

Toxicology and Risk

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Our Chemical World

• Chemical Abstracts	22,000,000+
– Commercial Products	100,000
• “Toxic Substances”	50,000
– Pesticides	1,000
– (Products 13,000)	

Insecticides and Use in Pest Management

- Pests
- Beginnings
- Food purity and residues
- Organics: DDT and Parathion
- *Silent Spring*
- Drift, biomonitoring, exposure
- Risk assessment

How does toxicology fit into the pesticide regulation?

Exposure sources: Acute Toxicity

	Highly toxic	Moderately toxic	Slightly toxic	Very low toxicity
Oral LD50 mg/kg	0-50	50-500	500-5000	>5000
Inhalation LC50 (mg/L)	<0.2	0.2-2	2-20	>20
Dermal LD50 mg/kg	<200	200-2000	2000-5000	>5000
Eye effects	corrosive	irritation persists 7 d	irritation reversible 7d	no irritation
Skin effects	corrosive	severe irritation @72 h	moderate irritation @ 72 h	mild irritation @ 72 h

In Vivo Dermal Absorption of Pesticides in Rats and Humans

Pesticide	Human Absorption	Rat Absorption	Ratio: Rat/Human
Atrazine	3	8	2.7
Azinphosmethyl	16	44	2.8
Chlorpyrifos	10	66	6.6
DEET	7	32	4.6
Diquat	1	3	3.0
Isofenphos	4	16	4.0
KBR 3023	4	23	5.8
Lindane	9	31	3.4
Malathion	6	28	4.7
Orthophenyl phenol	43	65	1.5
Parathion	10	95	9.5
Permethrin	2	28	14.0
Propoxur	20	50	2.3
Grand Mean ± SD	10 ± 11	38 ± 26	5.0 ± 3.4

Product Signal Words

Signal word	Acute Oral LD50 (mg/kg bw)
CAUTION <i>slightly toxic</i>	500-5000
WARNING <i>moderately toxic</i>	50-500
DANGER <i>highly toxic</i>	0-50

Acute, Sub-chronic, and Chronic

- Acute 1± day
- Short term to 28 days
- Sub-chronic few days to 10% lifetime
- Chronic lifetime

Chemical Risk: Dose/Exposure

Experimental

*Human
Exposure*

Hazard

Use

Dose-Response

Exposure

Risk Assessment

Management
Communication

Risk Assessment

- Lethal LD50
- Low observed adverse effect
- No observed adverse effect
- Uncertainty:
10 × species &
10 × variability

- $NOAEL/10/10 = RfD$
RfD=Reference Dose
- $RfD/E > 1$

Where do pesticides go?

- Routes (insecticides)
 - Inhalation
 - Ingestion
 - Skin absorption
- Distribution
 - Blood
- Elimination
(breakdown products)
 - Urine
 - Stool

- Storage
 - Blood: circulating
 - Short term: skin
 - Long term: fat

How little is OK? Biomonitoring

- Reactive, H₂O sol
- Short residence
 - Minutes
 - Hours
 - Days
- Urine, saliva

$$E (\mu\text{g/person}) = \text{Conc}(\mu\text{g/L}) \times \text{volume}$$

- Less reactive, oil sol
- Long residence
 - Months
 - Years
 - Lifetimes
- Blood, stool

$$E (\mu\text{g/person}) = \text{Conc}(\mu\text{g/ml}) \times \text{blood volume}$$

Toxicology Profile: Glyphosate

- LD50
- LOAEL
- NOAEL
- Death
 - >5000 mg/kg-bw
- Response
 - 3500 mg/kg-d maternal and developmental
- No response
 - 1000 mg/kg-d

LD50, LOAEL, NOAEL (mg/kg)

<u>Lethal Dosage</u> 50%	<u>LOAEL</u> (threshold)	<u>NOAEL</u>
Death	Organs Reproduction Growth	No effects

Toxicology Profile: 2,4-D

- LD50
- LOAEL
- NOAEL
- Death
 - 800-2000 mg/kg-bw
- Response
 - 60 mg/kg kidney
 - 300 mg/kg testes
- No response
 - 15_k mg/kg
 - 100_t mg/kg

2,4-D Reference Dose

- NOAEL 15 mg/kg kidney
- Uncertainty Factors
 - Species: animal to human (0.1) 1.5 mg/kg
 - Person-to-person (0.1) 0.15 mg/kg

$$\text{RfD} = \text{NOAEL} \times 0.1 \times 0.1$$

Table 2. Leading Causes of Death in the US: Unintentional Injuries Including Poisoning

Cause	Number	Deaths per 10 ⁵ Deaths
All unintentional injuries	101,537	35.6
Motor-vehicle	43,788	15.4
Falls	15,019	5.3
Poisoning	14,078	4.9
Pesticide	7	0.0025
Choking	4,185	1.5
Drowning	3,281	1.2
All other	21,186	7.4

National Safety Council, 2004

Table 1. Unintentional Injuries at Work by Industry in the US

Injury Division	Workers x 10 ³	Deaths 2003	Deaths per 10 ⁵ Workers
Agriculture	3,340	710	20.9
Mining	539	120	22.3
Construction	9,268	1,060	11.4
Manufacturing	17,708	490	2.8
All industries	138,988	4,500	3.2

National Safety Council, 2004

Table 3. Five Year Summary of California Pesticide Illness and Injury Data Classified by Definite, Probable, and Possible Exposures¹

Year	Total cases	Relationship of Illness or Injury to Pesticide Exposure					
		Definitely or Probably			Possible		
		Cases	Hospitalized	Lost work time	Cases	Hospitalized	Lost work time
1999	1,629	830	32	126	371	2	51
2000	1,144	637	33	144	256	3	51
2001	979	430	27	78	186	2	25
2002	1,859	924	19	106	291	6	42
2003	1,232	614	8	70	188	1	42

¹Definite: Signs and symptoms would be expected from exposure described. Probable: Close correspondence. Possible: Some correspondence.

Table 4. Substances Most Frequently Involved in Children Under 6 Years-of-age

Substance	Number x 10 ⁵	Per Cent
Cosmetics and personal care products	1.7	13.4
Cleaning substances	1.2	9.7
Analgesics	1.0	7.8
Foreign bodies	0.92	7.4
Topicals	0.92	7.4
Cough and cold preparations	0.68	5.5
Plants	0.58	4.6
Pesticides	0.51	4.1
Vitamins	0.45	3.6
Antimicrobials	0.35	2.8
All other	1.5	11.2
Total	12.5	--

The plural of anecdotal is not evidence!

- Collier Co. Florida, Oct 2005
 - 3 cases of child deformity, Moms 200ft
- “They have to stop spraying people”
- Phocomelia
- Deformed jaw
- Death 3d, severely disfigured

“That doesn’t rule it out. It’s just that we couldn’t make the link.” County Health Department

Margin-of-Exposure

RfD



Exposure (ADD)

Chemical exposures—you can't live without 'em

- Exposure is essential
- Exposure can be measured
- Exposure is not a disease

- Dose is the chemical part of risk
- Risk reduction is an ongoing process