What does LD50 mean?

LD stands for "Lethal Dose". LD50 is the amount of a material, given all at once, which causes the death of 50% (one half) of a group of test animals. The LD50 is one way to measure the short-term poisoning potential (acute toxicity) of a material.

Toxicologists can use many kinds of animals but most often testing is done with rats and mice. It is usually expressed as the amount of chemical administered (e.g., milligrams) per 100 grams (for smaller animals) or per kilogram (for bigger test subjects) of the body weight of the test animal. The LD50 can be found for any route of entry or administration but dermal (applied to the skin) and oral (given by mouth) administration methods are the most common.

What does LC50 mean?

LC stands for "Lethal Concentration". LC values usually refer to the concentration of a chemical in air but in environmental studies it can also mean the concentration of a chemical in water.

For inhalation experiments, the concentration of the chemical in air that kills 50% of the test animals in a given time (usually four hours) is the LC50 value.

Why study LD50's?

Chemicals can have a wide range of effects on our health. Depending on how the chemical will be used, many kinds of toxicity tests may be required.

Since different chemicals cause different toxic effects, comparing the toxicity of one with another is hard. We could measure the amount of a chemical that causes kidney damage, for example, but not all chemicals will damage the kidney. We could say that nerve damage is observed when 10 grams of chemical A is administered, and kidney damage is observed when 10 grams of chemical B is administered. However, this information does not tell us if A or B is more toxic because we do not know which damage is more critical or harmful.

Therefore, to compare the toxic potency or intensity of different chemicals, researchers must measure the same effect. One way is to carry out lethality testing (the LD50 tests) by measuring how much of a chemical is required to cause death. This type of test is also referred to as a "quantal" test because it is measures an effect that "occurs" or "does not occur".

Who invented the idea of an LD50?

In 1927, J.W. Trevan attempted to find a way to estimate the relative poisoning potency of drugs and medicines used at that time. He developed the LD50 test because the use of death as a "target" allows for comparisons between chemicals that poison the body in very different ways. Since Trevan's early work, other scientists have developed different approaches for more direct, faster methods of obtaining the LD50.

What are some other toxicity dose terms in common usage?

LD01 Lethal dose for 1% of the animal test population

LD100 Lethal dose for 100% of the animal test population

LDLO The lowest dose causing lethality

TDLO The lowest dose causing a toxic effect

Why are LD50 and LC50 values a measure of acute toxicity?

Acute toxicity is the ability of a chemical to cause ill effects relatively soon after one oral administration or a 4-hour exposure to a chemical in air. "Relatively soon" is usually defined as a period of minutes, hours (up to 24) or days (up to about 2 weeks) but rarely longer.

How are LD/LC50 tests done?

In nearly all cases, LD50 tests are performed using a pure form of the chemical. Mixtures are rarely studied.

The chemical may be given to the animals by mouth (oral); by applying on the skin (dermal); by injection at sites such as the blood veins (i.v.- intravenous), muscles (i.m. - intramuscular) or into the abdominal cavity (i.p. - intraperitoneal).

The LD50 value obtained at the end of the experiment is identified as the LD50 (oral), LD50 (skin), LD50 (i.v.), etc., as appropriate. Researchers can do the test with any animal species but they use rats or mice most often. Other species include dogs, hamsters, cats, guinea-pigs, rabbits, and monkeys. In each case, the LD50 value is expressed as the weight of chemical administered per kilogram body weight of the animal and it states the test animal used and route of exposure or administration; e.g., LD50 (oral, rat) - 5 mg/kg, LD50 (skin, rabbit) - 5 g/kg. So, the example "LD50 (oral, rat) 5 mg/kg" means that 5 milligrams of that chemical for every 1 kilogram body weight of the rat, when administered in one dose by mouth, causes the death of 50% of the test group.

If the lethal effects from breathing a compound are to be tested, the chemical (usually a gas or vapour) is first mixed in a known concentration in a special air chamber where the test animals will be placed. This concentration is usually quoted as parts per million (ppm) or milligrams per cubic metre (mg/m^3). In these experiments, the concentration that kills 50% of the animals is called an LC50 (Lethal Concentration 50) rather than an LD50. When an LC50 value is reported, it should also state the kind of test animal studied and the duration of the exposure, e.g., LC50 (rat) - 1000 ppm/ 4 hr or LC50 (mouse) - $5mg/m^3$/ 2hr.

Which LD50 information is the most important for occupational health and safety purposes?

Inhalation and skin absorption are the most common routes by which workplace chemicals enter the body. Thus, the most relevant from the occupational exposure

viewpoint are the inhalation and skin application tests. Despite this fact, the most frequently performed lethality study is the oral LD50. This difference occurs because giving chemicals to animals by mouth is much easier and less expensive than other techniques. However, the results of oral studies are important for drugs, food poisonings, and accidental domestic poisonings. Oral occupational poisonings might occur by contamination of food or cigarettes from unwashed hands, and by accidental swallowing.

How do I compare one LD50 value to another and what does it mean to humans?

In general, the smaller the LD50 value, the more toxic the chemical is. The opposite is also true: the larger the LD50 value, the lower the toxicity.

The LD50 gives a measure of the immediate or acute toxicity of a chemical in the strain, sex, and age group of a particular animal species being tested. Changing any of these variables (e.g., type animal or age) could result in finding a different LD50 value. The LD50 test was neither designed nor intended to give information on long-term exposure effects of a chemical.

Once you have an LD50 value, it can be compared to other values by using a toxicity scale. Confusion sometimes occurs because several different toxicity scales are in use. The two most common scales used are the "Hodge and Sterner Scale" and the "Gosselin, Smith and Hodge Scale". These tables differ in both the numerical rating given to each class and the terms used to describe each class. For example, a chemical with an oral LD50 value of 2 mg/kg, would be rated as "1" and "highly toxic" according to the Hodge and Sterner Scale (see Table 1) but rated as "6" and "super toxic" according to the Gosselin, Smith and Hodge Scale (see Table 2). It is important to reference the scale you used when classifying a compound.

It is also important to know that the actual LD50 value may be different for a given chemical depending on the route of exposure (e.g., oral, dermal, inhalation). For example, some LD50s for dichlorvos, an insecticide commonly used in household pesticide strips, are listed below:

- Oral LD50 (rat): 56 mg/kg
- Dermal LD50 (rat): 75 mg/kg
- Intraperitoneal LD50: (rat) 15 mg/kg
- Inhalation LC50 (rat): 1.7 ppm (15 mg/m3); 4-hour exposure
- Oral LD50 (rabbit) 10 mg/kg
- Oral LD50 (pigeon:): 23.7 mg/kg
- Oral LD50 (rat): 56 mg/kg
- Oral (mouse): 61 mg/kg
- Oral (dog): 100 mg/kg
- Oral (pig): 157 mg/kg

Differences in the LD50 toxicity ratings reflect the different routes of exposure. The toxicity rating can be different for different animals. The data above show that dichlorvos is much less toxic by ingestion in pigs or dogs than in rats. Using Table 1, dichlorvos is moderately toxic when swallowed (oral LD50) and extremely toxic when breathed (inhalation LC50) in the rat. Using Table 2, dichlorvos is considered very toxic when swallowed (oral LD50) by a rat.

Table 1: Toxicity Classes: Hodge and Sterner Scale					
		Routes of Administration			
		Oral LD50	Inhalation LC50	Dermal LD50	
Toxicity Rating	Commonly Used Term	(single dose to rats) mg/kg	(exposure of rats for 4 hours) ppm	(single application to skin of rabbits) mg/kg	Probable Lethal Dose for Man
1	Extremely Toxic	1 or less	10 or less	5 or less	1 grain (a taste, a drop)
2	Highly Toxic	1-50	10-100	5-43	4 ml (1 tsp)
3	Moderately Toxic	50-500	100-1000	44-340	30 ml (1 fl. oz.)
4	Slightly Toxic	500-5000	1000-10,000	350-2810	600 ml (1 pint)
5	Practically Non-toxic	5000-15,000	10,000-100,000	2820-22,590	1 litre (or 1 quart)
6	Relatively Harmless	15,000 or more	100,000	22,600 or more	1 litre (or 1 quart)

Table 2: Toxicity Classes: Gosselin, Smith and Hodge		
Probable Oral Lethal Dose (Human)		
Toxicity Rating or Class	Dose	For 70-kg Person (150 lbs)
6 Super Toxic	Less than 5 mg/kg	1 grain (a taste - less than 7 drops)
5 Extremely Toxic	5-50 mg/kg	4 ml (between 7 drops and 1 tsp)
4 Very Toxic	50-500 mg/kg	30 ml (between 1 tsp and 1 fl ounce)
3 Moderately Toxic	0.5-5 g/kg	30-600 ml (between 1 fl oz and 1 pint)
2 Slightly Toxic	5-15 g/kg	600-1200 ml (between 1 pint to 1 quart)
1 Practically Non-Toxic	Above 15 g/kg	More than 1200 ml (more than 1 quart)

Can animal LD50 data be applied to man?

In general, if the immediate toxicity is similar in all of the different animals tested, the degree of immediate toxicity will probably be similar for humans. When the LD50 values are different for various animal species, one has to make approximations and assumptions when estimating the probable lethal dose for man. Tables 1 and 2 have a column for estimated lethal doses in man. Special calculations are used when translating animal LD50 values to possible lethal dose values for humans. Safety factors of 10,000 or 1000 are usually included in such calculations to allow for the variability between individuals and how they react to a chemical, and for the uncertainties of experiment test results.

How should an LD50 value be used?

The LD50 can be used:

- As an aid in developing emergency procedures in case of a major spill or accident.
- To help develop guidelines for the use of appropriate safety clothing and equipment. For example, if the dermal LD50 value for a chemical is rated as extremely toxic, it is important to protect the skin with clothing, gloves (etc.) made of the right chemical-resistant material before handling. Alternatively, if a chemical has an inhalation LC50 value which indicates that it is relatively harmless, respiratory protective equipment may not be necessary (as long as the oxygen concentration in the air is in the normal range - around 18%).
- For the development of transportation regulations.
- As an aid in establishing occupational exposure limits.
- As a part of the information in Material Safety Data Sheets. Remember, the LD50 is only a ball park figure so that lethal toxicity can be compared. It says nothing about levels at which other acute toxic, but non-lethal, effects might occur.

The LD50 is only one source of toxicity information. For a more thorough picture of the immediate or acute toxicity of a chemical, additional information should be considered such as the lowest dose that causes a toxic effect (TDLO), the rate of recovery from a toxic effect, and the possibility that exposure to some mixtures may result in increasing the toxic effect of an individual chemical.

Where can I find LD50 and LC50 values?

The largest, single collection of LD50 and LC50 values is in the database Registry of Toxic Effects of Chemical Substances (RTECS**)** that is available by subscription on CD-ROM and on the Internet. Two other databases available from CCOHS, CHEMINFO and the Hazardous Substances Data Bank® (HSDB). Both of these are on the CHEMpendium CD-ROM; CHEMINFO is also accessible on the Internet.

Document last updated on June 16, 2005

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The LD_{50}

The LD_{50} is a standardized measure for expressing and comparing the toxicity of chemicals.

The LD_{50} is the dose that kills half (50%) of the animals tested (LD = "lethal dose"). The animals are usually rats or mice, although rabbits, guinea pigs, hamsters, and so on are sometimes used.

Because a single test may kill as many as 100 animals, the United States and other members of the Organization for Economic Cooperation and Development agreed in December 2000 to phase out the LD_{50} test in favor of alternatives that greatly reduce (or even eliminate) deaths of the test animals.

In all these tests, the dose must be calculated relative to the size of the animal. The most common units are milligrams of chemical per kilogram of test animal (mg/kg or ppm).

Chemical	Category	Oral LD_{50} in Rats (mg/kg)
Aldicarb ("Temik")	Carbamate	1
Carbaryl ("Sevin")	Carbamate	307
DDT	Chlorinated hydrocarbon	87
Dieldrin	Chlorinated hydrocarbon	40
Diflubenzuron ("Dimilin")	Chitin inhibitor	10,000
Malathion	Organophosphate	885
Methoprene	JH mimic	34,600
Methoxychlor	Chlorinated hydrocarbon	5,000
Parathion	Organophosphate	3
Piperonyl butoxide	Synergist	7,500
Pyrethrins	Plant extract	200
Rotenone	Plant extract	60

The table gives the LD_{50} values for some insecticides. In each case, the chemical was fed to laboratory rats. Note that the lower the LD_{50}, the more toxic the chemical. Even adjusting for the test animal's weight, the LD_{50} for one species is often quite different from that for another. Thus any LD_{50} value gives only a rough estimate of the risk to humans. The way in which the chemical is administered also has a marked effect on LD_{50} values. The chemical may be fed, injected, applied to the animal's skin, etc., and each method usually generates a different LD_{50}.