Commentary

EPA To Allow Human Testing with Pesticides

Proposal provides inadequate protections

By Laura Hepting

The Environmental Protection Agency's (EPA) proposed rule to allow human pesticide testing and the use of resulting data for pesticide registration was published in the September 12 *Federal Register*. The rule (70 FR 53838) sets long-anticipated restrictions on human pesticide testing, while continuing to allow intentional dosing experiments and having little impact on other types of human pesticide studies. It falls short of providing adequate protection to human subjects and does little to ensure critical ethical guidelines will be followed. The rule, which amends 40 CFR Part 26 *Protections for Subjects in Human Research*, is open to public comment until December 12, 2005.

Background

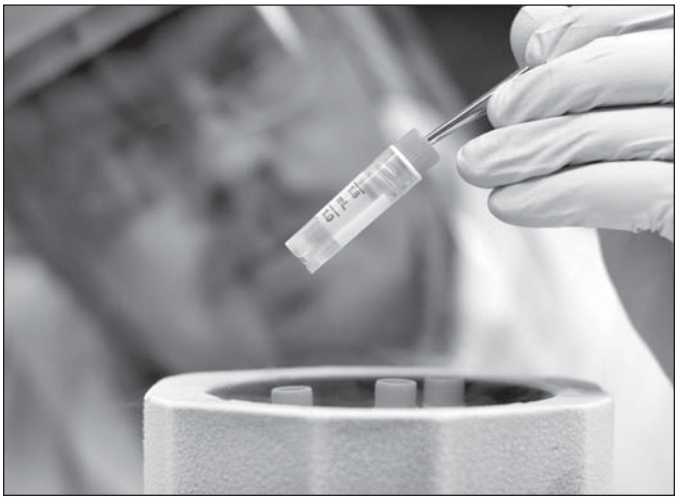
Human pesticide testing has long been a controversial issue, as human subjects have been used for decades in such tests by the chemical industry.[1] The last several years have been exceptionally contentious, resulting in a variety of reports, legal maneuvers, and committees. The issue, drawing widespread criticism over the rulemaking process, has escalated to the currently proposed rule.

EPA first addressed the ethical concerns inherent to human pesticide testing during the Clinton Administration, a period in which pesticide manufacturers were increasingly turning to human testing in attempts to reduce the uncertainty factors EPA uses for developing tolerable exposure levels (an unintended and unfortunate result of the *Food Quality Protection Act of 1996*). In response to the increase of human experiments and resulting public criticism, EPA Administrator Carol Browner enacted a moratorium in 1998.[2] EPA also created a joint committee to review the issue, which stressed the importance of rigorous ethics and stated that, "If the use of human subjects in pesticide testing can be justified, that justification cannot be to facilitate the interests of industry or of agriculture, but only to better safeguard the public health."[3]

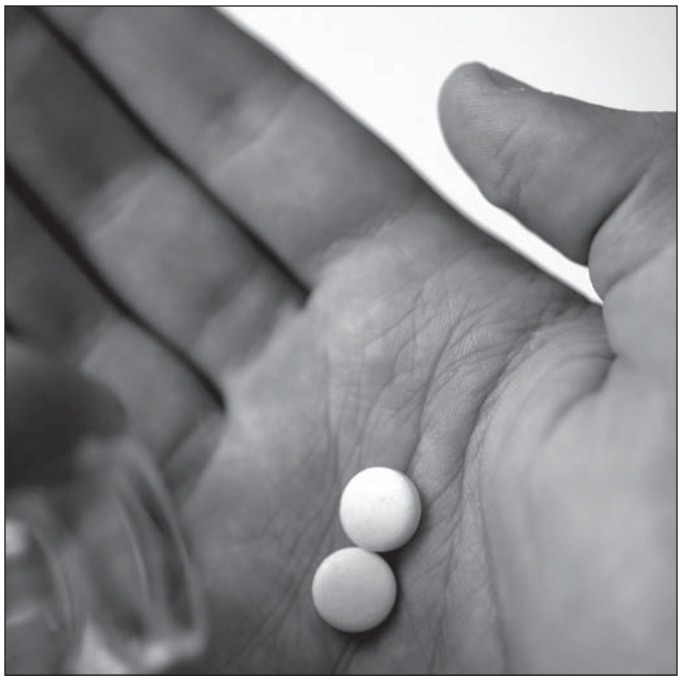
EPA ceased to use human pesticide experiments for consideration in the pesticide registration process for several subsequent years. Administrator Christie Todd Whitman upheld the moratorium, amid internal conflicts over EPA's human testing stance and a brief reversal of the ban in 2001, pending the completion of a review by the National Academy of Sciences (NAS).[4] The chemical industry challenged Whitman's moratorium by bringing suit in *CropLife America, et al. v. EPA*. The ban ended in 2003 when the U.S. Court of Appeals for the District of Columbia Circuit ruled that EPA's interim approach had not been established through required rulemaking procedures. The court also ruled, "as a consequence, the agency's previous practice of considering third-party human studies on a case-by-case basis, applying statutory requirements, the Common Rule,* and high ethical standards as a guide, is reinstated and remains in effect unless and until it is replaced by a lawfully promulgated regulation."[5] EPA made no effort to correct the procedural errors to reestablish a moratorium and continued its human testing policy without formal rulemaking or guidance.

In 2004, NAS completed its evaluation of the issue. The report, criticized as deficient and self-contradictory, concluded human testing with pesticides is ethical, and provided guidelines for developing regulations for human experiments. Regardless, EPA failed to acknowledge NAS recommendations and proceeded to accept third-party human pesticide studies without establishing a new rule to reflect NAS recommendations, and has continued to accept studies unless scientifically unsound or "fundamentally unethical."

In response, Senator Barbara Boxer (D-CA) and Representative Henry Waxman (D-CA) requested a congressional report on 22 studies that EPA provided out of a total of 24 the agency said it was reviewing or expected to review as of April 2005. Conducted from 1967 to 2005, approximately one-quarter of the studies were conducted in the United States. Review of the studies exposed gross scientific and ethical flaws, finding



* The Common Rule, promulgated by the Department of Health and Human Services (Subpart A, 45 CFR part 46), requires that all subjects are volunteers, adequately informed and equitably selected.



Studies dose subjects with pills containing pesticides.

the studies failed to obtain informed consent, used unethical liability waivers, lacked scientific validity, dismissed adverse outcomes, and failed to conduct long-term medical monitoring. Azinphos-methyl, carbofuran, chloropicrin, and dimethoate, as well as several other organophosphates, are examples of the pesticides that were used in the experiments through various exposure methods such as ingestion and inhalation. Methyl isothiocyanate, which is closely related to the chemical that killed thousands in Bhopal, India, was also tested. Under strict ethical guidelines, the majority of these studies would not be allowed, as many were designed to put subjects at risk, tested pesticides that already had a counterpart on the market, and advanced industry interests.

Congressional Action

After the overturn of EPA's ban on human pesticide experiments, Members of Congress made efforts to reestablish the moratorium. The first attempt, in 2003, was an amendment to EPA's budget bill that prohibits the agency from accepting, considering or relying on human pesticide testing. This amendment passed the House but was removed during conference.[6]

The second Congressional attempt to reenact a moratorium has led to the current rule in question. Earlier this year Representative Hilda Solis (D-CA) sponsored an amendment to the Interior Appropriations bill that prohibited:

> *… the use of funds by the Administrator of the Environmental Protection Agency to accept, consider, or rely on third-party intentional dosing human studies for pesticides or to conduct intentional dosing human studies for pesticides.*[7]

The amendment passed the House, and was followed by an identical amendment in the Senate, introduced by Senator Boxer, that also passed.[8]

However, a contradictory amendment on human pesticide testing sponsored by Senator Conrad Burns (R-MT) also passed, sending the issue to conference once again. The stated purpose of this amendment was:

> *[T]o direct the Administrator of the Environmental Protection Agency to conduct a review of all third party intentional human dosing studies to identify or quantify toxic effects.*[9]

The result was a compromised amendment that would continue to allow human testing, but would force an end to EPA's stalled rulemaking process. The language of the conference committee's report sets a temporary ban on human pesticide testing that will last until EPA implements the final version of the proposed rule. Several requirements for the final rule, including ethical guidelines, are included in the language of the committee's report:

> *None of the funds made available by this Act may be used by the Administrator of 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 the Administrator issues a final rulemaking on this subject. The Administrator shall allow for a period of not less than 90 days for public comment on the Agency's proposed rule before issuing a final rule. Such rule 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; and shall establish an independent Human Subjects Review Board. The final rule shall be issued no later than 180-days after enactment of this Act.*[10]

Upon completion of a draft rule, EPA's proposed rule on human testing was submitted for review to the Office of Management and Budget (OMB). The role of OMB is to review the rule, make recommendations, and give EPA the opportunity to make changes based on these recommendations. At the point EPA had submitted the internal draft to OMB, it was leaked to the public. This internal draft sparked strong criticism from medical experts, Members of Congress, environmental groups, EPA toxicologists, health experts, and lawyers. The general consensus was that the rules provided insufficient measures for protecting human subjects.[11] While some modifications were made to the language of the rule before it was published in the *Federal Register*, it still has many shortcomings.

Summary of Rule

The proposed rule, *Protections for Subjects in Human Research*, focuses on human testing that involves intentional pesticide exposure. Such tests are used to identify or measure toxic effects; examine absorption, metabolism, and other functions; test for insect repellent efficacy; and also includes some non-occupational exposure studies. EPA differentiates intentional dosing studies from other data collection tools (e.g., accident

and incident reports, epidemiological studies, and monitoring studies) available to EPA for risk assessment. Within intentional dosing studies, much of the rule discusses ethical guidelines and focuses on third-party testing of children and pregnant women.

The summary provided in the *Federal Register* reads:

> *EPA proposes and invites public comment on a rulemaking to ban intentional dosing human testing for pesticides when the subjects are pregnant women or children, to formalize and further strengthen existing protections for subjects in human research conducted or supported by EPA, and to extend new protections to adult subjects in intentional dosing human studies for pesticides conducted by others who intend to submit the research to EPA. This proposal, the first of several possible Agency actions, focuses on third-party intentional dosing human studies for pesticides, but invites public comment on alternative approaches with broader scope.*

Other pertinent issues addressed in the proposed rule include the extension of the Common Rule to third-party research, establishment of a Human Studies Review Board and the related role the Institutional Review Boards (IRBs) would play, deferral of additional protections for prisoners, consequences of non-compliance, and ethical standards used to determine whether to rely on human experiments conducted before and after promulgation of the rule for regulatory decisions.

Items for Comment

The following topics are major weaknesses in the proposed rule.

- **Observational studies excluded:** The proposed rule focuses only on intentional dosing studies. It excludes observational studies, which monitor the effects of pesticide use that is already taking place. However, as in the case of Los Angeles Unified School District, experimental and conditional use pesticides are often pushed on school districts and other institutions by the chemical industry (see "Governor Schwarzenegger Signs Bill Protecting Kids from Experimental Pesticides" on page 7 of this issue). It would also exclude studies such as the highly controversial, and at least temporarily derailed, Children's Environmental Exposure Research Study (CHEERS), which would have encouraged children's exposure to pesticides in the home. Senator Boxer called the CHEERS study "a reprehensible idea that never should have made it out of the boardroom." *For more information, see "EPA Cancels Study that Encouraged Children's Exposure to Pesticides" on page 4 of the Summer 2005 issue of* Pesticides and You *(Vol. 25, No. 2).*

- **Vulnerable populations:** Although pregnant women, infants and children are provided additional protections under this rule, populations vulnerable to coercion or undue influence are not. For example, EPA has chosen to defer the proposal of additional protections for prisoners even though the Department of Health and Human Services recommended EPA include additional protections for this population. Additionally, the proposed rule does not address additional protections for low-income and at-risk populations. Rather, EPA states the rule does not have an adverse impact on the environmental and health conditions of these communities, pointing out the rule does call for research procedures that ensure equitable selection of test subjects. However, to be adequate, additional protections must be extended to all vulnerable populations, including those with disabilities and those who already endure significant pesticide exposure on a regular basis.

- **Exceptions, exceptions, exceptions:** Loopholes in the proposed rule undermine the basic tenets that should be established. The rule states that *"under no circumstances"* will EPA, or an entity that submits findings to EPA from intentional dosing studies, be permitted to "*conduct or support research involving intentional dosing of any pregnant woman, fetus, or newborn."* However, another provision states, *"EPA shall not rely on any research involving intentional dosing of any pregnant women, fetuses, or newborns, except when such research is deemed scientifically sound and crucial to the protection of public health."* In other words, testing is prohibited on women and infants, yet EPA may still accept data from such studies, contradicting its categorical prohibition on such experiments.

  The proposed rule addresses intentional dosing of children under a separate provision. Within this provision, the rule is again undermined: *"[R]esearch conducted or supported by EPA outside the United States … in appropriate circumstances, the Administrator may … waive the applicability of some or all of the requirements of these regulations."* And again, EPA does not allow data from studies that involve intentional dosing of a child for consideration, *"except when such research is deemed scientifically sound and crucial to the protection of public health."*

  Another provision states, *"EPA will conduct or fund research in which the IRB finds that no greater than minimal risk to children is presented."* Additionally, when greater than minimal risk is expected, *"EPA will conduct or fund research in which … the risk is justified by the anticipated*

benefit … the risk is at least as favorable to the subjects as that presented by available alternative approaches . . . provisions are made for soliciting the assent of the children and permission of their parents or guardians." Even further problematic under the provisions affecting children in the proposed language, *"even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement."* As far as parental/guardian permission, the proposed rule reads, *"for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements."* This language increases children's vulnerability, rather than offering adequate protection.

- **Failure to establish hard-line rules:** EPA shies away from providing firm incentives not to conduct unethical experiments. Provisions of the rule allow EPA to rely on research conducted before the rule is enacted, unless 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 at the time."* (Note words such as fundamentally, seriously, and significantly leave the language of the rule open to interpretation.)

  Research accepted after promulgation of the rule, subject to these exceptions, will lead to circumstances that allow prohibited studies to be used by EPA. It is also worth noting that EPA's refusal to accept a study is the last action listed under the options for possible consequences of noncompliance.

- **The slippery slope of ethics:** In the end, the entirety of the proposed rule boils down to ethics. When reviewing such international ethical guidelines like the Nuremburg Code, with which Congress requires EPA to comply, it is hard to imagine any circumstance where there would be pesticide benefits that justify the intentional dosing of human subjects. The rule does establish an Independent Review Board to review proposed studies, and the Board will approve a study *"only if risks to subjects have been minimized and are reasonable in relation to anticipated benefits."* However, EPA does not by practice or rule generally evaluate the actual need for a pesticide to determine whether there is a less toxic approach to managing a defined pest. According to ethicists, there must be a highly significant societal benefit to justify jeopardizing the health of individuals. Pesticide testing is carried out by chemical companies in order to provide data for EPA registration, which then allows widespread human and environmental exposure. However, according to advocates, human testing of pesticides, which frequently have less-toxic equivalents, has no societal benefit.

Take Action: Submit Comments to EPA and Your Elected Officials

Please let EPA know the public will not tolerate weak ethical standards, especially in a rule that allows people to be exposed to unnecessary and potentially detrimental health risks and that the proposal fails to comply with the Congressional mandate. Comments should be received on or before December 12, 2005, but can be sent after that date. Send comments by e-mail to **opp-docket@epa.gov** or by mail to Public Information and Records Integrity Branch (PIRIB) (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, 1200 Pennsylvania Ave., NW, Washington, DC 20460-0001. Include "Docket ID Number OPP-2003-0132" in all comments to EPA.

When the comment period has ended or to improve the impact of your comments to EPA, send comments on human testing to your Senators and Members of Congress. Much of the movement on this issue has been initiated in Congress and may continue as a result of Congress responding to public outrage. To determine your Senators and Member of Congress, visit **www.congress.org** or contact Beyond Pesticides.

Citations

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