Anatomy of the banning of three pesticides

by Christopher Sann

On October 12, as part of the settlement of a lawsuit brought by the State of California, and others, the Environmental Protection Agency (EPA) said it was revoking the agricultural use registrations of 25 well-known pesticides for their use on food.

Listed among those 25 pesticides were 15 commonly used in turfgrass management. Within that group of 15 were [three pesticides], two fungicides, Iprodione and Bayleton, and one insect control, Orthene. All of these pesticides' agricultural use registrations, [including these three], have been revoked because the EPA has concluded that they "induce cancer". (*Ed. note: see News Brief on page 11.*)

What was the lawsuit about?

The lawsuit was brought because, despite previously introduced evidence by the plaintiffs, the EPA had continued to allow the use of these 25 pesticides for the production of food under the provisions of its food additive regulations even though measurable traces of these pesticides or their metabolites (break-down compounds) were detectable either in a raw agriculture commodity or its final processed form.

The plaintiffs contended that, by allowing detectable residues in food, the EPA was in violation of the "zero-tolerance" provisions of the so-called Delany clause of the Federal Food, Drug and Cosmetic Act (FFDCA). They maintained, and the Ninth Circuit U.S. Court of Appeals agreed that the Delany clause barred the establishment of food additive regulations, tolerances, or exceptions for residues of any pesticides that had been demonstrated to induce cancer, no matter how small the risk.

What happened to these pesticides?

In the announced settlement of this lawsuit, the EPA agreed to cancel the food additive tolerances that had previously existed for the listed 25 pesticides. In the process they revoked the use registrations for certain agricultural uses of each pesticide. Additionally the EPA agreed, over the next five years, to examine all of its remaining pesticide food additive regulations, or so-called 409s, to determine whether any of the remaining tolerances violate the Delany clause's zero-tolerance provisions for cancer inducing pesticide residues in the food supply. As violations of the Delany clause are found, the EPA will move to revoke the agricultural uses. The EPA estimates that the agricultural uses of an additional 49 pesticides could be affected.

What guidelines are used?

When trying to determine the ability of a compound to induce animal cancers, the EPA uses a "weight of the evidence" standard. The carcinogenisity of a substance in animals is determined when the substance is administered to test animals in a scientific study and a thorough examination of the test subjects at the end of the study yields a statistically significant increase in malignant neoplasms. This approach to determining a substances ability to induce cancer is conducted independently of the likelihood or risk that the same levels of exposure and duration imposed on the test animals may be reached in humans and is conducted in this manner to show potential for occurrence rather than actual occurrences. This technique for determining cancer causing potential meets the zero tolerance conditions of the Delany clause.

Using this weight of the evidence standard, tests conducted to meet these standards led the EPA to determine that the commonly used pesticides acephate (Orthene), triadimefon (Bayleton), and iprodione (Chipco 26019) induce cancer.

What were the test results?

Acephate or Orthene

After tests were conducted using acephate, the EPA concluded that "exposure to acephate results in the induction of malignant heptocellular carcinomas in female CD1 mice".

Both male and female CD1 mice were exposed to three levels of acephate: 50, 250, 1000 parts per million (ppm) of body weight, over a two year period. Of those test animals that were still alive at the end of the test, only the female mice that had been exposed to the 1000 ppm dosage showed signs of increased incidence of heptocellular and hyperplastic nodules of the liver that

were significantly higher than the historical range for that strain of test animals at that testing laboratory.

When acephate was tested under laboratory conditions for genotoxicity (the ability to mutate genes) it was found that exposure to acephate caused genetic mutations in Salmonella, E. coli, and S. cerevisiae strains of bacteria and lymphoma cells of mice, Chinese hamster ovary cells, and DNA recombinant in Saccharomycces (unicellular yeast) cells.

Based on the increased incidence of liver cancers in mice, the six positive indications for genotoxicity under laboratory conditions, and using its weight of the evidence standard, the EPA decided that sufficient evidence had been developed to warrant the identification of acephate as a substance that induces cancer.

Triadimefon or Bayleton

Testing results indicated that exposures of 1000 ppm of triadimefon caused significantly higher incidence of heptocellular adenomas in both male and female mice than the control animals and that the incidence of these adenomas was found to be dose related, i.e. the higher the dose, the higher the incidence of adenomas.

Initially, triadimefon was not thought to be responsible for this increase in tumors, but a peer review committee determined that information contained in a pathology report indicated that the pathological evidence required a second evaluation. When the original slides of the tumors from the original study were re-evaluated under the more stringent criteria of current analysis standards, it was determined that the lesions examined were heptocellular adenomas and carcinomas. Heptocellular adenomas are considered to be benign tumors but they can progress into carcinomas or malignancies. When indications of both liver adenomas and carcinomas are found during an examination, then the test substance is considered to have stronger ability to induce cancers. An additional two year study found that exposure to triadimefon caused dose-related increases in thyroid follicular cell adenomas and cystic hyperplasia.

When the triadimefon test data were combined with historic positive data from tests for induction of carcinomas by other closely related compounds which have indicated a tendency to induce adenomas and carcinomas, the EPA concluded that exposure to triadimefon causes heptocellular adenomas and carcinomas of the liver and thyroid follicular cell adenomas and cystic hyperplasia and that exposure to triadimefon induces cancer.

Iprodione or Chipco 26019

Test results indicated that exposure to iprodione produced increased incidences of heptocellular carcinomas in male mice, combined heptocellular adenomas and carcinomas in both male and female mice, ovarian lutenomas in female mice, and testicular interstitial cell tumors in male mice.

Ninety-nine week tests of mice exposed to 160, 800, 1400 ppm per body weight of iprodione found a significant increase in both benign and malignant liver cell tumors. At the higher doses male mice were found to have higher incidences of interstitial cell hyperplasia, benign tumors, and significant other changes to the structures of the testes. There was also an increase in lutenomas and tubular hyperplasia of the ovaries in female mice at the highest dose levels.

The EPA combined this test evidence with information about related compounds which have been associated with adverse effects on reproductive organs and the liver, and concluded that Chipco 26019 induces cancer.

TGT View — It is clear from this information, that turfgrass and landscape managers will have to start to ask more questions about the safety of their chemical pesticide tools. What managers do with that information will be up to them, but making an informed decision requires that all of the information about a products safety is available. The previous lack of information about the safety of these three pesticide products indicates that, in these three cases, the pesticide users, the people that buy pesticide products and keep pesticide manufacturers in business, have not been well served. Manufacturers have an obligation to the applicators of their products to keep them well informed about all aspects of their product's safety. It is the least they can do to those of us who have the greatest exposures. The source document for this article is EPA Document No. OPP-300360 "Acephate, Triadimefon, Iprodione, and Imazalil; Revocation of Food Additive Regulations" —CS ■