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.

Before any pesticide can receive 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 the 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, the 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 and updated several times since then, but by the present time, the science related to carcinogens had advanced significantly, prompting further revision.

1. **Carcinogenic to humans.** The 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.

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 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. **Inadequate information to assess carcinogenic potential.** The 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.** The 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.