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Chapter 4 - Risk Assessment and the Precautionary Principle

4.4.3.2 Human Testing of Pesticides

Perhaps the most unexpected and certainly the most perverse result of the new 10-fold safety margin intended to protect children, is the recently renewed[1] and increasing practice, by pesticide companies, to seek and often pay human "volunteers" to test for pesticide NOAEL's. The intention of this renewed testing is to eliminate one of the core 10-fold uncertainty factors by providing data on a NOAEL derived directly from experiments on humans. The result, if these studies are accepted, could well be to *increase* pesticide tolerances directly as a result of the passage of the supposedly child-safety-focused FQPA. Said another way, the FQPA requirement for an additional safety factor has unintentionally created an incentive to test pesticides in humans.[2]

At least twelve unpublished studies conducted by pesticide companies have been submitted to EPA and more are expected. They are systemic toxicity studies to establish a human NOAEL. Most were conducted in England and Scotland, often seeking volunteers from among company employees or offering to pay "volunteers" from the public at large.

The pesticides most commonly being studied in the human experiments are organophosphates and carbamates, the two categories of pesticides that have been the subject of the most heated debate in the U.S. during their reevaluation. The FQPA requirement to address the riskiest first as well as to first aggregate exposure from, and then assess chemicals with, common mechanisms of toxicity led to an initial focus on these two groups of pesticides. Since the 10-fold safety margin would be very likely applied to chemicals known or strongly suspected to negatively affect developing nervous systems, human testing offers a potential way out of lower tolerance levels.[3]

The human testing of pesticides has arisen within a policy vacuum at the EPA. It has been greeted with disgust and outrage and is opposed on moral, ethical and scientific grounds by the public interest, farmworker, religious, environmental, consumer, health

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[1] *Ibid*.; the 1972 study cited therein is: Coulston, F., L. Golberg, and T. Griffin, 1972. Safety Evaluation of DOWCO 179 in Human Volunteers, Institute of Experimental Pathology and Toxicology, Albany Medical College, Albany, New York. MRID No. 95175. HED Doc No. 000179, 03822, 04363.

[2] Staff Background Paper for November 30, 1999 Meeting of SAB/SAP Joint Subcommittee on Data from Human Subjects. Available at: www.epa.gov/oscpmont/sap/1999/november/background-1130.pdf

[3] Indeed, the process of revising down tolerances for these chemicals according to an additional 10-fold safety factor might well conclude that many ought to be banned to ensure avoidance of children's health effects.

and medical communities in the United States.[4] A 1998 report[5] and subsequent evaluations by the above-noted groups have charged that the practice is scientifically dubious and ethically indefensible. When the story hit the headlines in 1998, the EPA responded with concern and referred the matter to its independent Science Advisory Board for advice.

The referral to the Science Advisory Board (SAB) has resulted in a deeply controversial investigation. A Joint Science Advisory Board-Science Advisory Panel (SAB/SAP) Subcommittee on Data from Human Subjects is advising on policy to ensure that EPA can rely on data meeting the highest ethical and scientific standards.

The standard approach to toxicity testing at EPA has been the use of its authority to specify what tests are required and how they should be performed (via the guidelines discussed above). EPA has never developed guidelines for testing pesticide effects or establishing NOAELs in humans nor have such tests been considered necessary, or to be encouraged.[6] Pesticide companies and their farming supporters argue that human tests are more appropriate and reliable in making accurate estimates of human health risk during a risk assessment exercise.[7] In seeking the SAB/SAP committee's advice, EPA wants a policy that applies the protection of the Common Rule (see below) to this new area of inquiry but that also recognizes the wide range of human research that already exists in less controversial circumstances. EPA notes that general standards of conduct will apply to all research but specific standards of conduct and acceptability are necessary in this new area of research.

The SAB/SAP Committee has not been able to agree on this contentious issue. The rift in the Committee has delayed the setting of a policy by EPA. At issue has been debate over whether this testing, as science, is dubious or ethical. John McCarthy of the American Crop Protection Association states that testing pesticides on humans is no different from testing the toxicity of new drugs. Bioethicists disagree pointing out that pesticides are not therapeutic agents.[8]

The comparison to clinical drug trials is important because it takes this issue directly and appropriately into the field of medical ethics. The history of abuse within medical experimentation is a horrific tale. It runs the gamut from the appalling practices of systematic torture and total control over "patients" by the German Nazi doctors through to the Tuskegee syphilis study[9] and the seminal work of Henry Beecher.[10] The history of abuse has provided

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[4] See multiple letters to Carol Browner, Administrator, United States Environmental Protection Agency, from the farmworker community (www.cehn.org/cehn/farmltr.html), the religious community (www.cehn.org/cehn/reliltr.html), the consumer and environmental community (www.cehn.org/cehn/consltr.html) and the health and medical community (www.cehn.org/cehn/htletter.html) Re: Human Testing of Pesticides, November 18/19, 1999.

[5] Environmental Working Group, *The English Patients: Human Experiments and Pesticide Policy*, July, 1998. Available at: www.ewg.org

[6] Staff Background Paper for November 30, 1999 Meeting of SAB/SAP Joint Subcommittee on Data from Human Subjects. Available at: Available at: www.epa.gov/oscpmont/sap/1999/november/background-1130.pdf

[7] Stroshane, T. 1999, *op.cit.*

[8] Ibid.; Staff Background Paper, *op.cit.*; and Joint SAB and SAP Open Meeting, November 30, 1999. Data from Testing on Human Subjects Subcommittee, Baskerville Transcription, Vienna, VA. Available at: www.epa.gov/oscpmont/sap/1999/november/jointsab.sap.pdf

[9] The Tuskegee syphilis study was one of the most condemned experiments in US medical history. Although a cure for syphilis was found during the course of this multi-year investigation, the hundreds of

detailed understanding of the conditions necessary for ethically justifiable research. The Nuremburg Code was the first attempt to enshrine ethical conduct in medical research; the most recent expression of policy for the protection of human subjects in research is The Common Rule.[11]

Two mandatory components of such rules have included the notion of informed consent and a responsible investigator. While it is beyond the scope of this report to explore the details of these two components, several important points are relevant. First, there is a crucially important set of conditions to be met for the ethically justified medical research on humans. There are issues of scientific adequacy, therapeutic value, protection of subjects and informed, comprehending and voluntary consent. As a two-way transaction, informed consent is a matter of shared decision-making. Hence, informed consent is considered possible only between adults, not between an adult and a child. The irony here is brutal since the experiments conducted by pesticides companies on humans are being done for the purpose of avoiding safety factors intended to protect children.

A key aspect of the notion of a responsible investigator revolves around the central ethical problem of medical experimentation. Beecher's work addressing the continuum of abuse noted above found that while the Nazis had a systemic and racist contempt for their subjects, the less horrendous forms of abuse in medical research stem from a conflict of goals of the physician-researchers. Beecher found that the central ethical problem of medical experimentation concerned balancing the interests of individual subjects with the goals of both helping future patients and advancing careers. Clearly, a central issue to consider in the applicability of The Common Rule to toxicity testing of pesticides on human subjects is the vested interests of pesticide company investigators. Research results that would enable sustained or increased pesticide sales are comparable to the conditions upon which ethical conduct rules have had to be established within the sphere of medical research.[12] A related issue in these studies is whether the alleviation of poverty motivated the human subjects to participate.

TheSAB/SAP Subcommittee on Data from Human Subjects met in December of 1999 to re-consider these issues after failing to agree on policy proposals at an earlier meeting in August. No policy has yet been proposed by the committee or EPA. Meanwhile, EPA states that it expects to receive more results from pesticides companies conducting human testing for pesticide toxicity. As unpublished reports, the nature of informed consent within these studies is not the subject of independent peer review. Nor is there any independent review on the extent to which The Common Rule is being applied.

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poor southern black men infected with the disease and involved in the study were not given treatment so that researchers could learn more about the disease by seeing the study through to its fatal conclusion.

[10] Henry Beecher wrote the seminal work in medical ethics in the 1960s after conducting an exhaustive review of unethical conduct in medical research. He drew distinctions between the most heinous examples of the Nazi doctors and the Tuskegee syphilis study but also found extensive unethical conduct within medical studies reported in the peer-reviewed medical literature.

[11] The Federal Policy for Human Subjects Protections (The Common Rule): From the *Final Report, National Committee on Human Radiation Experiments, 1995,* (as reproduced in Environmental Working Group, 1998, *op.cit.*), sets out the responsibilities and obligations of those conducting research on human subjects to ensure protection of their subjects rights and well-being and to ensure the application of informed consent requirements.

[12] For two reviews of these issues see: Roy, D.J., J.R. Williams and B.M. Dickens, *Bioethics in Canada,* Chapter 13: When Treatments are Uncertain: The Ethics of Research with Human Beings, Prentice-Hall, 1994; and Pence, G.E., *Classic Cases in Medical Ethics,* Chapter 9: The Tuskegee Syphilis Study, McGraw-Hill Inc. 1990.