NIH HRPP Policies Related to Enrollment of Pregnant Women, Participants Lacking Capacity to Provide Informed Consent, and Prisoners: Current Status and Recent Updates

Peg Sanders, RN, MSN, MA, CIP
OHSRP Division of Compliance & Training

OHSRP Education Series
September 1, 2020

Policies 400-404

Release Date: 8/24/2020

Effective Date: 9/11/2020

400: Research Involving Pregnant Women, Human Fetuses and Neonates

401: Research Involving Prisoners

402: Research Involving Children

403: Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation

404: Research Involving NIH Staff as Subjects

Policies 400-404

Three policies have additional specific federal regulatory requirements which apply to all NIH research

- 400: Research Involving Pregnant Women, Human Fetuses and Neonates (Subpart B)
- 401: Research Involving Prisoners (Subpart C)
- 402: Research Involving Children (Subpart D)

These 2 NIH policies do not have specific regulatory requirements beyond Subpart A, but investigators must comply with NIH policy requirements

- 403: Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation
- 404: Research Involving NIH Staff as Subjects

Caveat

This presentation is meant to be a brief overview of the key points of policies 400-404. It is not an intended as in-depth discussion of the policy and not all points raised in the policies will be discussed. For example, the approved posted policies address instances where FDA regulations may vary from requirements under the HHS regulations (45 CFR 46), which may not be included in this session.

Therefore, **it is important to review the complete policy documents** posted on the IRBO website.

Topics for this session

- Reasons for enrolling pregnant women in clinical trials
- Circumstances under which pregnant women may be enrolled in human subjects research (HSR)
- What to do when a woman becomes pregnant while participating in a protocol not originally reviewed under regulations governing research involving pregnant women
- Circumstances when prisoners may be enrolled in HSR and PI responsibilities if a participant becomes incarcerated while on study
- Identifying and determining the appropriateness of the legally authorized representative for potential participants who lack capacity to provide informed consent for participation in HSR
- Temporary versus permanent loss of capacity to provide informed consent for participation in HSR

Why Enroll Pregnant Women in Clinical Trials?

1978: The Belmont Report

One of the three basic ethical principles discussed in the Belmont Report is Justice

- Exclusion of pregnant women from clinical research may result in an unfair denial of benefits to the woman or fetus that are unavailable outside the research setting
- Women need safe and effective treatment during pregnancy with pharmacokinetic information to identify appropriate therapeutic doses during pregnancy and to quantify risks of fetal exposure

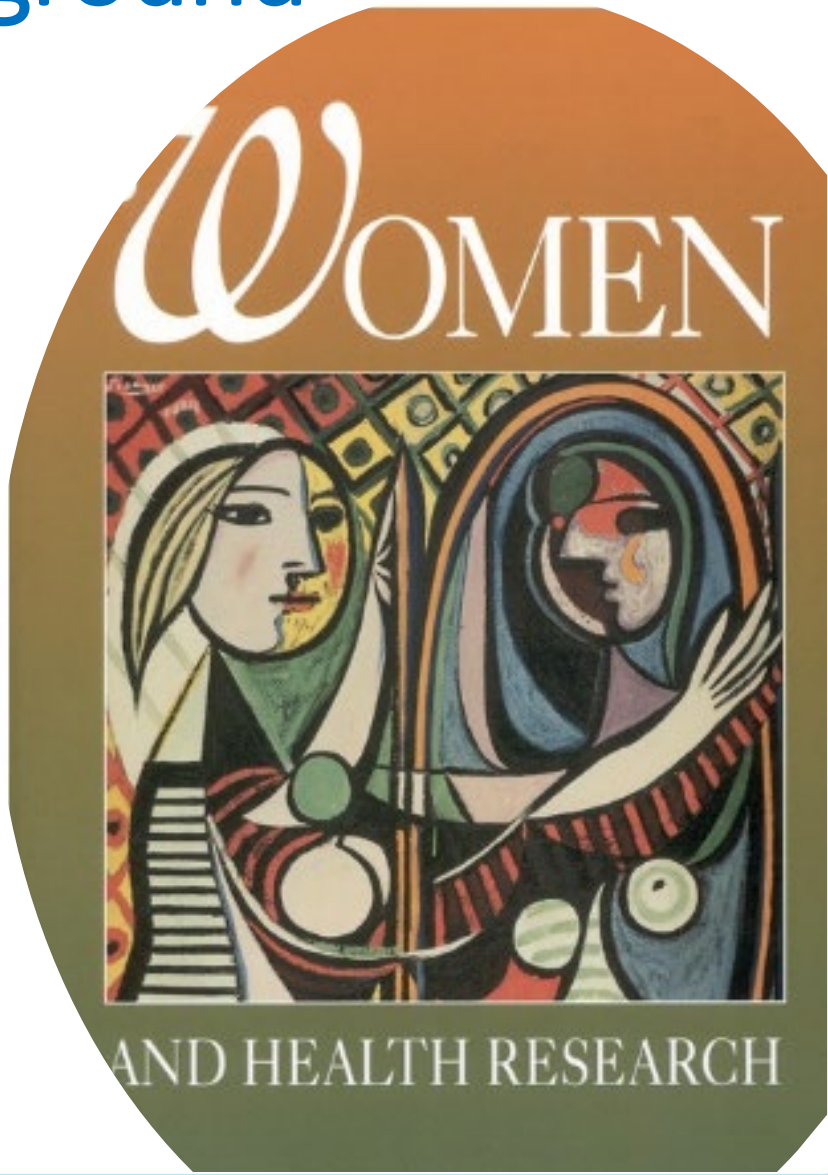
Historical Background

1975: HHS adopted regulations concerning pregnant women as research participants and included pregnant women as a "vulnerable population" deserving of special protection

- Regulations took a proscriptive approach: "No pregnant woman may be involved in research unless. . ."

Historical Background

1994: The Institute of Medicine (IOM) report, *Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies*, commented on the HHS regulations related to research with pregnant women (Subpart B) noting the following:

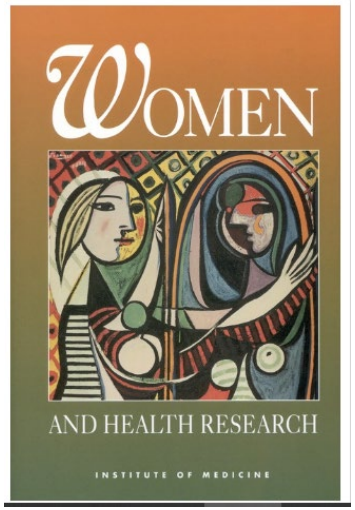


Historical Background

"Removal of pregnant women from the regulatory category of "vulnerable" potential participants would avoid any possible inference that pregnant women are less capable of making informed decisions by virtue of their pregnancy, than are other potential research participants."

The IOM:

- Urged that the prevailing presumption regarding the participation of pregnant women in clinical trials and other intervention studies be shifted from one of *exclusion* to one of *inclusion*



continued

Historical Background-IOM

The IOM:

- Unanimously endorsed the importance of recognizing in public policy and in the decisions made by IRBs and investigators, that pregnant women should be treated as competent adults capable of making their own decisions about participation in research
- Noted that it is the responsibility of investigators and IRBs to ensure that pregnant women are provided with adequate information about the risks and benefits to themselves, their pregnancies and their potential offspring

Historical Background-Regulatory Update

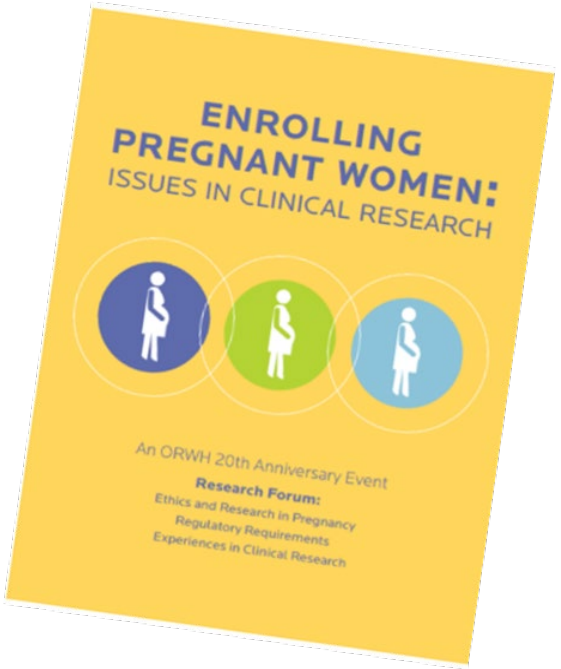
In 2001, Subpart B of 45 CFR 46 that addresses research with pregnant women, fetuses and neonates was modified to its current language

- Rather than the former proscriptive approach ("No pregnant woman may be involved in research unless. . ."), the 2001 regulations stated, "Pregnant women or fetuses may be involved in research if all the following conditions are met…."

Historical Background-Regulatory Update

In 2010, the NIH Office of Research on Women's Health (ORWH) convened a workshop, *Enrolling Pregnant Women: Issues in Clinical Research*

- As was the case in the IOM report, the ORWH emphasized the need to change the presumption of exclusion of pregnant women to one of inclusion
- Report reiterated that identifying pregnant women as a vulnerable population is a misnomer



Finally a Change! (But NOT to Subpart B)

Pre-2018 Common Rule:

"When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, *pregnant women*, mentally disabled persons, and economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects."[Emphasis added.]

Finally a Change! (But NOT to Subpart B)

The Revised Common Rule (the 2018 Requirements)*
The IRB should be particularly cognizant of the special problems of research ~~involving~~ that involves a category of subjects who are vulnerable ~~populations~~ to coercion or undue influence, such as children, prisoners, ~~pregnant women, mentally disabled persons~~ individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons

*Blue font is new wording

Subpart B: Enrollment of Pregnant Women, Fetuses or Neonates in Trials Supported or Conducted by HHS

Must meet all 10 conditions:

1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted ***and*** provide data for assessing potential risks to pregnant women and fetuses
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means

(continued)

45 CFR 46 (Subpart B): Enrollment of Pregnant Women or Fetuses in Trials Supported or Conducted by HHS

(continued)

3. Any risk is the least possible for achieving the objectives of the research
4. 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, [and] her consent is obtained in accord with the informed consent provisions of Subpart A

(continued)

45 CFR 46 (Subpart B): Enrollment of Pregnant Women or Fetuses in Trials Supported/Conducted by HHS

(continued)

5. 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 45 CFR 46, subpart A, 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
6. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate

(continued)

45 CFR 46 (Subpart B): Enrollment of Pregnant Women or Fetuses in Trials Supported or Conducted by HHS

(continued)

7. For children as defined in §46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D "*Additional Protections for Children Involved as Subjects in Research*"
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy
10. Individuals engaged in the research will have no part in determining the viability of a neonate

Can the Protocol be Approved by the IRB Under Subpart B?

- Does the research have the prospect of direct benefit to the mother and/or to the fetus?*
- Is the research no greater than minimal risk or does the research have a greater than minimal risk to the mother and/or the fetus?**

*Clinical Care is not considered a benefit of research

**Unlike HHS Subpart D regulations (research involving children), regulations for research involving pregnant women do not include consideration of research that represents a "minor increase over minimal risk."

When Research Involves Pregnant Women and Has Prospect of Direct Benefit

Research that has the prospect of direct benefit (DB) to the pregnant woman or the fetus is generally approvable even if greater than minimal risk when the other Subpart B requirements are also met

- Consent of the pregnant woman alone is sufficient in this case unless the research has the prospect of DB *only* for the fetus
- If the DB is *only* for the fetus, the consent of both the pregnant woman and the father is required unless the father is unable to provide consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest

When Research Involves Pregnant Women and There is NO Prospect of Direct Benefit

- When there is no prospect of DB to the mother or fetus, the IRB may only approve the research if the risk to the fetus is no greater than minimal, and the "*purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.*"
- For such a protocol, in order to gain the important biomedical knowledge that is the intent of the protocol, enrollment of pregnant women will be needed
- The PI must provide a justification in the protocol and the IRB must subsequently determine that the aim of gaining such knowledge cannot be achieved by enrolling only nonpregnant participants

Research > Minimal Risk with No Prospect of Direct Benefit

- Research involving pregnant women that is greater than minimal risk with no prospect of direct benefit to the pregnant woman or the fetus cannot be approved by the IRB

- For studies that do not enroll pregnant women and that are greater than minimal risk, the protocol should address what will happen if participants become pregnant during the course of the study

Research > Minimal Risk with No Prospect of Direct Benefit

- For treatment studies:
  - The protocol should indicate if pregnancy is an off-treatment criterion
  - If the participant's partner becomes pregnant and the intent is to continue to collect outcome data, the IRB must review and approve a consent form allows the partner to provide consent to have pregnancy outcome data collected, and the protocol should be revised to include a pregnant partner cohort
- For FDA regulated research, pregnancy outcome should be collected and reported

What if a Participant Becomes Pregnant While on a Study with No Prospect of DB for the Pregnant Woman or Fetus?

If the protocol indicates that the participant will remain on study, the IRB should make a Subpart B determination based on the PI's plan as documented in the protocol to include the following information:

- While pregnant, neither research interventions nor research tests or procedures that are greater than minimal risk will occur (because per the regulations, research with pregnant women that is > minimal risk is not approvable unless there is potential for direct benefit to the pregnant woman or fetus) **and**
- Explain the justification in the protocol for why the biomedical knowledge to be gained cannot be obtained from nonpregnant women

What if a Participant Becomes Pregnant While on a Study with No Prospect of DB for the Pregnant Woman or Fetus?

Example:

- In a natural history study of individuals with Lupus, the PI explains that the only way to learn about critical biological differences between pregnant and nonpregnant participants with this disease is to continue to follow pregnant women on study
- While pregnant, no research interventions, tests or procedures that are > minimal risk will be performed on the pregnant woman

In this case, continued participation of a woman who becomes pregnant can be approved by the IRB under the Subpart B regulations

Policy 400: Research Involving Pregnant Women, Human Fetuses and Neonates: Key Points

- Research involving pregnant women, human fetuses or neonates may not begin prior to IRB approval of the research
- When conducting research involving pregnant women, human fetuses or neonates, Principal Investigators (PIs) must:
  - Ensure that the protocol and the research comply both with the basic protections for human subjects specified at 45 CFR 46 Subpart A, and the additional requirements of 45 CFR 46 Subpart B
  - In addition, if this research also involves pregnant children (Subpart D), or pregnant prisoners (Subpart C), the other subparts of 45 CFR 46 also apply

(continued)

Policy 400: Key Points (continued)

- When conducting FDA-regulated research involving pregnant women, human fetuses or neonates, Principal Investigators (PIs) must also:
  - Follow all applicable FDA requirements
  - Note that the exception(s) from informed consent requirements for emergency research may not be applied to research that is also subject to Subpart B.

Policy 400: Additional Points

- Regulations under Subpart B:
  - The regulations also apply to research both with viable neonates and those of uncertain viability, and to fetal tissue use
  - Exempt research may proceed so long as it meets the requirements of 45 CFR 46.104(d) (2018 CR) or 45 CFR 46.101(b) (pre-2018 CR), as applicable
  - Investigators should also be mindful of applicable state or local law, including Tribal law

Policy 400: Other NIH Policies

- When conducting research involving pregnant women, research with human fetuses or human fetal tissue, Principal Investigators (PIs) should be aware that other regulations and NIH policies apply
- These other requirements, including prohibited research, are not covered in Policy 400. Therefore, PIs should also review the *OIR Sourcebook: Special Research Considerations* when conducting research involving:
  - human fetal tissue
  - human embryonic stem cells (hESCs)
  - human induced pluripotent stem cells (IPSCs), or
  - adult stem cells

Policy 401: Research Involving Prisoners

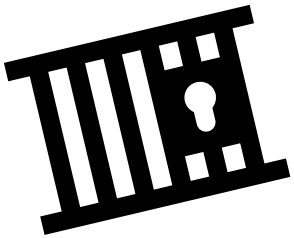
This policy describes the NIH policy for research involving prisoners, including when an NIH subject unexpectedly become incarcerated

- Research involving prisoners may not begin prior to approval of the research by both the IRB **and** the HHS Office of Human Research Protections (OHRP)
- When reviewing prisoner research, the composition of the IRB must include at least one prisoner representative
- When an NIH subject becomes incarcerated, research may not continue until IRB approval and OHRP approval is obtained (with one limited exception)
- In order to obtain OHRP approval, NIH must certify to the HHS Secretary that the IRB has approved the research consistent with Subpart C

Policy 401: Research Involving Prisoners

Prisoner– Any individual who is:

- Involuntarily confined or detained (ability to leave the institution is restricted) in a penal institution (e.g., prison) having been sentenced to such an institution under a criminal or civil statute
- Detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution
- Detained pending arraignment, trial or sentencing



(45 CFR 46.303(c))

Policy 401: Specified Categories of Research Involving Prisoners

- Non-exempt human subjects research involving prisoners must meet one of the 4 categories specified at 45 CFR 46.306
- The first 2 categories include research that must present **no more than minimal risk** and no more than inconvenience to the subjects and that relate to the study of:
  - Possible causes, effects, and processes of incarceration, and of criminal behavior

OR

  - Prisons as institutional structures or of prisoners as incarcerated persons

(continued)

Policy 401: Specified Categories of Research Involving Prisoners (continued)

- Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction and sexual assaults)
  - Studies in this category may proceed only after the Secretary has consulted with appropriate experts including experts in penology medicine and ethics and published notice in the Federal Register of the intent to approve such research

(continued)

Policy 401: Specified Categories of Research Involving Prisoners

- Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject
  - In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology medicine and ethics and published notice in the Federal Register of the intent to approve such research

Policy 401: Exempt Research

- Exempt research involving prisoners is not allowed in research approved under the pre-2018 Common Rule (CR)

- Under the 2018 (CR) research involving prisoners cannot be deemed exempt under 45 CFR 46.104(b), except for research aimed at involving a broader subject population that only incidentally includes prisoners. (45 CFR 46.104(b)(2))

Exempt Research That Only Incidentally Includes Prisoners- Examples

Examples provided in the preamble to the 2018 CR

#1: Exempt secondary research use of information or biospecimens from subjects who are prisoners, if that analysis is not seeking to examine prisoners as a population and only incidentally includes prisoners in the broader study

- Such inclusion would previously have required IRB review under Subpart C, including review by an IRB prisoner representative, followed by certification to and authorization by OHRP

(continued)

Exempt Research That Only Incidentally Includes Prisoners- Examples (continued)

#2: A subject could continue participation in exempt research if they became a prisoner during the course of an exempt study, assuming the study was aimed at a broad nonprisoner population, without the need for subpart C IRB review and certification to OHRP

- Example: an exempt study that recruited subjects from a local community center to participate in a comparison of HIV educational materials would continue to be exempt and would not trigger the need for review under subpart C, even if some of the subjects became prisoners after enrollment

Policy 401: Key Investigator Responsibilities

- When investigators anticipate the participation of prisoners on the research, this intent must be indicated in the protocol and any safeguards for prisoner-subjects must be described
- If a subject becomes incarcerated and the IRB and OHRP have not approved prisoner participation, the IRB must be notified ASAP, and all research interventions must cease until IRB and OHRP approval have been obtained. . . However. . .

(continued)

Policy 401: Key Investigator Responsibilities

(continued)

- However, in special circumstances if the PI believes it is in the best interest of the subject to remain on study, the PI must promptly notify IRBO and obtain permission from the IRB Chair to continue activities needed to ensure the safety and welfare of the now prisoner-subject until the IRB and OHRP approval is obtained
  - The Investigator must submit an amendment requesting permission for the prisoner-subject to remain on study and include any additional safeguards and changes to procedures (if any) needed for the now-prisoner-subject to remain on the research as consistent with this policy
- If the IRB disapproves continued participation of the prisoner-subject, the subject must be taken off study

Policy 402: Children in Research

Please review the October 2019 OHSRP Education Series session ***Research with Children-An Ethical and IRB Perspective*** presented by Dr. Green (Available on the OHSRP Compliance and Training webpage section- Presentation Archives)

Policy 402: Children in Research

- **Children** – Are 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. (45 CFR 46.402(a))
- For the purpose of consent when research is conducted at an **NIH site**, an adult is anyone 18 years or older
- Children who are legally emancipated are considered adults and the requirements of Policy 402 do not apply: Investigators **MUST** consult OHSRP who will contact OGC for guidance before considering a minor to be emancipated

Policy 402: Key Points & Investigator Responsibilities

- Research involving children may not begin prior to IRB approval of the research
- Investigators must ensure that the protocol and research comply with the basic protections for human subjects specified at 45 CFR 46 Subpart A and the additional requirements of 45 CFR 46 Subpart D
    - When research involves pregnant children (Subpart B), or child prisoners (Subpart C), the other subparts also apply
- For FDA-regulated research, investigators must also comply with all applicable FDA requirements

Policy 402: Subpart D Risk: Benefit Categories

46.404/50.51	research not involving > minimal risk
46.405/50.52	> minimal risk but with prospect of direct benefit (DB) to the individual subjects
46.406/50.53	no more than a minor increase over minimal risk and no PDB but likely to yield generalizable knowledge about the subject's disorder or condition
46.407/50.54	not otherwise approvable

Policy 402: Parental Permission*

No child may be enrolled, screened, or have research procedures initiated unless parental permission and child assent are obtained consistent with the Common Rule and, as applicable, FDA regulations

- Joint custody requires both parents' permission
- Both parents must give their permission for research covered under §46.406 and 46.407 unless one parent is deceased, unknown, or not reasonably available
  - ➢ Consult with the OHSRP, when questions arise about what constitutes being "not reasonably available."

* Note that federal regulations require additional steps if wards of the state will be enrolled. Consult policy 402 & OHSRP for additional information

Policy 402: Child Assent

Assent is the affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

- When the IRB determines that assent is required it determines whether and how assent must be documented
- The assent process may be either verbal or written
- The IRB may only waive assent of the child if it determines that specific conditions are met*

* 45 CFR 46.116, and 45 CFR 46.408 and, as applicable, 21 CFR 50.55

Policy 403: Research With Adults Who Lack Decision-making Capacity to Consent to Research Participation

This policy:

- Describes additional safeguards and considerations for research involving these participants
- Describes the circumstances under which the NIH IRP permits a Legally Authorized Representative (LAR) to provide consent for participants who lack decision-making capacity to consent to, or continue participation in research

This policy applies to:

- All research overseen by the NIH IRB
  - UNLESS research is conducted at a non-NIH site, when state law or local policy may supersede the hierarchy used to determine the LAR at that site
- NIH investigators conducting research at NIH sites, irrespective of whether NIH or another IRB is the Reviewing IRB

Policy 403:Research With Adults Who Lack Decision-making Capacity to Consent to Research Participation- Key Points

- Subjects without capacity cannot enroll or continue in research (except as described later) without IRB approval that grants permission for those subjects to participate

- For all research requiring informed consent and approved in advance by the IRB to involve subjects without capacity, legally effective informed consent must be obtained from the LAR prior to the initiation of any research activities, (except as described later)

Policy 403:Research With Adults Who Lack Decision-making Capacity to Consent to Research Participation-Protocol

- If the research will or may include such subjects, the protocol must describe:
  - A compelling justification for their inclusion
  - Any safeguards that will be in place
  - The process for assessing decisional capacity
  - The process for identifying the LAR
  - The process for determining the validity of the LAR

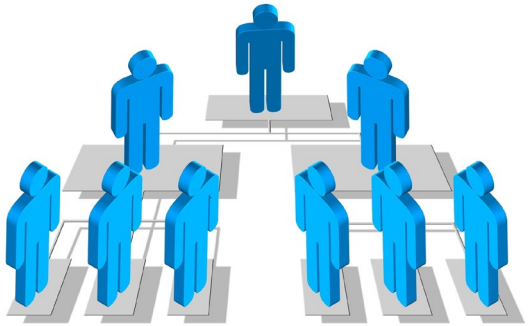
Policy 403: Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation

Category	Risk: Benefit
Category A	Minimal risk
Category B	> Minimal risk but with a prospect of direct benefit to the participant
Category C	> minimal risk without a prospect of direct benefit, if the risk is no more than a minor increase over minimal, and it does not adversely effect the rights, safety or welfare of the subject
Category D	> minimal risk with no prospect of direct benefit if it has undergone additional institutional review and approval by the NIH Institutional Official

Policy 403: LAR Hierarchy

Legally Authorized Representative (LAR) Hierarchy

- Court appointed guardian
- Appointed Durable Power of Attorney (DPA) for Healthcare
- If subject does not have either of the above but understands the DPA process, they may appoint at DPA
- If the above LARs do not apply, next of kin applies (in this order, and for Categories A, B and C **only**)
  - Spouse or domestic partner
  - Adult child
  - Parent
  - Adult Sibling
  - Other Relative



Temporary vs. Permanent Loss of Capacity *After* Enrollment

- When a subject with capacity who provided initial consent for research participation has a subsequent **temporary** loss of capacity (e.g., they are expected to regain capacity), reconsent of the subject by the LAR is **not** required for the subject's continued participation in the research
- If the research has not been approved by the IRB for inclusion of subjects without capacity, and a subject who had capacity previously provided consent for themselves subsequently loses capacity **permanently, AND**
- The research involves continued interactions or interventions with the subject (excluding only data or specimen analysis),

- The NIH PI/Lead Site Investigator **must** obtain IRB approval, and reconsent from the LAR in order for the subject without capacity to remain on the research

Policy 404: Research Involving NIH Staff

Key Points

- NIH staff and immediate family members of the study team are generally permitted to participate in NIH research, but must comply with NIH Policy including:
  - Prohibitions or restrictions by the staff member's Institute or Center
  - NIH compensation requirements
  - NIH leave requirements (See NIH Manual Chapter: 2300-630-3)
- NIH staff interested in participating in NIH Research should review the NIH Frequently Asked Questions (FAQs) for Staff Who are Considering Participation in NIH Research (This information has been updated since the prior policy regarding enrolling NIH staff as participants)

Policy 404: Research Involving NIH Staff- Prospect of DB vs. No Prospect of DB

- For research with **prospect of DB**, NIH PIs are not required to obtain IRB approval for enrollment of NIH staff or the immediate family members of the study team
- When research offers **no prospect of direct benefit**, the IRB must prospectively approve inclusion of this group, and the protocol must describe:
  - Whether staff or family members will be included
  - Safeguards for this population
  - Recruitment plan
    - Solicitation of subordinates should not be direct
    - Recruitment materials may be displayed only where public announcements are permitted

Summary Policies 400-404 Effective Date: 9/11/2020

400: Research Involving Pregnant Women, Human Fetuses and Neonates
401: Research Involving Prisoners
402: Research Involving Children
403: Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation
404: Research Involving NIH Staff as Subjects

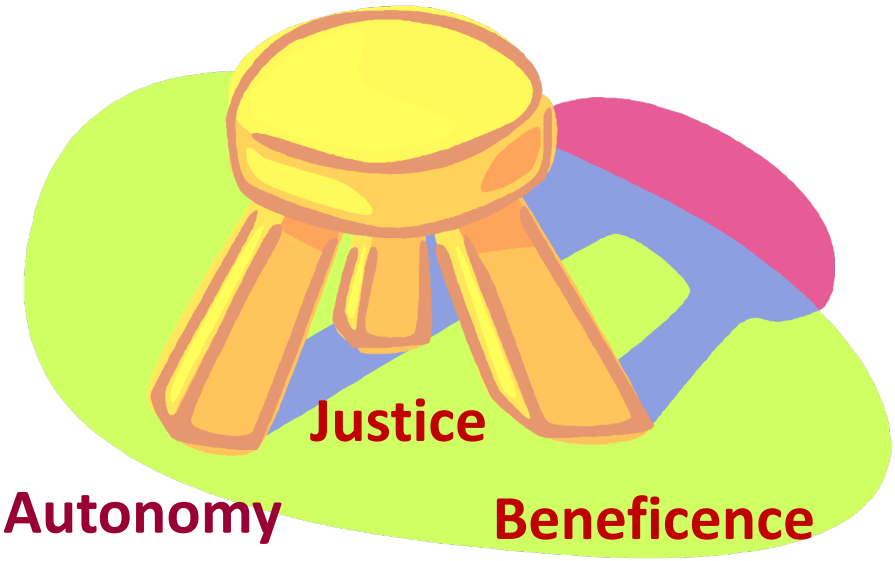
- This presentation was intended as a brief overview and a summary of changes
- **Please review the complete policies on the policy webpage on the OHSRP website**

Special thanks to

Jonathan Green, OHSRP Director
and
Heather Bridge and Chris Witwer
OHSRP Policy & Accreditation

for slides and guidance related to the new HRPP policies covering these topics

Thank You



IRB@od.nih.gov

OHSRP: (301) 402-3713

References and Links

NIH POLICIES

400: Research Involving Pregnant Women, Human Fetuses and Neonates

401: Research Involving Prisoners

402: Research Involving Children

403: Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation

404: Research Involving NIH Staff as Subjects

GENERAL

Belmont Report (1978)

45 CFR 46 (2018 Requirements)

RESEARCH INVOLVING PREGNANT WOMEN, HUMAN FETUSES AND NEONATES

Institute of Medicine. Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies, Volume 1. Washington, DC: The National Academies Press. 1994 https://doi.org/10.17226/2304 or via PubMed here

References and Links

Foulkes MA, Grady C, Spong C. Bates A, Clayton JA. Clinical research enrolling pregnant women: a workshop summary. *J Womens Health* 2011;20: 1429-1432. DOI: https://doi.org/10.1089/jwh.2011.3118

Lyerly AD, Little MO, Faden RR. Reframing the framework: toward fair inclusion of pregnant women as participants in research. *Am J Bioeth* 2011; 11(5): 50–68. DOI: https://doi.org/10.1080/15265161.2011.560353

NIH Office of Research on Women's Health, *Enrolling Pregnant Women: Issues in Clinical Research* (2010)

Task Force on Research Specific to Pregnant Women and Lactating Women, Report to Secretary, Health and Human Services Congress (September 2018)

RESEARCH INVOLVING PRISONERS

OHRP Guidance- Prisoner Involvement in Research (2003)

OHRP Prisoner Research FAQs

RESEARCH INVOLVING CHILDREN

OHRP Research with Children FAQs

OHRP Special Protections for Children as Research Subjects

References and Links

Children as Research Subjects and the HHS "407" Process

RESEARCH WITH SUBJECTS WHO LACK CAPACITY TO CONSENT TO RESEARCH

MAS 19-1 Determining Legally Authorized Representatives for Adult Patients Who Are Unable to Provide Informed Consent for Clinical Care or Re-Admission (26 March 2020)

Clinical Center (CC) Bioethics Consultation Service, including the Ability to Consent Assessment Team (ACAT)

NIMH Human Subjects Protection Unit

RESEARCH WITH NIH STAFF AS SUBJECTS

NIH Policy 2300-630-3 - Leave Policy for NIH Employees Participating in NIH Medical Research Studies