

**OFFICE OF RESEARCH AND DEVELOPMENT
VETERANS HEALTH ADMINISTRATION**

**GUIDANCE ON COLLECTING DATA ON PREGNANCY AND OUTCOMES OF PREGNANCY
FROM VA RESEARCH SUBJECTS AND PREGNANT PARTNERS
OF VA RESEARCH SUBJECTS FOR SAFETY MONITORING**

Date: April 18, 2014

This guidance supersedes ORD's June 10, 2009 guidance entitled: [Pregnancy and VA Research: Guidance on Collecting Data on Pregnancy and Outcomes of Pregnancy in VA Research Subjects and Pregnant Partners of VA Research Subjects](#)

For questions on the content of this guidance, email the VHA Office of Research and Development at VHACOORDResponseTeam@va.gov.

SCOPE: The Veterans Health Administration (VHA) Office of Research and Development (ORD) has received questions from industry and Investigators on collecting information about pregnancy progress and pregnancy outcomes for safety monitoring when pregnancy is not the research focus. This document describes ORD's current position on collecting data on pregnancy from or about female subjects who become pregnant during a VA research study, collecting data on pregnancy from or about pregnant partners of male subjects in VA research, IRB review considerations, and obtaining a waiver from the VHA Chief Research and Development Officer (CRADO) when information is collected about the newborn infant for safety monitoring in VA research. ORD offers guidance on the following topics:

1. Collecting pregnancy information from or about female subjects who become pregnant while participating in VA research.
2. Collecting pregnancy information from or about female partners of male subjects participating in VA research.
3. Collecting information about the newborn infant of female subjects or female partners of male subjects in VA research.
4. IRB considerations when collecting data on pregnancy progress and outcomes of pregnancy in VA research.
5. Applying the criteria for obtaining a waiver from the Chief Research and Development Officer (CRADO) when collection of information about the newborn infant for safety monitoring is proposed in VA research.
6. Submitting a waiver request to ORD for research involving children when collection of information about the newborn infant for safety monitoring is proposed in VA research.

BACKGROUND: The Department of Veterans Affairs (VA) is one of the seventeen Federal departments and agencies that have agreed to follow the Federal Policy for the Protection of Human Subjects, commonly referred to as the "Common Rule". VA's codification of the Common Rule ([45 CFR Part 46 Subpart A](#)) is [38 CFR Part 16](#). Common Rule regulations at [38 CFR §16.102\(e\)](#) define research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. A human

subject is defined in [38 CFR §16.102\(f\)](#) as a living individual about whom an investigator (whether professional or student) conducting research obtains

- (1) Data through intervention or interaction with the individual, or
- (2) Identifiable private information.

If an activity involving living individuals meets the above definition, it is human subjects research. Unless otherwise required by the department or agency heads or exempt from Common Rule regulations described in [38 CFR §16.101\(b\)](#), the activity must be reviewed and approved by an Institutional Review Board (IRB) holding an Federalwide Assurance (FWA). Specific VHA requirements regarding Assurances for VA facilities are described in [VHA Handbook 1058.03](#): Assurance of Protection for Human Subjects in Research. Specific VHA requirements regarding IRB composition are described in [VHA Handbook 1200.05](#).

Pregnant women, women of child-bearing potential, and children may be entered into VA research if VHA requirements are met as described in [VHA Handbook 1200.05](#). If the research is also subject to FDA regulations, FDA regulations would also apply.

- (1) If the research activity involves women who are pregnant at the time they are entered into a VA study, VHA requirements must be met as described in [VHA Handbook 1200.05](#).
- (2) Women of child-bearing potential may be entered into VA research. However, women of child-bearing potential may not be entered into VA studies involving the use of FDA Categories for Drug Use in Pregnancy's Category D or Category X drugs unless a waiver is obtained from the CRADO.
- (3) Children are defined in [38 CFR §16.102\(a\)](#) as persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. A waiver must be obtained from the CRADO if children are entered into VA research.

1. COLLECTING PREGNANCY INFORMATION FROM OR ABOUT FEMALE SUBJECTS WHO BECOME PREGNANT WHILE PARTICIPATING IN VA RESEARCH.

In the majority of studies conducted in the VA, pregnancy is not the focus of the research. In many research studies, particularly clinical investigations involving interventions with drugs or medical devices, the Investigator or Sponsor may want to obtain information about the progress of a pregnancy when a female subject becomes pregnant while participating in the research. In the majority of these studies, the female subject no longer receives the clinical intervention described in the IRB-approved protocol once the Investigator is made aware of the female subject's pregnancy, but monitoring of the pregnancy for safety is requested or recommended by the sponsor of the study.

If a female subject who becomes pregnant is withdrawn from the research intervention portion of the study by a VA Investigator, collection of any additional data by the Investigator from the female subject or obtaining identifiable private information about her after she is withdrawn would constitute human subject research activities. A subject can be withdrawn solely from receiving the research intervention, remain in the study, and the Investigator would be allowed to continue data collection and other follow-up activities if the data collection and follow-up activities are described in the protocol and informed consent approved by the IRB, the HIPAA authorization, and the subject does not revoke that portion of the informed consent and HIPAA authorization. Written authorization requirements for use and disclosure of protected health

information must be met as described in VHA Handbook 1605.01 (“Privacy and Release of Information”) and VHA Handbook 1200.05. When a subject is withdrawn from all aspects of the study by the subject’s or Investigator’s choice, the subject’s participation in that study ends and additional data and identifiable private information about that subject must not be collected or obtained.

2. COLLECTING PREGNANCY INFORMATION FROM OR ABOUT FEMALE PARTNERS OF MALE SUBJECTS PARTICIPATING IN VA RESEARCH.

The majority of studies conducted in VA involve recruitment of male subjects. In research studies, particularly clinical investigations, the investigator may want to obtain information about the progress of a pregnancy if the female partner of a male Veteran subject becomes pregnant during the interval when the male subject is participating in a VA research study.

VA applies the Common Rule to all human subjects research which is approved as VA research. Collection of data in the research through intervention or interaction with the female partner or obtaining identifiable private information about the female partner constitutes human subjects research. The female partner becomes a human subject according to the Common Rule and is given protections as a human subject as required in 38 CFR Part 16 and VHA Handbook 1200.05. In such cases, the IRB-approved protocol must include provisions for collecting information from the pregnant female partner of the male subject enrolled into the research. Informed consent as approved by the IRB must be obtained by the Investigator from the female partner prior to the collection of any data by the Investigator from the female partner or obtaining identifiable private information about her unless the IRB has waived informed consent in accordance with criteria described in 38 CFR § 16.116(c) or 38 CFR §16.116(d). Written authorization for use and disclosure of protected health information must be obtained from the female partner as described in VHA Handbook 1605.01: Privacy and Release of Information.

3. COLLECTING INFORMATION ABOUT THE NEWBORN INFANT IN VA RESEARCH.

When a VA Investigator conducting human subjects research collects identifiable private information about the newborn infant of subject enrolled in VA research, the infant is a human subject, and the Investigator is conducting VA research involving children. The IRB-approved protocol must include provisions for collecting information about the newborn infant. Informed consent as approved by the IRB and obtained from the adult subject(s) must contain sufficient information about the data to be obtained for the newborn. Written authorization for use and disclosure of protected health information must be obtained as described in VHA Handbook 1605.01: Privacy and Release of Information. A waiver must be obtained from the CRADO prior to collection of data about the newborn infant following IRB review and approval in accordance with VHA Handbook 1200.05 requirements.

4. IRB CONSIDERATIONS WHEN COLLECTING DATA ON PREGNANCY PROGRESS AND OUTCOMES OF PREGNANCY IN VA RESEARCH

When VA research involves collecting data from or about pregnancy and pregnancy outcomes, the IRB must still ensure that subjects’ ethical rights are protected. VHA follows 45 CFR §46.204 requirements for including pregnant women in VA research. IRBs are not expected or

required to review studies using the criteria described in 45 CFR §46.204 simply because the study involves women of child-bearing potential. However, once the reviewing IRB is made aware that information about a subject's pregnancy is being obtained in a VA study, the reviewing IRB must ensure that:

- (1) the IRB-approved protocol addresses the data collection procedures for obtaining data about the progress of the pregnancy and pregnancy outcomes (live birth with or without birth defects, stillborn, or aborted fetus);
- (2) informed consent has been obtained from the adult subject to obtain information about the progress of the pregnancy and pregnancy outcomes unless the IRB has waived informed consent in accordance with criteria described in [38 CFR § 16.116\(c\) or 38 CFR §16.116\(d\)](#);
- (3) the data collection involving the pregnant female subject described in the IRB-approved protocol meets the conditions described in [45 CFR §46.204](#); and
- (4) the data collection involving the newborn infant described in the IRB-approved protocol meets [45 CFR 46 Subpart D](#) requirements for research activities not involving greater than minimal risk ([45 CFR §46.404](#)).

5. APPLYING THE CRITERIA FOR OBTAINING A WAIVER FROM THE CHIEF RESEARCH AND DEVELOPMENT OFFICER (CRADO) WHEN COLLECTION OF INFORMATION ABOUT THE NEWBORN INFANT FOR SAFETY MONITORING IS PROPOSED IN VA RESEARCH.

When identifiable private information is collected about a newborn infant in VA research, the newborn infant is a research subject, and a waiver must be obtained from the CRADO. The criteria for waiver as described in VHA Handbook 1200.05 include the following:

- (1) The study represents no greater than minimal risk as determined by the IRB.
- (2) The study meets all requirements in [45 CFR 46, Subpart D](#), Additional Protections for Children Involved as Subjects in Research, Sections [46.401](#) through [46.404](#), and [46.408](#).
- (3) The IRB reviewing the study has appropriate membership to represent children's interests and pediatric expertise.
- (4) The IRB reviewing the study has specific SOPs regarding children in research.
- (5) The VA Facility Director certifies that the facility is able to respond to pediatric emergencies if the study includes interactions with children at the VA facility.

In studies requesting data collection on newborn infants for safety monitoring when children are not a primary subject population, the criteria requiring the VA Facility Director to certify that the VA facility is able to respond to pediatric emergencies is not applicable when there are no interactions between the VA Investigator and newborn at the VA facility.

If the research activities involving the newborn infant consist of data collection through review of records (no intervention or interaction with the infant), the criteria requiring the VA facility Director to confirm that a non-VA sponsor has procured appropriate liability insurance is also not applicable because liability insurance is not needed for the data collection activity.

The waiver for VA research involving children does not have to be obtained until the research involves children. There is no requirement to obtain a waiver for research involving children in VA research if a protocol includes women of child-bearing potential unless an event occurs in which data about the newborn infant from a female subject or the pregnant partner of a male VA subject will be collected in VA research. If the VA Investigator wishes to obtain a waiver for

research involving children following initial IRB approval as a “just-in-case” scenario, ORD will process those waiver requests as described in the following section.

6. SUBMITTING A WAIVER REQUEST TO ORD FOR RESEARCH INVOLVING CHILDREN WHEN COLLECTION OF INFORMATION ABOUT THE NEWBORN INFANT FOR SAFETY MONITORING IS PROPOSED IN VA RESEARCH.

VHA Handbook 1200.05 lists the following information as submission requirements for waiver requests when VA research includes children as research subjects:

- A. A cover letter signed by the VA facility Director that contains the following information:
 - (1) Certification by the VA facility Director that the facility is able to respond to pediatric emergencies if the study includes an interaction with children at the VA facility.
 - (2) Any additional safeguards that have been incorporated into the clinical site where children will be studied.
 - (3) Information on the study’s funding source and on liability coverage if the sponsor is not VA.
 - (4) Certification that the IRB has determined the study to be of no greater than minimal risk and has approved the study.
 - (5) A statement that the required elements of 45 CFR 46 Subpart D have been met.
 - (6) A description of the relevance to Veterans’ health of both the study and the inclusion of children in the study.

- B. A copy of the study protocol, the informed consent form, the assent document, and HIPAA authorization. The informed consent document signed by the parent or guardian is the vehicle for parent or guardian permission. Provisions for permission by parents or guardians must be documented in accordance with, and to the extent required by 38 CFR 16.117.

- C. Minutes of the IRB meeting approving the study. The IRB minutes need to reflect the discussion regarding level of risk, the informed consent and assent forms, the investigators’ qualifications to conduct research involving children, and any additional safeguards incorporated into the protocol.

- D. If the study involves biological specimens or data collected from children, in addition to the preceding requirements, the following must be submitted:
 - (1) A discussion of how the biological specimens or data were, or will be, obtained and under what consents or authorization.
 - (2) If the biological specimens or data were, or will be, collected for research purposes, the IRB approval, the informed consent form, and the HIPAA authorization for the research.
 - (3) If biological specimens or data were, or will be, collected from an international site, a waiver from the CRADO for international research.
 - (4) Plans for future use of biological specimens or data.

Some of the information described in VHA Handbook 1200.05 requires clarification for studies requesting data collection about newborn infants for safety monitoring when children are not a primary subject population:

- (1) There is no need for the VA Facility Director to certify in a cover letter to ORD that the VA facility is able to respond to pediatric emergencies when there are no interactions with children at the VA facility.
- (2) When record review is the activity involved in collecting data about the newborn infants for safety monitoring, there is also no need to address additional safeguards incorporated into the clinical site where children will be studied because VA is not a clinical site.
- (3) Although ORD does require the VA Facility Director's cover letter to address the funding source if the study is funded, information regarding liability coverage is not applicable for non-VA sponsored studies when the activity involves record review.
- (4) When information about the newborn infant is being obtained for safety monitoring for studies where pregnant women are not the target study population, a description of the relevance to Veterans' health of both the study and the inclusion of children in the study should contain statements clarifying that children are not the primary study population, pregnancy is not the primary research study focus, and information is being obtained about the newborn for safety monitoring of either a female subject who became pregnant or a female partner of a male subject who became pregnant or of the infant.
- (5) There will be no assent document if information is being obtained about a newborn infant.

When all documents are ready for submission, send three copies of the documents by hard copy to the address listed below.

Chief Research and Development Officer
VHA Office of Research and Development (10P9)
810 Vermont Avenue, NW
Washington, DC 20420

REGULATORY AND VHA POLICY REFERENCES:

[VHA Handbook 1058.03: Assurance of Protection for Human Subjects in Research](#)

[VHA Handbook 1200.05: Requirements for the Protection of Human Subjects in Research](#)

[VHA Handbook 1605.01: Privacy and Release of Information](#)

[38 CFR, Chapter 1 Department of Veterans Affairs, Part 16, Protection of Human Subjects](#)

[45 CFR Part 46, Subpart A, Basic HHS Policy for Protection of Human Research Subjects](#)

[45 CFR 46, Subpart B, Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research, Section 46.204](#)

[45 CFR 46, Subpart D, Additional Protections for Children Involved as Subjects in Research, Sections 46.401 through 46.404, and 46.408](#)