Summary of Requirements for Environmental Protection Agency (EPA) Supported Human Research

Human research supported by the EPA is subject to requirements and ethical standards outlined in 40 CFR 26 including Subparts B-D.

The EPA regulations for protecting human research participants apply to research supported by the EPA **and** research in which the intent is submission of data to the EPA.

In addition to this summary guidance, an IRB Checklist is available for use by the IRB in conducting review of EPA regulated research.

EPA Study Types:

EPA regulations implement protections applicable to two basic study types:

- **Intentional exposure** of a human subject is defined as a study where the exposure experienced by the subject would not have occurred but for the human subject's participation in the study. This includes any research in which the subject's exposure is artificially manipulated or controlled.
- **Observational research** means any research that does not involve intentional exposure. Studies that involve naturally occurring environmental exposures may meet the regulatory definition of observational.

Risk level is irrelevant to the determination of whether the research involves intentional exposure or is observational.

The following describes limitations and protections defined in the EPA regulation subparts for vulnerable subject populations involved in intentional exposure and observational research. Note: *The EPA subparts are different from Department of Health and Human Services (DHHS) subparts.*

INTENTIONAL EXPOSURE:

EPA has a categorical ban on research involving intentional exposure of pregnant women, nursing women, or children to any substance.

Subpart B Prohibition of Research Conducted or Supported by EPA Involving Intentional Exposure of Human Subjects who are Children or Pregnant or Nursing Women

This subpart prohibits intentional exposure research, under **all circumstances**, in children and women who are pregnant or nursing. All circumstances include studies involving controlled exposures to neutral substances (such as clean, filtered air), foods, or therapeutic drugs. This prohibition is absolute and does not incorporate reference to either risk level or potential benefit.

EPA extends the provisions of 40 CFR 26 to human research involving intentional exposure of non-pregnant, non-nursing adults to substances. **A substance** includes any chemical, biological organism, or physical property tracked or regulated by the EPA or identified in an environmental statute. The Substance Registry Services (SRS) is the EPA's central system for information about substances that are tracked or regulated by EPA.

OBSERVATIONAL RESEARCH:

Observational research supported by or submitted to the EPA may be permitted if conditions outlined in the following regulations are met.

Subpart C Observational Research: Additional Protections for Pregnant Women and Fetuses Involved as Subjects in Observational Research Conducted or Supported by EPA

Subpart C establishes rules for studies that involve pregnant women (and thus their fetuses) participating in **observational research**.

Research of this nature can be conducted when there is direct benefit to the woman or the fetus. However, in the absence of direct benefit, **if the risk is no greater than minimal to the fetus** and the research is important for biomedical knowledge which cannot be obtained in any other manner, the research is permissible by EPA.

Subpart D Observational Research: Additional Protections for Children Involved as Subjects in Observational Research Conducted or Supported by EPA

Subpart D establishes rules for studies that involve children participating in **observational research**.

Research of this nature, involving no more than minimal risk of this type, can be conducted on children.

Research involving greater than minimal risk can only be conducted when there is direct benefit to the subject. The IRB reviews and approves observational research involving children that does involve greater than minimal risk but presenting the prospect of direct benefit to the individual participants if the IRB finds and documents that:

- The intervention or procedure holds out the prospect of direct benefit to the individual participant or is likely to contribute to the participant's well-being.
- The risk is justified by the anticipated benefit to the participants.
- The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.
- Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 40 CFR 26.406.

The IRB reviews and approves observational research involving children that does not involve greater than minimal risk only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 40 CFR 26.406. Permission by parents or guardians shall be documented in accordance with and to the extent required by 40 CFR 26.117. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

There is no provision in the EPA rule for the conduct of research when there is greater than minimal risk and no direct benefit to the child. Also, EPA regulations do not recognize a category of research on children involving "a minor increase over minimal risk".

Subpart K - Basic Ethical Requirements for Third-Party Human Research for Pesticides Involving Intentional Exposure of Non-pregnant, Non-nursing Adults

EPA 2013 Final Rule – Enhanced protections for all other adult subjects in human research involving pesticides.

Defines pesticide as a substance or mixture of substances intended for pesticidal effect.

Informed Consent Requirements:

If the research involves intentional exposure of subjects to a pesticide, the subjects of the research must be informed of the identity of the pesticide and the nature of its pesticidal function. In consideration of risks currently unforeseen, investigator should include any potential risk to embryo or fetus, should subject become pregnant.

Subpart K does not include provision for consent by a subject's legally authorized representative (LAR). No investigator may involve a human being as a subject in pesticide research unless the investigator has obtained the legally effective informed consent of the subject.

Subpart L—Prohibition of Third-Party Research involving Intentional Exposure to a Pesticide of Human Subjects who are Children or Pregnant or Nursing Women

Submission of IRB Documentation to EPA for Project Review

The PI must submit the following documentation to the EPA Human Subjects Research Review Official (HSRRO) for final review and approval before the research can begin:

- ☐ UK's Federal-wide Assurance (FWA) number
- ☐ Copies of:
  - the IRB approval (or exemption) letter;
  - the study protocol(s) as submitted to the IRB (the pre-award document is not sufficient);
  - the IRB approved consent forms and subject recruitment materials if applicable; and
  - all supplementary IRB correspondence between the IRB and the investigator (i.e., submission, requested revisions, etc.).

Additional Resources:

- The online course, Human Subjects Research at the Environmental Protection Agency: Ethical Standards and Regulatory Requirements, provides training for investigators involved in human subject research supported by EPA.
- The online manual Scientific and Ethical Approaches for Observational Exposure Studies serves as a resource tool and source of information for researchers involved in the development and conduct of observational human exposure studies.

Sources:

40 CFR 26

Conducting Human Subjects Research (HSR) at EPA

Oversight of Human Research Regulated by EPA: Special Considerations for HRPPs, AAHRPP Presentation, 2010

Human Subjects Research at the Environmental Protection Agency: Ethical Standards and Regulatory Requirements