This document summarizes changes in *Policy 402 Research Involving Children* (referred to as Policy 402 in this document) that NIH investigators should be aware of, from the SOP(s) mentioned below.

The policy describes regulatory and policy requirements that apply when an NIH Institutional Review Board (IRB) is reviewing, or when an NIH investigator seeks to perform, research involving children. (See 45 CFR 46 Subpart D)

NIH investigators are responsible for reviewing Policy 402 and complying with the requirements of the policy.

Note: Text from the policy and other policy titles are italicized.

Policy 402 Research Involving Children	**SOP Superseded by Policy 402**
Policy 402 partially supersedes:	**SOP 14A Research Involving Vulnerable Subjects (General Considerations)** This SOP will not be replaced by an HRPP policy and will be inactivated. When inactivated, this SOP will be archived in the Policy archive.
Policy 402 supersedes	**SOP 14D Research Involving Children**

Applicability of Policy 402 - This policy applies to:

- all research involving children reviewed by the NIH IRB
- NIH investigators when conducting research at an NIH site, whether the reviewing IRB is the NIH IRB or an external IRB
- non-NIH investigators, including Lead Site Investigators, when the NIH IRB is the reviewing IRB

POLICY Requirement	**SOP Requirement**
Section C.1 – *The protection of the rights, welfare and safety of children that are research subjects is of paramount importance to the NIH Human Research Protection Program (HRPP). Therefore, the NIH Principal Investigator (PI)/Lead Site Investigator will not initiate or conduct research (e.g., screen, enroll or perform research procedures) that involves children without IRB approval for the inclusion of children.* (emphasis added) Policy 402 adds specificity for clarity. (See also E.1.a. in the policy.)	**SOP 14D.2.A** – *The NIH HRPP follows the requirements of this SOP which are consistent with Federal Regulations for the Protection of Human Subjects (45 CFR 46) Subpart D (see Appendix A). For the applicable requirements of the Food and Drug Administration (FDA), see 21 CFR 50, Subpart D – Additional Safeguards for Children in Clinical Investigations (see References). The requirements of this SOP are in addition to those imposed under other subparts of 45 CFR 46 and other relevant SOPs.*
Section C.4 – *Human subjects research that is subject to 45 CFR 46 subpart D may be exempt research under 45 CFR 46.104 of the 2018 Common Rule, as follows:* *a. Exemptions may be applied to the categories found at 45 CFR 46.104(d)(1), (4), (5), (6), (7), and (8), if the conditions*	**N/A –** the 2018 Common Rule was not in effect at the time of publication. Policy 402 describes the applicability of the revised exemption categories.

of the exemption are met. (45 CFR 46.104(b)(3) of the 2018 Common Rule). *b. Exemptions may be applied to the category found at 45 CFR 46.104(d)(2)(i) and (ii)), only when the research involves educational tests or the observation of public behavior when the investigator(s) does not participate in the activities being observed.* *c. As written in the 2018 Common Rule, the exemption category found at 45 CFR 46.104(d)(3)) applies only to adults. Further, the exemption category found at 45 CFR 46. 104(d)(2)(iii) cannot be applied or utilized.* Exempt research categories under the 2018 Common Rule exemptions are similar to those published in the pre-2018 Common Rule, with the exception of the new exemption for benign behavioral interventions. Of note, research involving children cannot be conducted under exempt category 3 for benign behavioral interventions. Such interventions constitute non-exempt research and must be IRB reviewed accordingly. Policy 402 is reorganized from the SOP for clarity.	
Section C.5 – *When the research involves children, no child may be enrolled, screened, or have research procedures initiated, unless parental permission and child assent is obtained consistent with 45 CFR 46.408 and, if applicable,* (FDA) *21 CFR 50.55, unless waived by the IRB. (45 CFR 46.116(f) of the 2018 Common Rule and 45 CFR 46.116(d) of the pre-2018 Common Rule)* *a. For research taking place at an NIH site, and in cases where parents share joint legal custody for medical decision-making of a child (e.g., by a custody agreement or court order), both parents must give their permission regardless of the risk level of the research. Exceptions may include if one parent has since died,*	**SOP 14D.6.1** – *When reviewing research involving children, the IRB must ensure, that adequate provisions have been made for soliciting the permission of each child's parent or guardian in accordance with, and to the extent that is required, by 45 CFR 46.116, and as described in SOP 12 - Requirements for Informed Consent. Additional requirements for obtaining permission are described in 45 CFR 46.408(b).* Policy 402 is reorganized from the SOP and adds specificity for clarity.

become incompetent, or is not reasonably available. *b. The Secretarial waiver of informed consent in certain emergency research may be applicable to research involving children. (45 CFR 46.101(a) and 46.401(a)(2))* There are no changes in requirements to obtain parental permission and child assent in accordance with the IRB's Subpart D determination(s). Please note that, as in SOP 14D, when parents share joint legal custody for medical decision-making, both parents must give their permission, even in minimal risk research in which one parent's signature would otherwise suffice.	**SOP 14D.2.D** – *The Secretarial waiver of informed consent in certain emergency research may be applicable to research involving children* Policy 402 is reorganized and adds specificity for clarity.
Section C.6 – *For the purpose of consent when research is conducted at an NIH site, an adult is anyone 18 years or older.* Policy 402 applies the definition of adult to all NIH sites, not just the NIH Clinical Center. Policy 402 does not address the definition of adult at non-NIH sites. Investigators should consult with the Office of General Counsel when questions arise. **Section C.6.a** – *For the purposes of the research, children who are legally emancipated are considered adults and the requirements of this policy do not apply.* Investigators MUST consult OHSRP who will discuss with OGC for guidance before considering a minor to be emancipated.	**SOP 14D.8.A** – *[1] For the purpose of consent at the NIH Clinical Center (CC), an adult is anyone 18 years or older or an emancipated minor (such as a minor who is married or a parent). At non-CC NIH sites applicable local, state or foreign law is followed in the absence of applicable U.S. Federal law.* Policy 402 also applies the definition of adult to all NIH sites, not just the NIH Clinical Center. Policy 402 requires that children be legally emancipated for the purposes of consenting as adults.
Section C.6.b – *Children that reach the age of majority during the period of the research, must provide consent in order to continue participation in the research, unless consent is not required (e.g., for certain exempt research) or if waived by the IRB.* Policy 402 adds specificity for clarity.	**SOP 14D.8.B** – *The PI should seek and obtain the legally effective informed consent of the now-adult subject unless the IRB has determined and documented that the requirements for obtaining informed consent can be waived under 45 CFR 46.116 (d).*

	There is no change in the obligation to provide consent, when applicable, for continued participation of child subjects who reach the age of consent.
Section C.6.c – *If the child who has reached the age of majority lacks the capacity to consent to the research, the NIH investigator will follow the requirements in Policy 403 Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation, unless the IRB has waived consent consistent with 45 CFR 46.116(f)(3) of the 2018 Common Rule and 45 CFR 46.116(d) of the pre-2018 Common Rule.* Policy 402 adds specificity for clarity.	**SOP 14D.8.E & F** – discuss obtaining consent from now-adults lacking capacity. The requirement to obtain legally effective informed consent (both initial and ongoing) from these participants has not changed.
Section E.1.b – *The NIH Principal Investigator (PI)/Lead Site Investigator is responsible for determining if it is scientifically and ethically appropriate to enroll children in the research protocol and must document this rationale in the protocol.* Policy 402 is reorganized and adds specificity for clarity.	**SOP 14D.5.1.B** – *"… Investigators must provide and IRBs are responsible for approving ethical and scientific justifications for recruiting children within the age range stipulated in the protocol."* There is no change in this requirement.
Section E.1.c – *In addition to the requirements for informed consent described in 45 CFR 46 Subpart A, when the research involves children, the consent requirements at 45 CFR 46 Subpart D must also be met.* *I. When the research involves children, the NIH PI/Lead Site Investigator must provide a plan in the protocol for obtaining parental permission as well as assent from the child, as applicable, or they must provide a justification for requesting a waiver of parental permission and/or assent (consistent with C.5. above).* Policy 402 is reorganized and adds specificity for clarity.	**SOP 14D.6.1** – *When parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research conducted under categories 1 and 2 (see 14D.5.2 above) and the IRB should document this finding. IRBs should also document if permission from both parents is required. Where research is conducted under categories 3 and 4 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.* IRB and PI/Lead Site Investigator responsibilities are described in separate sections of Policy 402. There are no changes to the parental permission and child assent obligations.
Section E.1.c.II – A*ll investigators are responsible for complying with the Reviewing IRB requirements for obtaining and documenting parental permission and assent,*	See above. These obligations apply to all NIH research involving children, regardless of whether the NIH IRB or an external IRB review the study.

and consistent with C.4. and C.5 above, as applicable. (45 CFR 46.408(d) and (e)) Policy 402 is reorganized and adds specificity for clarity.	
Section E.1.c.III *– When child subjects reach the age of majority, investigators must seek legally effective informed consent from the now-adult subject, consistent with C.6.(c) above, or withdraw the subject from the research. (See Policy 301 Informed Consent.)* *i. Alternatively, the investigator may request a waiver of consent from the IRB for the subjects continued participation if the ongoing research meets the criteria for a waiver specified in 45 CFR 46.116(f)(3) of the 2018 Common Rule and 45 CFR 46.116(d) of the pre-2018 Common Rule. For example, a request may be to continue to use tissue specimens collected when the participant was a minor.* *ii. If the now-adult subject is unable to provide legally effective informed consent, the requirements of Policy 403 Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation must be followed.* iii. If investigators will not seek informed consent from the now-adult subject for continued use of specimens or data, investigators must request a waiver of consent from the IRB in order to continue to use specimens or information collected when the participant was a child. iv. Research involving ongoing interactions or interventions will generally require consent from the now-adult subject.	**SOP 14D.8.B.** *– The PI should seek and obtain the legally effective informed consent of the now-adult subject unless the IRB has determined and documented that the requirements for obtaining informed consent can be waived under 45 CFR 46.116 (d).* **SOP D.8.C** *– The PI should seek and obtain the legally effective informed consent of the now-adult subject even if the research does not involve any ongoing interactions or interventions with the subject, but continues to meet the regulatory definition of "human subjects research" (e.g., it involves the continued analysis of identifiable specimens or data). In these circumstances, if appropriate, the IRB may consider a waiver under 45 CFR 46.116 (d).* Policy 402 is reorganized from the SOP for clarity.