Acute toxicity

Acute toxicity refers to the immediate effects (0-7 days) of exposure to a pesticide. Highly acutely toxic pesticides can be lethal at very low doses. Narrative toxicity categories (Danger, Warning, Caution) are based on the LD_{50} , the dose (in milligrams of substance per kilogram of body weight) that kills 50% of the test animals in a standard assay, through either oral or dermal exposure routes. For inhalation exposures, the LC_{50} is used--the concentration in air in mg per liter that kills 50% of the test animals. The U.S. EPA gives a narrative warning label to pesticide products based on LD_{50} s. See <u>table</u> for LD_{50} narrative equivalents.

- PAN Acute Toxicity Description
- WHO Acute Hazard Rankings
- U.S. EPA Acute Toxicity Rankings
- U.S. EPA Toxics Release Inventory Rankings
- U.S. NTP Acute Toxicity Rankings
 - Study Type
 - **■** Exposure Route
 - Species
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 - Units
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Pesticide Action Network (PAN) Acute Toxicity Description

There are several organizations that evaluate and rank chemicals for their acute toxicity. *Active ingredients* of pesticides are ranked by the World Health Organization (WHO). Information on LD₅₀s (which can be equated to a narrative ranking) can be obtained from the U.S. National Toxicology Program (NTP), U.S. EPA's Toxics Release Inventory (TRI) ranking, or materials safety data sheets (MSDS). *Formulated pesticide products* (which often include inert ingredients) are given a toxicity rating by the U.S. EPA which is shown as a warning label on the pesticide product.

Because toxicity designations from different sources sometimes conflict with each other, PAN created a summary acute toxicity designation that reflects the most toxic ranking assigned by any organization. In addition, the different terms used by different organizations to describe acute toxicity were translated into a consistent set of terms. For example, if WHO determined a pesticide to be "Highly Hazardous", we used the label "Highly Toxic." The equivalences between the different ranking systems are shown in the table below.

For a chemical to be classified as a <u>PAN Bad Actor</u>, it must be in either the **Extremely Toxic** or **Highly Toxic** PAN summary category.

PAN category	Equivalence in other ranking systems				
Extremely toxic	WHO: Extremely hazardous				
	U.S. EPA: Category I, DANGER				
	U.S. NTP: no parallel category				
	MSDS: no parallel category				

	TRI: no parallel category				
	WHO: Highly hazardous				
	U.S. EPA: Category I, DANGER				
Highly toxic	U.S. NTP: based on U.S. EPA's LD ₅₀ guidelines				
	MSDS: based on U.S. EPA's LD ₅₀ guidelines				
	TRI: Yes				
	WHO: Moderately hazardous				
	U.S. EPA: Category II, WARNING				
Moderately toxic	U.S. NTP: based on U.S. EPA's LD ₅₀ guidelines				
	MSDS: based on U.S. EPA's LD ₅₀ guidelines				
	TRI: no parallel category				
	WHO: Slightly hazardous				
	U.S. EPA: Category III, CAUTION				
Slightly toxic	U.S. NTP: based on U.S. EPA's LD ₅₀ guidelines				
	MSDS: based on U.S. EPA's LD ₅₀ guidelines				
	TRI: no parallel category				
	WHO: Unlikely to be hazardous				
	U.S. EPA: Category IV, CAUTION				
Not acutely toxic	U.S. NTP: based on U.S. EPA's LD ₅₀ guidelines				
	MSDS: based on U.S. EPA's LD ₅₀ guidelines				
	TRI: no parallel category				

World Health Organization (WHO) Acute Hazard Rankings

The WHO bases its ratings on the lowest published rat oral LD₅₀, the lethal dose (in milligrams of substance per kilogram of body weight) that kills 50% of the test animals in a standard assay. WHO gives a hazard ranking of Ia (Extremely Hazardous) to the most hazardous pesticide active ingredients. While the WHO ratings generally reflect acute toxicity, they also take into account other toxic effects such as reproductive and developmental toxicity. WHO does not evaluate the fumigants, a class of gaseous pesticides that are generally extremely hazardous, nor does it evaluate pesticides believed obsolete or discontinued, even though some of these "obsolete" pesticides are currently registered for use in the U.S.

WHO Toxicity Classification		Rat LD50 (mg of chemical per kg of body weight)				
Class	Description	Solids (oral)	Liquids (oral)	Solids (dermal)	Liquids (dermal)	
Ia	Extremely hazardous	< 5	< 20	< 10	< 40	
Ib	Highly hazardous	5-50	20-200	10-100	40-400	

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II	Moderately hazardous	50-500	200-2,000	100-1,000	400-4,000
III	Slightly hazardous	> 500	>2,000	>1000	> 4 , 000
Table 5	Unlikely to present acute hazard in normal use	> 2,000	> 3,000		
Table 6	Not classified: believed obsolete				
Table 7	Fumigants not classified by WHO				

About the Data: Accuracy, currency, comprehensiveness and source

This dataset was compiled by WHO and includes acute toxicity ratings for 575 pesticide chemicals. Not included in the WHO data are gaseous pesticides and any pesticide considered obsolete Note: (A number of "obsolete" chemicals are still in use in the U.S.) This list is updated biennially and was last published by WHO in 2005. The data presented in the PAN Pesticide Database were current as of October 2005.

Reference:

<u>The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification</u> 2004, World Health Organization, April 2005.

Materials Safety Data Sheets (MSDS)

Materials Safety Data Sheets (MSDSs) provide toxicity information and emergency procedures for chemical substances. MSDSs are available for most chemicals and must be supplied to purchasers of pure chemicals. MSDSs were only used in the PAN database to determine acute toxicity when data from other sources were not available. Narrative ratings were assigned based on LD₅₀ (oral, rat) values given in the MSDS, using the U.S. EPA acute toxicity guidelines (see <u>table</u>).Online sources for MSDS information are available as links from the Product Information page. To access this page, simply search for a product (detailed instructions <u>here</u>) and click on the More button in the search results list.

U.S. EPA Acute Toxicity Rankings

Formulated pesticide products (which often include inert ingredients) are given an <u>acute toxicity</u> rating by the U.S. EPA which is reflected in the warning label on the pesticide container. The U.S. EPA gives a warning label of Category 1 to the most acutely toxic pesticide products and Category 4 to the least acutely toxic pesticide products. The different toxicity categories are based on the LC₅₀, the lethal dose (in milligrams of substance per kilogram of body weight) that kills 50% of the test animals in a

standard assay. For inhalation exposures, the LC_{50} is used---the concentration in air in mg per liter that kills 50% of the test animals.

Active ingredients can be similarly ranked for toxicity on the basis of LD_{50} values. Thus, warning labels for single-active-ingredient pesticide products containing technical grade active ingredients over 90% pure can serve as a reasonable proxy for the toxicity of the active ingredient. However, many of these warning labels are not internally consistent, and different pesticide products containing essentially the same concentration of active ingredient are labeled with two or more different toxicity ratings. In this situation, the U.S. EPA acute toxicity rating for the chemical was noted as "No Consensus Value."

U.S. EPA Categories and Warning Labels		Acute Toxicity to Rats					
Category	PAN Narrative Rating	Warning Label	Oral LD ₅₀ (mg/kg)	Dermal LD ₅₀ (mg/kg)	Inhalation LC ₅₀ (mg/L)	Eye Effects	Skin Effects
1	Highly Toxic	Danger-Poison*	< 50	< 200	< 0.05		
1	Highly Toxic	Danger	< 50	< 200	< 0.05	Corrosive (irreversible destruction of ocular tissue) or corneal involvement or irritation persisting for more than 21 days.	Corrosive (tissue destruction into the dermis and/or scarring)
2	Moderately Toxic	Warning	50-500	200-2,000	0.05-0.5	Corneal involvement or irritation clearing in 8-21 days	Severe irritation at 72 hours (severe erythema or edema)
3	Slightly Toxic	Caution	500-5,000	2,000-5,000	0.5-2	Corneal involvement or irritation clearing in 7 days or less	Moderate irritation at 72 hours (moderate erythema)
4	Not Acutely Toxic	None	> 5,000	> 5,000	> 2	Minimal effects clearing in less than 24 hours	Mild or slight irritation (no irritation or slight

erythema)

About the Data: Accuracy, currency, comprehensiveness and source

All pesticide products registered for use in the U.S. are required to have an acute toxicity rating on the label. PAN staff obtained U.S. EPA acute toxicity rankings from the labels for single-active-ingredient products containing technical grade active ingredient at more than 90% concentration. Many of these warning labels are not internally consistent, with pesticide products containing essentially the same concentration of active ingredient labeled with several different toxicity ratings. When there was a *consistent* acute toxicity rating for a given active ingredient, we assigned an acute toxicity rating. Where ratings were inconsistent or when acute toxicity was apparently due to an inert ingredient, no rating was assigned. Initial analysis was conducted using U.S. EPA product data from August 2, 2000. Updates are planned on an as-needed basis.

References:

- 1. U.S. EPA Health Effects Test Guidelines: Acute Toxicity Background, U.S. EPA, download pdf. Viewed on October 29, 2002.
- 2. 40 Code of Federal Regulations, <u>Part 156.10</u>. Note: The toxicity guidelines given here are *different* than those given in reference 1. Those in reference 1 were used, since it was published as official guidance from U.S. EPA. Viewed on October 31, 2002.
- 3. U.S. EPA Pesticide Product Information System (PPIS). Viewed on October 29, 2002.
- 4. <u>CA DPR Pesticide Product Database</u>, California Department of Pesticide Regulation. Viewed on October 29, 2002.

U.S. EPA Toxics Release Inventory List

In 1986, Congress passed the Emergency Planning and Community Right-To-Know Act (EPCRA) and the Pollution Prevention Act (PPA), with the intent of increasing the transparency of the use and disposal of chemicals in manufacturing, mining, and other activities. Section 313 of the EPCRA and section 6607 of the PPA required companies that release toxic materials to provide information to U.S. EPA on the identity and amounts of these toxic chemicals they are releasing to air, land and water. This information is made available to the public through U.S. EPA as the Toxics Release Inventory (TRI), providing valuable information on the release and transport of toxic chemicals in the U.S.

U.S. EPA publishes a list of chemicals that must be reported. A chemical is placed on the list if it is toxic to humans or damaging to the environment. The current TRI toxic chemical list contains approximately 650 individually listed chemicals and 30 chemical groups. Of this group, only 350 individual chemicals and 25 chemical groups are pesticides or related compounds. Of these pesticide chemicals, only 222 have been formally ranked through the TRI program for their toxicity.

Toxicity categories evaluated for the TRI list of chemicals includes acute toxicity, carcinogenicity, reproductive and developmental toxicity, environmental toxicity and toxicity to organ systems including cardiovascular, liver, gastrointestinal, kidney, immune, hematological, and respiratory systems.

Environmental Defense maintains a web site called <u>Scorecard</u>, at which you can find information on the TRI chemicals being released in your neighborhood, with a map showing the location of the responsible facilities.

References:

^{*}This signal word is used for acute systemic poisons.

- 1. <u>Toxics Release Inventory and Community Right to Know,</u> U.S. EPA. Viewed on October 29, 2002.
- 2. What is the Toxics Release Inventory?, U.S. EPA, Viewed on October 29, 2002.
- 3. <u>Hazard Information on Toxic Chemicals Added to EPCRA Section 313 Under Chemical Expansion</u>, U.S. EPA, Viewed on October 29, 2002.

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U.S. National Toxicology Program (NTP) Acute Hazard Rankings

The U.S. NTP hazard rankings are based on LD_{50} or LC_{50} values (oral, dermal and inhalation) for all mammals that are reasonable analogs for humans, including rats, mice, rabbits, monkeys, dogs, cats, gerbils, and guinea pigs. The LD_{50} is the lethal dose (in milligrams of substance per kilogram of body weight) that kills 50% of the test animals in a standard assay.

Narrative hazard rankings (Highly Toxic, Moderately Toxic, Slightly Toxic, and Not Acutely Toxic) were assigned to the U.S. NTP LD₅₀ data according to U.S. EPA guidelines (see <u>table</u>).

About the Data: Accuracy, currency, comprehensiveness and source

This dataset was compiled by NTP from peer-reviewed sources and includes acute toxicity data for 1,581 chemicals, not all of which are pesticides. It is not known how frequently additions are made to this list. NTP data downloaded July 1, 2000.

References:

- 1. <u>Chemical Health and Safety Data</u>, U.S. National Toxicology Program. Viewed on October 31, 2002.
- 2. U.S. EPA Health Effects Test Guidelines: Acute Toxicity Background, U.S. EPA, download pdf. Viewed on October 31, 2002.

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Study Type

Study type defines the toxicity endpoint used for a particular study. For the U.S. National Toxicology Program data, the only endpoint evaluated is mortality. The toxicity endpoints used in the U.S. NTP data are LD_{50} , LC_{50} , LD_{Lo} , and LC_{Lo} .

The **LD**₅₀ is the dose of the pesticide in milligram (mg), microgram (ug), or nanogram (ng) of pesticide per kilogram (kg) of body weight that is lethal to 50% of the test organisms. This designation is used for routes of exposure where a known dose is administered (oral, dermal, intravenous, etc). Units used are: ppm (mg/kg), ppb (ug/kg), and ppt (ng/kg). (see definition of <u>conversion</u> factors between one unit and another).

The LC_{50} is only used for inhalation studies in the NTP data and is defined as the concentration of pesticide in air that is lethal to 50% of the test organisms within the stated study time. For the NTP studies, the LC_{50} is given in milligrams of pesticide per liter of air (mg/L), milligrams of pesticide per cubic meter (mg/m3), and grams of pesticide per cubic meter (g/m3). Other units used are parts per million (ppm), or parts per hundred (pph).

The LD_{Lo} is the lowest dose of pesticide that produces a lethal response in any test animal. Because the LD_{Lo} study type is not strictly defined as to the percentage of test animals affected, it is less useful for comparison purposes. Studies with an LD_{Lo} endpoint were not used to assign the <u>Toxicity Rating</u>.

The $\mathbf{LC_{Lo}}$ is only used for inhalation studies in the NTP data and is defined as the lowest concentration of pesticide in air that produces a lethal response in any test animal. For the NTP studies, the $\mathbf{LC_{Lo}}$ is given in milligrams of pesticide per liter of air (mg/L), milligrams of pesticide per cubic meter (mg/m3), parts per million (ppm), parts per billion (ppb). Because the $\mathbf{LC_{Lo}}$ study type is not strictly defined as to the percentage of test animals affected, it is less useful for comparison purposes. Studies with an $\mathbf{LC_{Lo}}$ endpoint were not used to assign the $\underline{\mathbf{Toxicity Rating}}$.

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Exposure Route

The exposure route is the route by which the test animals were exposed to the chemical. The most common exposure routes are oral (by mouth), dermal (applied to the skin), inhalation (by breathing the chemical). Since these three routes are the standard ones used for rating toxicity, only data from studies with these exposure types was used in assigning the <u>Toxicity Rating</u>.

Other exposure routes include:

Implant: Chemical is time-released from an implanted device. **Intraperitoneal:** Chemical is injected into the abdominal cavity.

Intravenous: Chemical is injected into a vein. **Intraarterial:** Chemical is injected into an artery.

Intraaural: Chemical is placed in the ear.

Intracerebral: Chemical is injected into the brain. **Intracervical:** Chemical is placed in the cervix.

Intraduodenal: Chemical is injected into the small intestine.

Intramuscular: Chemical is injected into a muscle. **Intratracheal:** Chemical is injected into the trachea.

Ocular: Chemical is placed in the eye

Parenteral: A general term meaning the chemical was *not* administered orally. Usually this means an

intramuscular or intravenous route was used.

Rectal: Chemical is adminstered through the rectum.

Subcutaneous: Chemical is injected in the upper layers of the skin.

Unknown or unreported: Some studies do not report the exposure route. View these with

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Species

The species is the type of animal on which the test was conducted.

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Result

The Result is the dose that caused the specified toxic endpoint. In most cases it is the dose that caused the death of 50% of the test animals.

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Units

The Units column defines the units on the dose, e.g. mg/kg, ppm, etc. For inhalation studies, the time of exposure is also noted, where H = hours and M = minutes. See <u>Study Type</u> for definitions of the different units.

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Acute Toxicity Rating

The Toxicity Rating is a narrative rating (Highly Toxic, Moderately Toxic, Slightly Toxic, and Not Acutely Toxic) derived from <u>LD50 or LC50</u> results according to U.S. EPA guidelines (see <u>table</u>). This rating was applied only to those studies with <u>LD50 or LC50</u> endpoints and oral, dermal and inhalation exposure routes for mammals that are reasonable analogs for humans (rats, mice, rabbits, monkeys, dogs, cats, gerbils, and guinea pigs). The term "No Rating" is used for all other studies.

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Used for Summary Rating

Based on the available NTP data, an acute toxicity range was determined. Not all NTP studies were used in this determindation. Only those studies with <u>LD50 or LC50</u> endpoints and oral, dermal and inhalation exposure routes for mammals that are reasonable analogs for humans (rats, mice, rabbits, monkeys, dogs, cats, gerbils, and guinea pigs) were used.

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