Pesticide regulation primer

■ Terms

Acceptable daily intake (ADI): See also *Reference dose (RfD).*

ADIs or Rfds are used in the regulation of noncarcinogens. For carcinogens, "cancer potency factors" are used.

Cancer potency factor: To regulate carcinogens, the EPA multiplies an exposure estimate by the cancer potency factor. EPA prefers that cancer risk be "negligible," or potentially causing one additional cancer in a million people. However, it is not required by law to limit pesticide-residue risk to a certain level (with the exception of pesticides covered by the Delaney Clause, which sets a zero-risk standard. See pp. 34, 35.) EPA is required to register pesticides based upon the entire picture of risks and benefits.

Federal Insecticide, Fungicide and Rodenticide Act (FIFRA): This act states that all pesticides used in the United States must be registered by the U.S. Environmental Protection Agency (EPA). Any pesticide used on food or feed must have a legally established residue tolerance for each crop to which it will be applied or to animal products such as meat and milk where residues may remain. Tolerances are the legal amounts of residues allowed on food crops when they leave the farm. In establishing tolerances on raw agricultural products, the EPA is required to evaluate and consider both the risks and benefits that will result if the pesticide is registered.

Federal Food, Drug and Cosmetic Act (FFDCA): This legislation regulates food, including pesticide residues. Although some parts of the act are implemented by the Food and Drug Administration (FDA), tolerances for pesticide residues are established by the EPA (which also regulates pesticides in the environment and in toxic waste). FDA, USDA and the states enforce the tolerances established by EPA.

Good agricultural practice: Growers observe "good agricultural practice" by adhering to pesticide label directions; the resulting food crops should have pesticide residues below tolerance levels. Tolerances are based on field tests that determine the maximum pesticide application that would be needed to control a worst-case infestation. Although health data is considered in setting tolerances, tolerances are not health-based. (see *Tolerance* and *Risk-benefit analysis* below.)

Negligible risk: Sometimes called *de minimis* risk, negligible risk is a target in carcinogen regulation. Agencies seek to limit involuntary risk from carcinogens to a negligible level, usually defined as the potential to cause one additional hypothetical cancer in a million people. The use of a negligible risk standard has been called into question by recent court interpretations of the Delaney Clause. (see p. 35 for "Delaney update," and p. 30 for discussion of pesticides affected by the zero-risk standard of the Delaney Clause.)

Reference dose (RfD): The reference dose is the level of daily exposure to a pesticide residue which, over a 70-year human life span is believed to have no negative effect. EPA now uses this term rather than acceptable daily intake (ADI). ADIs or Rfds are determined from studies using laboratory animals. The highest dose or exposure level that produces no noticeable toxic effect on test animals is divided by a safety factor, usually 100.

Registration: Registration means that the EPA, after reviewing required research results, has concluded that the benefits from the use of the pesticide outweigh the risks (see *Risk-benefit analysis* below).

To obtain registration, the company that developed the pesticide must submit the results of studies showing the pesticide's toxic effects on laboratory animals, at what doses it caused them, and studies of how the proposed pesticide behaves in the environment. If the pesticide leaves residues on food, the EPA will require that pesticide residue studies be performed.

Risk-benefit analysis: Under FIFRA, each pesticide registration is based upon a risk-benefit analysis. Risks may include pesticide applicator and farmworker hazards, adverse effects on the environment such as groundwater contamination, and consumers exposure to residues on the food they eat. Benefits may include longer crop-growing seasons, larger yields and more attractive, affordable food products that have less waste and longer shelf life.

In establishing tolerances on raw agricultural products, the EPA is required to evaluate and consider both the risks and benefits that will result if the pesticide is registered.

Tolerance: A tolerance is the maximum amount of a pesticide residue allowed on produce at the farmgate. Currently, tolerances are set by the EPA based on studies done in a variety of geographical locations under the most severe conditions — using maximum rates, maximum applications per year, and shortest interval between the last application and harvest. At the end of the studies, the maximum residue is determined. The pesticide manufacturer then requests that a tolerance, or maximum allowable residue level, be granted by the EPA that slightly exceeds the maximum residue observed.

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The EPA then calculates the theoretical maximum (worst-case) consumer exposure to the pesticide from all foods, compares it to the acceptable daily intake (ADI) developed through animal studies and calculates the cancer risk for carcinogens. If the theoretical exposure exceeds the reference dose or if the cancer risk exceeds 1 in a million, EPA calculates a more realistic exposure using data on percent crop treated, and residue levels on food at the time of consumption (as opposed to farm gate residue levels). EPA will only establish a tolerance (and register use) if the actual exposure is less than the reference dose and the cancer risk is less than 1 in a million.

■ Controversies

Scientific unknowns have given rise to several controversies. Other debates concern the practical difficulties in pesticide regulation.

Actual residues vs. tolerances

National studies have sometimes used maximum "tolerance levels" to estimate actual pesticide residues on food. These tolerance values — set in the registration process — are usually much higher than actual residue levels found in government monitoring programs.

Also, food processing, transportation and handling practices (such as washing, peeling and cooking) can decrease the amount of residue that is ultimately consumed. Some food processes such as concentration or dehydration may also magnify pesticide residues or breakdown products.

Health-based tolerances

The NAS committee called for tolerances that more fully protect human health, including the health of infants and children. While EPA takes toxicology data into consideration when setting tolerances (for example, tolerances are generally not granted unless they are less than the acceptable daily intake), it is just one part of the entire picture of risks and benefits that EPA must consider. EPA's charge is to register pesticides for which the benefits outweigh the risks.

Some have argued that tolerances — rather than being set to reflect "good agricultural practice" — should be health-based. Tolerances are currently based on field tests that determine the maximum pesticide application needed to control a worst-case infestation.

Interactive effects

The effects of combinations of pesticides are not usually considered when setting tolerances. The most common way for chemicals to interact is to cause additive effects. Chemicals may also be antagonistic, that is, the effects cancel each other. Or they may be synergistic, with the combined effect being more than the additive effect of the pesticides. Regulators believe that safety factors built into the risk management process compensate for these potential interactions, and for differences in sensitivity among people.

Natural carcinogens

Some scientists have proposed that natural carcinogens found in the food supply could have a greater impact on human cancer than synthetic carcinogens. The relative roles of natural carcinogens and synthetic chemicals in human cancer remain elusive and have been inadequately assessed.

UC Berkeley's Bruce Ames and Lois Gold have estimated that food plants contain between 5,000 and 10,000 natural pesticides and breakdown products that are potentially toxic in humans. Further, they have speculated that we eat as many as 10,000 times more natural pesticides than synthetic ones (strictly on a weight basis, not taking potency into consideration).

Like synthetic chemicals, several naturally occurring substances, such as aflatoxins, are carefully regulated in the diet because of their extreme toxicity. Many of the highly toxic natural substances have been identified; they typically occur at very low levels in the diet and thus do not appear to pose significant health risks.

Although several natural carcinogens have been studied, they probably have not been tested adequately to make valid toxicological comparisons. There is no current consensus on how many others should be tested and what priority should be assigned to substances for toxicological testing.

Reregistration: the EPA backlog

The great majority of pesticides in use today were registered before extensive toxicology testing was required. Although risk assessment studies were done, these older studies do not fulfill current requirements. Legislation in 1972 called for reregistration of these pesticides. However, of 405 groups of pesticides for which reregistration was required (and which industry has indicated it intends to support), only 47 had reached the stage of a final finding by the end of fiscal year 1993.

Congress in 1988 accelerated the timetable for a national reregistration, requiring pesticide manufacturers to fill in data gaps by 1997 to determine whether these older products should maintain their registrations (FIFRA, 1988). Critics of the system say that the reregistration process is moving too slowly and that certain older pesticides should not remain in use in the interim.

Sample size in tests

In all national residue testing programs, less than 2% of our food supply is actually sampled. The Total Diet Study, for instance, includes four market baskets of food items, each from a different region of the country. It has been criticized for offering a low level of statistical significance.

Small sample size may also reduce the effectiveness of monitoring programs. Limited time, money and technology may allow illegal uses to go undetected. However, evidence indicates that most illegal residues are chemicals that have been used on crops for which they are not registered. They may have been wrongfully used or inadvertently picked up from neighboring crops or soil residuals. They are not necessarily present at harmful levels. — *Editor*