

## Evaluation of Pesticides for Carcinogenic Potential<sup>1</sup>

Frederick M. Fishel<sup>2</sup>

The purpose of this guide is to discuss the 5-tiered scheme used by the Environmental Protection Agency (EPA) to classify the carcinogenic potential of pesticides.

Prior to any pesticide receiving its registration from the EPA, numerous studies must be conducted to determine the hazards of the particular pesticide and its use. For pesticides that will be used on food and some nonfood commodities, studies are conducted to determine their potential carcinogenicity. Studies are required in laboratory settings involving both sexes of two species (mice and rats). The results of the studies are peer-reviewed by the Cancer Assessment Review Committee. This committee then recommends a cancer classification for the active ingredient under review. The classification determines how EPA regulates the pesticide to minimize human risk. These studies may be reviewed again when a pesticide undergoes re-registration and the cancer classification may be re-evaluated, particularly if new studies have been submitted.

To indicate possible cancer risk posed by a pesticide, EPA ranks how strongly carcinogenic the chemical is and the potential for human exposure.

The EPA's guidelines for evaluating the potential carcinogenicity of chemicals have been updated over the years to reflect increased understanding of ways chemicals may cause cancer. The guidelines were first issued in 1976, updated several times since then, but by 1999, the science related to carcinogens had advanced significantly, thus prompting another revision.

EPA currently uses a 5-tiered classification system with pesticides that have undergone review since 1999. The classes in this system include:

- 1) Carcinogenic to humans. EPA assigns this descriptor to pesticides when there is convincing epidemiologic evidence demonstrating causality between human exposure and cancer. It is based on compelling evidence of carcinogenicity in animals and mechanistic information in animals and humans demonstrating similar mode(s) of carcinogenic action. The only actively registered pesticides in this group are the arsenicals, used for wood treatment. The use of arsenic for wood treatment has been severely restricted since the end of 2003.

1. This document is PI-37, one of a series of the Agronomy Department, Florida Cooperative Extension Service, Institute of Food and Agricultural Sciences, University of Florida. Original publication date March 2005. Reviewed April 2008. Visit the EDIS Web Site at <http://edis.ifas.ufl.edu>.

2. Frederick M. Fishel, Associate Professor, Agronomy Department, and Director, Pesticide Information Office; Florida Cooperative Extension Service, Institute of Food and Agricultural Sciences, University of Florida, Gainesville, FL 32611.

**Use pesticides safely. Read and follow directions on the manufacturer's label.**

The Institute of Food and Agricultural Sciences (IFAS) is an Equal Opportunity Institution authorized to provide research, educational information and other services only to individuals and institutions that function with non-discrimination with respect to race, creed, color, religion, age, disability, sex, sexual orientation, marital status, national origin, political opinions or affiliations. U.S. Department of Agriculture, Cooperative Extension Service, University of Florida, IFAS, Florida A. & M. University Cooperative Extension Program, and Boards of County Commissioners Cooperating. Larry Arrington, Dean

2) Likely to be carcinogenic to humans. This class is used when the available tumor effects and other key data for a pesticide are adequate to demonstrate carcinogenic potential to humans. Data within this class range from an association between human exposures to the pesticide and cancer to the weight of experimental evidence showing animal carcinogenicity by a mode of action assumed to be relevant to humans. Imazalil, a postharvest fungicide used in Florida citrus production, fits into this tier.

3) Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential. Examples of this assessment may include:

- evidence showing a marginal increase in tumors that may be exposure-related;
- evidence that is observed only in a single study; or
- evidence that is limited to certain high-background tumors in one sex of one species.

In this classification, further studies would be needed to determine human carcinogenic potential. Pyrethrins, insecticides used in a wide array of settings, are an example of active ingredients classed in this category.

4) Data are inadequate for an assessment of human carcinogenic potential. EPA uses this descriptor whenever there is a lack of pertinent or useful data or where existing evidence is conflicting. For example, some evidence is suggestive of carcinogenic effects, but other equally pertinent evidence does not confirm a concern. An example classed in this tier is pyraclostrobin, a biological-based fungicide applied to fruit and vegetable crops.

5) Not likely to be carcinogenic to humans. EPA places pesticides in this class when the findings of carcinogenicity studies reveal:

- evidence that extensive human experience demonstrates the lack of carcinogenic effect;

- animal evidence that shows a lack of carcinogenic effects in at least two well-designed and well-conducted studies in two appropriate animal species;
- any carcinogenic effects shown in animals are not considered relevant to humans;
- evidence that carcinogenic effects are not likely by a particular route of exposure; and,
- evidence that carcinogenic effects are not anticipated below a defined dose range.

The herbicide glyphosate, used widely in agricultural, residential and non-crop settings, is an example of a pesticide classed in this tier.

### **Additional Information**

The EPA Office of Pesticide Programs, Health Effects Division and Science Information Management Branch has released the listing of Chemicals Evaluated for Carcinogenic Potential. The document may be viewed at <http://www.pestmanagement.rutgers.edu/NJinPAS/postings/EPAcancerevalchem704.pdf>.

This list is current as of July 19, 2004. All pesticide active ingredients that have been submitted to EPA for registration, re-registration or special review are included. In some cases, the registration of certain pesticides has been canceled (although this is not noted in the list). Keep in mind that you can't necessarily correlate the potential for carcinogenic effects in systems used prior to 1999 to those used in the 1999 revised system.