Comments on EPA Final Proposed Rule on
Protections for Subjects in Human Research
December 2005

**These comments are submitted by Public Employees for Environmental Responsibility (PEER).**

**The following groups have signed on to PEER's comments:** Alliance for Human Research Protection (AHRP), Center for Environmental Health, Citizens Campaign for the Environment (CCE), Environmental Research Foundation, Health Care Without Harm, Organic Consumers Association, Protect All Children's Environment (PACE) and Center For Health, Environment and Justice

## Introductory Comments

On September 12, 2005, the U.S. Environmental Protection Agency proposed rules for protecting subjects in human research. As demonstrated by these comments, EPA's proposed rule is peppered with loopholes, encourages unethical conduct and omits key protections for infants, pregnant women and other vulnerable populations.

Among the principal concerns with EPA's plan are provisions that would allow –

- Dosing experiments involving infants and pregnant women using non-pesticide chemicals. Thus, companies will be free to test agents such as perchlorate on nursing mothers;

- A repeat of the infamous (and now canceled) CHEERS study in which parents were to be paid to spray pesticides in their infants' rooms at home. EPA pointedly omits any check against undue economic inducement (as in CHEERS), i.e., paying poor people amounts that would induce them to sign informed consent papers; and

- Reliance on unethical studies by EPA on the basis of a variety of loopholes. For example, the proposal says EPA can use any human dosing study conducted before the new rule's effective date on a case-by-case basis, applying the ethical norms prevalent at the time. Since, prior to the rule, EPA recognized no ethical standards at all, this means that all previous human studies can come in through EPA's wide open door.

EPA states in the preamble to the Proposed Rule that the agency "is open to considering an expanded scope for this proposed rule to address either a broader range of human research designs or decision-making under other statutory authorities." 70 Fed. Reg. 53,841. This statement is a backhanded acknowledgement of the limited and grudging nature of what the agency has proposed. These comments stress the importance of expanding both the scope and rigor for EPA to strengthen its final rule.

**Brief Background**

During the past 12 months, EPA policies on testing pesticides and chemicals on human subjects have rapidly evolved. Since the fall of 2004, the agency has gone from defending a very controversial Florida pesticide study, CHEERS, then withdrawing the study in April. In February 2005, EPA put forward the position that no ethical standards could be promulgated for human testing and by September the agency is now proposing to adopt standards that only months earlier defied promulgation.

A year ago EPA was determined to go into low-income homes in Duval County, Florida to test infant and toddler exposure to harmful pesticides and household chemicals, with funding from the leading industry group, American Chemistry Council. This study, called the Children's Environmental Exposure Research Study, or CHEERS, created a firestorm of public criticism initially causing the agency to postpone the study for further ethical review in November 2004. Finally, in April of this year, during Administrator Stephen Johnson's confirmation hearing, the agency announced it would cancel the study.

Meanwhile, the agency was accepting comments on a public notice it filed in February 2005 stating its current policy of accepting third-party human subject studies on a case-by-case basis. At that time EPA gave no indication of plans to adopt ethical standards for human subject studies conducted (first-party), supported (second-party) or relied upon (third-party) by EPA for use in agency decision-making.

In the wake of the agency's dogged defense of CHEERS and advocacy of human testing without fixed ethical safeguards, the U.S. Congress passed a provision in the EPA's 2006 Appropriations Act requiring the agency to promulgate rules protecting human subjects of intentional dosing studies conducted by third-party researchers, EPA researchers or supported by EPA. Specifically, the mandate calls on the agency to prohibit the use of pregnant women, infants or children as subjects, create an independent Human Subjects Review Board and adhere to the principles of the 2004 National Academy of Sciences (NAS) report and the Nuremberg Code.

In other words, Congress has told EPA that it must adopt ethics rules if it wants to remain in the human testing business. So this September, EPA jettisoned its proposed policy of accepting all human dosing studies on a "case-by-case" basis and has finally put forward some ethical standards.

The good news is that EPA is at last pledging to make an attempt to abide by the Nuremberg Code, adopted after World War II to prevent a repetition of the horrific Nazi human experiments. The bad news is that EPA's latest proposal is only a tiny half-step forward, which appears to have been written to please the chemical industry while attempting to comply with the Congressional mandate.

Human testing has become central to the regulatory plans of the chemical companies. These companies are challenging the utility of animal studies and demanding that EPA

use human subject tests as the new safety benchmark. Because human tests cannot use the same high chemical concentrations that are used in animal tests, increased reliance on human testing better enables companies to argue that there is no definitive proof of harm from the introduction of chemicals based upon small-scale human studies of dubious probative value.

Consideration of comments to the proposed rules and drafting the final rule is EPA's opportunity to ensure that all human subjects of research conducted by, supported by or intended for submission to EPA are protected by the highest ethical standards. In light of the growing industry reliance on human testing to market more products with higher concentrations of known toxic substances, EPA ethical standards for human subject protection are more important than ever.

## Specific Comments

### I. Proposed Rule Is Riddled with Loopholes: EPA Should Adopt a Comprehensive Approach

The proposed rule is extraordinarily limited in scope.

#### A. Pesticide Orientation Excludes Experiments With Other Chemicals.

EPA's final rule should protect human subjects of all research, conducted, supported or relied upon by EPA regardless of the purpose of the study or whether it is to be used for decision-making under pesticide laws or any other statutory or regulatory scheme.

EPA's reliance on a provision of Federal Insecticide, Fungicide, and Rodenticide Act which would extend some protections to research participants in other than intentional dosing studies is ineffective.[1] This provision only covers human studies of pesticides and there is no reasonable justification for limiting any provision of this rulemaking to human research being conducted using non-pesticide chemicals.

EPA offers as its justification for limiting the scope of this rule to pesticides that it is because "it is the most pressing of issues." 70 Fed. Reg. 53,841. Apart from the fact that EPA offers no empirical support of this conclusion, the logical reason for addressing studies on certain chemicals now and other more hazardous chemicals perhaps at some later date is not apparent. It is unclear why EPA considers product registration decisions more "pressing" to the Pesticide Program than decisions on particulate matter and ozone to the Air Program, decisions on arsenic to the Water Program or decisions on hormonal disrupters or other emerging contaminants to the Toxic Substances Control Act Program.

[1] EPA states, "FIFRA section 12(a)(2)(P) would apply because a pesticide is involved. This provision of FIFRA makes it unlawful for any person 'to use any pesticide in tests on human beings unless such human beings (i) are fully informed of the nature and purposes of the test and of any physical or mental health consequences which are reasonably foreseeable therefrom, and (ii) freely volunteer to participate in the test.'" 70 Fed. Reg. 53,847-48.

EPA should eliminate the need for future human subject rulemakings by publishing a final rule that is not limited in scope to studies conducted for consideration under pesticide laws.

**B. Researcher Intention Standard Is Artificial and Unworkable.**

EPA's proposal only extends the provisions of the Common Rule to third-party human research that involves "intentional dosing" and is "intended for submission to EPA under the pesticide laws." These two limitations place countless third-party human subject studies without any ethical protections.

The "intention restriction" serves no discernible public policy purpose. It is a predicate that is practically unenforceable and invites corporate evasion by insulating unethical studies conducted under another pretext.

**C. Intentional Dosing Standard Excludes Many Human Experiments.**

The proposed rule also limits its categorical prohibition of testing on pregnant women and children in first and second-party studies to those studies that meet the agency's definition of intentional dosing.

EPA defines intentional exposure research as "a study of an environmental substance in which the exposure to the substance experienced by a human subject participating in the study would not have occurred but for the human subject's participation in the study." Limiting third-party research standards in this way does not preclude the unethical practice of encouraging ongoing behaviors which the researcher knows risk harm to the subject in order to collect data. Studies in which researchers find subjects engaged in harmful behavior in order to study effects of toxic substances are spared from ethical standards.

This problem is most clearly demonstrated by the CHEERS Study Design. Researchers identified subjects who used neurotoxic pesticides in ways that were anticipated to result in exposures to their children, including newborns. Participating adults were told, "You and your child will not experience any risks from participating in this study" and they were encouraged to continue using pesticides in order to qualify for the study and earn monetary payments.

If third-parties are given the green light to conduct CHEERS-like studies without ethical standards, the EPA would open the door to industry-run studies that fail to inform subjects of the reasons for participation in the study and the possible harmful effects of continued exposure. The fact that "the exposures likely would have occurred anyway" should never be the basis for compromising the best interests of human research subjects, an inevitable result if the researcher isn't required to ensure subjects are fully informed of risks.

It is critical that studies such as CHEERS that the agency does not consider to be "intentional dosing studies" comply with the Common Rule so that participants are

protected by measures such as informed consent and independent review by an Institutional Review Board (IRB).

The Declaration of Helsinki states, "...in research on man, the interests of science and society should never take precedence over considerations related to the well being of the subject." This fundamental statement of human rights applies regardless of "intentional exposure." The EPA proposed rule falls well short of that standard.

The welfare of subjects must always outweigh research interests. The EPA cannot assert it is honoring that standard so long as it limits ethical standards and protections to participants involved in *intentional dosing* of *pesticides*.

### D. EPA Should Adopt a Comprehensive Approach.

It is ironic that EPA claims to be addressing the concerns of the public and members of Congress ignited by CHEERS with this proposed rule which offers no assurance of ethical standards for future studies identical to CHEERS but conducted by a third party researcher. If the agency fails to address this paradox in the final rule it should expect similar public outrage as it has experienced over the past year.

The Congressional mandate, which led to this proposed rule, is a response to EPA's continued insistence that CHEERS as designed was "ethically sound." EPA Administrator Steve Johnson so stated at an all-employee meeting in Denver as recently as June 2, 2005. If EPA is to have any credibility the final rule must –

- Not artificially limit ethical oversight to "intentional dosing" studies as defined by the agency;
- Create a consistent agency-wide approach for all human studies which EPA conducts, supports or relies upon;
- Not allow researchers to ethically observe, study or encourage ongoing harmful behavior or exposures of participants without fully informing them of the risks and ways to reduce those risks.

This Rule should create consistent standards for *all* research conducted, funded or used by all programs within EPA. The importance of creating an agency-wide approach now is underlined by absence of any timetable or commitment to a future "series of Agency actions" alluded to in the proposed rule.

To create uneven standards of subject protection in different EPA programs creates confusion both inside and outside the agency. This piecemeal approach will also force the agency to conduct additional and separate training for agency scientists and staff who review or oversee, or obligate grant money for such human subject research.

## II. Pregnant Women and Children Remain at Risk

### A. Proposed Rule Does Not Comply With Nuremberg Code.

In order to comply with the Nuremberg Code, and thus the 2006 Appropriations Act, the final rule must treat third-party research involving pregnant women, fetuses, newborns and children the same as first and second-party research and must ensure all members of these sensitive groups are protected against unethical research practices.

The proposed rule restricts the prohibition on testing of pregnant women and children to 1) intentional dosing studies conducted or supported by EPA and 2) third-party studies involving intentional dosing of pesticides. It therefore fails to prohibit EPA from relying on studies of pregnant women, fetuses, newborns and children submitted by third parties which fall outside its narrow definition of "intentional dosing." Also, the proposed extension of additional Common Rule protections for pregnant women, fetuses, newborns and children to studies involving other than intentional dosing methods does not apply to any third-party research.

The Appropriations Act directs EPA to promulgate its rules in accordance with "the principles of the Nuremberg Code with respect to human experimentation." Principle #5 of the Nuremberg Code states: *"No experiment should be conducted where there is a priori reason to believe that death or disabling injury will occur."* Principle #7 states: *"Proper preparations should be made and adequate facilities provided to protect the experimental subject against* ***even remote possibilities of injury, disability or death.****"* [Emphasis added.]

The rule as proposed does not offer a mechanism for prior review to ensure that the examples of studies mentioned above would meet these provisions of the Nuremberg Code. The sections of the final rule providing additional protections to pregnant women, fetuses, newborns and children should extend to 1) all categories of third-party research 2) intended for submission to EPA 3) involving any research methods 4) to study any class of environmental substances. This would enable the agency to identify and reject third-party studies designed in such as way as to violate the Nuremberg Code, thereby preventing human beings from being unnecessarily harmed by dangerous research practices.

**B. Infants and Children Will Be Subjects in Potentially Harmful Experiments.**

Under its proposed rule, these limited special protections and prohibitions would still permit EPA to rely on –

- "Observational" studies in which a pesticide manufacturer documented adverse effects to children from ongoing dangerous pesticide exposures which the manufacturer itself did not cause but which were normally occurring in the children's lives. Such studies could be conducted in countries where children are used to apply agricultural pesticides;

- Studies of children exposed to environmental hormone disruptors such as flame retardant polybrominated diphenyl ethers (PBDEs) for decision-making under the Toxic Substances Control Act; and

- Studies of fetuses and infants exposed to perchlorate in an effort to justify relaxed standards under the Safe Drinking Water Act.

Furthermore, sections 26.221 and 26.421 of the proposed rule, prohibiting EPA reliance on research involving intentional dosing of pregnant women, fetuses, newborns or children is limited to "its regulatory decisions-making under [FIFRA] or section 408 of the Federal Food, Drug, and Cosmetic Act." These sections should apply to research involving these sensitive classes of research subjects regardless of the statutory or regulatory scheme. Research relevant to any statute within EPA's jurisdiction has the potential to unethically place human subjects at risk, particularly when the subjects are of a sensitive class.

**III. Proposal Allows Undue Economic Inducements**

In the preamble to the proposed rule EPA "invites the public to comment on any specific provision of . . . the 2004 NAS report that may be appropriate for inclusion in the final rule." 70 Fed. Reg. 53,859. Perhaps the most glaring omission in this regard is the failure to include provisions that would protect all potential human research participants from undue economic inducement.

Payment for participation in human research was discussed by NAS in its 2004 report. NAS Recommendation 5-3 states:

> "[Instutional Review Boards], all relevant review boards, investigators, and research sponsors should ensure that payments to participants in intentional human dosing studies are neither so high as to constitute undue inducement nor so low as to be attractive only to individuals who are socio-economically disadvantaged. Proposed levels of and purposes for remuneration (e.g., time, inconvenience, and risk) should be scrutinized in light of the principles of justice and respect for persons.
>
> Moreover, EPA, in conjunction with other federal agencies, should consider developing further guidance on remuneration for participation in intentional human dosing studies, including guidance regarding whether remuneration should reflect the level of risk as well as the time and inconvenience involved."

EPA's proposed rule makes no mention of payment to participants. The final rule should include provisions for how the agency and the Human Subjects Review Board will protect all persons from undue economic inducement. At the very least, the agency should adopt the NAS recommendation by setting requirements that payment to participants be duly considered by all reviewing officials and people involved with the study.

Moreover, the agency should go beyond the NAS recommendation by protecting participants of other than intentional dosing studies from undue economic inducement. EPA must recognize that even research which could legitimately be considered passive observation, such as skin tests or urinalysis, can itself change behavior, especially in impressionable, socio-economically disadvantaged and trusting subjects. The risk is that when presented with the opportunity to participate in a study for payment, people may continue behavior or exposure which they have just been informed is potentially harmful. It is also entirely possible that potential participants would decide to adopt new behaviors to please researchers and qualify for the study's remuneration, falsely certifying that they already prescribed to the behaviors to be studied. The burden should therefore be on the agency to make sure that its first, second and third-party research does not allow for these unethical scenarios.

CHEERS, as described above, is an excellent example of why such safeguards are needed. The EPA should heed the public outcry over that study, which was largely centered on the cash and gift inducements, including over $900 and a camcorder, offered to participants who were intentionally recruited in socio-economically disadvantaged communities. Perhaps the most insidious incentive was that participants could keep the camcorder (and thus the home movies of their infant) only if they continued applying pesticides in the room primarily occupied by their infant for the entire two-year period of the study.

Disturbingly, EPA continues to defend CHEERS on the grounds that it was not designed to dose children with pesticides, all the while disregarding the high potential for poorly informed low-income families to change household pesticide use to qualify for a camcorder they may otherwise never have the resources to purchase.

These are undoubtedly the concerns behind NAS recommendation 5-3. EPA should adopt a process to ensure payment for participation is proper for all research that it conducts, supports, or relies upon in its decision-making, regardless of whether it involves intentional exposure as defined by the agency.

**IV. The Proposed Rule Allows Unjustified Exceptions to its Ethics Rules**

EPA proposes to rely on scientific data from studies conducted before the effective date of the final rule, "Unless there is clear evidence that the conduct of that research was fundamentally unethical (e.g., the research was intended to seriously harm participants or failed to obtain informed consent), or was significantly deficient relative to the ethical standards prevailing at the time the research was conducted." This is a stunningly low standard very similar to the highly criticized case-by-case review process EPA has been using for all human subject studies.

This provision would allow the agency to, for example, to set public health standards based upon some of the data from Nazi-era experiments, if it found such studies were not sufficiently deviant from "the ethical standards prevailing at the time."

According to a Congressional report prepared earlier this year for Senator Barbara Boxer and Representative Henry A. Waxman, the agency is in possession of at least 22 unethical human dosing studies submitted for use in EPA decision-making.[2] The studies reviewed for the report were found to have inflicted harm on human subjects, failed to obtain informed consent, and dismissed adverse outcomes as unrelated to the test chemical. The proposed rule is written in such a way as to allow the agency to rely on these unethical studies in setting public health standards.

The agency's view that ethical lapses must be "significant" indicates that EPA views "moderate" ethical lapses as acceptable. Even more alarming is the parenthetical offering "research intended to seriously harm participants" as an example of "fundamentally unethical." This indicates the agency is not deterred from relying on data from studies where the participants, even pregnant women and children, were harmed, so long as the harm was not intentional. This sends a chilling message about the level of concern the EPA has for keeping human subjects safe. Even from ostensibly "minor" ethical lapses such as paperwork violations (e.g., not fully protecting personal information) can have serious consequences for subjects.

Moreover, applying the Rule as a function of when the study was conducted indicates that EPA believes that the standards of human subject protection are situational, and may encourage future unethical studies by researchers in the hopes that the agency can be convinced to use them.

EPA must also be cognizant of the example it sets. Any use of unethical research by EPA encourages similar violations of ethics by entities which may use EPA's behavior as a standard, even if the research is never used or intended to be used by the agency. The preamble to the proposed rule even states that EPA's "rules might influence the conduct of a larger universe of research and thereby provide greater protection for human subjects." 70 Fed. Reg. 53,856.

The proposal also states that applying the Common Rule only to third-party research initiated after the effective date of the final rule "would allow researchers to come into compliance with the new requirements in an orderly manner." It is unclear what disorder would occur if EPA did not rely on the unethical studies it has in hand. The proposed rule suggests that EPA believes that it *needs* to rely on unethical research, or experiments on pregnant women, fetuses and children to make regulatory decisions. This is completely false. EPA should, as it has in the past, rely on data derived from studies not involving human subjects and the available *ethical* human data.

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[2] HOUSE GOVERNMENT REFORM COMMITTEE MINORITY STAFF AND THE OFFICE OF SENATOR BARBARA BOXER ENVIRONMENTAL STAFF, *HUMAN PESTICIDE EXPERIMENTS* (June 2005), *available at* http://www.democrats.reform.house.gov/Documents/20050616110407-47162.pdf.

Before EPA makes a decision to rely on data from human subject studies conducted before the effective date of the final rule, the individual or group submitting the information should prove to the agency that the study was conducted in accordance with the Common Rule and other human subject protections established by the final rule. This process should apply to all types of human subject studies and not be limited to intentional dosing studies being submitted for consideration under the pesticide laws.

The final rule should establish that EPA will not rely on studies that do not comply with the Common Rule regardless of when the research was conducted.

**V. The Proposed Catch-All Exception Undermines Ethical Standards**

Section 26.603 of the proposed rule would allow EPA to rely on studies that do not meet any of the proposed ethical standards or that involve intentional exposure of a pregnant woman, fetus, newborn or child if the data from such studies are "crucial to a regulatory decision that would be more protective of public health than could be justified without relying on the data."

This exception can be used to eliminate virtually any protection for human subjects proposed in the PR as well as to circumvent Congressional directives in EPA's 2006 Appropriations Act. The exception clearly states that the agency will use its loose provisions to "rely on data derived from a study that does not meet the applicable standards." EPA's promise to "include in the explanation of its decision a through discussion of the significant ethical deficiencies of the study" provides scant consolation.

EPA appears to be offering this catch-all exception, section 26.603, in lieu of sections included in the Department of Health and Human Services regulations allowing for use of otherwise unethical research if strict conditions are met. These HHS sections provided narrow circumstances where careful review by an IRB and the Secretary's consultation with a panel of experts would allow the agency to conduct or fund otherwise excluded research involving pregnant women, fetuses, neonates or children, so long as the study presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of the class.

Section 26.603 should not appear in the final rule in any form because it would cause the rulemaking to violate the Congressional mandate to prohibit all intentional dosing of pregnant women, infants and children. The language of EPA's exception does not provide for the rigorous review required in order for otherwise unacceptable studies to be used by HHS.

Furthermore, the EPA exception states that it will consider "whether the data are crucial to a regulatory decision that would be more protective of public health than could be justified without relying on the data" for ***every*** otherwise unacceptable study before rejecting it. 70 Fed. Reg. 53,866. This language in practice would mean that the default at EPA would be to accept every third-party study it can even if it involves intentional exposure of pregnant women and children. The threshold for ultimately rejecting an

admittedly unethical third-party intentional dosing study is a subjective decision by agency officials, only after "soliciting the views" of the inadequate Human Subject Review Board, as proposed, and providing an opportunity for public comment. This provides no assurance that humans will be protected from unethical third-party studies and it flies in the face of the Congressional mandate.

By drafting this language, EPA is seeking to use its mission to protect public health to justify unethical treatment of subjects. The phrase *"would be more protective of public health"* would allow EPA to use, for example –

- A study which caused permanent neurological damage to a small number of minority children, justified on the grounds that the study was necessary for registration of a pesticide that might prevent mosquito-borne disease in the larger population;

- Data derived from intentionally exposing fetuses to a novel pesticide, justified on the grounds that a pesticide which was registered based on such data would increase crop yields and lower the cost of foods important for children's nutrition;

- A study which released subjects' personal medical histories to their insurance companies, justified on the grounds that the study would support a new drinking water standard for the nation's water supply; and

- A study which exposed subjects, without informed consent, to dangerous levels of an inhaled toxicant, justified on the grounds that it led to a lower limit on that chemical's release to air.

Adoption of this provision would undermine this entire rulemaking process and reinforce the EPA's reputation for placing industry-influenced environmental standards above protection of human research subjects and internationally accepted human rights principles.

**VI. Proposed Rule Does Not Protect Prisoners and Other Captive Populations.**

EPA proposes to defer adopting any protections for prisoners, wards of the state or other involuntarily confined groups. In its proposal EPA attempts to explain this omission and the failure to adopt the HHS prisoner safeguards (45 CFR part 46, subpart C) because:

> (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."

Regardless of EPA's present intention, the proposed rule does not prohibit EPA from using research conducted with prisoners and specifically excludes prisoners from special

protections. In doing so, the proposed rule actually creates an incentive for third parties to use prisoner populations in research, as that research would be subject to fewer regulatory constraints.

To the extent that EPA regards the current subpart C of the Common Rule as too flawed to adopt, a superior approach would be for EPA to bar any conduct, support or use of studies conducted with prisoners until HHS revises Subpart C and EPA adopts the revision.

The current posture of EPA's proposed rule sends the unmistakable message that certain human subjects are not worthy of safeguards.

**VII. Proposed Human Subjects Review Board Lacks Independence.**

As proposed, the agency's rule does not assure that the new Human Subjects Review Board (HSRB) would be an independent, unbiased body. The final rule should include provisions to guarantee the HSRB created would have the specialized expertise needed to consider the diverse types of human subject studies submitted to the agency. Furthermore, the jurisdiction of the HSRB to review study protocols and reports of completed research should not be limited to "studies which EPA intends to rely on in its decision-making under FIFRA and FFDCA." 70 Fed. Reg. 53,863.

**A. Scope of Review is Too Narrow.**

The National Academy of Sciences recommended that EPA should establish an HSRB to review "...*all* studies . . . regardless of the sponsor or site of performance" (NAS recommendation 6-2, emphasis in original). The proposed rule, however, includes limitations that would place much of the research that EPA relies upon out of sight of the HSRB, including:

- All of EPA's first and second-party research;
- First and second-party research partially funded by regulated entities, such as CHEERS which received $2 million from the chemical industry; and
- Research which is outside the narrow definition of "intentional dosing" of pesticides.

The Congressional directive in EPA's 2006 Authorization Act to create a HSRB intended that the body would function as the NAS recommended, not hamstrung by restrictions on its oversight.

B. **Review Board is Too Small**.

EPA proposes that the HSRB be a "small group", but restrictions on its size could prevent the HSRB from effective and efficient review all of the research under its purview. It is instructive that the Centers for Disease Control and Prevention (CDC) employs an Institutional Review Board for each of its six divisions, and some of these boards have as many as 16 members. EPA should form an HSRB large enough to review all of the

research under its purview, and allow for expansion of that board should it prove necessary.

**C. Review Board Lacks Conflict of Interest Safeguards.**

The IRB organization employed by CDC provides that members of its HSRB do not have any conflict of interest. To be truly independent, EPA should enact strict recusal procedures to ensure that persons with financial or other ties to regulated entities do not review any studies which could affect those entities. It is unacceptable to allow HSRB members to review studies which might affect their own financial status, their employer, grantor or relative merely because they publicly state that they have a conflict of interest.

**D. Review Board Lacks Specified Expertise.**

The IRB organization employed by CDC also provides for the expertise necessary for review of wide ranging scientific and ethical characteristics of the studies needing review. In order to ensure EPA's HSRB has sufficient expertise to consider all types of human subject research, EPA should consider in the final rule creating the HSRB according to Common Rule Institutional Review Board specifications.

Furthermore, the HSRB should include, at the minimum: 1) an expert in the ethics of human subjects research; 2) a citizen representing populations vulnerable to coercion; 3) a clinician(s) and/or toxicologist(s); 4) an expert in the legal application of the Common Rule; and 5) appropriate subject matter expert(s). As with EPA's Science Advisory Board, EPA should establish appropriate standing committees to address the different types of studies to be reviewed.

**E. Review Board's Work Should Be Public.**

The HSRB should not be housed in any EPA Program Office, but should instead report to the EPA Administrator. In addition, all HSRB meetings should be announced in advance in the Federal Register; their meetings should be open to the public, and all of the information they review, and their final reports, with the exception of confidential business information, should be made publicly available.

## VIII. The Proposed Rule Suffers from Weak Enforcement.

The proposed practices to ensure ethical safeguards in research conducted, financed or relied upon by EPA are fundamentally flawed:

A. **Piecemeal Approach Invites Evasion.**

The penalties that EPA proposes are limited to third-party research submitted under FIFRA, indicating that EPA intends to take no action if it receives similarly unacceptable research under another statute. For example, the PR would allow EPA to use a study of pesticides on children to support decision-making under the Safe Drinking Water Act which it rejected for use under FIFRA because of unethical conduct.

If consequences for failure to comply are consistent across the agency EPA scientists or other employees who conduct, review or give grant monies for studies will have one set

of standards to apply, regardless of what EPA program they work in. Likewise, all entities submitting research to EPA will understand the standards to which their research will be held.

**B. Standard for Violation Impedes Enforcement.**

Section 26.505 (Debarment) states that EPA will require "repeated" or "egregious" violation of the regulations before it will recommend that an institution be declared ineligible to participate in EPA research. The terms "repeated" and "egregious" are not specifically defined. The context in which they are used suggests that EPA will ignore ethical violations unless they are so outrageous that they cannot be ignored.

It would behoove EPA to have clear standards for what would constitute actionable violations. Moreover, EPA should have a system of graduated penalties, rather than one single "one-size-fits all" penalty, so that the agency could apply sanctions to fit the offense.