Toxicology

A Brief Introduction to the Concepts of Toxicology-

So we can all speak the same language.

Units Used to Measure Chemicals in the Environment

- PPM – Parts per million
- PPB – Parts per billion
- PPT – Parts per trillion

One part per million is

- 1 inch in 16 miles
- 1 minute in two years
- 1 cent in $10,000
- 1 ounce of salt in 31 tons of potato chips
- 1 bad apple in 2,000 barrels of apples

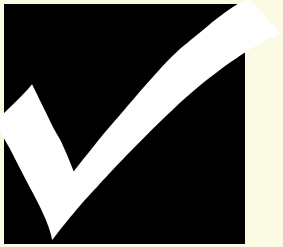
One part per billion is

- 1 inch in 16,000 miles
- 1 second in 32 years
- 1 cent in $10,000,000
- 1 pinch of salt in 10 tons of potato chips
- 1 bad apple in 2,000,000 barrels of apples

One part per trillion is

- 1 postage stamp in the area of the city of Dallas
- 1 inch in 16 million miles (more than 600 times around the earth)
- 1 second in 320 centuries
- 1 flea on 360 million elephants
- 1 grain of sugar in an Olympic sized pool
- 1 bad apple in 2 billion barrels

When Reporting Lab Results… We Also Assume..



1 liter of water = 1 kg

1 mg / kg = 1 ppm

$1mm^3$ / liter = 1 ppm

1 mg / liter = 1 ppm

Measures of Toxicity

- Toxicity of chemicals is determined in the laboratory
- The normal procedure is to expose test animals
  - By ingestion, application to the skin, by inhalation, gavage, or some other method which introduces the material into the body, or
  - By placing the test material in the water or air of the test animals' environment

Measures of Toxicity

- Toxicity is measured as clinical "endpoints" which include
  - Mortality (death)
  - Teratogenicity (ability to cause birth defects)
  - Carcinogenicity (ability to cause cancer), and,
  - Mutagenicity (ability to cause heritible change in the DNA)
- At this time we will discuss 2 measures of mortality – the LD_{50} and the LC_{50}

Measures of Toxicity: The Median Lethal Dose

LD_{50}

The amount (dose) of a chemical which produces death in 50% of a population of test animals to which it is administered by any of a variety of methods

mg/kg

Normally expressed as milligrams of substance per kilogram of animal body weight

Measures of Toxicity: The Median Lethal Concentration

LC_{50}

The concentration of a chemical in an environment (generally air or water) which produces death in 50% of an exposed population of test animals in a specified time frame

mg/L

Normally expressed as milligrams of substance per liter of air or water (or as ppm)

Primary Routes of Exposure to Pesticides

There are three primary routes by which organisms are exposed to pesticides

Oral

Dermal

Inhalation

Primary Routes of Exposure: Oral Exposure

Any exposure to pesticide which occurs when the chemical is taken in through the mouth and passes through the gastrointestinal tract

During oral exposure, although carried within the body, the pesticide is still outside of the body cavity

Primary Routes of Exposure: Dermal Exposure

Exposure of the skin to a pesticide

Most common route of human exposure

With proper hygiene this type of exposure is generally not serious unless there is a specific, rapid toxicological effect (often eye effects) which is of concern

Primary Routes of Exposure: Inhalation Exposure

Occurs when a pesticide is breathed into the lungs through the nose or mouth

Not of toxicological concern until it crosses from the lung into the body (unless the chemical is corrosive)

Duration of Exposure

Three terms are commonly used to describe the duration of dose(s)

Acute

Chronic

Subchronic

Duration of Exposure: Acute Exposure

Application of a single or short-term (generally less than a day) dosing by a chemical

If toxic symptoms are expressed, they are referred to as symptoms of “acute toxicity”

Duration of Exposure: Chronic Exposure

Expression of toxic symptoms only after repeated exposure to a chemical in doses regularly applied to the organism for a time greater than half of its life-expectancy

If toxic symptoms are expressed, they are referred to as symptoms of “chronic toxicity”

Duration of Exposure: Subchronic Exposure

Toxic symptoms are expressed after repeated applications for a timeframe less than half the life expectancy of the organism – but more often than a single dose or multiple doses applied for only a short time

If toxic symptoms are expressed, they are referred to as symptoms of “subchronic toxicity”

Remember –

- For pesticides – less is more when dealing with toxicity
- The less you need to cause a toxic effect – the more toxic the substance is
- Thus an LD_{50} of 25 mg/kg is more toxic than is one of 7,000 mg/kg

Is it Safe?

Low Risk

Signal Words

The relative acute toxicity of a pesticide is reflected on the label in the form of a “signal word”

The (toxicologically) appropriate signal word MUST appear on every pesticide label

The three possible signal words are

CAUTION

WARNING

DANGER

Signal Words: CAUTION

- "Caution" reflects the lowest degree of relative toxicity
- All pesticides with an LD_{50} of greater than 500 mg/kg must display this word on their label
- Actually includes two groups of pesticides – those classed by the EPA as "Relatively nontoxic (>5,000 mg/kg) and those classed as "slightly toxic" (500 – 5,000 mg/kg)

Signal Words: WARNING

- "Warning" reflects an intermediate degree of relative toxicity
- All pesticides with an LD_{50} of greater than 50 and less than 500 mg/kg must display this word on their label
- Pesticides in this category are classed as "moderately toxic"

Signal Words: DANGER

"Danger" reflects the highest degree of relative toxicity

All pesticides with an LD_{50} of less than 50 mg/kg must display this word on their label

Pesticides here are classed as "highly toxic"

POISON!!!

- Legally defined term – not just anything you don't like
- Any pesticide with an LD_{50} of 50 mg/kg or less
- Labels must reflect this classification
- Label must have the signal word "DANGER" plus the word "POISON"
- Label also must display the skull and crossbones icon

Relative toxicity

- Organisms can't differentiate between "natural" and "synthetic" chemicals
- "Synthetic" does not mean toxic or poisonous
- "Natural" does not mean safe or even low risk
- Chemicals must be evaluated in their biological context of behavior in organisms
- Mode of action, not source, is the concern of toxicologists and informed users of pesticides

Relative toxicity

Are All Pesticides Created Equal ???

- Most herbicides act on biological pathways not present in humans
- Some insecticides are highly toxic

Relative toxicity

- Some examples of pesticides and other chemicals are given to show relative risk of pesticides in the environment in which we live
- This is NOT to trivialize the pesticides
- Always treat them with caution and respect
- But, have a realistic recognition of their relative risk in a world of risks

Relative toxicity: Insecticides

• TCDD (Dioxin)	0.1	mg/kg
• Parathion	13.0	mg/kg
• Nicotine	50.0	mg/kg
• Sodium Fluoride	52.0	mg/kg
• Carbaryl	270.0	mg.kg
• Malathion	370.0	mg/kg

Relative Toxicity: Herbicides and Additives

	mg/kg
Paraquat	95
2,4-D	375
2,4-DP	532
Triclopyr	630
Tebuthiuron	644
Dicamba	757
Hexazinone	1,690
Glyphosate	4,320

	mg/kg
Limonene	5,000
Clopyralid	>5,000
Sulfometuron Met..	>5,000
Imazapyr	>5,000
Diesel oil	7,380
Picloram	8,200
Fosamine am..	24,400
Kerosene	28,000

Relative Toxicity: Comparative information

Highly toxic chemicals

0 – 50 mg/kg range

(taste → 1 teaspoonful)

	mg/kg
• Botulinus toxin	0.00001
• Dioxin	0.1
• Parathion	13.0
• Strychnine	30.0
• Nicotine	50.0

Moderately toxic chemicals

50- - 500 mg/kg range

(teaspoonful → 1 ounce)

	mg/kg
• Paraquat	95
• Caffeine	200
• Carbaryl	270
• Malathion	370
• 2,4-D	375

Relative Toxicity Comparative Information

Slightly toxic chemicals

500 – 5,000 mg/kg range

(1 ounce → 1 pint)

	mg/kg
• 2,4-DP	532
• Triclopyr	630
• Tebuthiuron	644
• Dicamba	757

	mg/kg
• Formaldehyde	800
• Hexazinone	1,690
• Asprin	1,700
• Vitamin B_3	1,700
• Household bleach	2,000
• Table salt	3,750
• Glyphosate	4,320

Relative Toxicity: Are all substances toxic?

YES!

- All are toxic to some quantifiable degree
- Sugar has an LD_{50} of 30,000 mg/kg
- Ethanol has an LD_{50} of only 13,700 mg/kg
- Even water has a recognized LD_{50} of slightly greater than 80,000 mg/kg

Relative Toxicity: The Last Word

- Pesticides are chemicals introduced into the environment to perform a function
- The source of a chemical (synthetic vs. natural) is irrelevant when considering its toxicity
- Pesticides should be treated with care and proper respect – but so should household cleaners, gasoline and kerosene, bleaches, paints and all other chemicals