May 9, 2005

VIA E-MAIL

Public Information and Records Integrity Branch
Office of Pesticide Programs
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460
ATTN: Docket ID Number OPP-2003-0132

Re: Human Testing; Proposed Plan and Description of Review Process

These comments are being submitted on behalf of Public Employees for Environmental Responsibility (PEER) in response to the Environmental Protection Agency's notice of its Human Testing Proposed Plan and Description of Review Process, published at 70 Fed. Reg. 6661 (Feb. 8, 2005). PEER is a national non-profit alliance of local, state and federal scientists, law enforcement officers, land managers and other professionals dedicated to upholding environmental laws and values.

Background and Summary of Comments

This Notice was published in the midst of a pesticide industry campaign to expand testing of pesticides on humans, in order to weaken health standards and increase profits. Due to the strict requirements of the Food Quality Protection Act of 1996 (FQPA), the pesticide industry has been under mounting pressure to reduce the risks that pesticides post to infants and children. In response, the industry continues to test pesticides on adult human subjects, thereby enabling them to remove safety factors and other protective requirements and submit older and extraordinarily unethical studies, including some with children test subjects. The result will be weaker and less scientifically valid health standards, while more adults, children and infant study participants are endangered along the way.

The Agency's current case-by-case review process for third-party human subject studies encourages the pesticide industry to continue testing on human subjects without adequate scientific and ethical review to ensure protection of the study participants. Under current EPA policy, human subjects involved in research to inform EPA decision-making regarding harmful pesticides and chemicals receive fewer protections than human subjects involved in research to inform decision-making by Dept. of Health and Human Services (HHS) agencies regarding drugs and devices having a countervailing benefit to the participants.

The Agency's forthcoming rulemaking should adopt subparts B (Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research), C (Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects), and D (Additional Protections for Children Involved as Subjects in Research) of the HHS regulations protecting populations of vulnerable research subjects.[1] Furthermore, EPA's rulemeaking should require that all third-party human subject studies submitted for EPA decision-making comply with the Common Rule[2] and the additional protections for the vulnerable populations.

<u>Recommendations</u>

This Notice merely establishes "a framework for making decisions about" certain third-party studies but leaves intact EPA's nebulous and subjective "case-by-case" approach which "binds no one to a particular process or result." Moreover, EPA states it "may act at variance from the process as described" until superceded by rulemaking.

The Agency's Advanced Notice of Proposed Rulemaking on Human Testing[3] is already two years old. Because EPA could delay rulemaking indefinitely and continue to make significant decisions with little consistency or transparency, it must establish a reasonable timetable for rulemaking and publish a proposed rulemaking taking into consideration these and other comments to the Feb. 8, 2005 Notice.

i. Third-party Human Studies

The Agency should deal immediately with third-party human studies conducted by pesticide manufacturers seeking registrations, and other regulated parties affirmatively submitting studies for decision-making purposes. In such cases the Agency has the authority to require and approve, a priori, study protocols. Specifically, the Agency should promptly publish a rule requiring that:

a) All third party studies submitted to the Agency for decision-making comply with the Common Rule, including any subparts to the Common Rule which EPA may adopt in the future;
b) Third-party researchers submit a proposed protocol to EPA prior to submitting studies to the Agency for decision-making; and
c) At a minimum, for each study protocol reviewed by the agency, the agency should exercise oversight during the course of the study to ensure it is conducted in compliance with the requirements of the Common Rule.

Furthermore, the Notice's description of EPA's current case-by-case review process only applies to third-party studies conducted "to identify or quantify a toxic endpoint."[4] The current process screens "all priority studies involving intentional dosing of human participants for toxic effects." However, third-party studies can also be conducted for other purposes. For example, many studies are designed to characterize the pharmacokinetics (absorption, distribution, metabolism, excretion) of a chemical. Such studies could be conducted unethically and injure subjects, even though the goal was

[1] 45 C.F.R. § 46.
[2] 40 C.F.R. § 26.
[3] 68 Fed. Reg. 24410 (May 7, 2003).
[4] 70 Fed. Reg. at 6666.

other than identifying a toxic endpoint.

EPA should not limit its description of or screening of third-party studies to only those that are intended to identify toxic endpoints such as NOAELs or LOAELs. EPA should screen ALL third-party studies for ethical competency.

The Notice states that EPA will continue to accept scientifically valid third-party studies unless there is “clear evidence” that the study “was intended to seriously harm participants” or “failed to obtain informed consent” or “was significantly deficient relative to the standards prevailing at the time the study was conducted.”[5]

It is hard to believe that these are truly the criteria by which EPA judges human subject studies, because they would be clear violations of HHS regulations. EPA should never accept or use data from any human subject study if there is even the slightest evidence of intentional harm, serious or otherwise. EPA should never accept or use data from any human subject study if there is any evidence that adequate informed consent was not obtained. To hold third-party researches to such low standards justifies past unethical behavior, encourages unethical behavior in the future and allows for unnecessary risks for countless human study participants. Certainly when EPA has the authority to require proof of ethical study protocols as part of a submission package before an entity begins a human study it should do so.

ii. Historical Studies

This Notice fails to explain exactly how EPA determines that a historical study is “significantly deficient” by historical standards. Has it set up a sliding scale of values? EPA should clearly state how it evaluates the ethical competency of historical studies, including an explanation of how such evaluations are consistent with Agency review of other human subject studies. EPA should not accept or use data from a historical study that it knows to be deficient by today’s high standards.

EPA needs to identify objective standards by which to determine if it will use data from all historical studies. Agency policy should explicitly state that the agency will not consider data from historical studies for which the Agency cannot obtain information or has only limited information about the ethical conduct of the study. It should define the minimal type and amount of information needed to make a determination of usefulness.

iii. Additional Protections for Vulnerable Populations

The Notice states that in conducting first- and second-party research, EPA “remains committed to full compliance with the Common Rule.”[6] However, EPA has still not adopted Subparts B, C or D of the HHS regulations (special protections for prisoners, pregnant women, fetuses, neonates, prisoners and children),[7] even though more than a

[5] 70 Fed. Reg. at 6666.
[6] *Id.* at 6664.
[7] 45 C.F.R. § 46.

year ago the National Academy of Sciences advised EPA to adopt Subpart D (Additional Protections for Children Involved as Subjects in Research).[8]

The recent release of the Study Design of EPA's research project, the Children's Health Environmental Exposure Study ("CHEERS"), revealed that EPA is not yet committed to full protection for children. That study would have coerced and unfairly induced parents (without clearly informing them of the study purposes or risks to their children) to continue pesticide use practices that the Agency determined would likely result in their infants' exposure to neurotoxic pesticides, merely for the purpose of refining risk assessment. Subpart D of the HHS rules explicitly forbids such practices. Thus, the Centers for Disease Control and Prevention, for example, would not have been able to conduct CHEERS without violating agency regulations for protection of research participants.

EPA should adopt subparts B, C and D of the HHS Human Subjects Protection regulations, found at 45 CFR 46, and apply them to all human subject studies (first-, second- and third-party).

iv. Institutional Review Boards and the Human Subjects Research Review Official

EPA currently has no independent Institutional Review Board to review studies conducted by or supported by the Agency (first- and second-party studies). Instead the Agency has only one Human Subjects Research Review Official (HSRRO) in the Office of Research & Development and one HSRRO assistant. This Notice proposes that this single HSRRO report instead to the Administrator to review certain third-party studies. The Agency claims that this will satisfy the NAS recommendation that EPA establish a Human Studies Review Board (HSRB) to ensure that IRB review is conducted in accordance with the Common Rule and other human subject protections.[9] On the contrary, the HSRRO, regardless of where the official is located within the Agency's organization, is in no way equivalent to the HSRB recommended by NAS.

Transferring the HSRRO to the Office of the Administrator will do nothing to establish the independence of the HSRRO and, in fact, may compromise it further. It is unreasonable for the Agency to charge one person with the responsibility of reviewing all first-, second- and third-party studies conducted by, supported by or submitted to EPA. By contrast, the Centers for Disease Control and Prevention has six independent IRBs.

Without an Agency independent IRB, all parts of the EPA outside the Office of Research & Development must rely on outside IRBs that may or may not judge studies consistently. As recommended by the NAS Report, EPA should immediately establish an

---

[8] National Academy of Sciences, National Research Council, *Intentional Human Dosing Studies for EPA Regulatory Purposes: Scientific and Ethical Issues* (2004), available at http://books.nap.edu/catalog/10927.html.
[9] *Id.* at 115.

agency-wide, but independent IRB.[10] This should consist of a sufficient number of persons with appropriate expertise to review all Agency studies (first, second and third party).

Concluding Remarks

Under the current review process at EPA there is no way for the public to know what studies EPA is conducting or supporting, or to know where in the review process those studies may be. It is even more alarming that until the CHEERS controversy surfaced, EPA regional office staff did not know that studies they conduct or support are subject to HHS regulations. To its credit, the Agency has scheduled ethics training for regional personnel, but none has been scheduled for headquarters personnel. EPA should establish a system to describe and track all human subject studies, and put this system on its website. It should establish agency-wide training on the requirements of the Common Rule for all staff conducting, granting money for, or reviewing human subject studies.

Pending completion of EPA's rulemaking regarding protection of human subjects, the Agency should apply current ethical and scientific norms embodied in domestic and international law and scientific convention. The Common Rule can and should be read to apply to third party studies submitted to EPA for regulatory purposes (such as pesticide registration or tolerance reassessment). In addition, the Nuremberg Code, Helsinki Declaration, and the International Covenant on Civil and Political Rights are customary international law, with which the Executive Order on the Implementation of Human Rights Treaties anticipates EPA compliance.[11] Each of these sources of law should be applied. Moreover, the recommendations contained in the EPA Science Advisory Board and the FIFRA Scientific Advisory Panel Report[12] and the NAS Report also establish fundamental ethical and scientific criteria for EPA to follow in reviewing studies.

EPA's approach to regulating pesticides and other harmful chemicals should invoke the highest and most rigorous review of ethical and health considerations. EPA must stop its policy of accepting research data from powerful corporations that dose babies, children and adults with toxins without safeguards. The Agency's case-by-case review fails to apply basic protections for human test subjects to countless studies conducted by private companies. EPA should promptly issue a rulemaking that requires safeguards for human subjects of industry studies before considering study data and adopts the HHS additional protections for vulnerable populations for all first-, second- and third-party human studies.

---

[10] *Id.* at 114.

[11] *See* Exec. Order No. 13107, 63 Fed. Reg. 68991 (Dec. 10, 1998). The basic purpose of this Executive Order was to recognize U.S. obligations under the ICCPR, the Convention Against Torture, and the Convention on All Forms of Racial Discrimination. The Executive Order specifically requires that "all executive departments and agencies…shall maintain a current awareness of United States international human rights obligations that are relevant to their functions and shall perform such functions so as to respect and implement those obligations fully." *Id.* This Order is further support that the United States has bound itself to the human rights norms codified in the treaties to which it is a party, including the primacy of full informed consent to any human experimentation.

[12] EPA Science Advisory Board and FIFRA Scientific Advisory Panel, *Comments on the Use of Data from the Testing of Human Subjects* (2000), available at http://www.epa.gov/sab/pdf/ec0017.pdf.

Thank you for the opportunity to provide these comments.

Respectfully submitted,

Jeff Ruch
PEER Executive Director

Rebecca Roose
PEER Program Director