



Study Number:

Reviewer Sheet Addendum - Children

45 CFR § 46 Subpart D affords special protections for children involved in research to prevent any unnecessary risk or harm. Under 45 CFR § 46.402(a), children are defined as "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." Massachusetts law contains a number of provisions which define minors and the limited number of circumstances under which children whom have not reached majority may consent to receive medical care, or to participate in research, and circumstances and conditions under which the child's parents or legal guardians may consent on their behalf. These provisions are outlined below:

Age of majority. Eighteen is the age of majority both in Massachusetts (M.G.L. c. 231, § 85P) and under federal policy. When a person turns 18, s/he is considered to be an adult under the law. (Buying and consuming alcohol, however, are two activities that are not legal until a person turns 21 in Massachusetts.)

Massachusetts law recognizes two instances when teenagers under the age of 18 may have the legal capacity to consent to medical treatment. These are the **emancipated minor** and **mature minor** rules. Note that these rules concern individuals in their capacity as **patients**, not as participants in research, and also that they apply only to persons in Massachusetts. These rules would not apply, for example, to research participants living in a foreign country, although that country might have analogous rules.

Emancipated minor. A patient under 18 years of age may consent to treatment of any kind, except abortion, and may authorize the release of his or her medical records if s/he is: (a) married/widowed/divorced, a parent, (b) a member of the armed forces, (c) living apart from parents and managing his or her own finances, or, in the case of a female, (d) pregnant or believes herself to be pregnant. M.G.L. c. 112 § 12F. A female under the age of 18 may consent to an abortion if she is or has been married. Otherwise, consent must be obtained from her parent(s) or the procedure must be authorized by court order. M.G.L. c. 112 § 12S. Further, patients under 18 years of age may consent to treatment and may authorize the release of their medical records relating to: diseases dangerous to the public health, drug dependency (but not alcohol dependency), and pregnancy (but not abortion, except in the case of those who had married).

Mature minor. Under Massachusetts case law, students under the age of 18 who are not emancipated under M.G.L. c. 112, § 12F, can, in certain circumstances, nevertheless consent to treatment and control access to their medical records. In such cases, the clinician proposing to provide the treatment may determine that the patient is a mature minor capable of consenting to treatment. To reach this determination, the clinician must

conclude that the minor is capable of giving informed consent to the treatment; and that it is in the best interest of the minor not to notify his or her parents of the intended medical treatment. In general, where a minor has the capacity to consent to medical treatment, that minor also has the capacity to control his or her medical records, including releasing them to others, such as researchers. In addition, there is an argument that a minor who has the capacity to consent to medical treatment also should have the capacity to consent to research that may accompany that treatment. However, this argument has not been tested in a Massachusetts court.

Parents or Guardians of minor children. In general, and as more fully explained below, parents and guardians may provide consent to participation in research for their minor children or wards. The definition of who is a parent or guardian differs in some respects under federal and Massachusetts laws. The Massachusetts Uniform Statutory Will Act (the “Will Act”) indirectly defines “parent” in its definition of “child.” See M.G.L. c. 191B, § 1(1). Under this law, the “parent” is the biological or adoptive mother or father of a child. However, a father of a child who is not married to the child’s mother may not always be considered a parent; his status would depend on whether he openly treats the child as his offspring or on whether a court has made a paternity determination. Under the Will Act, the term “parent” does not include step-parents who have not formally adopted the child, foster parents, grandparents or other relatives. *Id.* In general, the term “guardian” is widely understood to mean a person lawfully invested with the power, and charged with the duty, of taking care of and managing the property and rights of someone who is considered incapable of administering his or her own affairs. This definition includes a person who legally has responsibility for the care and management of the person or estate or both of a child during his or her minority. Parents are usually considered the guardians of their minor children under Massachusetts law. For example, with respect to children, the Department of Mental Retardation defines “guardian” in its regulations concerning research as “a natural or adoptive parent, or the individual or agency with legal guardianship of the person.” 115 CMR 10.02.

Legal guardianship in Massachusetts usually is created through a court process, most often through the Probate Court, M.G.L. c. 201 § 2, although parents may designate another adult to be a guardian without having to invoke a court proceeding. This kind of guardian, once appointed, is also referred to as a “standby proxy,” whose authority becomes enforceable when the parent dies, becomes incapacitated or is unavailable to care for the child. M.G.L. c. 201 §§ 2B – 2D. The Department of Social Services (DSS) or other state agencies may become the legal guardian of children it takes into custody. The CHS will make a determination based on the risk/benefits to determine whether to accept DSS, or other agency consent for children in their custody.

In general, a parent or legal guardian is considered under federal policy to be the legally authorized representative of a child, and thus may consent to the child’s participation in a research project. Thus, for a child participant in research, a parent or guardian acting as a legally authorized representative can give permission (consent) on behalf of the child to participate in research. As discussed above, an exception to this general rule is where the

research involves medical treatment and the child has the capacity to consent under the emancipated minor or mature minor rules.

1. Determination of Risk to the Children in the Research, *mark which is true:*

a. Research Not Involving Greater than Minimal Risk

Mark if true:

- Under **45 CFR § 46.404**, where the CHS has found that the proposed research presents no greater than minimal risk to the children, it may approve the research *only if it also finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 45 CFR § 46.408*. (Note that 45 CFR § 46.408(b) the permission of both parents is required 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 CHS may find that the permission of one parent is sufficient for research to be conducted under 45 CFR §§ 46.404-.405 even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.)

b. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child participants

Under **45 CFR § 46.405**, where the CHS has found that the proposed research presents more than minimal risk to the children but involves either an intervention or procedure that holds out the prospect of direct benefit for the individual participant, or a monitoring procedure that is likely to contribute to the participant's well being, it may approve the research *only if it also finds that:*

Mark if true:

- a. the risk is justified by the anticipated benefits to the subjects;
- b. the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; *and*
- c. adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in HHS regulations at 45 CFR § 46.408.

(Note that 45 CFR § 46.408(b) the permission of both parents is required 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 CHS may find that the permission of one parent is sufficient for research to be conducted under 45 CFR §§.46.404-.405 even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for care and custody of the child.)

c. Research involving greater than minimal risk and no prospect of direct benefit to the individual child participants, but likely to yield generalizable knowledge about the participant's disorder or condition

Under **45 CFR § 46.406**, where the CHS has found that the proposed research presents more than minimal risk to the children and involves either an intervention or procedure that does not hold out the prospect of direct benefit for the individual participant, or a monitoring procedure that is not likely to contribute to the participant's well being, it may approve the research *only if it also finds that*:

- a. the risk of the research represents a minor increase over minimal risk;
- b. the intervention or procedure presents experiences to the child subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations;
- c. the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; *and*
- d. adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 45 CFR § 46.408.

(Note that, under 45 CFR § 46.408(b), where research to be conducted under 45 CFR § 406, and permission is to be obtained from parents, both parents must give their permission unless either: one parent is deceased, unknown, incompetent, or not reasonably available, deceased; or only one parent has legal responsibility for the care and custody of the child.)

d. Research not otherwise approvable that presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children

Under **45 CFR § 46.407**, where the CHS does not believe that the proposed research meets the requirements of 45 CFR §§ 46.404, 46.405, or 46.406, but does believe that it presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, it may refer the protocol to DHHS for review. The research may proceed only if the Secretary of DHHS, after consulting with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following an opportunity for public review and comment, determines either: (1) that the research in fact satisfies the conditions of 45 CFR § 46.404, § 46.405, or § 46.406, or (2) the following:

- a) the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- b) the research will be conducted in accordance with sound ethical principles; *and*
- c) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth at 45 CFR 46.408.

(Note that, under 45 CFR § 46.408(b), where research to be conducted under 45 CFR § 407, and permission is to be obtained from parents, both parents must give their permission unless either: one parent is deceased, unknown, incompetent, or not reasonably available, deceased; or only one parent has legal responsibility for the care and custody of the child.)

2. Requirements for Permission by Parents or Guardians

Under 45 CFR § 46.408(b), for research involving children, the CHS must determine, in accordance with and to the extent required by 45 CFR § 46.116, that adequate provisions are made for soliciting the permission of each child's parents or guardian. As noted above, for research conducted under 45 CFR §§ 46.404-405 (minimal risk), the CHS may find that the permission of one parent is sufficient. Where research is to be conducted under 45 CFR §§ 46.406-407 (greater than minimal risk), and permission is to be obtained from parents, both parents must give their permission unless either: one parent is deceased, unknown, incompetent or not reasonably available; or only one parent has legal responsibility for the care and custody of the child.

Under 45 CFR § 46.408(c), in addition to the provisions for waiver set forth in 45 CFR § 46.116, if the CHS finds that a study is designed for conditions or for a participant population for which parental or guardian permission is not a reasonable requirement to protect the participants (for example, neglected or abused children), then it may waive consent, provided an appropriate mechanism for protecting the children is substituted, and provided further that the research is not FDA-regulated and the waiver is not inconsistent with federal, state or local law. The choice of an appropriate mechanism depends on the nature and purpose of the proposed activities, the risk and anticipated benefit to the research participants, and their age, maturity, status and condition.

Under 45 CFR § 46.408(d), permission of parents or guardians for their children to participate in research must be documented by a signature on the consent/permission form, unless a waiver of consent/permission or documentation is approved by the CHS.

Mark if true:

- There are adequate provisions for parental permission;
- The research meets the definition of minimal risk;
 - An alteration of some or all of the elements of parental permission is warranted
Indicate waived elements: _____
 - Parental permission may be waived.
- If more than minimal risk, permission will be sought from both parents;
- If more than minimal risk and only one parent's permission is being sought, one parent is deceased, unknown, incompetent or not reasonably available; or only one parent has legal responsibility for the care and custody of the child.
- The research is designed for conditions or for a participant population for which parental or guardian permission is not a reasonable requirement to protect the participants.

- An appropriate mechanism for protecting children who will participate as participants in the research is substituted.
- The research is not FDA-regulated.

3. Requirements for Assent by Children

“Assent” means agreement – specifically, in this context, a child’s agreement to participate in research. Assent, like consent, is a process that should be documented.

Under 45 CFR § 46.408(a), when, in the CHS’ judgment, children are capable of providing assent, the CHS must determine that adequate provisions are made for soliciting their assent. In determining whether children are capable of assenting, the CHS takes into account their ages, maturity, and psychological state. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the CHS deems appropriate. If the CHS determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or 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 and is available only in the context of the research, then the assent of the children is not a necessary condition for proceeding with the research. Even where the CHS determines that the participants are capable of assenting, the CHS still may waive the assent requirement in accord with 45 CFR § 46.116.

Under 45 CFR § 46.408(e), when the CHS determines that assent is required it shall also determine whether and how assent must be documented. Assent forms are designed similarly to consent forms and should include the purpose, procedures, risks and benefits of participating in a particular research study. The assent should be written at the age level of the children, with jargon and technical terms explained or removed.

For children ages seven and under, the CHS recommends that the Investigators verbally explain the study to the child, including its purpose, procedures, and potential risks and benefits (if appropriate, depending on the child’s age, maturity and development). For children ages seven through 17 years, the CHS typically requires written assent from the child, although this may be waived by the CHS. Assent should be obtained in the presence of a parent or legal guardian, unless the study procedures are taking place in a setting (such as a school) where parents are not usually present. However, in nearly all cases, a child’s assent must be accompanied by the permission or consent of the child’s parent or guardian.

Mark if true:

- Assent will be obtained from
 - All of the children
 - Some of the children. Indicate which children will be assented: _____
 - None of the children
- The age, maturity and psychological state is appropriate for assent.

- The age, maturity and psychological state is appropriate for some children to assent.
- The assent includes the purpose of the research, the procedures involved with participating in the research, and the risks and benefits of participating in the research
- Written assent will be obtained and documented from the children.
- Verbal assent will be obtained from the children (if yes, indicate which of the following is true):
 - Verbal assent will be obtained from the children and *observed* by the parent or guardian.
 - Verbal assent will be obtained from the children and *documented* by the parent or guardian.
 - Verbal assent will be obtained from the children and documented by a child advocate or consent monitor.
 - Verbal assent will be obtained from the children and documented by the researcher.
 - Verbal assent will be obtained from the children, but not documented by the researcher.
- The age maturity and psychological state is not appropriate for assent
- 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 and is available only in the context of the research, then the assent of the children is not a necessary condition for proceeding with the research.
- The child is able to assent, but the CHS waives the assent requirement in accord with 45 CFR § 46.116 (c) (d) ,45CFR46.117 (c) .

4. Additional Requirements for Wards and Foster Children

Under 45 CFR § 46.409(a), children who are wards of the state or any other agency, institution, or entity can be included in research approved under § 46.406 or § 46.407 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 participants are not wards.

Even if such research is approved under 45 CFR § 46.409(a), 45 CFR § 46.409(b) requires the 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 or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the CHS) with the research, the Investigator(s), or the guardian organization.

Massachusetts law (MGL Chapter 119, et. seq.) allows the Department of Social Services (DSS) to remove children from their parents' custody in certain circumstances, but the placement of a child in foster care does not automatically terminate all parental rights.

Because these situations are complicated, investigators who wish to use foster children as participants in their research are urged to consult in advance with the CHS.

Will children in the research be wards of the state or foster children: Yes No

If yes, *the following must be true:*

- The research is related to the children's status as wards;
- The research will be conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.
- A child advocate will be appointed for each child.
- The child advocate has the background and experience to act in the best interests of the child(ren).
- The child advocate is not associated with the research.
- If a guardian has been appointed for the child, the guardian will also provide permission.
- If the child is in foster care and the child's parents have maintained their parental rights, appropriate provisions have been made for the permission of the parent.

Reviewer Name

Date