Veterans Health Administration
Research & Development
Improving Veterans' Lives — www.research.va.gov

**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:** March 9, 2015

This guidance supersedes ORD's April 18, 2014 guidance entitled: Guidance *on Collecting Data on Pregnancy and Outcomes of Pregnancy from VA Research Subjects and Pregnant Partners of VA Research Subjects for Safety Monitoring*

*For questions on the content of this guidance, email the VHA Office of Research and Development through* FIND Pro.

**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 required VA Facility Director approval for VA research involving children and pregnant women. 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. Obtaining VA Facility Director approval for collecting data about the newborn infant.

6. Obtaining VA Facility Director certification for collecting data about the female subject who becomes pregnant or the pregnant partner of a male subject in VA research.

**BACKGROUND:** The Department of Veterans Affairs (VA) is one of the eighteen 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 § 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 § 516.101(b), the activity must be reviewed and approved by an Institutional Review Board (IRB) holding a 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 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. 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 §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. The VA facility director must approve participation of children in the research 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. Obtaining VA Facility Director approval for collecting data about the newborn infant

When identifiable private information or de-identifiable information is collected about a newborn infant in VA research, the newborn infant is a research subject who is also a child. Following IRB, other applicable subcommittees, and R&D Committee approvals, the VA Facility Director must approve this activity which constitutes VA research involving children as research subjects. This VA Facility Director approval should be in the investigator's study files and in the R&D file in the Research Office.

VA Facility Director approval for VA research involving children does not have to be obtained until the research involves children. There is no ORD requirement to obtain VA Facility Director approval 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 research activities involving the newborn infant consist of data collection through review of records (no intervention or interaction with the infant), considerations that the VA Medical Center Director may evaluate during the approval process such as procuring

liability insurance to allow collection or data or considering whether the VA Facility is able to respond to pediatric emergencies is not applicable because the research activity consists of data collection in the absence of interventions or interactions.
Additional guidance from ORD issued to assist IRBs, R&D Committees, and VA Facility Directors in their review and approval of VA research that meets the definition of children's research is available at http://www.research.va.gov/resources/policies/guidance/research-involving-children.pdf

**6. Obtaining VA Facility Director Certification for Collecting Data about the Female Subject who Becomes Pregnant or the Pregnant Partner of a Male Subject in VA Research**

When identifiable private information is collected about or from the female subject who becomes pregnant or the pregnant partner of a male subject, VA research involving pregnant women is being conducted. Following IRB, other applicable subcommittee, and R&D Committee approval, the VA Facility Director is required to certify that the Medical Facility has sufficient expertise in women's health to conduct this activity. This VA Facility Director approval should be in the investigator's study files and in the R&D file in the Research Office.

If the research activities with collecting pregnancy progress and pregnancy outcome data involves minimal risk activities (e.g., no obstetric interventions being done at the VA Facility to collect data), considerations that the VA Medical Center Director may evaluate as part of the certification process such as ensuring that the VA facility is able to respond to obstetric emergencies is not applicable because the research activity is not associated with obstetric emergencies.

**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