

Certain anti-thyroid pesticides are known to cause thyroid tumors in animals after long-term exposure. It has been argued lately that anti-thyroid compounds should be considered separately from other carcinogens, because, as the theory goes, there might conceivably be a threshold below

which no toxic effects on the gland would occur, and therefore no tumors would develop. The herbicide oryzalin (trade-name Surflan TM) is an example of such a compound. Originally classified as a Class B2 (probable human) carcinogen, oryzalin was downgraded to a Class C (possible human) carcinogen on the basis of this new theory after a

FIFRA Scientific Advisory Panel (SAP) review in 1986.

Oryzalin is a pre-emergence, dinitroaniline sulfonamide herbicide manufactured by Eli Lilly Co. since 1974. It controls 46 different annual grasses and broadleafs by inhibiting growth of germinating weeds. More than 80% of usage is on soybeans, but oryzalin is also used in almond orchards, vineyards, grains, potatoes and other crops. It can be formulated with trifluralin, another Class C carcinogen. Several formulations of a crabgrass killer/fertilizer combination with and without another Lilly herbicide (Benefin or BalanTM) can be used on lawns and golf courses, especially in the South and on rights-of-way.

According to a 1987 EPA Registration Standard, oryzalin causes a "significantly elevated incidence of thyroid gland tumors and three different categories of

chemicalWATCH Stats:

CAS Registry Number: 19044-88-3 Chemical Class: 2,6-dinitroaniline herbicide Use: A pre-emergent herbicide to control annual grasses, broadleaf weeds and woody shrubs by inhibiting growth Toxicity rating: Moderate toxicity Signal Words: Caution, Warning Health Effects: Classified as a Group C carcinogen- possible human carcinogen Environmental Effects: Moderately toxic to fish and aquatic invertebrates. Oryzalin degrades slowly in soil and may leach to groundwater.

> skin tumors in male and female (Fischer 344) rats." Benign liver tumors are seen in male rats at high doses, and benign mammary tumors in females. No tumors were seen in mice, although "mean weights of uteri (including ovaries) were decreased in dose-related fashion, and markedly so, in oryzalintreated females." Mutagenicity tests were also negative, with the exception of a single test. EPA reviewers note the presence of certain unidentified (trade-secret) impurities, one of which was mutagenic in an Ames test, and another known carcinogen/mutagen. A nitrosamine contaminant at levels of less

than 1 ppm is present in oryzalin technical. Most of the nitrosamines, which have been tested, have been found to be potent carcinogens.

EPA noted in the Standard that structural analogues of oryzalin cause thyroid tumors in rats. Two other examples of anti-

> thyroid pesticides are: the herbicide amitrole, banned in Massachusetts, and ethylene thiourea (ETU), a breakdown product of EBDC fungicides, like maneb and mancozeb, currently under special review at EPA. Apparently, these compounds depress formation of thyroxin by the thyroid gland, stimulating the pituitary by a feedback

mechanism to circulate thyroid stimulating hormone (TSH), which then stimulates the thyroid to make more thyroxin. Overstimulation of the gland results in hyperplasia, and later, tumors. Lilly, the manufacturer, contends (without supporting evidence) that oryzalin's anti-thyroid effects are probably specific to rats and would not occur in human beings exposed to the product.

Another concern explored by EPA relates to inconclusive joint investigations by the International

Chemical Workers Union and the Occupational Safety and Health Administration into allegations that production workers a t the oryzalin factory in Renssalaer, IN fathered children with heart defects. Four birth defects studies in rats and rabbits were negative, although oryzalin was found to be fetotoxic. EPA noted "a potential adverse effect of oryzalin on eyes of rats exposed in utero and later ... " which they felt required further clarification. There is no information on the metabolism of oryzalin in animals or plants, and tolerances (legal residue limits on

food) include the parent compound only. Dermal absorption studies indicated that only 1.6% of the applied dose is absorbed in monkey studies. EPA has requested further information on oryzalin metabolism, and has required grazing and rootcrop rotation restrictions.

EPA's 1987 review found that the upper-bound dietary risk to the public consuming food residues of oryzalin was 10-5-10-6, but the Agency still concluded, "that the risks posed by oryzalin are minimal and hence initiation of a special review is not necessary at this time... [Furthermore]... the benefits of oryzalin... outweigh its risks." No valid environmental fate chemistry studies were available in 1985, although according to the manufacturer, weed control lasts from 2 to 12 months. Oryzalin is moderately mobile in sandy soil bioassays, and has the potential for soil residue accumulation. Since existing tolerances are not properly supported by toxicology data from the identified most sensitive species (the dog), EPA required chronic toxicity study one year or longer in length.

Reprinted from Volume 8, No.4, October 1989

UPDATE: October 2007

The residential lawn and turf use of oryzalin are no longer eligible for reregistration since there is concern about a potential for continued, substantial contact with treated surfaces, especially among children. Until data are submitted and evaluated for turf grass uses, residential use is ineligible. Several agricultural uses have been cancelled for oryzalin, with the only remaining uses for berries, vines and orchard crops.

Oryzalin is listed as a known carcinogen in the state of California. There is no evidence that links oryzalin to developmental or reproductive effects, however when fed to rats there were some changes in blood parameters and organ weights at moderate to high doses. Procedures to limit occupational exposure have been outlined by the EPA in the Reregristration Eligibility Decision (RED) signed in September 1994. Personal protective equipment (PPE), including coveralls and chemical resistant footwear, is now required for handlers. Along with PPEs, there is a 24-hr restricted entry interval (REI) which is twice as stringent than that proposed by the worker protection standard (WPS).

Oryzalin chemicalWATCH Factsheet Bibliography

"EPA & SAP agree on oryzalin as Class C carcinogen," Pesticide & Toxic Chemical News, February 19, 1986.

EPA. (1994). Reregistration Eligibility Decision (RED). Oryzalin. Office of Prevention, Pesticides and Toxic Substances. Washington, DC.

EPA. (1987). Guidance for the reregistration of pesticide products containing oryzalin as the active ingredient. Office of Pesticide Programs. Washington, DC.

EPA. (1985). Memorandum: Oryzalin: Highlights of problems/ issues- End of phase ll. March 8, 1985. Office of Pesticides & Toxic Substances. Washington, DC.

EPA. (1981). Memorandum: Toxicology Branch/Hazard Evaluation Division comments on ELi Lilly responses of 3/6/81 and 2/ 24/81 to EP A letter of 2/ 4/81 to Lilly, oryzalin (SurflanTM). Office of Pesticides & Toxic Substances. Washington, DC.

Washington Sate Department of Transportation. (2006). Oryzalin- Roadside Vegetation Management Herbicide Factsheet. http://www.wsdot.wa.gov/maintenance/pdf/oryzalin.pdf