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Oversight of Human Research Regulated by EPA: Special Considerations for HRPPs

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Historical Background

- The state of affairs prior to 1996
- The 1996 Food Quality Protection Act and the response of third-party pesticide manufacturers
- The public debate over the ensuing decade
- The 2006 Appropriations Act
- The 2006 revision of the EPA Human Studies Rule

The 2006 Appropriations Act

- None of the funds…may be used by…the Environmental Protection Agency to accept, consider or rely on third-party intentional dosing human toxicity studies for pesticides, or to conduct intentional dosing human toxicity studies for pesticides until…final rulemaking on this subject.

- Such rule shall not permit the use of pregnant women, infants or children as subjects;…

The 2006 EPA Human Studies Rule (40 CFR 26)

- Retains EPA's prior codification of the Common Rule (Subpart A)
- Adds three subparts (Subparts B-D) that incorporate prohibitions and additional protections for pregnant women, nursing women, and children in research conducted or supported by EPA
- Adds a series of subparts (Subparts K-Q) that include rules for third-party research for pesticides intended for submission to EPA under the pesticide laws

EPA's Subpart L

- Regulates third-party human research for pesticides involving the intentional exposure of pregnant women, nursing women, or children
- Defines *research involving the intentional exposure of a human subject* as the "study of a substance in which the exposure to the subject would not have occurred but for the subject's participation in the research"
- Categorically prohibits all research subject to this subpart

EPA's Subpart K

- Regulates third-party human research for pesticides involving the intentional exposure of non-pregnant, non-nursing adults
- Defines *research involving the intentional exposure of a human subject* exactly as in Subpart L
- Applies the Common Rule IRB and informed consent requirements to research subject to this subpart

EPA's Subpart B

- Regulates research conducted or supported by EPA involving the intentional exposure of pregnant women, nursing women, or children
- Does not mention pesticides (or any other substances)
- Defines *research involving the intentional exposure of a human subject* exactly as in Subparts K and L
- Categorically prohibits all research subject to this subpart

EPA's Subpart B

- The prohibition on intentional exposure research is absolute and does not incorporate reference to either risk level or prospect of benefit, including direct benefit

- Research prohibited by Subpart B in pregnant women, nursing women, and children includes:
  - Pharmacokinetic studies involving below ambient exposures
  - Studies involving controlled exposures to neutral substances (such as clean, filtered air)
  - Nutritional studies involving the controlled administration of foods
  - Therapeutic drug trials

EPA's Subpart C

- Regulates observational research conducted or supported by EPA involving pregnant women and fetuses

- Defines *observational research* as "any human research that does not meet the definition of *research involving intentional exposure of a human subject*"

EPA's Subpart C

- Applies the additional protections found in 45 CFR 46 Subpart B to research subject to this subpart, but

- Does not address, and thus does not provide a mechanism for, research "not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women (or) fetuses…"

EPA's Subpart D

- Regulates observational research conducted or supported by EPA involving children
- Defines *observational research* exactly as in Subpart C
- Applies the additional protections found in 45 CFR 46 Subpart D to research subject to this subpart for:
  - Research not involving greater than minimal risk
  - Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects

EPA's Subpart D

- Does not address, and thus does not provide a mechanism for:
  - Research involving greater than minimal risk without prospect of direct benefit but "likely to yield generalizable knowledge about the subject's disorder or condition"
  - Research "not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children"

Summary of EPA vs. HHS for Pregnant Women and Fetuses

- Categorical ban on intentional exposure research
- No mechanism for research “not otherwise approvable”

- No such categorical ban
- Research “not otherwise approvable” may be conducted under special circumstances

Summary of EPA vs. HHS for Children

- Categorical ban on intentional exposure research
- No such categorical ban
- No mechanism for greater than minimal risk research without prospect of direct benefit
- Greater than minimal risk research without prospect of direct benefit may be conducted under special circumstances

Summary of EPA vs. HHS for Children

- No mechanism for research “not otherwise approvable”
- Research “not otherwise approvable” may be conducted under special circumstances

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