Weed Killer in the Crosshairs Concerns prompt reexamination of atrazine's safety

With hooded sprayers, farmers can direct herbicide to areas between crops (sorghum shown), limiting possible drift. U.S. Department of Agriculture/Photo Researchers, Inc.

Each year, American farmers and turf managers apply some 34 million kilograms of atrazine to quash broad-leaved and grassy weeds. Most treatments go to protect corn, sorghum, sugarcane and cotton, though golf courses sometimes tap the weed killer to maintain immaculate fairways and putting greens.

In recent years, however, questions have surfaced about atrazine's safety, especially after monitoring programs picked up the chemical in drinking water and lab studies demonstrated the pollutant's ability to emasculate - if not deform - amphibians and fish. Last fall, the U.S. Environmental Protection Agency announced it was reopening what industry had hoped was a closed chapter on allegations in the United States of atrazine's risks.

Atrazine, an organic compound belonging to the triazine family of herbicides, stops pre- and post-emergent weeds by inhibiting electron transport, ultimately blocking photosynthesis. The EPA reexamined data on the herbicide's putative toxicity four years ago as part of a systematic review of the safety of older pesticides - those initially registered for use before 1984. Atrazine was reregistered - meaning it could continue to be sold - after the EPA concluded that its regulated use could continue without posing undue risks to health and the environment. The chemical is banned by the European Union and, ironically, in Switzerland, where atrazine's leading manufacturer, Syngenta, is headquartered.

In a surprising turnabout, the EPA instructed its Scientific Advisory Panel on pesticides, a group of outside experts, to reevaluate the weed killer's safety through three meetings this year, the first of which took place earlier this month. The panel will review human data and any studies, including animal or test-tube assays, that might suggest risks to people.

EPA admits this new review was prompted by a flurry of recent news stories and critical reports by advocacy groups, which continue to show that large numbers of people are being exposed to atrazine through drinking water (SN: 11/3/01, p. 285) and which offer new data suggesting health concerns.

Among these new criticisms was a report in August by the Natural Resources Defense Council: "Poisoning the Well: How the EPA is ignoring atrazine contamination in surface and drinking water in the central United States." Its analysis of data that the EPA collected - but didn't publicly release -shows that traces of atrazine frequently pollute not only rivers but also water exiting the tap, oftentimes at concentrations exceeding EPA's 3-parts-per-billion limit for drinking water.

For its part, Syngenta Crop Protection, based in Greensboro, N.C., the largest U.S. producer of atrazine, argues EPA's new review is unnecessary. "After seven Scientific Advisory Panels, 15 years of special review and the reregistration of atrazine in 2006, the science stands for itself," says company toxicologist Tim Pastoor. Reviewing the data again "seems over the top," he contends, and poses unnecessary costs to taxpayers.

Yet there are plenty of new data that have not previously been part of any systematic federal review.

Sentinels of risk

Atrazine's ability to provoke hormonal perturbations in test animals is one of the more dramatic signs of its toxicity to emerge throughout the past decade, says biologist Tyrone Hayes of the University of California, Berkeley. He points to studies from his lab (SN: 11/2/02, p. 275) and by others that have demonstrated that this weed killer can inappropriately - and sometimes quite deleteriously - boost estrogen concentrations in male animals, from rats and fish to frogs and alligators.

The presence of too much estrogen or estrogen at the wrong time can not only alter reproductive development but also can pose cancer risks, so toxicologists have expressed concern over hormonal changes in test animals. Whether atrazine poses such risks to people, however, remains unknown.

Robust data suggestive of hormonal effects, including partial gender reassignment, come from amphibians and fish. And a review in the January Environmental Health Perspectives

This analysis didn't include all available studies, Rohr acknowledges, because "we had very strict quality criteria," requiring such things as "proper

experimental design, proper reporting or application of statistics," and data showing there had been no contamination of supposedly unexposed animals.

Trends observed across the studies that did make the cut indicate that atrazine alters rates of amphibian metamorphosis, reduces immune function in 33 of 43 measures and increases risk of infection in 13 of 16 measures. Exposure to the weed killer altered at least one aspect of gonad structure and function in seven of 10 studies, with some animals exhibiting "sexually ambiguous" gonad tissue. Atrazine also altered sperm production in the two studies that investigated it and changed sex-hormone concentrations in six of seven studies.

This review's findings contradict those reported in a February 2009 paper in Toxicological Sciences by Werner Kloas of the Leibniz-Institute of Freshwater Ecology and Inland Fisheries, in Berlin, and his coauthors (one of whom, Alan Hosmer, is a Syngenta employee).

According to Syngenta's Pastoor, the paper by Kloas' team is "the most comprehensive, complete and extensive study ever done on frogs looking at sexual development." Some 3,000 African clawed frogs were exposed to five doses of atrazine spanning four orders of magnitude. "And from that," he says, "it was definitively shown that atrazine has no effect."

Rohr and McCoy omitted most data in that paper from their review, however, arguing its statistical deficiencies made evaluation of the data "impossible."

Previous EPA analyses of atrazine safety had access to four earlier reviews of animal data, Rohr notes - all funded at least in part by industry. He maintains that his is the first review that is free of industry involvement. Funding for his assessment came from the EPA, the National Science Foundation and the U.S. Department of Agriculture. Atrazine at the surface Map source: USGS watershed regressions for pesticides atrazine model at infotrek.er.usgs.gov/warp; chart source: "Pesticides in the Nation's Stream and Ground Water." 1992-2001/USGS

Two rat studies in the November Toxicological Sciences point to an apparent stress response that may explain how atrazine could alter reproductive development. EPA scientists showed that the weed killer elevates stress-related hormones such as adrenocorticotropic hormone, or ACTH.

If levels of this hormone get out of balance in females, it "can interfere with normal regulation of the ovaries and ovulation," notes Ralph Cooper, chief of endocrinology at EPA's laboratory in Research Triangle Park, N.C. This, in turn, "will interfere with fertility," he points out. The hormone changes "indicated to us that the pituitary was responsive to atrazine directly," he says, "by secreting ACTH." Similar changes were seen in exposed male rats, suggesting a possible stress-system mechanism by which atrazine might impair sex-hormone production in males.

The witnessed changes might help explain the impaired reproduction previously linked to atrazine in animal studies, including delayed puberty, impaired fertility and inflamed prostates (in the male pups of exposed female rats), Cooper says. However, he cautions, exposures in his studies, though brief, far exceeded what would ever occur in drinking water.

Tied together, with caveats

Several studies have linked problems in human newborns to water supplies polluted with atrazine. The limitation of these papers is substantial: The water contained other farm chemicals that might be toxic in high doses as well.

A paper in Acta Paediatrica inApril 2009, for instance, identified a recurring seasonal increase in U.S. birth defects for babies conceived from April through July. The data, compiled from 1996 to 2002 by the Centers for Disease Control and Prevention, came from an assessment of more than 30 million live births.

Surface-water contaminant measurements by the U.S. Geological Survey during the same years show these months are when concentrations of agricultural chemicals - chiefly nitrate fertilizers and atrazine - peak, says Paul Winchester, a neonatologist at the Indiana University School of Medicine in Indianapolis.

Compared with the rest of the year, Winchester's team found, babies who were conceived from late spring to early summer showed a 3 percent higher rate of birth defects, such as spina bifida, cleft lip, urogenital defects and Down syndrome. And while a mix of farm pesticides usually showed up in that seasonal runoff into waterways, Winchester observes that "far and away, the most prevalent pesticide - and the one which exceeds safety limits

most often - is atrazine." The weed killer's statistically significant association with birth defects is intriguing, he says, and deserves further exploration.

A related investigation linked atrazine concentrations in Indiana drinking-water supplies to the chance that a baby would be very small at birth. "Atrazine concentrations above 0.1 part per billion were associated with, on average, a 17 percent increase in the risk of having a small baby," says Hugo Ochoa-Acu Purdue University in West Lafayette, Ind. Such contamination, well below the EPA's 3-ppb limit, can be common. Biweekly drinking-water data suggested that in Fort Wayne, Ind., for example, atrazine concentrations exceed 0.2 ppb on 265 days a year, and exceed 0.5 ppb more than one out of every three days.

Each 1 ppb increase of atrazine in drinking water, for consumption averaged throughout a pregnancy, increased by 15 percent a woman's chance of giving birth to a baby in the lowest 10 percent of weight for its gestational age. Such babies have a poorer chance of survival.

The weed killer's correlation with low birth weight proved most robust for contamination during a woman's third trimester, the Purdue team reports in the October Environmental Health Perspectives . "And that makes sense," Ochoa-Acu So a small effect there would produce a big difference."

As Winchester's group found, many other pesticides tended to coexist with atrazine in water, but their levels weren't nearly as high.

At his agency's February Scientific Advisory Panel meeting, the EPA's Aaron Niman reviewed these and additional new studies correlating the levels of atrazine in drinking water to birth defects and low birth weights. The strength of Winchester's study, he said, "is that it provides for an overall snapshot of trends in both birth defects and atrazine levels in the environment. For this reason, it's useful in hypothesis generation ... but can only be used to demonstrate correlation" - not causation.

The study by Ochoa-Acu Niman said, because it offers individual exposure estimates and is able to adjust for several potentially confounding factors, such as seasonality. Still, Niman acknowledged, there are limitations to even this study. But he also noted that this is to be expected when looking at complex, real-world exposures - not the controlled environments of lab rats.

Overall, researchers concede that no smoking guns exist regarding atrazine risks. Data are suggestive, based on high-dose rodent tests, real-world wildlife exposures and epidemiological surveys of people exposed to a mix of pollutants.

Although there have been charges that Syngenta has hidden troubling data from regulators and the public, Pastoor counters that the company's research "is publicly available," and that "EPA has all of our raw data" for every study. Indeed, he says, "When we submit a study, it undergoes the kind of scrutiny that would rival an Internal Revenue Service review."

So regardless of the concerns that have been circulating in news accounts and reports by public interest groups, Pastoor says he's confident that as long EPA bases its new safety assessment on science, "any further opening up of atrazine's scientific history is welcome."

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