Technically Speaking

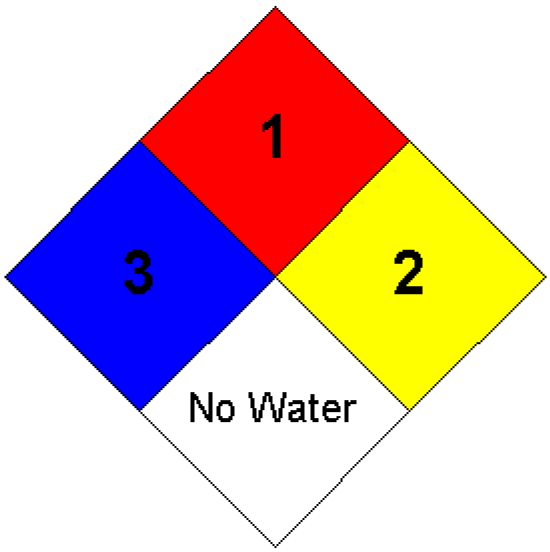
Health and Toxicity

by John S. Nordin, Ph.D.

This is a very broad topic. We will start with the National Fire Protection Association diamond.

National Fire Protection Association diamond

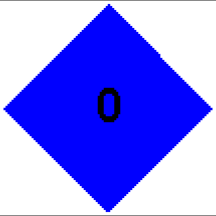
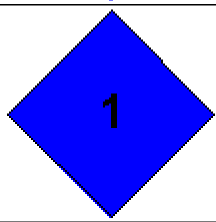
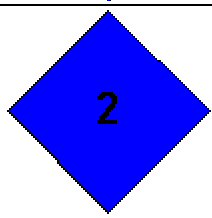
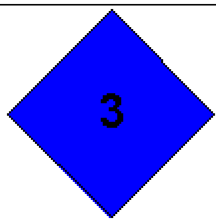
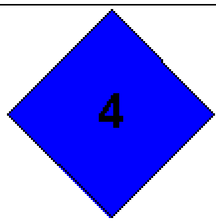
You have seen the NFPA diamond that should accompany hazardous chemicals that are stored or used.



The blue diamond above represents health hazard ratings. The red diamond at the top represents flammability. The yellow diamond at the right represents reactivity. The white diamond at the bottom may convey additional information, but for many chemicals the white diamond is left blank. The colored diamonds each contain a hazard rating number from 0 to 4 with 4 being the most hazardous rating and 0 being the least hazardous.

Remember that we are talking about how the National Fire Protection Association (NFPA) considers health hazard ratings. Other organizations such as the Occupational Safety and Health Administration (OSHA) or the National Institute for Occupational Safety and Health (NIOSH) communicate heath hazard information differently.

The NFPA rating system is listed below:

	The material presents no unusual health hazard. Under fire conditions, the material would offer no hazard beyond that of ordinary combustible material.
	Materials which on exposure would cause irritation but only minor residual injury even if no treatment is given.
	Materials which on intense or continued exposure could cause temporary incapacity or possible residual injury unless prompt medical treatment is given.
	Materials which on short exposure could cause serious temporary or residual injury even though prompt medical treatment is given.
	Materials which on very short exposure could cause death or major residual injury even though prompt medical treatment is given.

When using the NFPA diamond, several cautions are advised. By exposure is meant inhalation or skin contact and does not consider irritation or burns if splashed into the eyes, or hazards from ingestion of the material. Unusually sensitized individuals, the elderly, or infants are not considered in this rating system. Long term effects from exposure such as carcinogenetic effects (may cause cancer later in life) may not be considered in the rating system.

Notice that the word “materials” rather then “chemicals” is used in the NFPA rating system definitions. From a chemist point of view, all materials are made up of chemicals, whether natural or man-made. This includes things like air, water, and the ground upon which a person stands. However, the general public may have a much more restrictive definition of the word chemical, usually substances that are man-made and may be harmful to his/her health. To avoid ambiguity, the word “materials” is used. Many natural substances or materials are indeed harmful. Many man-made substances are quite harmless.

Dose and Routes of Exposure

Let's look at how a person is exposed to the chemical or material. Routes of exposure may be by (1) inhalation, (2) ingestion, (3) through the skin, (4) through the eyes, (5) or by inoculation as in a puncture wound. Sometimes four routes of exposure are listed in reference sources with eye contact considered as a variation of skin or dermal absorption. Eyes are particularly vulnerable because they are very vascular and provide rapid transport of many chemicals into the body.

Some chemicals are corrosive to human flesh and do considerable damage to the skin or eyes on contact. Some chemicals are sensitizers, that is they cause rashes or asthmatic conditions upon repeated exposure.

The two major routes of entry in the case of first responders are (1) inhalation and (2) dermal or skin contact. We will assume that the responders practice good hygiene and take care not to contaminate food or water intake. Some materials are readily absorbed through the skin but have low vapor pressures and not likely to be inhaled. Some chemicals are corrosive and burn human flesh but do not readily absorb into the body. Some materials cause the most harm if inhaled. Asbestos fibers might be safely handled but if inhaled may result in a fatal form of lung cancer later in life.

Let us look at a couple of definitions:

Dose: The amount of chemical (or material) administered or taken up by an organism. For example, if a person consumes one gram of methanol, his/her dose is one gram.

Dosage: The amount of chemical (or material) administered or taken up by the organism expressed as some function (e.g. per unit weight) of the organism. For example, if the person weighs 70 kilograms and consumes one gram of methanol, his/her dosage is 1/70 = 0.01429 grams per kilogram of body weight, or 14.3 mg/kg. If he/she consumes 1 gram of methanol daily, the dosage is 14.3 mg/kg/day.

Some chemicals (or materials) may be taken up by the body and later excreted unchanged in the urine or feces and/or through respiration. Other chemicals such as methanol are metabolized usually in the liver and excreted as a different chemical. Some chemicals or their metabolites accumulate in the body and are not excreted or only partly excreted over a long period of time. Examples of chemicals which accumulate in the body are many toxic metals such as mercury and lead, polychlorinated biphenyls (PCB), and many radioactive isotopes. These have the potential to do great harm to the body.

How Is Toxicity Measured?

Most information on toxicity comes from test animals which are exposed to varying amounts of the chemical or material. Additional information comes from workers who have been exposed to the material, from prison test volunteers, poison case victims, and even (in the case of chlorine) from use as a chemical warfare agent in the battlefield. The use of test animals allows the information to be obtained under a controlled situation. Usually the animal is a rat, but often mice and rabbits and other animals are used.

Acute toxicity is measured by exposing the test animals to the chemical, and determining the dosage required to kill 50% of the test animals. The route of absorption is critical to the test: the chemical might be placed in the animal's food, or the animal partly shaved and the chemical placed in a patch attached to the skin, or the animal placed in a chamber and allowed to breathe vapors or gases or aerosols for a specified time.

Dermal and oral ingestion test results are usually expressed in terms of LD_{50} values, defined as the quantity of material required to kill 50% of the test animal, and is expressed in grams or milligrams per kilogram of body weight. (LD = lethal dosage)

Inhalation test results are usually expressed as LC_{50} values, defined as the lethal concentration in air of a toxicant which kills 50% of the test animals when administered over a specific time period. The time period usually used in animal tests is 1 or 4 hours.

Sometimes tests are run on fish or aquatic invertebrates. This information is of particular interest to regulators who establish discharge limits on chemicals in surface runoff or in industrial effluents. In case of a spill, the material often must be contained and cannot be allowed to appear in surface waters, or the regulatory agency may allow release over a time period so as not to kill the fish. Toxicity results are expressed as LC_{50} values, defined as the lethal concentration in water (parts per million, mg/liter, micrograms/liter or other units) that kills 50% of the test organisms over a specific time period, usually 96 hours.

Chronic toxicity is measured by exposing the test animals to a lower dosage than the acute toxicity tests, but the dosage is repeated daily. The tests may take weeks, months, even years. Sometimes dogs are used as the test animal. Measurements of the toxicant and possible metabolites may be made in the animal's urine and feces. Birth defects in the offspring may be studied. The animals are sacrificed at the end of the tests and changes in body organs noted including any evidence of cancer.

Animal toxicity is never the same as for humans, but the LD_{50} or LC_{50} can give an idea of what the basic toxicity should be so that appropriate measures can be taken. For example, if LD_{50} for rats is 10 mg/kg, it is reasonable to expect that a dose of 700 mg would kill a 70 kg man. Remember the LD_{50} or LC_{50} numbers are derived from acute toxicity tests where the animal is delivered a single dose and that these numbers do not consider possible long-term effects such as developing cancer. Chronic toxicity is particularly insidious because of the long latency period.

Another number sometimes reported from animal inhalation tests is LC_{Lo} or the lowest reported concentration in air that kills any of the test animals breathing the air for a specified time period. Again, only acute toxicity is considered. More Definitions

TLV: Threshold Limit Value. This is expressed as the time-weighted average (TWA) airborne concentration or as a ceiling value (C) to which healthy, adult workers can be exposed during an 8-hour day without adverse effects. The ceiling concentration should not be exceeded. These numbers were developed by the American Conference of Governmental Industrial Hygienists (ACGIH). Sometimes the number is called ACGIH TLV TWA for the time-weighed average or ACGIH TLV Ceiling for the ceiling value.

STEL: Short Term Exposure Limit. This is the 15-minute, time weighted average concentration (TWA) that should not be exceeded at anytime during the day. There should not be any more than 4 incidences during an 8-hour day. These numbers were developed by the American Conference of Governmental Industrial Hygienists. Sometimes the number is called ACGIH TLV STEL.

NIOSH REL: National Institute for Occupational Safety and Health, Recommended Exposure Limits. NIOSH is the governmental organization which develops and periodically revises recommended exposure limits (RELs) for hazardous substances or conditions in the workplace. These recommendations are published and transmitted to the Occupational

Safety and Health Administration (OSHA) for use in promulgating legal standards. NIOSH considers many sources in developing their REL values, including ACGIH. NIOSH recommends 8-hour time weighted average (TWA) numbers, ceiling numbers, and STEL.

IDLH: Immediately Dangerous to Life and Health. This exposure concentration is developed by the National Institute of Occupational Safety and Health. This concentration represents a maximum level that a person could escape within 30 minutes without any escape-impairing symptoms or any irreversible acute health effects. Usually this concentration number is used in the context of use and selection of a respirator. Sometimes the number is called NIOSH IDLH.

PEL: Permissible Exposure Limit. This is the concentration in the air that the Occupational Safety and Health Administration (OSHA) uses in setting regulatory limits in the workplace.

EEL: Emergency Exposure Level. This number is published by the American Industrial Hygiene Association, and is sometimes called AIHA EEL. The EEL is the concentration of contaminant that can be tolerated without adversely affecting health but not necessarily without acute discomfort or other evidence of irritation or intoxication. They are intended to give guidance in the management of single, brief exposures to airborne contaminants in the working environment. Reference is made to the publication by J.P. Frawley, "Emergency Exposure Limits", Amer. Ind. Hyg. Assn. Journal, 25, pages 578-586, 1964.

ERPG: Emergency Response Planning Guideline. These airborne concentrations numbers developed by the American Industrial Hygiene Association are considered by many authorities including the U.S. Department of Transportation to be the best available criteria for deriving isolation and protective action distances in case of a chemical release incident. To date, ERPG numbers have been published for a little more than 100 chemicals. About 7 new chemicals are added each year. Three levels of concern are developed:

- ERPG-1: The maximum airborne concentration below which most individuals could be exposed for up to one hour without experiencing anything other than mild transient adverse health effects or perceiving a clearly defined objectionable odor.

- ERPG-2: The maximum airborne concentration below which most individuals could be exposed for up to one hour without experiencing or developing irreversible or other serious health effects, or symptoms that could impair their ability to take protective action.

- ERPG-3: The maximum airborne concentration below which most individuals could be exposed for up to one hour without experiencing or developing life-threatening health effects.

TEEL: Temporary Emergency Exposure Limit. The U.S. Department of Energy has published a list of Temporary Emergency Exposure Limits to be used by DOE contractors to serve as temporary values until the American Industrial Hygiene Association comes up with their ERPG list. TEEL-1, TEEL-2, and TEEL-3 numbers have been published for almost 2000 chemicals. This list available at the website, http://www.bnl.gov/scapa/teels.htm

HSE SLOT: Health and Safety Executive Specified Levels of Toxicity. These numbers are generated for use in the United Kingdom. Reference: Turner, D. and S. Fairhurst, 1989. "Assessment of the Toxicity of Major Hazard Substances. Report 21". Health and Safety Executive, London, UK.

What about Cancer and Other Long Term Effects?

This is a controversial topic. Development of cancer later in life is usually what comes to mind, but other things can happen. There have been several documented cases where workers have been exposed to the pesticide azinophos-methyl, even a single acute exposure, and several weeks later started to develop numbness and tingling in the extremities (arms and lower legs) which eventually resulted in paralysis. Over the years the persons partly recovered but some were left with a permanent disability. Some chemicals such as mercury, lead, and certain pesticides can accumulate in the body leading to loss in motor control and cognitive ability. Some can result in birth defects and in chromosome damage.

This kind of information is difficult to carry out in animal tests. It is relatively easy to give rats or mice test animals a single acute exposure and establishing a LC_{50} or LD_{50} concentration or dosage which kills 50% of the animals. But the tests do not answer the question of whether the surviving animals develop cancer or have other disabilities because the tests are not set up that way. Other tests are carried out where the animals are given a daily dosage, usually orally, and after a period of time may be sacrificed and organs examined to look for cancer. Again there are time constraints on the tests, usually 2 years is a practical limit. Sometimes ambiguous results occur in the tests, where liver tumors might appear in an animal receiving a lower dosage but tumors do not appear in an animal receiving a higher dosage. Sometimes tumors appear in mice but not rats or dogs or rabbits.

The International Agency for Research on Cancer (IARC) publishes a list of chemicals which are known or probable human carcinogens. This list is used by OSHA and the information must be communicated to workers by regulation. Additional suspected carcinogens may be designated by NIOSH (see Pocket Guide to Chemical Hazards) and under the National Toxicology Program. A person exposed to these chemicals may not necessarily develop cancer. A big unknown is what is the minimum exposure that is safe. A major part of the answer is that it varies with the individual. Smokers are at a disadvantage.

Known or Probable Human Carcinogens (according to OSHA using IARC list, 1991, condensed)

Acrylonitrile
Actinolite
Actinomycin D
Adriamycin
Aflatoxin B1
4-Aminobiphenyl
Amitrole
Amosite
Anthophyllite
Arsenic
Lead chromate
Lead chromate (VI) oxide
Magenta manufacture
Melphalan
Mestranol
Methoxsalen with ultraviolet
Metronidazole
certain Mineral oil additives and impurities
Mustard gas
2-Nephthylamide

Arsenic pentoxide
Arsenic trioxide
Arsenic, inorganic compounds
Asbestos
Auramine
Azathioprine
Benzene
Benzidene
Benzo(a)pyrene
Benzotrichloride
Beryl
Beryllium
Beryllium aluminum alloy
Beryllium compounds
Bischloroethyl nitrosourea (BCNU)
1,4-Butanediol dimethanesulphonate
Cadmium
Cadmium dust
Cadmium compounds
Calcium chromate
Carbon tetrachloride
Carbonic acid, nickel salt
Chemotherapy chemicals, certain kinds
Chlorambucil
Chloramphenicol
Chlornaphazine
1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea
Chloroform
bis-Chloromethyl ether
Chlorophenols
Chromium
Chromium trioxide, sintered
Chromium compounds
Cisplatin
Coal tar pitches
Cresote(s)
Cyclophosphamide
Dacarbazine
3,3'-Dichlorobenzidine
Dienoestrol
Diethyl sulfate
Diethylstilbestrol

3,3'-Dimethoxybenzidine

Dimethyl sulfate

Nickel
Nickel carbonyl
Nickel compounds
Nickel refining
Nickel subsulfide
Nickelocene
Nitrogen mustard
Norethisterone
Oestrogens, conjugated
Oestrone
Oil shale soot extracts
Oral contraceptives, combined
Oxymetholone
Phenacetin, incl. analgesic mixtures
Phenazopyridine
Phenoxyacetic acid herbicides
Phenytoin
Polychlorinated byphenyls (PCBs)
Procarbazine
Progesterone
Propylthiouracil
Shale oils, bitumens
Shale oils, commercial blends
Shale oils, crude distillation fractions
Shale oils, crude-high temperature fractions
Shale oils, crude-low temperature fractions
Sodium arsenate
Sodium arsenite
Soots, tars and mineral oils
Strontium chromate
Tetrachlorodibenzo-dioxin (TCDD)
o-Toluidine
Tremolite
Treosulfan
2,4,6-Trichlorophenol
Tris(aziridinyl)-para-benzoquinone
Tris(aziridinyl) phosphine sulfide
Uracil mustard
Vinyl chloride
Zinc beryllium silicate
Zinc chromate

Dimethylcarbamoyl chloride
Dioxane

Direct black 38, technical grade
Direct blue 6, technical grade
Direct brown 95, technical grade

DDT

Epichlorohydrin

Estradiol

Ethinyloestradiol

Ethylene dibromide

Ethylene oxide

Ethylene thiourea
Formaldehyde (gas)

Hematite (underground mining, radon exp.)
Hydrazine

Isopropyl alcohol manufacture by strong acid process

One obvious point is that the chemical must enter the body (a person must be exposed to the chemical) to be cancerous. Many of the materials such as nickel and chromium metal and pads made of asbestos may be safely handled, but fines or dusts of the same chemical if inhaled are dangerous. Many other chemicals cannot be safely handled because they are absorbed through the skin.

The above listing is not complete. The U.S. Department of Health under the National Toxicology Program has its listing of carcinogens. For this listing, visit the website,

http://ntp-server.niehs.nih.gov/NewHomeRoc/AboutRoC.html

and pull up the 10th report. Information on each listed chemical may be obtained in this report.