBJECTS BY UVM STUDENTS ............................................. 14

   6.A.2. Responsibility of Course Instructors When Class Projects are Exempt ................................................................. 16

   6.A.3. Individual Research Projects, that are Exempt ........................................................................................................ 16

   6.A.4. Individual Research Projects, Directed or Independent that are Not Exempt .......................................................... 17

   6.A.5. Responsibility of Course Instructors/Faculty Sponsors When Class Projects are Not Exempt ................................ 17

7. TYPES OF COMMITTEE REVIEWS ........................................................................... 17

   7.A. “FULL” COMMITTEE REVIEW ........................................................................... 17

   7.B. “EXPEDITED” REVIEW .................................................................................... 18

   7.C. “EXEMPT” RESEARCH REVIEW ...................................................................... 19

   7.D. “RESEARCH NOT INVOLVING HUMAN SUBJECTS” REVIEW AND DETERMINATION .......................................................... 21

   7.E. PROJECTS WHERE THE ONLY PROCEDURE INVOLVES CHART REVIEW .............................................................................. 22

   7.F. REVIEW OF QUALITATIVE RESEARCH .......................................................... 24

   7.G. COORDINATION WITH OTHER COMPLIANCE COMMITTEES/DIVISIONS ......... 27

      7.G.1. The University of Vermont Cancer Center Protocol Review and Management Committee (PRMC) .......................................................... 27

      7.G.2. Scientific Advisory Committee (SAC) ......................................................... 27

      7.G.3. Office of Biotechnology Activities/Recombinant DNA Advisory Committee .................................................................................. 27

      7.G.4. Institutional Biosafety Committee (IBC) .................................................... 27

      7.G.5. Radiation Safety Office (RSO) .................................................................... 28

      7.G.6. Sponsored Project Administration (SPA) .................................................... 28

      7.G.7. Office for Clinical Trials Research (OCTR) ............................................. 28

      7.G.8. UVM Medical Center Compliance Office .................................................. 28

8. REQUIREMENTS AND SUBMISSION MATERIALS FOR INITIAL REVIEW ......... 28

   8.A. PROTOCOL .......................................................................................................... 28

      8.A.1. Elements ....................................................................................................... 28

      8.A.2. Qualitative Research Protocol .................................................................... 37

      8.A.3. Placeholder ................................................................................................... 37


      8.A.5. Biological Specimens/Data Repository Protocols ......................................... 39


   8.B. LEGALLY EFFECTIVE AND PROSPECTIVELY OBTAINED INFORMED CONSENT AND DOCUMENTATION OF CONSENT .................................................................................. 42

      8.B.1. Consent Requirements/Elements in the Form ............................................ 45

      8.B.2. HIPAA Authorization Requirements .......................................................... 47


      8.B.4. Waiver of Informed Consent, Alteration of Informed Consent, or Waiver of Documentation ................................................. 50

      8.B.5. Waiver or Alteration of HIPAA Authorization ............................................ 53

      8.B.6. Request for Waiver of Informed Consent/Authorization/Documentation Form .................................................................................. 54


      8.B.8. Request for Partial Waiver of Authorization for Recruitment Purposes Form ........................................................................ 54


      8.B.10. Children Reaching Legal Age of Consent While Enrolled in a Study Policy ........................................................................ 56

      8.B.11. Media Consent ............................................................................................. 56

8.C. DOCUMENTATION ................................................................................................. 57

8.D. DATA MANAGEMENT GUIDANCE – SEE APPENDIX O ........................................ 57

8.E. REVIEW OF GRANTS/CONTRACTS/REVIEW FEES ........................................ 57
9. SUBMISSION OF MATERIALS AFTER INITIAL APPROVAL IS OBTAINED ........................................... 59

9.A. CONTINUING REVIEW ................................................................................................................. 60
9.A.1. Requirements ......................................................................................................................... 60
9.B. UNANTICIPATED PROBLEMS REPORTING (INCLUDES ADVERSE EVENTS) ...................... 62
9.B.2. Documentation ......................................................................................................................... 65
9.C. REQUEST FOR MODIFICATION/AMENDMENT TO PREVIOUSLY APPROVED PROTOCOL ...... 65
9.C.1. Requirements ........................................................................................................................... 65
9.C.2. Immediate Hazard .................................................................................................................... 67
9.C.3. When to Request ....................................................................................................................... 68
9.C.4. The Request for Modification / Amendment to Approved Protocol Form .................................. 68
9.C.5. Documentation .......................................................................................................................... 68
9.D. NOTICE OF PROTOCOL CLOSURE OR REQUEST TO REOPEN A CLOSED PROTOCOL ... 69

10. INVESTIGATOR RESPONSIBILITIES ............................................................................................. 70

10.A. EXPECTATIONS OF AN INVESTIGATOR ................................................................................. 69
10.B. REQUIREMENTS OF THE PRINCIPAL INVESTIGATOR .......................................................... 70
10.B.1. Ensure Proper Training of the Research Team ........................................................................ 70
10.B.2. Ensure Protocol Adherence .................................................................................................... 70
10.B.3. Create a Process of Informed Consent and HIPAA Authorization ........................................ 70
10.B.4. Provide Reports on the Progress of the Study ....................................................................... 71
10.B.5. Coverage for PI or Faculty Sponsor ....................................................................................... 72
10.B.6 Investigator’s Responsibilities when Leaving the University ................................................. 72
10.C. GUIDANCE FOR THE INVESTIGATOR AND RESEARCH PERSONNEL .............................. 73
10.C.1. Communication with the IRB ................................................................................................. 73
10.C.2. Written Communication of IRB Decisions ............................................................................ 74
10.C.3. Retention of Research Records ............................................................................................. 74
10.C.4. Accessibility of Records ......................................................................................................... 74
10.C.5. Enrollment Incentives ............................................................................................................ 75
10.C.6. Investigator Financial Interest ................................................................................................. 75

11. ADDITIONAL PROTECTIONS FOR SPECIAL POPULATIONS ..................................................... 78

11.A. GUIDELINES ............................................................................................................................... 78
11.B. PREGNANT WOMEN, FETUSES, AND NEONATES ................................................................. 79
11.C. PRISONERS ............................................................................................................................... 81
11.D. CHILDREN ................................................................................................................................. 83
11.E. NON-ENGLISH SPEAKING INDIVIDUALS .............................................................................. 85
11.F. COGNITIVELY IMPAIRED INDIVIDUALS ................................................................................ 85

12. INVESTIGATIONAL DRUGS (INCLUDING BIOLOGICS) AND DEVICES .................................... 87

12.A. RESEARCH INVOLVING INVESTIGATIONAL DRUGS ............................................................ 87
12.A.1. Definition of an Investigational Drug from the FDA Regulations: ........................................ 87
12.A.2. Use of Approved Drugs for Off-Label Indications: ............................................................... 88
12.A.3. Expanded Access of Investigational Drugs (also sometimes referred to as compassionate use): 88
12.B. RESEARCH INVOLVING MEDICAL DEVICES ...................................................................... 92
12.B.1. Definition of an Investigational Device .................................................................................... 92
12.B.2. IRB Review of Investigational Device Protocols ................................................................. 92
12.C. HUMANITARIAN USE DEVICES .............................................................................................. 93
13. MULTI-INSTITUTIONAL RESEARCH STUDIES

13.A. MANAGING IRB REVIEW IN COLLABORATIVE RESEARCH STUDIES ................................. 94
   13.A.1. Institutions Without an IRB Engaged in Federally Funded Research ............................ 94
   13.A.5. Collaborative Research Studies FLOWCHART ..................................................... 95
13.B. NON-COLLaborATIVE RESEARCH AND IRB REVIEW .................................................. 97
13.C. UVM/UVM MEDICAL CENTER RESEARCHER AS THE LEAD PI IN A MULTI-INSTITUTIONAL STUDY ................. 97

Attachments
A: Emergency Use of an Investigational Drug, Biologic, or Device Certification of Compliance Form ........... 100
B: POLICY – Attachment B is blank intentionally ........................................................................ 101
C. POLICY – Fees for Committee on Human Research Review of Sponsored Trials ...................... 102
Attachment D ................................................................................................................................ 104
D: Elements for De-Identification for Protected Health Information .............................................. 104
E: Statement of Compliance for the Committees on Human Research ........................................... 105
F: POLICY – Human Subject Research Monitoring Program ...................................................... 106
G: Guidance on Research Involving Coded Private Information or Biological Specimens ................. 107
H: Standards and Language for Studies Involving MRI ............................................................... 111
J. Guidance on Engagement in Research .................................................................................... 117
K. Types of Research ................................................................................................................ 121
L. Pregnancy Testing in Minor Research Subjects ......................................................................... 122
M. Certificates of Confidentiality ............................................................................................... 123
N. Exceptions to Confidentiality Guidance ................................................................................ 127
O. Guidance on Data Management in Human Subjects Research ............................................... 128
P. Requirement to include a full Protocol Title in the Electronic Medical Record (PRISM) ............ 138
Q. NONCOMPLIANCE POLICY AND PROCEDURES – 9/23/2016 ........................................ 139
R. Electronic Signature Policy .................................................................................................... 144
S. Research Tissue Acquisition Policy ....................................................................................... 146

Manual for Human Subject Research – 2/17/17

6
1. COMMITTEE’S MISSION

The University of Vermont and UVM Medical Center are responsible for safeguarding the rights and welfare of human subjects involved in any research activity. According to institutional policy, all such research, funded or unfunded, conducted by University and/or UVM Medical Center personnel, including students, or done under the auspices or sponsorship of either institution must be reviewed by one of the Institutional Review Boards (IRBs): the Committee on Human Research in the Medical Sciences (CHRMS) or the Committee on Human Research in the Behavioral and Social Sciences (CHRBSS). Approval must be obtained BEFORE the research activity starts and the project must be reviewed at least annually for as long as it is active.

2. COMMITTEE’S RESPONSIBILITIES/AUTHORITY

The Committees on Human Research are charged with certain responsibilities and authority according to federal regulations and institutional policy:

A. Review and have authority to approve, require modifications in, or disapprove research activities.

B. Require that information given to subjects as part of informed consent with all requirements and may require that information, in addition to that specifically mentioned in the regulations, be given to the subject when, in the IRB’s judgement, the information would add to the protection of the rights and welfare of subjects.

C. Require documentation of informed consent or waive documentation in accordance with the regulations.

D. Require that waivers or alterations of consent comply with the requirements outlined in the federal regulations.

E. Conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and research.

F. Investigate and report to the appropriate institutional officials, Office of Human Research, DHHS (OHRP), and, when applicable US Food and Drug Administration (FDA) and/or funding agency, any serious or continuing noncompliance with the federal regulations and requirements and determinations of the IRB.

G. Suspend or terminate approval of research that is not being conducted in accordance with the federal regulations and the IRB’s requirements or has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall be reported promptly to the investigator, appropriate institutional officials, OHRP, and/or FDA when applicable.

H. Provide training for all individuals involved in the conduct of research involving human subjects, regardless of funding source.

I. Review all adverse events and unanticipated problems to subjects and others meeting local IRB criteria.

J. Function as the Privacy Board by reviewing all HIPAA authorization language or requests to waive authorization for research undertaken at both UVM and UVM Medical Center.
K. Monitor active projects to ensure compliance with the IRB-approved protocol and with applicable human subject protection guidelines and regulations.

POLICY: OVERSIGHT OF HUMAN RESEARCH PROTOCOLS POLICY AND PROCEDURES;
06/08/2007

The commitment of UVM and UVM Medical Center to high quality protection of human subjects underlies the policy of the IRBs to provide an appropriate level of oversight for research involving the use of human participants. The program for oversight and monitoring of research is designed to continue to increase the safety and well-being of participants in research studies.

Program for Oversight of Human Research Protocols

Training in the Protection of Human Subjects: Completion of the UVM/UVM Medical Center approved training is required. We currently use Collaborative Institutional Training Initiative (CITI) for this requirement. This training is required for all individuals involved in the conduct of research involving human subjects, regardless of funding source. The IRB does not release the approvals for new and continuing protocols until all individuals involved with human subjects on the project (i.e., direct contact with subjects or access to data) have completed their training. This assures that investigators and their staff are appropriately trained in their regulatory and safety responsibilities prior to commencing research activities.

Continuing Review of Protocols: In addition to the training requirements, the IRB utilizes forms for researchers to report on the status and activity in their research protocols. These forms gather substantive information which allows the IRB to effectively evaluate the on-going conduct of the research projects. The internal forms that IRB members use in doing the initial and continuing reviews contain checklists that promote consistency and thoroughness in these processes.

Adverse Event Review: Internal processes provide for a timely and effective review and follow-up on adverse events and unanticipated problems which are reported to the IRB. The IRB staff does a preliminary analysis and obtains additional information as needed. A sub-committee of the IRB provides a more in-depth review of adverse events and unanticipated problems which have been identified as requiring additional review and analysis.

Compliance Monitoring: The IRB has a process for monitoring on-going research to ensure compliance with the IRB-approved protocol and with applicable human subject protection guidelines and regulations. The process is intended to be educational for the personnel involved in the human subjects research, with a primary goal of fostering a collegial environment, thus developing a culture of compliance. The IRB monitoring plan includes the following elements: 1) site visits with researcher; 2) review of protocol documents; 3) review of the consent process; and 4) review of other processes as appropriate, e.g., adverse event and unanticipated problem reporting. See monitoring policy Attachment F.

3. CONTACTS

The administrative office of the Committees on Human Research is located in 213 Waterman Bldg, 85 South Prospect St, Burlington, VT 05405, (802) 656-5040. The RPO staff as well as a list of the current Committee Chairs is located under contacts on our website.

4. DETERMINATION IF THE INSTITUTION(S) IS ENGAGED, WHETHER THE PROJECT IS CONSIDERED RESEARCH AND IF THE RESEARCH INVOLVES HUMAN SUBJECTS

A. As it is the Committee’s responsibility to safeguard the rights and welfare of the
“human subjects” in “research”, before developing a proposal for research activity, you should ask yourself these three critical questions:

1. Is the activity RESEARCH?
2. Will the activity involve HUMAN SUBJECTS?
3. Is UVM or UVM Medical Center engaged in the research?

Federal Regulations (45 CFR 46: HHS Policy for the Protection of Human Research Subjects) provide the following definitions on which to base an initial decision.

1. **RESEARCH**: "A systematic investigation including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."
2. **HUMAN SUBJECT**: "A living individual about whom an investigator (whether professional or student) conducting research obtains (i) data through intervention or interaction with the individual or (ii) identifiable private information."
3. **INTERVENTION**: "...includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes."
4. **INTERACTION**: "...includes communication or interpersonal contact between investigator and subject."
5. **PRIVATE INFORMATION**: "...includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical or school record)."
6. **ENGAGEMENT IN RESEARCH**
   An institution is considered engaged in human research when employees or agents for the purposes of the nonexempt research project, obtains: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research. An institution is also considered engaged when the institution receives a direct federal award to conduct human subject research, even when all activities involving human subjects are carried out by a subcontractor.
   Researchers may utilize the Engagement Determination checklist located on our website to assist with this determination. It is not a requirement that this determination be made by the IRB, however we can review and acknowledge the determination upon request. See Appendix J.

See **Appendix K** for a list of various types of research.
4.A.1. Is the activity RESEARCH?

**ASSESSING WHETHER YOUR PROJECT IS "RESEARCH" REGULATED BY THE IRB**

For Assessing Projects Such As Program Evaluation, Quality Improvement, Quality Assurance, or Public Health Practice

**Is this a Quality Activities (Quality Assurance/Quality Improvement) or Program Evaluation Project?**
- Purpose to assess a process, program, or system, the intent to make the same process, program or system (e.g., cost-effectiveness, efficiency, etc.).

**Is this a Public Health Project?**
- Analysis or collection of data for a public health project, may or may not include activities that could be considered as "research." (See Note 1)

**Other Projects?**
- Use this chart to determine if your project is "research."

**Does this activity meet the definition of "research"?**
- To make an accurate determination, answer the question below.
- If you respond "YES" to any question, it is most likely research.
- If you respond "NO" to all questions, it is most likely not research.

1. Is the activity intended to generate new knowledge that will contribute to the scientific literature (i.e., that revises or improves upon an existing principle, theory, or knowledge)?

2. Are any of the project activities experimental, i.e., is there any testing of new or unproven treatments or strategies that are not yet known to be efficacious?

3. Are the participants in the activity randomized to an intervention so that the results of the activity can be generalized to a larger population?

4. Does the activity involve additional risks imposed on participants in order to make the results generalizable beyond the participants themselves?

5. Is there an intent to publish or present the results of a human subject research question to the scientific community?

6. Is there an evaluation/assessment part of your project that is designed to develop or contribute to generalizable knowledge (will info be shared beyond those involved in overseeing the program/process/system)?

**Your project may not involve human subjects**

- See "Assessing Whether There Are Human Subjects" Research Form and submit to IRB for official determination.

**Does this research activity involve human subjects?**
- Interaction with human subjects and/or personally identifiable private info about human subjects. (See Note 2)

**Submit Project to IRB As Research Involving Human Subjects**
- Submit applicable materials to IRB for appropriate level of review.
- See website for more info: [http://www.nihsf.edu](http://www.nihsf.edu)

**NOTES:**

**NOTE 1:** Examples: SAMHSA projects for which you are collecting required performance measures to monitor the effectiveness of the program projects where the primary intent is to identify and control a health problem; or projects where the primary intent is to directly benefit a population or group of individuals.

**NOTE 2:** Analysis of data that are not individually identifiable (i.e., permanently stripped of all patient identifiers) that do not involve human subjects or data that meet the definition of "Public Health Project" may not involve human subjects. (See Note 3)

**NOTE 3:** Intent to publish is an insufficient criterion alone for determining if a project is research. There are other purposes for publishing descriptions of non-research activities. For example, quality improvement projects are often disseminated outside the institution for the purpose of sharing the process (the QC methodology) not the healthcare outcomes or implications. This would not be considered research.
Examples of when an activity may be determined to not be “research”.

Activities conducted solely for the intent of maintaining or improving quality of services provided by an institution (UVM, UVM Medical Center, etc.) are not considered research activities.

Quality improvement project outcomes are often disseminated outside the institution for the purpose of sharing the process (the QA/QI methodology) not the health care outcomes or implications. This would not be considered research.

Case Studies – The IRB has defined a case study as a retrospective analysis of one, two or three clinical cases. Publishing retrospective case studies does not constitute research, and therefore, does not require prior IRB review and approval. However, investigators need to keep in mind that if there are any individual identifiers associated with the protected health information to which HIPAA applies, patients may need to provide authorization for use of their data. In these cases you should seek advice from the UVM Medical Center privacy officer on how to proceed.

Program Evaluation done for internal use only.

An interview for a newspaper article.

Oral history activities, such as open ended interviews, that ONLY document a specific historical event or the experiences of individuals without an intent to draw conclusions or generalize findings would NOT constitute "research" and would not require IRB review.

- Example: An oral history video recording of interviews with World Trade Center (WTC) survivors is created for viewing in a museum. The creation of the videotape does NOT intend to draw conclusions, inform policy, or generalize findings. The sole purpose is to create a historical record of specific personal events and experiences related to the attack on the WTC and provide a venue for WTC survivors to tell their stories.

If your proposed activity meets the criteria for RESEARCH, you need to ascertain if the research involves HUMAN SUBJECTS. Proceed to 4.A.2. which presents another flow to assist you in making that determination.
4.A.2. Assessing whether there are “HUMAN SUBJECTS” in research.

B. Grant Proposals Lacking Definite Plans for Involvement of Human Subjects

Certain types of applications may involve human subjects (within the funding period) but definite plans are not included in the application or protocol. This type of application would include such activities as institutional grants, training grants, and projects in which human subjects’ involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. The IRB must certify
that all human subjects research contained within a grant application has been reviewed and approved prior to release of funds, even if the plans for human subject involvement is unknown. Therefore, investigators should submit the “Initial Review of an Administrative Tool or Projects to be Developed” form. This will allow the IRB to certify what is in the grant with the caveat that not all activities specific to human subject involvement have been reviewed. This will allow the release of grant funds so that work may begin.

However, no research involving human subjects may commence until the human subjects activities have been reviewed and approved by the Committee.

5. TRAINING REQUIREMENTS

<table>
<thead>
<tr>
<th>POLICY: PROTECTION OF HUMAN SUBJECTS IN RESEARCH TRAINING POLICY AND GUIDELINES 07/14/11</th>
</tr>
</thead>
<tbody>
<tr>
<td>The University of Vermont and UVM Medical Center have pledged a commitment to the protection of all human subjects in research and have a long-standing history in extending protections required by federal funding to all research activities. In keeping with this commitment, completion of the UVM and UVM Medical Center approved human subjects training is required for all individuals involved in the conduct of research involving human subjects, regardless of funding source. The Committee on Human Research (also known as the IRB) will not release the approvals for new and continuing protocols until all individuals involved with human subjects on the project (i.e., direct contact with subjects or access to data) have completed their training.</td>
</tr>
<tr>
<td>For a description of the continuing education program, see our required human subjects training guidelines and FAQs (<a href="http://www.uvm.edu/~irb/?Page=training_faqs.html">http://www.uvm.edu/~irb/?Page=training_faqs.html</a>).</td>
</tr>
<tr>
<td>What happens if my training expires? If a PI’s training expires, this will result in the withdrawal of protocol approval. Protocol related research activities must stop until training is complete and protocol approval is re-instituted. If the study is a treatment trial and withholding the treatment is not in the best interest of the subjects, the PI must contact the Research Protections Office immediately to determine the appropriate action.</td>
</tr>
<tr>
<td>If a Faculty Sponsor’s training expires, the PI must find an alternate Faculty Sponsor until the training is complete. The individual has 30 days to find an alternate sponsor or his/her approval will be withdrawn as well.</td>
</tr>
</tbody>
</table>

6. NON-FACULTY RESEARCHERS WHO CONDUCT HUMAN SUBJECT RESEARCH

<table>
<thead>
<tr>
<th>POLICY: Requirements for the Oversight of Non-Faculty Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>A non-faculty researcher includes, but is not limited to, any of the following: fellow, resident, post-doctoral fellow, post-doctoral associate, post-doctoral trainee, and any student (graduate or undergraduate). Non-faculty researchers cannot conduct human subject research without having a faculty sponsor or faculty course instructor who is responsible for overseeing the conduct of the research activities. The faculty sponsor must be employed by the institution (UVM or UVM Medical Center) and these duties must fall within their role.</td>
</tr>
<tr>
<td>The applicable definition of research is any systematic investigation, including research development (pilot testing); designed to develop or contribute to generalizable knowledge. A human subject is a living individual about whom a researcher conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information.</td>
</tr>
</tbody>
</table>
### Role of the Faculty Sponsor or Course Instructor

Non-faculty often are not fully aware of University policy or experienced in preparing research protocols for submission to the Committee. This lack of experience can lead to multiple protocol revisions, significant delays in the review and approval process, and a shift in the mentoring role to the IRB staff. Therefore, all non-faculty researchers must have a faculty sponsor or course instructor.

**Policy Statement:** The faculty sponsor or course instructor will assume the role of the responsible investigator on all research involving human subjects which is designed and carried out by non-faculty. The responsible investigator will advise the non-faculty researcher throughout the process of protocol development, submission, and review, as well as in the implementation of the research project. As the responsible investigator, the faculty sponsor or course instructor is required to complete the UVM and UVM Medical Center approved human subjects training. Protocol approvals will not be released until that requirement has been met.

The faculty sponsor or course instructor, as the responsible investigator, will guide the non-faculty researcher in the development of the protocol, thus assuring that the content, quality, and timing of the submission meet the requirements of the Committee.

Furthermore, the faculty sponsor or course instructor as the responsible investigator is accountable for ensuring that non-faculty researchers are aware of their responsibilities as investigators, and for ensuring that the Committee is immediately notified in the event of research-related, unanticipated events or findings during the study that would affect the risks or benefits of participation.

### Role of the Non-Faculty Researcher

Non-faculty researchers have responsibilities as listed in Section 10 under “Investigator Responsibilities.”

---

### 6.A. Use of Human Subjects by UVM Students

**POLICY: Use of Human Subjects by UVM Students**  
- 7/14/04 (Revised 04/15/15)

Research projects involving human subjects in an institutional setting (i.e., educational projects, independent student research, research practica, course-assigned research) must be submitted to the Committees on Human Research regardless of whether or not the project meets the strict federal definition of “research.” See section 4 for federal definition of research.

Both graduate and undergraduate students at UVM conduct research with human subjects. The purpose of this policy is to clarify how student research is reviewed by the Committee.

The Committee strongly recommends that undergraduate research fall into the “exempt” category. See section 7.C for the exemption categories.

**6.A.2. Responsibility of Course Instructors When Class Projects are Exempt**

[See section 7.C.]

When course-assigned projects fall within an EXEMPT category under the "Federal Policy for the Protection of Human Subjects", the course instructor bears the responsibility for determining that projects are exempt and certifies this process with the Committee using the Instructor’s Assurance form. Again, course instructors are required to complete the UVM and UVM Medical Center approved human subjects training.

The Instructor Assurance form covers one course. As long as the research assignment remains the same, and the course and instructor do not change, the Instructor Assurance form is valid for one year. Annual updates of course content and continued determination of exemption is required each year. **All requests for review or certification of exemption must be received by the IRB at least one month before the students will begin their projects.**
6.A.3. Individual Research Projects, that are Exempt

See section 7.C.

6.A.4. Individual Research Projects, Directed or Independent that are Not Exempt

See section 7.C.

Any research projects to be conducted by students (graduate or undergraduate), that are not exempt, and that involve human subjects, must be submitted to the Committee for review and approval. This includes, but is not limited to, independent undergraduate research projects and honor's theses, master's theses, and dissertations. It is possible that a research project may be exempt from ongoing Committee review, but it must meet explicit criteria and must be submitted to the IRB for certification of the exemption.

Students are required to have a faculty sponsor (this will most often be the course instructor) who is responsible for oversight of the student's research activity. The faculty sponsor is required to complete the UVM and UVM Medical Center approved human subjects training. The faculty sponsor must make it clear to students that their project cannot begin until they have been approved by the Committee.

Examples of Research that would require Full Committee Review – Requires IRB Submission

Any research involving the following populations and procedures most likely will require a full committee review. The Committee on Human Research in the Behavioral and Social Sciences strongly discourages research in these categories by undergraduates.

1. Vulnerable populations:
   - Children (persons under 18 yrs)
   - Mentally disabled/incompetent
   - Pregnant Women
   - Prisoners
2. Physically invasive procedures - Drugs, devices, x-rays, strenuous exercise, etc.
3. Psychologically or emotionally distressing situations
4. Manipulation of behavior - Deception, hypnosis, etc.
5. Collection of sensitive data - Criminal behavior, illicit drug or alcohol abuse, sexual habits (where identifiers are attached).

Examples of Expeditable Research - Requires IRB submission

1. Voice or image recordings or photographs of individuals made for research purposes, such as investigations of speech defects.
2. Research on individual or group behavior or characteristics of individuals, such as studies of perception, cognition, game theory, or test development, where the investigator does not modify subject's behavior and the research will not involve stress to subjects.
3. The study of existing documents, data, records or diagnostic specimens which are not publicly available and which will be identifiable.
4. Recording of data from subjects 18 years of age or older using noninvasive procedures routinely employed in clinical practice. This includes the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject or act as an invasion of the subject's privacy. This category also includes such procedures as weighing, testing sensory acuity, EKG, EEG, thermography. Exposure to electromagnetic radiation outside the visible range (e.g. x-rays, microwaves) requires FULL REVIEW.

6.A.5. Responsibility of Course Instructors/Faculty Sponsors When Class Projects are Not Exempt

When student research activities fall into either of the two categories above, the Course Instructor or Faculty Sponsor have all of the responsibilities listed in Section 10 under “Investigator Responsibilities.”

Additional mentoring responsibilities:
1. reviewing the materials for submission to the Committee on Human Research for accuracy and
completeness;
2. assisting and supporting the student in his/her interaction with the Committee on Human Research and for overseeing the resolution of any issues arising during the review process; and
3. oversight of the student’s research to ensure that human subjects are protected, e.g., the protocol is followed as approved, any unanticipated events are reported as required, etc.
4. verifying that prior approval of Thesis or Dissertation Committee, if applicable, has been obtained.


Student researchers have responsibilities as listed in Section 10 under “Investigator Responsibilities.”

Typically student projects are short in duration and in many cases are completed in less than a year. It is important that the IRB be notified when the project is completed so that the IRB file may be closed.

7. TYPES OF COMMITTEE REVIEWS

See Attachment C for the IRB policy on fees.

7.A. “Full” Committee Review

The full Committee review process is used for all protocols that present more than minimal risk, do not fall within the expedited review categories, (section 7.B below), or are determined to require additional review secondary to inclusion of a vulnerable subject population.

One or more Committee member(s) are assigned to review the complete protocol or amendment, consent form, Investigational Drug/Device Brochure and any other protocol materials. The reviewer(s) summarize the protocol or amendment for the full Committee at a convened meeting and answer questions during the discussion. All other Committee members are provided summary information and the protocol consent form. Members may review any documentation related to the study.

Note about review of MRI/fMRI procedures: UVM has determined MRI procedures to be greater than minimal risk whenever the device is employed for research purposes if intravenous contrast, sedation, or drugs are also being used, since the probability and magnitude of harm or discomfort anticipated in the research are greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests [45 CFR 46.102(i)]. These protocols would require full review.

For studies involving normal, healthy subjects in which sedation, drugs, or contrast are not used, or studies involving subjects with a disease/condition when the MRI/fMRI does not pose any additional risk, the study may be deemed to present no greater than minimal risk, as the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. These protocols can undergo an expedited review.

7.B. “Expedited” Review

Protocols, amendments, or continuing reviews that meet specific criteria outlined below qualify for an expedited review. The complete protocol, consent form, and any other protocol materials receive review and approval by the Chairperson or one or more designated Committee members.
POLICY: Categories of Research that may be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure

Applicability

(A) Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

(B) The categories in this list regardless of the age of subjects, except as noted.

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

(D) The expedited review procedure may not be used for classified (military) research involving human subjects.

(E) The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review -- expedited or convened -- utilized by the IRB.

(F) Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

Research Categories

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
   a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (NOTE: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review).
   b. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
   a. From healthy, non-pregnant adults who weight at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
   b. From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, and the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

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

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications). Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involved input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have collected or will be collected, solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101 (b)(4) This listing refers only to research that is not exempt.) Note: A project may not constitute “human subjects research” if the investigators/collaborators will not have access to the identities of the subjects. See guidance on Research Involving Coded Private Information or Biological Specimens, Attachment G.

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

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

8. Continuing review of research previously approved by the convened IRB as follows: (a) where (i) the research is permanently closed to the enrollment of new subjects, (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or (b) where no subjects have been enrolled and no additional risks have been identified; or (c) where the remaining research activities are limited to data analysis.

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

7.C. “Exempt” Research Review

According to federal regulations, Committee review is not required for certain categories of research activities that involve little or no risk to human subjects. However, the University and UVM Medical Center have an obligation to be apprised of all human subjects’ research being conducted under their auspices in the event any questions or problems arise and in order to assure that, regardless of risk, all research subjects are afforded the same protection.

Research involving surveys or interview procedures in children is not exempt from a Committee review. HHS believes that children being surveyed or interviewed by an investigator may not be capable of recognizing that their responses to questions on sensitive issues could be potentially damaging to themselves or others. For this reason, the
IRB is required to at least review such research to determine whether the rights and welfare of the children participating as subjects are adequately protected.

In most exempt projectsthe participant’s signature on a consent form is not necessary. Consent may be obtained verbally or may be implied by the completion of the research requirement. It is suggested that an Information Sheet be developed for the potential participant’s reference. If you are planning on using an Information Sheet, the Committee must review it.

Research which is determined to be exempt from Committee review must comply with all University of Vermont policies and procedures, as well as with applicable federal, state and local laws regarding the protection of human subjects in research.

Note, that any revisions to the research affecting human subjects may affect the original determination of exemption and therefore must be prospectively submitted for review and subsequent determination of exemption.

<table>
<thead>
<tr>
<th>POLICY: Categories of Exempt Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Updated 04/15/15</td>
</tr>
</tbody>
</table>

Research activities in which the only involvement of human subjects will be in one or more of the categories listed below may be considered "exempt". Please note, however, that although the research is exempt from formal review, it is not necessarily exempt from informed consent requirements.

The Department of Health and Human Services has identified categories of research qualifying for exemption from certain federal regulations applicable to research involving human subjects. The IRB makes federal exemption determinations according to 45 CFR 46.101.

One additional non-federal exemption category may be applied to non-federally supported or otherwise non-federally regulated studies. Exemption category #7 is based upon commonly accepted, minimal risk research practice originally defined in 45 CRF 46.110 receiving expedited IRB review procedure.

Exemption #1: Normal Educational Practices and Settings
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.

Exemption #2*: Educational Tests, Surveys, Interviews, or Observations
Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observations 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, or deals with sensitive aspects of the subject's own behavior, such as illegal conduct, drug abuse, sexual behavior or the use of alcohol.

*Note: The exemption at 45 CFR 46.101(b)(2), for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, subpart D, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

Exemption #3: Identifiable Subjects in Special Circumstances
Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observations of public behavior that is not exempt under exemption #2, 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.

**Exemption #4: Collection or Study of Existing Data**

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 the subjects cannot be identified, directly or through identifiers linked to the subjects. **Note:** This may not constitute “human subjects research” if the investigators/collaborators will not have access to the identities of the subjects. See guidance on Research Involving Coded Private Information or Biological Specimens, Attachment G.

**Exemption #5: Public Benefit or Service Programs**

Research and demonstration projects which are conducted by or subject to the approval of the [Federal] 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.

**Exemption #6: Taste and Food Evaluation and Acceptance Studies**

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 and Safety and Inspection Service of the U.S. Department of Agriculture.

**Non-Federal Exemption #7**: Research involving collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, where this information is personally identifiable or coded. **Note:** Prisoner research, research that is federally funded, and data that includes Protected Health Information (PHI) do not meet the criteria for this exemption.

### 7.D. “Research Not Involving Human Subjects” Review and Determination

Federal guidance states that there is a distinction between (a) research involving coded private information or specimens that does not involve human subjects and (b) human subject research that is exempt from the requirements of the Department of Health and Human Service (DHHS) regulations.

When conducting research using data or specimens, the human subject determination noted above, the type of application, the informed consent requirements, and the level of review by the IRB depends primarily on one factor: whether the data or specimens can be linked to an individual person by the principal investigator or key personnel. Please refer to Section 4.A.2. regarding whether an activity involves human subjects.

Determinations of whether research involving coded private information or biological specimens is considered to be “human subjects research” must be made by the IRB. The investigator should submit a Research Not Involving Human Subjects Review and Determination form, located on the website.

### 7.E. Projects Where the Only Procedure Involves Chart Review

Chart refers to medical records, electronic or paper, pathological specimens or
diagnostic specimens, or any other type of existing record (e.g. educational record, criminal records, etc.)

- **A retrospective chart review** evaluates data that is existing at the time the project is submitted to the IRB for initial review.
- **A prospective chart review** will evaluate data that does not yet exist at the time the project is submitted to the IRB for initial review.

**Categories of IRB Review**

- **Exemption Category 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.
  - All data/material must be in existence at the time of IRB submission.
  - No identifiers or links can be recorded. Your study will not qualify for exemption if you intend on recording any of the following identifiers:

| 1. Names | 10. Certificate/license numbers |
| 2. All geographic subdivisions smaller than a state* | 11. Vehicle identifiers and serial numbers, including license plate numbers |
| 3. Telephone numbers | 12. Device identifiers and serial numbers |
| 4. Fax numbers | 13. Web Universal Resource Locators (URLs) |
| 5. Electronic mail addresses | 14. Internet Protocol (IP) address numbers |
| 6. Social Security numbers | 15. Biometric identifiers, including finger and voice prints |
| 7. Medical record numbers | 16. Full face photographic images and any comparable images |
| 8. Health plan beneficiary numbers | 17. All elements of dates (except year)** |
| 9. Account numbers | 18. Any other unique identifying number, characteristic or code |

*including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code, if according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.

**for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.

If this study involves chart review of Prisoners it must be submitted for a full board review.

**Exemption Category 4 Addressing Informed Consent and HIPAA Authorization**

- **Waiver of Consent is applicable**
- **HIPAA is not applicable if there is no protected health information (PHI)**
  - When PHI is included, de-identified PHI is exempt from HIPAA requirements as long as a certification of de-identification is in place. Certification means that even though researchers are seeing identifying information during chart review data extraction, the researchers will NOT record any identifying information. The only methods by which data may be classified as de-identified are
- by certifying that none of the 18 HIPAA-defined identifiers are used, reviewed, or recorded by the research staff
- by certifying that as a member of our covered entity the individual using PHI to create a de-identified data set
  - keeps all information seen in the process of creating the de-identified data strictly confidential
  - does not record any of the identifiers defined by HIPAA
  - cannot link the data back to the individual in any way, or
- by certifying through statistical analysis on each identifier that is contained within the data that the likelihood of an individual being identified by using the data in whole or part is very small. Statistical de-identification must be done by a qualified statistician and the methods and results of the analysis must be documented.

When protected health information is being accessed, researchers will be required to complete the Certification of De-Identification section of the exemption form. This area must be signed by the PI and all person(s) who will be extracting data from charts.

- **Expedited Category 5:** Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected, solely for non-research purposes (such as medical treatment or diagnosis).
  - Allows for the prospective collection of data that is later reviewed for research purposes.
  - Identifiers and/or links can be recorded if necessary.

If this study involves chart review of Prisoners it must be submitted for a full board review.

**Expedited Category 5 Addressing Informed Consent and HIPAA Authorization**

- Obtaining consent must be addressed, whether you are requesting a waiver of the entire consent process, obtaining written consent, or requesting a waiver of documentation of consent.
- Obtaining HIPAA must be addressed when identifiers are retained. The HIPAA-approved language must be included within the consent form.
  - Waiver or alteration of HIPAA authorization may be requested in certain circumstances. The principal investigator must submit a request for waiver of authorization to the IRB for review and approval. To approve the waiver the following elements must be satisfied:
    - The use and/disclosure of the PHI involves not more than a minimal risk to the privacy of individuals;
    - The research could not practicably be conducted without the waiver; and
    - The research could not practicably be conducted without access to and the use of the PHI.

To request a waiver or alteration of the requirement for a HIPAA authorization, complete and submit the form titled “Request for Waiver of Informed Consent/Authorization/Documentation”.

**7.F. Review of Qualitative Research**

Proposals that primarily are composed of qualitative methods, e.g., research “in the
field," phenomenological or ethnographic research proposals may not fit a traditional research design or IRB review model. Still, from the standpoint of federal regulations and professional ethical codes in the social sciences, the same principles and guidelines for protection of the rights and welfare of subjects/participants apply. The IRB has developed a specific “Qualitative Research” protocol form to assist with member review.

You must accurately determine if what you are proposing is qualitative research. **Qualitative research** is the gathering of data primarily through the methods of participant observation, observation, face-to-face interviews, or open-ended surveys or questionnaires, often for the purpose of addressing questions pertaining to social and/or cultural issues. There are several kinds of qualitative research, such as ethnography, historical, field research, phenomenological, grounded theory, and case studies. Such research may describe a social situation as a whole, or it may focus on specific problems or situations within a larger social context.

**Quantitative research** generates numerical data or information that can be converted into numbers.

**Medical research** means direct medical intervention or interaction, clinical trials for new drugs/devices, FDA regulated activities, invasive or non-invasive medical procedures for research purposes or the collection or use of private health information for research purposes in the biomedical arena.

Sometimes research protocols combine both qualitative and quantitative research methods, referred to as **mixed-method research**. If you are doing mixed methods research with equal parts qualitative and quantitative methodology, you will need to choose the submission form that best describes your research to someone outside of the study team (i.e. for IRB staff and Committee Members to review).

The IRB appreciates that qualitative research has the following special characteristics (Arwood, T., and McGough, H., 2007 PRIM&R SBER Conference):

- It is experiential
- It is interactive
- It is not easily bounded by time and place
- It is often exploratory
- It morphs easily and often (new questions emerge during research)
- The boundaries between normal activities and communication and data collection are blurred

In order for the IRB to understand these special characteristics and the nature and scope of a particular qualitative research project, the following issues should be addressed in the Qualitative Research Protocol, if applicable.

**Participant Population**

- The kinds of people who will be involved in the research should be described. If there are different groups or categories of people, the groups and the approximate number of participants in each group anticipated to be enrolled must be described. If potentially vulnerable populations are included, any additional protections should be explained. If an exact number of people to be enrolled are unknown, a range should be provided. An amendment should be submitted to the IRB when/if actual numbers exceed those estimates.

**Description of Procedures**
• The length of time to be spent at the field site(s) should be described. If unsure, an approximate length of time should be provided (e.g., one year, two summer months, etc.). Also the approximate length of time of the interaction with subjects (i.e., 2 hour interviews, day-long observation) and the number of anticipated interactions (i.e., 3 interviews over a 4 month period) should be provided. An amendment should be submitted to the IRB when/if actual dates exceed those estimates.

• The research techniques that will be used to conduct the research (such as participant observation, interviews, focus groups, use of public, private governmental or other records, administration of test, etc.) should be described. The topics or research domains to be covered as well as what will be observed (such as individual behaviors, community rituals, societal norms, etc.) should be described. This will help the IRB get a sense of what will be learned from and about the participants in the research.

• Explain how the maximum number of participants is determined or what criteria will be used to determine when data collection is completed.

Research Site(s) or Location(s):

• Explain where the research will be conducted and explain why this particular research setting was chosen.

• Has the researcher conducted research at this site or with the population previously? If so, briefly describe the topics and duration of your previous research.

• Is local governmental or community permission to conduct research required at any of the sites? If so, explain how you will obtain this permission. If there is formal documentation of this permission, attach it to the application form or indicate when it will be received and forward to the IRB.

• Will you work with local collaborators (interviewers, interpreters, translators, guides, etc.)? If so, please explain who these collaborators are and how they will be involved in the research. Will they need to obtain local ethics committee approval for their role in the study?

• Many countries have the expectation that foreign scholars will collaborate with local scholars and institutions. Explain whether this applies to your research and if local IRB or other type of ethical review board approval will be obtained.

Risks and Inconveniences

Risk of harm in qualitative research is usually limited to what may result from invasion of privacy, stigmatization, or breach of confidentiality. Harm may happen to individuals and to the groups or communities to which they belong.

• Identify the risks of harm that may result from this research.

• Describe the steps you will take to minimize the risks of harm. If harm occurs, what plans do you have to manage it?

• If there are different risks of harm for different groups of participants, please identify the risks for each group. Sometimes this cannot be known in advance of entering the field. If unanticipated problems occur, research has begun, the incidents must be reported to the IRB. When appropriate, the study can be modified to address any issues that arise.

Benefits

• Is it possible that individuals who take part in your research can reliably expect a direct benefit from taking part? If yes, describe.
- Describe the anticipated benefits of this research for the community you will study, for your profession, or for society in general.

Confidentiality

- Describe how you will find out how people in this setting feel about the fact that you will write articles about them. Will you consult with the people from whom you collected data before you publish?
- Are any portions of the research material you may collect not publicly available and expected by community standards to be private? If yes, describe the materials that are private and explain (1) how you will store the private information or materials while you are in the field so that the confidentiality of the data is protected; (2) explain how you will store the private information or materials after you leave the field so that confidentiality is protected; (3) explain whether you will retain information that could lead to identification of the research site and explain any negative consequences this could have; (4) explain if you will record any direct participant identifiers (such as names or contact information) that could be linked to the private research material.
- If you will record identifiers (# 4 above) explain why and describe how you will protect against disclosure of this information or explain why this is not necessary. If you will retain the identifiers linked to the data, explain (1) how long the identifiers will be kept, (2) how confidentiality will be maintained during this period, (3) who will have access to data (such as sponsors, advisors, government agencies, etc.). In each case, explain whether they will have access to study data with identifiers or only to coded data with no access to the identifying study code. If identifiers will be maintained indefinitely, explain why. For example, do you intend to re-contact participants or communicate with them over a long period of time, or is the data identifiable by its nature (recordings, genealogies, etc.). Explain how you will protect the data from a breach of confidentiality or why this is not necessary.
- If you will retain data that may place participants at risk for criminal or civil liability or be damaging to their financial standing, employability or reputation, please explain. It may be advisable to obtain a federal Certificate of Confidentiality.
- The IRB acknowledges that sometimes it is not possible or desirable to maintain anonymity. For example, when a researcher works with a small group of people only found in a particular region with whom others have worked. In order to advance ethnographic knowledge about the group, their identity must be made known.

Sometimes individuals or whole communities do not want to remain anonymous. If this is the case, explain how you learned of this and describe why. If there are differences in the community about this, describe how this will be handled.

Consent Procedures/Process

- Explain how you will introduce yourself as a researcher to potential participants. If you already know them, please explain the circumstances.
- How will you inform people about your research and obtain their consent to participate? If you plan to use an oral consent process and to work informed consent procedures into your introduction to a group, or the beginning of an interview, please provide a general script or a list of points you will cover.
- Describe how people in this setting let you know if they don’t want to talk with you.
- Identify who is responsible for giving consent in the research setting (for instance, if a tribal council or community leader provides consent for the entire
group). Sometimes the consent process can be multi-layered in community settings. Be sure to describe what the full process is in the setting in which the research will take place.

- Describe how you will handle situations in which group consent is provided, but individuals to not want to participate and vice versa.

7.G. Coordination with Other Compliance Committees/Divisions

7.G.1. The University of Vermont Cancer Center Protocol Review and Management Committee (PRMC)
Any initial review or change to protocols regarding the study of cancer, require prior review by the PRC. Review by the PRC is independent of the review by the Institutional Review Board (IRB). PRC and IRB, however do share their Committee review correspondence and outcomes with each other. While submissions may be made to both Committees at the same time, the PRC must approve the protocol or approve with clarifications (that do not require a subsequent full committee review) prior to the IRB review. This is to make certain the PRC clarifications and responses can be taken into consideration during the IRB review. This is required for all initial submissions and amendments.

7.G.2. Scientific Advisory Committee (SAC)
Any protocols wishing to utilize resources of the Clinical Research Center require review by the SAC. Review by the SAC is independent of the review by the Institutional Review Board (IRB). However, the findings from the IRB review are communicated to the SAC. Submissions may be made to both Committees at the same time, however SAC will not approve until the IRB has approved the project.

7.G.3. Office of Biotechnology Activities/Recombinant DNA Advisory Committee
Novel Human Gene Therapy experiments are required to undergo extensive review and final approval through the Office of Biotechnology Activities/Recombinant DNA Advisory Committee (OBA/RAC) which is a government entity. The IRB requires documentation of the OBA/RAC approval prior to IRB protocol review.

7.G.4. Institutional Biosafety Committee (IBC)
Any protocols that involve the use of gene therapy require review by the IBC. Approval to begin activities will not be released until IBC approval is obtained. Submissions may be made to both Committees simultaneously but human subject activities must not begin until both Committees have approved the protocol.

7.G.5. Radiation Safety Office (RSO)
The RSO at UVM oversees the use of ionizing radiation sources on campus and ensures compliance with state and federal regulations, to protect UVM employees, students, the public, and the environment. The RSO also provides safety related services for UVM. Any protocols involving the application of radioactive materials, radioisotopes, and/or radiation treatment to humans for nonclinical purposes must undergo review by the UVM Radiation Safety Office if the research procedures are taking place at UVM. If the research procedures are taking place in UVM Medical Center, you should contact the UVM Medical Center Radiation Safety Committee.
7.G6. **Sponsored Project Administration (SPA)**
SPA requires documentation of protocol approvals prior to release of funds for sponsored projects. IRB staff share protocol statuses with SPA for this purpose.

7.G7. **Office for Clinical Trials Research (OCTR)**
OCTR assists with the majority of the industry-funded protocols by developing contracts, invoicing and collecting IRB fees for the investigators. Protocol information is shared for these purposes.

7.G8. **UVM Medical Center Compliance Office**
The 2010 Affiliation Agreement between the University of Vermont (UVM) and UVM Medical Center requires approval of a billing plan by UVM Medical Center Compliance for all protocols utilizing UVM Medical Center resources regardless of whether they are UVM or UVM Medical Center studies. The IRB assists UVM Medical Center Compliance in identifying protocols that require a billing plan and will release final protocol approvals to UVM Medical Center Compliance if the billing plan is the only outstanding item.

8. Requirements and Submission Materials for Initial Review

8.A. **Protocol**

A complete protocol is required for Committee review. Researchers who are participating in a multi-center protocol may submit the lead investigator/sponsor’s protocol. The Committee requires that the “Human Research Protocol” form be utilized any time a local researcher is writing his/her own protocol, or when a grant is being submitted for review. This form includes all of the elements as listed below in a format that is easy to complete and easy for Committee members to review. The form can be found on our forms page.

The “Qualitative Research Protocol Form” should be used instead of the “Human Research Protocol” form when submitting qualitative research or primarily qualitative research and when medical procedures are not included in your research.

8.A.1. **Elements**

The following elements, when applicable, should be included in your protocol. The Committee may request that additional sections be added to a protocol to address additional protections for certain categories of human subjects when applicable.

8.A.1.a. **Title Page.** A title page should include the title of the project, number of project if applicable, and the Principal Investigator’s address, e-mail, and phone numbers. Include any of the following names and contact information if applicable: sub-investigators, statistician and research coordinator. (not a required element)

8.A.1.b. **Table of Contents** (not a required element)

8.A.1.c. **Introduction.** The importance of the research and the potential knowledge to be gained should be explained in detail. Give background information, including references to prior human or animal research and references that are relevant to the design and conduct of the study.

8.A.1.d. **Objectives.** Clearly state the primary objective(s) of the study.
8.A.1.e. **Study Design.** Describe the research design and the procedures to be used to accomplish the specific aims of the project. Include how the data will be collected, analyzed, and interpreted as well as the data sharing plan as appropriate. Describe any new methodology and its advantage over existing methodologies. Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the objectives. As part of this section, provide a tentative sequence or timetable for the project. Point out any procedures, situations, or materials that may be hazardous to personnel and the precautions to be exercised.

8.A.1.f. **Inclusion/Exclusion Criteria:** Eligibility and ineligibility criteria should be specific. Changes to the eligibility criteria at a later phase of the research have the potential to invalidate the research.

8.A.1.g. **Methods.** Describe the types, frequency and duration of tests, study visits, interviews, questionnaires, etc. Include required screening procedures performed before enrollment and while on study.

8.A.1.h. **Withdrawal Procedures.** Define the precise criteria for withdrawing subjects from the study. Also include a description of study requirements for when a subject withdraws him or herself from the study (if applicable).

8.A.1.i. **Statistical Considerations.** Delineate the precise outcomes to be measured and analyzed. Describe how these results will be measured and statistically analyzed. Delineate methods used to estimate the required number of subjects. Describe power calculations if the study involves comparisons. Perform this analysis on each of the primary and secondary endpoints, if possible.

8.A.1.j. **Human Subject Protections.**

8.A.1.j.1. **Subject Selection:** Provide rationale for subject selection in terms of the scientific objectives and proposed study design.

Include as appropriate:

**Inclusion of Minorities and Women:** Describe efforts to include minorities and women. If either minorities or women are excluded, include a justification for the exclusion.

For protocols including the use of an investigational drug, indicate whether women of childbearing potential have been included and, if not, include appropriate justification.

If HIV testing is included specifically for research purposes explain how the test results will be protected against unauthorized disclosure. Include if the subjects are to be informed of the test results. If yes, include the process and provision for counseling. If no, a rationale for not informing the subjects should be included.

**Special Populations:** Explain the rationale for involvement of special classes of subjects, if any. Discuss what procedures or practices will be used in the protocol to minimize their susceptibility to undue influences and unnecessary risk (physical, psychological, etc.). See Section 11.
Inclusion of Children: Describe efforts to include children. Inclusion is required unless a clear and compelling rationale shows that inclusion is inappropriate with respect to the health of the subjects or that inclusion is inappropriate for the purpose of the study. If children are included, the description of the plan should include a rationale for selecting or excluding a specific age range of children. When included, the plan must also describe the expertise of the investigative team in working with children, the appropriateness of the available facilities to accommodate children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study. If children are excluded then provide appropriate justification. Provide target accrual for this population. See Section 11D.

8.A.1.j.2. Plans for Recruitment/Retention

All methods for subject recruitment need to be reviewed by the IRB. This review ensures equitable selection, that the plans and information accurately portray the protocol, and that the method is free from coercion.

Common methods of human subject recruitment follow:

PI/Collaborators recruit own subjects
Any UVM Medical Center health care provider or his/her immediate practice group who has a direct treatment relationship with the patient may recruit for an IRB-approved protocol.

PI sends letter to colleagues asking for referrals of eligible patients who are interested in the research study
The referral letter and process needs IRB approval prior to use. This recruitment strategy depends on the potentially interested subject to contact the researcher. The researcher cannot contact the potentially eligible subject(s) directly, since a treating relationship does not exist.

PI sends letter to colleagues asking these physicians to send out the “Dear Patient” letter describing the research study
The “Dear Patient” letter and process needs IRB approval prior to use. The interested subject must contact the researcher. The researcher cannot have access to the patient names or addresses for mailing purposes.

Review of patient medical record to determine eligibility
Researchers who have a treating relationship may have access to their patient files to determine eligibility without prior IRB approval. When the researcher does not have a treatment relationship with the subject, prior IRB review and approval of the planned recruitment procedures is necessary. Researchers wishing to access protected health information for the purpose of establishing suitability for subject inclusion may wish to request a partial waiver of the HIPAA authorization requirement. This partial waiver allows access to the information that is needed for the recruitment, but does not allow the researcher to take the information from the medical record. Complete “Request for Partial Waiver of Authorization for Recruitment Purposes” form if you wish to waive authorization to review information.
Further IRB review and approval would be necessary to allow removal of information or to further contact potential patients. Please refer to Section 8.B. for additional HIPAA information.

Advertisements or Media

All recruitment materials including recruitment letters, posters, newspaper ads, radio spots, TV commercials or public service announcements are to be forwarded to the IRB for review and approval prior to use. Generally, advertisements used to recruit research subjects should be limited to information that a potential subject would need to determine if they are eligible and interested in participating. More specifically, the ads should include information such as:

a. Name and address of the research facility;
b. The condition or disease that will be the focus of the research;
c. A clear statement that the study is research; (required)
d. Summary of criteria for eligibility to participate;
e. Time and commitments that will be required of the subject;
f. Location of the study and the contact for information.

The ads should not:

a. Contain explicit or implicit claims of safety and efficacy or equivalency or superiority to other approved treatments;
b. Emphasize the amount of reimbursement that subjects will receive. The ads may state that reimbursement may be provided;
   For example, posters in which the compensation amounts are too large or are too prominently presented (i.e. bold typeface or large fonts) will not be approved;
c. Promise a favorable outcome or benefit.

Recruitment materials should be placed in areas which allow for equitable recruitment of subjects. You need to indicate where the material will be placed.

For example, if a researcher advertises in the classified section of the newspaper, the personal column or a “block ad” is considered most appropriate. These should never be placed in the “employment section” of any type of media, (e.g. newspaper or Craig’s list). Particular attention should be paid to emphasize the “volunteer” and “research” aspects associated with participation.

If recruitment is media-based, provide script, if available, and what stations will air it.

If there is a national campaign, provide the press release as soon as it is available and list which stations will air the release.

Recruitment mailings to subjects’ should be stamped confidential or personal. We recommend the use of window envelopes to avoid errors in mailing.

Phone recruitment scripts need to be submitted for review and approval.
Conversation with parties other than the subject you are trying to contact should not reveal the purpose of the call. Phone mail messages revealing the purpose of the call should be avoided.

It should be carefully explained to a potential subject that voluntary participation in a research project does not constitute employment.

**Direct Mail Recruitment**

Direct mail campaigns obtain subjects’ names and contact information through large marketing firms who have conducted voluntary surveys of U.S. households. The collected information and consent of the survey volunteer to receive information are placed in a database. This information is then used by direct mail vendors to alert these individuals of new offers or information pertaining to their selected responses.

Details about the mail campaign and the proposed letter and/or materials must be reviewed and approved by the Committee prior to vendor distribution. The letter and/or materials must contain local information such as PI, address, and a telephone number for the subjects to contact. There should also be mention of the how the subjects’ contact information was obtained for the mail campaign.

**Direct E-Mail Recruitment**

Use of a company or university list-serve for recruitment purposes must be approved by the institution that manages/owns that list-serve. The IRB will request proof that permission has been granted by the institution.

**Students and Employees**

Though the research may be careful to avoid potentially coercive behavior, the very nature of the relationship with the subject can create the appearance of coercion. Even subtle cues of compromise can place subjects in a position of involuntary participation in a research project. For this reason, researchers should be aware of the potential for coercion that exists when a research subject is also a student, employee, colleague, or subordinate of the researcher.

Various procedures have been suggested to reduce the possibility of unintended coercion, while still permitting their participation as subjects in research. These include:

- Posting IRB approved advertisements/posters throughout the university to recruit subjects from a broad base;
- Avoiding any personal solicitations of students by faculty, graduate assistants, or fellow students. In seeking potential subjects among employees, the best strategy is to utilize a third party unassociated with the work relationship;
- Providing a number of research projects from which to choose, if participating as a subject is a course requirement;
- Providing alternative and equal methods for meeting course credit (or extra credit) requirements, such as attending a series of research presentations by faculty, writing a brief paper, conducting one’s own research;
- Making it clear in the consent form that refusal to participate will not affect class standing, grades, status on an athletic team, or job standing.
It is IRB practice not to approve recruitment procedures that include employees from the investigator’s own lab or office, especially when the procedures are more than minimal risk. The IRB, however, may reconsider this practice on a case-by-case basis.

Investigator Self-Experimentation
Some researchers may want to participate in their own studies, a practice known as “self-experimentation.” The federal regulations are silent on this point, making no distinction between self-experimentation and participation by others. The IRB requires that such self-experimentation be fully described in a protocol that is submitted for IRB review. This policy (1) may protect researchers from unwarranted risks and (2) allows a neutral third party to raise concerns, if any, regarding credibility of resulting data.

Note: There is a difference between being a participant in the research and research development/evaluation or testing designed to validate tools for the research project. If the investigator is involved in development only, this would not be considered research and therefore a research study consent form does not apply. However, if any of the procedures involves more than minimal risk, a consent or acknowledgement of understanding should be conducted and documented within the research files.

A main concern for the IRB when reviewing a protocol that involves self-experimentation, is that the ideation of a novel concept may outweigh the investigator’s concern for his/her own welfare.

The IRB may institute additional safeguards for the research project, such as shorter review periods, monthly progress reports, or require that an IRB member obtain informed consent from the investigator.

Subject Retention
It is understood that many studies require long-term followup for disease and survival data. The protocol should account for this followup from the outset and subjects should be made aware of this requirement at the time of consent to participate.

The Committee generally discourages use of subject locator services. Contact by a service rather than the treating physician/researcher may be potentially upsetting to the subject and subjects appear to lose their right to privacy when a service, unbeknownst to them, is using different methods to locate them. Requests for use of a locator service are considered on a case-by-case basis and will only be approved if the methods are appropriate and the need for finding a subject is justified.

Any items such as money, small tokens, gift certificates, etc, which are given to the subject to retain their participation in research is considered a form of compensation and needs prior approval by the IRB.

Subject Compensation
Compensation may be in the form of money, course points, travel expenses, gift cards, etc. The compensation for participation in the
research will be reviewed on a protocol-by-protocol basis. The amount should be commensurate with what is being asked of the participants and can not be considered coercive. Compensation should not be dependent upon completion of the protocol and there should be a proration schedule. Participation cannot be required for academic course credit or course completion. Researchers should consider how compensation could impact participant’s state or federal benefits (i.e., SSI, SSDI) eligibility in their consideration of compensation type and amount.

Compensation Guidance when Minors are Involved

The level of risk to which a child is exposed is an important consideration for the IRB in determining the appropriateness of payment. The IRB shall ensure that the amount, type, and timing of payment does not unduly pressure or influence the decision making of parents or legal guardians to enroll their child in the research activity.

In pediatric research, inducements are generally tailored to the child participant. Inducements may also be made to the parents or legal guardians of children taking part in research. For example, researchers may provide a payment that represents partial compensation to parents for their time away from work for example when a research study visit requires a full day of the parent's time to accompany their child for a research visit.

Inducements to children shall be age appropriate and respectful and sensitive to children and families. Researchers providing inducements to children shall be encouraged to have several options available for children and families that allow children and families to choose an inducement that is consistent with the family’s values. The IRB encourages non-cash payments, e.g., gift cards/certificates, movie/event tickets, toys, books, as forms of payment that are respectful to children and reduce the potential for unduly influencing the child's legal representative's decision regarding participation.

Compensation from UVM Funds

Research subjects who are eligible for compensation through UVM are required to provide personal information such as name, address and social security number in order that they are paid. In addition to cash, this includes gifts, tokens and gift certificates. The social security number is only needed if a single payment is more than $100.00. If the total sum of payments within one year are expected to be greater than $600.00, the social security number is required at the time of their first visit only. See UVM’s Procurement site for additional information and detail about processing subject payments.

Compensation from UVM Medical Center

Research subjects who are eligible for reimbursement from the research study through UVM Medical Center have to provide their social security number at the first visit regardless of the amount of payment. UVM Medical Center assigns a unique ID upon the first payment visit and uses that ID going forward to reimburse subjects.

In both cases all correspondence should be sealed in an envelope and marked confidential.

Note: Principal Investigators are not allowed to use their own personal
funds to compensate participants.

8.A.1.j.3. Risks/Benefits: Describe any potential risks. This includes physical, psychological, social, legal or other risks. Describe the planned procedures for protecting against or minimizing potential risks and assess their likely effectiveness. Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Discuss the potential benefits of the research to the subjects and others. Discuss why the risks to the subjects are reasonable in relation to the anticipated benefits to subjects and others. Discuss the importance of the knowledge gained or to be gained as a result of the proposed research and why the risks are reasonable in relation to the knowledge that reasonably may result.

NOTE: If the study involves the collection, storage or analysis of genetic information, the Genetic Information Nondiscrimination Act (GINA) is invoked. GINA language must be included in the subject consent form. Language can be found in the IRB consent template located on our forms page.

8.A.1.j.4. Confidentiality: Provide a statement describing the extent to which confidentiality of materials (data and specimens) identifying the subject will be maintained and that notes the possibility that the Institutional Review Board and regulatory authorities may inspect the materials.

8.A.1.j.5. Data Safety and Monitoring: The specific design of a Data and Safety Monitoring Plan (DSMP) for a protocol may vary extensively depending on the potential risks, size, and complexity of the research study. For a minimal risk study, a DSMP could be as simple as a description of the Principal Investigator’s plan for monitoring the data and performance of safety reviews or it could be as complex as the initiation of an external, independent Data Safety and Monitoring Board (DSMB).

The data and safety monitoring plan should provide for a regular review of accrued research data and other relevant information to ensure the validity and integrity of the data and that there is no change to the anticipated benefit-to-risk ratio of study participation. In addition, there should be an ongoing review of study procedures to ensure that the privacy of research subjects and the confidentiality of research data has not been violated.

The following general principles should be considered when addressing an appropriate data and safety monitoring plan:

- Protocols with interventions require some level of monitoring;
- Monitoring should be commensurate with risks;
- Monitoring should be commensurate with the size and complexity of the study;
- Monitoring should be performed on a regular basis;
- Conclusions of monitoring should be reported to the appropriate individuals/groups.

Specific monitoring requirements may be necessary for the following: NIH grant applications for Phase I/II/III clinical trials; Clinical Research Center protocols; University of Vermont Cancer Center protocols; NCI-funded
clinical trials; gene therapy trials; or multi-center trials when UVM is the lead institution.

A **Data Safety and Monitoring Board** (DSMB) is an external, independent committee of scientists, physicians, statisticians, and others that collects and analyzes data during the course of a study to monitor for adverse effects and other trends (such as an indication that one treatment is significantly better than another, particularly when one arm of the study involves a placebo control) that would warrant modification or termination of the study or notification to study participants about new information that might affect their willingness to continue in the study. Typically, protocols that are industry sponsored accrue multiple subjects at multiple sites and are required to have the appropriate resources to capture and report issues of safety and do this by means of a board or equivalent.

**8.A.1.j.6. Unanticipated Problems to Subjects and Others Reporting:** All protocols should specify that, in the absence of more stringent reporting requirements, the guidelines established in the Committees on Human Research “Unanticipated Problems Reporting Policy and Procedures” will be followed. The UVM/UVM Medical Center requirements for reporting adverse events and unanticipated problems to subjects and others should be included in the DSMP.

For research protocols utilizing the UVM 3T research magnet, you must have a plan for handling incidental findings. Refer to guidance on incidental findings in Attachment I.

For protocols using the CRC, additional adverse event reporting mechanisms exist. The CRC Office of Research Subject Advocacy is available to assist you in meeting these requirements. Please call the RSA Office (847-0433) or visit the CRC website for sample language on this topic to include in your protocols.

**8.A.1.j.7. Sources of Materials:** Identify sources of research material obtained from individually identifiable human subjects in the form of specimens, records or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records or data.

**8.A.1.j.8. Collaborating Sites.** When research involving human subjects will take place at collaborating sites or other performance sites when UVM/UVM Medical Center is the lead site, the principal investigator must provide in this section a list of the collaborating sites and their Federalwide Assurance numbers when applicable. Sites added after initial approval must be submitted as an amendment to the IRB and must adhere to the same requirements. Additional agreements may be required, see Section 13.

**8.A.1.j.9. Consent and HIPAA Authorization.** The consent form with incorporated HIPAA authorization language (if protected health information (PHI) is included, (see Section 8.B for further information about PHI)) should accompany the protocol as an appendix or attachment.

**8.A.1.j.10. References.** Include references.
8.A.2. Qualitative Research Protocol

The Qualitative Research Protocol form SHOULD be used for proposals where the significant majority of the research methods are qualitative. It SHOULD NOT be used for studies involving human specimens or medical procedures even if the study is primarily qualitative because of the additional regulatory requirements for human subject protection. See Section 7.F. for more information regarding Review of Qualitative Research.

8.A.3. Placeholder


There is a category of expedited protocols that includes only the collection of blood. Researchers conducting bench science often times require human cells for their laboratory research, and they and their staff, will donate blood for these scientific purposes. While the activity of drawing blood is not a "research protocol", the collection of the cells is for research, and therefore falls under the IRB purview. What follows is guidance for blood collection protocols.
OHRP has ruled that for all Federally-sponsored research, informed consent must be obtained before identifiable specimens may be collected for research purposes. This applies to any research that is done at an institution that receives Federal funding. The following guidance and the new Blood Collection Protocol form have been developed to comply with these requirements and to help standardize procedures to establish safe practices in the collection of human blood and human blood products for research purposes.

Submission of the Blood Collection Protocol for review and approval will assist the IRB in ensuring that donors who are participating are protected.

**Blood Collection in Non-Clinical Settings**

Blood draws in spaces outside of clinical care areas should be conducted in a room that is separated by a door from bench space, biological safety cabinets or other laboratory equipment that is used to handle or store biological infectious agents. Space utilized for blood draws should be separated from active manipulation of infectious biological agents and active work with hazardous chemical agents prior to the blood draw (for area disinfection purposes), at the time of the blood draw, and until disinfection procedures have been completed after the blood draw.

Blood draw areas must follow all BSL-2 work practices including:

1. **Furniture** – Blood draw chair or table should be made of materials that can easily be disinfected (example vinyl or plastic furniture)
2. **Sharps containers** – An approved Sharps disposal container should be available in the blood draw area at the point of use. All glass items and needles must be disposed of in an approved Sharps container.
3. **Disinfectant** – Bleach solution or an EPA registered disinfectant should be available in the draw area in the event of a spill.
4. Spill or Emergency Procedure - A procedure to handle spill cleanup or emergency response information should be posted at the point of use.
5. Biohazardous Waste Disposal - Biohazardous waste bags and boxes must be used to dispose of all plastic ware and personnel protective equipment.
6. Biohazardous Signage and Labeling – All clinical laboratory spaces must be labeled with a biohazardous door sign designating the space as BLS-2. All equipment used to store and handle human blood and blood products must be labeled with a biohazardous sticker.
7. Personnel Protective Equipment – Personnel conducting blood draws are required to wear the appropriate personnel protective equipment (PPE). This includes liquid barrier gloves (latex or nitrile), face protection (full face shield or surgical mask and safety glasses) and lab coat or lab gown that can be laundered or disposed in event of a blood splash or spill.

Personnel Conducting Blood Draws

The principal investigator is responsible for verifying that personnel performing blood draws have sufficient training and experience in conducting human blood sampling. Qualifications may include prior experience as a trained phlebotomist, nurse or emergency medical technician. All research personnel conducting human blood draws or work with human blood and blood products must complete bloodborne pathogen training on an annual basis. Information on training is available on the University Environmental Safety website or is part of the UVM Medical Center mandates.

Approved Standard Practices for Obtaining Blood

1. Healthy adults individuals will be asked to participate in this minimal risk procedure. Education and review of the consent will be performed.
2. After the consent is signed, the volunteer will be brought to ______________________
3. Phlebotomy of a peripheral arm vein will be performed by ______________________ using sterile procedures and seated position. A sterile bandage will cover the phlebotomy site after the procedure and the arm will be elevated to ensure that bleeding has stopped.
4. The volunteer will be observed for any lightheadedness, bruising or bleeding during and after the procedure.
5. If the volunteer is lightheaded, he/she will be reclined and monitored until symptoms resolve.
6. If the volunteer is asymptomatic after the phlebotomy procedure, he/she will be released.
7. Any volunteer with any side effects during or after phlebotomy will not be used again to obtain the blood products. In addition, any volunteer that requires more than three attempts to access a vein will also not be used as a volunteer.

8.A.5. Biological Specimens/Data Repository Protocols

There is a category of expedited protocols that include the collection of samples or data for future research. What follows is policy and guidance for repository protocols. We have developed a submission form “Biological Specimens/Data Repository Protocol” to address management of repository activities.

NOTE: UVM investigators sending data or specimens outside of the institution should contact the UVM Office of Technology Commercialization to determine if a Material Transfer Agreement or any other agreement defining the respective institutional responsibilities is warranted.

Biological Specimens/Data Repository Policy – 01-09

The use and control of human tissue and medical charts for research is governed and restricted by federal and state laws and local regulations to ensure human protection measures are adequate. In the past tissue registries, tissue banks, pathology archives, research waste materials, hospital and clinic charts, and other databases have often been accessible to medical researchers. Often this “tissue” material was acquired from human subjects (living persons and fetuses) for non-research purposes such as diagnosis, medical therapy, public health control, quality assurance and transfusion/transplantation therapy. Researchers were often permitted access to these materials without adequate human protection mechanisms in place. More recently, human protection standards on use of tissue material have become more stringent and less trivial based on newly identified issues such as medical/legal privacy acts, HIV status, genetic confidentiality issues, religious and ethical beliefs, fetal restrictions, and other issues. The days of free access to personal...
data and tissues by researchers without subject consent have passed.

Operation of a specimen/data repository is now subject to oversight by the committee. The committee will review and approve a protocol specifying the conditions under which sample collection occurs and then all subsequent requests to access the specimens or data for research purposes. This is done to ensure adequate provisions to protect the privacy of subjects and maintain the confidentiality of data.

8.A.5.a. Definitions

**Human tissue and data repositories** collect, store, and distribute human tissue materials and data for research purposes. Repository activities involve three components: (i) collection of the tissue samples or data; (ii) storage of the tissues samples or data; and (iii) future use of stored tissue or data.

**Tissues** include any cell tissue, fluid, or excreta from which measures of normal or pathologic human physiologic function can be obtained. The term, “tissue” includes, but is not limited to pathological specimens, diagnostic specimens, hair and nail clippings, deciduous and permanent teeth, dental plaque and calculus, sweat, uncanulledated saliva, placenta removed at delivery, amniotic fluid, cerebrospinal fluid, genetic material, urine, blood and other bodily fluids.

**Data** includes any private medical or non-medical information obtained from the subject, informant or the medical chart.

**Coded or De-Identified** means that identifying information (HIPAA Identifiers List) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain, has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

8.A.5.b. Protocol Requirements

The IRB has developed a “repository” protocol form and process that covers all the following requirements.

1. person responsible;
2. description of all tissue/data that will accumulate in the bank;
3. physical location and security measures of the bank;
4. a separate “repository consent form” or request for a waiver of consent/authorization;
5. pledge that the responsible party will not use or release tissue or data unless an IRB application is submitted for every proposed analysis of that data;
6. internal monitoring in place to cross check samples, data, consents and withdrawals;
7. safeguards against identification; use of a third party system;
8. process to evaluate tissue utilization;
9. length of time specimens or data are kept; how destroyed; and
10. what information will be shared with subject(s).

As is usual, the protocol should discuss these issues in enough detail for the IRB members to evaluate the plans; a somewhat briefer description should be included in the consent form.

OHRP strongly recommends that a Certificate of Confidentiality be obtained to protect confidentiality of human cell repository specimens and data.

8.A.5.c. Consent Form Requirements

The IRB has developed a standard specimen collection consent form which includes the following elements:

1. operation and security of the repository;
2. specific types of research to be conducted (as specific as possible with the basic idea to determine if there is any type of research to which the subject might object);
3. conditions under which data and specimens will be released to recipient-investigators; (other site must have IRB approval);
4. procedures for protecting the privacy of subjects and maintaining the confidentiality of data;
5. sensitivity of the generated information (E.g. information that could affect a subjects employment, insurance coverage etc., (if DNA typing is involved include information on consequences (paternity));
6. non-exculpatory language through which subjects are made to waive or appear to waive any legal rights;
7. freedom to withdraw: how will confidentiality risk be terminated;
8. whether or not it is anticipated that the subject may be approached for follow-up information or follow-up samples in the future (a process to which the subject should have the opportunity to give or deny consent);
9. voluntariness of participation;
10. the degree to which ongoing access to medical records is being sought for correlative information, and the duration of such access; and
11. the kind of information that will be provided to subject(s).

8.A.5.d. Reporting Individual Results to Subjects

For general repository activities, it is probably best to plan not to provide results of future studies to the subjects. Much of the future research will be conducted without identifiers, and it is unlikely that most research will yield results that, if known, would affect the patients’ health care or family planning. In fact, there are many cases in which it would be unethical to provide results to patients, such as when the research is in the early stages and the clinical significance has not been established. On the other hand, if there is a good chance that research will yield results that could affect the subjects’ medical care, it may be appropriate to tell subjects that if such identifiable results are obtained, the subjects will be contacted and asked if they wish to be informed of the results. The decision about whether to provide any results to subjects will depend on the ethical implications of each protocol.

Note: Results obtained from a laboratory that does not meet the standards of CLIA (Clinical Laboratory Improvement Act) may not be used to direct patient care. In these cases, the subject could be notified that an issue has been identified, and that the subject or in some cases the investigator can notify the subject’s physician so that their physician may follow-up with standardized testing when appropriate.

8.A.5.e. Receiving or Purchasing Tissue/Data from Other Researchers

For protocols in which there are plans to collect specimens or data from outside institutions, the committee will review a “collection” protocol (can use same “repository” protocol form), informed consent /authorization document (if applicable) for distribution to these outside specimen/data collectors and their local IRBs.

A written agreement is required for collector-investigators, which requires written informed consent of the donor-subjects utilizing an informed consent document or a waiver approved by each of the local IRBs. It should also contain an acknowledgment that collector-investigators are prohibited from providing recipient-investigators with access to the identities of donor-subjects or to information through which the identities of donor-subjects may readily be ascertained.

8.A.5.f. Giving Tissue/Data to Other Researchers

IRB review required: A UVM/UVM Medical Center researcher who is responsible for a tissue or data bank cannot release tissues or data to other researchers (local or not local) until he or she has determined that those researchers have received appropriate approval or determination of exemption from a duly constituted Institutional Review Board (IRB).

Researchers at other institutions or companies are not subject to review by UVM/UVM Medical Center IRB, and the IRB has no jurisdiction over how non-UVM/UVM Medical Center researchers will protect subjects' privacy and interests in the future research. Researchers who are funded by private foundations or industries may be conducting research which is not necessarily subject to Federal regulations protecting human subjects. Therefore, to apply the same level of protection for all subjects involved in UVM/UVM Medical Center research, the IRB generally will not permit providing subject identifiers along with tissues or data to non-UVM/UVM Medical Center researchers. If necessary, the samples/data may be coded, but the key must be maintained at UVM/UVM Medical Center. For those University of Vermont or UVM Medical Center protocols in which there are plans to release tissue or data to an outside institution, a written usage agreement for recipient-investigators is required.

Other researchers at UVM/UVM Medical Center wishing to use samples or data previously collected under an approved protocol should contact the IRB office for assistance with determining what paperwork is required for review.

8.A.5.g. Specimen Collection as Part of a Larger Protocol

Tissues are routinely used for a variety of tests within treatment and epidemiological protocols, and most researchers are accustomed to describing the sampling procedures and risks in their protocols and consent forms. However, if some of the samples will be saved for unspecified future research, additional discussion is needed in the protocol and consent form. All of the concerns that apply to independent tissue collection protocols apply here as well.

Making Tissue Collection Optional: In treatment studies with a potential benefit for subjects, the IRB recommends that collection of tissues for repositories (as opposed to collection for treatment-related analyses) be made optional. That is, in general, patients should not be denied a promising experimental treatment because they are unwilling to
allow their tissue to be banked for unspecified future purposes. The IRB is aware that some national cooperative study
groups make banking of samples a condition of study participation. Approval for such repositories will be considered
very carefully and denied only when there are over-riding ethical concerns.

**Consent within a larger protocol:** A consent form should emphasize the major procedures and risks of the research
study. If the study primarily involves banking of specimens in repositories for future research use, then the major part
of the procedures and risks sections should discuss this long term storage. On the other hand, when banking is done
as a small and preferably optional part of a treatment study (a cancer treatment regimen, for example) the concern
about banking is relatively small compared to deciding how to treat a life-threatening condition.

One acceptable method of discussing banking within a consent form for a treatment study is to include a separate
paragraph between the Procedures and Risks section, briefly discussing the banking and its implications. If banking in
a repository is optional, two appropriately labeled lines for initials should be included with the signature section, so that
subjects can indicate whether or not they are willing to have specimens banked.

The IRB recommends the following language:

“Biologic Studies: Portions of your tissues which are removed as part of care and are not required for
routine diagnosis or treatment may be used now or in the future for research purposes. These tissue
samples may be used to learn more about how cancer or other diseases develop and/or may result in
new products, tests or discoveries. In some instances, these may have potential commercial value. These
tissues to be kept for research purposes will be obtained only at the same time as your regular
procedures are performed; you will not have to undergo any special procedures for this purpose. There
will be no additional charge, and you will not receive any payment or financial benefit from any products,
tests or discoveries. You may also be asked in the future if you are willing to be in additional research
studies. You will not be told the results of any future research. Participation in this extra research is
voluntary, and if you choose not to allow the extra research it will in no way affect your care on the main
study. You may at any time contact the researchers to request that your samples be withdrawn from
research use, and any identifiable samples still in their possession will be destroyed. Please indicate
whether you are willing to allow this extra research by initialing one of the lines at the end of the form.”

Just before the signature lines in the treatment consent form:

* ______ I do not want my tissue and blood samples used for any research or tests other than those
needed for the main research study.

______ The researchers may keep my extra tissue and blood samples for future research.

______ I am willing to be contacted in the future about any additional research studies.”


The Committee receives many projects where the only procedure is gathering health
information (e.g., data mining, chart review). If your project includes any additional
procedures, this form would not be appropriate.

Any project that requires access to protected health information from a covered entity is
required to undergo an expedited review. The covered entities are UVMMC and UVM
Eleanor M. Luse Center. We have combined the necessary data points from each of our
submission forms into one form for the Committee to conduct this review. This form may
be found on the forms page of our website. See section 7.E. for additional information.

Please note that if you are utilizing the Jeffords Institute for Quality, you must obtain
approval from them prior to sending to the IRB for review.

8.B. Legally Effective and Prospectively Obtained Informed Consent and
Documentation of Consent
The Committee evaluates both the consent process and the procedures for documenting informed consent to ensure that adequate informed consent is obtained from participants unless a waiver of consent has been approved by the Committee. Except as provided in Section 8.B.5. of these procedures, the use of a written consent form approved by the Committee is required to document informed consent. The following procedures describe Committee review of the consent process and documentation of consent.

Definitions:

1. **Assent**: An individual’s affirmative agreement to participate in research obtained in conjunction with permission from the individual’s parents or legally authorized representative. Mere failure to object should not, absent affirmative agreement, be construed as assent. Assent is typically conducted with children 11 years of age or older.

2. **Children**: Any person who has not attained 18 years of age.

3. **Health Care Decision-Maker**: In the case of an incompetent individual, or an individual who lacks decision-making capacity, the individual’s health care decision-maker is designated in order of reference as one of the following: the individual’s court-appointed legal guardian or conservator with health care decision-making authority (e.g., Durable Power of Attorney for Health Care or DPAHC); the individual’s health care agent as specified in an advance directive; or the individual’s Health Care Decision-Maker.

4. **Informed Consent**: An individual’s voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure.

5. **Legally Authorized Representative (LAR)**. A legally authorized representative is an individual or body authorized under applicable law to provide permission on behalf of a prospective subject to the subject’s participation in the procedures involved in the research. For the purposes of this policy, a legally authorized representative may include:

   - the parent or parents having custody of a prospective subject under the age of 18;
   - a person appointed as a health care agent under a Durable Power of Attorney for Health Care (DPAHC);
   - next-of-kin (only for research involving a potential for health care benefits), in the following order of priority unless otherwise specified by applicable state law: spouse, adult child (18 years of age or older), parent, adult sibling (18 years of age or older), grandparent, or adult grandchild (18 years of age or older). This applies only to adult participants who are incompetent or lack decision-making capacity, AND do not have a valid Court-appointed guardian or health care agent. The next-of-kin should be an adult who has exhibited special care and concern for the patient and who is familiar with the patient’s personal morals and values;
   - a court-appointed guardian of the person (legal guardian).

I. The IRB ensures that provisions are made to obtain legally effective informed consent prospectively from each prospective research participant or permission from his/her legally authorized representative, in accordance with and to the extent required by 45 CFR 46.116 and 21 CFR 50.20. However, there are circumstances in which the IRB may grant a waiver of informed consent in accordance with Federal regulations (See 8.B.5).

   **A. Cases of Physical Compromise**  A person who can understand and comprehend spoken English, but is physically unable to talk or write, can be entered into a study if they are competent and able to indicate approval or disapproval by other means. If (1) the person retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally (still competent) and (2) is able to indicate approval or disapproval to study entry, they may be entered into the study. The consent form should document the method used for communication with the prospective subject and the specific means by which
the prospective subject communicated agreement to participate in the study. An impartial third party should witness the entire consent process and sign the consent document.

This consent process must be approved prior to use. Please explain that the subject will be assessed for their comprehension and understanding and asked if they are able to sign and date for themselves. If they can understand but cannot sign, an impartial witness will be made available to witness the discussion and the agreement of the subject to participation. If they are able to sign and date for themselves, no witness will be necessary. The witness cannot be the same person who is obtaining the consent, it has to be someone impartial. Below is an example of the signature page that may be appended to the approved consent in these situations.

_________________________________________  __________
Signature of Subject (mark here with "X" if unable to write)  Date

Name of Subject Printed (research staff may complete if subject is unable to write)

_________________________________________
Impartial Witness (to be used in the event the subject is unable to write)  Date

_________________________________________  __________
Signature of Principal Investigator or Designee  Date

Name of Principal Investigator or Designee Printed

II. Documentation of informed consent is to be obtained unless alternate procedures are approved by the IRB, in accordance with 45 CFR 46.117 and 21 CFR 50.27. The IRB reviews all informed consent documents to assure the adequacy of the information contained in the consent document, and adherence to Federal regulations regarding the required elements of informed consent.

III. Informed consent is obtained from the participant or permission from a legally authorized representative prior to initiating research activities. This includes recruitment and screening procedures. Contact with a potential subject for recruitment purposes may be made prior to written consent if the criteria for a waiver of written documentation or an alteration in the process is requested and approved. Written informed consent must be obtained on the most recently-approved version of the consent document.

A. Children. For subjects less than 18 years of age, their parent(s) or other legal guardians are the legally authorized representatives who may grant permission for their participation in research (in accordance with 45 CFR 46 (children’s subpart). (REFER TO VULNERABLE POPULATIONS SECTION – 11.D.).

1. Parents. Only the parent(s) may grant permission for the child’s participation in research. Assent is to be sought from the child, only after permission has been obtained from one or both of the parents. Grandparents and other relatives or caregivers may not grant permission unless they have been granted formal custody of the child by a court. In such cases, the Principal Investigator (PI) must obtain a copy of the court order as evidence of that person’s authority to grant permission for participation in research on the child’s behalf. See additional information regarding consent process in Section 11.D.
2. Children in State Custody (Wards of State). According to the Department of Children and Families (DCF) applicable policies and by virtue of the court order granting DCF legal custody of certain children (e.g., foster children), that Department is the agency that is authorized to grant permission for participation in research for children in their custody. The decision of whether to grant permission for research is made on a case-by-case basis by DCF and consent is provided by an appropriate representative of DCF. If a child has begun research procedures with the consent of a parent but is subsequently placed in the custody of DCF while undergoing research interventions, consent must be sought again from the appointed advocate for the child at DCF in order to continue participation in the research. See additional information in Section 11.D.

3. Emancipated Minor. According to Vermont Statute, an emancipated minor means a minor who:
   a. has entered into a valid marriage, whether or not such marriage was terminated by dissolution;
   b. is on active duty with any of the armed forces of the United States of America; or
   c. has been, by a court of law, ordered emancipated.

In order to become an “emancipated minor” the minor must petition the probate court. There are multiple stipulations that must be met by the minor and the court must find that emancipation would be in the best interest of the minor. If the stipulations are met, the court will issue an order of emancipation.

In certain limited circumstances, it may be appropriate to allow an emancipated minor to consent to participate in a research study in the absence of the permission of a parent or legal guardian if the minor has the sufficient capacity to consent to the procedures involved in the research study. Each situation is judged on a case-by-case basis.

B. Adult Subjects lacking capacity to consent (including cognitively impaired).

1. If a prospective adult subject lacks the capacity to consent, his or her legally authorized representative or a Health Care Decision-Maker (see definitions above) may grant permission, on their behalf, for their participation in research, within prescribed limitations. For non-medical studies (research that does not provide a potential for health care benefits) a Health Care Decision-Maker cannot be used; another form of legally authorized representative must consent on behalf of the cognitively impaired adult. For minimal risk studies it may be possible to obtain a waiver or alteration of consent. It is unlikely that the IRB will approve non-therapeutic research involving cognitively impaired adult subjects that is more than minimal risk.

2. Research over Extended Periods. Studies involving subjects who are decisionally-impaired may take place over extended periods of time. The IRB considers whether and when periodic re-consenting of individuals is required to assure that a subject’s continued involvement is voluntary. The IRB may require that the Investigator re-consent subjects after taking into account the study’s anticipated length and the condition of the individuals to be included (e.g., subjects with progressive neurological disorders). Additionally, the IRB considers whether and when to require a reassessment of decision-making capacity.

Protocols must include details about the proposed use of “legally authorized representatives” for the consent process.

8.B.1. Consent Requirements/Elements in the Form
An investigator may not involve a human subject in research without first obtaining the informed consent (with HIPAA authorization language included when Protected Health Information (PHI) is used/disclosed) of the subject or the subject's legally authorized representative. This must be obtained in writing, or verbally (if the specific criteria as described below are met). In either case, informed consent (and HIPAA, when applicable) must be obtained under circumstances which allow sufficient opportunity to consider participation and that minimize the possibility of any coercion or undue influence.

The information that is given to subjects must be in a language understandable to them or their representative. Whether informed consent is written or oral, it must not include any exculpatory language through which the subject or representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, sponsor, institution or its agents from liability for negligence.

If genetic materials are to be collected, stored or analyzed, GINA language must be included in the subject consent form. Language can be found in the IRB consent template located on our forms page.

The IRB provides instructions and a consent template to assist with consent form development. The elements are listed below.

**Basic Elements of Informed Consent:**

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

b. A description of any reasonably foreseeable risks (physical, psychological, social, legal, or others) or discomforts to the subject.

   NOTE: See section 8.A.1.j.3. Risks/Benefits, for additional information regarding GINA.

c. A description of any benefits to the subject or to others which may reasonably be expected from the research. If there is no direct benefit to the subject, this should be stated.

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

e. A statement describing the extent to which confidentiality of records will be maintained.

f. For research involving more than minimal risk, an explanation as to whether compensation and any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained. When applicable, standard language from the template must be used as written.

g. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

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

i. The name, address, and telephone number of the principal investigator(s) or contact person(s).

j. The amount of compensation, if any, for participation.
Additional Elements of Informed Consent:

a. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.

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

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

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

e. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.

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

g. When HIV testing is conducted as part of the research procedures, individuals whose test results are associated with personal identifiers must be informed that they will be provided with their test results and provided with the opportunity to receive appropriate counseling. It should also be stated that both HIV and AIDS cases must, by law, be reported to the Vermont Department of Health and disclosure of a positive test may result in discrimination by friends, family, employers, insurance companies and others. See consent template for additional guidance.

For consent form document guidance as well as templates for various types of consents, see the forms section of the IRB website.

8.B.2. HIPAA Authorization Requirements

HIPAA refers to the Health Insurance and Portability Act of 1996. It is a broad federal law, only part of which is intended to protect the privacy of healthcare information. It is divided into three parts: portability, accountability, and administrative simplification. The most important regulation under HIPAA for research are the privacy regulations, often referred to as the Privacy Rule. Covered entities are entities that bill electronically for healthcare services.

The intent of the Privacy Rule is to protect the private individual’s health care information also referred to as Protected Health Information (PHI). It defines the means by which individuals/human research subjects can be informed of how their PHI will be used or disclosed and it gives individuals a number of rights with regard to their health information. The authorization language is now included within the consent as of 7/30/16.

The UVM Medical Center is a covered entity and the University is considered a hybrid covered entity as specific departments within the University, such as the Luse Center, bill for healthcare services.


The Department of Health and Human Services (DHHS) regulations for the protection of human subjects require that informed consent information be presented in “language understandable to the subject,” and, in most situations, that informed consent be documented in writing (45 CFR §46.116 and §46.117).

In order for non-English speaking subjects to participate in a research study, steps must
be taken to assure true informed consent is obtained. This does not simply mean that a form is signed, but rather that steps are taken to assure the study and voluntary nature of the research is understood by the subject. A translator may need to be involved in the informed consent discussion and a translated consent document may be needed. Further, the IRB may require the investigator to submit a back-translation of the informed consent.

If the majority of subjects are expected to be non-English speaking, use of the Long Form Consent and Authorization Process (Section 8.B.3.a.) is required.

If the protocol is already approved for English speaking subjects and a non-English speaking subject presents for participation, the Oral Translation with Short Form Consent Process and Authorization Process (Section 8.B.3.c.) may be used. To do this, researchers must submit an amendment to include a non-English speaking individual as a subject addressing all of the requirements listed in that section.

8.B.3.a. Long Form Consent and Authorization Process §46.117(b)(1)
When the subject population of any research study is expected to include a significant number of subjects who are not fluent in English but are fluent in another language, the IRB requires a full translation of the English version of the approved consent document (a “Long Form Consent Document”) along with the translator’s documentation of qualifications.

Note: Interpreter Services at UVMMC meet the standards, therefore, additional documentation is not required. We do, however, require documentation of qualifications for any other translator services.

IRB Review
In addition to the standard initial review submission materials, submit the following:

1. English language version of consent (it is recommended that you hold on translation until after the IRB has approved the English version)
2.
3. A plan for ensuring that the subject understands the requirements and the voluntary nature of the research

The following items must be resubmitted for final approval of the foreign language documents:

1. Foreign language version of the consent.
2.
3. Documentation describing the qualifications of the translator and the date of translation.

8.B.3.b. Long Form Consent Documents – Request for Back-Translation
If the research is deemed “high” risk or is very complex, or there are other relevant concerns, the IRB reserves the right to request that the foreign language consent be translated back into English to ensure the foreign language consent is written in understandable terms and contains all key elements of consent.

The IRB requires documentation that this back-translation was done by a different translator than the one who did the original translation and documentation of that second translator’s qualifications is required as well.
Consent and Record-keeping Requirements with Translated Long Form
1. Conduct the subject’s informed consent process with the researcher and a
   translator fluent in both English and the foreign language present
2. The subject signs the foreign language informed consent document
3. The researcher or designee signs the informed consent document
4. The translator (or other witness fluent in both languages) signs the
   informed consent form
5. The subject is given a copy of informed consent form
6. A copy of the signed documents are maintained in the study records
7. A copy of the signed documents should be included in the subject’s
   medical records if that is the standard practice for this particular study

8.B.3.c. Oral Translation with Short Form Consent and Authorization
   Process
Alternatively, §46.117(b)(2) permits oral presentation of informed consent
   information in conjunction with a short form written consent document in the
   subject’s language (stating that the elements of consent have been presented
   orally). Additionally, the subject is provided with the IRB-approved English
   version of the consent form.

Typically this option is used when a single subject is found to be eligible to
   participate in research and there is no long form consent translation. A witness
to the oral presentation is required.

IRB Review
Submit the following for review:

1. Amendment form
2. Request for Waiver or Alteration of Informed
   Consent/Authorization/Documentation
3. English version of short form (template located on our forms page)
4. Foreign language version of short form
5. Documentation describing the qualifications of the translator(s) and date of
   translation.
6. IRB-approved version of the English language version of the consent
   form for the protocol
7. A plan for ensuring that the subject understands the requirements and the
   voluntary nature of the research

Consent and Record-keeping Requirements when using a Short Form
   Informed Consent Document
Per the Office of Human Research Protections (OHRP), the following steps
must be followed after IRB approval.

1. Conduct the subject’s informed consent process with the researcher, a
   witness, and a translator fluent in both English and the foreign language
   present
2. The subject signs the ‘short form’ informed consent document
3. The researcher signs the IRB-approved English version of the informed
   consent document
4. The witness (fluent in both languages) signs BOTH the short form and
   the written informed consent form. (Note, the translator may also serve
   as the witness or the investigator, but not as the investigator and the
   witness and the translator).
5. The subject is given a copy of the signed short form and signed written summary/informed consent form 
6. Provide the English version of the signed informed consent form even though the subject may not understand English. 
7. A copy of the signed documents are maintained in the study records along with clear documentation of the consent process and who was involved. *(consent process documentation form is available on the IRB website)* 
8. A copy of the signed documents should be included in the subject's medical records *if that is the standard practice for this particular study.*

Any deviation from these alternatives requires review and approval by the IRB.

8.B.3.d. Effective Communication During Study Participation
In order for consent to be legally effective, the subject must be provided with all relevant research-related information and must clearly understand such information. When non-English speaking subjects are being invited to participate in a study, investigators must ensure that there is adequate communication between the research team and the subjects.

Unless the principal investigator or a member of the research team is fluent in the prospective non-English speaking subject’s language, a translator will be necessary to facilitate the conversation during the consent process and for communication throughout the course of the study. Translators should be fluent in English as well as in the language of the non-English speaking subject.

8.B.3.e. Other Considerations
Recruitment materials such as flyers must be translated in order to accommodate expected non-English speaking subjects *(i.e., a significant number of subjects who are not fluent in English).* All translations of recruitment materials must be completed by a certified translator and approved by the IRB prior to their use.

Study instruments may be in English and translated orally by a translator or a member of the research team who is fluent in the language spoken by the non-English speaking subject. If an investigator prefers to have any study instruments translated, the translations must be completed by a certified translator and approved by the IRB.

8.B.4. Waiver of Informed Consent, Alteration of Informed Consent, or Waiver of Documentation

A. Waiver of Informed Consent: In some research, written or verbal consent is not possible. A typical example would be retrospective record or pathology reviews for limited information that is not sensitive in nature and the data are derived from clinically indicated procedures. Consent is not possible because the subjects are not available to sign a consent form.

UVM Waivers Cannot be Used at Other Institutions
Waivers of consent and HIPAA authorizations are only possible when all the criteria for a waiver are met and the clinical records are UVM Medical Center records. UVM waivers would not and cannot be applied to different hospitals or clinics. Waivers of consent assume that there is no risk to the subject. Allowing specific records reviews under a UVM/UVM Medical Center waiver outside of our own institution increases the risk to not only the
subject (increasing the chances of a breach of confidentiality by going outside of the institution) but also to UVM and/or UVM Medical Center. Under the HIPAA regulations, patients have the right to request an access report of their medical records. If a subject were to ever make such a request from the other hospital or clinic, they would then realize that their records have been reviewed by someone from UVM, which is not something that they would have been aware of until that point.

Currently, there is not a way within the regulations or for the continued protection of our subjects for researchers to access protected information from other entities without obtaining consent.

B. Alteration of Consent: In some research, an alteration of the individual’s informed consent or elements of the process may be waived. An example would be when research requires deception. In these cases, some of the elements of informed consent are met but not all. Information typically held would be the basis for the research and subjects are debriefed after the research is complete. The requirement to obtain written or verbal informed consent may be waived or altered if:

a. The research involves no more than minimal risk to the subjects.
b. The waiver or alteration will not adversely affect the rights and welfare of the subjects.
c. The research could not practicably be carried out without the waiver or alteration. **AND**
d. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

**NOTE:** The FDA does not typically allow for a waiver of consent when regulated test articles are being used. In the case of emergency care treatment, a waiver will be considered, see below 8.B.5.C.

To apply for a waiver of written or verbal informed consent, the Principal Investigator must complete Section I of the Request for Waiver of Informed Consent/Authorization/Documentation form and submit it to the IRB with the other initial submission documents. The IRB will evaluate the request to ensure that the waiver criteria set forth above are met. If the waiver is granted, then the waiver approval signed by the IRB chair or designee shall be returned to the principal investigator.

**Note:** If the protocol requires protected health information (PHI) and you are applying for a waiver of consent, then a waiver of authorization must also be applied for. To do this, complete both Sections I and II of the Request for Waiver of Informed Consent/Authorization/Documentation. If there is no protected health information, HIPAA regulations do not apply and a waiver of authorization would not be required.

C. Waiver or Alteration of Informed Consent: “Treatment Use in an Emergent Situation” If your protocol includes an FDA-regulated test article (drug or device), an exemption from the consent requirement is permitted for “Emergency Use for Treatment” providing the additional following four conditions are met and certification of compliance is provided to the IRB by both the investigator and a physician who is not otherwise participating in the clinical investigation prior to use of the test article, if possible.
1) The human subject is confronted by a life-threatening situation necessitating use of the test article;
2) Informed consent cannot be obtained from the subject because of an inability to communicate with or obtain legally effective consent from the subject;
3) Time is not sufficient to obtain consent from the subject's legal representative; and
4) There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject. (21 CFR 50.23(a))

If certification of compliance with the four conditions specified above cannot be obtained prior to using the test article, certification (See Attachment A) must be submitted to the IRB within 5 working days after the use of the test article.

The Committee is aware of the difficulty in addressing these issues; however, this is a specific regulatory requirement.

D. FDA Requirement for Exception from Informed Consent Requirement for Emergency Research: For situations in an emergency setting when a subject is unable to consent and there is no “legally authorized representative” who can provide prospective informed consent for the subject, there is only the following option available. In order for the Committee to approve proposed research activities which contain an exception to consent for emergency research, referred to as an “Emergency Research Consent Waiver,” the Committee must ensure that the activities meet the strict limited conditions set forth by FDA regulation, 21 CFR Section 50.24. It is the policy of the Committee to follow these regulations when all of the specified conditions are met. The Committee has not, at this time, invoked the “Emergency Research Consent Waiver.”

E. Waiver of Documentation of Informed Consent: In some research, verbal or implied consent of the subject is sufficient and a signed consent form is not necessary. A typical example would be a mailed survey with a cover letter explaining the research. The receipt of a completed survey implies that the subject wanted to participate. The requirement for the investigator to obtain a signed consent from some or all subjects may be waived if:

a. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context.

OR

b. The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. All subjects, however, must be asked whether they want documentation linking them with the research. The subject's wishes will govern and should be adequately documented, regardless of final decision.

In cases where the documentation requirement is waived, the investigator may wish to provide the subjects with a simply written statement or information sheet that describes the research. This written statement must be reviewed and
approved by the Committee prior to use. See forms page on our website for template. For protocols where verbal consent is obtained, the principal investigator or a research team member must document in the research file that verbal consent was obtained. See forms page on our website for consent process documentation form.

To apply for a waiver of consent documentation, the principal investigator must complete Section III of the Request for “Waiver of Informed Consent /Authorization/Documentation” form. The IRB will evaluate the request to ensure that the waiver criteria set forth above are met. If granted, the waiver is approved by the IRB chair or designee and will be returned to the principal investigator.

8.B.5. Waiver or Alteration of HIPAA Authorization

UVM Medical Center may use or disclose PHI for research purposes without patient authorization if the IRB (functioning as the Privacy Board) has approved a “Waiver of Authorization.”

In order to use or disclose PHI with a waiver of authorization, the IRB or Privacy Board must find:

(a) The use or disclosure of PHI involves no more than minimal risk to the privacy of individuals, based on, at least, the presence of the following criteria:

(1) An adequate plan to protect the identifiers from improper use and disclosure;
(2) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law;
(3) Adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of PHI would be permitted under the HIPAA privacy rule.

(b) The research could not practicably be conducted without the alteration or waiver; and
(c) The research could not practicably be conducted without access to and use of the protected health information.

An alteration of HIPAA Authorization may be granted when there is also a request to waive the documentation of consent.

To apply for a waiver or alteration of authorization for research purposes, the Principal Investigator must complete Sections I and II of the “Request for Waiver of Informed Consent /Authorization/Documentation” form and submit it to the IRB with the initial submission documents. The IRB will evaluate the request to ensure that the waiver criteria set forth above are met. If granted, the waiver is approved by the IRB chair or designee and will be returned to the Principal Investigator.
8.B.6. Request for Waiver of Informed Consent /Authorization/Documentation Form

Note: The “Request for Waiver of Informed Consent /Authorization/Documentation” Form is a form utilized by the Committees on Human Research to review the specifics of any requested waiver of normally required research materials. If you are applying for a waiver of both consent and authorization, only one form need be completed and submitted. We recommend that you contact our office for assistance prior to protocol submission.

All the necessary forms are located in the forms section of our website and should be downloaded each time you need one.


Recruitment of potential research subjects at UVM Medical Center/UVM is a regulated research activity and must be conducted in accordance with the policies and procedures promulgated by the UVM Institutional Review Board.

A UVM Medical Center Health Care Provider or his/her agent may, without patient authorization, review the medical records of patients with whom he or she has a current clinical relationship to determine whether they meet the eligibility criteria for enrollment into a research study, and then contact prospective subjects directly by telephone or by letter, explaining the research study and requesting a decision concerning the individual’s potential interest in the study.

A “UVM Medical Center Health Care Provider” is defined as a licensed health care professional who is employed on a full-time or part-time basis by UVM Medical Center, regardless of whether or not the provider holds a faculty appointment at UVM or has an employment relationship with UVM. This includes the provider’s immediate practice group or coverage group.

A “current clinical relationship” shall be deemed to exist whenever the patient, at the time the recruitment activity is taking place, is considered to be under the care of the provider engaged in the recruitment activity or a member of the provider’s immediate practice group or coverage group.

An “agent” is defined as an individual who is under the direct supervision and control of the UVM Medical Center Health Care Provider engaged in the recruitment activity or under the direct supervision and control of a member of the provider’s immediate practice group or coverage group.

In all other cases, UVM Medical Center may only use or disclose PHI for recruitment purposes if the use or disclosure has been authorized by the patient or the researcher has obtained an IRB waiver of authorization. To obtain a partial waiver for recruitment purposes, complete form “Request for Waiver of Authorization for Recruitment Purposes” and submit to the IRB at the time of initial submission.


“Request for Partial Waiver of Authorization for Recruitment Purposes” Form is a form utilized by the Committees on Human Research, which are operating as the Privacy Board for UVM Medical Center, to waive HIPAA Authorization, prior to enrollment, for recruitment purposes only. Every partial waiver of Authorization for recruitment purposes approved by the Committees/Privacy Board must have a “Request for Partial
Waiver of Authorization for Recruitment Purposes Form.

8.B.9. Ongoing Consent

Over the course of a study new information may become available that may impact a subject's willingness to continue in a study. If new information becomes available, the researcher must submit an amendment for review and approval. The Principal Investigator will be requested to answer the following questions:

1. How will new findings be communicated?
2. What is the expected timeframe to relay this information to all subjects?
3. How will you determine if the subject is willing to continue study participation?
4. How will ongoing consent be documented?

New information must be relayed to the subjects as soon as possible so that they have the necessary information to make an informed decision as to whether they want to continue their participation. The following are acceptable options for sharing new information.

1. Verbal Exchange
   Information should only be shared in this way if it does not affect risk to subject. The exchange can be conducted during a routine study visit or by phone. Researcher needs to document discussion in the research record.

2. Informational Sheet
   Information shared in this way typically does not substantially affect risk to subject. This option does not require a subject signature, but the researcher needs to document that information was provided to the subject in a research record. IRB review/approval is required prior to distributing to subjects.

3. Informed Consent Addendum
   A consent addendum provides the subject with an update to the originally signed consent form. This option is typically used when there is a substantive change to the risk/benefit profile. The addendum document includes only that information which is new or different from the originally signed document, reducing the potential for participant confusion. The subject's signature indicates their willingness to continue participation in the study given the new information. Use of a consent addendum requires IRB review/approval and an IRB stamp of approval. An addendum is to be reviewed, signed and dated by both the subject and researcher in the same manner as the original consent document process.

4. Full Consent
   IRB policy is that a consent addendum be used instead of requesting the subject sign a full copy of the newly revised consent. Requesting subjects sign a full consent each time there is a revision is a practice that can confuse subjects unnecessarily. Note: Changes to this policy will be reviewed on a case-by-case basis.

Note: Consent form version numbers or dates

The Committee requires that a consent form version number or date appear in the footer of the consent form document. This ensures both the investigator and the Committee are working with the current consent version.

Some sponsors, however, are requesting that investigators update their consent form every year at time of continuing review or with every protocol amendment, even if there have been no actual changes to language in the consent form. The Committee does not
allow this practice for the reason stated above. The consent version number or date must remain the same when no changes have been made to the consent language. When language changes are necessary as a result of new information, only then should the version number or date be changed.

8.B.10. Children Reaching Legal Age of Consent While Enrolled in a Study Policy

When a child who was enrolled in research with parental or guardian permission subsequently reaches the legal age of consent to the procedures involved in ongoing research, the subject’s participation in the research is no longer regulated by the requirements of 45 CFR part 46.408 regarding parental or guardian permission and subject assent.

The researcher should seek and obtain the legally effective informed consent, as described in 45 CFR 46.116, for the now-adult subject for any ongoing interactions or interventions with the subjects. This is because the prior parental permission and child assent are not equivalent to legally effective informed consent for the now-adult subject.

As long as the participation continues to meet the regulatory definition of “human subjects research” (for example, it involves the continued analysis of specimens or data for which the subject’s identity is readily identifiable to the researcher), then it would be necessary for the researcher to seek and obtain legally effective informed consent of the now-adult subjects.

However, the IRB could approve a waiver of informed consent under 45 CFR 46.116(d), if the project meets the required conditions for a waiver of consent. The investigator must complete and submit the “Request for Waiver of Informed Consent” form to the IRB for this determination.

The IRB developed a sample consent form for “Continued Participation in a Research Study” that should be used when consenting the now-adult subjects. Since this document was created by the IRB, it does not require the IRB approval stamp. However, if you wish to change the contents, an amendment would be required prior to use. This consent form is essentially a continuation cover consent that explains why the now-adult subject is being consented at this time. A copy of the originally signed parental permission and assent (if applicable) should be attached to this continuation consent form and presented to the now-adult subject. Another HIPAA authorization must also be obtained at this time. Subjects should be reminded of their right to withdraw from the study including: (a) their right to revoke HIPAA authorization, to the extent that such authorization is revocable under the terms of the informed consent and the authorization signed by the parent(s) or guardian; and (b) their right to revoke any other right granted in the study, (e.g., rights with respect to use of tissue samples) to the extent it would be revocable by the parent(s) or guardian when the subject was a minor.

8.B.11. Media Consent

If a subject consents to participate in a protocol and then agrees to be interviewed regarding their research participation, another consent document must be signed. This consent document is referred to as “media” consent. It is required because the originally signed protocol consent form states that the subject’s information will be protected and kept confidential. The “media” consent indicates that they are freely giving up that protection by agreeing to take part in the interview. This applies when there is a direct or indirect interview, videotaping, and photographs of the individual for TV/radio broadcast or publication. This “media” consent is located on our website forms page and should be completed by the subject prior to the interview. The IRB does not need to review this activity.
8.C. Documentation

The PI must keep a copy of all forms/documents submitted to the IRB (perhaps in a Research Regulatory Binder) as evidence of IRB submissions and approval record. NOTE: Initial protocol approval periods begin on the date the IRB chair or designee verifies that the IRB-specified conditions for approval have been satisfied, not the date of the original convened IRB meeting.

8.D. Data Management Guidance – see Appendix O


RPO, SPA and the Office of Clinical Trials Research work together to ensure all institutional and sponsor approvals and contracts are in place prior to the initiation of sponsored research involving human subjects. The IRB is required to ensure that all research described in a grant application or proposal is entirely consistent with any corresponding protocol(s) reviewed and approved by the IRB. Any discrepancies must be resolved prior to the start of the project. The IRB works with SPA and the Office for Clinical Trials Research to establish that an appropriate connection is made between the application and the protocol being reviewed.

Relevant information regarding sponsored projects is shared between Offices (e.g. conflict of interest, study incentives, key personnel). Protocol approvals are not released until applicable contracts or agreements have been fully executed.

8.E.1. New Competing or Competing Renewal Grant Applications

To meet the requirement listed above, any time you will be submitting a new competing grant or a competing renewal application, a new protocol must be submitted to the IRB for review and approval. SPA will not clear funds for release until there is an approved protocol. Continued approvals will be checked on an annual basis for the life of the grant.

Note: It is very important that the proposal and protocol be matched correctly for the reason mentioned above and to ensure that the required reference to the sponsor made in the consent form is accurate.

8.E.2. When the Project is a New Competing or a Competing Renewal Application and the New Protocol is Identical or Substantially Similar to an Approved Protocol

Obtaining grant funding is extremely competitive. The same grant proposal may be submitted to multiple funding agencies at once or the same agency at different time points. If you obtain new funding, it is your responsibility to submit the corresponding grant and protocol for IRB review and approval.

The IRB treats identical protocols as new applications, however, a new committee review may not be required if the project is the same or substantially similar to the previously approved protocol.

If this is the case, you must submit the following:

1. One copy of your new grant application and any corresponding protocol.
2. One copy of an updated Common Protocol Cover Form.
3. One copy of a Request for Waiver of Consent/Authorization (if applicable).
4. A copy of the Consent Form(s).
5. A letter to the committee chair explaining that you are submitting a similar grant application to a different funding agency. State that this new protocol application is identical to the old one (provide CHRBSS/CHRMS file #) with regard to hypotheses, specific aims, and human subject involvement (or describe minor differences).

If this application is essentially the same as the previously approved application with only minor differences clearly described in a letter, the protocol will receive administrative review. If substantial changes are proposed, then a new committee review may be required.

8.E.3. Competing Resubmissions or Supplements

Grant resubmissions require an amendment to a previously approved protocol if it is identical or substantially similar to that protocol and grant. The amendment form and a copy of the resubmitted grant application are to be submitted for review and approval. Administrative and competitive supplements also require an amendment to a previously approved protocol. The amendment form and a copy of the supplement are to be submitted for review and approval.


What is “Just-in-Time” Review
The NIH just-in-time policy allows grant applications to be submitted to NIH for peer review without prior IRB approval. This policy has been extended by the University to all UVM grant proposals where the granting agency does not require IRB approval at the time the proposal is submitted. Researchers should check with SPA to determine the funding agency’s IRB approval requirements.

Process for “Just-in-Time” Review
If the sponsor accepts just-in-time human subjects review, as soon as the researcher is notified that the proposal received a favorable priority ranking from the granting agency, the protocol should be submitted to the IRB for review. If the project is a new or competing renewal and is identical or substantially similar to a previously approved protocol, see section 8.E.2. for further guidance. If the project is not identical or substantially similar, researchers should check the IRB submission deadlines for the next available IRB meeting as special requests for insertion onto an agenda after the scheduled deadline may not be possible. **NOTE:** It is not necessary for the researcher to submit a protocol if the priority ranking is unfavorable.

If the just-in-time request is for a resubmission, see section 8.E.3. for submission guidance.

The delay in submission of a protocol for IRB review approval may delay an award but should not affect the receipt of an award.

8.E.5. Grant Proposals Lacking Definite Plans for Involvement of Human Subjects

Certain types of applications may involve human subjects (within the funding period) but definite plans are not included in the application or protocol. The NIH refers to these as “delayed onset awards”. These applications may not need to be reviewed by the Committee before an award can be made by DHHS or another federal agency. Examples of this may include activities such as research training programs, research, pilot, or developmental projects in which human subjects’ involvement will depend upon development of instruments or pre-clinical animal studies.

NIH guidance states that PIs are required to obtain prior approval from the sponsor for the
addition of human subject research activity prior to implementation. See notice below for additional information.

- Prior NIH Approval of Human Subjects Research in Active Awards Initially Submitted without Definitive Plans for Human Subjects Involvement (Delayed Onset Awards) (NOT-OD-12-130) National Institutes of Health

If the sponsor requires an IRB approval of the grant prior to involvement of human subjects, the IRB will send bi-annual notices to investigators to remind them of this NIH requirement and the IRB requirement to obtain prior approval of the human subject activities.

No human subjects may be involved until the project has been reviewed and approved by the IRB and certification of approval submitted to the funding agency.

8.E.6. Contracts/Agreements

Protocols which are supported by an industry sponsor where money, materials (test articles, equipment, or other supplies), or intellectual property are exchanged require a contract or agreement be in place between the sponsor and either UVM or UVM Medical Center. Most industry-sponsored research contract review is done through the Office of Clinical Trial Research (OCTR) however a select few are handled through SPA.

The IRB requires a copy of the final contract prior to release of a protocol approval. OCTR/SPA will forward a copy of the final contract to the IRB who will review for potential conflicts of interest and appropriate subject payments. Many times this contract review is the final step to protocol approval and release, so researchers should plan accordingly and submit their contracts to the appropriate individuals early in the review process.

8.E.7. Review Fees

Refer to fee policy in Appendix C.

8.E.8. Changes to the Scope of a NIH Awarded Project

While most of the University’s NIH grants are under Expanded Authorities, eliminating the need for prior approval for most budget changes, NIH still requires prior approval before making changes that NIH considers changes in project scope.

The NIH Grant Policy Statement provides examples of actions requiring approval before they are made. Investigators should consult the complete policy statement (link below) for changes that may involve a change in scope.


In 2012 the NIH issued additional guidance for changes that involve human subjects in active awards and that will require prior NIH approval. (NOT-OD-12-129).

Some actions that may require prior approval as they represent a change in scope include:

- Change in the specific aims approved at the time of award
- Substitution of one animal model for another
- Any change from the approved use of animals or human subjects
• Shift of the research emphasis from one disease area to another
• Application of a new technology
• Transfer of the performance of substantive programmatic work to a third party if the third party is a foreign component
• Change in key personnel including withdraw from the project, absence during any continuous period of three-months or more, reduction in time devoted to the project by twenty-five percent or more.

Prior approvals may be requested by an email from a University Authorized Official to the project’s Grants Management Officer. If you would like to request prior approval for any of the changes mentioned above, please be in touch with your SPA administrator. Your administrator will advise you on the content of the email request, review it, and forward it to the University’s Authorized Official who will send it on to NIH.

9. Submission of Materials After Initial Approval is Obtained

The following are materials that require submission after initial approval.

9.A. Continuing Review

9.A.1. Requirements

Federal Policy: Continuing review of research activity is required by federal regulations [(45CFR46.109 subpart (e)].

It is the policy of the IRB to review human research appropriate to the degree of risk involved, but not less than once per year. “Higher risk” research (as determined by the Committees on Human Research – hereafter “Committee”) may require more frequent reviews.

The purpose of continuing review is to determine:

1) whether the risks to subjects continue to be minimized and reasonable in relation to the anticipated benefits;
2) whether the selection of subjects continues to be equitable;
3) whether the informed consent continues to be appropriate;
4) changes in key personnel and whether mandatory training is complete;
5) whether there continue to be:
   a. adequate provisions for monitoring the data collected to ensure the safety of the subjects, when appropriate;
   b. adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data, when appropriate; and
   c. appropriate safeguards for vulnerable populations.

All research protocols (except protocols determined by the Committee to qualify for exempt status) must undergo continuing review at least once a year, unless all research activity, including data analysis, has been completed.

Continued Approval Policy: (updated 11/11)

In order to resolve the issue of indefinitely reviewing and reapproving protocols annually for which work has not ever been started, the IRB approved the following policy:
If the work on a research protocol has not yet begun after a three-year period, the protocol will be administratively closed by the IRB. A new protocol must be submitted for review at the point in time when activity is anticipated to begin. Exceptions may be made if the funding period exceeds three years and the human subjects’ protocol is not scheduled to begin until after that time period. You must indicate that is the case on your continuing review form.

In addition, the committee will be closing at time of continuing review any non-treatment protocols in which there has been no activity within the last 5 years.

This policy does not apply to protocols that have been and plan to remain open to accrual but have just not had any enrollment to date, such as many of the oncology group protocols that are approved for rare tumors. For that situation, the category “active - work in progress” should be checked on the continuing review form.

9.A.2. When to Report:

The Committee will send a “Request for Continuing Review” form to the PI approximately three months before the approval is due to expire. Reminders will be sent at two months and one month prior to expiration.

Identifying the Point When Continuing Review is no Longer Necessary

OHRP Guidance Released November 10, 2010

K. Identifying the Point When Continuing Review is no Longer Necessary

Continuing review and re-approval of a research project at least annually is required so long as the project continues to involve human subjects. OHRP considers a research project to continue to involve human subjects as long as the investigators conducting the research continue to obtain:

- Data about the subjects of the research through intervention or interaction with them; or
- Identifiable private information about the subjects of the research.

With respect to obtaining identifiable private information, OHRP considers this to include obtaining identifiable biological specimens originating from living individuals. Furthermore, OHRP considers obtaining identifiable private information to include:

- Collecting or receiving identifiable private information (including identifiable biological specimens) from any source (i.e., not already in the possession of the investigator);
- Collecting identifiable private information by observing or recording private behavior without interacting or intervening with the human subjects; and
- Using, studying, or analyzing identifiable private information (including identifiable biological specimens), even if the information was already in the possession of the investigator before the research begins. This includes using, studying, or analyzing any of the following:
  - Identifiable private information obtained by interacting or intervening with the human subjects;
- Identifiable private information stored in documents, records, photographs, images, video recordings, or audio recordings provided to the investigators from any source;
- Identifiable private information stored in documents, records, photographs, images, video recordings, or audio recordings already in the possession of the investigator before the research begins;
- Identifiable private information obtained about an individual by interviewing other people (e.g., an individual's healthcare provider or teacher);
- Identifiable biological specimens provided to the investigators from any source; or
- Identifiable biological specimens already in the possession of the investigator before the research begins.

A research project no longer involves human subjects once the investigators have finished obtaining data through interaction or intervention with subjects or obtaining identifiable private information about the subjects, which includes the using, studying, or analyzing identifiable private information. Once all such activities described in the IRB-approved protocol are finished, the research project no longer needs to undergo continuing review. For example, when the only remaining activity of a research project involves the analysis of aggregate data sets without individual subject identifiers, no further continuing review is necessary. At that point the IRB can formally close the IRB file for that project and advise the investigator of that action.

The Committee requires the PI to submit final closeout report for all protocols when a research study no longer involves human subjects. The PI must submit a continuing review form to officially change the designation to “Not Human Subjects”. A “Not Humans Subjects” certification will be forwarded to the PI for their records. Once the protocol has been certified with this designation, continuing reviews are no longer required.

**Expired Approvals**

Extensions beyond the expiration date cannot be granted. If the expiration date has passed, or is in jeopardy of passing, the Committee must be notified as soon as possible.

- **a)** If the Committee does not provide continued approval of the research by the specified expiration date, subject accrual is suspended pending continued approval of the research by the Committee. **Note**: A valid consent form will not be available until after the Committee reviews and approves a continuation of the research.
- **b)** Where subjects are patients in treatment studies, continuation of research interventions or interactions is allowable for the safety and well-being of the individual and is reportable to the IRB.
- **c)** Department chairs and Faculty Sponsors (if applicable) will be notified of a lapse in a researcher’s IRB approval.
- **d)** Researchers found to be collecting data without a current IRB approval may not be allowed use the data.

As part of the continuing review process, the Committee may require that the research be restricted, modified, reviewed more frequently or terminated/suspended if risks have changed during the review period. Alternatively, special precautions or Committee-imposed restrictions, or shortened review periods, may be modified if current data support such actions. Ongoing approval will not be released until requested clarifications or changes have been received.
The most visible element of the continuing review process is the stamped IRB approval date on the signature page of the consent form.

9.A.3. Request for Continuing Review Form

The “Request for Continuing Review” form is intended to capture all of the required elements for a significant review of the research. This is located in the continuing review of our forms page and should be downloaded each time you need one. Incomplete forms will be sent back to the investigator.

9.A.4. Documentation

a. Once approved, the Committee will return a signed Protection of Human Subjects Assurance and a stamped consent form (if applicable) to the PI via email.

b. Proof of continuing review must be kept by the PI (perhaps in a Research Regulatory Binder) as evidence that Continuing Review has occurred. The documentation should include:

   i. An IRB Approval Memo;
   ii. A signed Protection of Human Subjects Assurance;
   iii. A stamped and dated consent form (if applicable);
   iv. Copies of all additional documentation (e.g. amendments) submitted to the Committee at the time of Continuing Review.

c. Stamped Consent Forms: Copies of the newly approved consent form with the Committee approval stamp should be made directly from the copy placed in the research binder. These copies must be used for all new subjects.

d. All previous unsigned versions of the consent form should be destroyed (with the exception of a copy in the Research Binder) to prevent the accidental use of expired consent forms.

**** The single most important practice to ensure compliance with the continuing review process is to make certain that the consent form given to the subjects is current (i.e., with a Committee approval stamp) ****

9.B. Unanticipated Problems Reporting (includes adverse events)

9.B.1. Policies

a) Federal Policy: Review of unanticipated problems involving risk to subjects or others (hereinafter referred to as unanticipated problems) is required by federal regulations (45CFR46.103 section b (5) and for FDA regulated articles 21 CFR 312 and 21 CFR 812), and is an essential element of the continuing review of research involving human subjects.

b) Local Policy: (below)

POLICY: Unanticipated Problems (includes adverse events) Reporting Policy and Procedures
Updated 03/21/12
The IRB is required under 45 CFR part 46 to submit to the Office for Human Research Protections (OHRP) any unanticipated problems involving risk to subjects or others (UAPs). [21 CFR 56.108 (b)(1) & 45 CFR 46.103(b)(5)(i)]. OHRP considers UAPs, in general, to include any incident, experience, or outcome that meets all the following criteria:

1. unexpected (in terms of nature (type of event), severity (extent of harmfulness), or frequency (number of like events higher than anticipated) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
2. related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
3. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

All UAPs must be promptly reported to the IRB. To assist investigators in identifying a UAP we have listed below four general categories of unanticipated problems that may require local reporting to the Committee. Investigators are encouraged to contact the Committee office for clarification in ambiguous circumstances.

1. **LOCAL ADVERSE EVENTS (including death)** whether serious or not serious, that are unexpected AND possibly, probably, or definitely related to study participation require reporting to the Committee utilizing the "Unanticipated Problem Potentially Involving Risk..." form.

1.a. **A LOCAL ADVERSE EVENT** is a negative side effect resulting from the study intervention that occurred to a subject enrolled at UVM, UVM Medical Center, or other research site under the jurisdiction of the UVM IRB.

1.b. **UNEXPECTED**: Any adverse event occurring in one or more subjects participating in a research protocol, the nature, severity, or frequency of which is not consistent with either:
   1.b.i. the known foreseeable risk of adverse events associated with the protocol procedures described in the (a) IRB-approved protocol, any drug or device brochure, and the IRB-approved informed consent, and (b) other relevant sources of information, such as product labeling and packing inserts; or
   1.b.ii. the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

   The vast majority of adverse events occurring in the context of research are expected in light of (1) the known toxicities and side effects of the research procedures; (2) the expected natural progression of subjects' underlying diseases; and (3) subjects' predisposing risk factors. Thus, most individual adverse events do not meet this criterion for an unanticipated problem and do not need to be reported.

1.c. **RELATED**: An adverse event is considered to be related if there is a reasonable possibility that the event may have been caused by the protocol or study interventions. A related event has a strong temporal relationship to the drug, device or intervention, and an alternative etiology is unlikely. Adverse events that are determined to be solely caused by (2) or (3) above would be considered unrelated to participation. If it cannot be determined whether an event is related, it should be reported as "possibly related."

**NOTE:** The IRB may, in coordination with other institutional oversight committees, categorize a protocol as "higher risk" and require the Investigator to follow a specific “high risk” reporting procedure. This high risk determination will be made at time of initial review or anytime after initial review if the IRB feels it is warranted. This determination and the requirements will be clearly communicated back to the Investigator. Examples of higher risk protocols of clinical trials for which the IRB may institute more stringent reporting are: local, investigator-initiated early phase (Phase I, Phase I/II) study without a DSMB; local, investigator-initiated trial in extremely vulnerable populations, e.g., very sick patients, subjects unable to consent for themselves, prisoners.

Adverse events that are not reportable to the Committee may also require reporting to UVM Medical Center SAFE, UVM Medical Center or UVM Risk Management, the sponsor and/or the FDA. Please do not forward copies of reports that do not meet local reporting criteria to the Committee.
Event submissions that do not meet local reporting criteria will be returned to the study contact via email pdf attachment and the IRB paper copy will be discarded.

2. INTERIM FINDINGS/NEW SAFETY INFORMATION

2.a. New Safety Information that requires a change to the protocol or consent form must be reported to the IRB utilizing the "Unanticipated Problem Potentially Involving Risk..." form. A "Request for Amendment" form and applicable materials must accompany the report. Examples of new safety information are below:

- Revised Investigator Drug/Device Brochures (IDB);
- Toxicity Reports/NCI Action Letters;
- Data and Safety Monitoring Reports/Progress Reports;
- Literature Reviews; or
- other safety information that may impact human subject welfare.

2.b. New Safety Information that does not require a change to the protocol or consent form must be reported to the IRB utilizing the "New Safety Information Not Affecting Risk to Subjects" form. Receipt of these submissions will be acknowledged.

3. PROTOCOL DEVIATIONS

A protocol deviation is a divergence or departure from the expected conduct of an IRB-approved study that is not consistent with the current, approved research protocol, consent process or document or study addenda. The significance of a protocol deviation, in terms of subject safety, depends on the nature of the deviation and the study.

3.a Those protocol deviations that involve harm or have the potential to impact the health or welfare of the subject(s) or others must be reported in writing to the IRB by utilizing the "Unanticipated Problem Potentially Involving Risk..." form. Examples of reportable deviations are below:

- Medication or Laboratory Errors;
- Improper or Unapproved Consent Process or Consent Form;
- Unintentional change to the protocol without prior IRB approval;
- Intentional change to the protocol without prior IRB approval to eliminate immediate hazard to research subject.

3.b. Those protocol deviations (e.g., missed appointment, labs one day late) that do not involve harm or have the potential to impact the health or welfare of the subject(s) or others do not need to be individually reported. The PI needs to make this determination for each deviation. Deviations not affecting risk to subjects or others should be summarized and reported at time of continuing review.

4. OTHER UNANTICIPATED PROBLEMS

Other unanticipated problems are those which are 1) unexpected, 2) related, AND 3) involve harm or have the potential for harm to subjects or others. Below are examples of other types of protocol-related problems that must be reported to the IRB:

- Complaint by a subject;
- Breach of confidentiality/HIPAA violation;
- Enforcement action e.g., unfavorable audit report, suspension or disqualification of investigator, FDA Form 483 or Warning Letter;
- Study personnel misconduct;
- Study personnel not on protocol;
- Incarceration of a research subject during participation;
- Other untoward events that present risk to the subject, investigator, research staff or others.
These unanticipated problems are to be reported to the IRB utilizing the “UNANTICIPATED PROBLEM POTENTIALLY INVOLVING RISK…” form.

Note Regarding IND Safety Reports and Study Progress Reports

Individual IND Safety Reports do not necessarily meet the reportable criteria and are recognized by OHRP and the FDA to not yield information that is useful to IRBs. The reports often lack context and detail, are often incomplete and unanalyzed, and as such, inhibit an IRB's ability to assure the protection of human subjects. Therefore, IND safety reports do not require submission to the IRB. Similarly, study progress reports do not provide any additional safety information and are not reportable to the IRB.

However, if an individual IND report results in a revision to the protocol or consent, an a copy of the specific IND safety report, an Amendment Request form along with applicable materials, as well as an “Unanticipated Problem Potentially Involving Risk…” must be submitted.

Notification Timelines for Reporting Unanticipated Problems

All unanticipated problems are to be reported as soon as possible. If all information is not available within 7 days, submit an initial report at 7 days and then follow-up with the IRB as information becomes available.

Disposition of Submissions and Communications Regarding Submissions

- Unanticipated problems, as defined above, will be reviewed by the Safety Subcommittee.
  - If it is determined that the protocol or consent require revision or there are other corrective actions that are necessary, a request will be sent to the PI and/or study contact.
  - If the protocol and or consent do not require revision and there are no other corrective measures that are necessary, a memo stating that no further action is required will be sent to the study contact.
  - Only the full Committee will make determinations regarding additional reporting to the Office for Human Subject Protections (OHRP).
- Adverse events that do not meet the criteria as UAPs will be returned to the study contact via email pdf attachment and the IRB paper copy will be discarded.
- For new safety information that is not considered a UAP (e.g. does not require protocol or consent revisions), a memo of acknowledgement will be sent to the study contact.

9.B.2. Documentation

a. The PI must keep a copy of the “Unanticipated Problem Potentially Involving Risk…” form (perhaps in a subject’s Research Binder) as evidence of IRB submission.

9.C. Request for Modification/Amendment to Previously Approved Protocol

9.C.1. Requirements

Review of any changes to previously approved research is required by federal regulation [45CFR46.103(b)(4)] and is an essential element of the continuing review of research involving human subjects.

The IRB recognizes that research is a continuous process and that changes in the conduct of a study and/or changes to the consent document are necessary.
However, no changes to an approved protocol should be implemented until the Committee has reviewed and approved the changes. This includes, but is not limited to, subject recruitment methods, consent form changes, treatment changes, amendments to the sponsor’s master protocol as well as changes or additions in study sites, investigators, or key personnel.

Major modifications/amendments potentially affecting the risk/benefit ratio are reviewed through the full committee review process, minor modifications not affecting the risk to subjects may be reviewed through the expedited review process.

When amendments impact the safety of subjects previously enrolled who continue to receive study interventions, it may be necessary to convey this information (e.g., to obtain the consent of the subjects) by means of an addendum to the existing consent form or providing the subjects with an informational sheet regarding the update (see 8.B.1.a Ongoing Consent). The IRB may determine, for example, that such subjects must be notified of new findings or toxicities not noted at the time they were originally consented. Such notification is consistent with the view of informed consent as a continuous process, and affords subjects the opportunity to determine whether or not they wish to continue their participation in the research. The IRB shall determine on a case-by-case basis when such notification, and its documentation, is required. The amendment review process does not affect continuing review expiration dates.

9.C.2. Immediate Hazard

Federal regulations mandate that changes cannot occur until after IRB review and approval “except when necessary to eliminate apparent immediate hazards to the subject.” The FDA has comparable criteria for implementing changes [FDA: 21CFR56.108(a)(4)].

Immediate Hazard: The definition for immediate hazard, as stated in the federal regulations for amendments, encompasses only those few instances where the immediate well-being of the subject is at risk. To that end, the subject’s well-being must benefit from (1) continuing the research itself (rather than just discontinuing the research intervention and treating with standard of care) and (2) the research must be changed immediately for the well-being of the subject. Subjects may always be treated based on a physician’s determination of their needs, but might not be eligible to continue in the research protocol. If a protocol is clinically faulted it should be corrected (through the amendment process) and the patient should normally be removed from the protocol and treated with the standard of care.

Example of “Immediate Hazard”: A subject has been enrolled on a local surgical protocol. The protocol requires that a certain immune-suppressing medication be administered to the subject during surgery, but the subject has an allergic reaction to that medication once surgery commences. The physician would determine the appropriate medical course of action and, if appropriate, the procedure would proceed.

Immediately following the procedure the PI must:
- notify the IRB; then
- the PI must submit a “Unanticipated Problem Potentially Involving Risk...” form documenting the event;
- the PI should submit a “Request for Modification / Amendment to Approved Protocol” form altering the protocol to allow for treatment or optional medications in case of allergic reactions (if appropriate); and
- the PI must ask the Committee to determine if the subject can be included in the study population as the protocol, as approved by the Committee, was not followed for this subject.

9.C.3. When to Request

Requests for approval of modifications may be submitted at any time. Complete a “Request for Modification / Amendment to Approved Protocol” form. The changes must be approved, before any changes can be implemented in the conduct of the protocol. If the amendment requires a revision to the consent form, the revised consent will be stamped with a new IRB approval date. This helps to track which consents apply to which version of the approved protocol. There will be no letter designation if the Request for Continuing Review form and the Request for Modification / Amendment to Approved Protocol form are submitted together and approved at the same time.

9.C.4. The Request for Modification / Amendment to Approved Protocol Form

The “Request for Modification / Amendment to Approved Protocol” form is intended to capture all of the required elements for a significant review of changes and amendments. When submitting amendments, you are not required to resubmit the entire protocol. Submit a completed “Request for Modification / Amendment to Approved Protocol” form to the Committee with all supporting documents that have been modified (i.e., protocol pages, questionnaires, recruitment flyers, consents, etc.).

If the protocol is NIH funded you may be required to obtain prior approval of the amendment from the sponsor, see section 8.C.8. for guidance.

Please Note: The CRC and UVMCC also require review of changes to protocols under their purview. Check their respective websites for further guidance.

9.C.5. Documentation:

Once approved, the Committee will return a signed “Request for Modification / Amendment to Approved Protocol” form and a stamped consent form form (if applicable) to the PI via email. Proof of the amendment/change approval as well as the stamped consent form must be kept by the PI (perhaps in a Research Regulatory Binder) as evidence that the Committee has approved the change.

Note: The newly revised consent form will have the same expiration date (if not outdated at the time of amendment request) as the pre-amendment consent form. There will now be an identifying letter along with the expiration date. This letter is associated with the approved amendment. Care must be taken to verify that the most current version is being used.

Investigators have the responsibility to formally close a study with current IRB approval once it is completed or discontinued. Among other reasons for closing out a study, this informs the IRB on the conduct and outcomes of the study, including any risks or problems that may have arisen since the last study renewal and which may need to be disclosed to the study participants or others.

**Do not close-out** a study if **any** of the following six conditions apply. Such studies must remain active and continue to receive ongoing IRB review and approval.

- Enrollment ongoing.
- Research-related interventions and/or follow-up ongoing.
- Subject follow-up ongoing.
- Biological specimens containing personally identifiable information are being maintained in a repository that has been approved as part of this study or upon which analysis or research is ongoing. If, however, specimens have been transferred to a separate repository that has ongoing IRB approval, the study may be closed.
- Primary data analysis or manuscript preparation that involves the use or access to personally identifiable information ongoing.
- If there is an external study sponsor and the sponsor has not provided permission to close the study with the IRB.

Notification must be done by completing a “**Request for Continuing Review**” form. This provides the opportunity for the researcher to summarize all the activities into a final report. Researchers can not use an amendment form to close a protocol.

In addition to informing the IRB of the closure, the PI must store the research records for the required length of time in accordance with the federal regulations, UVM policy, and any additional requirements stipulated by research sponsors and/or investigators’ professional associations. The PI must continue to follow appropriate data security procedures.

Subsequent use of data from closed research, whether by the original investigator or other investigators, may constitute human subjects research requiring IRB approval or a determination of Exemption from IRB review (see section 7.c.). For further information about storage of data, determinations of not human subjects, or future use and secondary uses of data, please consult the RPO for guidance.

If the principal investigator is leaving the institution, it is the principal investigator’s responsibility to either close the study or transfer the protocol to another UVM/UVM Medical Center principal investigator.

The IRB may close projects without UVM/UVM Medical Center investigator notification in the following circumstances:

- If the work on a research protocol has not yet begun after a three-year period.
- Non-treatment protocols in which there has been no activity within the last 5 years.
- If it is determined that the investigator is no longer affiliated with UVM/UVM Medical Center.
- If the approval period for the research has expired, the study is closed to subject accrual and the IRB has not permitted ongoing research procedures for the safety of continuing subjects.
- If the investigator has not responded to the IRB’s requests for revisions and/or clarifications within a reasonable timeframe, 120 days, and an extension has not been requested.
- If the IRB approval has been terminated. This would only occur after IRB review and communication with the investigator. Termination of IRB approval is reportable to the appropriate federal department or agency head and institutional officials.

In any of the situations described above, the IRB office will notify the PI of the study closure.

Note: If the investigator needs to reopen a protocol and less than one year has passed since closure, a completed continuing review form must be submitted for review and approval. If the study is billable, it will be invoiced for this review regardless of the amount of time that has passed. If the study has been closed for greater than one year, a new protocol submission is required. If the study is billable, the review will be invoiced.

10. Investigator Responsibilities

10.A. Expectations of an Investigator

There are certain expectations of a Principal Investigator (PI). Those expectations are outlined in the “Investigator’s Agreement” which is part of the Common Protocol Form. By signing the Common Protocol Cover Form you have agreed to the expectations as listed below:

14. INVESTIGATOR’S AGREEMENT

As Principal Investigator of this study, I assure the Committees on Human Research that the following statements are true:

The information that is provided in this form is correct. I will seek and obtain prior written approval from the IRB for any modifications in the proposal, including changes in procedures, co-investigators, etc. All of the members of the research team have completed the applicable institutional credentialing processes required to conduct this research. I will promptly forward any reportable adverse events and unanticipated problems to subjects or others that may occur in the course of this study. I will report in writing any significant new findings that develop during the course of this study that may affect the risks and benefits to participation. I will not begin my research until I have received written notification of IRB approval. I will comply with all IRB requests to report on the status of the study. I assure that the information I obtain as part of this research including PHI will not be reused or disclosed to any other person or entity other than those listed on this form, except as required by law or for authorized oversight of the research project. If at any time I want to reuse this information for other purposes or disclose the information to other individuals or entities, I will seek prior IRB approval. I will maintain records of this research according to applicable guidelines. If I am seeking IRB approval for a sponsored project, I hereby certify that the application that I have submitted to my funding agency accurately and completely reflects what is contained in this application. Agreement allows invoicing and collection of IRB review fees.

X____________________________________ __________________________
Original Signature of PI Date

Subinvestigators have an equally important role in that they are often assigned with the day-to-day conduct of the study.

All investigators participating in industry sponsored research should be aware and adhere to the Good Clinical Practice guidelines when applicable. Additional information regarding GCPs can be accessed at http://www.fda.gov/oc/gcp/default.htm. Our statement of compliance with GCPs
can be found in Appendix E.

10.B. Requirements of the Principal Investigator

As the principal investigator you must:

- Ensure proper training of the research team;
- Ensure protocol adherence;
- Create a process of informed consent; and
- Provide reports on the progress of the study.

10.B.1. Ensure Proper Training of the Research Team

The principal investigator is responsible for ensuring that the research team has appropriate training prior to and during the conduct of the study. All research team personnel are required to complete the UVM and UVM Medical Center approved human subject training. They also need to have specific training for the given protocol. Dependent upon delegated responsibilities, this training could take the form of attendance at investigator meetings, regular local research team meetings, or daily mentorship from the principal investigator.

10.B.2. Ensure Protocol Adherence

It is the principal investigator’s responsibility to ensure that the IRB-approved protocol is being followed by the research team. This includes making sure that amendments are submitted for IRB review in a timely fashion and once approved, are then implemented by the research team.


Informed consent is one of the basic ethical obligations for all research involving human participants. Informed consent is not just a form. It is a process of information exchange that takes place between the subject and the investigator or the study team, before, during and sometimes after the completion of the study. The amount of information that needs to be presented both in writing and verbally is directly related to the risk that the study presents and the complexity of the study design and related procedures.

The information in the HIPAA authorization language conveys how the institution will use and disclose the subjects’ protected health information in the context of the research study. Some research studies do not use protected health information and therefore would not need the authorization language included in the consent form.

The manner and context in which information is conveyed is as important as the information itself. There must be no coercion or undue influence. Potential subjects must have sufficient time to decide and should be allowed to consult with family and/or others if needed.

The purpose of a consent form is to provide a written source of information and documentation that a subject’s consent and authorization have been obtained. Consent forms must be signed and dated by the subject prior to conducting any research related procedures or data collection.

The IRB reviews the consent form to ensure that it contains required information.
in sufficient detail to protect the rights and welfare of human research subjects. The IRB stamps its approval on this document. If changes are made, the revised form must be submitted and approved. A new approval date is placed on the revised form. Form templates are available on our website under the forms section.

The investigator should be certain that the most current IRB approved consent form is being used at all times.

**a. Obtaining informed consent:**
- **a.** Written informed consent must be obtained from every subject who enters a research study, before any study related procedures are undertaken.
- **b.** The subject must be provided the information outlined in Section 8.B., both verbally and in writing.
- **c.** Once the subject has decided to participate, both the person obtaining consent, and the research subject should sign and date the form. NOTE: The PI or designee should never pre-sign or pre-date consent forms.
- **d.** The subject must receive a signed and dated copy of all executed documents, including subsequent updates to the consent.

**b. Delegating the informed consent:**
The principal investigator may delegate the consent process to an appropriately qualified person. This person must be listed on the protocol as key personnel and have taken the required human subjects training. Consider the complexity of the protocol and level of risk when designating responsibility for obtaining informed consent.

**c. Documentation of informed consent:**
The signed informed consent is documentation and must be retained. It is recommended that the discussion with the subject regarding potential participation and the informed consent process be documented in a source document. The most likely source document would be the medical record, but could also be a note to the research record.

**10.B.4. Provide Reports on the Progress of the Study**

During the course of a research study, new information might become available about safety or the study population under investigation. As new information becomes available, the principal investigator is obligated to report to the IRB. Common items that need to be reported in a timely fashion to the IRB are described in detail below

**a. Continuing review of approved studies**
It is the responsibility of the principal investigator to submit the current status of active protocols at least annually. Some protocols require more frequent review based on risk. The IRB makes this determination and notifies the principal investigator. Please refer to Section 9.A. for additional information on submission of continuing reviews.

**b. Reporting adverse events, deaths and unanticipated problems to subjects or others**
Refer to Section 9.B. for reporting information.
c. Amendments to a previously approved protocol
Any changes to the protocol, consent form or recruitment materials require IRB approval. Requests for changes (amendments) to approved studies may be submitted at any time but before the change is implemented, it must receive IRB approval. Refer to Section 9.C, for further instructions on how to submit an amendment.

d. Development of subject recruitment and retention materials
Recruitment strategies are very important to the success of a protocol and often change over the course of a protocol. Recruitment and retention materials (e.g., advertisements, flyers, letters) need to be submitted for IRB review and approval. If the materials require posting, the Committee needs to know where the materials will be posted. Materials cannot be used until IRB approval has been provided. When submitting recruitment material(s) with new protocols, check the appropriate box on the Common Protocol Cover Form and attach the materials for review. When materials are submitted after the initial submission, complete the Request for Modification / Amendment to the Approved Protocol form and attach the materials for review. See IRB guidelines for recruitment Section 8.A.1.j.2.

e. Change in research team
It is required that the investigator notifies the IRB office when there are any additions or deletions to research staff participating in a protocol. Update the current key personnel list by completing a Request for Change in Key Personnel form.

All key personnel are required to take the UVM and UVM Medical Center approved human subjects training before their active participation on the protocol and every 3 years thereafter. Refer to Section 5 to learn more about required training.

f. Premature termination/suspension
The IRB should be notified when a protocol has been terminated or suspended prematurely. The IRB also needs to know the reason for premature termination or suspension. To notify the IRB complete the Request for Modification / Amendment to the Approved Protocol form and send to the IRB office.

g. Study closures or requests to reopen closed protocols
See Section 9.D, for reporting requirements.

10.B.5 Coverage for PI or Faculty Sponsor

In order to fulfill the PI or faculty sponsor responsibilities, the IRB must be notified when a sabbatical or extended leave of absence of more than four weeks will be taken. IRB notification needs to include a designated investigator who will comply with the requirements noted above. This does not apply when the investigator or faculty sponsor does not have active protocols for which they are responsible.

10.B.6 Investigator’s Responsibilities when Leaving the University

If the investigator is leaving the institution, it is the investigator’s responsibility to contact the IRB to discuss their institutional status in regards to ongoing research activities and to close or appropriately transfer protocols before their departure. If this is not accomplished prior to leaving the institution, all protocols may be administratively closed by the IRB.
10.C. Guidance for the Investigator and Research Personnel

10.C.1. Communication with the IRB

When you are in communication with the office, whether in writing, by telephone, fax or e-mail, you should have the following information available.

- CHRMS or CHRBSS number, if assigned at time of contact
- Principal investigator’s name
- Protocol title
- Date and type of submission (if applicable)

We cannot readily assist you without this information.

All submissions must be in paper form and may be submitted by:

1) Inter-departmental mail or Hand Delivery

Research Protections Office
UVM Committees on Human Research
213 Waterman Bldg

2) US Postal Service for off-campus personnel:

Research Protections Office
UVM Committees on Human Research
213 Waterman Bldg
85 South Prospect Street
Burlington, VT 05048

10.C.2. Written Communication of IRB Decisions

Decisions made by the IRB will be communicated to the principal investigator (or designee if provided) through a memorandum outlining the approval status and/or concerns, questions and/or comments of the IRB.

NOTE: Initial protocol approval periods begin on the date the protocol was reviewed by the fully convened IRB, not on the date the IRB chair or designee verifies that IRB-specified conditions for approval have been satisfied.

The IRB staff will convey one of the following four decisions in writing to the investigator promptly after the meeting:

1. Approval
   The principal investigator may begin the research study upon written notification of approval of the research protocol and the informed consent form (if applicable) from the IRB chairperson.

2. Approval Withheld Pending Clarifications
   This decision is determined when the protocol is recommended for approval by the IRB pending the investigator’s response to IRB-directed questions and/or revisions. The principal investigator must provide a memorandum responding to the IRB’s recommendations. We ask that
you indicate the CHRMS/CHRBSS number on this correspondence and attach a revised protocol (if applicable), and revised consent form (if applicable).

3. Tabled
More substantive issues regarding the protocol and/or consent form must be addressed. Clarifications or requested revisions may have a significant impact on subject safety or understanding. A memorandum is sent to the investigator requesting that these issues be addressed. Full committee review of the investigator’s response is required prior to approval.

4. Disapproved
Questions regarding the rights and welfare of the subjects are of such significance that the committee finds approval of the study to be unwarranted. The authority of the Committee on Human Research to disapprove a human research study may not be overridden.

NOTE: The IRB has a 30, 60, 90 day reminder system for all pending protocol items. The investigator is reminded that the IRB has requested something from them in regards to a protocol and is awaiting his/her response. At the 120 day mark the protocol is withdrawn from the Committee’s consideration. This helps to ensure that changes to protocols are handled in a timely fashion.

10.C.3. Retention of Research Records
At a minimum research records should be retained for 3 years after research is complete. This meets the federal requirements for IRB protocol file records. UVM’s policy on Data and Retention forExternally funded research may require a longer period (3-5 years). See UVM Data and Retention Policy http://www.uvm.edu/policies/general_html/recordretention.pdf.

There also may be additional requirements from sponsors such as: the investigator is required to maintain a file of study records, including informed consent documents, for at least two years after the last approval of a marketing application (ICH Guidelines for GCP, 4.9.5). If clinical development is discontinued, or an NDA is not submitted or is later disapproved, study records must also be retained for at least two years after the termination of the investigation.

It is the responsibility of the sponsor to inform the investigator when research documents no longer need to be retained (21 CFR, 312.62). However, when no sponsor exists, it is up to the investigator to maintain research records as referenced above.

When the retention period has been met and materials are to be destroyed, we recommend that paperwork be shredded for confidentiality purposes.

10.C.4. Accessibility of Records
The investigator must provide direct access to all research records to the IRB staff. Dependent upon the protocol sponsorship there may be others with access needs, such as study monitors, FDA, and other regulatory authorities. There may be other units internally (e.g., OCTR, UVMCC, CRC, UVM Medical Center Risk Management) with oversight responsibilities that must be granted access as well.
NOTE: Unless otherwise indicated in a protocol and/or consent form, a subject’s specific research data is generally not provided to the research subject or his/her representative.

10.C.5. Enrollment Incentives

Enrollment incentives are any form of direct or indirect inducement (cash or non-cash) offered or received in exchange for enrolling subjects into research studies: (i) that is paid as reimbursement in excess of the reasonable cost of conducting the research protocol, or (ii) that is paid extra-contractually, including any bonus, reward, award, grant, gift, benefit, or other quid pro quo, or (iii) that creates a financial incentive that UVM and/or UVM Medical Center determine is contrary to the best interests of human subjects participating in the research.

The use of enrollment incentives in research involving human subjects creates a significant potential for conflicts of interest. Enrollment incentives are not reasonable payments made to subjects for their participation in research or to the actual costs researchers incur when enrolling subjects. Enrollment incentives are any special incentives, finders fees, bonuses or other similar forms of compensation provided to institutions or researchers as a means to encourage the enrollment of subjects in research, including clinical trials. Such incentives may create conflicts of interest. Enrollment incentives may also have an adverse effect on human subjects because such incentives may compromise the informed consent process or increase the likelihood for enrollment of ineligible persons as participants in the research.

Policy:

It is the policy of the Committees on Human Research not to approve human subjects research involving use of enrollment incentives. This prohibits any payment to investigators, study personnel or departments for additional compensation that: 1) encourages the recruitment of subjects (whether it is for identification, referral, recruitment, or enrollment of any subject); or 2) is tied in any way to the rate or timeframe for recruitment or enrollment.

References:
Univ. of Washington Enrollment Incentives Policy and Yale Univ. Policy Regarding Recruitment of Subjects

10.C.6. Investigator Financial Interest

POLICY REGARDING INVESTIGATOR FINANCIAL INTEREST – 2/16/05
(Updated Consent Template Language 10/20/10)

Statement of Principles:
The basic ethical principles that underlie research are respect for persons, beneficence and justice. The first two principles require an open and honest sharing of information so that potential human subjects may make informed choices about participating or refusing participation in research.

Patients are already concerned about conflicts of interest related to managed medical care and may become increasingly concerned over conflicts of interest in the conduct of research.

The doctrine of informed consent, which requires a patient to consider the risks, benefits, and alternatives to the suggested research intervention, requires that patients be given all the information
that would be reasonably relevant to their choice.

Disclosure of significant financial interests which pose potential conflicts of interest is essential to the integrity and ethical propriety of the informed consent process and to maintaining public trust in and support for the research endeavor.

**Policy:**
As part of the protocol submission, investigators must inform the Institutional Review Board (IRB) whether or not they or other key personnel have a significant financial interest as defined in this policy, and must describe the nature of that interest.

The IRB shall, as part of its reviews of research protocols, consider and evaluate all disclosures of significant financial interests made by investigators hereunder and shall determine whether the disclosed interests could potentially compromise or influence the investigator’s professional judgment or actions in the performance of the study (e.g. the design, conduct, oversight, evaluation or reporting of the results of the study) or could otherwise adversely affect the rights and welfare of human subjects. Financial interests determined by the IRB to have potentially negative impacts shall be deemed “relevant significant financial interests”. The IRB shall take such “relevant significant financial interests” into account in determining whether to approve the study and what protocol modifications or conditions, if any, to impose on the study in order to appropriately minimize or eliminate the potential negative impacts of the financial interest. The IRB shall also require that the existence of such financial interests be disclosed to study subjects, as required by this policy.

During the course of the study, new information that falls within the reporting requirements of this policy must be disclosed to the IRB in a timely manner.

An IRB member with a significant financial interest in a specific study or its sponsor must not participate in review and approval of that study, except to provide information as requested by the IRB.

**Definition of significant financial interest:**
Significant financial interests include any monetary or in-kind payments or gifts received from the research study sponsor, including cash, consulting fees, honoraria or other payments received from the sponsor, or stocks or other ownership interests in the sponsor, if any (single) or all of the (combined) payments or ownership interests paid to or held by the Investigator in one year (including payments to or interests held by his or her spouse and dependent children) are expected to be more than $5,000 and/or constitute more than a two percent (2%) ownership interest in the sponsor. Significant financial interests also include patents, copyrights or other intellectual property rights, and royalties or other future payments to be derived from the licensing, assignment, or use of intellectual property rights, the value or amount of which could be favorably affected by the research study. The term “sponsor” as used herein shall be deemed to include any corporate parent owning a controlling interest in the corporation sponsoring the research study.

**Role of the IRB:**
The IRB should be cognizant of the source of funding and funding arrangement for each protocol and assess the potential impact of the funding arrangement on subject welfare. Moreover, when a significant financial interest is identified as part of the protocol submission, the IRB shall determine whether the disclosed interests are “relevant significant financial interests” as described in the preceding policy statement and must determine how the relationship should be managed.

One factor to be considered is whether a financial interest is of such a magnitude that simply disclosing it is not sufficient. If this is the case, the IRB must determine whether additional steps should be taken to manage, reduce, or eliminate the conflict.

The IRB should carefully consider specific mechanisms proposed to minimize the potential adverse consequences of the conflict in an effort to optimally protect the interests of the research subjects. In general, if there may be significant financial conflict of interest issues on the part of the Investigator, as determined by the IRB, he or she should not be directly engaged in those aspects of the trial that could be influenced inappropriately by that conflict. These could include: the design of the trial, monitoring the trial, obtaining the informed consent, adverse event and unanticipated problem reporting, and analyzing the data. In all cases, good judgment, openness of process, and reliance upon objective, third party oversight may effectively minimize the potential for harm to subjects and safeguard the
Disclosure to potential subjects:
As part of the informed consent process, potential subjects shall be informed of the existence of relevant significant financial interests (as defined above) held by the investigator(s). The following language (or other appropriate language approved by the IRB, in those exceptional cases meriting special language) shall be included in all informed consent forms:

“You should also know that [investigator] has a significant financial interest (e.g. a separate relationship with the sponsor or a related company involving ownership or stock, payment for services or other significant financial payments) that could potentially compromise or influence the investigator’s professional judgment or actions in the performance of the study (e.g. the design, conduct, oversight, evaluation or reporting of the results of the study). The investigator has disclosed that personal financial interest to the IRB responsible for approving this study. The IRB reviewed the [investigator’s] financial interest and determined that any potential conflicts are being appropriately managed. However, negative impacts on subjects participating in this study, are always possible, and therefore the potential conflict is being disclosed to you. Please discuss with the Investigator any questions you may have about this.”

11. Additional Protections For Special Populations

11.A. Guidelines

If there is a possibility that any group of research subjects may be vulnerable to injury, coercion or undue influence, the investigator should include additional safeguards in the consent process and protocol that attempt to minimize, to the greatest extent possible given the specific research, those risks. The special populations for which there are currently additional federal regulations providing additional protections are:

- Pregnant Women and Fetuses;
- Neonates;
- Prisoners; and
- Children.

Additional populations not currently specifically covered by federal regulations but for which additional unspecified safeguards could be required by the IRB, are listed below.

1. Economically disadvantaged subjects;
2. Students;
3. Subjects with HIV;
4. Cognitively impaired subjects;
5. Mentally ill subjects (including, but not limited to the following);
   - Dementia (including Alzheimer’s)
   - Anxiety disorders
   - Depression
   - Obsessive / compulsive disorders
   - Manic / bipolar disorders
   - Personality disorders
   - Mental retardation
   - Psychoses
6. Subjects with drug and/or alcohol addictions (certificates of confidentiality are strongly recommended for this group);
7. Subjects with other disabilities; or
8. Non-English speaking subjects.
Depending on the research, exclusion of any of the above populations might be construed as unfair and attempts should be made to include these populations, with appropriate protections, if they are applicable to the research question. If the protocol is records or specimen collection only and the vulnerable population cannot be identified or there is no risk to the vulnerable subject they should not be listed as targeted subjects on your protocol cover form.

11.B. Pregnant Women, Fetuses, and Neonates

11.B.1. Pregnant women or fetuses may be involved in research if all of the following conditions are met:

1. Preclinical studies (studies on pregnant animals, and clinical studies, including studies on non-pregnant women), have been conducted and provide data for assessing potential risks to pregnant women and fetuses, if appropriate;
2. If there is the prospect of direct benefit for the woman or the fetus; the risk to the fetus is caused solely by interventions or procedures;
3. If there is no prospect of benefit for the woman or the fetus; the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
4. Any risk is the least possible for achieving the objectives of the research;
5. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
6. Researchers will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
7. Researchers will have no part in determining the viability of a neonate.

Consent: The consent of the pregnant woman and the father should be obtained in accordance with normal informed consent processes. Individuals providing consent should be fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.

The father's informed consent is not required if:

1. The purpose of the activity is to meet the health needs of the mother (direct benefit to the mother); OR
2. The purpose of the activity is to meet the health needs of the mother and fetus (direct benefit to the mother and fetus); OR
3. When risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means; OR
4. He is unavailable; OR
5. His competency is in question; OR
6. He is temporarily incapacitated; OR
7. The pregnancy resulted from rape or incest.

The father's informed consent should be secured when:

1. The purpose of the activity is to meet the health needs of the fetus (direct benefit to the fetus) only.

For children who are pregnant (less than 18 yo) assent and permission
11.B.2. Neonates of uncertain viability may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
2. Researchers engaged in the research will have no part in determining the viability of a neonate.
3. The IRB determines that:
   a) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or
   b) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research.

Consent Regarding Neonates of Uncertain Viability:

1. Informed consent can be obtained from either parent of the neonate. If neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of either of the parents’ legally authorized representatives should be obtained. If the pregnancy resulted from rape or incest, consent need not be obtained from the father nor his legally authorized representative;
2. Each individual providing consent must be fully informed regarding the reasonably foreseeable impact of the research on the neonate.

Nonviable neonates may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
2. Researchers engaged in the research will have no part in determining the viability of a neonate;
3. Vital functions of the neonate will not be artificially maintained;
4. The research will not terminate the heartbeat or respiration of the neonate;
5. There will be no added risk to the neonate resulting from the research; and
6. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means.

Consent Regarding Nonviable neonates:

1. Informed consent must be obtained from both parents of the neonate. In some cases a waiver and/or alteration of consent is applicable, see Sec. 46.116(c) and (d). However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements. If the pregnancy resulted from rape or
incest, consent need not be obtained from the father. Informed consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements for consent; and

2. Each individual providing consent must be fully informed regarding the reasonably foreseeable impact of the research on the neonate.

Viable neonates. A neonate, after delivery, that has been determined to be viable may be included in research only in accordance with the policies for including children in research (see children below).

Consent for viable neonates. See Section 11.D. (Children)

11.B.3. Research involving, after delivery, the placenta, the dead fetus or fetal material.

Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities.

If information associated with material described in this section is recorded for research purposes in a manner that individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent regulations are applicable.

11.C. Prisoners

Consult 45 CFR 46 Subpart C (Sections 301, 302, 303, 304, 305 and 306)

Prisoners as defined by HHS regulations are any individuals involuntarily confined, detained, or incarcerated in a penal institution or other alternative facility (by virtue of statuses or commitment procedures) and individuals detained pending arraignment, trial, or sentencing.

OHRP does not automatically consider a person under a court order to be a “prisoner” under Subpart C. Study participants on parole or probation are NOT considered to be prisoners under Subpart C. Persons in post-release criminal justice halfway houses are presumptively NOT considered by OHRP to fit the Subpart C definition of prisoners. This is dependent upon whether detainment or confinement is voluntary.

The only categories of research permitted with prisoners are:

1) Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

2) Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

3) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction and sexual assaults) provided that the study may proceed only after the Secretary of Health and Human Services (HHS) has consulted with appropriate experts including experts in penology, medicine and ethics, and published notice in the Federal Register of his intent to approve such research;
4) Research on practices, both innovative and accepted, that have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups that may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine and ethics, and published notice in the Federal Register of his intent to approve such research.

The IRB must make the following findings during its review in order to approve the research:

1) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
2) The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
3) The procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless you provide to the IRB justification in writing for allowing some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;
4) The information is presented in language that is understandable to the participant population;
5) Adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and
6) Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing participants of this fact.

What happens if a human subject becomes a prisoner during the course of a research study?

If a human subject involved in ongoing research becomes a prisoner during the course of the study, and the relevant research proposal was not reviewed and approved by the IRB in accordance with the requirements for research involving prisoners under subpart C of 45 CFR part 46, the investigator must promptly notify the IRB. All research interactions and interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must be suspended immediately, except as noted below. Upon receipt of the investigator’s report that a previously enrolled research subject has become a prisoner, if the investigator wishes to have the prisoner subject continue to participate in the research, the IRB must promptly re-review the proposal in accordance with the requirements of subpart C, and the institution(s) engaged in the research involving the prisoner subject must send a certification to OHRP and wait for a letter of authorization in reply when federal funds support the research. Otherwise, the prisoner subject must stop participating in the research, except as noted below.

OHRP allows one important exception to the requirement that all research interactions or interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must cease until the regulatory requirements for research involving prisoners are met. In special circumstances in which the investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated, the subject may continue to participate in the research until the requirements of subpart C are satisfied. The investigator must promptly notify the IRB of this occurrence, so that the IRB can re-review the study. Note
that in these circumstances, some of the findings required by 45 CFR 46.305(a) may not be applicable; for example, the finding required under 45 CFR 46.305(a)(4) regarding the selection of subjects within the prison may not be applicable, if the subject was recruited outside of an incarcerated context. The IRB will need to document findings of non-applicability accordingly.

When preparing for an amendment to your protocol to request the continuation of a research subject who has become a prisoner, it is unlikely that previous review of the research and the consent document contemplated the constraints imposed by incarceration. In this case, an amendment that includes appropriate justification (benefits to the individual outweigh the additional risks due to incarceration) should be written including specific examples of benefits to the individual prisoner-subject. As part of the submission a consent addendum that the now prisoner-subject will need to sign in addition to the original consent must also be submitted for review and approval.

11.D. Children

Research that is allowable with children is determined by the degree of risk involved. These categories of allowable research are:

1) No greater than minimal risk where adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

2) Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects, if the IRB finds that:
   a. The risk is justified by the anticipated benefits to the subjects;
   b. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; AND,
   c. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

3) Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition, if the IRB finds that:
   a. The risk represents a minor increase over minimal risk;
   b. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations;
   c. The intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the subject's disorder or condition; AND
   d. Adequate provisions are made for soliciting assent of the children and permission of the parents or guardians.

4) Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children if:
   a. The IRB finds the above to be true; AND
   b. The Secretary of HHS, after consultation with a panel of experts in pertinent disciplines has determined:
      1. The research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children is present;
      2. the research will be conducted in accordance with sound ethical principles;
      3. adequate provisions are made for soliciting the assent of children and
NOTE: The regulations define **Minimal Risk** as the risks of harm anticipated in the proposed research are not greater, considering the probability and magnitude, than ordinarily encountered in the daily life of the research subject, or during the performance of routine physical or psychological examinations or tests. Physical, psychological, social, legal or other risks should be assessed/considered.

**Children Who Are in State Custody**

Children who are wards of the State or any other agency, institution, or entity may be included in research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition, only if such research is:

1. Related to their status as ward; or

2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

If the research meets the condition(s) above, an advocate should be appointed for each child who is a ward (one individual may serve as advocate for more than one child), in addition to any other individual acting on behalf of the child as legal guardian or in loco parentis.

The advocate should be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child’s participation in the research and who is not associated in any way (except in the role as advocate) with the research, the investigators, or the guardian organization. The advocate does not provide informed consent, that is only provided by the legal guardian as determined by DCF.

**Consent:**

The consent process of children should meet the following Requirements for Assent and Parental Permission:

For research in the categories “Research involving greater than minimal risk…” and “Research otherwise not approvable...” permission is to be obtained from both parents, unless one parent is deceased, unknown, incompetent or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

The IRB may determine that the permission of one parent is sufficient for research not involving greater than minimal risk or for research that does involve greater than minimal risk, but presents the prospect of direct benefit to individual subjects.

*** The assent of a child is not a necessary condition for proceeding with the research if the IRB finds that the capability of some or all of the children is so limited that they cannot be reasonably consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research. Permission of the parents/guardians is still a requirement.

**Waiver of Consent (and HIPAA Authorization if PHI is involved):** If the IRB determines that a research protocol is designed for conditions or for a subject population, for which parental or guardian permission is not a reasonable requirement to
protect the subjects (for example, neglected or abused children), the IRB may waive the consent requirements, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risks and anticipated benefits to the research subjects, age, maturity, and condition.

**NOTE:** The FDA does not typically allow for a waiver of consent when regulated test articles are being used. In the case of emergency care treatment, (not research in an emergency setting) a waiver will be considered, see section 8.B.5.

**Exemptions:** The following are examples of research with children considered "exempt" from a formal Committee review. This research, though considered exempt from formal review, does require IRB review to determine whether the rights and welfare of the children participating as subjects are adequately protected. See additional information on "exempt" research, Section 7.C.

- **a.** 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. (Exemption Category #1)

- **b.** Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), 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. (Exemption Category #2)

- **c.** 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. (Exemption Category #4)

- **d.** Research involving the observation of public behavior is in the exempt category only if the investigator does not participate in the activities being observed. (Exemption Category #2)

OHRP has a new set of Frequently Asked Questions (FAQs) to help clarify issues related to research involving children. You may access these FAQs from their website.

**11.E. Non-English Speaking Individuals**

The Common Rule (45 CFR 46.116), states “the information that is given to the subject or representative should be in language understandable to the subject or the representative.”

Please reference Section 8.B.3. FAQs are under development.

**11.F. Cognitively Impaired Individuals**

There are no specific federal regulations concerning the inclusion of cognitively impaired or mentally disabled subjects. These vulnerable subjects have the same rights as other individuals to participate in research, but special care must be taken to ensure adequate informed consent. Some research protocols involving the cognitively impaired specifically focus on their special...
problems. Examples include, but are not limited to, patients with dementia, schizophrenia, delirium, mental retardation, bipolar disorder and stroke. Other protocols may include a variety of subjects and only incidentally include individuals with questionable capacity to consent. In either case, special considerations should be made to ensure that the informed consent process is adequate and appropriate.

It is important to recognize when a prospective subject is of questionable capacity to consent. If an investigator either knows or suspects that a subject falls into this category, the investigator or designee must determine whether the individual is able to give informed consent. The specific procedures used to determine competence to give informed consent must be described in the protocol if the investigator anticipates enrolling subjects with questionable capacity to consent. If the subject is not able to give informed consent, then the investigator must determine whether there is a legally authorized representative for the subject and/or a family member who is usually involved in decisions about his/her health and other important matters. These guidelines apply to both therapeutic (with potential direct benefit to the subject) and non-therapeutic (no direct benefit).

"Legally Authorized Representatives" for Provision of Consent for Research

See Section 8.B. Definitions for a list of "legally authorized representatives" who may be allowed to provide informed consent for individuals unable to provide consent for themselves.

Guidelines for Obtaining Informed Consent from Individuals with Questionable Capacity to Consent

When therapeutic research represents an appropriate treatment option in the opinion of the health care provider, a policy that creates an obstacle to the conduct of that research activity is ethically unsound. With the above issues in mind, the Committee has established the following policy for research studies that may involve adult subjects who are not competent to give informed consent for participation in a research study.

When a study involves subjects who are not competent to give informed consent, the investigator must identify whether he/she plans to allow his/her legally authorized representative to consent to participation in the research study. Specifically, the investigator must inform the Committee if he/she would like to consider a next-of-kin as the legally authorized representative with the ability to provide permission for an incompetent individual to participate in research study.

When an investigator proposes use of a legally authorized representative to consent for participation in a research study involving a subject who is not competent to give informed consent, the investigator must consider the following questions as part of the protocol submission:

1) Could the subject receive the same clinical management that he/she would receive in the research study outside the setting of a research protocol?
2) Will participation in the study increase the risk of harm or discomfort compared to what is expected with the management that the subject would receive if he/she did not participate in the research study?
3) Could this study be practicably done without the use of next-of-kin consent? If not, why not?
4) Will participating in the study provide a reasonable chance that the subject would experience a favorable outcome compared to what would be expected with the management that the subject would receive if he/she did not participate in the research study?
5) What is the magnitude of the benefit that future patients, or society in general, may experience as a result of the subject participating in this study?
6) Would the process of appointing a legal guardian, which may take several months, compromise patient care?

NIH guidance notes the importance of respecting the autonomy of individuals with impaired decision making capacity. The Committee concurs that these individuals’ assent to participation must be obtained whenever possible and their decision to withdraw from a study at any time must be honored. It is also important to keep in mind that decision making capacity may fluctuate, requiring ongoing assessment during the course of the research; thus the consent process should be ongoing.

If a legally authorized representative consent for participation in a research study is used for a subject who was temporarily not competent to give informed consent, whenever possible, the subject should be debriefed when he/she does become competent.

Even with the permission of the legally authorized representative, it is unlikely that the Committee will permit a cognitively impaired subject who is not competent (to give informed consent) to participate in a research study that offers little chance of DIRECT BENEFIT to the research subject over what he/she would receive outside the research setting, and involves more than minimal risk of harm or discomfort, regardless of the potential gain to future subjects or society in general.

When there is a meaningful chance of DIRECT BENEFIT to the cognitively impaired research subject over what he/she could receive outside the research setting, the Committee will decide who may consent to participation in the study.

Additional Requirements for Use of "Next-of-Kin" Consent in Research involving Subjects with Questionable Capacity to Consent:

Requirements for use of next-of-kin in research involving subjects with questionable capacity to consent:

1) No subject will be entered into the protocol if there is not consensus amongst all kin who have been contacted.
2) The determination of appropriate "legally authorized representative" will be made in accordance with the standard practices used in provision of medical care.
3) Detailed documentation of all attempts to obtain consent from the patient and/or the patient's legally authorized representative will be kept.

This guidance clarifies the Committee’s interpretation of what constitutes informed consent from a subject's "legally authorized representative" and does NOT constitute a waiver of consent.

12. Investigational Drugs (including Biologics) and Devices

Food and Drug Administration (FDA) regulations that govern the use of investigational drugs, devices, or biological products (a biologic is a preparation, such as a drug, a vaccine, or an antitoxin, that is synthesized from living organisms or their products and used as a diagnostic, preventative, or therapeutic agent) in human subjects are substantially similar to the HHS regulations as outlined in these Guidelines. However, they have some requirements for approval, record keeping and reporting that are more rigid than HHS. The FDA audits projects and inspects files, including subject records and, for this reason, subjects must be informed (in the consent form) that FDA may inspect their research records.

12.A. Research Involving Investigational Drugs
12.A1. Definition of an Investigational Drug from the FDA Regulations:
   a. A new drug in any of the clinical phases of evaluation which has not been released by the FDA for general use or cleared for sale in interstate commerce.
   b. A drug that is commercially available in the U.S. may be considered investigational and require that an investigational new drug (IND) form be filed with the FDA if the proposed use involves a controlled study aimed towards seeking a significant change in the labeling, advertising, route of administration, dosage level, or other factor that affects the risks associated with the use of the product.
   c. Drugs which are not on the Hospital Formulary and are to be dispensed within the context of research protocols will also be considered “investigational”.

12.A2. Use of Approved Drugs for Off-Label Indications:

12.A2.a. Investigational Purposes:
   If an investigator is using an approved drug in the context of a study protocol (i.e., to gather data for the purpose of changing the drug’s labeling) then the investigation would be subject to IRB review and approval, including informed consent requirements and may also be subject to regulation by the FDA.

12.A2.b. Non-Investigational Purposes:
   If a physician prescribes a marketed drug for an indication not in the approved labeling, s/he has the responsibility to be well informed about the product and to base its use on a firm scientific rationale and on sound medical evidence, and to maintain records of the products and its effects. However, use of a product in this manner as part of the practice of medicine, where no data will be gathered for research purposes, does not require the approval of the IRB.

12.A3. Expanded Access of Investigational Drugs (also sometimes referred to as compassionate use):

Investigational products are sometimes used for treatment of serious or life-threatening conditions either for a single subject or for a group of subjects. The procedures that have evolved for an investigational new drug (IND) used for these purposes reflect the recognition by the Food and Drug Administration (FDA) that, when no satisfactory alternative treatment exists, subjects are generally willing to accept greater risks from test articles that may treat life-threatening and debilitating illnesses. The following mechanisms expand access to promising therapeutic agents without compromising the protection afforded to human subjects or the thoroughness and scientific integrity of product development and marketing approval.

If a researcher wishes to treat a patient who is eligible to receive an expanded access investigational drug, the IRB must be notified immediately. The IRB has the ability to convene a special meeting to review and approve these types of protocols (aka compassionate use) in an expeditious manner. The IRB will need to know the timeline for treatment, and be provided with a protocol (which can be from the sponsor or investigator written), a consent (which can be developed from either the sponsor template or the IRB template), and, information about the drug.

   These are usually uncontrolled studies, carried out to obtain additional safety data (Phase 3 studies). They are typically used when the controlled trial has ended and treatment is continued so that the subjects and the
controls may continue to receive the benefits of the investigational drug until marketing approval is obtained. These studies require prospective Institutional Review Board (IRB) review, and informed consent.


The treatment IND [21 CFR 312.34] is a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. A treatment IND may be granted after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks. Because data related to safety and side effects are collected, treatment INDs also serve to expand the body of knowledge about the drug.

There are four requirements that must be met before a treatment IND can be issued:

1) the drug is intended to treat a serious or immediately life-threatening disease (defined as the stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment, e.g., advanced cases of AIDS, advanced congestive heart failure, advanced MS);
2) there is no satisfactory alternative treatment available in the intended patient population;
3) the drug is already under investigation, or trials have been completed; and
4) the trial sponsor is actively pursuing marketing approval.

Physicians should first ensure that the manufacturer of the unapproved drug is willing to provide the drug. If the manufacturer agrees to provide the drug, the physicians then must submit an IND application to the appropriate review division at FDA. See the FDA guidance on “Physician Request for an Individual Patient IND under Expanded Access for Non-Emergency or Emergency Use”.

Individual patient treatment INDs require prospective IRB review and informed consent. The IRB will need to know the urgency of the request, and for review, the eIND application, the proposed consent, and procedures for treatment.


The need for an investigational drug may arise in an emergency situation that does not allow time for submission of an IND in the usual manner. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND. In such cases, FDA may authorize shipment of the drug for the specified use [21 CFR 312.36]. Such authorization is usually conditioned upon the sponsor filing an appropriate application as soon as practicable.

Prospective IRB review is required unless the conditions for exemption are met [21 CFR 56.104(c) and 56.102(d)]. Informed consent is required
unless the conditions for exception are met.

See additional FDA guidance at “Physician Request for an Individual Patient IND under Expanded Access for Non-Emergency or Emergency Use”.

NOTE: Data derived from an emergency use before IRB approval may not be used for research purposes (the use was for medical care, not research), but safety information should be reported to the FDA or the manufacturer as appropriate.

POLICY: GUIDELINES FOR EMERGENCY USE OF AN INVESTIGATIONAL DRUG OR BIOLOGIC OR INVESTIGATIONAL DEVICE – updated 7/14/11

The following are guidelines for obtaining emergency exemption from prospective IRB approval.

1. The proposed use must meet the following definition from the FDA regulations:

   "Emergency use means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval." 21 CFR 56.102(d)

2. If the proposed use meets this definition, the investigator must contact the IRB office to request approval to proceed with the administration of the test article.

   **During normal business hours:**

   The investigator should contact the Research Protections Office at 656-5040 and identify the issue as an emergency use exemption.

   **Outside of normal business hours:**

   1. David Kaminsky, M.D., CHRMS Chair
   2. Alan Homans, M.D., Executive Chair

3. The IRB Chair or his/her designee will want to speak with the investigator regarding the request. The information that will be required is as follows:

   a. Basic clinical information about the proposed use.
   b. Information regarding the status of the emergency IND or IDE that will cover this use (either existing protocol, company IND or IDE or through FDA directly).
   c. Whenever possible, a copy of the consent form to be used is requested in advance (generally a standard form exists and the IRB does not require that it be put into the usual institutional format for an emergency use). The IRB has a consent template located on its forms page for use.
   d. If obtaining informed consent is not possible from the subject or the subject's legally authorized representative, the investigator and a physician not otherwise involved, must certify in writing that the following four conditions have been met:
• the subject is confronted by a life-threatening situation necessitating the use of the test article;
• informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
• time is not sufficient to obtain consent from the subject's legal representative; and
• no alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life” (21 CFR 50.23(2)).

If, in the investigator's opinion, immediate use is required to preserve the subject's life and if time is not sufficient to obtain an independent physician's determination that the four conditions apply, within 5 working days after the use of the article, the investigator must have the use reviewed and evaluated in writing by an independent physician to evaluate whether the four conditions were met. **Form is located on the web page under Medical (CHRMS) Committee Review.**

4. If the IRB Chair or his/her designee has no concerns about any of the above, concurrence to proceed with the use of the article will be given. This concurrence to proceed does not imply that IRB review and approval has occurred. It is a confirmation that the proposed use meets the guidelines for emergency exemption from prospective IRB approval.

5. The investigator must provide a follow-up report to the IRB within 5 working days of the use of the article. **Use form in Attachment A.**

6. In accordance with FDA regulations, no subsequent use of that investigational drug or biologic or investigational device will be permitted at this institution without a full review by the IRB.

---

12.A.3.d. **Group C Treatment IND**

The "Group C" treatment IND was established by agreement between FDA and the National Cancer Institute (NCI). The Group C program is a means for the distribution of investigational agents to oncologists for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are generally Phase 3 study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can generally be administered by properly trained physicians without the need for specialized supportive care facilities. Group C drugs are distributed only by the National Institutes of Health under NCI protocols. Although treatment is the primary objective and patients treated under Group C guidelines are not part of a clinical trial, safety and effectiveness data are collected. Local IRB review and approval is required for these studies.

12.A.3.e. **Parallel Track**

The FDA's Parallel Track policy [57 FR 13250] permits wider access to promising new drugs for AIDS/HIV related diseases under a separate "expanded access" protocol that "parallels" the controlled clinical trials that are essential to establish the safety and effectiveness of new drugs. It provides an administrative system that expands the availability of drugs for treating AIDS/HIV. Local IRB review and approval is required for these studies.

12.B. **Research Involving Medical Devices**

12.B.1. **Definition of an Investigational Device**

Investigational devices are medical devices which are the object of clinical research to
determine their safety or effectiveness. Studies undertaken to develop safety and effectiveness data for medical devices involving human subjects must be conducted according to the requirements of the Investigational Device Exemption (IDE) regulations (21 CFR 812). Investigational devices are classified as either significant risk or non-significant risk devices.

12.B.1.a. Non-Significant Risk Device
A non-significant risk device is one that does not present a potential for serious risk to the health, safety, or welfare of the subject. Examples of non-significant risk devices are: most daily wear contact lenses, lens solutions, heel cups, antibacterial surgical garments, incontinence devices, oral training splints, and ultrasonic tooth cleaners. Unless otherwise notified by FDA, an investigation of a non-significant risk device is considered to have an approved IDE if the sponsor fulfills the abbreviated requirements of the IDE regulations. These regulations require, in part, that IRB approval be obtained and maintained throughout the investigation and that informed consent be obtained and documented.

12.B.1.b. Significant Risk Device
A significant risk device is one that presents a potential for serious risk to the health, safety, or welfare of the subject. Such a device is intended as an implant; is to be used in supporting or sustaining human life; or is of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health. Examples of significant risk devices are catheters (other than urological), ventilators, CPR devices, TMJ prostheses, stents, lithotripters, sutures and absorbable bandages/materials, ECT devices, extended wear contact lenses, pacemakers, contraceptive devices, most laser systems, and most hemodialysis systems. Investigations involving significant risk devices must meet the full IDE requirements including the submission of an IDE application to the FDA. As with non-significant risk devices, IRB approval is required prior to conducting clinical trials of the investigational device.

12.B.2. IRB Review of Investigational Device Protocols
In addition to determining whether a study should be approved, the IRB will also determine whether the device presents significant or non-significant risk.

In deciding if a device presents significant or non-significant risks, the IRB will consider the device’s total risks, and not compare these with the risks of alternative devices or procedures. If the device is used in conjunction with a procedure involving risk, the IRB will consider the risks of the procedure in conjunction with the risks of the device.

Once a decision on the degree of risk is reached, the IRB will consider whether the study should be approved or not. Some studies involving non-significant risk devices may also be considered minimal risk studies and thus may be reviewed through the expedited review procedure established by the IRB. FDA considers studies of all significant risk devices to present more than minimal risk; thus, IRB review at a convened meeting is required for all studies involving significant risk devices. In considering whether a study should be approved, the IRB will use the same criteria it would use in considering approval of any research involving an FDA-regulated product. In considering the risks of the device, the IRB will not simply judge the increase in risk over standard treatment, but rather the risk of the procedure as a whole. The IRB will consider the risks and benefits of the test medical device compared to the risks and benefits of alternative devices or procedures in deciding the approvability of a study.
# 12.C. Humanitarian Use Devices

## POLICY: Guidelines for Treatment Use Humanitarian Use Devices

Revised 09/21/11  Original policy 1/15/03

### Background Information (quoted from FDA guidelines):

On June 26, 1996, FDA issued a final rule to carry out provisions of the Safe Medical Devices Act of 1990 regarding humanitarian use devices (HUDs). This regulation became effective on October 24, 1996. **An HUD is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year.** A device manufacturer's research and development costs could exceed its market returns for diseases or conditions affecting small patient populations. FDA, therefore, developed and published this regulation to provide an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting these populations.

The regulation provides for the submission of an humanitarian device exemption (HDE) application, which is similar in both form and content to a premarket approval (PMA) application, but is exempt from the effectiveness requirements of a PMA.

An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Additionally, the applicant must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that they could not otherwise bring the device to market.

An approved HDE authorizes marketing of the HUD. **However, a HUD may only be used after IRB approval has been obtained for the use of the device for the FDA approved indication.** The labeling for an HUD must state that the device is an humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.

### Initial and Continuing Review

The proposed use of the humanitarian use device must be reviewed and approved at a convened meeting of the IRB, in accordance with the FDA's "Final Guidance for Industry."

FDA recommends the use of an expedited procedure for subsequent continuing reviews because a HUD is a legally marketed device and no safety and effectiveness information is being collected systematically, as is required for a research protocol.

### Consent

Prospective consent is not always attainable or necessarily in the best interest of the patient in these cases. Often, the use of the particular HUD is not anticipated yet does not meet the criteria for an "Emergency Use" either. FDA regulations and guidance leave it to the discretion of the local IRB whether or not to require prospective written consent. Thus, the Committee concluded that written consent for all HUD protocols is no longer required. Physicians should document consent in the medical chart whenever possible.

### Reporting/Administrative Requirements:

1. Submit any proposed changes to the protocol for approval prior to initiation on the Committees on Human Research "Request for Modification/Amendment to Approved Protocol" form.
2. Report adverse events and unanticipated problems to subjects or others related to the use of the device to the IRB and the sponsor in accordance with FDA regulations and UVM/UVM Medical Center Adverse Event and Unanticipated Problems Reporting Policy and Procedures.
3. Complete and submit continuing review forms as requested (at least once annually). Attach
Using HUDs in Compassionate Use Situations

If a HUD is used outside its approved indication(s), FDA recommends that the physician obtain informed consent from the patient and ensure that reasonable patient protection measures are followed, such as devising schedules to monitor the patient, taking into consideration the patient's specific needs and the limited information available about the risks and benefits of the device. FDA further recommends that the physician submit a follow-up report on the patient's condition to the HDE holder.

In such circumstances, the physician shall, after the use of the device, notify the Committee of the use within five working days. The date on which the device was used, along with the reason for the use should be reported using the “Unanticipated Problem Potentially Involving Risk…” form.

Using HUDs in Emergency Use Situations

If a HUD is used in an emergency situation and consent is unable to be obtained then the Committee’s policy on waiver of consent for emergency use is applied, see policy POLICY: GUIDELINES FOR EMERGENCY USE OF AN INVESTIGATIONAL DRUG OR BIOLOGIC OR INVESTIGATIONAL DEVICE.

13. Multi-Institutional Research Studies

13.A. Managing IRB Review in Collaborative Research Studies

The University recognizes that investigators frequently collaborate with researchers from outside of the University when designing and/or conducting human research and that such collaboration is vital to maintaining the University’s robust research program. Research may extend beyond the boundaries of a single institution to encompass other academic entities, community organizations and agencies, local medical practices, and/or non-affiliated individuals whose expertise is needed for the effective conduct of a study.

Whenever the University will engage institutions or individuals not otherwise affiliated with the University in human research, appropriate written agreements with the collaborating institution or investigator will be obtained to ensure that all University human research is conducted in accordance with IRB approval and oversight requirements. Under such agreements, the University may choose to provide IRB oversight to the project or to rely on the oversight of another federally registered IRB.

Definitions

Assured (Federally Registered IRB) Institution
An institution with a Federalwide Assurance (FWA) that is approved by the Office for Human Research Protections (OHRP).

Collaborating Investigator
An individual who is conducting collaborative research activities with a UVM/UVM Medical Center investigator, but is not an employee or agent of either UVM/UVM Medical Center

Engagement in Research
An individual is considered engaged in human research when he/she for the purposes of the nonexempt research project, obtains: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research. An institution is considered engaged when its employees or agents conduct the above activities, or when the
institution receives a direct federal award to conduct human subject research, even when all activities involving human subjects are carried out by a subcontractor. See Appendix J.

**Federalwide Assurance (FWA):**
A formal written, binding attestation in which an institution assures to DHHS that it will comply with applicable regulations governing research with human subjects.

A formal, written, binding agreement in which UVM agrees to serve as the IRB for another institution or vice versa. The IAA sets out terms and conditions for the institutions.

**Individual Project Agreement (IPA)**
A formal, written, binding agreement in which UVM agrees to serve as the IRB for another institution, when the other institution either has no IRB or the IRB is not federally registered. The IPA sets out terms and conditions for the institutions.

**Institutional Support Letter (e.g., schools, nursing homes)**
A letter signed by an executive director, chief executive officer, board president or other individual with authority to commit the institution’s resources, acknowledging the proposed research activity, and granting permission for the engagement of their employee and facilities (if applicable) in that activity. A template of our support letter is located in our forms page.

13.A.1. Institutions Without an IRB Engaged in Federally Funded Research
When institutions engaged in federally funded research do not have an IRB, or are not affiliated with an IRB, it may be in the interest of both UVM/UVM Medical Center and the institution to establish a research partnership whereby UVM/UVM Medical Center will provide IRB oversight for research involving the other institution. In such cases, the institution would file a Federalwide Assurance with OHRP designating UVM/UVM Medical Center as the institution’s IRB of record and would enter into an IRB Authorization Agreement with UVM/UVM Medical Center. This affiliation may be for a single protocol, several protocols, or for all research conducted by the other institution.

13.A.2. Institutions Without an IRB Engaged in Non-Federally Funded Research
When institutions without a federally registered IRB or FWA are engaged in non-federally funded University human research, UVM/UVM Medical Center will enter into an Individual Project Agreement with the institution who will be investigators or study personnel for the research.

13.A.3. Institutions With an IRB
When a research protocol is to be conducted with another institution and that institution has an IRB that is registered with OHRP, there are a couple of options. Each respective IRB can review the protocol, with the lead site obtaining IRB approvals from the other institution. UVM/UVM Medical Center and the other institution may enter into an IRB Authorization Agreement, naming either UVM/UVM Medical Center or the other institution as one of the IRBs of record for the study. This option may eliminate the need for multiple protocol reviews. Agreements may be made for single or multiple projects. In such agreements, UVM/UVM Medical Center IRBs may serve as IRB of record, or UVM/UVMMC may designate another federally registered IRB as IRB of record.

When an individual is proposed to be involved in the conduct of a UVM/UVM Medical Center human research study and the individual is not affiliated with an IRB, he or she must enter into an Individual Project Agreement.
13.A.5. Collaborative Research Studies FLOWCHART

Is there an IRB?

---

YES

Does the Collaborator have a Federally Registered IRB associated with a FWA?

---

YES

A. The outside Collaborator’s local IRB would be the IRB of Record and reviews and approves the research. UVM’s IRB also needs to conduct their local review. Collaborator needs to send the UVM/FAHC IRB a copy of their local IRB approval prior to research activities.

---

NO

B. The outside Collaborators may want to rely on the outside Collaborator’s IRB for review and approval of the research. Contact the IRB for assistance with this process as this would require the execution of an IRB Authorization Agreement between the FWA institutions outlining research responsibilities and amending the respective FWA to rely on that IRB.

---

NO

C. UVM/FAHC investigators may want to rely on the outside Collaborator’s IRB for review and approval of the research. Contact the IRB for assistance with this process as this would require the execution of an IRB Authorization Agreement between the FWA institutions outlining research responsibilities and amending the respective FWA to rely on that IRB.

---

NO

D. If the IRB is not Federally Registered (does not have a FWA), and there is no federal funds supporting the research, the collaborators could rely on the UVM/FAHC IRB with the execution of an Individual Project Assurance and a Memorandum of Understanding. Contact the IRB for this paperwork.

---

If there is no IRB and there is federal funding supporting the research, the Collaborators need to apply for a FWA and could rely on the UVM/FAHC IRB with the execution of an agreement outlining research responsibilities and a Memorandum of Understanding. Contact the IRB for this paperwork.

---

If there is no IRB and there is no federal funding supporting the research, the Collaborators could rely on the IRB of Record and reviews and approves the research. UVM’s IRB also needs to conduct their local review. Collaborator needs to send the UVM/FAHC IRB a copy of their local IRB approval prior to research activities.
13.B. Non-Collaborative Research and IRB Review

The IRB is often approached by outside entities or individuals to act as the IRB of record for their specific project. The IRB does not usually provide services to non-UVM or non-UVM Medical Center entities or individuals when there is no collaborative relationship with researchers at UVM or UVM Medical Center as discussed above. We discourage this practice primarily due to challenges in monitoring non-institutionally based projects. We encourage outside entities to utilize an independent IRB as it is their purpose to provide service to non-local or unrelated entities. There are many independent IRBs and they often have a variable fee dependent upon the level of risk for the project. Here is a link to a list of possible external IRBs http://www.consortiumofirb.org/cirb_members.htm.

13.C. UVM/UVM Medical Center Researcher as the Lead PI in a Multi-Institutional Study

When a UVM/UVM Medical Center investigator is the PI on a multi-site study, the UVM/UVM Medical Center investigator is responsible for the overall conduct of the study. The IRB will determine and document that the operations center has sufficient mechanisms in place to ensure the following;

1. That management, data analysis, and Data and Safety Monitoring (DSM) systems are adequate, given the nature of the research involved;
2. Sample protocols and informed consent documents are developed and distributed to each collaborating institution;
3. Each collaborating institution holds an applicable OHRP-approved Federalwide Assurance (FWA) if applicable;
4. Each protocol is reviewed and approved by the IRB at the collaborating institution prior to the enrollment of subjects;
5. Any substantive modification by the collaborating institution of consent information related to risks or alternative procedures is appropriately justified;
6. Informed consent is obtained from each subject in compliance with federal regulations; and
7. The privacy of subjects and confidentiality of data are adequately maintained.

The investigator must initially;

1. Develop an operations center protocol;
2. Develop an operations center procedure manual;
3. Negotiate and execute agreements with each site (UVM SPA must be involved);
4. Submit the “Common Protocol Cover” form, “Operations Center Activities Supplement” form along with numbers 1-3 to the UVM/UVM Medical Center IRB for review.

For ongoing oversight the investigator must submit to the IRB;

1. DSM minutes or DSMB reports as they are complete (reports should discuss safety information gathered to date);
2. If a site has been audited, a copy of report from the visit must be forwarded;
3. Any site protocol deviations or noncompliance that suggests potential to harm subjects must be submitted as they are identified (copy of local site report is sufficient);
4. Continuing review materials must be submitted as requested.
POLICY: Requirements for Conducting Multi-Institutional Studies when UVM/UVM Medical Center is the Operations Center (OC) 12/21/09

Replaces Policy: INSTITUTIONAL REVIEW BOARD (IRB) GUIDELINES FOR MULTI-INSTITUTIONAL STUDIES ORIGINATING AT AND/OR UNDER THE LEADERSHIP OF UVM/UVM Medical Center

This section provides an overview of the processes and oversight an Operations Center should have in place to ensure proper study management of a multicenter clinical trial. These elements must be addressed either in the protocol or in a study operations manual. Deviations from these elements will be reviewed on a case-by-case basis.

Purpose and Function of Operations Center (OC)

The OC provides administrative, data management, and organizational support in the conduct of the multi-center trial. Follows is a list of responsibilities:

- Central location for all trial documents
- Initial IRB protocol review and approval
- Distribution of approved protocol materials to participating sites
- Process for central subject registration
- Process for submitting adverse events and unanticipated problems to the Primary Principal Investigator and appropriate oversight entities
- Coordinate staff training
- Facilitate monitoring and auditing visits for all participating sites

Primary Principal Investigator (PPI) Responsibilities

The PPI has the responsibility to monitor the progress and safety of the protocol across all participating sites. Follows are a list of responsibilities, some of which may be delegated back to the OC:

- Coordination and development of the protocol, and its subsequent amendments
- Study staff training
- Regulatory reporting requirements
- Timely review of all serious adverse events (SAE) reports from all sites
- Review of all study data submitted for analysis
- Regular communication with all participating sites
- May delegate authority for ongoing trial management

Note: A PPI who holds an IND is bound to the investigator and sponsor requirements written in 21 CFR part 312.

Participating Investigator Responsibilities

PIs are responsible for the conduct of the trial at their individual site. It is the responsibility of the site PI to ensure that his or her study team has the current version of the protocol and informed consent documents and that the study team is conducting the clinical trial within the guidelines of Good Clinical Practice. Additional responsibilities of the PI include:

- Designating a study coordinator and/or research nurse as the study contact
- Timely submission of data
- Prompt reporting of serious adverse events (SAEs) and unanticipated problems involving research to their local IRB and the OC.

Regulatory Binder

Each must compile a regulatory binder specific to its function. The documents should be maintained or updated, as appropriate, throughout the course of the trial. The OC will identify the required contents.
**Central Subject Registration**
The OC serves as the central location for registering all subjects enrolled. Subject registration requires a registration checklist and copy of the signed informed consent. The OC will maintain a subject registration list and copies of the above for each participating site.

**Adverse Event Reporting**
The PPI is responsible for the timely review of all SAE reports to assure the safety of subjects. The OC is the central location for the collection and maintenance of adverse event documentation and promptly submits SAE report to the PPI.

The OC maintains documentation of all adverse events for each site. Each site maintains its own documentation as required.

All adverse events must be reported as outlined in the protocol. Participating sites may need to report adverse events to their own IRB as well as to the OC.

Note: A PPI who is the IND holder is ultimately responsible for reporting to FDA.

**Data Collection**
The participating sites should submit case report forms (CRFs) to the OC according to the protocol. Sites should be aware that they might need to send source documentation to the OC.

**Quality Assurance**
The PPI with support from the OC is responsible for the integrity and accuracy of data collected at each participating site. The monitoring and auditing plans should be based on the complexity and risk level of the trial. Typical monitoring and auditing visits may include review of original consent forms, case report forms and source documentation, treatment administration records, protocol compliance, and drug accountability. Sites should be aware that they might be audited by the OC in addition to any oversight delegated to an external Contract Organization.

Note: The participating site should notify the OC immediately they have been cited for an FDA audit.

**Site Communication**
The PPI and OC should have regular and documented communications with the participating sites to update and inform them about the progress of the trial.

**Drug Ordering**
Each participating site is responsible for the ordering, storing, and dispensing of investigational agent(s) from the sponsor or company that is supporting the trial.

**Inter-Institutional Agreement**
A formal agreement/contract is required for each protocol. The agreement must be reviewed and approved by SPA at UVM.
Attachment A

University of Vermont
Committees on Human Research

A: Emergency Use of an Investigational Drug, Biologic, or Device Certification of Compliance Form

Form is now located on the forms page under Medical (CHRMS) Committee Review.
B: POLICY – Attachment B is blank intentionally
Attachment C

C. POLICY – Fees for Committee on Human Research Review of Sponsored Trials

Updated: April 15, 2015    Effective Date: April 15, 2015

Policy
The University’s Institutional Review Boards (IRBs) charge fees for initial and annual continuing review for all University of Vermont (UVM) and University of Vermont Medical Center (UVMMC) studies sponsored by industry, pharmaceutical companies, and other for-profit entities, and to review protocols for organizations unaffiliated with UVM or UVMMC outside. Fees are not charged for University of Vermont or University of Vermont Medical Center federal or federal flow through, oncology group, non-profit, or departmentally-funded studies. The fee schedule is reviewed each year by the IRB and is subject to change.

Process Background
On July 1, 2009, the IRB ceased its practice of holding documentation of approvals until payment had been received from the sponsor. This change created a serious delay in sponsor payment. To correct this situation, effective April 16, 2010, the IRB reinstituted the practice of holding documentation of initial approvals until payment is received. This process change did not impact continuing review approvals. Documentation of continuing review approval is sent as soon as the review is complete.

IRB Fee Schedule (Effective July 1, 2009)
Initial review: $2,500.00  
Continuing review: $1,500.00  
Amendments: No Fee  
Adverse Events and Unanticipated Problems: No Fee  
Other actions: No Fee

Budgeting for IRB Fees
For industry-initiated projects, the University of Vermont Medical Center Office of Clinical Trials Research (OCTR) works with sponsors to include the IRB fees in project budgets during the proposal and award negotiation processes. For investigator-initiated, industry sponsored projects, OCTR works with UVM Sponsored Project Administration (SPA) to include the IRB fees in project budgets. OCTR identifies IRB fees and protocol start up fees as separate line items in a budget.

FAQ’s
When will the initial review fee be charged?
The initial IRB fee is invoiced for new protocols at the time the IRB receives them for review.

How are sponsors invoiced for IRB fees?
For industry-initiated projects, which are processed through OCTR, University of Vermont Medical Center Accounting invoices sponsors through Financial Edge. For investigator-initiated projects, which are processed through SPA, the Research Protections Office (RPO) prepares invoices for IRB fees and forwards them to the SPA billing/AR team. SPA invoices the sponsor according to the terms of the agreement and includes the IRB fees in the invoice. Upon receipt of sponsor payment, the SPA billing/AR team transfers the payment for IRB fees to an RPO chartstring.

What happens if the contract or study is not approved?
The fee is for IRB review of the protocol. If the IRB has reviewed the protocol, payment is expected regardless of contractual arrangements or review outcome.

When will the continuing review fee be charged?
The continuing review fees will be invoiced after the protocol has been reviewed and approved.
Note: If you have requested that a protocol be re-opened after it has been closed, a continuing review will be conducted at that time and the fee will be applied to that review regardless of when the prior review was conducted.

Will there be exceptions made to this policy?
Exceptions to this policy will be considered on a case-by-case basis by appropriate institutional officials. Requests for consideration must be submitted by the Principal Investigator or Sponsor in writing to the IRB. Requests for outright waiver of the fee must be received prior to protocol submission to the IRB.
Attachment D
D: Elements for De-Identification for Protected Health Information

1. Names
2. All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.

The population of a zip code can be identified on the web site of the U.S. Census Bureau at the following url: http://www.census.gov/popfinder/

3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
4. Telephone numbers
5. Fax numbers
6. Electronic mail addresses
7. Social security numbers
8. Medical record numbers
9. Health plan beneficiary numbers
10. Account numbers
11. Certificate/license numbers
12. Vehicle identifiers and serial numbers, including license plate numbers
13. Device identifiers and serial numbers
14. Web Universal Resource Locators (URLs)
15. Internet Protocol (IP) address numbers
16. Biometric identifiers, including finger and voice prints
17. Full face photographic images and any comparable images
18. Any other unique identifying number, characteristic, or code, except a code or other means of record identification that allows information de-identified to be re-identified by the covered entity, provided that:
   a. The code or other means of record identification is not derived from or related to information about the individual and is not otherwise capable of being translated so as to identify the individual; and
   b. The code or other means of record identification is not used or disclosed for any other purpose, and does not disclose the mechanism for re-identification.

And

No actual knowledge exists that the information could be used alone or in combination with other information to identify an individual who is a subject of the information.
Attachment E
E: Statement of Compliance for the Committees on Human Research

The University of Vermont
Committees on Human Research
Serving the University of Vermont and
University of Vermont Medical Center

Statement of Compliance

The Committees on Human Research (also known as the IRBs) conduct all of their activities in compliance with the Federal Policy for the Protection of Human Subjects (the Common Rule, codified for DHHS at 45 CFR 46) and consistent with the applicable Federal-Wide Assurances. In addition, the FDA-regulated studies, the activities are in compliance with the applicable sections of the Code of Federal Regulations (usually 21 CFR 50, 56, 812) and consistent with the ICH guidance GCP for IRBs, as it corresponds to the HHS and FDA regulations.

Alan Homans, M.D., Executive Chair  
Date 2/16/2016
Policy:

The IRB has developed a system for monitoring on-going research to ensure congruence with the IRB-approved protocol and compliance with applicable human subject protection guidelines and regulations. The IRB is committed to administering a process that is educational for the personnel involved in the human subjects research, with the goal of fostering a collegial environment, and thus contributing to a culture of compliance.

Our monitoring program covers a sampling of all studies that are currently active. Highest priority is given to investigator-initiated studies that do not have other formal monitoring processes in place.

The monitoring process may include representatives from other institutional entities which oversee the specific protocol to be monitored. The IRB is currently collaborating with the University of Vermont Cancer Center (UVMCC) and with the Research Subject Advocate (RSA) Office of the Clinical Research Center (CRC).

The monitoring process includes a review to determine that:

1. the protocol on file with the IRB is the protocol being used and being followed;
2. all modifications have been submitted to and approved by the IRB and have been implemented;
3. the consent document being used is that which was approved by the IRB;
4. the consent forms are appropriately signed and dated; and
5. adverse event and unanticipated problem reporting guidelines are being followed.

Monitors:
- IRB Staff
- Others as necessary, i.e., IRB Chair, IRB Administrator, or other IRB member
- When appropriate, representative(s) from collaborating units, i.e., CRC RSA Office or UVMCC

Notice:
- Investigator will be given advance notice of the monitoring visit and a list of studies to be reviewed.
- A representative number of subject research files will be reviewed. Copies of any documents reviewed at the site visit may be requested at that time.
- Investigator and/or designee should be prepared to answer questions about the timing of procedures for the specific subjects identified.

Review:
Data will be reviewed to determine whether: 1) the signed consent forms were the correct version; 2) the date of informed consent corresponds with date of procedures; 3) approved protocol is being used; 4) amendments were approved and are being followed; 5) adverse reactions and unanticipated problems were reported according to IRB policy; and 6) other items deemed appropriate for review during collaborative monitoring visits are in compliance.

Possible Outcomes:
An immediate exit interview will be conducted with the principal investigator or his/her designee. After a preliminary report has been reviewed internally, a final report will be forwarded to the principal investigator. Categories of possible monitoring outcomes are as follows:

- Acceptable;
- Additional action required by Investigator; or
- Further Committee review required.
G: Guidance on Research Involving Coded Private Information or Biological Specimens

Version 5/5/05

1. Basic Policy

Research using private information or biological specimens that is categorized as "human subjects research" can only be conducted after receiving the appropriate Committee review under the normal established guidelines.

There is now federal guidance that clarifies the distinction between (a) research involving coded private information or specimens that does not involve human subjects and (b) human subject research that is exempt from the requirements of the Department of Health and Human Service (DHHS) regulations. The guidance also provides new definitions of key terms to assist in making these determinations because it fits into specific categories. When conducting research using data or specimens, the human subject determination noted above, the type of application, the informed consent requirements, and the level of review by the IRB depends primarily on one factor: whether the data or specimens are identifiable to the principal investigator or key personnel.

Determinations of whether research involving coded private information or biological specimens is considered to be "human subjects research" must be made by the IRB, not the investigator.

2. Definitions

**Human Subject:** The DHHS regulations "Protection of Human Subjects" (45 CFR Part 46, administered by the Office for Human Research Protections (OHRP) define human subject as a living individual about whom an investigator conducting research obtains:

data through intervention or interaction with the individual or identifiable private information

**Investigator:** The OHRP considers the term investigator to include anyone involved in conducting the research. OHRP does not consider the act of solely providing coded private information or specimens (for example, by a specimen repository) to constitute involvement in the conduct of the research. However, if the individuals who provide coded information or specimens also collaborate on other activities related to the conduct of the research with the investigators who receive such information or specimens, they will be considered to be involved in the conduct of the research. [OHRP’s Coded Specimen Guidance]

**Research:** HHS regulations define research at 45 CFR 46.102(d) as follows:
Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

**Obtains:** In its guidance for use of coded specimens, OHRP has determined that under the definition of human subject at 45 CFR 46.102(f), obtaining identifiable private information or identifiable specimens for research purposes constitutes human subjects research. Obtaining means receiving or accessing identifiable private information or identifiable biological specimens for research purposes. OHRP interprets obtaining to include an investigator’s use, study, or analysis for research purposes of identifiable private information or identifiable biological specimens.

**Intervention** includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes. (45 CFR 46.102(f))
Interaction includes communication or interpersonal contact between investigator and subject. (45 CFR 46.102(f))

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. (45 CFR 46.102(f))

Individually Identifiable Private Information: According to its guidance for use of coded specimens, OHRP generally considers private information or specimens to be individually identifiable as defined at 45 CFR 46.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. Conversely, OHRP considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Coded: With respect to private information or human biological specimens, coded means that:

(1) identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol or combination thereof (i.e., the code); and
(2) a key to decipher the code exists, enabling linkage of the identifying information with the private information or specimens.

3. Does Your Proposed Research Involve Human Subjects?

Regulatory requirements (Federal and state) to protect human subjects apply to a much broader range of research than many investigators realize, and researchers using data and/or specimens are often unsure about how regulations apply to their research. Regulatory obligations to protect human subjects would apply, for example, to research that uses –

1. Bodily materials, such as cells, blood or urine, specimens, organs, hair or nail clippings, from living individuals who are individually identifiable to the investigator(s), even if these materials were collected by others;

2. Residual diagnostic specimens from living individuals that are individually identifiable to the investigator(s), including specimens obtained for routine patient care that would have been discarded if not used for research;

3. Private information, such as medical information, about living individuals that is individually identifiable to the investigator(s), even if the information was not specifically collected for the study in question. This includes research on genetic information that can be readily associated by the investigator(s) with identifiable living individuals.

The definition of “human subject” includes, but is not limited to, human organs, specimens, and body fluids from living individuals, as well as private graphic, written, or recorded information about living individuals, if (1) there is interaction or intervention with a living individual to obtain the data or specimens for research purposes, or (2) the identity of the subjects can be readily ascertained by the investigator or other members of the research team.

Research that involves only coded private information/data or coded human biological specimens may not constitute human subjects research under the HHS human subjects
regulations (45 CFR Part 46) if:

1. The private information and/or specimens were not collected specifically for the currently proposed research project through an interaction/intervention with living individuals, **AND**

2. the investigator(s) (including collaborators) on the proposed research cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain (e.g., the researcher’s access to subject identities is prohibited by written repository procedures and policies and/or through an agreement signed between the recipient researcher and the repository providing the data or specimens).

Individuals who provide coded information or specimens for proposed research and who also collaborate on the research involving such information or specimens are considered to be involved in the conduct of human subjects research.

The same data/specimens may be identifiable or not for different researchers. For example, if Researcher A stores or receives data/specimens with a code number and has a key linking the numbers to subjects’ identities, the data/specimens are identifiable for Researcher A. On the other hand, if Researcher A passes the data/specimens to Researcher B and there is a written agreement that Researcher A will in no circumstances give identifying information to Researcher B, then for Researcher B’s research the data/specimens are not identifiable and not considered research involving human subjects.

4. **Who Determines Whether Human Subjects are Involved in Research**

   The decisions about when research involving data and/or specimens from subjects is considered human subjects research are complex. The project must be submitted to the IRB for this determination utilizing the form titled “Research Not Involving Human Subjects Review and Determination.”

5. **Retrospective versus Prospective Collection of Data or Specimens**

   The criteria the IRB must use to determine whether research involves human subjects under this policy are based on the following types of data/specimen collection methods and how the data/specimens are identified.

   **a. Retrospective data or specimens** are data or specimens that are already existing or "on the shelf" when the research is proposed. Specimens or data are considered existing only if they were gathered before the research is proposed. Example: Data previously collected for medical care or specimens that are left over from surgery or previous research studies.

   **Existing, Not Identifiable (i.e., not coded) data or specimens:** This category includes data or specimens obtained without identifiers from a data or specimen repository at UVM/UVM Medical Center or elsewhere. Research utilizing such existing coded data or specimens would not be considered “research with human subjects.” The investigator would need to complete and submit the “Research Not Involving Human Subjects Review and Determination” form.

   **Existing, Identifiable data or specimens:** This category includes data or specimens that can be individually identified with the patient/subject and therefore would be considered “human subject research.” This type of research may meet the federal criteria for exemption from IRB research. See guidance on exempt review in the Research Manual.
b. **Prospectively gathered data or specimens:** Conversely, data or specimens that will be taken from patients or subjects after proposal of the research are considered to be prospectively gathered.

**Prospectively Gathered, Not identifiable (i.e., not coded) data or specimens:** If you are prospectively obtaining data or specimens which are left over from another purpose (clinical, diagnostic procedures or another research study), and they are not individually identifiable (coded) to the investigator, it may be considered not “research with human subjects.”

**Prospectively Gathered, identifiable data or specimens:** If the data or specimens are to be gathered specifically for the research project, it is considered “human subject research” and would not qualify for exemption, however might qualify for expedited review. See Research Manual for guidance regarding expedited review.
H: Standards and Language for Studies Involving MRI

Revised 3/21/14

This document reflects standard procedures accepted by the IRB for research protocols involving magnetic resonance imaging (MRI) and functional MRI (fMRI). It provides guidelines for how to describe the procedures in the protocol and consent form. These standards do not apply to therapeutic imaging.

Research Protocol Screening and MRI Procedures
To date, over 150 million patients have had MRI examinations. Every year, approximately 10 million patients undergo MRI procedures. MRI has been shown to be extremely safe as long as proper safety precautions are taken. In general, the MRI procedure produces no pain and causes no known short-term or long-term tissue damage of any kind.

MRI Risk Information for Researchers
1. Risks due to the static magnetic field of the scanner
The powerful magnetic field of the scanner can attract certain metallic objects known as “ferromagnetic” objects, causing them to move suddenly and with great force towards the center of the MR system (projectiles). This may pose a risk to the patient or anyone in the way of the object, and has resulted in several deaths worldwide.
- Great care must be taken to prevent ferromagnetic objects from entering the MR scan room. It is vital that anyone entering the scan room removes metallic objects, including watches, jewelry, and items of clothing that have metallic threads or fasteners.

The powerful magnetic field of the scanner can also exert a force on metallic implants and other materials inside the subject’s body, including (but not limited to) aneurysm clips, metallic fragments in the eye, and bullets. Movement of such objects can cause serious injury or death.
- Researchers must screen potential subjects for possible metal in their body and assume that such metal is unsafe, unless it has been approved by qualified personnel.

2. Risks due to time-varying magnetic field gradients
MRI uses spatial and time-varying magnetic field gradients to form images. Switching the electrical current used to generate these gradients results in the loud sounds associated with MRI. These rapidly varying magnetic fields can also induce electrical currents into conducting wires, such as cardiac monitoring leads and implanted electrical devices (which might cause the device to fail). It is also possible to stimulate nerves (peripheral nerve stimulation), although the scanner is designed to operate at FDA-approved limits below this level.
- Subjects are required to wear earplugs or headphones to protect their hearing.
- Care must be taken to use only MRI-compatible electrical devices. Correct placement of leads and devices is essential to their safe operation.
- Patients with implantable electrical devices are not to be scanned
- Subjects to be instructed not to cross their hands or feet to minimize the chance of peripheral nerve stimulation.

3. Risks due to radio-frequency (RF) power
The MRI uses RF transmission and reception, at similar frequencies to those used for FM radio. Some of this RF energy is absorbed by the body, and may cause a small temperature rise. The scanner is designed to operate at FDA-approved limits on patient heating. RF can also cause electrically conducting materials such as aluminum foil to heat up, and have caused severe burns to patients.
- Medication patches may contain aluminum backing, and so should not be worn during the MRI scan
- Metallic tattoos must be evaluated for safety
- Extra caution should be exercised in patients with poor temperature regulation
4. Risks due to the use of MRI contrast agents

**FDA-approved gadolinium-based contrast agents**

Gadolinium contrast agents have been approved for use since the late 1980s. Although these agents can be differentiated on the basis of stability, viscosity, and osmolality, they cannot be differentiated on the basis of efficacy. Gadolinium chelates are extremely well tolerated by the vast majority of patients in whom they are injected. Acute adverse reactions are encountered with a lower frequency than is observed after administration of iodinated contrast media.

When gadolinium-based contrast is being used, subjects need to be screened for possible kidney or liver impairments and excluded appropriately.

Patients who answer yes to the following criteria must have had a blood serum creatinine drawn within 60 days of the MRI scan to determine if gadolinium can be safely administered:

- Renal disease history (including solitary kidney, renal transplant, renal tumor)
- Liver disease
- Age >60
- History of hypertension
- History of diabetes

It is the Principal Investigator’s responsibility to obtain the above laboratory values prior to subject’s research scan.

Gadolinium contrast administered to patients with acute renal failure or severe chronic kidney disease can result in a syndrome of nephrogenic systemic fibrosis (NSF).

Nephrogenic systemic fibrosis (NSF) is a fibrosing disease, primarily involving the skin and subcutaneous tissues but also known to involve other organs, such as the lungs, esophagus, heart, and skeletal muscles. Initial symptoms typically include skin thickening and/or pruritis.

**Other contrast agents**

If your research study involves the use of an investigational agent or an agent other than gadolinium, the risk section must be specific to the agent being studied. Please check with your sponsor or the package insert. Consult with MRI staff if you are unsure about the contrast needs for your research.

5. High risk individuals

**Pregnancy**

The protocol must state that the risk of MRI to pregnant women and fetuses is currently unknown. Women must be informed of this fact and must take a pregnancy test prior to MRI. The protocol must specify whether female subjects who test positive are not allowed to participate in (1) the study or (2) the MRI component of the study.

**Enrollment of Minor Research Subjects**

For studies where minors will be scanned, parents/guardians may not have knowledge of the minor subject’s complete health history. For example, minors can consent to certain medical procedures, like requesting birth control procedures, supplies or information. On the other hand, a minor may not have knowledge of their own complete health history, so parents/guardians should not be excluded from the screening process. Extra measures may need to be taken to protect the privacy and confidentiality of these subjects, as well as to obtain a complete medical history. This should be taken into account when designing screening procedures for minors. Additionally, see policy “Pregnancy Testing in Minor Research Subjects.”

**Common Contraindications to MRI**

The magnetic field of the MRI environment has the potential to cause burns or bodily injury if ferrous metal objects are implanted in the body or if personal articles containing ferrous material are brought into the environment. The protocol must specify how participants with contraindications for MRI studies (internal/implanted defibrillator or pacemaker, surgical brain aneurysm clips, cochlear implant, or known metal fragments embedded in the body) will be excluded.
The protocol must specify how participants with medical or electronic devices that may interfere with the scan or pose a risk will be evaluated and how risks to these participants will be minimized. Examples of such devices include but are not limited to:

- Artificial heart valves;
- Implanted drug infusion ports;
- Artificial limbs or metallic joint prostheses;
- Implanted nerve stimulators;
- Metal pins, screws, plates, stents or surgical staples.

**Incidental Findings**

There is a risk that the image will reveal a potentially clinically important finding, but which is beyond the aims of the study. In the event of the confirmation of a significant anomaly, this information will likely be distressing to the subject and constitutes a psychological risk. Additionally, see policy “Incidental Findings in Neuroimaging Protocols – Detection and Management”

**Informed Consent Text**

**MRI Procedure Section**

As part of your participation in this research study, you will have a magnetic resonance imaging (MRI) scan or a functional MRI (fMRI). MRI makes images of your body by using magnetic fields and radiowaves. The MRI exam will take approximately _________ minutes. Prior to your scan, you will be asked to complete a standard safety questionnaire. The purpose of this questionnaire is to ensure that you are able to safely enter the MRI area.

The MRI scan is performed in a special room that houses the MRI system or “scanner”. You will be escorted into the room and asked to lie down on a comfortably padded table that gently glides you into the scanner. The MRI scanner is an upright donut shape with a tube through the middle. The table will move to ensure that the part of your body that we are imaging close to the center of the tube. Even though the tube is open at both ends, some people may feel confined (claustrophobic). If this bothers you, please notify the MRI staff. You will be required to wear earplugs and/or headphones to protect your hearing from the loud tapping, buzzing and beeping noises made as images are being acquired. These loud noises are a normal part of the MRI procedure. The MRI scanner is equipped with an intercom system that allows the MRI staff to communicate with you during the scan. However, while images are being acquired, the noise of the scanner will be too loud for them to hear you. You will be given a squeeze bulb to alert the staff if you become uncomfortable or anxious.

The most important thing for you to do is to relax and lie still. You will be asked to remain as still as possible during the time the imaging takes place, but between sets of images some minor movement may be allowed. The MRI staff will advise you accordingly.

You may end your participation in this study at any time by telling the MRI staff.

**Risk Section**

The effects of magnetic fields in an MRI scanner have been extensively studied, and there are no known significant risks with an MRI exam. You may, however, be bothered by feelings of confinement (claustrophobia), and by the noise made by the magnet during the procedure. There is a small risk of decreased hearing immediately after an MRI scan. To help lessen this risk, you will be asked to wear earplugs or earphones while in the magnet. Some degree of fatigue or anxiety could occur while undergoing testing. Should this occur, efforts will be made to minimize discomfort.

*If contrast is used, explain risks here...example follows:* With the IV catheter insertion you may experience discomfort with insertion of the needle and a flushing sensation when the contrast agent is injected. A bruise to the area may develop afterwards.
If gadolinium-based contrast is utilized use the following risk language:
The contrast agent you will receive is FDA-approved and used routinely for MRI exams. It contains a material called gadolinium. The injection of contrast may cause discomfort, tingling or warmth in the lips, metallic taste in the mouth, tingling in the arm, nausea, or headache. These symptoms occur in less than 1% (less than 1 in 100) of people and go away quickly.

There is a small risk of an allergic reaction to gadolinium; however, a severe allergic reaction occurs in less than one in 300,000 people.

People with moderate to advanced kidney failure or chronic liver disease are at risk for developing nephrogenic systemic fibrosis (NSF) is a serious progressive disease which causes thickening of the skin and other organs resulting in decreased movement and possibly death. The cause is unknown and not treatable. If you answer yes to the following criteria you will need to have a blood serum creatinine drawn to determine if gadolinium can be safely administered:
Renal disease history (including solitary kidney, renal transplant, renal tumor), liver disease, history of hypertension, history of diabetes and/or if you are of age 60 or older.

If your research study involves the use of an investigational agent or an agent other than gadolinium, the risk section must be specific to the agent being studied. Please check with your sponsor or the package insert. Consult with MRI staff if you are unsure about the contrast needs for your research.

The presence of certain metals or devices in the body may present a risk (due to movement of the metal or mis-operation of the device) if placed in a very strong magnetic field. You may not be allowed to enter the MRI scanner if you have any of the following: cardiac pacemakers or implantable defibrillators, aneurysm clips, neural stimulators, artificial heart valves, ear implants, implanted devices such as insulin pump or drug infusion device, IUDs, magnetic dental appliances, metal fragments or foreign objects in the eyes, skin or body, metal plates, screws and prosthetics, non-removable metal piercings, tattoos on the head and neck, other certain older tattoos with metal containing inks, and permanent makeup (eyeliner). Some medicated patches that are applied to the skin may contain aluminum or other metals. The metal may not be visible. Wearing a patch with a metal backing during a MRI may result in a burn on the skin. You should make the MRI staff aware of any medicated patches that you are wearing prior to your MRI.

If you have other metals in your body, we will need to evaluate your case before you can participate in the study.

There are no known long-term risks associated with MRI scans.

The risk of MRI to pregnant women and fetuses is currently unknown.

There is a possibility that while reviewing your (insert test) we may see an abnormality that may have health implications that we did not expect to see. This is what is called an "incidental finding."

If we see an incidental finding, a qualified person (usually a member of the research team) will communicate the information to you. If you wish, we will provide information about this incidental finding to your primary doctor or we will refer you to an appropriate doctor for further evaluation.

This study is neither designed nor intended to detect health problems. The imaging that you will have as part of this research study does not substitute for an appropriate medical examination by a qualified health care provider. Your images will not be routinely reviewed by a doctor specializing in interpreting such images. If you suspect that you might be suffering from injury or illness, you should not rely on this study as a way to determine your health status. The information from these images will not be shared with you or your personal physician, unless (as mentioned above) there is an incidental finding.

An incidental finding may cause you to feel anxious. If you have further tests done, those results will
then become part of your medical record, which may affect current and future health or life insurance. The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility.
Attachment I


University and UVM Medical Center researchers must make adequate provisions for monitoring the data collected to ensure the safety of subjects. In the course of study monitoring, information incidental to the research goals may be identified which may impact the safety and/or wellbeing of the subjects. Scientists and clinicians should anticipate the potential for incidental findings in experimental design and establish a process to handle the discovery of an incidental finding.

Incidental Finding - Definition
A finding discovered in the course of research participation for which there is potential health importance. An incidental finding is beyond the specific aims of the protocol.

Note: The UVM MRI Research Center 3T magnet is not considered a clinical magnet and therefore neither the images nor reports can be incorporated into the subjects' clinical medical record and should not be used for diagnosing or treating medical conditions. Any abnormality found utilizing this magnet would be considered an incidental finding.

IRB Requirements Regarding Protocols Which May Have Incidental Findings
The IRB requires that the way in which incidental findings will be handled is made explicit in the study design. The IRB also requires that the way in which incidental findings will be handled is made explicit to any potential research subject through the informed consent process.

Research x-rays that are included in a protocol should not be designed nor intended to detect health problems in subjects. The x-rays required as part of a research study do not substitute for an appropriate medical examination by a qualified health care provider. The information from these x-rays should not be shared with the subject or their personal physician, unless there is an incidental finding.

Disclosure of clinically meaningful findings should be conducted by a licensed physician (or psychologist, genetic counselor, or other professional as appropriate) whenever possible. The person responsible for communicating an incidental finding must be referenced in the plan for disclosure submitted to the IRB.

Consent Template Section
Incidental Findings
There is a possibility that while reviewing your (insert test) we may see an abnormality that may have health implications that we did not expect to see. This is what is called an “incidental finding.”

If we see an incidental finding, a qualified person (usually a member of the research team) will communicate the information to you. If you wish, we will provide information about this incidental finding to your primary doctor or we will refer you to an appropriate doctor for further evaluation.

This study is neither designed nor intended to detect health problems. The imaging that you will have as part of this research study does not substitute for an appropriate medical examination by a qualified health care provider. If you suspect that you might be suffering from injury or illness, you should not rely on this study as a way to determine your health status. The information from this image will not be shared with you or your personal physician, unless (as mentioned above) there is an incidental finding.

An incidental finding may cause you to feel anxious. If you have further tests done, those results will then become part of your medical record, which may affect current and future health or life insurance. The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility.
### J. Guidance on Engagement in Research

<table>
<thead>
<tr>
<th>Category</th>
<th>Description of UVM Activities</th>
<th>UVM Engaged?</th>
<th>Other Site Engaged?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Funding Only/No Direct UVM Involvement</td>
<td>UVM receives a direct grant or award to perform human subjects research, even if all of the activities are performed off-site by subcontractors or collaborators and UVM itself never intervenes or interacts directly with human subjects and never receives identifiable private information.</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Pre-Research Activities</td>
<td>UVM performs a feasibility study to determine whether sufficient data or prospective participants exist to formulate a hypothesis or conduct a study.</td>
<td>MAYBE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>UVM performs a small pilot study to work out details of an anticipated future research project.</td>
<td>YES</td>
<td>n/a</td>
</tr>
<tr>
<td></td>
<td>UVM intervenes or interacts with individuals who meet study eligibility criteria to develop study protocol.</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>PR/Publicity/Pre-Screening Activities</td>
<td>UVM informs potentially eligible subjects about research occurring elsewhere and provides them with information about how to contact the researchers.</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td></td>
<td>UVM sends letters to prospective subjects describing a study and letting them know they may later be contacted to participate.</td>
<td>YES</td>
<td>MAYBE</td>
</tr>
<tr>
<td>Study Recruitment/Informed Consent</td>
<td>UVM informs prospective subjects about the availability of research conducted elsewhere; provides prospective subjects with written information about research (including the relevant informed consent document and other IRB-approved materials); provides prospective subjects with information about contacting investigators for information or enrollment; or obtains and appropriately documents prospective subjects’ permission for investigators to contact them. *Generally, a UVM clinician may discuss the study with the prospective subject as the subject’s clinician but not as a researcher or part of the study team. *Documentation of permission must be HIPAA-compliant if the UVM investigator is affiliated with a unit covered by HIPAA.</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td></td>
<td>UVM faculty, staff, trainees, or agents conduct the consent interview, obtain subject signature on the consent form, or otherwise act as authoritative representatives of the investigators.</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td></td>
<td>UVM researchers obtain permission from a school or nursing home to observe, audio/video, or distribute surveys/questionnaires for research purposes. The students or residents are</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Data/Specimen Repositories</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td><strong>UVM data steward queries UVM database on behalf of external researchers.</strong></td>
<td>NO</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td><strong>UVM releases information and/or specimens to investigators at other site in non-identifiable (i.e., non-linkable) form, when the information and/or specimens were originally obtained for non-research purposes.</strong></td>
<td>NO (Not Human Subjects)</td>
<td>NO</td>
<td></td>
</tr>
<tr>
<td><strong>UVM receives information or specimens for research from established repositories operating in accord with an FWA, OHRP guidance on repositories, and a written agreement unequivocally prohibiting release of identifying information to UVM investigators.</strong></td>
<td>NO (Not Human Subjects)</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td><strong>UVM obtains, receives, or possesses identifiable (directly or with links/codes) private information from another site for research purposes.</strong></td>
<td>YES</td>
<td>YES</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Multi-Site Research</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UVM is Statistical/Data Coordinating Center</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>UVM obtains, receives, or possesses identifiable (directly or through links) private information to operate a ‘statistical or data’ coordinating center for multi-site collaborative research. If the UVM investigator is within the covered entity, i.e. affiliated with a unit covered by HIPAA they are required to obtain the appropriate documentation of HIPAA compliance from the site(s) submitting identifiable private information. If UVM has no other interaction or intervention with subjects, and the principal risk associated with institutional activities is limited to the potential harm resulting from breach of confidentiality, then the UVM IRB need not review each underlying collaborative protocol. However, the IRB should determine and document that: (i) the statistical/data coordinating center has sufficient mechanisms in place to ensure the privacy of subjects and confidentiality of data are adequately maintained; (ii) each collaborating institution holds an FWA or other appropriate assurance; (iii) each protocol is reviewed and approved by the IRB at the collaborating institution prior to enrollment of subjects; and (iv) informed consent is obtained from each subject in compliance with HHS regulations, the Common Rule, and any other applicable federal policy.</strong></td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Multi-Site Research</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UVM is the Lead or Operations Coordinating Center</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>UVM obtains, receives, or possesses identifiable (directly or through links) private information to operate a &quot;lead or operations coordinating center&quot; for multi-site collaborative research. If UVM as the lead/operations coordinating center has no other interaction or intervention with subjects, the UVM IRB need not review each underlying collaborative</strong></td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>
However, the IRB should determine (i) management, data analysis, and Data Safety and Monitoring (DSM) systems are adequate, given the nature of the research involved; (ii) sample protocols and informed consents are developed and distributed to each collaborating institution; and (iii) each collaborating institution holds an applicable OHRP-approved Federalwide Assurance (FWA); (iv) each protocol is reviewed and approved by the IRB at the collaborating institution prior to enrollment of subjects; and (v) any substantive modification by the collaborating institutions of sample informed consent information related to risks or alternative procedures is appropriately justified; and (vi) informed consent is obtained from each subject in compliance with HHS regulations, the Common Rule, and any other applicable federal policy.

<table>
<thead>
<tr>
<th>Medical Care/Standard Clinical Practice</th>
<th>UVM provides unforeseeable but medically appropriate clinical treatment incident to a patient's participation in a clinical trial elsewhere, e.g., when patient suffers an adverse event that is treated at UVM by her regular health care provider.</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient is hospitalized at UVM and attending physician decides continued participation on protocol at outside institution is ok.</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical Care/Little or No Direct UVM Involvement/Data Not Collected for Study</th>
<th>UVM administers test article and performs normal monitoring, but does not perform data collection.</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UVM performs blood draw for a genetics study occurring at another institution but sends the samples to the other institution for analysis.</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>UVM provides pre- and/or post-test genetic counseling to study participants regarding tests conducted by and results reported from other institution.</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subinvestigators</th>
<th>UVM consents prospective subjects (even if for &quot;someone else’s study&quot;).</th>
<th>Yes</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UVM performs physicals or other eligibility testing to be sent to investigators at another site.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>UVM collects and reports data to investigators at another site.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Contracted Medical/Professional Services</th>
<th>UVM performs physicals or other eligibility testing to be sent to investigators at another site.</th>
<th>No</th>
<th>UVM must adhere to commonly recognized professional standards for maintaining</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UVM performs and/or analyzes blood draw for genetics study occurring at other institution and furnishes the results to the investigator.</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>UVM collects and reports data to investigators at another site.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Consulting Services

(See "multi-site research" above for additional details.)

| Consultant does not obtain, receive or possess identifiable private information (e.g., the consultant analyzes data that cannot be linked to individual subjects, directly or through a coding system, by any member of the research team). | NO | YES |
| Consultant accesses or uses identifiable private information while visiting the research team's institution. | NO | YES |
| But consultant's activities become subject to the other institution's IRB. | YES |
| Consultant obtains coded data for analysis at UVM (and there is not a written agreement unequivocally prohibiting release of identifying codes to the consultant). | YES | YES |
### K. Types of Research

<table>
<thead>
<tr>
<th>Types</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applied</td>
<td>Scientific investigations conducted to answer specific clinical questions or solve practice-related problems.</td>
</tr>
<tr>
<td>Basic</td>
<td>Scientific investigation that involves the generation of new knowledge or development of new theories; its results often cannot be applied directly to specific clinical situations.</td>
</tr>
<tr>
<td>Correlational</td>
<td>The systematic investigation of relationships among two or more variables, without necessarily determining cause and effect.</td>
</tr>
<tr>
<td>Descriptive</td>
<td>Research that provides an accurate portrayal of characteristics of a particular individual, situation, or group. These studies are a means of discovering new meaning, describing what exists, determining the frequency with which something occurs, and categorizing information.</td>
</tr>
<tr>
<td>Ethnographic</td>
<td>The investigation of a culture through an in-depth study of the members of the culture; it involves the systematic collection, description, and analysis of data for development of theories of cultural behavior.</td>
</tr>
<tr>
<td>Experimental</td>
<td>Objective, systematic, controlled investigation for the purpose of predicting and controlling phenomena and examine probability and causality among selected variables.</td>
</tr>
<tr>
<td>Exploratory</td>
<td>Studies that are merely formative, for the purpose of gaining new insights, discovering new ideas, and increasing knowledge of phenomena.</td>
</tr>
<tr>
<td>Grounded Theory</td>
<td>A research approach designed to discover what problems exist in a given social environment and how the persons involved handle them; it involves formulation, testing, and reformulation of propositions until a theory is developed.</td>
</tr>
<tr>
<td>Historical</td>
<td>Research involving analysis of events that occurred in the remote or recent past.</td>
</tr>
<tr>
<td>Phenomenological</td>
<td>An inductive, description research approach developed from phenomenological philosophy; its aim is to describe an experience as it is actually lived by the person.</td>
</tr>
<tr>
<td>Qualitative</td>
<td>Research dealing with phenomena that are difficult or impossible to quantify mathematically, such as beliefs, meanings, attributes and symbols.</td>
</tr>
<tr>
<td>Quantitative</td>
<td>Research involving formal, objective information about the world, with mathematical quantification; it can be used to describe test relationships and to examine cause and effect relationships.</td>
</tr>
</tbody>
</table>

Note: The practice of telephone screening and consent for potential subjects is considered research and could occur in any of the above types of research.
L. Pregnancy Testing in Minor Research Subjects

A minor is defined as a person under the legal age of full responsibility. All persons under 18 years of age are considered minors.

Research involving minors requires special consideration on the part of both the research team as well as the IRB. This is particularly so if the study requires pregnancy testing of minor subjects, either to confirm eligibility or as part of routine safety monitoring, for example, before the administration of study drug. Researchers must consider how results of such tests will be handled and to whom they will be disclosed. This plan must be clearly outlined in the protocol as well as in any consent and assent documents.

Any protocols that utilize UVM Medical Center resources, would require point-of-care pregnancy testing. UVM Medical Center staff should refer to UVM Medical Center Policies and Procedures Labpoc110.21 for information about those procedures. There is no pregnancy testing policy for protocols that only utilize UVM resources.

If pregnancy is an exclusion criterion and screening procedures to determine eligibility require a pregnancy test, the researcher must determine whether the results of screening tests will be disclosed to the minor subject’s parent(s)/legal guardian or only to the minor subject. There are factors that may necessitate disclosure to parents even for a screening pregnancy test, or that may make reporting to parents after enrollment inappropriate. Researchers may consider both the age and maturity of the minor subjects, as well as any other factors that may impact the reporting decision, such as developmental delays or other relevant physical or mental characteristics of the subject population being studied. For example, if a researcher is enrolling autistic subjects, a positive pregnancy test in this population, regardless of age, would almost certainly need to be disclosed to the parents whether it was a screening test or not. On the other hand, a pregnancy in a 17-year old participating in a study for which parental permission was waived (see section 11.D. Children, Waiver of Consent would not necessarily need to be reported to parents.

Reporting Pregnancy of a Minor to Authorities
Researchers should be aware that there is no age specified at which point the researcher becomes required to report the pregnancy of a minor under state law. Pregnancy of a minor does not necessarily indicate suspected abuse and many other factors may need to be considered. Researchers may consider both the age and maturity of the minor subjects, as well as any other factors that may impact the reporting decision, such as developmental delays or other relevant physical or mental characteristics of the subject population being studied. State child abuse laws governing healthcare providers or persons receiving information about a child who has received healthcare services outline when mandatory reporting is required. See Appendix N. Exceptions to Confidentiality.

Language in Consent Form
Regardless of the specifics of the reporting plan, both the parental consent form and the minor’s assent form (they may be the same form depending on the age of the minor subjects) should clearly outline when pregnancy tests will be performed, to whom the results will be disclosed, and whether there may be any exceptions to this. Additionally, an exception to confidentiality statement must be included when it is possible that suspected child abuse or neglect be revealed, requiring mandatory reporting to regulatory authorities.
M. Certificates of Confidentiality

Purpose
Certificates of Confidentiality (CoCs) protect participants enrolled in highly sensitive research studies from the risks of legally mandated release of information for use in federal, state, or local civil, criminal, administrative, legislative, or other legal proceedings. A Certificate allows a researcher to refuse to disclose any identifying information about their research participants.

Who Issues CoCs
CoCs are issued by the Department of Health and Human Services (DHHS) to protect identifiable research information from forced disclosure.

Click below for a flowchart of institutes that can currently issue a CoC. (taken from the NIH Certificates of Confidentiality Kiosk)

The Food and Drug Administration (FDA) is authorized to issue CoCs for studies with an IND/IDE that do not have other DHHS funding. Additionally, NIH is authorized to issue CoCs for sensitive research that is not federally funded, at its discretion, if the research is related to the NIH mission.

Extent and Limitations of Coverage
Certificates can be used for biomedical, behavioral, clinical or other types of research that is sensitive. By sensitive, we mean that disclosure of identifying information could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. A list of research areas which are considered sensitive is below in Step 1.

• Circumstances where a CoC cannot be used to resist disclosure
  A CoC cannot be used to resist disclosure if the disclosure is requested in writing by the research participant, their legal guardian, or legal representative. The Certificate also cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

• Circumstances where information about study participants may be voluntarily disclosed by the Investigator or Institution
  Investigators and their Institutions may (and should be prepared to) make disclosures to prevent serious harm to the participant or someone else, including abuse and to voluntarily comply with state and local reporting requirements for communicable diseases. The consent form must explain these and any other circumstances of voluntary disclosure.

• Protection of identifiable research information obtained prior to issuance of a CoC
  A CoC protects identifiable information about research participants that is maintained by an investigator during any time the CoC is in effect, even if the participant was enrolled before a study obtained a CoC.

Steps to Obtain CoC
1. Determine if a CoC is Appropriate

Research projects that collect personally identifiable, sensitive information and have been approved by the UVM/UVM Medical Center IRB are eligible for a CoC. Federal funding as mentioned above is not a pre-requisite for an NIH-issued CoC, however, the subject matter of the research must fall within NIH mission areas. Requesting sensitive information from a participant does not automatically make it eligible for a CoC.

Some research areas that are eligible for a CoC are:
- Research on HIV, AIDS, and other STDs;
- Studies that collect information on sexual attitudes, preferences, or practices;
- Studies on the use of alcohol, drugs or other addictive products;
- Studies that collect information on illegal conduct;
- Studies that gather information that if released could be damaging to a participant’s financial standing, employability, or reputation within the community;
- Research involving information that might lead to social stigmatization or discrimination if it were disclosed;
- Research on participant’s psychological well-being or mental health;
- Genetic studies, including those that collect and store biological samples for future use;
- Research on behavioral interventions and epidemiologic studies.

Projects that are not eligible for a certificate are:
- not research based;
- not collecting sensitive information or information that, if released publicly, might harm the research participants,
- not collecting personally identifiable information, or
- not involving a subject matter that is within a mission area of the National Institutes of Health.

2. IRB Review

The protocol should include the fact that the study will have a CoC. If during its review of research for which an investigator has not identified the need for a CoC, the IRB may recommend applying for a CoC. The IRB does not allow participant recruitment until the CoC has been obtained and is on file with the IRB.

Generally, an application for a CoC is submitted after the IRB responsible for its review approves the research project. This is because certificate issuance is conditioned upon IRB approval, see Step 3. Given this pre-requisite, the IRB will approve the protocol prior to CoC issuance; however, a written consent form would be released marked as, “For use only after a CoC is in place.” You must submit the CoC certificate to the IRB in order to receive the approved IRB stamped consent form for use.

The informed consent form must include a description of the protections and limitations of the CoC in the confidentiality section, including the circumstances in which the investigators plan to disclose voluntarily identifying information about research subjects (see Appendix N. Exceptions to Confidentiality)

Confidentiality Section
We will do everything we can to keep others from learning about your participation in the research. To further help us protect your privacy, we
have obtained a Certificate of Confidentiality from the Department of Health and Human Services. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below:

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances: discovery of abuse and neglect, or harm to self or others.

3. Applying for a Certificate
Certificates are granted to institutions (not investigators nor IRBs), based upon an investigator’s application, for single, well-defined research project. Certificates are sometimes issued for cooperative multi-site projects which must have a coordinating center or lead institution. The coordinating center/lead institution can apply on behalf of all institutions associated with the multi-site project and must ensure that all participating institutions conform to the application assurances. Please see FAQ C6 for more details and lead site responsibilities (http://grants.nih.gov/grants/policy/coc/faqs.htm#364)

Applications must be signed by the PI and UVM's authorized institutional official. The UVM Board has delegated authority to the Associate Vice President for Research Administration as an institutional official that meets this definition. You may send applications in need of a signature to the IRB administrator with whom you are working.

Certificate Expirations
Certificates are not open-ended. They have an expiration date. If you determine that the research project will not be completed by the CoC expiration date, you must work with your NIH coordinator to submit a written request for an extension of the Certificate three (3) months prior to the expiration date.

Amending a Certificate
Sometimes a research project is amended to collect additional sensitive data. When this occurs, in addition to submission to the IRB, researchers should consider whether the Certificate needs to be amended. We advise that you speak with the NIH coordinator to establish whether the Certificate still covers the data and for instructions
on how to amend. See below for contacts.

**Application Contacts**

For a list of NIH IC Certificate Contacts, see [http://grants.nih.gov/grants/policy/coc/contacts.htm](http://grants.nih.gov/grants/policy/coc/contacts.htm). Some ICs use an online application process which is noted under the IC name on the Contacts List.

The Food and Drug Administration handles requests for Certificate of Confidentiality protection for studies that obtain an Investigational New Drug (IND) authorization or other FDA authorization. Projects with INDs or IDEs should apply to the FDA (Kevin Prohaska, D.O., M.P.H., Captain, U.S. Public Health Service Corps, Medical Officer, Division of Scientific Investigations, kevin.prohaska@fda.hhs.gov, 301-796-3707 OR Patricia Holobaugh, Bioresearch Monitoring Branch, HFM-664, Center for Biologics Evaluation and Research, patricia.holobaugh@fda.hhs.gov, 301-827-6347).
N. Exceptions to Confidentiality Guidance

**Mandatory Reporting:** Vermont law requires health care providers and other professionals to take specific actions and to submit specified reports when certain facts or conditions become known to them (i.e. child abuse, elder abuse and imminent harm to self or others). These laws apply to the professional as a condition of their license or employment; and thus to any information gained by that person during the conduct of research.

The IRB expects that the PI will, when appropriate, communicate these potential exceptions to confidentiality to prospective research subjects during the informed consent process. This applies both to research projects specifically gathering such information and to projects where these circumstances or conditions may become known to the researcher even though the researcher does not directly seek this information (i.e. abuse of a child may be evident during a physical exam).

**Do I need to include an Exceptions to Confidentiality section in my consent form?** If you are subject to mandatory reporting laws AND there is a reasonable possibility that you could discover information that would require you to break confidentiality then your consent form should include an Exceptions to Confidentiality section.

**Am I (or any Key Personnel on this study) subject to mandatory reporting laws?** Health care workers, mental health providers, social workers, educators, members of the clergy, and law enforcement officers are examples of professionals who are mandated reporters in Vermont. Check with your professional licensing board if you are unsure if you are a mandated reporter. In addition, **UVM requires any employee** who has reasonable cause to believe that a minor participating in a program or activity at the University has been sexually abused or neglected to report the concern promptly to the Vermont Department for Children and Families (DCF).

**What is the likelihood that in the course of carrying out my protocol I will discover information that requires mandatory reporting?** If the likelihood is low then the consent form does not need to include additional language. If during the conduct of the research a situation that required mandatory reporting arises, the PI should first and foremost act ethically to protect a potential victim (i.e. report suspected child abuse to the authorities). In addition the PI should report this to the IRB as the breach of confidentiality would be an Unanticipated Problem.

If there is a reasonable possibility, this should be disclosed as an exception to confidentiality to the potential participant during the informed consent process.

Suggested Consent Language:

**Exceptions to Confidentiality:** There is one exception to confidentiality that you should know about. By law, it is our responsibility to report to the appropriate authority suspicion of harm to children or to others.

*If appropriate add:* However, we are not seeking this type of information in our study nor will you be asked questions about these issues.
O. Guidance on Data Management in Human Subjects Research

I. Background

This guidance is intended to assist researchers in developing data management plans for human research data. The guidance presents relevant definitions and key concepts concerning human research data, describes the roles and responsibilities for data management, outlines the elements of a research data management plan, and describes requirements for maintaining and using human research information once projects are completed.

The protection of privacy and the confidentiality of information about research subjects is a special concern for IRBs in their review of research data management. Research subjects must have a reasonable expectation that personal information will be disclosed only with their permission or in ways that are consistent the consent process, and in compliance with the laws and regulations. Violations of confidentiality could have serious consequences for research subjects, including potential discrimination, misuse of genetic information, loss of insurance, or loss of privacy. Even with all the appropriate state and federal laws, University and hospital policies, and requirements of IRBs all aimed at protecting the confidentiality of a research subject’s individually identifiable private information, violations of privacy can and do occur. Such violations may be inadvertent (accidental) or due to carelessness, deliberate or compelled by regulation or law.

Clearly defined and faithfully followed procedures to protect the confidentiality of human subjects can significantly reduce the possibility of violations to the confidentiality of human research data and should be part of every study design.

In addition to this guidance, researchers may need technical support from either UVM’s Enterprise Technology Services (ETS) or the College of Medicine Technology Services (COMTS) for assistance with development of an adequate research data protection protocol. Contacts are listed below.

UVM Information Security Operations Team
iso@uvm.edu

COM IT Information Security
infosecurity@med.uvm.edu

University of Vermont (UVM) policies referenced in this document:
Information Security Procedures
Intellectual Property

UVM Medical Center policies:
UVMMC employees may view related policies on the UVMMC Intranet.

Please note that the information in this guidance was current when the guidance was issued Summer 2015. As technologies and social norms advance, however, the standards for managing data may change.

II. Definitions and Key Concepts

A. Anonymization

This process removes information from data that allows recognition of particular individuals. Common strategies for anonymizing data are deleting or masking personal identifiers, such as name and social security number, and suppressing or generalizing quasi-identifiers, such as date of birth and zip code. Cell size restrictions may also be applied. Typically anonymized
data is not coded; it ordinarily contains no link to individually identifying information that may be available to the researcher.

B. Coding

Coding is a process in which individually identifying information is replaced with a number, letter, symbol, or combination thereof and a key linking the code to identifiers is created. The key is usually maintained separately from the coded data. Coding is one means to protect the confidentiality of research data.

The HIPAA Privacy Rule requires that a code for the re-identification of health information does not derive from or be related to identifiers for an individual and not be capable of translation to identify an individual. This requirement can eliminate the use of so-called hash codes.

C. Confidentiality

Confidentiality means restricting access to information that an individual has disclosed in circumstances that the individual can reasonably expect the information will not be made public. The relationship between a researcher and a study participant is ordinarily one of trust. This relationship often includes an expectation that personal information collected for research that is ordinarily regarded as private will not be divulged outside the research team without explicit permission or in ways that are inconsistent with consent to research participation.

D. Covered Entity

Those entities to which HIPAA Privacy Rule standards apply are called “covered entities”. They are defined as (1) health insurance plans, (2) health care clearinghouses, and (3) health care providers that electronically transmit health information in connection with medical service transactions.

E. Data

The Merriam-Webster Dictionary (2005) defines data as “factual information (as measurements or statistics) used as a basis for reasoning, discussion, or calculation.” There are many ways to categorize data; for the purpose of this guidance, the terms as used in this document are described below.

Research data refers to collected and recorded factual information commonly accepted in scientific and scholarly communities as necessary to validate research findings. Research data can be classified as:

- **Anonymous research data**: Research data that lacks information that would allow the recognition of particular individuals by the researcher.

- **Health data**: Health information created or received by health care providers, insurance plans, and clearinghouses that is individually identifiable is protected by federal and state laws, including the **Health Insurance Portability and Accountability Act of 1996** (HIPAA; see the definition below.).

- **Identifiable research data**: Research data containing information that allows recognition of particular individuals from the data by the researcher.
• **Indirectly identifiable research data:** Research data that are coded with a key linking the data to individually identifying information. The key may or may not be available to the researcher.

• **Limited data set:** See the definition below.

• **Processed research data:** Analyses, descriptions, and conclusions prepared as reports, manuscripts, theses, or papers.

• **Published research data:** Written information distributed to people beyond those involved in research data acquisition.

• **Raw or primary research data:** Information recorded as notes, images, video recordings, paper surveys, computer files, etc., pertaining to a specific research project. Examples of such data are: survey responses, observations of behaviors, observations of medical symptoms, temperature readings, behavioral or medical test results, biological samples, and radiographic images.

F. De-Identification

As required by the **HIPAA Privacy Rule**, this process involves the removal of the following informational elements from health information.

1. Names.
2. All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP Code, and their equivalent geocodes, except for the initial three digits of a ZIP Code if, according to the current publicly available data from the Bureau of the Census:
   a. The geographic unit formed by combining all ZIP Codes with the same three initial digits contains more than 20,000 people, and
   b. The initial three digits of a ZIP Code for all such geographic units containing 20,000 or fewer people are changed to 000.
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older. The population of a zip code can be identified on the web site of the U.S. Census Bureau at the following url: [http://www.census.gov/popfinder/](http://www.census.gov/popfinder/)
4. Telephone numbers.
5. Facsimile numbers.
6. Electronic mail addresses.
7. Social security numbers.
8. Medical record numbers.
9. Health insurance plan beneficiary numbers.
10. Account numbers.
12. Vehicle identifiers and serial numbers, including license plate numbers.
15. Internet protocol (IP) address numbers.
16. Biometric identifiers, including fingerprints and voiceprints.
17. Full-face photographic images and any comparable images.
18. Any other unique identifying number, characteristic, or code, unless permitted by the

**HIPAA Privacy Rule** standard for re-identification.

In addition, health information can be de-identified if (a) a person with appropriate knowledge of
and experience with generally accepted statistical and scientific principles and methods
determines that the risk is very small that the health information could be used to identify an
individual and documents the methods and results of this analysis, or (b) the covered entity from
which health information is being obtained does not have actual knowledge that the information
could be used to identify an individual.

G. Encryption

Encryption is the process of comprehensively encoding information in such a way that only
authorized parties can read it. Encryption limits access to data by controlling the distribution of
the decoding algorithm to authorized individuals. Encryption is one means of protecting the
confidentiality of research data. Under **HIPAA**, if protected health information is encrypted, this
action provides a “safe harbor” from violating **HIPAA**.

H. Health Insurance and Portability and Accountability Act of 1996 (HIPAA)

**HIPAA** is federal legislation that, along with its implementing regulations, produced legal
protections for health information. This legislation has had an impact on the conduct of
research involving health information. A critical part of **HIPAA** for research activities is the so-
called privacy regulations, often referred to as the **Privacy Rule**. The intent of the **HIPAA Privacy Rule** is to protect the confidentiality of health care information and define the rights of
patients regarding their health information. The **HIPAA Privacy Rule** created the concept of
“protected health information” or “**PHI**”, which is individually identifiable health information
created or received by a covered entity (See the definition of covered entity above.)

Under the **HIPAA Privacy Rule**, specific permission from patients for research use of health
information may be obtained using an **Authorization** in addition to the consent process. The
**HIPAA Privacy Rule** specifies the kinds of information included in the **Authorization** language.
Provided certain regulatory criteria are satisfied, an IRB may waive or alter the information
included in the **Authorization** language.

I. Honest Broker

An honest broker obtains legally protected data from their source and typically codes and then
de-identifies the data or creates a limited data set for research use. The honest broker retains
the key linking the code to identifiers for individual contributors of the data. If questions arise
about the validity or accuracy of the data, the honest broker can typically resolve them without
revealing the identity of individuals to the researcher. As a result of the activities of the honest
broker, the research conducted with processed data may not involve human subjects, because
the data lacks identifiable private information.

An investigator actively involved in the research in which the data are used cannot be an honest
broker, nor can any person under the investigator’s supervision.

J. Identifiers
Identifiers are specific informational elements that permit the recognition of a particular person.

K. Limited Data Set

Under the **HIPAA Privacy Rule**, a limited data set is defined as protected health information that excludes the following direct identifiers of an individual or of relatives, employers, or household members of that individual:

1. Names
2. Postal address information, other than town or city, State, and zip code
3. Telephone numbers
4. Fax numbers
5. Electronic mail addresses
6. Social security numbers
7. Medical record numbers
8. Health plan beneficiary numbers
9. Account numbers
10. Certificate/license numbers
11. Vehicle identifiers and serial numbers, including license plate numbers
12. Device identifiers and serial numbers;
13. Web Universal Resource Locators (URLs);
14. Internet Protocol (IP) address numbers;
15. Biometric identifiers, including finger and voice prints; and
16. Full face photographic images and any comparable images.

A limited data set may only be used for the purposes of research, public health, or health care operations.

A data use agreement between the source of the protected health information and the recipient is needed for use of a limited data set. This agreement restricts the uses and disclosures of the limited data set, requires the recipient to establish appropriate safeguards to limit further uses and disclosures, applies the **HIPAA Privacy Rule** to the use of the limited data set, and prohibits identifying or contact with the individuals who contributed the data.

L. Repository

A repository compiles data, specimens, or both for future research purposes. The repository receives, processes, stores, and distributes data with or without specimens to researchers. The repository may or may not be an honest broker.

M. Sensitive Data

Data that are individually identifiable and private usually are considered sensitive and should be protected appropriately. Identifiable data that if disclosed could have adverse consequences for subjects or could damage their financial standing, employability, insurability, or reputation are considered highly sensitive. The IRB may recommend that a Certificate of Confidentiality be applied in these cases to allow researchers to refuse to disclose names or other identifying characteristics of research subjects in response to legal demands. A list of research in which resultant data would be considered highly sensitive can be found in Appendix M., Section 1. Very stringent security precautions need to be in place to protect research data while in storage or being transferred.

III. Roles and Responsibilities for Human Subject Data Management
A. Principal Investigators (PIs)
PIs are responsible for developing an appropriate data management plan (see Section IV) as well as ensuring that research staff members are thoroughly trained to maintain the integrity of the research data that is collected. These responsibilities include determining how to best collect, store, protect, analyze, and disseminate research data.

B. Research Team Members
The primary research data management responsibilities of research coordinators, research assistants, and those in similar positions are usually involved with research data collection, ensuring the reliable and accurate collection of the research data and protecting the confidentiality of research data that are collected.

Statisticians are primarily responsible for ensuring comprehensive and appropriate research data analysis.

C. The Institutional Review Boards (IRBs)
The IRBs are responsible for review and approval of proposed data management plans so that the rights and welfare of research subjects are acceptably protected.

IV. The Research Data Management Plan

A summary of four basic types of research data appears in the table below.

<table>
<thead>
<tr>
<th>DIRECTLY IDENTIFIABLE RESEARCH DATA</th>
<th>INDIRECTLY IDENTIFIABLE RESEARCH DATA</th>
<th>ANONYMIZED RESEARCH DATA</th>
<th>DE-IDENTIFIED RESEARCH DATA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data contains informational elements that allow the data to be associated with a living unique individual.</td>
<td>Direct identifiers among the data are replaced by a code and a key to the code links it to individual identities. Re-identification of the data is possible.</td>
<td>Individual identifiers were never recorded or have been stripped from the dataset and the data has been manipulated to make it very difficult to re-identify individuals. The data is not coded.</td>
<td>Certain specified informational elements are absent from the data. The data may or may not be coded.</td>
</tr>
</tbody>
</table>

Before starting a new scientific research project, the PI and research team should address the following activities related to research data management.

A. Data Collection
The information below is intended as general advice to researchers about devising a data management plan.

The data management plan should reflect whether or not the project requires that data to include

- Direct identifiers,
- If a code should be used, resulting in indirectly identifiable data,
- If the research data should be anonymized, or
- If the data should be collected without any identifiers at all.

The use of identifiers should have a clear justification, because it will increase risks to the confidentiality of subject data. If the research data is coded, the plan should describe the coding methodology, and the security arrangements for storage of the “key” linking the code to identifiers. In general, the key should be stored separately from the data.
B. Data Storage
Researchers should decide how they are going to store research data, in what format, and for how long. Considerations should include the data retention requirements of UVM and UVMMC, sponsors, and publishers, plus intellectual property protection, and potential data sharing.

Generally speaking, enough research data should be retained so that the findings of a project can be reconstructed with ease. While this does not mean that a project needs to retain all the raw research data that were collected, relevant statistics and analyses from this research data should be saved, along with any notes or observations.

Some key issues for electronic research data storage are: (1) thorough documentation to allow research data to be appropriately used in the future and (2) using storage formats that are adaptable to evolving computer hardware and software. There are also some additional considerations that are unique to electronic research data storage, including rapid access to the data, fast read/write rates, ability to archive and remove the data, low cost, and a backup system.

C. Data Retention and Disposal
Research sponsor requirements, clinical trial contracts, federal grant terms and conditions, data sharing plans, intellectual property protection, publishers’ policies, and the potential future value of the research data often require long retention periods. In addition, UVMMC’s policies apply to clinical care and other health services delivery data. In general, the UVM records retention policy applies. It can be found at http://www.uvm.edu/policies/general_html/recordretention.pdf

The IRB strongly recommends that researchers remove direct identifiers, such as those listed in the HIPAA Privacy Rule standard for de-identification, so that the identity of individual research subjects cannot be readily ascertained from the data. Additionally, researchers should arrange to securely archive signed consent forms. Such procedures for stored research data serve to minimize risks to subjects. The IRB review process includes asking researchers to describe their plans and procedures for long-term maintenance of research data involving human subjects when study protocols are closed.

D. Destruction of Research Data
When researchers decide that research data should no longer be maintained, the data should be thoroughly and completely destroyed. Effective destruction ensures that research data cannot be extracted or reconstructed. Many document storage companies now offer onsite shredding and secure destruction of written and electronic media.

For electronic research data, the IRB advises researchers to contact either the College of Medicine Technology Services COMTS or Enterprise Technology Services (ETS) to assist with development of an adequate data destruction plan, as simply deleting the data files is insufficient.

E. Data Security
Research data management plans should ensure that hard copy and electronic research data are securely stored to prevent unauthorized access, disclosure, or loss. Hard copy records should be stored in a manner that limits access to authorized individuals. For example, filing cabinets/areas should be locked and placed in rooms that are routinely locked when not in use.

Electronic research data should be stored on a device that has appropriate security safeguards, such as unique identification of authorized users, password protection, encryption, automated operating system patch (bug fix) management, anti-virus controls, firewall configuration, and scheduled and automatic backups to protect against research data loss or theft. If a researcher chooses to store directly identifiable private research data locally on the computer’s hard drive, that computer, whether a laptop or desktop, must be encrypted. The use of the
network and servers maintained by the University is preferable to saving data on a local hard drive.

Laptops, Smart Phones, Tablets, removable hard drives, “jump” or “thumb” or “flash” drives, CDs, DVDs, and other portable devices and removable media are convenient to ensure your research data are always at your fingertips. External hard drives are a cost effective and convenient way to back up your research data. These devices, however, require encryption solutions if they are used to store or transfer directly identifiable private information. This requirement may be waived depending upon the sensitivity of the data being collected. The IRB will make that determination.

Because email is not secure, directly identifiable private research data that will be transferred via email, requires that the data file be encrypted prior to sending.

The IRB advises researchers to refer to the University Information Security Procedures Policy or to contact the appropriate technical support from either the College of Medicine Technology Services (COMTS) or Enterprise Technology Services (ETS) for assistance with development of an adequate research data protection protocol.

V. Data Analysis and IRB Approval

Primary Analysis
Primary analysis refers to how raw research data are chosen, evaluated, and interpreted into meaningful and significant conclusions. Once the primary research data analysis for a protocol is complete, the protocol should be closed with the IRB. Any subsequent analysis of the same research data, however, is usually considered secondary research data analysis.

During analysis, when subjects are typically no longer being enrolled, a researcher may apply for IRB approval to anonymize the research data by completing a continuing review application describing how identifiers will be removed. When the IRB approves a proposal to remove identifiers from remaining research data, IRB oversight of the study stops, and the researcher may continue to analyze the now anonymized research data.

Secondary Analysis
Any new, subsequent secondary analysis of existing human subject research data either requires: 1) IRB review and approval prior to access to or access to the research data; or 2) an IRB determination that its review is not necessary. See the chart below.

The IRB is responsible for determining whether or not 1) secondary analysis of research data increases risks to subjects, and 2) subjects were adequately informed during the original consent process about the possibility of secondary research use, maintenance of confidentiality, and destruction of identifiers. Based on these determinations the IRB may require the investigator to obtain informed consent from the subjects for secondary analysis.

Unless a dataset is anonymous, namely contains no direct identifiers and no code linked to identifiers, investigators who obtain research data from other researchers for secondary analysis should obtain IRB review and approval, or the IRB’s determination that the research does not require further IRB review, prior to obtaining the research data. The researcher providing the data may need to consult with his or her institution before sharing research data with local investigators. Guidance about data acquisition, management, sharing, and ownership at UVM can be found at the following URL. http://www.uvm.edu/spa/?Page=dataacquisition.html
<table>
<thead>
<tr>
<th>Does The Research Data Have Identifiers?</th>
<th>Proposed New Analysis Plan</th>
<th>Requirement For IRB Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Change to analysis of anonymous or anonymized data in an existing research project</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>Change to data analysis for a currently approved research protocol.</td>
<td>Submit an amendment to original study for IRB review of the proposed modifications. Likely to qualify for Expedited Review unless risks to subjects would be increased.</td>
</tr>
<tr>
<td>Analysis of research data from previously approved research after the original study is closed.</td>
<td>Submit a new application for IRB review with a protocol describing the research data and its analysis plan. Include a copy of the IRB approval letter and IRB approved consent form for the original study that collected the data. Note: If the original IRB approved protocol and consent did not include information about the new proposed analysis, the application for review should include a procedure for obtaining consent or a request for waiver of informed consent and authorization if PHI is involved. Likely to qualify for Expedited Review unless risks to subjects would be increased.</td>
<td></td>
</tr>
<tr>
<td>Share research data with a UVM or UVMMC colleague.</td>
<td>If sharing is not in the current protocol, amend protocol to allow sharing. The investigator receiving the research data should submit a application for IRB review for the new project. Likely to qualify for Expedited Review, Exemption from Review, or a Not Human Subjects determination depending on whether identifiers are included with the research data, and the consent form for the study collecting the data contained information about the sharing of data.</td>
<td></td>
</tr>
<tr>
<td>Share research data with a non-UVM or non-UVMMC colleague.</td>
<td>If sharing is not in the current protocol, amend protocol to allow sharing outside of UVM and UVMMC. Likely to qualify for Expedited Review, Exemption from Review, or a Not Human Subjects determination depending on whether identifiers are included with the research data and the consent form for the study collecting the data contained information about the sharing of data. The investigator receiving the research data should provide documentation of local IRB approval. A Materials Transfer Agreement may be needed prior to release of the data.</td>
<td></td>
</tr>
<tr>
<td>Storage of research data to share with colleagues or students in the future.</td>
<td>Submit a new application for review of a repository.</td>
<td></td>
</tr>
</tbody>
</table>
**Data Sharing and the IRB**

Researchers who intend to share research data with colleagues from an on-going study should obtain IRB review of a study amendment before doing so. They should also request documentation of IRB review for the colleagues’ project if the data will contain individual identifiers. The IRB usually requests the removal of direct identifiers prior to release; if UVM researchers intend to maintain identifiers, even if indirectly through use of a code, there should be an appropriate scientific justification for doing so.

Research data sharing may occur after the original study has been completed. If a researcher intends to share research data from a study that has been closed, then the researcher should consult with the IRB. The consultation with the IRB is needed to determine whether or not the consent process for the original study included such data sharing. If not, then only de-identified data that may or may not be coded would be eligible for sharing.

UVM investigators sending research data outside of the institution should contact the UVM Office of Technology Commercialization to determine if a Materials Transfer Agreement or other agreement is needed.

**VI. Information for Human Subjects**

Subjects should be informed during the consent process about the following study procedures:

1. What information will be collected as research data,
2. How the confidentiality of their personal or private information will be protected,
3. How long the research data will be kept after the initial study analysis is completed,
4. If data sharing is contemplated, how their identities will be protected when the data is shared.

See the “Protecting Your Confidential Information” section of the IRB’s consent form template for sample wording.
P. Requirement to include a full Protocol Title in the Electronic Medical Record (PRISM)

UVMMC requires that certain information (full protocol title, CHRMS/CHRBSS protocol number, Principal Investigator and Principal Investigator’s contact information) about research study participation be included in the Research Flag area of each participant’s electronic medical record. This requirement is for participant safety and billing compliance.

It is expected that full protocol titles are included in PRISM, however it is recognized that there may be rare circumstances in which inclusion of the full study title is inappropriate.

If the Principal Investigator feels that including the full protocol title in the PRISM record is not in the best interest of the participant, they may request a waiver of this requirement. The waiver request will either be that the protocol title is withheld completely (PRISM will indicate “Protocol title withheld due to the confidential nature of the research”), or that an alternate title, proposed by the Principal Investigator, is substituted.

Examples of appropriate justification to waive the requirement to include the full protocol title or alter the title:

- There is more than negligible risk of stigmatization or discrimination by health care providers, health insurance plans, employers, or others by placing the protocol title in the medical records of participants.
- There is an expected deterrent effect on research participation by including the protocol title in the medical records of the study population.
- There is misleading information (for example disease condition, drug names) that might lead to conclusions about the person’s condition or related treatment which may increase potential for risk to the participant.

Example of inadequate justification to waive the requirement to include the full protocol title or alter the title:

- Participant privacy by itself is not considered an appropriate justification as electronic medical records are considered private. All personnel with access to the Research Flag in PRISM have completed training in confidentiality and privacy matters and the appropriate access and use of patient medical information. In addition, UVM Medical Center tracks all PRISM access and audit trails are in place to monitor access.
Q. NONCOMPLIANCE POLICY AND PROCEDURES – 9/23/2016

OVERVIEW

It is the responsibility of the Committees on Human Research (also referred to as CHRMS, CHRBSS, the Committee(s), or the IRB(s)), in accordance with the Federal-Wide Assurances between UVM/UVM Medical Center and the Department of Health and Human Services Office of Human Research Protections (OHRP), to investigate and review possible noncompliance; develop and ensure implementation of appropriate corrective actions; and ensure required reporting of any serious and/or continuing noncompliance. In all cases of noncompliance, the IRBs must assess the level of risk of harm, determine whether the research may safely continue, and specify those conditions necessary for the continued protection of human subjects. This document describes the procedures for handling these matters. This policy is not all encompassing, and the IRB reserves the right to use its discretion in individual cases.

DEFINITIONS

Noncompliance is defined as the conduct of research in a manner that deviates from the approved protocol or disregards or violates federal regulations or institutional policies and procedures applicable to human subjects research. Noncompliance may result from actions or omissions by study personnel, and can range from relatively minor or technical deviations to serious deviations that threaten subjects’ rights or welfare.

Serious Noncompliance is defined as noncompliance that, in the judgement of the IRB, potentially increases the risk of harm to research subjects, reduces benefits to human subjects, or compromises the integrity of the research oversight process.

Continuing Noncompliance is defined as a pattern of noncompliance (recurring or ongoing) that, in the judgement of the IRB, may indicate an underlying deficiency in knowledge of the regulations or IRB requirements or an unwillingness or inability to comply with these regulations/requirements.

GENERAL NONCOMPLIANCE REVIEW PROCEDURES

The investigation of potential noncompliance begins when the IRB becomes aware of potential noncompliance. This may include an allegation (unproved assertion) of noncompliance, a self-disclosure of noncompliance, or any other indication that noncompliance may have occurred. The process for the review of potential noncompliance involves initial administrative review, followed by an inquiry/fact finding process if indicated. Once complete, the IRB makes a determination as to whether the noncompliance is serious, continuing, or neither. The IRB determination will be documented in a summary report that contains a corrective action plan in cases of serious or continuing noncompliance. This process is detailed below, however at any point in the review process, the IRB designee may at their discretion:

- Recommend intervention for the safety of the research subjects
- Recommend the suspension of research activities
- Inform, involve, and/or provide salient documents to the PI, members of the research team, the Department Chair, Dean, legal counsel, or Institutional Officials, as appropriate
- Initiate reporting per federal regulations
- Initiate a monitoring visit
- Recommend immediate corrective actions

PROCESS OF NONCOMPLIANCE REVIEW AND DETERMINATION
**Initial Review of Allegation or Indication of Noncompliance:** When there is an allegation or indication of noncompliance, the first step is an administrative review to determine if, in the judgement of the person(s) conducting the review, there is the potential for serious or continuing noncompliance. The initial review may be conducted by the RPO Director, RPO Assistant Director(s), an IRB Chair (Executive Chair, Associate Chair, or Chair), or another Institutional Representative. Allegations/indications which are determined to have no potential to be serious and/or continuing noncompliance are resolved with either no follow-up (i.e. when an allegation or indication has no merit) or directly with the PI.

**Inquiry/Fact Finding Process:** If it is determined that the noncompliance has the potential to be serious or continuing or if questions remain following the initial review, then an inquiry (fact finding) process will begin. The particular circumstances of the noncompliance will determine when the fact finding begins and when the committee is briefed. The fact finding may be conducted by any IRB designee including a sub-committee or subcommittee member, the RPO Director, Assistant Director(s), an IRB Chair (Executive Chair, Associate Chair, or Chair) or other Institutional Representatives. The IRB may be briefed at any point throughout the fact finding process, as deemed appropriate by the designee. The fact finding process continues until the designee has arrived at a recommendation of determination (i.e. serious noncompliance and/or continuing noncompliance, or neither). A fact finding report is then prepared and includes the recommendation of determination and draft corrective actions. This fact finding report will be shared with the PI, and if applicable, other person(s) involved. All parties will be provided an opportunity to respond to any factual inaccuracies within the report before the committee deliberates.

**Deliberation by the IRB:** At a convened meeting, the IRB will consider all available information and make a determination as to whether the fact finding revealed serious noncompliance and/or continuing noncompliance, or neither. The following factors will be taken into consideration by the IRB or designee in making their initial determination as to whether the noncompliance is serious and/or continuing noncompliance. As each situation is unique, the indicators of noncompliance that are important in one case may not be relevant in other cases.

**Factors in the Determination of Serious Noncompliance:**
- Level of risk or potential risk to subjects
- Severity of violation of the research process
- Frequency or number of minor deviations or errors
- Intent
- Threat to integrity of the IRB review processes and requirements for the protection of human subjects (i.e. falsification of IRB documents)
- Other factors that, in the judgement of the IRB or designee, are relevant to the situation being reviewed.

**Factors in the Determination of Continuing Noncompliance:**
- Similarity of noncompliance to previous deviations and/or noncompliance within the same protocol.
- Similarity of noncompliance to previous deviations and/or noncompliance in other protocols conducted by the investigator.
- Likelihood that instances of noncompliance will continue without intervention

**Final Determination of the IRB:** If, in the judgement of the committee, the noncompliance is neither serious nor continuing, this determination will be shared with the PI. If, in the judgement of the
committee, the noncompliance is serious and/or continuing. The designee will prepare a summary report including the IRB’s determination and an approved corrective action plan. This report will be shared with the PI, who will be given 14 days to review it before it becomes final.

**Development of Corrective Action Plans:**
The IRB/designee will develop a proposed plan for corrective actions based on the information gathered during fact-finding and input from the principal investigator and/or other affected individuals. The proposed plan may:

- Require no further action
- Require minor corrective actions to achieve compliance
- Institute limitations on the use of data
- Require additional education
- Require the investigator and/or other affected individuals to develop and implement procedures to prevent recurrence
- Review internal departmental or institutional mechanisms and systems for opportunities to prevent recurrence or similar occurrences by others
- Require additional oversight (e.g., by other faculty member or department process)
- Require more frequent IRB reviews
- Require internal monitoring visits or monitoring plans
- Suspend or terminate individual protocols
- Restrict researcher’s research activities

**REQUESTS FOR RECONSIDERATION**
A PI may request a reconsideration of the IRB’s determination. Requests must be limited to claims that either (1) the process was faulty, resulting in considerable risk that the outcome was incorrect; or (2) that the findings and/or corrective actions imposed by the IRB were excessive or unjustified. The written request must be submitted within 14 days of receipt of the summary report and must specify the nature of any claimed procedural error or the perceived unfairness of actions taken. Reconsiderations will be conducted by an IRB Chair (Executive Chair, Chair, or Associate Chair), or Designee. The reconsideration process will result in one of three outcomes, either the summary report will stand and it will become final, the summary report will be modified and become final, or further investigation is necessary and will be initiated.

**REQUIRED REPORTING**
When noncompliance is determined to be serious and/or continuing, the final report will be forwarded to federal regulators if required, and to applicable Institutional Officials, the Departmental Chair, the Dean, and sponsors, if applicable.

**GUIDING PRINCIPLES FOR NONCOMPLIANCE REVIEW**

**Protection of Human Subjects:** The University of Vermont and UVM Medical Center are responsible for safeguarding the rights and welfare of human subjects involved in any research activity.

**Fairness:** The IRB strives to maintain a review that is impartial and honest, free from self-interest, prejudice or favoritism.

**Communication:** The committee will communicate with the PI during the review process at points determined to be appropriate by the IRB designee.
Confidentiality: All IRB discussions and documents regarding a situation of noncompliance are considered sensitive and will be handled in a confidential manner and in accordance with state and federal regulations. The IRB cannot, however, guarantee complete anonymity to informants or witnesses. Confidentiality will be maintained to the extent possible to protect privacy and prevent retaliation, while still allowing for a full and fair review. Information may be shared, as described above under Required Reporting.

Conflict of Interest: Any IRB member who feels that they have a conflicting interest must recuse themselves from reviewing the issue of noncompliance. IRB members who are also listed as key personnel on the protocol(s) will not participate in the review but may be asked for information.

Procedures: In addition to what has been stated within this policy, the Committee will follow all applicable procedures that are outlined within the Committee Operating Procedures document.
R. Electronic Signatures Policy 2016

<table>
<thead>
<tr>
<th>Policy</th>
<th>Electronic Records and Signatures in the InfoEd Electronic Submission Software</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective Date</td>
<td>12/14/16</td>
</tr>
<tr>
<td>Regulation</td>
<td>FDA 21 CFR Part 11  Electronic Records; Electronic Signatures</td>
</tr>
</tbody>
</table>

**Requirement for Compliance**
In March of 1997, FDA issued final part 11 regulations that provide criteria for FDA acceptance of, under certain circumstances, electronic records, electronic signatures, and handwritten signatures executed to electronic records as equivalent to paper records and handwritten signatures executed on paper. These regulations, which apply to all FDA program areas, were intended to permit the widest possible use of electronic technology, compatible with FDA’s responsibility to protect the public health.

Part 11 requires assurances in three basic areas: Record Archiving (audit trail), Electronic Signatures, and Security Controls.

**Achieving Compliance**
InfoEd in combination with institutional controls, meets the regulatory requirements in each of the areas of Record Archiving (audit trail), Electronic Signatures, and Security Controls.

The system and information tracked in it includes, but is not limited to, versioning of submissions, time and date stamps on routing, time and date stamps on status history, record access history and login history.

Institutional policy regarding authentication, configuration of security and workflow controls, and limits on access to the database, this supports the record archiving (audit trail) and security controls necessary for compliance.

The electronic signature procedure, which secures the user authentication (proof of claimed identity) at the same time the signature is generated, provides the same assurance as an original signature on a paper document, and signifies acceptance and adherence to the Committees’ certification and investigator agreement.

**Definitions**

**Principal Investigator (PI)** – The researcher who is responsible for the conduct of a research study at an institutional site.

**InfoEd** – An online protocol submission and review system utilized by the Research Protections Office, also referred to as “the system.”

**InfoEd Delegate** – The PI has the option to delegate a specific person or persons to create submissions and in some instances submit the protocol package. The delegation feature in the InfoEd system allows the assigned delegate(s) to view everything that the PI can view within the InfoEd system, including all protocol and grant information for that PI.

**InfoEd electronic signature** – InfoEd electronic signatures are based on use of a UVM NetID and the associated network account password (authentication). Authentication ensures no two individuals have the same combination of identification. Passwords must be regularly updated in accordance with University information security policies.

**Current Procedure for Signatures on Paper Applications Uploaded to the System**
The PI signs and dates the paper application, and the signed application is submitted electronically through the InfoEd system. The PI must submit the application in InfoEd or alternatively, the PI may request to the RPO office that their primary contact person be delegated the ability to submit the application on his/her behalf. Consistent with PI requirements, delegates are required to sign into the system with a UVM NetID and password.
Future Procedure for Electronic Signatures within the System
In the future, the electronic submission of documents will be replaced with electronic forms directly in the system. At that point there will no longer be a physical PI signature on the application. To meet the regulatory requirement for a valid electronic signature, all protocol submissions utilizing InfoEd’s electronic form sets must be submitted by the PI and may no longer be submitted by a primary contacted who has been delegated that authority. The PI may request to the RPO office that their primary contact person be delegated the ability to assist in the preparation of the protocol submission. Once a delegate has completed his/her work on the submission, the PI must then enter their NetID and password into InfoEd to review the materials, agree to the Investigator Certification language, and click the submit button.

Food and Drug Administration
Office of Regional Operations (HFC-100)
5600 Fishers Lane
Rockville, MD 20857

To Whom It May Concern:

Pursuant to Section 11.100 of title 21 of the Code of Federal Regulations, this is to certify that the University of Vermont, including its constituent parts, University of Vermont Medical Center, Inc. and University of Vermont Health Network, intends that all electronic signatures executed for research purposes, by our employees, agents, or representatives, located anywhere in the world, are the legally binding equivalent of traditional handwritten signatures.

Sincerely,

Richard Galbraith, MD, PhD
Vice President for Research
S. Research Tissue Acquisition Policy

UVM’s IRB has adapted the UVMMC’s 6-1-2014 Tissue Acquisition Policy as stated below.

Specimens obtained as part of research protocols:
Patients sometimes enroll in research studies and agree to have tissue obtained for study purposes. It is essential however, that sufficient tissue be obtained for complete examination in the Department of Pathology to ensure an accurate diagnosis for the patient even when samples are required for research purposes. Therefore, research protocols requiring tissue that would otherwise be sent to pathology for examination must (i) include procedures for ensuring the adequacy of diagnostic tissue for pathologic examination and (ii) receive approval from the surgical pathology quality assurance subcommittee on research specimens prior to activation. Such protocols must acknowledge that if feasible, tissue diverted from pathologic examination for investigative purposes will be provided to the Department of pathology for diagnostic or other patient management purposes as clinically indicated. Pertinent information for patients regarding the use of their tissue for research purposes (e.g. risks and benefits) must be included in the informed consent for such research studies.