Experts: Human pesticide tests unethical, useless

By Keith Mulvihill

NEW YORK, Mar 01 (Reuters Health) - Scientists, ethicists and policymakers gathered last week at the New York Academy of Sciences in Manhattan to discuss growing concerns about the pesticide industry's use of human test subjects to evaluate their products' health effects.

Such testing is being used as a means, said one of the conference's organizers, to justify less stringent standards on pesticide use. Attendees also questioned the ethics of this testing, which is being done outside the US and often involves paying participants considerable sums of money.

And finally, some attending the conference said data gained through such tests on young adults is useless in gauging the health effects of pesticide exposure on infants and children.

"We believe that the reason they are doing the testing in humans is so that they can basically use the human data to justify more relaxed pesticide standards that would permit the application of higher amounts of pesticides to the foods that we eat," said Dr. Philip J. Landrigan, a pediatrician at Mount Sinai School of Medicine and director of the Mount Sinai Center for Children's Health and the Environment, the group that sponsored the event.

At the heart of the issue, according to Landrigan, is a 1996 law passed by Congress, called the Food Quality Protection Act (FQPA).

Traditionally, pesticide toxicity has been tested on rodents. Results from animal tests are extrapolated to humans in two steps. The safe rodent level is first divided by 10 to account for extrapolation from rodent to human. The resulting figure is again divided by 10 in order to account for the variability of a chemical's effects among humans, as some people will be more sensitive to pesticide exposure than others.

The FQPA requires the Environmental Protection Agency (EPA), in certain cases, to apply a child protective safety factor to the resulting figure. This means dividing it by 10 once more to account for the difference between infants and adults. So ultimately, the "safe" exposure level for rodents is divided by 1,000.

Landrigan and other experts believe that pesticide makers are using human tests to avoid the first 10-fold reduction in safety levels, thereby effectively keeping permissible pesticide exposure levels at pre-1996 levels.

"As we see it, (testing pesticides in humans) seemingly involves an attempt by manufacturers to bypass the requirement for a child protective safety factor in standard setting," Landrigan explained.

After the passage of the FQPA, Landrigan noted, the use of paid human volunteers in pesticide has steadily increased. The bulk of such testing, he said, occurs overseas where ethical standards for human testing are presumably more lax.

For example, Dr. Herbert L. Needleman, a professor of pediatrics at the University of Pittsburgh in Pennsylvania, told Reuters Health that commercial testing firms in Scotland pay college students and other jobless citizens up to $600 per day, for as many as 18 days, to ingest organophosphates. This family of compounds includes chemicals used as pesticides, fertilizers and nerve gas.

While much of modern medicine has relied heavily on advances achieved through the use of human test subjects, Landrigan pointed out that such human testing has generally

been deemed ethically acceptable only if the test offers the promise of some benefit to the individual or society at large.

Generally accepted ethical standards require informed consent from any research subject, meaning that he or she must be made completely aware of any potential risks of a procedure, according to Dr. Mary Faith Marshall, a professor of bioethics at the University of Kansas Medical Center in Kansas City, who spoke at the meeting.

Marshall also noted that that the research at hand has to be important enough to justify the use of a human being as a research subject. "If not, researchers shouldn't even be doing the study in the first place," she said.

Whether or not pesticide testing in humans passes that ethical litmus test was just one of the many points of contention expressed at the conference.

Another speaker, Dr. Marc Lappe, the executive director of the Center of Bioethics and Toxics at the University of California at Berkeley, pointed out that pesticide testing in humans is nothing new. For example, he noted, some chemicals have been tested in children to establish dosages for treating head lice or scabies.

"In those circumstances it's critical to know the dose response," said Lappe. "However, those are (examples of) medical benefits that are not claimed in the testing being proposed to help industry allow higher tolerances of pesticides in foodstuffs," he added. "And for that reason ethicists might justifiably question the specific industry sponsored studies that are at stake in the conference today."

With regard to the large sums of money being offered to volunteers to be exposed to pesticides, Lappe said, "We have people being asked to be involved with the research for a fee...to participate for payment to do work which is not even claimed to afford benefit to them, to their neighbors, or to society as a whole."

"And for that purpose, some ethicists have considered this type of research to be possibly out of bounds...inappropriate...unethical," he added.

NO REGULATION OF HUMAN PESTICIDE TESTING

The EPA has no standards governing pesticide testing in humans, according to Dr. Lynn R. Goldman, a professor of public health at Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. Goldman was assistant administrator in the EPA's Office of Prevention, Pesticides and Toxic Substances during the Clinton administration.

"This leaves the whole issue wide open for abuse...and, in a way, constitutes an encouragement for companies to do (these kinds) of studies," said Goldman, who also noted that regulatory approval of a pesticide can be worth hundreds of millions of dollars in profits for a company.

Confusing matters further, in 1998 the EPA placed a moratorium on accepting data from human testing used to establish toxicity thresholds for the regulation of a pesticide.

But the Bush administration later reversed that decision and sided with the manufacturers, saying that they would accept data from such tests.

Public outcry about the issue forced the current administration to reinstate the moratorium and to send the whole matter to the National Academy of Sciences for guidance, according to Landrigan.

But, Goldman noted, until industry gets an answer they can always hold on to hope that the data will be admissible and continue their studies.

ETHICS ASIDE, STUDIES DEEMED UNSCIENTIFIC

Despite the storm brewing over whether or not such human testing is ethically acceptable, several of the attendees questioned the quality of the studies that are being conducted.

Landrigan told Reuters Health that "the testing that's being done is all being focused on young adults and therefore the data that are being generated really is not very relevant to the protection of infants and children."

In addition, Needleman and Goldman each pointed out that many of the studies they have seen are very small, including fewer than 20 subjects. Ordinarily, studies that aim to assess a toxic effect in people, like those used in drug trials, require the use of thousands of people to establish safe levels of exposure.

Experts attending last Wednesday's conference unanimously agreed, Landrigan told Reuters Health, that "the current studies say nothing about the toxicity of pesticides to infants and children."

Over the next several weeks Landrigan said he and his colleagues plan to write up the conference proceedings for publication. They also plan, he said, to outline their concerns in letters to EPA administrator Christie Whitman and the National Human Research Protections Advisory Committee of the Department of Health and Human Services.

Commenting on some of the issues presented at the conference, Jay Vroom president of the trade association CropLife America (formerly the American Crop Protection Association) told Reuters Health that these types of test are important because they help refine and make more certain the relevance of pesticides to real human risk compared to animal data.

"We believe that there is a very important place for human clinical tests for a wide range of risk assessment purposes as long as those tests are conducted in carefully controlled and ethically sound manner," said Vroom.

"Our position about this kind of testing is that it is appropriate and a valuable tool for regulators to consider," he added.

CropLife American represents all of the major manufactures, formulators and distributors of crop protection chemicals, like pesticides, and crop biotechnology, according to Vroom, who did not attend last weeks conference and spoke to Reuters Health by telephone from his office in Washington, DC.