Chapter 12

Mammalian Toxicology: Insecticides, Acaricides, and Transgenic Crops

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The use of insecticides, acaricides, and transgenic crops is intended to protect human health from diseases spread by insects, mites, and ticks; to increase the yield of crops; and to improve the natural beauty of our environment. For example, insecticides can be used to control the following: insects that transmit bacterial or viral diseases or allergens to plants or humans; insects that directly eat crops and leaves or bark of plants, shrubs, or trees; structural and household pests, such as termites, carpenter and fire ants, and cockroaches; and grubs and worms that feed on the roots of turf and field crops. Acaricides are agents specific to mites and ticks that attack crops and animals.

A more recent advancement in the pesticide industry is the development of transgenic crops that have been genetically manipulated to be more resistant to pests by internal synthesis of plant toxins that specifically kill insects, but are nontoxic to mammals. Transgenic crops, which produce plant pesticides, are in a new regulatory class of pesticides referred to as biopesticides and microbial pest control agents (MPCAs). MPCAs also include bacteria, viruses, and other naturally occurring agents that are specifically toxic to insects, mites, and ticks, etc., but are harmless to mammals.

Fundamentally, pesticides are medicines developed to treat diseases and prevent the spread of disease and predator destruction of trees, shrubs, grasses, and crops. As a result, pesticides prevent the vector-borne spread of diseases to humans and plants and increase crop yields, which provide an inexpensive and reliable source of fruits and vegetables necessary for maintaining optimum human health.

Regulations Requiring Mammalian Toxicity Studies

The original legislation entitled the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was passed in 1947 and provided labeling authority of pesticides to the U.S. Department of Agriculture. The most significant amendment to FIFRA occurred in 1972; it transferred most regulatory authority for pesticides to the newly formed (1970) U.S. Environmental Protection Agency (EPA). Under this amendment, pesticides would be registered as either general-use or restricted-use pesticides, for which the latter required handling only by individuals certified by the states. This amendment required that pesticides not only be registered with the EPA, but also reregistered by the EPA, so that reevaluation of the safety of pesticides would be done according to present day safety standards. Additional federal actions since 1972—the most recent entitled "The Food Quality Protection Act" (FQPA, 1996)—are intended to expand the requirements and standards for registering and reregistering pesticides to protect humans, especially children, and the environment. These more recent federal actions seek to minimize the level of risk in the use of pesticides, i.e., by providing a standard of "reasonable certainty of no harm."

The Office of Pesticide Programs (OPP), which regulates the pesticide industry under FIFRA is within the Office of Prevention, Pesticides, and Toxic Substances (OPPTS) (Table 1). The Health Effects Division requires mammalian toxicology testing to evaluate the risk to humans from pesticide use. The Environmental Fate and Effects Division requires ecological toxicology testing and environmental fate analyses to determine potential risks to birds, fish, wildlife, invertebrates, and nontarget plants in terrestrial and aquatic environments.

Testing Requirements

A broad selection of toxicology studies is used for pesticides, whose general use patterns include terrestrial, aquatic, and greenhouse uses for food and nonfood crops; and forestry, domestic outdoor and indoor uses for nonfood-related products. Each chemical is assessed for dietary, worker, and nonworker risks. The requirements for testing were proposed in the Federal Register (October 24, 1984) and are now listed in 40 CFR 158.340. For these studies listed in Table 2, the EPA 870 Series Data Requirements/Test Guidelines are available (Table 3).

Acute and short-term studies may use varying routes of exposure (e.g., dermal, inhalation, oral intubation [gavage]). Longer term studies are generally performed by administering the pesticide in the diet, which is consistent with general long-term exposure of humans to pesticide residues in the food. However, these pesticides are tested up to a maximum tolerated dose or a limit-dose of 1,000