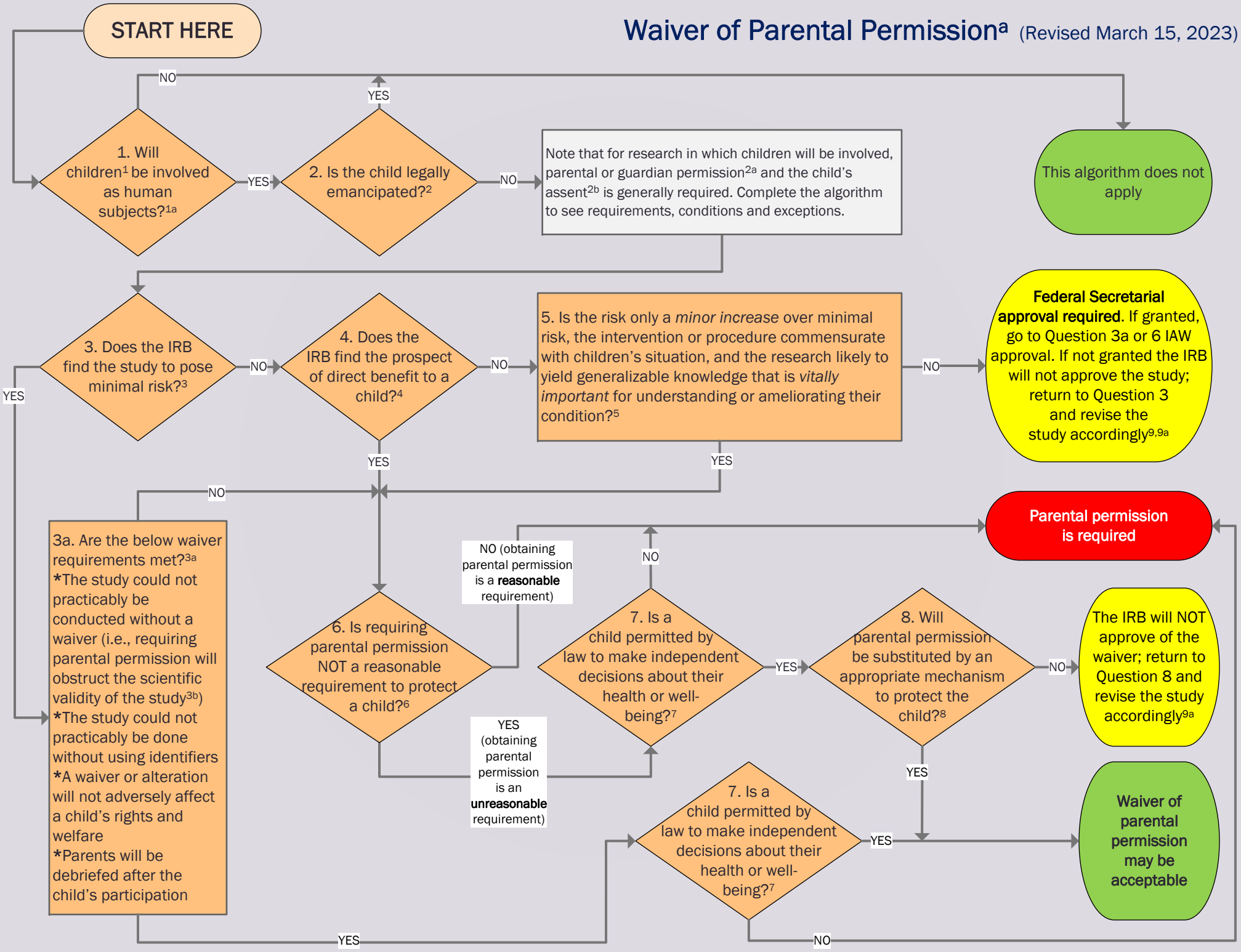
Waiver of Parental Permission[a] (Revised March 15, 2023)



NOTES (March 15, 2023)

[a] This algorithm illustrates key decisions points, pathways, and outcomes regarding FSU Institutional Review Board (IRB) review of researchers' requests for waivers of parental permission for children to take part in research as human subjects. Such review is governed by federal law at Title 45 of the U.S. Code of Federal Regulations, Part 46 (45 C.F.R. 46), §§ 46.111(b), 46.116, 46.408(c)). Waiver of parental permission means that for research that may involve a child as a human subject, that the child's *parent* or *guardian* are not provided by researchers with information about the research and/or are not asked to provide permission for their child to take part in the research. For purposes of this algorithm, the terms "child" or "*children*" means a person or persons who have not attained the legal age for consent to treatments or procedures involved in the research (See Note 1 below). The term "*parent*(s)" and "parental" includes a child's biological or adoptive parent or guardian, and the term "*guardian*" means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care (§ 46.402(d), (e)).

There are two pathways to such waivers: (1) for research that pose only minimal risk to children and (2) for research for which, regardless of risk, parental permission would not serve to protect a child. This algorithm and the notes below describe the conditions that may apply for each pathway, decision point and outcome. If the conditions are satisfied, an IRB may—**but is not required to**—approve of a waiver; the IRB may also impose other conditions for approval.

> *References throughout to "§ 46.xxx" relate to sections of 45 CFR 46 of the federal regulations. To locate any citation listed in this algorithm, see https://www.ecfr.gov/ and search for the referenced Title and §s. The eCFR is not an official edition of the CFR (click here for the official legal version) but is more readily accessible and may be more current.*

[1] *Children* are defined as "persons who have not attained the legal age to consent to treatment or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted" (§46.402(a)). In Florida, persons under the age of 18 are considered minors for consent purposes unless the "disability" of their nonage has been removed under specified conditions or for certain activities (e.g., unwed pregnant minors who may consent to their own or their child's medical care; certified unaccompanied homeless youth who may consent to their own or their child's medical and other care. Florida Statutes (FLA. STAT.) §§ 743.065, 743.067). Other jurisdictions may or may not be similar in this regard.

[1a] Children will be involved as *human subjects* when, for a research purpose, information will be obtained from children through intervention or interaction with the children OR when information or biospecimens about children will be accessed or obtained (with or without intervention or interaction with children). If "No" then this algorithm does not apply.

[2] Whether a child is considered legally emancipated is also governed by the law of the jurisdiction that applies to the child. In Florida, persons may be considered legally emancipated under specified conditions (e.g., when a person reaches the age of 18 years; through marriage; by circuit court order. FLA. STAT. §§ 743.07, 743.01, 743.015). Again, other jurisdictions may or may not be similar in this regard. Answer "No" if the status about a child's legal emancipation is unknown. If "Yes" AND the IRB is provided with sufficient documentation* of the child's legal emancipation (e.g., court order if <18 years; other indication of age ≥18 years), then this algorithm does not apply.

[2a] *Permission*. Before involving a child as a human subject, researchers must generally—in addition to obtaining the child's assent[2b]—obtain the permission of each child's parents or guardian (§ 46.408(b)). Whether permission must be obtained from one or both parents may depend upon the risks and benefits of the proposed research; refer to Questions 3, 4 and 5. Parental permission must be consistent with the following:

- General requirements (i.e., be legally effective; without coercion or undue influence; in a language that the parent would understand; includes information that a reasonable parent would want, and an opportunity for the parent to discuss the information with the researcher; begins with a concise and focused presentation of key information; includes sufficient detail and is organized so as to facilitate the parent's understanding of the reasons for taking part or not taking part; and without any exculpatory language) (§ 46.116(a));

- Basic and additional elements (e.g., descriptions or statements about the purposes of research, risks and discomforts, benefits, confidentiality, research injury, incidental findings, voluntariness, cost, incidental findings) (see § 46.116(b) and (c) for a complete list).

See also NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, REPORT AND RECOMMENDATIONS: RESEARCH INVOLVING CHILDREN, 1977) (NATIONAL COMMISSION: RESEARCH INVOLVING CHILDREN).

[2b] *Assent*. Aside from parental permission, researchers must obtain children's assent (i.e., affirmative agreement) to take part in research if the IRB finds that the children are capable of providing assent (§§ 46.402(b) and 46.408(a)). Unless affirmatively deemed to lack capacity of providing assent, children who are seven (7) years of age or older are considered capable of understanding the procedures and general purpose of research and indicating their wishes regarding participation. The IRB shall—as the IRB may deem appropriate—consider each individual child or all the children's age, maturity, and psychological state.

If the IRB finds that (1) the capability of some or all of the children is so limited that the child/children cannot reasonably be consulted or (2) 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 IRB may find that assent is not a necessary condition for approving of the research (§ 46.408(a)). However, the prospect of direct benefit must be considered significant and the direct benefit possible only through the child's participation in the study. The IRB will expect researchers to provide sufficient evidence* about the significance of the possible direct benefit and its availability only through the study. For a discussion about the prospect of direct benefit, see Note 4 below.

Finally, even where the IRB determines that children are capable of assenting, the IRB may still, providing other conditions are satisfied, approve of a waiver of the assent requirement. See Note 3a below; see also NATIONAL COMMISSION: RESEARCH INVOLVING CHILDREN.

[3] *Minimal Risk.* Among the criteria for approving research, the IRB must evaluate the risks posed to human subjects; when research will involve children, the risks posed to children will govern parental permission requirements. *Minimal risk* "means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests" (§ 46.102(j)). The standard of minimal risk for research involving children is applied by the IRB as follows:

1. those risks that may be encountered in the daily life of a normal, average, healthy child;
2. who is living in a safe environment; and,
3. the risk is indexed to the experiences of children of the same age and developmental stage as the proposed subject population.

NATIONAL ACADEMIES, ETHICAL CONDUCT OF CLINICAL RESEARCH INVOLVING CHILDREN, 2004; THE SECRETARY'S ADVISORY COMMITTEE ON HUMAN RESEARCH PROTECTIONS (SACHRP): APPENDIX B RECOMMENDATIONS REGARDING RISK IN RESEARCH INVOLVING CHILDREN (2005); U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, FOOD AND DRUG ADMINISTRATION, ETHICAL CONSIDERATIONS FOR CLINICAL INVESTIGATIONS OF MEDICAL PRODUCTS INVOLVING CHILDREN: GUIDANCE FOR INDUSTRY, SPONSORS AND IRBS, 2022 (Draft)).

If the research presents a risk to a child subject outside of the standard (i)-(iii) above, then the research is deemed greater than minimal risk (note that even a minor increase over minimal risk is considered greater than minimal risk; see note 5). Whether a study poses minimal risks is a determination made solely by the FSU IRB (§§ 46.111, 46.404). Every component of the study is separately evaluated, and each component must pose only minimal risk for the entire study to be determined minimal risk. For a list of factors that may be considered by the FSU IRB for evaluating risks, refer to GUIDANCE: Risk Levels, Risk Types, Examples & FSU IRB Review Pathway, available in RAMP IRB under the IRB, Library and General tabs. For a study that the IRB finds poses only minimal risk, the IRB may—**but is not required to**—find that the permission of one parent is sufficient (§ 46.408(b)).

[3a] Waiver Requirements. For minimal risk research, IRB may—**but is not required to**—waive or alter the usual requirements for informed consent, BUT ONLY IF a number of conditions that apply are satisfied (§ 46.116(f)). Before an IRB may approve of a waiver of informed consent or to approve of an alteration to a required informed consent element, the IRB is required to find and document ALL the five (5) following conditions:

1. the research involves no more than minimal risk;
2. the research could not practicably be conducted without the requested waiver or alteration;
3. if the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be conducted without using such information or biospecimens in an identifiable format;
4. the waiver or alteration will not adversely affect the rights and welfare of the subjects; and,
5. whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation (i.e., debriefing).

Researchers must provide the IRB with sufficient documentation and explanation* in order for the IRB to make the above regulatory findings (e.g., that without a waiver or alteration that the study cannot be conducted or will lack scientific validity; that a child's parents will be debriefed after a child's participation, and provide a copy of the debriefing statement or form; and that no right to which a child is entitled or for which the child's welfare is protected—such as qualification for or access to any benefits, services or treatment as usual—will be delayed, lost, reduced or otherwise abridged in any way by a waiver or alteration). See also Note 3b below. Only answer "Yes" to this Question 3a if the IRB finds and documents that the above requirements are satisfied.

[3b] The requirement to obtain parental permission may arguably serve to bias recruitment or accrual of children or the veracity of children's responses such that the research could not practicably be conducted. Note that "not practicably" (i.e., not possible or not feasible—such as the parents and guardians of some or all of the children are lost to contact; the parents of children needed for the study routinely withhold their permission for studies of the type or subject matter proposed) is not the same as "not practical" (i.e., obtaining parental permission may be inefficient, costly or inconvenient—such as it takes too many study staff or too much time, telephone calls or emails to locate parents or to obtain parental permission).

For researchers to claim that requiring parental permission will undermine or obstruct the study's scientific validity, such as prevent findings from being generalizable to a sample or population of interest, then researchers must provide the IRB with sufficient scientific evidence* to support their claim. The data must be clear and evidenced based, and researchers must demonstrate how such evidence of bias (and the underlying factual patterns) and their proposed study are similarly situated (e.g., children's conditions; family and social environments; risks and benefits of the research) such that such bias is likely to detrimentally affect their proposed study by making the study not practicable to conduct (see, e.g., Bauman et al., *Whether to Waive Parental Permission in HIV Prevention Research Among Adolescents: Ethical and Legal Considerations,* JOURNAL OF LAW, MEDICINE & ETHICS 48(1) (2020); Liu et al., *The Effects of Requiring Parental Consent for Research on Adolescents' Risk Behaviors: A Meta-Analysis*, JOURNAL OF ADOLESCENT HEALTH 61(1) (2017); Mustanski and Fisher, *HIV Rates are Increasing in Gay/Bisexual Teens: IRB Barriers to Research Must be Resolved to Bend the Curve*, AMERICAN JOURNAL OF PREVENTIVE MEDICINE 51(2) (2016)).

[4] Direct Benefit. For purposes of determining parental permission requirements in research that may pose greater than minimal risks to children, the IRB must first have evaluated whether the intervention or procedure that is being studied presents the prospect of direct benefit to the individual child or will include a procedure that is necessary to monitor the effects of the intervention in order to maintain or contribute to the individual child's well-being (e.g., obtaining a blood sample or spinal fluid for purposes of determining whether the intervention is safe or effective for the child). The prospect of direct benefit refers to the potential benefit to the individual child that will accrue from the child's exposure to the research intervention or procedure being studied, *not* from ancillary interventions or procedures such as physical, psychological, or other examinations or tests that are conducted as part of the research, but which examinations or tests are not themselves being for studied for their effect on the child's biomedical, social, behavioral, or educational outcome (§ 46.405; NATIONAL COMMISSION: RESEARCH INVOLVING CHILDREN). The IRB is not to consider the benefits of therapies that a child would receive even if the child did not participate in the research (§ 46.111(a)(2)).

After finding the prospect of direct benefit, the IRB must next have found that the risk is justified by the anticipated benefit to the child, and that the relation of the anticipated benefit to the risk is at least as favorable as any available alternatives. In its evaluation, the IRB will consider the adequacy of the evidence (see below) provided by researchers, which evidence arguably establishes proof of concept about a potential direct benefit, and whether the proposed exposure (e.g., duration, frequency, amount, dose) to the intervention or procedure is enough to offer a potential direct benefit to the individual child. Additionally, for any monitoring procedure claimed by the study team to provide a direct benefit, the proposed monitoring procedure must have the intended, *not incidental*, potential benefit of influencing the management of the child's diseases or condition. Finally, any intervention or procedure must be compatible with the child's age and developmental stage such that a benefit is anticipated.

The IRB will expect researchers to provide sufficient evidence* for the IRB to unambiguously find that the research will provide potential direct benefit to each child; this evidence may for example include one or more sources of the following information:

- When adult data are available in conditions that exist both in adults and children, evidence of direct benefit in adults from the intervention or procedure being studied provides support for prospect of direct benefit in children.
- Evidence of direct benefit in older aged children from the intervention or procedure being studied supports the prospect of direct benefit in younger aged children.
- For conditions with manifestations that occur exclusively in children, the availability or collection of adult data evaluating the intervention or procedure may not be available, applicable, or feasible.
- For conditions with a phenotype that extends from childhood into adulthood, demonstration of a studied intervention or procedure's positive effect on a biomarker or surrogate endpoint linked to the causal pathway of the condition in adults supports the prospect of direct benefit in children.
- Finally, nonclinical data obtained in relevant animal studies or in vitro models for some health-related conditions of interest may sometimes be the only source of information to support the prospect of direct benefit in children.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, FOOD AND DRUG ADMINISTRATION, ETHICAL CONSIDERATIONS FOR CLINICAL INVESTIGATIONS OF MEDICAL PRODUCTS INVOLVING CHILDREN: GUIDANCE FOR INDUSTRY, SPONSORS AND IRBS, 2022 (Draft)); THE SECRETARY'S ADVISORY COMMITTEE ON HUMAN RESEARCH PROTECTIONS (SACHRP): APPENDIX B: RECOMMENDATIONS REGARDING RISK IN RESEARCH INVOLVING CHILDREN (2005).

If the IRB does find the prospect of direct benefit to the individual child, the IRB may—**but is not required to**—find that the permission of one parent is sufficient (§§ 46.405, 46.408(b)).

[5] Minor Increase over Minimal Risk. For the purposes of determining parental permission requirements in research that may pose greater than minimal risks to children but for which research the proposed intervention or procedure being studied does not provide the prospect of direct benefit to the individual child or the monitoring procedure is NOT likely to contribute to a child's well-being, the IRB must first have evaluated each of the following (1)-(3):

1. Whether the risks of the research represent only a *minor increase* over minimal risk (§ 46.406(a)). The criteria for "only a minor increase over minimal risk" include:
    a. that the intervention or procedure being studied does not meet minimal risk criteria; and,
    b. that the investigator presents sufficient evidence* to the IRB about the intervention, procedure, population, and the qualifications of the study team for the IRB to find that:
        i. the increase in the probability and magnitude of harm is only slightly more than minimal risk;
        ii. any potential harms associated with the intervention or procedure will be transient and reversible in consideration of the nature of the harm (restricted to time of procedure or short post-experimental period); and,
        iii. there is no or an extremely small probability that any child subject will experience as severe the potential pain, discomfort, stress, or harm associated with the intervention or procedure (SACHRP: APPENDIX B RECOMMENDATIONS REGARDING RISK IN RESEARCH INVOLVING CHILDREN).

2. Whether the intervention or procedure being studied presents experiences to subjects that are reasonably commensurate with those inherent in the children's actual or expected medical, dental, psychological, social, or educational situations (§ 46.406(b)); and,
3. Whether the intervention or procedure being studied is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition (§ 46.406(c)). For interventions or procedures to be considered of "vital importance" the researchers must provide the IRB with sufficient scientific evidence* that intervention or procedure's use is likely to yield generalizable knowledge that would contribute to understanding the etiology, prevention, diagnosis, pathophysiology, amelioration or treatment of the subjects' condition or disorder.

The documentation and evidence* provided by researchers to the IRB must be clear and evidenced based, with the primary objective of the proposed research to contribute to understanding the etiology, prevention, diagnosis, pathophysiology, amelioration or treatment of the subject's disorder or condition.

For a study that the IRB finds poses greater than minimal risk to child subjects without the prospect of direct benefit AND that the IRB finds that the study will satisfy the conditions (1)-(3) above, 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 (§§ 46.406, 46.408(b)). If the research does not satisfy the conditions (1)-(3) above, then the IRB will not approve of the study without federal agency Secretarial review and approval (see Note 9 for details).

[6] For purposes of considering whether to waive parental permission, the IRB may—in addition to the provisions for waiver of informed consent at § 46.116(f) for minimal risk research—waive parental permission if the IRB determines that the research is designed for conditions or for a child for which parental or guardian permission is not a reasonable requirement to protect the child (§ 46.408(c)), BUT ONLY IF the IRB determines that (1) an appropriate mechanism for protecting the children is substituted (see Note 8), and (2) the waiver would not be inconsistent with Federal, state or local law (see Note 7). Note that unlike a waiver under § 46.116(f), a waiver of parental permission under § 46.408(c) may—assuming other conditions are satisfied—be granted for research regardless of risk.

Some conditions for which permission may not be a reasonable requirement to protect a child include among the following:

- The child's parents or guardian are legally incompetent or functionally unable to provide permission.
- The research is designed to study children who are neglected or abused.
- Children may be at risk of physical or psychological harm if their parents are informed about their children's interest or participation in a study activity.
- The research is designed to study children who are engaged in high-risk behaviors such as illegal alcohol or drug use or sexual activities.
- A child's participation in a study activity may result in conflicts with the child's parent, leading to significant emotional distress or disconnect or risk to a child's psychosocial well-being.

Researchers must provide the IRB with sufficient documentation* (e.g., that a child's parents have been found by a court to be legally incompetent; that the children have been deemed by a child welfare agency as neglected or abused due to parental act or omissions) or scientific evidence (e.g., that the literature demonstrates that children similarly situated as the study's prospective subjects are at risk of harm if their parents knew about their children's participation in an activity which is being studied) for the IRB to make the above findings. Scientific data must be clear and evidenced based, and researchers must demonstrate how such evidence and their proposed study are similarly situated or substantially related (e.g., children's conditions; family and social environments; risks and benefits of the research). Some evidence might include current literature on harm or punishment inflicted by parents on children engaged in drug-seeking behaviors; stigmatization or ostracizing of children considered members of a sexual minority; or conflicts that are experienced by children interested in cognitive behavioral strategies for coping with family trauma.

[7] In addition to the conditions for waiver of parental permission outlined in Note 6, a waiver must not be inconsistent with other applicable laws (§§ 46.408(c), 46.101(e)-(g)). The IRB will expect researchers to provide the IRB with sufficient, authoritative evidence* so that the IRB may unambiguously make this finding about each child, since depending upon the jurisdiction to which the research is subject or in which the child is protected, the law may differ or even conflict.

The documentation may for Florida law be in the form of a copy of a current Florida statute (e.g., https://www.flsenate.gov/Laws/Statutes) and for federal law in the form of a copy of a current federal regulation (e.g., https://www.ecfr.gov/). For international laws, the laws of states other than Florida, and tribal laws that may be applicable to the research, the documentation must be in the form of official legal memoranda or other legal communication that has been provided to the study team to confirm that parental or guardian permission, consent or knowledge for those jurisdictions is not required. The documentation must be dated; must provide an unequivocal statement to the effect that current applicable law permits children of the age, maturity, status, condition or circumstances sought as prospective human subjects for the proposed study may independently decide to take part in the proposed study without the need for parent or guardian permission or knowledge; must further provide if not obvious from the memoranda or communication the legal citation/reference for the law; and must indicate that current applicable law would not prohibit, restrict, or otherwise limit children from taking part in research of the type proposed.

Examples of some areas of a child's health and well-being for which Florida laws may under certain conditions permit children to independently make decisions include:

- Sexually transmitted diseases, including Human Immunodeficiency Virus testing and prophylaxis (e.g., FLA. STAT. 384.30).
- Alcohol or drug abuse counseling or treatment (e.g., FLA. STAT. 397.601(4)(a)).
- Family planning or prenatal care (e.g., FLA. STAT. 381.0051(4)).
- Outpatient mental health diagnostic and evaluative services or crisis intervention, therapy, and counseling services (e.g., FLA. STAT. 394.4784(1) and (2)).
- Emergency medical care or treatment (e.g., FLA. STAT. 743.064)

The above are only examples, are subject to certain conditions and limit, and are current as of the publication of this algorithm. Referring to these examples should not be relied upon in lieu of providing the IRB with sufficient, authoritative, and current evidence. Because such laws and the conditions that may apply may change over time, and may clearly fall under the ambit of another jurisdiction's authority, are numerous and may be difficult to locate, may not be recognized in other jurisdictions, and may substantially differ among jurisdictions, it is essential that researchers provide the IRB with the current status for any law claimed to permit children to independently make decisions regarding their health or well-being about which the study specifically pertains.

[8] In addition to the conditions for waiver of parental permission outlined in Note 7, a waiver may be granted only if the IRB finds that researchers will, as a substitute for parental permission, put into place an appropriate mechanism for protecting the children (§ 46.408(c)). Specifically—

- Researchers must provide sufficient documentation* of a suitable and detailed plan to put into place an appropriate mechanism to protect children. The appropriateness of such mechanism(s) will depend upon study parameters such as the nature and purpose of the activities described in the protocol, the risk and anticipated benefit of the research to children, and the children's age, maturity, status, and condition; separate mechanisms may therefore be required for different children depending upon these and other study parameters.
- Mechanisms that might substitute for parental permission may include, for example, the following:
    - Court approval of or legal authority designating a surrogate to make decisions on behalf of a child.
    - Having a professional (e.g., social worker, teacher, health care provider, counselor, case worker) who is not affiliated with the research—but who has the background and experience in matters pertaining to child health or welfare and who is knowledgeable about the study's experimental and standard-of-care procedures, risks and benefits—*adequately explain the study to the child* in terms that the child will understand.
    - Having a professional (see above examples) who is not affiliated with the research—but who has the background and experience in matters pertaining to child health or welfare and who is knowledgeable about the study's experimental and standard-of-care procedures, risks and benefits—*observe and monitor the assent procedure* and to separately (without any member of the study team present) confirm with the child the child's understanding.

- Designating a competent adult who may be related to the child, for which child the adult is a suitable substitute for a parent, who comprehends as well as understands the proposed research, and who is otherwise not conflicted by the research or by the participation of the child—*to adequately explain the study to the child* in terms that the child will understand (SACHRP: APPENDIX A RECOMMENDATIONS RELATIVE TO RESEARCH INVOLVING CHILDREN (2006)).

The IRB may impose other requirements or require mechanisms in addition to those listed above.

[9] Federal law does not permit the IRB to approve of research involving children that does not fall within one of the three categories of approvable research (minimal risk; greater than minimal risk with prospect of direct benefit; minor increase over minimal risk with no prospect of direct benefit), absent federal U.S. Department of Health and Human Services (DHHS) Secretarial (for DHHS-funded research) or equivalent (for non-DHHS-funded research) review and approval. For research that the IRB finds is not otherwise approvable and before submitting such research for DHHS or equivalent review, the FSU IRB is required to find, based upon sufficient scientific evidence* provided by researchers, that "the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children" (§ 46.407(a), (b)); for examples of evidence, see Note 4. For federal guidance on Secretarial or equivalent review, see § 46.407(b) or this OHRP link.

If DHHS Secretarial or equivalent approval is granted, the research may be resubmitted to the FSU IRB for review; proceed to Question 3a if the Secretarial or equivalent federal agency deems the research as minimal risk, or Question 6 if deemed otherwise. Note that while not dispositive—i.e., other applicable laws, including e.g., international, federal, state, or local laws that provide additional protections for human subjects, including children, may still apply—DHHS Secretarial or equivalent approval should be given substantial weight by the IRB. If DHHS Secretarial or equivalent approval is NOT granted, the IRB will not approve of the study.

[9a] For studies that are not otherwise approvable, researchers are strongly advised to ensure, as may be applicable, that before submitting their studies for IRB review or by revising their submissions to the IRB's satisfaction, that all research risks are reduced to an acceptable level (i.e., that research will involve only minimal risk or only a minor increase over minimal risk); that their studies will unequivocally provide the possibility of direct benefit to a child or (for studies involving a minor increase over minimal risk) yield generalizable knowledge about the child's disorder or condition; that steps are taken to provide a substitute for parental permission as an appropriate mechanism to protect children; and/or that sufficient documentation or evidence is provided to the IRB as may be required above. Doing so may allow the IRB to find that a waiver or alteration of parental permission may meet regulatory requirements such that the study may be approved. As usual, the IRB has inherent discretion in determining whether research satisfies regulatory criteria for approval; FSU institutional officials may not approve of any such research that has not been approved by the IRB (§§ 46.109(a), 46.112).

* The threshold for "sufficient" documentation or evidence is greater than relying on the opinion or claims of the investigator, and that the determination of the sufficiency of the documentation or evidence to support or prove any matter or issue requiring consideration or evaluation by the IRB is a subjective analysis that must be deliberated by the IRB (§46.109 et seq.; NATIONAL COMMISSION, RESEARCH INVOLVING CHILDREN). IRB submissions that lack sufficient documentation or evidence will be returned, deferred, disapproved or approval conditioned upon receipt of appropriate documentation or evidence.