

## **Part 7 - Participant Protection (July 2009)**

*All non-exempt human research subject to the HRPP is reviewed and must be approved by the applicable Institutional Review Board or other duly constituted committee approved by the Office of the Vice President for Research using criteria similar to those applied to federally-funded research and consistent with the principles outlined in the Belmont Report. This section describes some of the ways research participants are protected under the HRPP.*

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### **I. HRPP PROTECTION EXTENDS TO ALL SUBJECTS**

The HRPP protects the rights and welfare of all individuals who participate in University research as human subjects, regardless of whether they are intended “primary” subjects of the research or their participation is ancillary to the main study intervention.

For example, an individual’s participation in a study (directly or through contribution of data) may be needed simply as a measure of outcomes of interventions with other individuals or institutions. Thus, a protocol intended to measure the effectiveness of an educational intervention designed to encourage primary care physicians treating diabetic patients to perform annual foot exams might include provisions to review patient records pre- and post-intervention. Although the primary subjects of the intervention are the physicians, the patients whose records are reviewed also are human subjects. See [Part 2\(A\)](#) of this Operations Manual for a definition of “human subjects.”

Similarly, a survey might ask primary participants for private information about their friends, family members, or other individuals. Thus, a study of alcoholism in a given community might request from primary subjects information about the drinking habits of their relatives and peers. Again, although the main subjects are those who answer the survey, any additional individuals who are identified in the course of the study also are considered human subjects.

The classification of certain individuals or groups of individuals as human subjects or not human subjects is important because it triggers a number of requirements under federal regulations and the HRPP. For example, written informed consent of all prospective subjects is required unless the principal investigator demonstrates to the IRB’s satisfaction that the requirements for a waiver or alteration of consent, or waiver of documentation, have been met. Who is considered a human subject for purposes of the [Common Rule](#) continues to be a matter of continuing debate and discussion. For additional information, see “Clarification of the Status of Third Parties When Referenced by Human Subjects in Research” <http://www.hhs.gov/ohrp/nhrpac/documents/third.pdf>.

### **II. DATA AND SAFETY MONITORING PLANS**

The issue of data and safety monitoring makes relates most directly to clinical research. It is a process designed to protect the safety of individual participants in research studies and ensure the validity of research results and scientific integrity of a study. The portions of a protocol that describe the steps the research team will take to identify, address and report physical, social, or psychological events that may result from participation in a study constitute a data safety and monitoring plan (DSMP). A DSMP typically describes the timing, tools and/or methods to be employed for monitoring and evaluating study data during the course of the project, procedures for treatment or resolution (including a description of circumstances that will result in halting or terminating research), and procedures for and timing of reports to oversight bodies, such as the IRB, an independent monitor, an internal committee, a data safety monitoring board (DSMB), NIH, or FDA. University IRBs are required to ensure that, when appropriate, research plans make adequate provision for monitoring data collected to ensure subject safety.

In some cases, for example in high-risk research or where institutional or individual conflicts of interest dictate the need for external review mechanisms, a DSMB may be established as part of the DSMP. A DSMB is a formally chartered, independent committee whose stated goal is to protect the welfare and safety of the subjects participating in a specified research study. On a periodic basis, DSMBs assess the

accumulating study data to assure its integrity, its relevance to the scientific question, the appropriateness of continuing the study, and to assess any reported adverse events. Not all studies require a DSMB; the principal investigator and responsible IRB should assess the need for one based on the risk to study participants, the complexity of the study, and the size of the study. For example, DSMBs may be chartered when:

- The study is intended to provide definitive information about the effectiveness and/or safety of a medical intervention.
- Prior work suggests that the intervention under investigation may induce a potentially unacceptable toxicity.
- The study will evaluate mortality, morbidity, or other significant endpoints such that the inferiority of one treatment arm has safety as well as effectiveness implications.
- The study raises ethical issues and it would be important for the study to stop early if the primary scientific question had been definitively answered, even if secondary questions or complete safety information were not yet fully addressed.

A DSMB charter should include at least the following elements:

- A detailed description of the membership, including qualifications and experience;
- Roles and responsibilities of the DSMB;
- Authority of the DSMB;
- Timing and purpose of DSMB meetings;
- Procedures for maintaining confidentiality;
- Format, content and frequency of DSMB reports;
- Guidelines outlining the procedure for the principal investigator's; interaction with the board and whether the investigator may be invited to attend any open sessions;
- Statistical procedures, including monitoring guidelines, used to monitor the identified primary, secondary, and safety outcome variables; and
- Plans for changing the frequency of interim analyses as well as procedures for recommending protocol changes.

DSMB membership generally should include:

- Multidisciplinary representation of at least three individuals, including physicians and scientists from relevant specialties and a biostatistician;
- Members free of apparent significant conflicts of interest, whether they are financial, intellectual, professional, or regulatory in nature; and
- An appropriate number of members (beyond three, as necessary) to address the size and complexity of the study.

To protect patient safety and promote scientific integrity, a DSMB performs a variety of activities. It approves proposed safety measures for a protocol, provides written documentation of protocol review and agreement with study design, reviews study progress as provided in its charter, reviews cumulative data at established intervals to assess safety and efficacy, consults with principal investigators concerning safety or integrity issues arising during the course of the study, and provides written reports to the principal investigator, IRB and other oversight authorities summarizing its oversight activities (*e.g.*, results of chart reviews, summaries of consultations with the PI, concerns regarding subject safety, *etc.*), and any recommendations (*e.g.*, continuing the study, continuing the study with modifications, suspending the study for interim analysis, or terminating the study).

### III. PAYMENT TO RESEARCH SUBJECTS

The University recognizes the importance of encouraging individuals to participate in research as human subjects and the value of the time, effort and risk subjects contribute to University research efforts. The University permits payments to be made or other consideration provided to subjects to compensate them for these contributions, as long as the following criteria are met:

- Payment arrangements are specifically approved in advance by the relevant IRB.
- Payments or other consideration provided to subjects in return for their participation are not so significant as to be coercive or unduly influential (e.g., inducing subjects to accept unreasonable risks).
- Payments are prorated when appropriate to avoid inducing subjects to continue participation in a study when they otherwise would withdraw.
- Arrangements are made by the principal investigator to assure proper accounting of payments made to subjects, and required reporting to tax authorities, as required by University policy, with due consideration of privacy concerns.

Note: See [Standard Practice Guide 501.7](#), Research Subject Fees.

### IV. VULNERABLE SUBJECTS

Special rules apply to research involving vulnerable populations. These groups include but are not limited to:

- Children (individuals who have not attained the legal age for consent to the treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted);
- Pregnant women and fetuses;
- Prisoners (individuals involuntarily confined or detained in a penal institution, including individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing);
- Individuals who are cognitively impaired or lack decision-making capacity; and
- Individuals who otherwise may be subject to coercion or undue influence (e.g., economically or educationally disadvantaged persons; employees or students of investigators conducting the study; patients of physician-investigators).

When members of any of these groups participate in research, University IRBs require investigators to specify what additional protections, if any, will be provided to these persons to protect their rights and welfare (e.g., minimize risks unique to these groups and the possibility of coercion or undue influence). In reviewing these research projects, the IRBs ascertain that inclusion of a vulnerable population is adequately justified and that safeguards are implemented to minimize risks unique to that population.

Laws governing research involving vulnerable populations, including laws on who may consent on behalf of children or cognitively impaired or incapacitated adults, vary from state to state. [See Part 11\(D\)](#) for a detailed description on Michigan requirements and guidance for determining the nature of requirements applicable to research proceeding outside of Michigan.

#### **Standards for Review of Research Involving Vulnerable Populations**

The University IRBs apply the following standards when reviewing research involving vulnerable populations:

1. For federally supported research, the IRBs comply with all of the requirements of 45 C.F.R. part 46, to the extent the sponsoring agency has adopted the standards reflected in subparts B-D.
2. For FDA-regulated research involving children, the IRBs comply with the requirements of 21 C.F.R. part 50, subpart D.
3. For research not subject to the above regulations, the IRBs comply with the standards listed in the next section "Standards for IRB Review of Research Not Supported by Federal Agencies that Have Adopted the Standards Reflected in 45 C.F.R. part 46, subparts B-D and Not Regulated by FDA Under 21 C.F.R. part 50." As noted in the standards, the Institutional Official assumes the HHS secretary role for consideration of applications of the subparts. Requests for exceptions to the application of the subparts are forwarded by the IRB to the Institutional Official or the Deputy Institutional Official. The IO or DIO may seek the recommendation of the IRB Council in considering a proposed change in policy. Approved changes will appear as amendments to the Operations Manual and, if applicable, to IRB standard operating procedures, prior to implementation.

**Standards for IRB Review of Research Not Supported by Federal Agencies that Have Adopted the Standards Reflected in 45 C.F.R. part 46, subparts B-D and Not Regulated by FDA Under 21 C.F.R. part 50**

**A. Research Involving Pregnant Women, Fetuses, and Neonates**

A University IRB may approve a project involving pregnant women, fetuses, or neonates as subjects only if the following requirements are met:

***1. Research Involving Pregnant Women or Fetuses***

The IRBs may approve the involvement of pregnant women or fetuses only if all of the following conditions are met:

- Where scientifically appropriate, preclinical studies, including 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:
- The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important knowledge which cannot be obtained by any other means;
- Any risk is the least possible for achieving the objectives of the research;
- If the risk holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions required in 45 C.F.R. part 46, subpart B.
- If the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions in 45 C.F.R. part 46, subpart B, which provides an exception to paternal consent if the father is unable to consent because of unavailability, incompetence, or temporary incapacity, or the pregnancy resulted from rape or incest.
- Each individual providing consent is fully informed regarding the reasonable foreseeable impact of the research on the fetus or neonate;

- For minors who are pregnant, assent and permission are obtained in accord with this Section, if state law allows the minors to consent on their own to the treatment or procedures involved in the research (i.e., if the minors are not “children”), or, otherwise, under the children’s rules described below;
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- Individuals engaged in the research will have no part in determining the viability of a neonate.

## 2. *Research Involving Neonates*

- i. An IRB may approve research involving neonates of uncertain viability and non-viable neonates only if all of the following requirements are met:
  - Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
  - Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
  - Individuals engaged in the research will have no part in determining the viability of a neonate.
- ii. The following additional conditions apply to research involving neonates of uncertain viability:
  - The IRB determines that 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 the purpose of the research is the development of important knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
  - The legally effective informed consent of either parent of the neonate, or if neither is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent’s legally authorized representative is secured as required under 45 C.F.R. part 46, subpart B.
- iii. The IRB must determine that the following additional requirements will be met for proposed research involving non-viable neonates after delivery:
  - Vital functions of the neonate will not be artificially maintained;
  - The research will not terminate the heartbeat or respiration of the neonate;
  - There will be no added risk to the neonate resulting from the research;
  - The purpose of the research is the development of important knowledge that cannot be obtained by other means; and
  - The legally effective informed consent of both parents of the neonate is obtained as required under 45 C.F.R. part 46, subpart B (the IRB may not approve a waiver or alteration of consent for these studies). 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, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. If neither parent is available or competent, the consent of a legally authorized representative of one or both parents is not sufficient to support participation of the non-viable neonate in the research.
- iv. Research involving viable neonates is subject to the children’s research requirements described below.

### 3. *Research Involving, After Delivery, the Placenta, the Dead Fetus, or Fetal Material*

An IRB may approve research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus only if:

- Compliance with applicable state laws is assured (see [Part 11\(III\)\(D\)](#) for information about Michigan laws or contact the Health System Legal Office for assistance with other state laws).
- If information associated with the material described above is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent human research protections, including requirements for informed consent apply.

### 4. *Research Not Otherwise Approvable*

Research that is not approvable under one of the above provisions may still be approved by a University IRB if the IRB determines that all of the following conditions have been met:

- The research presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; and
- Approval is secured from the Institutional Official or Deputy Institutional Official after consultation with a panel of experts in pertinent disciplines. In granting the approval, the IO or the DIO must determine that the research will be conducted in accord with sound ethical principles and informed consent will be obtained in accord with the informed consent standards described in the 45 C.F.R. 46 subpart A: and
- Notice of the proposal is posted to the [HRPP website](#) for review and comment.

## B. Research Involving Prisoners

### 1. *Who is a Prisoner?*

A “prisoner” means any individual involuntarily confined or detained in a penal institution such as a prison, jail, or juvenile offender facility, and their ability to leave the institution is restricted. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of states or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing. Prisoners may be convicted felons, or may be untried persons who are detained pending judicial action, for example, arraignment, or trial. This policy applies to those persons incarcerated prior to participation in research and those who become incarcerated after participation has commenced.

The following are examples of individuals who are considered to be prisoners:

- Individuals who are detained in a residential facility for court-ordered substance abuse treatment as a form of sentencing or alternative to incarceration are prisoners; however, individuals who are receiving non-residential court-ordered substance abuse treatment and are residing in the community are not prisoners.
- Individuals with psychiatric illnesses who have been committed involuntarily to an institution as an alternative to a criminal prosecution or incarceration are prisoners; however, individuals who have been voluntarily admitted to an institution for treatment of a psychiatric illness, or who have been civilly committed to non-penal institutions for treatment because their illness makes them a danger to themselves or others, are not prisoners.
- Parolees who are detained in a treatment center as a condition of parole are prisoners; however, persons living in the community and sentenced to community-supervised monitoring, including parolees, are not prisoners.

- Probationers and individuals wearing monitoring devices are generally not considered to be prisoners; however, situations of this kind frequently require an analysis of the particular circumstances of the planned subject population.

## 2. *IRB Composition*

A University IRB may approve research that may involve prisoners only if its composition at the time of its determination meets the following requirements:

- A majority of the Board (exclusive of prisoner members) has no association with the prison(s) involved, apart from their membership on the Board; and
- At least one member of the Board is a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one Board only one Board need satisfy this requirement.

## 3. *Additional Conditions on Research Involving Prisoners*

An IRB must determine the following criteria will be met before approving research involving prisoners.

- The research under review represents one of the categories of research permissible as provided in subsection 4 below:
- 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;
- The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
- 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 the principal investigator provides to the Board justification in writing for following 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;
- The information is presented in language which is understandable to the subject population;
- 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
- Where the Board 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.

Prior to enrolling any prisoners on a study, the IRB must certify that these requirements have been fulfilled to the Institutional Official or Deputy Institutional Official except as allowed in urgent situations where the best interests of the subject requires participation in the research prior to fulfillment of all requirements as described in federal guidance at <http://www.hhs.gov/ohrp/humansubjects/guidance/prisoner.htm> section J, #3 and <http://www.hhs.gov/ohrp/prisonerfaq.html#q19>

#### 4. Permitted Categories of Research

Only the following categories of research may involve prisoners:

- 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;
- 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;
- 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 Institutional Official or Deputy Institutional Official has consulted with appropriate experts including experts in penology, medicine, and ethics, and notice of the proposal is posted to the [HRPP website](#) for review and comment;
- Research on practices, both innovative and accepted, which 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 which may not have any added benefit over standard care the study may proceed only after the Institutional Official or Deputy Institutional Official has consulted with appropriate experts, including experts in penology, medicine, and ethics, and notice of the proposal is posted to the [HRPP website](#) for review and comment; or
- Epidemiological research, consistent with the standards published in the [Federal Register](#) on June 20, 2003.

The IRBs follow the guidance published at <http://www.hhs.gov/ohrp/policy/index.html#prisoners>; and <http://www.med.umich.edu/irbmed/guicance.htm> (scroll down to "Prisoners and Research") when a research participant becomes a prisoner during the course of a study, except that the Institutional Official or Deputy Institutional assumes the role of the HHS Secretary for studies requiring certification or approval.

#### C. Research Involving Children

"Child" is a term of art under federal research regulations and refers to an individual who has not yet reached "the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted" 45 C.F.R. § 46.402(a); 21 C.F.R. § 50.3(o). Detailed guidance on who is considered a "child" for purposes of human research conducted at the University of Michigan or by University researchers is provided in Part 11 of this Operations Manual. Similarly, [Part 11](#) defines the term "guardian" for purposes of determining whose permission may be required for a child to participate in research when his or her parents are unavailable.

A University IRB may approve a project involving children as subjects only if the following requirements are met:

### *1. Research Involving No More Than Minimal Risk*

Research involving no more than minimal risk may be approved only if the IRB finds and documents that adequate provisions have been made for soliciting assent from the children and permission from at least one parent or the guardian of each child participant, unless waivers or substitute mechanisms are approved under the standards described in 45 C.F.R. part 46, subpart D.

### *2. Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Subjects*

Research involving greater than minimal risk and no prospect of direct benefit may be approved if the IRB finds and documents that:

- The intervention or procedure under investigation holds out the prospect of direct benefit to individual participants, or the monitoring procedure is likely to contribute to the subject's well-being; and
- The risk is justified by the anticipated benefit to participants; and
- The relation of the anticipated benefit to the risk is at least as favorable to participants as that presented by available alternative approaches; and
- Adequate provisions have been made for soliciting assent from the children and permission from at least one parent or guardian of each child participant, unless waivers or substitute mechanisms are approved under the standards described in 45 C.F.R. part 46, subpart D.

### *3. Research Involving Greater Than Minimal Risk and With No Prospect of Direct Benefit to Individual Subjects*

Research involving greater than minimal risk and no prospect of direct benefit may be approved if the IRB finds and documents that:

- The risk represents a minor increase over minimal risk; and
- The intervention or procedure presents experiences to subjects that are reasonable and commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations; and
- The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
- Adequate provisions are made for soliciting assent of the children and permission of both parents or the child's guardian, unless waivers or substitute mechanisms are requested and meet the standards described in 45 C.F.R. part 46, subpart D. If one parent is deceased, unknown, incompetent, or not reasonable available, or if one parent has sole legal custody of the child, only one parent's consent is required.

### *4. Otherwise Unapprovable Research*

Research that is not approvable under one of the above categories may still be approved by a University IRB if:

- The IRB finds and documents that the research presents a reasonable opportunity to further understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
- Approval is secured from the Institutional Official or Deputy Institutional Official after consultation with a panel of experts in pertinent disciplines. In granting the approval, the IO or the DIO must determine that the research will be conducted in accord with sound ethical principles and adequate provisions are made for soliciting the assent of

- children and the permission of their parents or guardians consistent with the standards described in 45 C.F.R. § 46.408; and
- Notice of the proposal is posted to the [HRPP website](#) for review and comment.

#### D. Research Involving Adults with Cognitive Impairment or Otherwise Impaired Decision-making Capacity

Impaired or limited decision-making capacity covers a broad spectrum of conditions. A health person in shock may be temporarily decisionally impaired. Another may have been severely mentally retarded since birth, while yet a third who has schizophrenia may have fluctuating capacity.

Federal regulations do not include specific protections for adults with impaired decision-making capacity similar to regulations governing research with pregnant women, prisoners, and children. Through eResearch, however, the IRBs determine whether research involves participants who have diminished decision-making capacity. The IRBs also consider limiting the types of research in which cognitively impaired adults may be enrolled based on the purpose, risk, and potential benefit of the research and whether the research question could be answered by enrolling adults who are able to consent.

In each such identified case, the protocol or application must describe any additional safeguards planned to assure appropriate consent. The IRB then must evaluate the appropriateness of the research and the adequacy of the investigator's proposed plan for initial and, if applicable, ongoing assessment of participants' capacity to consent. For those participants unable to consent, the IRB must determine whether assent must be secured and, if so, whether the investigator's proposed plan for assent is adequate. The requirement for assent may be waived by the IRB only if: (i) the capability of some or all of the subjects is so limited that they cannot reasonably be consulted; (ii) the intervention or procedure holds out the prospect of direct benefit to the health or well-being of the subjects and is available only in the context of the research; or (iii) the research otherwise meets the conditions for waiver of consent consistent with the standards described at 45 C.F.R. §§ 46.116 or 46.117.

An IRB may approve participation of adults with cognitive impairment or diminished decisionmaking capacity only under the following circumstances:

##### *1. Research Involving No More Than Minimal Risk*

Research involving no more than minimal risk may be approved only if the IRB finds and documents that adequate provisions have been made for soliciting assent from the subject, if appropriate, and permission of the subject's legally authorized representative (e.g., next-of-kin or legal guardian). The IRB may approve an exception to the assent requirements if the standards described in 45 C.F.R. § 46.408(a) are met. The IRB may approve an exception to the requirement for permission of the subject's LAR if a waiver of consent or documentation would be acceptable under 45 C.F.R. §§ 46.116 or 46.117.

##### *2. Research Involving Greater Than Minimal Risk But Presenting the Prospect of Direct Benefit to the Individual Subjects*

Research involving greater than minimal risk may be approved if the IRB finds and documents that:

- The intervention or procedure under investigation holds out the prospect of direct benefit to individual participants, or the monitoring procedure is likely to contribute to the subject's well-being; and
- The risk is justified by the anticipated benefit to participants; and

- The relation of the anticipated benefit to the risk is at least as favorable to participants as that presented by available alternative approaches; and Adequate provisions have been made for soliciting assent from the subject and permission from the subject's legally authorized representative (e.g., next-of-kin or legal guardian), or assent is waived consistent with the standards described in 45 C.F.R. § 46.408(a).

### *3. Research Involving Greater Than Minimal Risk and With No Prospect of Direct Benefit to Individual Subjects*

Research that is not approvable under one of the above categories may still be approved by a University IRB if the IRB finds and documents that:

- The research presents a reasonable opportunity to further understanding, prevention, or alleviation of a serious problem affecting the health or welfare of cognitively impaired adults or adults with diminished decisionmaking capacity;
- Approval is secured from the Institutional Official or Deputy Institutional Official, after consultation with a panel of experts in pertinent disciplines; determination that the research will be conducted consistent with sound ethical principles; and determination that adequate provisions have been made to solicit the assent of the participant and permission of his or her LAR, consistent with the standards described at 45 C.F.R. 46.408(a); and
- Notice of the proposal is posted to the [HRPP website](#) for review and comment.

## **V. COMPENSATION FOR INJURIES**

University policy and IRB procedures require that for research involving more than minimal risk, the informed consent process provide an explanation as to whether any compensation or treatment will be provided to an injured subject (injury in this context refers both to physical injuries and to less tangible injuries, such as injury to reputation or legal rights). If so, the compensation and treatment is described, or the subject is told where to find additional information. Exculpatory language (e.g., language that provides that a subject "assumes the risk" for participation in a study) is prohibited in informed consent documents. [See http://www.hhs.gov/ohrp/humansubjects/guidance/exculp.htm for additional examples of exculpatory and non-exculpatory language.](http://www.hhs.gov/ohrp/humansubjects/guidance/exculp.htm)