IRB Tools and Tips

Issue 19: Assent of Minors

The IRB Tools and Tips newsletter was developed to provide you with knowledge in various IRB related topics. Each newsletter, highlights a particular form, policy or concern. At times this format may be used to provide IRB updates and share timely, useful information. Please feel free to contact the IRB office with questions. Frequently asked questions appear periodically in issues of the newsletter.

Which of the following is true:
A) Federal regulations dictate the age at which assent must be obtained from minors.
B) A child’s failure to object to enrollment into a study should be interpreted as assent.
C) In general, Marshfield’s IRB recommends obtaining assent from children who are ten years of age or older.
D) If the research is non-therapeutic and of no benefit to the child, the child must have the final say regarding participation.

The only true statement is D) – the child must have the final say regarding participation if the research is non-therapeutic and of no benefit to the child. Read on to find out what makes the other statements false.

Background:
Federal regulations provide additional protections for minors involved as subjects in research. These regulations also outline requirements for permission by parents or guardians and for assent by minors.

When an investigator proposes to use children in a research project, the IRB must assure that additional approval criteria are satisfied. These criteria differ depending on the level of risk involved in the project. One criterion that remains constant, however, is that adequate provisions must be made for soliciting the assent of the children.

Guidance:
While children may be legally incapable of giving informed consent, they nevertheless may possess the ability to assent to or dissent from participation. Out of respect for children as developing persons, they should be asked whether or not they wish to participate in the research, particularly if:

1) the research does not involve interventions likely to be of benefit to the subjects; and
2) the children can comprehend and appreciate what it means to be a volunteer for the benefit of others.

In what type of research is assent required?
If the research is non-therapeutic and of no benefit to the child, the child must have the final say regarding participation. When the research offers the child the possibility of a direct benefit that is important to the health or well-being of the child and is available only in the context of the research, the IRB may determine that the assent of the child is not required. In such circumstances, a child’s dissent may be overruled by the child’s parent(s) or legal guardian(s). (This will be discussed in greater detail later.)

When is a child capable of assent?
There is no absolute regulatory or ethical standard for assent. 45 CFR 46.408(a) requires that "adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent."

Determining the actual age of assent is the IRB’s call. But some regulatory guidance is offered: "In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved."

As a general "rule of thumb," many IRBs (including Marshfield's) use the age of seven years as the approximate time when it becomes appropriate to seek assent. Moral theologians have used this age for several centuries as the "age of reason," at which one becomes capable of knowing right from wrong.

Minor - an individual who is less than 18 years of age.
Assent – to agree or concur.

* Information in this newsletter is taken from 46 CFR Subpart D Additional DHHS Protections for Children Involved as Subjects in Research; MCRF Guidance #787 Assent of Minors; and, “Children in Research” by Linda E. Krach, MD, Director of Research Administration, Gillette Children’s Specialty Healthcare.
For each protocol, the IRB must determine, depending on such factors as the nature of the research and the age, status and condition of the potential subjects, whether all or some of the children are capable of assenting to participation. For research staff however, it is more important to look at the individual child than it is to look at the age. A bright child who’s asking questions should be involved in the process, even if s/he’s only 6. A child who’s more delayed may be hard to involve until later than 7. And of course, a child with a cognitive disability may not be capable of assent until much later.

The approval letter the investigator receives from the IRB will document whether or not assent is required and the age for which assent must be obtained.

**What is the process for obtaining and documenting assent?**

When the IRB determines that assent of the child is required, it must also determine that provisions for obtaining and documenting assent are adequate. The IRB expects the researcher to verbally convey the information that is contained in the consent form to the child in a manner that is understandable to him/her.

The discussion with a child should at a minimum include:

1. an explanation of the purpose of the research;
2. any discomforts and inconveniences the child may experience if he or she agrees to participate;
3. the benefits of participation;
4. any alternatives that are available; and
5. the fact that the child may say “no” at any time without having it held against them.

Keep in mind that assent is a child’s affirmative agreement to participate in research. Mere failure to object should not be interpreted as assent.

When the IRB requires assent of minors, the approved consent form will contain an assent page that asks for the minor’s signature if they agree to be a part of the study. When, in the investigator’s opinion, a minor in this age range is intellectually unable to understand and weigh the risks and benefits of the study and therefore unable to provide assent (e.g., mentally disabled individual), the investigator must certify such on the assent form and may proceed with the research with the parent or guardian’s permission. It is expected that these cases will be rare. Consultation with the IRB on individual cases is encouraged. Where appropriate, IRBs may choose to review on a case-by-case basis whether assent should be sought from given individual subjects. Investigators are also encouraged to consult the IRB document "Information that May Be Considered in Assessing Children’s Capacity for Informed Assent.”

**Is assent always required?**

There is an assent requirement for each of the four categories of allowable research (45 CFR 46.404-407-Children Involved as Subjects in Research). However, the IRB has the same authority to waive the requirement that it has to waive consent in other contexts. The first requirement for the waiver of consent is that the research not involve greater than minimal risk.

**There is a special consideration.** A parent or guardian may choose to have a child receive medical treatment over the child’s objections. When a study provides access to a therapy not otherwise available, and that therapy seems likely to be superior to anything available outside of a study context, the parents’ right to make medical decisions for a child may be at odds with the child’s right to grant or withhold assent. In that case, an IRB may waive the requirement for assent. In most cases, this should have no impact on the level of information that is appropriate to provide to the child. But the exchange becomes an information-only process rather than an information-and-assent process.

**What if a minor wants to refuse therapy?**

From a legal perspective, the parents’ authority to make medical decisions for a child overrides the child’s decision not to grant assent. When research involves experimental therapies for life-threatening diseases such as cancer, however, IRBs and investigators should be sensitive to the fact that parents may wish to try anything, even when the likelihood of success is marginal and the probability of extreme discomfort is high. It is appropriate for investigators to be aware that the parents’ authority may not be
absolute in this context. Courts have on many occasions ruled that a "mature adolescent" may decide against further medical care and that such a decision should be honored. In general in this situation, if the child is a mature adolescent and death is imminent, the child's wishes should be respected.

**Is parental permission always required?**

There is a parental permission requirement for each of the four categories of allowable research. However, the IRB has the same authority to waive the requirement that it has to waive consent in other contexts (as set forth by Federal regulations). The first requirement for the waiver of consent is that the research not involve greater than minimal risk.

The specific example cited in 45 CFR 46.408(c) is a study of abused or neglected children. In that case, the IRB may waive the requirement for parental permission, provided that adequate protections are in place to protect the rights and welfare of the children. Appropriate protections would be very study-specific. For the example cited, there may be a person-appointed by a court or a child protection agency who would be an appropriate person to approve the inclusion of the child in the study.

The regulatory requirement is for permission from both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. If there are two parents and they disagree about allowing the child to participate in the research, the child may not be enrolled in the research. *Note: in the circumstance where the research has real potential benefit, (45 CFR 46.405) the two-parent rule does not apply.*

**What if the child is a ward of the court?**

Children who are wards of the State or any other agency, institution, or entity can be included in research only if such research is:

1. related to their status as wards; or
2. conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

If the research is approved in these cases, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian. One individual may serve as advocate for more than one child. The advocate must have the background and experience to act in, and must agree to act in, the best interests of the child for the duration of the child's participation in the research. Additionally, the advocate must not be associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

**What about emancipated minors?**

Emancipated minors are not specifically covered by federal research regulations, and emancipated minor laws do not address research participation. By many state laws a person may become “emancipated” before the age of majority by marrying or by being in the military. The child may have most of the legal rights of an adult—including the full right to consent to medical care. Although no emancipated minor statute specifically addresses consent for research participation, the authority to grant such consent seems a reasonable inference from the other legal entitlements of the emancipated state.

Less clear is the situation of “selective emancipation.” Many states have laws allowing minors to seek medical attention for certain problems such as drug abuse, pregnancy, contraception, sexual assault, sexually transmitted diseases or the results of parental abuse or neglect. Sometimes the provision is a part of the emancipated minor statute; sometimes it’s separate. However, there is no law offering guidance and IRBs have traditionally been very cautious on this point. If the research would qualify for waiver of parental permission, that finding is more clearly allowable than is a finding that the child can be his or her own consent authority. If the research would not qualify for such a waiver, many IRBs would be reluctant to approve it.
Updates and Reminders

Research Compliance Intranet website: You may find it helpful to know that in addition to the Clinic’s Forms library, all Research Compliance forms can also be accessed from the intranet website. And, the forms on the website include a description of their use which you may find helpful. To locate the website, open the Intranet site for MCRF. From there click on Administration & Support Services, then Research Compliance/Committee forms.

Continuing Review Auditing: As you may be aware, we have made a change in our internal audit procedures in regard to the continuing review audits. Previously, any study that was approved with a requirement for written informed consent and had at least one subject enrolled and did not have a monitor's visit in the last year was audited at continuing review time. To reduce the burden, we have revised this to limit the audits to one per coordinator per month. On a monthly basis, after receipt of continuing review forms, the qualifying studies (described above) will be categorized by coordinator, and one study per coordinator will be randomly selected for audit. We believe this will reduce the burden on research coordinators and still give reasonable assurance to the IRB that proper procedures for obtaining and documenting consent are being employed.

Consent Revisions: Please note, when you make revisions to approved consent forms, it is no longer necessary to attach a paper copy of the red-lined consent to the Amendment/Revision/Update form. When the form is received in the IRB office and you have checked the box “yes” for consent revisions, IRB staff will automatically go into the Transfer Directory to get the revised consent.

When an amendment includes sponsor-required consent form changes, remember to include the sponsors consent form with the submitted documentation. If the sponsor communicates the proposed revisions to you via e-mail, include a copy of the e-mail with your submission. Additionally, when you are making changes to the consent, be sure that all the sponsor-requested changes are made in the electronic consent. If IRB staff notice a difference between the sponsor consent and local consent, we will assume that the changes are not to be made to the local consent (e.g., perhaps they don't apply to our site, or the local investigator is not in agreement with them.)

Completeness: Remember to respond to all questions when completing forms for submission. If a question is not applicable, indicate such in your response. If you leave the question blank we assume that you simply forgot to answer it and it will be returned to you.

Correct Forms: Remember to submit the correct form for the item you are submitting. Pay particular attention when choosing a Continuing Review Report form to ensure that the form matches the type of research (clinical, non-clinical, database, joint, etc.) It is sometimes easy in the Forms library to inadvertently click on the wrong form. When the form opens, look at the title to ensure it’s the correct form. And only use forms from the Forms library or the Research Compliance website. Do not save templates into your own personal directory as you may not be using the most current version of the form.

Electronic copy of sponsor consent for new protocols: When completing and submitting a new protocol to the IRB, remember to place an electronic copy of the sponsor’s consent into the Transfer Directory/IRB Sponsor consents folder and enter the electronic file name in the appropriate space on the checklist portion of the IRB application.

Adverse Event Reporting: Remember that the IRB only accepts adverse events that meet the reporting criteria (as defined in the policy “Adverse Events - IRB Reporting and Review.”) Events other than those described in the policy should not be submitted and will not be acknowledged or reviewed if submitted.

Investigators and completed education on human subject protection requirements: Remember when submitting a protocol application or amendment form adding co-investigators, if it is known that a particular individual has not completed the required “IRB Education on Human Research Subject Protections,” do not send a request to add that individual to a study until s/he has completed the training. (Department of Clinical Research secretaries have access to the educational database.)