Human exposure to pesticide testing and experimentation are not warranted without a stringent ethical review.

Environmental Ethics

The U.S. Environmental Protection Agency (EPA) held the first meeting on environmental ethics sponsored by the Scientific Advisory Panel and Board on 10–11 December 1998 in Arlington, Virginia (*1*). The report from the meeting will more completely inform scientists and the community of current issues. This editorial should serve as an initial brief of this meeting [which was held on the fiftieth anniversary of the Declaration of Human Rights (adopted by the United Nations on 10 December 1948)].

A number of chemical pesticide manufacturers now use human subjects in their pesticide studies. This is to ascertain and develop biomarkers, to examine agricultural worker exposure, and primarily to better understand human exposure and risk. The human studies, many in other countries, are an attempt to establish new safety factors, usually to implement the broader use of a pesticide or to establish human no-observed-adverse-effect levels (NOAELs) for new agents being developed. Much of the justification for these private human research studies is based on the human drug paradigm. Further, these studies are typically presented to the EPA without their prior knowledge and without standing EPA human studies and ethics committees to review these studies. If an ethics committee were active, the accepted ethical basis of these studies would be the "Common Rule" or policy [40 CFR 26 (*2*); less restrictive than the Helsinki Declaration (*3*) or Article Five of the Nuremberg Code (*4*), which requires researchers to participate in their own studies; Common Rule also urges more children and women to participate, which would not be operative in this scenario. Surprisingly, it has also been reported that pesticide patch tests have been performed on teenagers with parental approval, and pesticides have been administered to patients with Alzheimer disease (*1,5*)].

Criteria for various human studies are available, but they vary from country to country if not hospital to hospital (institutional review boards, who are already overburdened, may suffer conflict of interest when approving internal studies of their colleagues). Given these complexities that bedevil the hospital and medical school human research communities, it seems that criteria for human studies are quite new and complex in agribusiness and in the regulatory community, where a long tradition of human studies does not exist.

One primary use for these studies is regulatory. These studies are not instituted to improve general or population health care directly (like a drug), nor are they constructed to improve the health of an individual suffering from a disease. These agents are accepted as toxic, and their regulatory toxicology (not scientific toxicology) is being defined. These studies fall into "risk–risk" assessment, not "risk–benefit," which is the classical model of drug study design. It is not common practice to administer a toxic compound; for example, we do not administer lead to children to ascertain risk [although historically lead was administered to adults to ascertain risk (*1*)]. Some "trivial risk" studies with ozone have been performed, but these must be examined individually. It is a matter of concern that known toxic agents, many of which are neurotoxic, have been administered, even when the state of the scientific art at this time cannot demonstrate harm (although with future technology, harm may be more evident); even the smallest details of these decisions must be questioned. These studies should not be performed without a complete review of all of the animal studies available (typically voluminous and sometimes overlooked). Further, use of these agents with the intent to alter existing regulations should not be allowed without a complete review of poison control center reports, in which thousands of cases are recorded (although they are not reported under accepted human studies circumstances).

Another major concern is remuneration: organizations that perform these studies recruit people who may receive $600–800/week, but, at the initial time of recruitment, the subjects may not appreciate what agents they will be exposed to. This quandary is avoided by paying people for time spent, not for the actual risk exposure of the experiment. Also, money is used to reward agents for supplying patients; this offers opportunities for ethical conflict. Many of these volunteers will likely be people from lower socioeconomic levels who will not derive direct significant personal benefit, or people who have already been exposed to high levels of other similar agents (e.g., agricultural workers and their families, or residents of inner-city urban areas where indoor air quality, pesticides, and vermicides may be evident, although this may not be documented before testing or other experimental exposures). Although "proper" informed consent may be obtained during experimental initiation, the concept of duress by economic incentive cannot be dismissed. Obviously, few if any of these studies are initiated by investigators who normally achieve funding from independent agencies. These studies are most often conceived by corporations who seek investigators (and pay them well) (*1*); are these investigators able to avoid corporate influence and bias? Further, these studies typically remain unpublished and exist as confidential information for the company; these studies would have to be duplicated by another company developing similar products before the results could be released (still not to the public, because these results are "confidential business"). This also raises ethical concerns.

Even if a small population is recruited for these pesticide studies (usually 4 controls and 12 experimental patients), they are usually not applicable to children, the elderly, and certain patients on heart, psychiatric, or neurologic drugs. These are huge populations, as are all of the special populations in the United States.

Regarding possible consideration and justification for human testing, the actual chemical and agricultural industry workers who produce the pesticides in factories, as well as farm workers and their families (children can be many times overexposed to these agents) are stakeholders in human studies. They understand that the results of human studies may apply very directly to them. Ultimately, these types of studies should only be allowed when no alternatives are available.

We appear to be in an early era of environmental human testing. Similarly, when we were in this era in genetic research (far more cogent to humans who were suffering from diseases for which the gene or its product would lead to cure), we called a moratorium on human research until our social and ethics policies could catch up (these policies are coupled and must move forward in tandem). Human exposure to pesticide testing and experimentation are not warranted without a stringent ethical review. Further, it is time for the EPA to consider developing a standing ethics committee (including reviews of animal testing) and an institutional review board to better understand these matters and to give guidance to corporations (foreign and domestic), scientists, and potential volunteers. This ethics committee must include community representation, and it must also set leadership standards in this murky, newly evolving arena. There is an overarching concern to educate investigators, regulators, and corporations in the need to incorporate the ethos of ethics in their human and animal studies trials on a regular basis. If all of these lofty issues are resolved (although the practical matter of health insurance has not been resolved, and compensation for complications or untoward sequelae of pesticide testing is nonexistent), the EPA, wise in its understanding to initiate this dialogue, should establish a standing Ethics and Human Studies Committee, answerable to the administrator, who should exercise prudent oversight on all matters referred to the committee from both inside and outside the agency.

The opinions stated in this editorial are the author's own and do not represent any organization.

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