DEPARTMENT OF HEALTH AND HUMAN SERVICES

45 CFR Part 46

RIN 0937–AA09

Department of Health and Human Services Policy for the Protection of Human Research Subjects: Update to the Additional Protections for Specific Populations

AGENCY: Department of Health and Human Services.

ACTION: Final rule.

SUMMARY: In this final rule, the Department of Health and Human Services (HHS) is amending its regulations that govern the protection of human subjects for conformity with 2018 revisions made to the Federal policy for protection of human research subjects (the ''Common Rule''), as well as to maintain consistency with the prior version of the Common Rule for research that remains subject to those requirements. Amendments include updating citations that were renumbered, adding updated descriptions of the applicability of exemptions, and correcting a technical error. No substantive amendments are included in this final rule.

DATES: This final rule is effective October 24, 2024.

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SUPPLEMENTARY INFORMATION:

I. Background

A. Revision of the Common Rule

The Common Rule, codified by HHS at subpart A of 45 CFR part 46, was revised by a final rule published in the **Federal Register** on January 19, 2017 (82 FR 7149), and subsequently amended by an interim final rule published in the **Federal Register** on January 22, 2018 (83 FR 2885), and a final rule published on June 19, 2018 (83 FR 28497). The revised Common Rule is defined in the regulatory text as the ''2018 Requirements.'' The prior version of the Common Rule, initially promulgated on June 18, 1991 (56 FR 28002), and amended on June 23, 2005 (70 FR 36325), published in the 2016 Code of Federal Regulations and effective October 1, 2017, is defined by the revised Common Rule as the ''pre-2018 Requirements.'' For brevity, in the regulatory text of subparts B, C, and D, HHS is shortening the full explanation of the ''pre-2018 Requirements'' to ''[t]he pre-2018 Requirements means 45 CFR part 46, subpart A, as revised October 1, 2016'' and the ''2018 Requirements'' to ''[t]he 2018 Requirements means 45 CFR part 46, subpart A, as revised October 1, 2018.'' The applicability of the pre-2018 or 2018 Requirements is defined by § 46.101(l) of the 2018 Requirements. Importantly, research that was approved under the pre-2018 Requirements may continue to follow that rule for the duration of the study; however, research initiated on or after January 21, 2019, must comply with the 2018 Requirements.

The preamble of the January 19, 2017 final rule indicated that, to the extent appropriate, HHS intended to amend the other subparts of the HHS human subjects protection regulations to align with the revisions to the Common Rule codified at subpart A. Through this final rule, HHS is updating subparts B, C, and D to reference both the pre-2018 Requirements and the 2018 Requirements, as appropriate. HHS intends to separately amend subpart E to conform with both the pre-2018 and 2018 Requirements.

B. Subparts B, C, and D Background

Subpart B of 45 CFR part 46, ''Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research,'' was first promulgated on August 8, 1975. The most recent revision to subpart B was published in the **Federal Register** on November 13, 2001 (66 FR 56775).

On November 16, 1978, the then Department of Health, Education, and Welfare published a final rule promulgating subpart C, ''Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects'' (43 FR 53652). On January 26, 1981, the Common Rule was first published, which substantially updated subpart A of 45 CFR part 46 (46 FR 8366). As part of this update, HHS also published an amendment to subpart C in which citations were corrected or updated and other technical amendments were made.

On March 8, 1983, HHS published the final rule promulgating subpart D, ''Additional Protections for Children Involved as Subjects in Research'' (43 FR 9814).

II. Amendments to Subparts B, C, and D of 45 CFR Part 46

As described above, HHS is amending subparts B, C, and D for conformity with both the pre-2018 and 2018 Requirements. Through this rule, HHS is:

- Adding language to subparts B, C, and D to specify when references to subpart A provisions refer to the pre-2018 Requirements or the 2018 Requirements.
- Adding language to clarify the meaning of ''pre-2018 Requirements'' and ''2018 Requirements.''
- Updating language in subparts B, C, and D that explains the applicability of the exemptions to research regulated under each subpart to reflect the additional exemptions allowed by § 46.104(b) of the 2018 Requirements.
- Correcting a technical error contained in subpart D.

A. Amendments to Subpart B

In this final rule, HHS makes eight amendments to subpart B, ''Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research.'' First, 45 CFR 46.201(b) is amended to state that for purposes of this subpart, the pre-2018 Requirements means subpart A as published in the 2016 edition of the Code of Federal Regulations. The version of subpart A referenced in the definition of the term ''2018 Requirements'' refers to 45 CFR part 46, subpart A, as revised October 1, 2018. Section 46.201(b)(1) is added to provide that research subject to the pre-2018 Requirements may apply the exemptions at § 46.101(b)(1) through (6) of the pre-2018 Requirements, while § 46.201(b)(2) is added to provide that research subject to the 2018 Requirements may apply the exemptions at § 46.104(d)(1) through (8) of the 2018 Requirements.

Second, § 46.202 is amended to clarify that the definitions found in § 46.102 of the pre-2018 Requirements or the 2018 Requirements, as applicable, shall be applicable to this subpart.

Third, § 46.202(h) is amended to clarify that if a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of subpart A of the pre-2018 Requirements or the 2018 Requirements, as applicable, and subpart D of part 46.

Fourth, § 46.204(d) is amended to clarify that the pregnant woman's consent must be obtained in accordance with the informed consent provisions of subpart A of the pre-2018 Requirements or the 2018 Requirements, as applicable.

Fifth, § 46.204(e) is amended to state that the consent of the pregnant woman and the father must be obtained in accordance with the informed consent provisions of subpart A of the pre-2018 Requirements or the 2018 Requirements, as applicable, except that the father's

consent need not be obtained if he is unable to consent for the reasons stated therein.

Sixth, § 46.205(b)(2) is amended to state that the consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with the pre-2018 Requirements or the 2018 Requirements, as applicable, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

Seventh, references in subpart B at § 46.205(c)(5) to subpart A's waiver and alteration of consent provisions are updated to reflect conformity with the pre-2018 Requirements as well as the 2018 Requirements. In order for the citation to be consistent with the section numbering of both the pre-2018 and 2018 Requirements, the prior pinpoint citation to § 46.116(c) and (d) has been modified to instead refer to § 46.116 of both the pre-2018 and 2018 Requirements.

Finally, the language of subpart B at § 46.205(d) has been revised to replace the reference to subpart A with reference to the pre-2018 Requirements or the 2018 Requirements, as applicable.

B. Amendments to Subpart C

In this final rule, HHS makes six amendments to subpart C, ''Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects.''

First, 45 CFR 46.301(c) is revised to provide that the requirements of this subpart are in addition to those imposed under the other subparts, including the 2018 Requirements and the pre-2018 Requirements, as applicable. This section is further revised to provide that the term ''pre-2018 Requirements'' means subpart A as published in the 2016 edition of the Code of Federal Regulations. The term ''2018 Requirements'' refers to 45 CFR part 46, subpart A, as revised October 1, 2018.

Second, § 46.304 is modified to clarify that in addition to satisfying the requirements in § 46.107 of the pre-2018 Requirements or the 2018 Requirements, as applicable, an institutional review board (IRB), carrying out responsibilities with respect to this subpart, shall also meet the specific requirements further detailed in this section.

Third, § 46.306(a) is modified to add the word ''nonexempt'' in order to clarify that, except for research involving prisoners that qualifies for exemption, research subject to subpart C must involve only a category of research reflected in 45 CFR 46.306(a)(2)(i) through (iv).

Fourth, § 46.306(b) is revised to provide that research conducted or supported by DHHS (the Department of Health and Human Services) shall not involve prisoners except as provided in § 46.306(b)(1) and (2).

Fifth, § 46.306(b)(1) is added to state that for research subject to the pre-2018 Requirements and this subpart, except as provided in § 46.306(a), biomedical or behavioral research conducted or supported by DHHS shall not involve prisoners as subjects.

Sixth, § 46.306(b)(2) is added to state that for research subject to the 2018 Requirements and this subpart, except as provided in § 46.306(a) or for research that is exempt pursuant to § 46.104(b)(2) and (d)(1) through (8), biomedical or behavioral research conducted or supported by DHHS shall not involve prisoners as subjects.

C. Amendments to Subpart D

In this final rule, HHS makes 12 amendments to subpart D, ''Additional Protections for Children Involved as Subjects in Research.''

First, HHS revises 45 CFR 46.401(a) to provide that the term ''pre-2018 Requirements'' means subpart A as published in the 2016 edition of the Code of Federal Regulations; and that the term ''2018 Requirements'' means 45 CFR part 46, subpart A, as revised October 1, 2018.

Second, given that there is a new § 46.401(a), the language of the previous § 46.401(a)(1) and (2) is renumbered as § 46.401(b)(1) and (2).

Third, HHS is correcting a technical error in the renumbered § 46.401(b)(2) in the citation to the provision of subpart A that allows the Secretary to waive some or all regulatory requirements. Subpart D cites the provision as § 46.101(e). However, the Secretarial waiver provision in subpart A appears at § 46.101(i), not § 46.101(e), in both the pre-2018 and the 2018 Requirements. This rule corrects this technical error, and revises the reference to ''subpart A'' to instead reference the pre-2018 and 2018 Requirements.

Fourth, 45 CFR 46.401(c) is amended to include an explanation of how the exemptions provided in the pre-2018 Requirements and the 2018 Requirements apply to research regulated by subpart D.

Fifth, § 46.401(c)(1) is added to provide that, for research subject to the pre-2018 Requirements, the exemptions at § 46.101(b)(1) and (3) through (6) of the pre-2018 Requirements are applicable to research subject to subpart D. In addition, the exemption at § 46.101(b)(2) of the pre-2018 Requirements regarding educational tests is also applicable to research subject to subpart D, with the caveat that the exemption at § 46.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research subject to subpart D, except for research involving observation of public behavior when the investigator(s) does (do) not participate in the activities being observed.

Sixth, § 46.401(c)(2) is added to provide that, for research subject to the 2018 Requirements, the exemptions at § 46.104(d)(1), (4), (5), (6), (7), and (8) of the 2018 Requirements may be applied to research subject to subpart D; the exemptions at § 46.104(d)(2)(i) and (ii) of the 2018 Requirements may only apply to research subject to this subpart involving educational tests or the observation of public behavior when the investigator(s) does (do) not participate in the activities being observed; and the exemptions at §§ 46.104(d)(2)(iii) and (d)(3) of the 2018 Requirements may not be applied to research subject to this subpart.

Seventh, the language formerly found at 45 CFR 46.401(c) has been updated to reference the pre-2018 Requirements and the 2018 Requirements, instead of ''subpart A,'' and moved to a new § 46.401(d).

Eighth, 45 CFR 46.402 is revised to provide that the definitions in § 46.102 of the pre-2018 Requirements and § 46.102 of the 2018 Requirements, as applicable, shall be applicable to this subpart.

Ninth, 45 CFR 46.408(a) is modified to provide that 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 the pre-2018 Requirements or the 2018 Requirements, as applicable.

Tenth, § 46.408(b) is modified to provide that in addition to the determinations required under other applicable sections of this subpart, the IRB shall determine, in accordance with and to the extent that consent is required by § 46.116 of the pre-2018 Requirements or the 2018 Requirements, as applicable, that adequate provisions are made for soliciting the permission of each child's parents or guardian.

Eleventh, § 46.408(c) is modified to provide that in addition to the provisions for waiver contained in § 46.116 of the pre-2018 Requirements or the 2018 Requirements, as applicable, if the IRB determines that a research

protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (*e.g.,* neglected or abused children), it may waive the consent requirements in § 46.116 of the pre-2018 Requirements or the 2018 Requirements, as applicable, and § 46.408(b), provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with Federal, State, or local law.

Twelfth, § 46.408(d) is modified to provide that permission by parents or guardians shall be documented in accordance with, and to the extent required by, § 46.117 of the pre-2018 Requirements or the 2018 Requirements, as applicable.

III. Legal Authority

The legal authority is as follows: 5 U.S.C. 301; 42 U.S.C. 289(a); 42 U.S.C. 300v–1(b).

IV. 5 U.S.C. 553(b)(B) of the Administrative Procedure Act, 5 U.S.C. 551–559

HHS finds that there is good cause to issue these amendments without advance notice and an opportunity for public comment. This final rule reflects changes that conform subparts B, C, and D to both the pre-2018 and 2018 Requirements and correct a technical error in subpart D that predates the publication of the 2018 Requirements. This final rule merely (i) adds language to each subpart specifying how the regulatory exemptions and provisions apply under the pre-2018 or 2018 Requirements, as applicable; (ii) corrects an erroneous citation in subpart D; and (iii) changes the citation to the subpart A provisions that allow waiver and alteration of informed consent in § 46.205(c)(5) from § 46.116(c) and (d) to § 46.116, in order to generally reference the waiver and alteration of informed consent provisions in both the pre-2018 and 2018 versions of the Common Rule. HHS determines that advance notice and public comment are unnecessary. Pursuant to 5 U.S.C. 553(b)(B) of the Administrative Procedure Act, HHS finds good cause to dispense with advance notice and public comment as these procedures are unnecessary, because this rule only serves to update subparts B, C, and D to conform with provisions in the pre-2018 and 2018 Requirements of 45 CFR part 46, which are already in effect, and to correct a citation error. HHS further finds good cause for this rule to be effective upon publication in accordance with 5 U.S.C. 553(d)(3) because the provisions of the pre-2018 and 2018 Requirements to which these revisions conform are already in effect, and regulated entities already are required to comply with these provisions.

V. Regulatory Impact Analyses

We have examined the effects of this final rule under Executive Order 12866 on Regulatory Planning and Review (September 30, 1993), Executive Order 13563 on Improving Regulation and Regulatory Review (January 18, 2011), Executive Order 14094 on Modernizing Regulatory Review (April 6, 2023), the Paperwork Reduction Act of 1995 (Pub. L. 104–13), the Regulatory Flexibility Act, (Pub. L. 96–354, September 19, 1980), the Congressional Review Act (5 U.S.C. 801, Pub. L. 104–121), the Unfunded Mandates Reform Act of 1995 (Pub. L. 104–4), Executive Order 13132 on Federalism (August 4, 1999), and section 1102(b) of the Social Security Act.

A. Executive Orders 12866, 13563, and 14094

Executive Orders 12866, 13563, and 14094 direct agencies to assess all benefits, costs, and transfers of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Rules are ''significant'' under Executive Order 12866 section 3(f)(1) (as amended by Executive Order 14094) if they have an annual effect on the economy of $200 million or more (adjusted every 3 years by the Administrator of the Office of Information and Regulatory Affairs (OIRA) for changes in gross domestic product); or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, territorial, or tribal governments or communities.

This rule makes technical corrections to subparts B, C, and D that reflect existing requirements contained in the 2018 Requirements. The impacts of the 2018 Requirements are accounted for in three prior regulatory impact analyses (82 FR 7231, 83 FR 2880, 83 FR 28505). Compared to a baseline scenario of the 2018 Requirements, HHS finds that this rule will not have an impact on human subjects research or human subjects research review. This rule has not been designated as a ''significant regulatory action'' under section 3(f) of Executive Order 12866 (as amended by Executive Order 14094).

B. Paperwork Reduction Act

This final rule does not impose any additional information collection burden under the Paperwork Reduction Act and does not contain any information collection activities beyond the information collection already approved by Office of Management and Budget under control numbers 0990–0260, 0990–0473 and 0990–0481.

C. Regulatory Flexibility Act

The Regulatory Flexibility Act (5 U.S.C. 601 *et seq.*) (RFA) and the Small Business Regulatory Enforcement Fairness Act of 1996, which amended the RFA, require agencies that issue a regulation to analyze options for regulatory relief for small businesses. If a rule has a significant impact on a substantial number of small entities, agencies must specifically consider the economic effect of the rule on small entities and analyze regulatory options that could lessen the impact of the rule. The RFA generally defines a ''small entity'' as (1) a proprietary firm meeting the size standards of the Small Business Administration; (2) a nonprofit organization that is not dominant in its field; or (3) a small government jurisdiction with a population of less than 50,000 (states and individuals are not included in the definition of ''small entity''). HHS considers a rule to have a significant economic impact on a substantial number of small entities if at least 5 percent of small entities experience an impact of more than 3 percent of revenue. In making this determination, the impact of concern is any significant adverse economic impact on small entities. An agency may certify that a rule will not have a significant economic impact on a substantial number of small entities if the rule relieves regulatory burden, has no net burden, or otherwise has a positive economic effect on the small entities subject to the rule.

This action does not have a significant economic impact on a substantial number of small entities under the RFA. Therefore, the regulatory flexibility analysis provided for under the RFA is not required.

D. Unfunded Mandates Reform Act

Section 202(a) of the Unfunded Mandates Reform Act (UMRA) of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000

or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $183 million, using the 2023 implicit price deflator for the gross domestic product. We do not expect this final rule to result in expenditures that will exceed this amount. This action does not contain any unfunded mandate as described in UMRA, 2 U.S.C. 1531–1538, and does not significantly or uniquely affect small governments.

E. Executive Order 13132: Federalism

Executive Order 13132 establishes certain requirements that an agency must meet when it promulgates a rule that imposes substantial direct requirement costs on State and local governments or has federalism implications. HHS has determined that this rule does not contain policies that have substantial direct effects on the States, on the relationship between the Federal Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we have concluded that this final rule does not contain policies that have federalism implications as defined in the order and, consequently, a federalism summary impact statement is not required.

List of Subjects in 45 CFR Part 46

Human research subjects, Reporting and recordkeeping requirements, Research.

For the reasons set forth in the preamble, the Department of Health and Human Services amends 45 CFR part 46 as follows:

PART 46—PROTECTION OF HUMAN SUBJECTS

■ 1. The authority citation for part 46 continues to read as follows:

Authority: 5 U.S.C. 301; 42 U.S.C. 289(a); 42 U.S.C. 300v–1(b).

Subpart B—Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research

■ 2. Amend § 46.201 by revising paragraph (b) to read as follows:

§ 46.201 To what do these regulations apply?

* * * * *

(b) The *pre-2018 Requirements* means 45 CFR part 46, subpart A, as revised October 1, 2016. The *2018 Requirements* means 45 CFR part 46, subpart A, as revised October 1, 2018.

(1) For research subject to the pre-2018 Requirements and this subpart, the exemptions at § 46.101(b)(1) through (6) of the pre-2018 Requirements are applicable to this subpart.

(2) For research subject to the 2018 Requirements and this subpart, the exemptions at § 46.104(d)(1) through (8) of the 2018 Requirements may be applied.

* * * * *

■ 3. Amend § 46.202 by revising the introductory text and paragraph (h) to read as follows:

§ 46.202 Definitions.

The definitions in § 46.102 of the pre-2018 Requirements and the 2018 Requirements, as applicable, shall be applicable to this subpart as well. In addition, as used in this subpart:

* * * * *

(h) *Viable,* as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the **Federal Register** guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of the pre-2018 Requirements or the 2018 Requirements, as applicable, and subpart D of this part.

■ 4. Amend § 46.204 by revising paragraphs (d) and (e) to read as follows:

§ 46.204 Research involving pregnant women or fetuses.

* * * * *

(d) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of the pre-2018 Requirements or the 2018 Requirements, as applicable;

(e) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of the pre-2018 Requirements or the 2018 Requirements, as applicable, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;

* * * * *

■ 5. Amend § 46.205 by revising paragraphs (b)(2), (c)(5), and (d) to read as follows:

§ 46.205 Research involving neonates.

* * * * *

(b) * * *

(2) The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with the pre-2018 Requirements or the 2018 Requirements, as applicable, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

(c) * * *

(5) The legally effective informed consent of both parents of the neonate is obtained in accord with the pre-2018 Requirements or the 2018 Requirements, as applicable, except that the waiver and alteration provisions of § 46.116 of the pre-2018 Requirements or the 2018 Requirements do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph (c)(5).

(d) *Viable neonates.* A neonate, after delivery, that has been determined to be viable may be included in the research only to the extent permitted by and in accord with the requirements of the pre-2018 Requirements or the 2018 Requirements, as applicable, and subpart D of this part.

Subpart C—Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects

■ 6. Amend § 46.301 by revising paragraph (c) to read as follows:

§ 46.301 Applicability.

* * * * *

(c) The requirements of this subpart are in addition to those imposed under the other subparts in this part and

includes the pre-2018 Requirements and the 2018 Requirements, as applicable. The *pre-2018 Requirements* means 45 CFR part 46, subpart A, as revised October 1, 2016. The *2018 Requirements* means 45 CFR part 46, subpart A, as revised October 1, 2018.

■ 7. Amend § 46.304 by revising the introductory text to read as follows:

§ 46.304 Composition of Institutional Review Boards where prisoners are involved.

In addition to satisfying the requirements in § 46.107 of the pre-2018 Requirements or the 2018 Requirements, as applicable, an Institutional Review Board, carrying out responsibilities with respect to this subpart, shall also meet the following specific requirements:

* * * * *

■ 8. Amend § 46.306 by revising paragraphs (a) introductory text and (b) to read as follows:

§ 46.306 Permitted research involving prisoners.

(a) Nonexempt biomedical or behavioral research conducted or supported by DHHS may involve prisoners as subjects only if:

* * * * *

(b) Biomedical or behavioral research conducted or supported by DHHS shall not involve prisoners except as follows:

(1) For research subject to the pre-2018 Requirements and this subpart, except as provided in paragraph (a) of this section, biomedical or behavioral research conducted or supported by DHHS shall not involve prisoners as subjects.

(2) For research subject to the 2018 Requirements and this subpart, except as provided in paragraph (a) of this section or for research that is exempt pursuant to § 46.104(b)(2) and (d)(1) through (8) of the 2018 Requirements, biomedical or behavioral research conducted or supported by DHHS shall not involve prisoners as subjects.

Subpart D—Additional Protections for Children Involved as Subjects in Research

■ 9. Revise § 46.401 to read as follows:

§ 46.401 To what does this subpart apply?

(a) The *pre-2018 Requirements* means 45 CFR part 46, subpart A, as revised October 1, 2016. The *2018 Requirements* means 45 CFR part 46, subpart A, as revised October 1, 2018.

(b) This subpart applies to all research involving children as subjects, conducted or supported by the Department of Health and Human Services.

(1) This includes research conducted by Department employees, except that each head of an Operating Division of the Department may adopt such nonsubstantive, procedural modifications as may be appropriate from an administrative standpoint.

(2) It also includes research conducted or supported by the Department of Health and Human Services outside the United States, but in appropriate circumstances, the Secretary may, under § 46.101(i) of the pre-2018 Requirements or the 2018 Requirements, waive the applicability of some or all of the requirements of this subpart for research of this type.

(c) The application of the exemptions to this subpart is as follows:

(1) For research subject to the pre-2018 Requirements and this subpart, the exemptions at § 46.101(b)(1) and (b)(3) through (6) of the pre-2018 Requirements are applicable to this subpart. The exemption at § 46.101(b)(2) of the pre-2018 Requirements regarding educational tests also is applicable to this subpart. However, the exemption at § 46.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.

(2) For research subject to the 2018 Requirements and this subpart, the exemptions at § 46.104(d)(1), (4), (5), (6), (7), and (8) of the 2018 Requirements are applicable to this subpart. The exemptions at § 46.104(d)(2)(i) and (ii) of the 2018 Requirements may only apply to research subject to this subpart that involves educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed. The exemptions at § 46.104(d)(2)(iii) and (d)(3) of the 2018 Requirements may not be applied to research subject to this subpart.

(d) The exceptions, additions, and provisions for waiver as they appear in § 46.101(c) through (i) of the pre-2018 Requirements or the 2018 Requirements are applicable to this subpart.

■ 10. Amend § 46.402 by revising the introductory text to read as follows:

§ 46.402 Definitions.

The definitions in § 46.102 of the pre-2018 Requirements and the 2018 Requirements, as applicable, shall be applicable to this subpart as well. In addition, as used in this subpart:

* * * * *

■ 11. Amend § 46.408 by revising paragraphs (a) through (d) to read as follows:

§ 46.408 Requirements for permission by parents or guardians and for assent by children.

(a) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine 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. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB 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, 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 the pre-2018 Requirements or of the 2018 Requirements, as applicable.

(b) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine, in accordance with and to the extent that consent is required by § 46.116 of the pre-2018 Requirements or the 2018 Requirements, as applicable, that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under § 46.404 or § 46.405. Where research is covered by §§ 46.406 and 46.407 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.

(c) In addition to the provisions for waiver contained in § 46.116 of the pre-2018 Requirements or the 2018 Requirements, as applicable, if the IRB determines that a research protocol is

designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in § 46.116 of the pre-2018 Requirements or 2018 Requirements, as applicable, and paragraph (b) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with Federal, State, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

(d) Permission by parents or guardians shall be documented in accordance with and to the extent required by § 46.117 of the pre-2018 Requirements or the 2018 Requirements, as applicable.

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Xavier Beccera,

Secretary, U.S. Department of Health and Human Services.

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