



Informed Consent/Permission/Assent Process

Policy

- A key requirement of human subject protection is voluntary participation. The informed consent/assent process must assure that both the child/adolescent and the parents/guardians fully understand the research, understand what they are being asked to do, and understand the associated risks and benefits of the research for which they are providing consent/assent.
- It is the policy of Children's Hospital to comply with all federal and state regulations that pertain to informed consent, parental permission, and assent.

Definitions

Informed Consent	<p>Informed consent is not merely a signature on a form, but a process of mutual communication. The process starts before any form is signed and continues throughout the entire study. The process begins by meeting with patients and their families and discussing the research. In pediatrics, this must be a family centered activity that involves the child/adolescent, the parent/guardian, and, sometimes, other caregivers.</p> <p>The written consent form is a formalization of the agreement to participate, and it is used to document a process. Investigators must explain the research in terms that both the children and the parents/guardians can understand. Informed consent is not the mere disclosure of information; it is an interactive process. Subjects and families must be able to describe what they are consenting to do. Because informed consent continues throughout the entire research activity, subjects and their families must be kept apprised of new information regarding the study. They must have the opportunity to ask, and be encouraged to ask, ongoing questions. Subjects and families are kept up-to-date through verbal discussions, written materials, and, when necessary, by having a subject re-sign a written informed consent document that contains additional information. It is important to keep in mind that subjects/families retain the right to withdraw at anytime, and to remind them of that fact.</p> <p>Within pediatrics the concept of informed consent shifts from that of a competent adult who grants informed consent to participate in research, to that of parents who grant permission to involve their children in research. This document uses the term informed consent for simplicity; however, it should be recognized that, in the case of children, it is actually parental permission that is being documented and granted,</p>
Assent	Assent is defined as a child's "affirmative agreement" to participate in



	<p>research. Federal regulations require that assent be obtained directly from the child/adolescent, in addition to obtaining written parental/guardian permission. Assent is required unless:</p> <p>The subject is incapable of providing it because of immaturity or cognitive abilities; or</p> <p>The research holds out the prospect of a direct benefit that is only available through participation in the research. This most frequently occurs in research that offers a therapeutic benefit.</p> <p>In these situations a parent's decision may override a child's refusal to assent. Even when assent is not required, the child is to be provided with information regarding the research. To obtain assent, the research procedure, and its risks and benefits, must be explained to the child/adolescent in language, and at a level, that they can understand. This will vary greatly depending on the age and cognitive ability of the child. The Committee on Clinical Investigation (CCI) will determine, on a protocol by protocol basis, whether assent is required. This decision is based on the population being studied and the potential for direct benefit. The final letter of protocol approval sent to an investigator indicates whether assent is required.</p>
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1. What are the Principles of Informed Consent/Assent?

The Belmont Report informs us that respect for persons requires that subjects "to the degree they are capable, be given the opportunity to choose what shall or shall not happen to them". A subject's choice incorporates three elements: information, comprehension, and voluntariness.

- **Information** is critical for a person to make an informed choice as to whether he or she, or his or her child, should participate in research. The Belmont Report suggests providing information that the "reasonable volunteer" will want to know. It is important that families understand the difference between what is necessary for their care and what is being proposed specifically for research. It is also important to recognize that some families will want more information than others, and investigators must be prepared to provide what a reasonable person would want to know, and more information, if requested.
- **Comprehension** will vary subject to subject and family to family. The manner in which information is provided may impact comprehension. It must be recognized that individuals may need to be presented information in a variety of ways in order to comprehend the information. Comprehension may require that time be provided to allow subjects to think about participation and to ask questions..
- **Voluntariness** requires conditions free of coercion and/or undue influence, including conditions under which an individual or family may agree or disagree without any fear of repercussions.

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The decision to participate in research should be a family-centered decision with special consideration and attention given to each parent and the pertinent child or adolescent. In some situations it may be appropriate to spend time with the child/adolescent alone, without the parent/guardian present. This may make it easier for the child to ask questions and not feel coerced by a parent/guardian. Consideration is to be given to the best method for obtaining consent and assent, and is to include issues such as the nature, location, and urgency of the research and family dynamics.

Investigators are to consider innovative and creative ways to provide children and families with information about the study during the informed consent process. Examples include:

- videotapes/photographs of research procedures
- pre-visits to the site of the research to see equipment (e.g., MRIs)
- encouraging and arranging for potential families to speak with families/patients who have participated in research
- distributing educational material about clinical research or specific types of research procedures (e.g., gene therapy, cancer trial pamphlets)

The burden of ensuring that a parent, guardian, child, or adolescent who might participate in research genuinely understands the research falls on the researcher. It is recommended that the researcher not only answer questions, but also ask questions to be certain that family members understand the research before a subject enrolls in a study. Asking questions can further discussion, prompt the subject and parents to think more carefully about their involvement, and help the researcher decide whether the subject and parent/guardian adequately understand the project. The questions that an investigator may consider asking are to be open-ended and nondirective. Some examples of such questions include:

- "Could you explain to me what we are going to ask you to do in this study? This will help me be to be sure that you understand the research."
Instead of:
"Do you understand the research and what will happen?"
- "What more would you like to know about this study?"
Instead of:
"Do you have any questions?"
- "Can you tell me the possible good and bad things that may happen if you take the experimental drug?" Instead of:
"Do you understand there are some good and bad things that could happen if you take this drug?"

2. Who Should Obtain Consent/Assent ?

Investigators are responsible, on a per protocol basis, for designating appropriate individuals to obtain consent/assent for a protocol. Only members of the research team who have experience in all elements of the study may provide a complete and accurate description of the research, and answer questions and concerns. Some considerations include:



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- The technicality of the details of the protocol, and who can best explain them.
- Who is best able to answer the questions that may come up?
- It may be possible to have two individuals involved in the consent process. Often the investigator provides information, and a research nurse is made available to follow-up and provide additional information.
- Who is able to spend as much time with the families as they require?
- If an investigator is also the family's physician, can the family distinguish the different roles?

3. Who Should Provide Consent/Assent?

A. General Requirements Consent

Both HHS and FDA regulations require that informed consent be obtained for the subject or legally authorized representative. For subjects who are minors, parents and guardians are asked to document their permission to allow their children to participate in research by signing an Informed Consent Form prior to enrollment. The consent of both parents is required unless the determination has been made that the consent of one parent is sufficient. The CCI will advise investigators as to whether the signature of one or both parents is required.

Informed consent must be documented on a written consent form approved by the CCI and signed by the subject or the subject's legally authorized representative unless the IRB has approved a waiver of consent, the required elements or approved another method of obtaining consent as specified in the regulations. A copy is to be given to the person signing the form. Unless otherwise approved by the CCI, a copy of the signed consent form is to be placed in the medical record if the study involves medical interventions, to ensure the safety of the patients who participate in research. Informed consent must be obtained before the initiation of any screening processes performed solely for the purpose of research.

The study investigator or designee is also required to sign the consent document to attest to the fact that all the elements of informed consent have been explained to the subject/legally authorized representative (parent/guardian) and all questions have been answered to the best of the investigator's ability.

B. Parents' Right to Consent to Participation of Their Children in Research

Competent parents may generally approve a minor's participation in research, assuming that regulatory and other ethical requirements for the research are met, including the minor's assent where indicated (see below). This is allowed by special regulations governing research involving children. For this purpose, "children" are persons "who have not attained 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". In Massachusetts, the general age of consent is 18 years old, and for the vast amount of research, persons under 18 will therefore be "children" for whom a parent's consent will be valid. Of course, assent for minors



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may still be necessary, and as a minor ages, that assent may look more and more like a consent document reviewed by the parents. But nonetheless, the operative consent is still that of the parents.

C. Determining Whether Permission Should be Obtained From One or Both Parents/Guardians for Children and Adolescents who Participate in Research

The Committee On Clinical Investigation shall determine, in accordance with and to the extent that consent is required by [§46.116](#) of [Subpart A](#) and FDA 50.20, that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under [§46.404](#), 50.51 (minimal risk) or [§46.405](#), 50.52 (greater than minimal risk, potential for direct benefit). Where research is covered by [§46.406](#), 50.53 and [§46.407](#), 50.54 (greater than minimal risk no prospect of direct benefit) and permission is to be obtained from parents, both parents must give their permission 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 permission from both parents is required in the following situations:

- In accordance with the regulations, permission from both parents, if reasonably available, is required if the research presents greater than minimal risk with no potential for direct benefit
- The CCI will generally require that permission be obtained from both parents or guardians, if reasonably available and competent to consent, even when the research potentially offers direct benefit, when:
 - the research presents significant increases in magnitude or probability of risk, above the alternative approaches; or
 - the research procedure is so novel that the risks are unknown; or
 - the research presents potential risks that could be **life threatening or severely debilitating**, or that have the **potential to cause major irreversible morbidity** (e.g., blindness, hearing loss, paralysis, stroke).

Guidelines for determining if a parent is "reasonably available" are as follows:

- The parent's role in the care and/or decision-making of the child, even on a limited basis, is such that his or her involvement and availability may be readily ascertained from Children's Hospital records; or
- The parent's whereabouts are known at the time the child is approached for research Purposes.
- If, in situations in which the above referenced criteria are met, the investigator is unable to make contact with the parent, the investigator is to document the attempts made, including the date of the attempt and the method of attempted contact (e.g., phone, fax, email). After multiple attempts at contact are made (usually three at a minimum), it may be reasonable to conclude that the parent/guardian is not reasonably available.

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Although the CCI generally requires both parents' signatures, situations may exist in which one parent accompanies a child to an acute care visit or emergency, and to require the signature of both parents or guardians would represent a significant impediment to the initiation of an investigational procedure that carries a potential for direct benefit. In such situations, if the provision of immediate and emergent care would be thwarted by the process of seeking both parents' consent in advance, and only one parent is reasonably available, one parent's consent may be relied upon. However, the rationale for proceeding in this situation is to be well documented in the research and medical records, as appropriate, and reasonable attempts are to be made to notify the other parent as soon as possible.

Even where a protocol generally requires both parents' permission, the permission of both parents is NOT required if a court grants decision-making authority solely to one parent, excluding any court-ordered consent role for the other (this happens rarely, and primarily in cases of abuse); or if only one parent is alive or competent; or if some person or agency other than the parent has been assigned legal custody of the child by law or court order. In cases where a child has been removed from parental custody, and legal custody in some form has been granted to the Department of Children and Families, an agency, or foster parents, it is advisable to discuss the case with the Office of General Counsel.

If the CCI finds that permission from one parent is sufficient for the research when the research is minimal risk or greater than minimal risk with the potential for direct benefit, investigators are to consider the issues, below, to determine whether it is prudent or in the child's best interests to seek the permission of both parents or guardians. Investigators may encounter individual family situations in which additional steps must be taken. Investigators must be sensitive to each subject's family dynamics, and the implications of such dynamics on decisions regarding whether or not permission from both parents is reasonable in order to proceed with the research.

When children are under the shared legally custody of two parents or guardians, each parent's rights of decision-making are to be respected to the greatest extent possible. Researchers are to be guided by sound clinical and ethical judgment, and are to be alert to the need for family consensus, just as they are with clinical interventions. Those situations in which it is reasonable to believe that it is in the best interests of the family and child to obtain permission from both parents/guardians include the following:

- When both parents are known to be involved in the child's care, and the investigator has reason to believe that there may not be family consensus on participation in research.
- When a non-custodial parent consents to research that will affect the child's care by a custodial parent, or impose obligations on the custodial parent.
- When the family has shown signs of mutual antagonism or stress related to reaching consensus on clinical decisions.
- When consent by one parent might reasonably or predictably affect the potential subject's relationship with the other parent.
- When one parent is known to disregard the wishes of the other parent.
- When one parent is known to object to the research for reasons that, accordingly, would caution against proceeding with a clinical intervention in similar circumstances.



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The Office of General Counsel is to be consulted when the subject has been removed from parental custody, and legal custody in some form has been granted to the Department of Children and Families, an agency, or foster parents. Moreover, all questions are to be directed to the Office of General Counsel.

D. Age of Assent from Minor Subjects

It is generally believed that children seven to eighteen years of age may be capable of providing assent. However, individual subjects or populations of subjects may not have the cognitive and emotional maturity to understand the research project and decide whether or not to participate. Although the CCI may require that assent be obtained, investigators must use their discretion to determine whether the subject is capable of providing assent.

If the IRB asks that assent be obtained, investigators are to document the rationale when assent is not obtained is a specific justified situation

E. Minors' Right to Consent in Certain Circumstances

There are certain exceptions to this generalization, that flow from special provisions allowing consent for individuals under 18 years of age. For example, in rare circumstances, such as in some public health studies involving blood draws, consent by a 17-year old or younger may be specifically allowed or required. More commonly, researchers have to consider the applicability of Massachusetts law authorizing a minor to consent to his or her own "medical or dental care" if (a) married, widowed, or divorced; (b) is the father or mother of a child; (c) is a member of any of the armed forces; (d) is pregnant or believes herself to be pregnant; (e) is living separate and apart from a parent or guardian and is managing his or her own financial affairs; or (f) is seeking care for a disease defined by public health authorities as dangerous to the public health, although in that instance the right to consent is limited to the diagnosis and treatment of that disease.

Despite the apparent objectivity of this definition, there are two key complexities in applying it to research:

- First, even in a non-research, purely clinical context, this law does not compel clinicians to treat minors in those categories as able to consent despite a sound clinical judgment that in fact the person is not able to understand the nature and consequences of what they are offered. In addition, although the law is not clear on this point, many attorneys would read the provisions focused on certain conditions (e.g., substance abuse treatment, or pregnancy) as implicitly limited to care directly related to those conditions, rather than authorizing consent to any health care whatsoever. It is therefore the policy of Children's Hospital to recognize that minors within some of these categories may not only need or benefit from family or other adult assistance, advice, and support but that for example, the fact of parenthood may not equate with a fully adult ability to appreciate the risks, benefits, and alternatives for indicated care. For that reason, sound and sensitive clinical judgment that is attentive to both a minor's rights *and* the

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minor's actual competence and needs is to be brought to bear, and is to include a determination as to whether involvement of family or other adults familiar to the minor is necessary and appropriate. In addition, special care is to be taken where the decision is of extraordinary impact, or when the physician or members of another care team have concerns about the wisdom, appropriateness, or depth of the minor's expressed preference or decision. The Office of General Counsel is always to be consulted concerning the application of this statute in such situations, (use the 24/7 attorney-on-call beeper if necessary and such consultation is to address, assuming the care team agrees with the minor on designated care, whether some sort of judicial ratification is to be sought.

- Second, by its terms, the statute applies to clinical care, and is of unsettled application to research. Where research is "therapeutic," where it offers care not available outside of the research, or where it presents care alternatives for which there is genuine equipoise concerning which treatment is preferred, and the greater part of the research consists in this otherwise-clinical care and related measurements to assess it, it is safe to rely on the statute as authorizing a minor to consent on his or her own behalf, assuming the CCI finds an ethically appropriate balance of risks and benefits, and the clinical team believes that the minor understands the decision and its ramifications in accordance with the standards described above and is truly capable of engaging in adult like consent. Similarly, if the research is minimal risk, with some prospect of direct benefit of a clinical nature, and the greatest part of the research consists in this otherwise clinical care and related measurements to assess it, it is generally safe to rely on this statute as authorizing not just non- research care, but care in a research context. However, in any circumstance in which there is doubt including any other circumstances than those described above, the Office of Clinical Research Compliance and the Office of General Counsel are to be consulted. These Offices will assess whether the statutory categories are apt, will relate them to sound application of the Belmont principles, and will also identify any conflicts between the clinical best interests of the minor and the minor's participation in the research.

Investigators are also to be aware that a parent's right to consent for a minors is open to question when research presents more than a minor increase over minimal risk, with no prospect for direct benefit. Unlike the first exception above, in which minors may consent for themselves because of categorical capacity related to their personal circumstances, this exception tends to arise on a protocol-wide basis as a result of the study design. Recent judicial decisions outside of Massachusetts, if applied here, would suggest that parents have no right to consent to expose their children to substantial risks without direct therapeutic benefit in a research context without judicial approval. This category of research, if federally funded, is subject to a so-called "407 panel review.". Although federal regulations require the consent of both parents if reasonably available, the CCI, with guidance from General Counsel, may in some circumstances recommend additional judicial approval, beyond the requirements of the "407" regulation. (It is not expected that this type of situation will arise for all research that falls within the 407 category.)



Researchers should note that this area of law is evolving rapidly, and that Children's Hospital will take the steps necessary to comply with the law.

F. Consent by Judicially Approved Guardians and other Surrogates

Under federal regulations, consent to participate in research may be obtained from the subject's "legally authorized representative." For a child subject whose parents are deceased, not competent, or judicially deprived of the right to consent (as in certain abuse and neglect cases), a "legally authorized representative" is a guardian appointed by a court. Investigators are not to assume that a guardian is authorized to consent to a child's participation in all research. Within the state of Massachusetts, guardian powers, including those of government agencies such as the Department of Children and Families, may be limited by the terms of a court order to certain forms of care decision, and it is not uncommon for a guardian to be required to return to court for decisions not specifically countenanced by the court order. In addition, the authority to make health care decisions is not the same as the authority to consent to research participation. For these reasons, investigators are to be clear on the terms of the guardian's authority (a guardian should be able to readily produce a copy of the pertinent court order); are to consult with the Office of General Counsel; and are to recognize that a court is most likely to approve such authority in situations where the research is "therapeutic," where it offers care not available outside of the research, or where it presents care alternatives for which there is genuine equipoise concerning which treatment is preferred.

In the state of Massachusetts, non-parent family members who are not court-appointed guardians are generally not authorized to consent to participation in research, unless their role can be justified on other grounds, such as the emergency nature of the minor's condition. Nonetheless, such family members can play an important supportive role for a minor who is technically able to consent as described above.

G. Surrogate Consent for Decisionally Impaired Adults

Please refer to the Children's Hospital separate policy "Research Involving Individuals with Decisional Impairment"

H. Obtaining Consent when Minor Subjects Become Adults or otherwise Acquire Capacity to Consent During the Course of research

Any research study that involves continuing diagnostic or therapeutic procedures, or any form of research intervention (e.g., surveys), is not to proceed with a minor subject after that subject becomes an adult until the subject provides informed consent as described in this policy. This is to occur regardless of the sophistication of the minor subject when assent was provided, or the level of detail provided in the assent document.



Moreover, the conduct of all forms of research in which there are continuing interactions with the subject (e.g., result reporting, informational follow-up) requires that such subjects 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 their parents 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 their parents or guardians were they still minors. In situations such as tissue banks where samples are collected before the subject is 18 however there is continued use of the tissue as defined by 'human subject research' the now adult subjects should provide consent for the continued use of the tissue or the CCI may consider waivers/alterations of informed consent as specified in the regulations. Other considerations to avoid the need for consent may include making the tissue/data anonymous etc.

4. What is the Appropriate Timing For Informed Consent?

Special consideration is to be given to the timing and location of all communications concerning informed consent, including when and where informed consent is given. When possible, potential subjects/parents are not to be presented with all of the information at once, or at the last minute. The amount of time required will vary with protocols and individuals. Busy and hectic environments may also distract a child's, adolescent's or parent's attention. When possible, all family members are to be given time to think about whether they want to participate, and are to have the opportunity to speak with others before proceeding. The consent process may be segmented; conversations, further questions, and the signing of the informed consent form may take place over several visits, and the time between discussion of the protocol and the signing of the consent may vary

5. Are there Special Informed Consent Considerations for Research Data Retention for FDA Regulated Research

When a subject withdraws from a study, the data collected on the subject to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the subject the option of having data removed.

The investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject must distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through chart review, and address the maintenance of privacy and confidentiality of the subject's information.

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The Researcher must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). The IRB must approve the consent document.

If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent. However, a researcher may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

Document Attributes

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