DHR HEALTH INSTITUTE FOR RESEARCH & DEVELOPMENT
POLICY AND PROCEDURE

SUBJECT: Considerations for Special Subject Populations	Policy #: CRP-1044
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DEPARTMENT: DHR Health Institute for Research & Development	
	EFFECTIVE: 02/19
APPROVED BY: Sohail Rao, MD, D.PHIL, President & Chief Executive Officer (Institutional Official, OHRP, DHHS)	REVIEWED/REVISED: 02/19, 02/20, 11/20, 01/21, 04/21, 05/21, 03/22

Purpose:
The purpose of this document is to describe the DHR Health Institute for Research and Development standard for conducting research with Special Subject Populations.

Applies To:
This policy applies to the following: staff and members of the Institutional Review Board; potential research investigator; Physician staff employed by RMF and its affiliates; staff employed by DHR Health and its affiliates; faculty, fellows, residents, students of academic institutions with a current affiliation agreement with DHR Health Institute for Research & Development; staff and physicians of non-academic institutions with a current affiliation agreement with DHR Health Institute for Research & Development; Physicians with privileges to practice medicine in DHR Health, Physicians and staff employed by Starr County Memorial Hospital and its affiliates; faculty, fellows, residents, students of academic institutions with a current affiliation agreement with Starr County Memorial Hospital and its affiliates; staff and physicians of non-academic institutions with a current affiliation agreement with Starr County Memorial Hospital and its affiliates; Physicians with privileges to practice medicine in Starr County Memorial Hospital and its affiliates.

Research Involving Children:
The DHR Health Institute for Research and Development adheres to the regulatory requirements for research with children as outlined in 45 CFR 46 Subpart D and 21 CFR 50 Subpart D. When reviewing research with children, the IRB membership includes at least one member who is knowledgeable about or experienced in working with children.

Definitions:

A. Children - Federal law defines "children" as persons who have not attained the legal age for consent to treatment for procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. Under the State of Texas law, persons under the age of eighteen (18) generally meet this definition of "children" with the exceptions noted below. As a result, permission of the child's parent(s) or guardian(s) must generally be obtained prior to the participation of that child in research.

- The provisions that permit a minor to be considered emancipated vary depending upon the circumstance. Unless a minor has been emancipated by court order, which should be confirmed by requesting a copy of the order, a minor should NOT be considered emancipated for purposes of consenting to participation in research.

B. Guardian - Under federal law, "guardian" means an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

- A child's "guardian" may provide legally effective informed consent for participation in research. If a guardian provides consent, the court order or legal authorization to consent to general medical care should be copied and included in the research records with the consent document. It is important to note that physical custody and legal guardianship may not be the same for some children, and that courts may only grant partial or joint custody in some cases. Review of the court order or other legal documentation establishing the guardianship is

- necessary to determine who may provide consent for participation in research on behalf of the child.

C. Permission - The agreement of parent(s) or guardian to the participation of the child in research.

D. Assent - An affirmative agreement by the child to participate in research. Mere failure to object should not be construed as assent without an affirmative agreement.

E. Parent - A child's biological or adoptive parent.

Applicable Categories of Research:
The IRB reviews all research involving children as participants and approves only research that satisfies all of the conditions of applicable federal regulatory subpart sections. The IRB assesses the potential risks and benefits for each research proposal, and the provisions for permission and assent, to determine if the activity satisfies the conditions for a category of research permitted for children, as specified in DHHS 45 CFR 46.404, 46.405, 46.406, 46.407 and 46.409 and FDA 21 CFR 50.51, 50.52, 50.53, 50.54 and 50.56.

The research categories are described as follows:

(45 CFRF 46.404 and 21 CFR 50.51) Research that does not involve greater than minimal risk may be approved if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

(45 CFR 46.405 and 21 CFR 50.52) Research involving greater than minimal risk, but presenting the prospect of direct benefit to an individual participant, or a monitoring procedure that is likely to contribute to the participant's well-being may be approved if the IRB finds that:

- The risk is justified by the anticipated benefit to the participant;
- The relationship of anticipated benefit to risk is at least as favorable as that presented by available alternative approaches; and
- Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

(45 CFR 46.406 and 21 CFR 50.53) Research involving greater than minimal risk with no prospect of direct benefit to individual participants, but likely to yield generalizable knowledge about the participant's disorder or condition may be approved if the IRB finds that:

- the risk represents a minor increase over minimal risk;
- the intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations;
- the intervention or procedure is likely to yield generalizable knowledge about the participant's disorder or condition which is of vital importance for the understanding or amelioration of the participant's disorder or condition; and

- adequate provisions are made for soliciting assent of the children or permission of their parents or guardians.

(45 CFR 46.407 and 21 CFR 50.54) Research that is not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health of welfare of children may be approved if the IRB and the Secretary of Health and Human Services (DHHS), after consultation with a panel of experts in pertinent disciplines and following an opportunity for public review and comment, find that the research in fact satisfies one of the above three categories; or satisfies all of the following requirements

- the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health and welfare of children;
- the research will be conducted in accordance with sound ethical principles; and
- adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

If the research study is not Federally-supported or subject to FDA regulation, the IRB Office will request review by a panel of pediatric experts to determine the applicability of approval under Section 45 CFR 46.407.

Consent Requirements
If a research study is designated as meeting the criteria for (45 CFR 46.404 or 21 CFR 50.51); or (45 CFR 46.405 or 21 CFR 50.52), the IRB will determine whether adequate provisions have been made to solicit the permission of each child's parents or guardians, unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless one parent has sole legal responsibility for the care and custody of the child. Where parent permission must be obtained, the IRB may determine that the permission of one parent is sufficient.

If a research study is designated as meeting the criteria for (45 CFR 406 or 21 CFR 50.53); or (45 CFR 46.407 or 21 CFR 50.54), the IRB requires the permission of both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless one parent has sole legal responsibility for the care and custody of the child.

The permission of the child's parent(s) must be documented by the inclusion of a signature on the consent form indicating that the child is under the age of 18 and therefore cannot provide direct consent.

Waiver of Parental Consent for Abused or Neglected Children
The IRB may waive the requirement for parental consent if it determines that the research study is designated for conditions or for a subject population (e.g., neglected or abused children) for which parental or guardian permission is not a reasonable requirement to protect the subjects (see 45 CFR 46.408). If the IRB grants this type of waiver based on this criterion, it must substitute an appropriate mechanism for protecting the children-subjects. The choice of such mechanism will depend on the

nature and purposes of the proposed research activities; the risk and anticipate benefit to the children-subjects; and the age, maturity, status, and condition of the proposed subject population.

The IRB will not waive the requirement to obtain parent or guardian permission based on the above-stated criterion if the research study is subject to FDA regulations (21 CFR Parts 50 and 56) governing human subject protections (i.e., the research study involves an evaluation of any article regulated by the FDA).

Consent for Continued Participation
If the research study involves children (age < 18 years old) who will continue to undergo research interventions (including the collection of identifiable private information) after they become adults, the IRB research protocol should address a mechanism (e.g., addendum informed consent document with copy of originally signed consent form attached; new consent form) whereby direct consent for continued participation in the research study will be obtained from these individuals at the time they reach adult status.

Assent Requirements
Adequate provisions must be made for soliciting the assent of the children-subjects when, in the judgment of the IRB, the children-subjects are capable of providing assent. In determining whether children-subjects are capable of providing assent, the IRB will take into account the ages, maturity, and psychological state of the involved children. This judgment may be made for all children to be involved in given research study, or for each child, as the IRB deems appropriate. The assent of a child-subject will not be a necessary condition for proceeding with the child's research participation if the IRB determines:

- that the capability of some or all of the children-subjects is so limited that they cannot reasonably be consulted;
- 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-subjects and is available only in the context of the research; or
- the IRB finds and documents that:
    - the research involves no more than minimal risk to the children-subjects;
    - the waiver of assent will not adversely affect the rights and welfare of the children-subjects;
    - the research could not practicably be carried out without the waiver; and
    - whenever appropriate, the children-subjects will be provided with additional pertinent information after participation.

Children who are developmentally able to provide written assent will sign the consent document in addition to the parent(s). For children who are not determined to be developmentally able to sign the consent document, the investigator must certify that the purpose and nature of the research was explained in age appropriate language and that the child provided positive affirmation to participate.

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Research Involving Prisoners:
The DHR Health Institute for Research and Development IRB adheres to the regulatory requirements for research which involves a prisoner as outlined in 45 CFR 46 Subpart C.

Definitions:

A. Prisoner - A prisoner is defined as "an individual involuntarily confined or detained in a penal institution" and encompasses individuals sentenced to such an institution under criminal or civil statute, 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.

B. Prisoner Representative - An individual who is currently or formerly a prisoner or an individual who has a close working knowledge, understanding and appreciation of prison conditions from the perspective of the prisoner (e.g., prison chaplain, prison social worker, prison health care worker.)

C. Minimal Risk - For research involving prisoners, the IRB will use the following definition for "minimal risk": "Minimal risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons."

Regulatory Requirements
Research involving prisoners that is federally funded or which is conducted in a federal prison will be reviewed by a convened IRB committee which includes at least one member who is a prisoner or a prisoner representative with appropriate background and experience to serve in that capacity. All other studies involving prisoners will include a prisoner representative as a consultant. This includes initial review, continuing review, full-board modifications, and reportable unexpected or unanticipated problems.

- Modifications that would otherwise be approvable by expedited review can be expedited (with the exception of DoD funded studies) as long as the prisoner representative receives a copy of the modification and concurs that it does not adversely affect the prisoners.

The IRB will approve the research only if it finds and documents that:

1. The research meets one of the regulatory criteria for approval addressed under 45 CFR 46.306 (a)(2); that is the research is a 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;
   - 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;
   - 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 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; or
- 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 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 the intent to approve such research.

2. any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, and quality of food, amenities and opportunity for earnings in the prison, are not of such 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;
3. the risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
4. 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 IRB 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 research project;
5. the information is presented in a language which is understandable to the subject population;
6. 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;
7. where the IRB finds there may be a need for follow-up examination or care of subjects 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 subjects of this fact.

Note: An IRB finding that follow-up examination or care of the prisoner-subjects may be needed after the end of their study participation will necessitate a change in the standard Compensation for Injury section of the informed consent document. The change will need to address the provision of long-term care for this subject population and must be prior approved by legal counsel to the IRB.

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If a study utilizing prisoners as research participants is federally funded, the DHR Health Institute for Research and Development will send a letter to the Office for Human Research Protections (OHRP) indicating it has approved a study that will include prisoners, the category the study fits into as well as how the study satisfies the six criteria noted under the regulations. A research study is not permitted to commence for DHHS supported research until written approval is received from OHRP on behalf of the DHHS Secretary under the provisions of 45 CFR 46.306(a)(2).

If a subject becomes a prisoner after enrollment in a research study the investigator should notify the IRB immediately. Either the prisoner-subject must be withdrawn from study participation; or the IRB must, at the earliest opportunity, re-review the research protocol and consent form in accordance with the listed requirements. The IRB can either (a) approve the involvement of the prisoner-subject in the research or (b) determine that this subject must be withdrawn from the research. Note that if the subject-prisoner is withdrawn from study participation, s/he must be fully informed of the reason for such action

Research Conducted in the Federal Bureau of Prisons

The Federal Bureau of Prisons has adopted extensive regulations for researchers seeking to use federal prisoners as research subjects. Among other things, these regulations prohibit use of prisoners within federal facilities for "medical experimentation, cosmetic research, or pharmaceutical testing." 28 C.F.R. 512.11(a)(3). In addition, strict limitations are imposed on incentives to prisoner/participants, and researchers may not promise confidentiality to subjects who reveal a future intent to engage in criminal behavior.

Research Involving Pregnant Women, Neonates, and Fetuses

Definitions

A. Dead fetus means a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

B. Delivery means complete separation of the fetus from the woman by expulsion or extraction or any other means.

C. Fetus means the product of conception from implantation until delivery.

D. Neonate means a newborn.

E. Nonviable neonate means a neonate after delivery that, although living, is not viable.

F. Pregnancy encompasses the period of time from implantation until delivery. A woman will be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

G. Viable, as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the Federal Register guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of subparts A and D of this part.

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Regulatory Requirements
For research involving pregnant women, fetuses, or neonates the IRB will approve the conduct of the research only if it finds that the research meets the regulatory criteria for approval addressed under the federal regulations at 45 CFR 46 Subpart B (45 CFR 46.204, "Research involving pregnant women or fetuses prior to delivery"; 45 CFR 46.205, "Research involving neonates"; 45 CFR 46.206, "Research involving, after delivery, the placenta, the dead fetus, or fetal material").

For research that does not meet the criteria for approval addressed under 45 CFR 46.204, "Research involving pregnant women or fetuses prior to delivery"; 45 CFR 46.205, "Research involving fetuses after delivery"; or 45 CFR 46.206, "Research involving, after delivery, the placenta, the dead fetus, or fetal material," the IRB must find that:

- the research presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women or fetuses; and

- the research, if federally supported, will be submitted for review and approval by the Secretary, DHHS, in accordance with the provisions of 45 CFR 46.207, “Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women or fetuses”. If the research study is not federally-supported, the IRB will use a review by a panel of obstetrician/ gynecology experts (2 members with expertise in the area who are not currently IRB members) and an ethicist to recommend whether to approve the study as research that presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women or fetuses.

Consent
Pregnant Women/Fetus Prior to Delivery
For research involving pregnant women or the fetus prior to delivery, the documented, written informed consent of the pregnant women or her authorized representative will be obtained in accordance with the provisions of 45 CFR 46.204; unless the IRB grants either a waiver of informed consent in accordance with 45 CFR 46.116(f) or a waiver of the requirement to document informed consent in accordance with 45 CFR 46.117(c).

Neonates of Uncertain Viability
For research involving neonates of uncertain viability, the documented, written informed consent of either parent or the authorized representative of either parent will be obtained in accordance with the provisions of 45 CFR 46.205; unless the IRB grants either a waiver of informed consent in accordance with 45 CFR 46.116(f) or a waiver of the requirement to document informed consent in accordance with 45 CFR 46.117(c).

Nonviable Neonates
For research involving nonviable neonates (i.e., neonates determined to be unable, after delivery, to survive to the point of independently maintaining heartbeat and respiration), the documented, written informed consent of both parents will be obtained in accordance with the provisions of 45 CFR 46.205.

- If either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the IRB may approve the research based on the consent of one parent. (Note: the consent of the father need not be obtained if the pregnancy resulted from rape or incest.)
- Note: the IRB may not grant approval for authorized representative (i.e., proxy) consent or a waiver of the requirement to obtain consent (i.e., 45 CFR 46.116 (c) or 45 CFR 46.116 (d)) for research involving nonviable neonates.

Fetal Material Derived from Abortion
For research involving the dead fetus or fetal material derived from an induced abortion, the documented written informed consent of the mother must be obtained.

- The research protocol must specify that informed consent for use of the fetal tissue for research will be obtained separately from, and after, the consent is obtained for the abortion.
- No remuneration, compensation or other consideration of any kind may be offered to a woman to consent to the use of fetal tissues for research.
- The donor may not designate the recipient of fetal tissue.

All persons who participate in the procurement, use or transplantation of fetal tissue must be informed as to the source of the tissue (e.g., abortion, miscarriage, still birth, ectopic pregnancy). Any protocol that involves an intervention derived from fetal tissue must include the information as part of the informed consent document and/or process.

If researchers are obtaining fetal tissues or organs from sources outside of the DHR Health system, confirmation must be provided from the outside source that the material was collected with appropriately obtained consent under applicable laws.

Fetal research funded by the DOD must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.

Research Involving Mentally Disabled Individuals

Definitions

A. Mentally disabled persons are those who have a psychiatric, organic, developmental or other disorder that affects cognitive or emotional functions, or may result from the effect of drugs or alcohol diminished capacity. This may impair their ability to understand the risks and benefits for participation in research and to autonomously provide informed consent. The impairment may be temporary, permanent or may fluctuate.

B. Legally Authorized Representative: An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

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Internal Review Requirements

The DHR Health Institute for Research and Development requires additional safeguards for research involving persons with mental disabilities. The IRB will approve the research only if it finds that:

1. the research bears a direct relationship to the mentally disabled subject's condition or circumstance;
2. the research meets one of the following criteria:
   - presenting no greater than minimal risk to the involved subjects;
   - presents an increase over minimal risk to involved subjects, but which offers the potential for direct individual benefit to the subject;
   - presents a minor increase over minimal risk to involved subjects and which does not have the potential for direct individual benefit; provided that the knowledge sought has direct relevance for understanding or eventually alleviating the subjects' disorder or condition

In evaluating a protocol involving the enrollment of persons with mental disabilities, The IRB may consider requiring additional safeguards, as appropriate, for a given protocol. Such safeguards may include any of the following:

- use of an independent party (independent of the study investigator with appropriate expertise) to assess the capacity of the potential subject;
- use of standardized assessment of cognition and/or decisional capacity;
- use of informational or educational techniques;
- use of an independent person to monitor the consent process;
- use of waiting periods to allow for additional time to consider information about the research study;
- use of proxy consent;
- use of assent in addition to proxy consent in order to respect the autonomy of individuals with decisional impairment;
- use of a witness. The IRB will determine the following when choosing this option:
  - whether the witness needs to be unbiased (which means the individual is not part of the study team nor a family member of the potential participant)
  - whether the witness will observe the entire consent process or just the signature

Consent

In general, all adults, regardless of diagnosis or condition, should be presumed competent to consent to participation in research unless there is evidence of serious disability that would impair reasoning or judgment. In making the determination about whether it is appropriate for investigator's to utilize proxy consent, the IRB will take into consideration the following:

- the rationale for the need to obtain proxy consent;
- the criteria that will be used in determining whether a potential subject has a mental disability sufficient to require the use of proxy consent, including any use of standardized assessment tools;

- whether any additional methods are proposed to enhance subjects' ability to achieve decisional capacity with regard to the proposed study (e.g., reading of the consent form may not be sufficient and use of other tools such as videos, educational materials, post-test, etc. might be considered to assist potential subjects in understanding what is involved with the research);
- who will be approached, and in what order, to provide proxy consent.

The following are specific procedures that must be followed if proxy consent is utilized:

- Persons with a mental disability may also have been adjudicated legally incapacitated by a court decision. If such persons are considered for enrollment in a research protocol, the only party who may provide proxy consent is the court-appointed guardian. The guardian may only provide proxy consent if the court order, appointing them guardian, specifically states that they have the authority to enroll the incapacitated person into a research protocol. For this category of subjects, a copy of the court order appointing the guardian and granting the guardian authority to enroll the person into a research study should be attached to the informed consent document.
- Persons may also, through a health care proxy appointed by a power of attorney, designate a person to make decisions for them in the event that they are subsequently incapacitated. This person may give proxy consent for enrollment of a subject in research.
- If a potential subject has neither a guardian, nor a health care proxy designated, the investigator may obtain the informed consent of the subject's legally authorized representative. Where neither a court-appointed guardian, nor a health care proxy exists, investigators may seek informed consent from the following individuals, in the order listed below:
    - spouse, unless an action for divorce is pending, and the adult children of the principal are not the children of the spouse;
    - adult child
    - a parent (natural or adoptive);
    - adult brother or sister;
    - adult grandchild
    - an adult who has knowledge of the principal's preferences and values, including, but not limited to, religious and moral beliefs, to assess how the principal would make health care decisions

When a person is giving proxy consent, the proxy should be informed that, where possible, s/he should base the decision on substituted judgment, reflecting the views that the subject expressed while decisionally capable. The proxy should be fully informed on the risks, benefits and alternatives to the research. If the values of the subject are not known with respect to a proposed research study, the proxy should act in the best interest of the subject.

If a person with a mental disability is capable of exercising some judgment concerning the nature of the research and participation in it, the investigator should obtain the subject's assent in addition to the consent of his/her legally authorized representative.

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The verbal objection of an adult with a mental disability to participate in the research should be binding.

If the subject, at any time, objects to continuing in the research study, such objection should be respected.

Where the condition causing the subject's mental disability is of an intermittent or temporary nature, the informed consent process should include a mechanism for obtaining the subject's subsequent direct informed consent to participate in the research. If a subject regains decision making capacity and declines to continue in the research, the decision must be respected.

Documentation of Consent and Assent: Informed Consent Document
Adult subjects, not deemed to have a decisional impairment as a result of a mental disability, should read and sign the informed consent document in the standard manner.

For adult persons with decisional impairment as a result of a mental disability, the investigator should document the following before obtaining the consent and signature of the subject's legally authorized representative or guardian and the signature of the unbiased witness to this consent, if required by the IRB:

- the conclusion that the subject is incapable of understanding the information presented regarding the research, to appreciate the consequences of acting (or not acting) on that information, and to make a choice;
- the information provided to the subject's legally authorized representative regarding the cognitive and health status of the subject, the risks and benefits of the research, and the role of the proxy.

To document obtaining the assent of a subject with a mental disability, a Verification of Explanation statement should appear on the consent document and be signed and dated by the Principal Investigator, listed co-investigator, or other research staff when authorized by the IRB.

Documentation of Consent and Assent: Research Record
In studies in which some or all participants may have a mental disability, it is recommended that at the time of obtaining consent the following be documented in a note to file for the subject's research record:

- whether the subject demonstrated the ability to understand the nature of the research procedures, the potential risks and benefits, the voluntary nature of the participation and to make a personal judgment about participation;
- use of any supplemental methods to enhance or evaluate decisional capacity;
- a summary of the matters discussed with the subject's legally authorized representative.

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Research Involving Terminally Ill Patients

Research involving terminally ill patients presents additional concerns in that potential subjects tend to be more vulnerable to coercion or undue influence, and the research is likely to present greater than minimal risk. As a result, special attention should be given to the informed consent process. The following elements must be emphasized:

- Accurate information concerning eligibility for participation and risks and benefits should be conveyed clearly and in a manner that will not either engender false hope or eliminate all hope;
- Patients should be fully informed of the availability of treatment alternatives, including at what point their participation in the research study should or may be terminated to permit a treatment alternative, and that an alternative may include no additional treatment;
- Any costs to the patient associated with research study participation should be stated explicitly.