

## Section 15: Vulnerable Populations

---

People are autonomous when they can deliberate personal goals and act accordingly. Some individuals may have limited autonomy and be unable to give informed consent. Additional protections may be warranted in these instances.

### 15.1 Inclusion of Children as Participants in Research

In cases where the investigator plans to involve children as research participants, the following will be considered:

1. **Whether or not the research represents minimal risk to the child.** The IRB will consider if it is possible to obtain assent from the children who will take part in the study and whether at least one parent or guardian is available to give permission for the child to take part in the research. The IRB will review such issues as the relative risk to the population of children under review. If these risks were perceived to be the risks that are encountered by children in ordinary life, the committee or IRB member would find and document this information in the study's approval.
2. **Whether the research is greater than minimal risk but offers the prospect of direct benefit.** In cases where the research being proposed is of greater than minimal risk to the child but may offer the prospect of direct benefit to the child, the IRB will consider whether or not some, all or none of the children are capable of giving assent and that permission will be sought from both parents as they are available. The IRB will also consider that the research being proposed has an anticipated benefit that is at least as favorable as that of the alternative approaches. The committee would base this decision on the type of research being proposed. For example, studies about potential new treatments for disease may indeed propose the opportunity for direct benefit to the children in question. IRB determinations will be documented in the minutes of the IRB or otherwise in the IRB documents.
3. **Whether the research is greater than minimal risk and does not offer the prospect of a direct benefit.** When the research being proposed offers greater than minimal risk and no prospect of direct benefit the IRB will consider whether or not some, all or none of the children are capable of giving assent and that permission will be sought from both parents as they are available. The IRB will also consider whether the proposed research is likely to yield generalizable knowledge about the disease or disorder. For example, studies about potential new treatments for disease may indeed propose the opportunity for direct benefit to the children in question, especially when this disease has little or no treatment options. The IRB determinations will be documented in the minutes of the IRB or otherwise in IRB documents.

#### Requirements for permission of parents or guardians and for assent by children

While reviewing studies that involve children, the IRB will assess the investigator's plan for obtaining permission from parents/guardians as well as plans for obtaining assent from the children.

In cases where the studies are of minimal risk to the child, the permission of one parent may be sufficient. In cases where the research presents more than minimal risk to the child but there is the prospect for direct benefit, the IRB may also find it sufficient to ask for permission from one parent.

When the IRB reviews studies that involve more than minimal risk for the child and do not hold out the prospect for direct benefit but do offer an opportunity to learn more about the disease under study, the IRB will require the permission of both parents when both are reasonably available.

In making this determination the IRB will work with the investigator to determine whether or not the permission of both parents should be sought, when both parents are reasonably available or when it is sufficient to obtain permission from one parent.

## **15.2 Pregnant Women and Fetuses in Research**

Generally DF/HCC institutions do not perform cancer related research that targets pregnant women. In rare situations where this would be the case, the IRB will consult with experts in this area. The IRB will also perform a careful review of the regulations governing pregnant women in research.

Some researchers do perform research involving tissue from dead fetuses. In these cases, the investigator is asked to confirm that the collection of this tissue was done in accordance with Massachusetts state law, that fetal tissue was not collected from women who are under the age of 18 and that no woman was induced to abortion for the purposes of the research.

## **15.3 Cognitively Impaired Persons Involved in Clinical Research**

Individuals in a wide variety of situations may have impaired decision-making capacity. Impaired capacity is not limited to individuals with neurologic, psychiatric, or substance abuse problems; for example, impairment may occur at times of great stress. Understanding and identifying the range of, and fluctuations in, decision-making capacity are therefore the first steps to providing appropriate protections in the clinical research setting.

While limited decision-making capacity should not prevent participation in research, the IRB is committed to providing additional scrutiny and protections for studies involving this population. The Department of Health and Human Services (DHHS) does not have specific regulations to govern research with cognitively impaired participants, unlike research involving children, prisoners, pregnant women, and fetuses. However, the federal regulators offer the following "Points to Consider" to assist the IRB and clinical investigators in their effort to protect participants in research who are, may be, or may become decisionally impaired. The DFCI IRB has adopted these "Points to Consider" as the guideline for all its clinical research studies involving the decisionally impaired.

Potential and actual research participants, especially those with permanent or transient cognitive impairments, may find it difficult to understand the difference between research and treatment, and to understand researchers' multiple roles, making "therapeutic misconceptions" particularly problematic, and possibly creating confusion among participants and their families.

It is essential that the consent process clearly indicate differences both between individualized treatment and research and between clinician and clinical investigator.

An individual's capacities, impairments, and needs must be taken into account in order to develop practical and ethical approaches to enable them to participate in research. A clear understanding of the implications of various cognitive impairments, along with a careful consideration of proposed clinical research methodology, is required. Assessment is complex; simply answering a certain number of factual questions about a protocol may not be an adequate assessment. A key factor in participants' decision-making is their appreciation of how the risks, benefits, and alternatives to participation in the study apply to them personally.

Limited decision-making capacity covers a broad spectrum. A healthy 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. Researchers should be sensitive to the differing levels of capacity and use assessment methods tailored to the specific situation. Further, researchers

should carefully consider the timing of assessment to avoid periods of heightened vulnerability when individuals may not be able to provide valid informed consent.

Both the IRB and clinical investigators must keep in mind that decision-making capacity may fluctuate, requiring ongoing assessment during the course of the research. The consent process should be ongoing and therefore the study should be explained again after enrollment. The IRB, at its discretion, may require an outside witness to observe the consent process.

Because no generally accepted criteria for determining competence to consent to research exists for persons whose mental status is uncertain or fluctuating, the role of the IRB in assessing the criteria proposed by the investigator is of major importance. The selection of an appropriate representative to give permission on behalf of those unable to consent for themselves must be accomplished without clear guidance from statutes, case law, or regulations. In cases of high risk studies, the IRB may also call on the primary care physician of individual subjects to comment on the subject's ability to give consent to participate.

Investigators are encouraged to review the following article: The American Journal of Psychiatry, 155:11, November 1998, entitled "[Guidelines for Assessing the Decision-Making Capacities of Potential Research Subjects with Cognitive Impairment.](#)"

The determination of a participant's ability to understand the implications of the decision to participate in research is best made by the clinician/investigator. In most cases, the clinician/investigator is in the ideal position to evaluate the participant's ability to understand the implications of the research and whether the participant is making a rational decision to participate. Likewise, it is the clinician/investigator that makes a judgment of the participant's ability to understand and follow the protocol.

There is no universally accepted test or standard for making a determination of comprehension. This process should operate in research studies in much the same manner as the informed consent process in clinical treatment that does not involve research. However, protocols involving participants with the potential for developing impaired decision-making capacity during the course of the study must outline the steps a researcher should take when such change in capacity occurs.

Closely related to the determination of the ability to comprehend the nature of the study is the importance of ensuring that participants' participation is completely voluntary. Some knowledge and assessment of the participant's competence is relevant to a determination of whether voluntary participation is evidenced by a written consent, or in the case of persons lacking legal capacity to consent, their assent. Research should not be conducted against the wishes of the participant, and making certain that the written documents are indeed a reflection of reality is the function of the individual researcher and the IRB.

There are many situations in which a participant should be encouraged to include the involvement of family members. However, the permission of another party will be required only when the participant is determined to lack the legal ability to provide his or her own informed consent. This would include minors (persons under the age of 18) and persons adjudicated incompetent. This also includes persons who are not capable of understanding the nature of their illness or the risks, benefits, and natural consequences of participation.

### **Definitions and Issues for Review when Studies Involve those with Diminished Capacity**

The IRB defines the legally authorized representative as a court appointed representative or an individual named as a health care proxy to make decisions for another individual about participation in research. This means the person who is possessed of the legal and rightful power to act for or on behalf of another.

The IRB will approve such research when:

1. The research holds out the prospect for direct benefit to the participant; the benefit is only available in the context of the research, and permission will be obtained through the legally authorized representative; or
2. The research is of minimal risk, the research question cannot be answered using adults able to provide consent, permission will be obtained from the legally authorized representative, and when possible, assent will be obtained from the participant; or
3. The research is of more than minimal risk, the research question cannot be answered using adults able to consent, the research holds out a prospect of direct benefit to all participants, permission will be obtained from the legally authorized representative, and when possible, assent will be obtained from each participant.

### **Obtaining Assent from those with Diminished Capacity**

While reviewing studies that involve children, the IRB will assess the investigator's plan for obtaining permission from legally authorized representatives as well as plans for obtaining assent from the participants.

In developing the assent, the investigator is obligated to incorporate any special accommodations necessary to assure that the subject population and or their authorized representatives comprehend the nature and purpose of the study. Useful techniques may include simplified consent documents, supplemental summary sheets, and formal Q&A sessions for the subject and legally authorized representative. Finally, the investigator should consider "waiting periods" after the initial discussion before the prospective participant actually enrolls.

## **15.4 Research Involving Prisoners**

Generally DF/HCC does not conduct research that plans to involve prisoners as participants. At times participants may become unexpectedly incarcerated. In such cases, investigators must contact OHRS as soon as they receive information that a current research participant has been incarcerated.

The PI will be asked to address the following:

1. Whether the participant is receiving any treatment as part of the research;
2. Whether all treatment can be provided as standard care
3. Whether alternative treatments are available as standard care and would be acceptable substitutes for treatments available only in the context of the research.

If any of the above is true, the presumption will be that the participant should be withdrawn from the research.

If there is a reason for the participant to remain in the research, the research will be re-reviewed by the IRB with participation from a prisoner representative to affirm that it is appropriate for the incarcerated individual to remain as a participant in the research.