Introduction

Research that involves children – defined in Wisconsin as individuals under the age of 18 – requires consideration of obtaining and documenting the assent of children to participate in the research.

However, the regulations are not proscriptive, but rather assign responsibility to the IRB of record to assess and determine whether assent should be required, what the process should look like, and whether documentation is required and how a is recorded. "The Federal regulations do not specify any of the elements of informed assent and do not indicate an age at which assent ought to be possible. The assent process should be developmentally appropriate based on the age and capability of the child to understand the information" (IRB Management and Function, Third Ed; Bankert E. et. al.)

This inherent flexibility provides opportunity for researchers to propose an assent process in line with the CW HRPP perspective (which will be described throughout this article), and the opportunity to inform the IRB of record about the rationale for a proposed assent process to aid the IRB in making their determinations.

Requirement to Obtain Assent

"Assent" is defined by the regulations as follows:

"Assent" means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent."(45 CFR 46.402(b)).

This means the child must actively show his or her willingness to participate in the research, rather than just complying with directions to participate and not resisting in any way. This active demonstration of willingness could be the child verbalizing their agreement to participate as well as documenting with a signature their willingness to participate.

"If a child is capable of assent and the Institutional Review Board (IRB) requires that assent be sought, it must be obtained before the child can participate in the research activity. Thus, if the child dissents from participating in research, even if his or her parents or guardian have granted permission, the child's decision prevails. Conversely, if a child assents to participate in research, and parental permission has not been waived by the IRB, the permission of the parents or guardian is also required before the child can be enrolled in the research." Research with Children FAQs - HHS

The federal regulations state that the IRB (not the investigator) is responsible for determining whether the assent of child participants is required for proposed research activities, or whether this requirement can be waived and under what circumstances. The IRB should require assent unless it determines that the proposed subject population, or an individual participant, is not capable of

assent. The IRB has the discretion to make assent determination for all minor participants or an individual participant. In making this determination the IRB:

- "shall take into account the ages, maturity, and psychological state of the children involved." 45 CFR 46.408.
    1. There is no minimum age at which assent should be obtained defined in the regulations
    2. Children's Wisconsin SOPs do not define a minimum age at which assent should be obtained
    3. Age alone is not the sole determinant – understanding varies among children of the same age
- Should take into account the nature of the proposed research activity
    1. For example, an oncology study may be too complex for children younger than 12 or 14 to understand but a study limited to collecting a blood sample might be understandable to a 6 or 7 year old.
- Whether the proposed assent procedure reflects a reasonable effort to enable the child to understand, to the degree the child is capable, what their participation in the research will look like

NOTE: **The PI should describe the above considerations in their proposal to assist the CW HRPP and the IRB of record in making a judgment regarding assent. The more information the IRB and the HRPP office has about the above points, the less likely there will be questions or the need for modifications, and delays in approval can be avoided.**

The CW HRPP strongly encourages flexibility and creativity in using age appropriate and engaging mediums to help the child understand what their participation means – focusing on things that would be most important to the child in making a decision about their participation (what will I have to do, will it hurt, how long will it take.)

One prerequisite to a child being able to make a decision about their participation in research is their understanding of what research is. There are graphic novels and videos, published by Boston Children's Hospital that could be helpful in explaining this to children in an engaging way. If an investigator plans to utilize this, or other resources to assist the child in understanding, these materials should be submitted to the IRB of record for approval with a description of their intended use.

Sophie's Science Project (graphic novel)

Sophie's Science Project (YouTube Video)

Requirement for Documentation of Assent

The IRB is also responsible for determining whether and how the child must document their assent. There are no federal regulations that requires documentation of a child participant's assent. "The IRB has the discretion to determine the appropriate manner, if any, of documenting child assent. Based on such considerations as the child's age, maturity, and degree of literacy, the IRB should decide what form of documentation, if any, is most appropriate. If adolescents are involved in the research where a consent form would have been used if the subjects were adults, it would generally be appropriate to use a similar form to document an adolescent's assent" (for example the parental permission form)

"If young children are involved who are as of yet unable to read, documentation should take a form that is appropriate for the purpose of recording that assent took place. The IRB may also decide that documentation of assent is not warranted."

NOTE: **The CW SOPs do not define how the assent of a child participant should be documented, or on what type of form. There is no CW requirement defining what age ranges should sign a separate assent form v. the parental permission form, or that a child's signature is even necessary. It is perfectly acceptable to have all children sign a separate assent form. It is also acceptable for all children to sign the parental permission form as long as ALL children are presented with age-appropriate information in the assent discussion to aid their understanding of what their participation means so they can decide whether they are willing to participate.**

"The abilities and needs of children vary widely and investigators should provide the information in a format tailored to the child in front of them. In many cases, assent forms are simplified consent forms that include elements that are irrelevant to assent (e.g. risk assessment, confidentiality) and are rarely written with sufficient simplicity of style and readability to achieve their intended objective." CHOP

The perspective of the CW HRPP is that investigators should carefully consider whether a child's signature is appropriate and describe the rationale in the proposal for IRB consideration. "Signature" in this case means whatever the child's mark entails including their printed name - it is not specific to a cursive signature.

When the research targets children unable or with limited capacity to read or write, an oral presentation accompanied perhaps by some pictures and/or other mediums (video, cartoons, graphic novels, etc.) with documentation by the person obtaining assent in a research note is likely more appropriate than providing the child a form to sign. In this case, the investigator should provide the IRB with a proposed script and any materials that they intend to use to explain the research.

The signature, if required, should be meaningful for the person signing the document. It is questionable that the act of signing an assent form would be meaningful for the child. It is also important to consider how a parent may perceive a requirement for a young child to sign a document. This could be confusing and concerning to parents, and if the IRB of record has determined a signature of the child is required, investigators should be prepared to explain to

parents and children what this means and the reason for documenting the child's assent in this manner.

"Older children may be well acquainted with signing documents through prior experience with testing, licensing and/or other procedures normally encountered in their lives. Signing a form to give their assent for research would not be perceived as unusual and would be reasonable. Younger children, however, may never have had the experience of signing a document. For these children, requiring a signature may not be appropriate, and some other technique to verify assent could be used. For example, a third party may verify, by signature, that the assent of the child was obtained."

Institutional Review Boards Frequently Asked Questions, FDA

Waiver of the Requirement to Obtain Assent

The IRB may determine that the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with §46.116 of Subpart A.

The HHS regulations at 45 CFR 46.408(a) identify three types of circumstances where the IRB may determine that waiver of children's assent is appropriate:

- if the capability of some or all of the children is so limited that they cannot reasonably be consulted;
- if the intervention or procedure involved in the research holds out the prospect of direct benefit to the health or well-being of the children and is available only in the context of the research.
- if the research meets the same conditions as those for waiver or alteration of informed consent in research involving adults, as specified in the regulations at either 45 CFR 46.116(c) or 45 CFR 46.116(d).

The FDA regulations at 21 CFR 50.55 identify 2 types of circumstances where the IRB may determine that a waiver of children's assent is appropriate:

1. The assent of the children is not a necessary condition for proceeding with the clinical investigation if the IRB determines:
2. That the capability of some or all of the children is so limited that they cannot reasonably be consulted, or
3. That the intervention or procedure involved in the clinical investigation holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the clinical investigation.

Expectations of the CW HRPP - Process of Obtaining and Documenting Assent

Obtaining assent from children in human subjects research is a nuanced process that requires sensitivity, respect, and an understanding of a child's developmental stage.

Researchers should strive to ensure that children comprehend what participation entails and feel genuinely willing to participate.

When the research targets children who are likely able to read and write, investigators should propose a process and form that is age appropriate and study specific, taking into account the typical child's experience and level of understanding, and composing a document that treats the child respectfully and conveys the essential information about the study.

1. Tell why the research is being conducted;
2. Describe what will happen and for how long or how often;
3. Say it is up to the child whether to participate and that it is okay to say no;
4. Explain if it will hurt and if so for how long and how often;
5. Say what the child's other choices are;
6. Describe any good things that might happen;
7. Say whether there is any compensation for participating; and
8. Ask for questions

The discussion:

- Provide the child opportunity to express and discuss their willingness to participate
- Provide the child the opportunity to ask questions
- Provide the child to think about their decision
- Pay attention to any coercion by parents/family members – the decision must be the child's voluntary willingness to participate free from coercion or influence
- Tailor the approach to each child's ability to comprehend the research
- Explain the study in language that is easily understandable to the child – use relatable examples
- Foster and open and non-coercive environment – create a supportive environment where children feel comfortable asking question and expressing concerns
- Engage parents/guardians
    1. To the extent to provide comfort to the child and address questions the child may have
    2. However, sometimes separate discussions with parents and children can ensure the child is not unduly influenced

Materials and Documentation:

- Use supplemental, age appropriate, engaging medium to enhance a child's understanding during the discussion
    1. Use charts, drawings, or interactive methods to facilitate understanding
- The assent form, if being used to document a child's assent, should be limited to one page as much as possible, and be conducive to the child
    1. Incorporate illustrations
    2. Larger type
- When the study involves older children or adolescents, and documentation of assent is required, the assent for should include more information and may use more complex language.
    1. When deemed appropriate, the parental permission form may be used to document the older child's assent

What happens when assent was not required when the subject was initially enrolled but the subject has reached an age when consent is required?

The CW HRPP expects that even when the IRB of record decides assent is not required from a minor subject, or for minor subjects who are not capable, the researcher should still involve the child as much as possible to help the child understand what will happen to them. While the child's assent may not be required to enroll the child, the child should still be given an opportunity to ask questions, express fears or concerns, and have those concerns addressed in an age appropriate way. This could include providing the child with age appropriate materials that help them understand even when their assent is not a requirement. When a child who is already enrolled reaches the age at which the IRB has decided assent is required for new enrollment, there should be a discussion with the child about their continued willingness to participate and this should be documented in the child's medical record. As with consent and parental permission, the process of assent is ongoing and there should be regular discussions with the minor subject about their understanding of the research and what is happening to them, and their continued willingness to participate.

The only times that a new signature is needed for a subject's ongoing participation are (1) at the time the subject reaches age of majority, when you no longer have legally effective informed consent; and (2) with new information, when the IRB has determined "re-consent" (parental permission) is required because the new information could affect a subject's willingness to continue participating. In the case of the latter, the HRPP Office suggests documenting assent consistent with the IRB determination for that age group for initial enrollment.