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FLASH REPORT

NEW EPA PROPOSAL ENCOURAGES HUMAN PESTICIDE EXPERIMENTS

PREPARED FOR

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EXECUTIVE SUMMARY

The Environmental Protection Agency has drafted a rule, slated for proposal next month, which will allow the systematic testing of pesticides on humans. The rule does not comply with the recommendations of the National Academy of Sciences and EPA's own advisory committee, and it contains multiple loopholes that invite abuse.

Human pesticide experiments are controversial. Unlike pharmaceutical products, pesticides are designed to be toxic. And unlike pharmaceutical studies, experiments that expose human subjects to doses of pesticides offer no promise of therapeutic benefit to the subjects. For these reasons, former EPA Administrator Carol Browner implemented a moratorium in 1998 on considering or relying upon human pesticide experiments.

The Bush Administration reversed this moratorium at the urging of pesticide manufacturers. As described in a recently released report, EPA is evaluating dozens of human pesticide experiments that contain serious ethical and scientific flaws. In fact, new documents reveal that EPA used one experiment despite a written finding by agency officials that the experiment showed "little concern for the safety or welfare of the research subjects."

The proposed rule being developed by EPA would further legitimize experiments that intentionally dose humans with pesticides. The rule fails to establish a national review panel to prevent abusive experiments, fails to provide full protections for children and other vulnerable populations, and includes multiple loopholes that undermine its effectiveness.

I. EPA CONSIDERATION OF FLAWED HUMAN PESTICIDE EXPERIMENTS

On June 16, 2005, Senator Barbara Boxer and Representative Henry A. Waxman released a report entitled *Human Pesticide Experiments*.[1] This report contained a detailed analysis of 22 human pesticide experiments that EPA is reviewing as part of its efforts to set exposure standards for pesticides. The report found that the experiments were rife with ethical and scientific defects. Some of the experiments put human subjects at risk of significant harm without any promise of health or environmental benefit. Others failed to obtain the informed consent of subjects, dismissed adverse outcomes, or conducted no long-term medical monitoring.

New documents now confirm that EPA has considered and relied upon a human pesticide experiment that even its own officials consider unethical. The experiment involved methyl isothiocyanate (MITC), a dangerous chemical that is closely related to methyl isocyanate, the chemical that killed thousands in Bhopal, India. MITC is a breakdown product of the pesticide metam sodium, one of "the most widely used agricultural pesticides in the U.S. with an estimated total of 51 million pounds applied annually."[2] The experiment was sponsored by the Metam Sodium Task Force, a consortium of pesticide manufacturers formed to share the costs of developing defensive data following a spill of metam sodium into the Sacramento River.

The MITC experiment had two parts. First, 33 subjects inhaled methyl isothiocyanate to determine the human odor detection threshold. Second, the eyes of 70 test subjects were exposed to methyl isothiocyanate through modified laboratory safety goggles for up to eight hours. Some subjects reported that the eye irritation they experienced neared or reached the "maximum" level. No informed consent forms were provided to EPA.[3]

EPA staff reviewed the MITC experiment for ethical considerations and documented the review in a January 23, 2004, memorandum entitled, "Ethical

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1 Minority Staff of the House Government Reform Committee and the Office of Senator Barbara Boxer, *Human Pesticide Experiments* (June 2005) (online at http://www.democrats.reform.house.gov/story.asp?ID=869).

2 U.S. Environmental Protection Agency, *Metam Sodium/Metam Potassium: The HED Chapter of the Reregistration Eligibility Decision Document (RED)* (Aug. 19, 2004).

3 Michael J. Russell and T.I. Rush., *Methyl Isothiocyanate: Determination of Human Olfactory Detection Threshold and Human No Observable Effect Level for Eye Irritation* (Sept. 10, 1996).

Screen of Human Studies with MITC."[4] According to the agency memo, the societal benefit of the experiment was "not clear" and the risk-benefit ratio was "not clearly favorable."[5] The memo also reported that there was insufficient information to assess the independence or the quality of ethical review or the quality of the informed consent. The memo concludes: "In summary, this study as reported shows little concern for the safety or welfare of the research subjects."[6]

Despite these concerns, EPA considered and relied upon the MITC study in the completion of the revised human health assessment for metam sodium.[7] In fact, the memo itself states: "I am aware of no barrier in current law or Agency policy to your giving this study full consideration in your risk assessment."[8]

II. THE EPA REGULATORY PROPOSAL

In response to criticism of its review of human pesticide experiments, an EPA spokesman said earlier this month that the agency "is expediting the process to issue its first-ever regulation."[9] Consistent with this statement, EPA circulated internally a draft proposed rule among EPA's various offices on June 20, 2005. According to the Director of the Regulatory Coordination Staff in EPA's Office of Prevention, Pesticides and Toxic Substances, the draft rule was circulated to provide a "final opportunity" for comments before the rule is submitted to the White House for review.[10] A draft agency communication plan indicates that EPA projects the proposal to be announced in late July 2005.[11]

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4 U.S. Environmental Protection Agency, *Ethical Screen of Human Studies with MITC* (Jan. 23, 2004).

5 *Id.*

6 *Id.*

7 U.S. Environmental Protection Agency, *Metam Sodium/Metam Potassium: The HED Chapter of the Reregistration Eligibility Decision Document (RED)* (Aug. 19, 2004).

8 *Ethical Screen of Human Studies with MITC, supra* note 4.

9 *EPA Using Data From Chemical Tests on Humans*, Washington Post (June 17, 2005).

10 U.S. Environmental Protection Agency, Memorandum from Angela Hofmann, Office of Prevention, Pesticides, and Toxic Substances, to Action Development Participants (Workgroup Members/Contacts) (June 20, 2005).

11 U.S. Environmental Protections Agency, Draft Communications Plan; Protections for Test Subjects in Human Research; Proposed Rule (June 20, 2005).

A copy of the proposed rule was obtained by the offices of Rep. Hilda Solis and Sen. Barbara Boxer. According to the draft, the goals for the draft proposed rule are (1) to strengthen protections for human research subjects, (2) to ensure scientifically sound data are considered and used appropriately, and (3) to ensure new burdens imposed on researchers and the Agency are reasonable.[12]

In fact, the draft proposal omits key safeguards recommended by the National Academy of Sciences and an expert EPA advisory committee. It also contains significant loopholes that will undermine its effectiveness.

III. FAILURE TO ESTABLISH AN EXPERT REVIEW BOARD

In 2002, the National Academy of Sciences convened a panel to examine the issue of intentionally dosing human subjects with pesticides and other toxic substances. The report of the National Academy of Sciences recognized that these experiments can be "troubling" and in some cases "repugnant."[13] For this reason, the Academy concluded that to be "ethically justified," a human pesticide experiment must pass "rigorous scrutiny on both scientific and ethical grounds."[14]

To address these ethical issues, the National Academy of Sciences recommended that EPA establish a "Human Studies Review Board."[15] According to the Academy, a specialized board could develop the expertise needed to evaluate the complex ethical and scientific issues raised by human pesticide experiments. The Academy recommended that all proposed human pesticide experiments be reviewed and approved by this expert EPA board in addition to the regular institutional review boards (IRBs) at the laboratories actually conducting the experiments. In the Academy's view, "it was not clear to the committee that local IRBs can be expected to conduct a thorough assessment of this kind of research."[16]

The draft regulations do not include this key safeguard, however. EPA states, "The Agency has decided not to include any proposed requirements relating to a

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12 U.S. Environmental Protection Agency, Final Agency Review Draft, Protections for Test Subjects in Human Research; Proposed Rule at 11 (June 20, 2005).

13 National Academy of Sciences, *Intentional Human Dosing Studies for EPA Regulatory Purposes: Scientific and Ethical Issues* (Feb. 2004) (cited hereafter as the "NAS Report").

14 NAS Report, *supra* note 13 at 112.

15 NAS Report, *supra* note 13 at 135.

16 NAS Report, *supra* note 13 at 137.

Human Studies Review Board" as suggested by the National Academy.[17] The rationale provided by the agency is that acting upon the Academy recommendation would "unnecessarily confine EPA's discretion."[18]

The failure to establish a Human Studies Review Board could substantially undermine the proposed rule. The report released by Sen. Boxer and Rep. Waxman revealed that many of the unethical pesticide experiments currently being considered by EPA were reviewed by IRBs associated with the private laboratories chosen by the pesticide manufacturer that sponsored these studies. These IRBs did not do an effective job in screening out improper studies. To the contrary, they affirmatively approved experiments that failed to obtain proper informed consent and included improper waivers of liability, among other violations.[19]

IV. FAILURE TO PROVIDE FULL PROTECTIONS FOR CHILDREN AND OTHER VULNERABLE POPULATIONS

In July 1998, EPA convened a joint advisory committee to examine human pesticide experiments. The joint committee was made up of EPA's Science Advisory Board (SAB) and the Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP). Like the National Academy of Sciences, the advisory committee found that these experiments pose difficult ethical issues.

One of the key recommendations of the advisory committee was opposition to pesticide experiments upon children and adolescents. The committee stated that pesticide experiments involving children were "ethically unacceptable" because "[t]here are too many unknown dangers to justify the effort, even under the most extraordinary circumstances."[20] The committee concluded: "In no case should developing humans (i.e., the fetus, infant, young children, or adolescents) be exposed to neurotoxic chemicals."[21]

The EPA proposal does not contain these prohibitions. Instead, it would allow pesticide manufacturers to conduct experiments on children so long as the

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17 Final Agency Review Draft, *supra* note 12 at 21.

18 Final Agency Review Draft, *supra* note 12 at 21.

19 *Human Pesticide Experiments, supra* note 1.

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

21 *Id.*

institutional review board at the laboratory determined that the risk was no greater than "minimal."[22] According to the National Academy of Sciences, this is not an appropriate standard because "the concept of minimal risk [is] of limited value as a guide to decision making in the context of human dosing studies."[23] As EPA itself recognizes in the draft rule, the Academy panel "could not conceive of any situation in which an investigator … could satisfy the ethical standards for testing a toxic material on children to determine whether (or at what level) it caused adverse effects."[24]

The National Academy of Sciences recognized the need for additional protections for other vulnerable populations, such as persons with mental disabilities. The Academy stated:

> it is not justifiable to enroll persons who lack the capacity to consent to their involvement … when the research offers them no prospect of direct personal benefit and carries more than minimal risk or when the needed information could be obtained through studies with individuals who have the capacity to consent.[25]

Contrary to these recommendations, however, the EPA draft proposal contains no additional safeguards for the mentally ill or other vulnerable populations. In fact, the draft proposal does not even discuss the need for protection for persons with mental disabilities.

V. MULTIPLE LOOPHOLES

In additional to these problems, the draft rule contains multiple loopholes. These loopholes significantly limit the scope of the protections in the rule, allow EPA to consider human pesticide experiments that violate the rule, and permit EPA to continue relying on old unethical studies.

Narrow Definition of Covered Experiments. By its terms, the draft regulation applies to only a subset of experiments with pesticides that may be conducted upon humans. The regulation does not apply to a human pesticide experiment

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22 Final Agency Review Draft, *supra* note 12 at 59.

23 NAS Report, *supra* note 55 at 115.

24 Final Agency Review Draft, *supra* note 12 at 26.

25 NAS Report, *supra* note 13 at 115.

unless (1) the experiment is "intended" to identify or quantify a toxic effect and (2) the experiment is conducted for submission to EPA's pesticide program.[26]

There are multiple problematic experiments that could be conducted that fall outside of this narrow scope. Under EPA's proposal, human test subjects, including children, would not be subject to any protections unless the stated objective of the experiment is to identify or quantify a toxic effect. Under this standard, an experiment in which human subjects are administered pesticides for other purposes — for example, to measure how a pesticide is metabolized in the body — would not be subject to the EPA regulation.

Similarly, human subjects would not be protected by the rule if the sponsor or researcher maintained that "at or before the time [the experiment] was initiated," there was no intention to submit the experiment to EPA's pesticide program.[27] Under this limitation, unscrupulous sponsors could conduct a wide range of human pesticide experiments without complying with the protections of the rule.

Consideration of Experiments that "Substantially" Comply. The EPA draft proposal does not require that pesticide experiments comply with its new standards. To the contrary, EPA proposes to accept all experiments as long as they "substantially" comply.[28]

This provision overtly undercuts the protections in the rule. The vague standard of substantial compliance sends the signal that EPA will not demand strict adherence to ethical standards in human pesticide experiments.

Consideration of Old Unethical Experiments. The National Academy of Sciences recommended that EPA not use studies concluded before the issuance of its rules that are "deficient relative to then-prevailing ethical standards."[29] EPA proposes to modify this standard to limit consideration of only those experiments that are "significantly deficient" compared to prevailing ethical standards, stating that refusing to rely on data should be reserved for only the most egregious conduct.[30] In effect, this provision rewards pesticide manufacturers that violated ethical standards in human research.

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[26] Final Agency Review Draft, *supra* note 12 at 14.

[27] Final Agency Review Draft, *supra* note 12 at 16.

[28] Final Agency Review Draft, *supra* note 12 at 42.

[29] NAS Report, *supra* note 13 at 20.

[30] Final Agency Review Draft, *supra* note 12 at 41.

VI. CONCLUSION

Human pesticide experiments are inherently controversial. They involve intentionally exposing human subjects to chemicals that are designed to have toxic effects. EPA's draft regulation would legitimize and encourage these experiments. Moreover, the regulation lacks key safeguards for ensuring that human pesticide experiments are conducted in an ethical manner. The regulation fails to adopt key recommendations of the National Academy of Sciences and EPA's own advisory committee, and it includes loopholes that invite abuse.