

December 12, 2005

Public Information and Records Integrity Branch (PIRIB)  
7502C  
Attn: Docket ID Number OPP-2003-0132  
Office of Pesticide Programs (OPP)  
1200 Pennsylvania Avenue, N.W.  
Washington, DC 20460-0001

Re: Federal Register  
Vol. 70, No. 175  
September 12, 2005

Dear Mr. Johnson:

On behalf of the approximately 8,000 employees of the Environmental Protection Agency (EPA) represented by the American Federation of Government Employees, AFL-CIO (AFGE), I am writing to address EPA's proposed regulations to change the rules that would permit conducting and reviewing human studies that intentionally expose participants to pesticides. Although AFGE strongly supports rulemaking to ban intentional dosing human testing for pesticides, AFGE is concerned that EPA's proposal is not stringent enough to effectively eliminate the ethical problems that these procedures may cause.

**I. Background**

EPA is charged with protecting public health and the environment by regulating releases of pollutants and some uses of hazardous and toxic substances. The agency generally evaluates health risks to people by performing and analyzing tests on laboratory animals. However, EPA has asserted that there are critical data gaps in understanding how certain substances affect the body, and that the agency can better understand the potential risks of toxicants by analyzing human exposure to the toxicants. Although human exposure studies may improve EPA's risk assessments, these studies also pose risks to the human test subjects. Societal concern over ethically deficient human research is understandable. As the EPA openly acknowledges, "...the history of human research contains well-known examples of unethical behavior in the name of

science...” These historical tragedies have brought about a change in the way the world views human exposure research and have necessitated ethical guidelines for how these studies should be conducted.

The **Common Rule**, put into place in 1991, establishes an ethical framework for the review and conduct of proposed human research across most of the federal government. The central requirements of the Common Rule are: (1) that *people who participate as subjects in covered research are selected equitably and give their fully informed, fully voluntary written consent*; and (2) that *proposed research be reviewed by an independent oversight group referred to as an Institutional Review Board (IRB), and approved only if risks to subjects have been minimized and are reasonable in relation to anticipated benefits, if any, to the subjects, and the importance of the knowledge that may reasonably be expected to result.* (Emphasis added)

While it is encouraging that EPA acknowledges the need for more comprehensive ethical standards to govern human testing, this proposal falls short in many ways. Unfortunately, the proposed rule has so many exceptions that, if adopted, it could force EPA’s Bargaining Unit members to accept data from 3<sup>rd</sup> party human studies that were conducted in an unethical manner. Since the proposed rule contains too many exemptions to make it an effective “ethical safeguard” for human studies, AFGE stands opposed to its implementation.

## **II. Extending the Common Rule to Future Third-Party Human Research**

Currently, the requirements of EPA’s codification of the Common Rule do not generally apply to third-party human research intended for submission to or considered by EPA. EPA proposes to extend the requirements of the Common Rule to third-party research that involves intentional exposure of human subjects if the researcher *intended* to submit the resulting information to EPA or to hold the information for later inspection by the EPA. Whether an investigator “intended” to submit research to the EPA will be determined based on the investigator’s decision to submit the research to the EPA when the research was initiated. If, on the contrary, an investigator decides that he or she wishes to submit his or her research to EPA after the research is initiated, the guidelines of the Common Rule may not apply.

Basing the applicability of the rule upon the investigator’s intent essentially allows the exception to this rule to swallow the rule itself. An investigator’s intent in submitting a research project to the EPA should not be allowed to override ethical conduct in choosing human subjects and proper oversight in carrying out scientific experiments involving human subjects. Although EPA asserts that the commitment to comply with the Common Rule must be made before conducting the research because the rule imposes certain procedural requirements on the conduct of the research, AFGE strongly believes that if intentional dosing of a

human subject must exist, third-party compliance with the Common Rule should be a requirement, not a choice. In order to accomplish this goal, EPA should strongly consider extending the application of EPA's Common Rule to all research with human subjects that EPA uses in its decision-making, rather than limiting it to research "*intended*" for submission to EPA.

This proposal also states that these regulations, if enacted, would apply prospectively, only affecting research initiated after the effective date of this rule. This still obligates the EPA to rely on earlier study results that do not conform to accepted ethical guidelines. AFGE is strongly opposed to this. If the EPA wishes to establish a credible ethical framework for conducting human exposure studies, EPA must apply agency guidelines uniformly and ensure that all research and studies, regardless of when they are initiated, are held to the same standards.

### **III. Additional Protections for Children**

EPA proposes to "categorically prohibit" third parties engaged in research covered by the proposed extension of EPA's Common Rule from conducting any study involving intentional dosing of children, and to apply the same prohibition to human research that EPA conducts or supports.

Although the EPA has strengthened guidelines that govern use of data from tests that expose children to toxic pesticides, the rules still do not adequately protect children. For instance, Section 26.401 (a)(1) allows intentional dosing studies on children if the head of an Office of the Agency believes that nonsubstantive, procedural modifications are appropriate from an administrative standpoint. This exception could result in different offices within EPA having different sets of procedures for children's intentional dosing studies. If EPA or a "second" or "third" party performs research on child subjects in circumstances that may pose a health risk to the children, the researchers have an affirmative moral obligation to inform the children and their parents of all potential health risks to those children, and the purpose of the research. This is the plain requirement of the Common Rule. EPA opens itself and its employees to criticism, and potentially liability, by condoning a weaker standard than the Common Rule for human subjects research by making use of this "catch-all" exception.

While AFGE acknowledge that in some instances the EPA can better understand the potential risks of a toxicant through human exposure studies, AFGE strongly believe that certain types of human research should never be acceptable. Deliberate exposure of children to pesticides is one such type of research that the EPA should never sink to using. As EPA has recognized, using children as potential subjects in human research raise varied ethical concerns. Not only do children have less capacity to understand the consequences from participation in a human study, but they are vulnerable to influence and in some instances

coercion by adults. The National Academy of Sciences (NAS) even noted in its report entitled “Intentional Human Dosing Studies for EPA Regulatory Purposes,” (February 2004) that no such testing could ever be justified.

AFGE strongly believes that any ethical safeguard adopted by EPA should be uniformly enforced across all offices within the agency. AFGE, therefore, recommends that the EPA broaden the scope of the ban on using children in pesticide exposure research studies, without exception. EPA should prohibit third parties from using unethical research on children as subjects in human exposure studies, and apply the same prohibition to human research that EPA conducts and/or supports.

#### **IV. Additional Protections for Pregnant Women, Fetuses, and Certain Newborns**

Although EPA proposes to “categorically prohibit” third parties engaged in research from conducting any study involving intentional dosing of pregnant women, fetuses, or newborns, the proposed regulations are misleading. Although the EPA does state that it is proposing to adopt and incorporate 40 CFR part 26, the preamble of the proposed rule does not acknowledge that Section 26 of this regulation is laden with exceptions.

Although the proposed rule allegedly bans testing on pregnant women, fetuses, or newborn children, Section 26.603 makes an exception for this ban. It allows EPA to accept data from “intentional dosing” studies done on pregnant women, newborns and fetuses if the data from the studies are “crucial to regulatory decision(s) that would be more protective of public health than could be justified without relying on the data.” AFGE believes under no circumstances should EPA accept data from studies where pregnant women, newborn infants, or fetuses have been deliberately exposed to pesticides or other chemicals.

AFGE recommends that the EPA broaden the scope of the ban on using pregnant women, newborn infants, or fetuses in human subject studies by prohibiting EPA from considering any intentional or unethical studies. EPA should apply the same prohibition to human research that EPA conducts and/or supports.

#### **V. Additional Protections for Prisoners**

The proposed rule explicitly states that EPA will “defer” adoption of rules that provide “additional protection of prisoners” who might participate in deliberate dosing studies. In its proposal EPA attempts to explain this omission and the failure to adopt the HHS prisoner safeguards (45 CFR part 46, subpart C) by stating:

- (a) “many people in the ethics community believe these rules create as many problems as they solve;” (b) HHS...and its advisory committee are actively considering revisions to the HHA Subpart C;” (c) “EPA has never conducted or supported any human studies with prisoner subjects, and has no intention to do so in the future;” and (d) “We do not expect any to be submitted to us in the future.”

The decision not to adopt additional protections for prisoners based on the conjecture that the agency may not receive studies of this nature in the future is simply foolish. If the agency does receive a human dosing study that involves prisoners, the agency will be unprepared to make a determination about whether that study is ethical and properly access the proven benefits or risks of that particular study. It is equally foolish to decide against adopting ethical guidelines for human dosing studies involving prisoners based on the presumption that it will ultimately create “problems.” Designing ethical guidelines for intentional dosing studies that involve prisoners may in fact be tenuous since these individuals compromise a unique sect of society and may be subject to certain legal or constitutional restrictions that other persons are not. However, choosing to sit by idly and do nothing leaves these individuals at risk for exploitation. This is unacceptable.

Although prisoners that participate in studies conducted by EPA or third parties would still be covered by the provision in EPA’s Common Rule, AFGE strongly believes that the proposed rule’s provisions “reserving” protections for prisoners gives the green light to conduct studies without sufficient ethical standards. AFGE recommends that the EPA formally adopt a ban on using prisoners in human subject studies where there is any intentional dosing.

#### **VI. Ethical Standards for Determining Whether to Rely on Scientifically Sound, Completed Human Studies with Ethical Deficiencies**

Although this proposal was purportedly drafted with an eye toward strengthening ethics in human research, this section of the proposal, in particular, negates the entire policy behind ensuring human safety. The EPA states that with regard to human studies initiated before a final rule becomes effective, EPA proposes to rely on data from human research even if there is evidence to show the conduct for the research was unethical or deficient relative to the ethical standards prevailing at the time the research was conducted.

While the EPA asserts that it would be “inequitable” to measure the conduct of human studies initiated before the date of the effective rule by using contemporary ethical standards, we believe that it would be immoral to do otherwise. If the proposed guidelines become regulation, EPA will be obligated to consider earlier unethical studies. What is most disturbing is that EPA

“recognizes that the...refusal to rely on the results of research that does not meet appropriate ethical standards may influence the behavior of third parties.” In essence, EPA encourages submission of unethical research if it adopts this regulation. If EPA is willing to overlook ethical lapses on a “situational” basis, EPA encourages the regulated community to exploit EPA’s lapse. If the EPA wishes to establish a comprehensive ethical framework for conducting human exposure studies, they must apply agency guidelines uniformly and ensure that all research and studies, regardless of when they are initiated, are held to the same standards.

Regarding the level of evidentiary proof the EPA should use in the consideration of reports that are unethical, NAS recommendation 5-7 states that the EPA should accept scientifically valid studies conducted before its new rules are implemented unless there is “clear and convincing evidence” that the conduct of those studies was fundamentally unethical. Although AFGE does not support or endorse the EPA’s use of *any* study that is ethically deficient, we believe NAS’ recommendation is superior to the Agency’s recommended standard stating that their refuse to rely on past studies only when they are “significantly deficient.”

Despite the fact that ethical lapses in human subject studies must be “significant,” EPA is willing to accept human subject studies that are in fact unethical, and could be equally as harmful to the participants involved in the study.

## **VII. EPA’s 2006 Appropriations Act**

Section 201 of the Department of the Interior, Environment, and Related Agencies Appropriations Act of 2006 addresses EPA activities regarding intentional dosing human toxicity studies for pesticides, and clearly states that the agency should issue a rule on this subject that,

...shall not permit the use of pregnant women, infants or children as subjects; shall be consistent with the principles proposed in the 2004 report of the National Academy of Sciences on intentional human dosing and the principles of the Nuremberg code with respect to human experimentation...

This act makes it plainly clear that Congress did not intend for EPA to rely upon, or to conduct itself, any studies on pregnant women, infants or children. Since the ban on testing of children, as well as pregnant women, newborns and fetuses is limited (as discussed in Section III and IV above) the proposed rule does not effectively protect human subjects of “third party” pesticide exposure studies and thus defies the requirements of EPA’s 2006 Appropriations Act.

This proposal also contradicts the requirements of the EPA's 2006 Appropriations Act because it violates several principles of the Nuremberg Code. Principal 5 states that, "No experiment should be conducted where there is a priori reason to believe that death or disabling injury will occur..."<sup>1</sup> Principle 7 states that, "proper preparations should be made and adequate facilities provided to protect the experimental subject against even **remote** possibilities of injury, disability or death."<sup>2</sup> (Emphasis added) The EPA's decision to implement a proposal that is riddled with exceptions fails to protect human subjects from exposure to substances that are known to be unhealthy. We strongly recommend that the EPA rewrite its regulations and propose an absolute ban on all testing for pregnant women, children, infants and newborns as the current appropriations act requires.

### **VIII. Conclusion**

Although the EPA has theoretically drafted a proposal that will strengthen ethical practices in human exposure studies, the regulations actually seem to encourage non-compliance with the agency's own standards. AFGE is seriously concerned that the current proposal endorses the philosophy that certain groups of people are more deserving of health protection than others. Not only do the proposed regulations fail to comply with accepted national and international legal standards, these rules potentially force bargaining unit employees into violating the Nuremberg Code and the 2006 Appropriations Act as a condition of employment. AFGE is not only concerned about our members being coerced into performing unethical procedures while carrying out human subject research, we are equally concerned about the participants who will take part in these human subject studies. AFGE is hopeful that the EPA will give our comments serious consideration when revising the rule before final publication, and ensure that exceptions are stricken from the rule before it is adopted.

Sincerely,

John Gage  
National President

---

<sup>1</sup> <http://ohsr.od.nih.gov/guidelines/nuremberg.html>, Reprinted from *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10, Vol. 2, pp. 181-182.* Washington, D.C.: U.S. Government Printing Office, 1949.

<sup>2</sup> <http://ohsr.od.nih.gov/guidelines/nuremberg.html>, Reprinted from *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10, Vol. 2, pp. 181-182.* Washington, D.C.: U.S. Government Printing Office, 1949.