

The Toxicology and Regulation of Chlorphenapyr, Fipronil, Imidacloprid, and Thiamethoxam

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Personal Chemical Exposure Program

Helen Vega, Administrative Assistant

Today's Menu

- **Chemicals and Public Perceptions**
- **General Pesticide Science**
- **Advanced Pesticide Science**
- **Health Records**
- **Regulate: Margin-of-Exposure**
- **Safe Pesticide Use**

Sign-up Envelope: Quiz will be on internet Monday a.m.
4-digit Number on Zip-Scan, 35 questions/**pencil**;
postmark on or before **4/6/06**

 **\$40** Lottery from all completed returns (Survey & Z-Scan)



**Chemicals are our
everywhere. ...the
environment!**

Chemicals are our everywhere....the environment

- Food (residues)
- Water (contaminants)
 - Air (pollutants)
- Home (residues)

Individual Views of Chemical Exposures

“How little is OK?” “How much is too much?”

Response

“Dose makes the poison” “All-or-none”

Amount

Safe levels of everything Small exposures--certain harm

Laboratory Studies

Awareness of limitations Little confidence in
of testing in animals relevance of testing

Active Ingredients vs Products



Primary Flavor Constituents (>2 FU)

All Beers

- Ethanol
- Hop bittering compounds
- Carbon dioxide


Specialty Beers

- Hop aroma compounds
- Caramel and roasted flavor compounds
- Esters and alcohols (high gravity beers)
- Short-chain acids

Defective Beers

- 2-trans-Nonenal (oxidation)
- Vicinal diketones (diacetyl)
- Sulfur compounds (H_2S , DMS)
- Acetic acid (contamination)
- 3-Methyl-2-butene-1-thiol (lightstruck)
- Others (contamination)

Specialty Beers

- “No Alcohol” beers contain 0.3-0.7% EtOH
- Cobalt head stabilizer killed alcoholics in U.S. and Canada in 1960s (heart; 40-140 ug/kg-day)
-  *NicoShot* beer (Germany) contains 6.3% ethanol and 3 mg nicotine/250 ml “shot” can—3 cans (\approx 1 pack cigarettes) will make you illegal behind the wheel in all 50 states!



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Secondary Flavor Constituents (0.5-2 FU)

Volatiles

- Banana esters (e.g., isoamyl acetate)
- Apple esters (e.g., ethyl hexanoate)
- Fusel alcohols (e.g., isoamyl alcohol)
- C6, C8, C10 aliphatic acids
- Ethyl acetate
- Butyric and isovaleric acids
- Phenylacetic acid

Nonvolatiles

- Polyphenols
- Various acids, sugars, and hop compounds

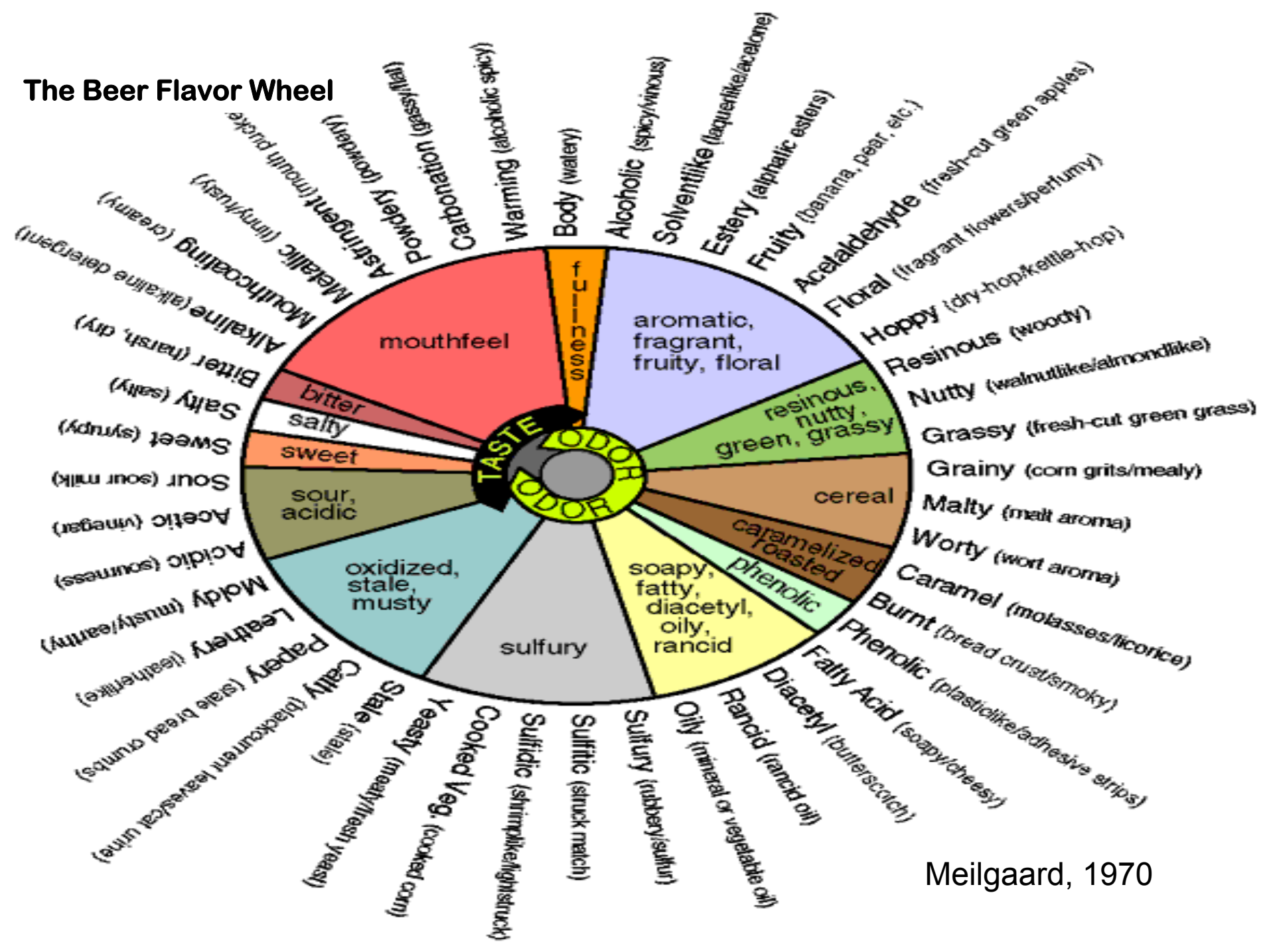
Tertiary flavor constituents (0.1-0.5 FU)

- 2-Penethyl acetate, o-amino acetophenone
- Isovaleraldehyde, methional, acetoin
- 4-Ethylguaiacol, g-valerolactone

Background flavor constituents (< 0.1 FU)

- Remaining chemicals of more than 1,000

The Beer Flavor Wheel



Meilgaard, 1970



BEER



2006 General

Pesticide Science

Department of Entomology

UCR

Properties

- Appearance: tan, brown, amber, light yellow, light tan
- Water solubility: low (relative to salt)
- Vapor pressure: low (10^{-7} to 10^{-12} mm Hg)
- Odor: mild

Pesticides Are Chemical Mixtures^a

- Formulation: Solid, Liquid, Gas
- Active ingredient
- Inert (preferably “Other”) ingredients
 - Solubility
 - Acid/Base
 - Chemical stability
 - Spreaders
 - Stickers

^a Almost everything is!

Formulations: Use specific

Inert ingredients

Or

Other ingredients

Propylene glycol

Diatomaceous earth

Crystalline silica
(quartz)

Starch

etc, etc, etc

Ingredient 1611

“Trade secret”

Adverse Effects: Toxicity

- Dosage (mg chemical/kg bw)
- Time
- ↑↓ Natural organic processes
- “There is a safe level of everything.”

Minimize Your Exposures

- Labeled or not!
- Use best judgment
- Share experience!

Recommendations

- respirator/dust
- eye protection
- WPS + gloves
- ventilation

2006 Advanced Pesticide Science

- ✓ Chlorfenapryl
- › Fipronil
- › Imidacloprid
- › Thiamethoxam

Organic Chemicals: Actives

Pesticides

Chlorfenapryl

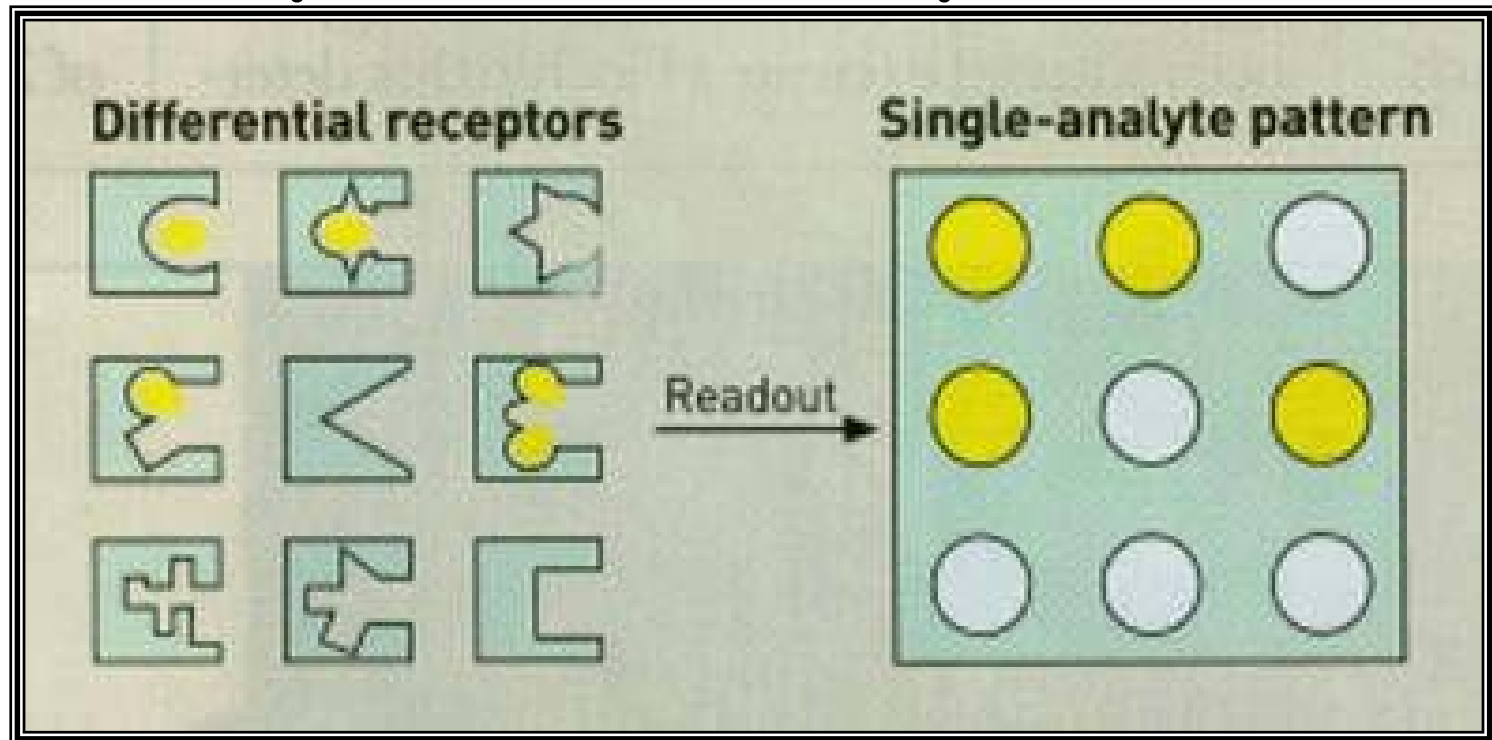
Fipronil

Imidacloprid

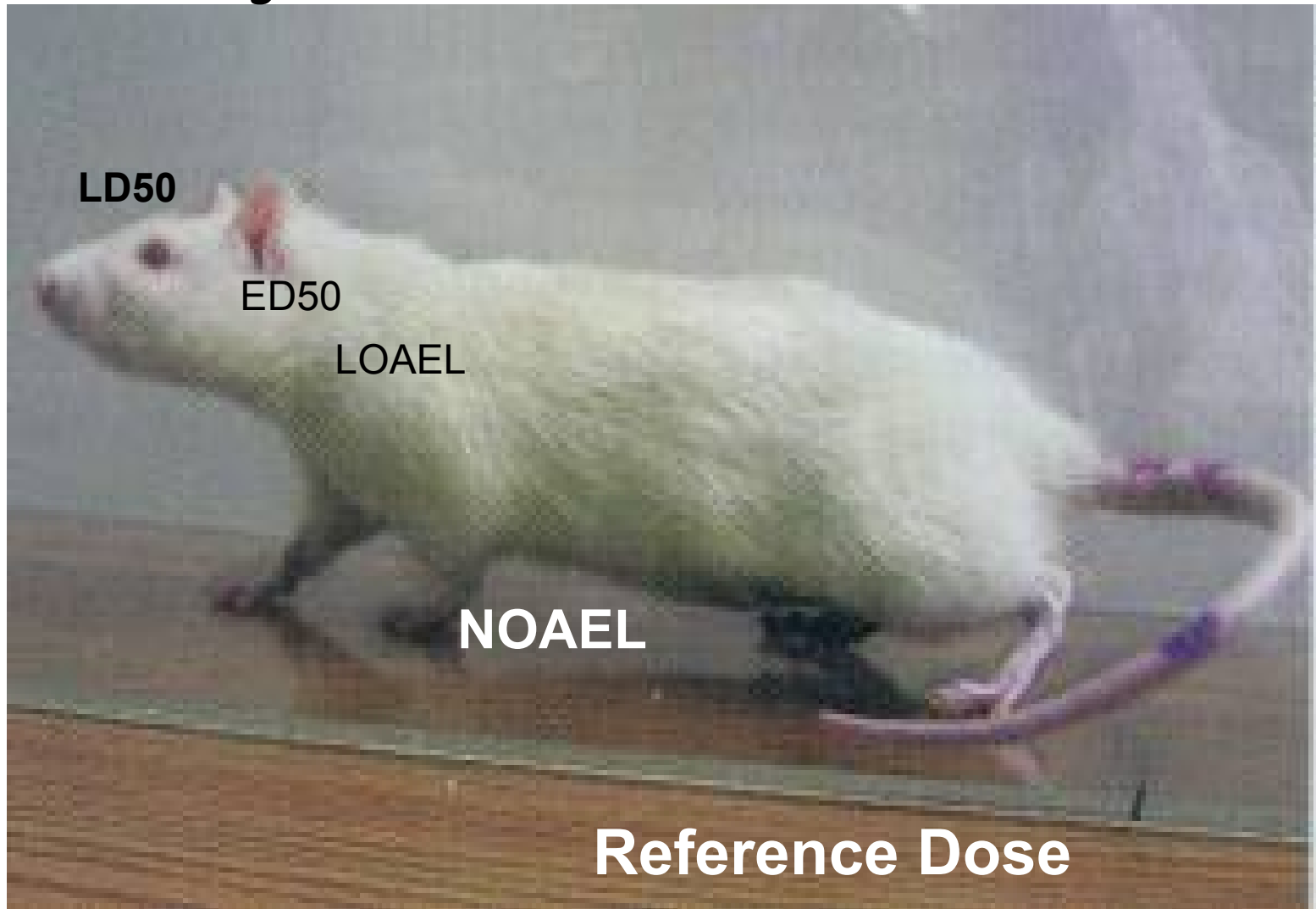
Thiamethoxam

<u>C</u>	<u>H</u>	<u>F</u>	<u>Cl</u>	<u>Br</u>	<u>N</u>	<u>O</u>	<u>P</u>	<u>S</u>
15	11	3	1	1	2	1	0	0
12	4	6	2	0	4	0	0	0
9	10	0	1	0	5	2	0	0
8	11	0	1	0	5	3	0	1

Receptors and Responses



Toxicity: Adverse Effects



6-Pack Toxicology

Pesticides

Chlorfenapryl

Fipronil

Imidacloprid

Thiamethoxam

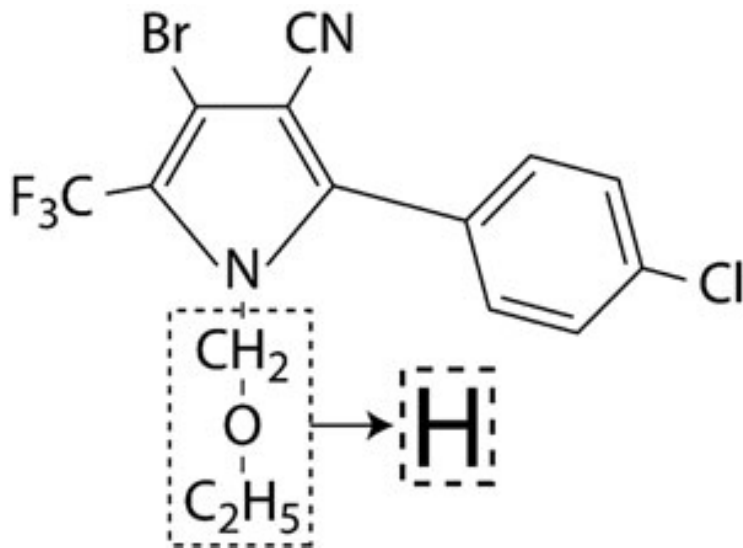
DANGER

Warning

Caution

Toxicology

Chlorfenapyr



Metabolic activation

Pyrrole mw 408

Appearance: Tan liquid

Volatility: low (10^{-7} mm)

Odor: mild "sweet"

Phantom® termiticide insecticide

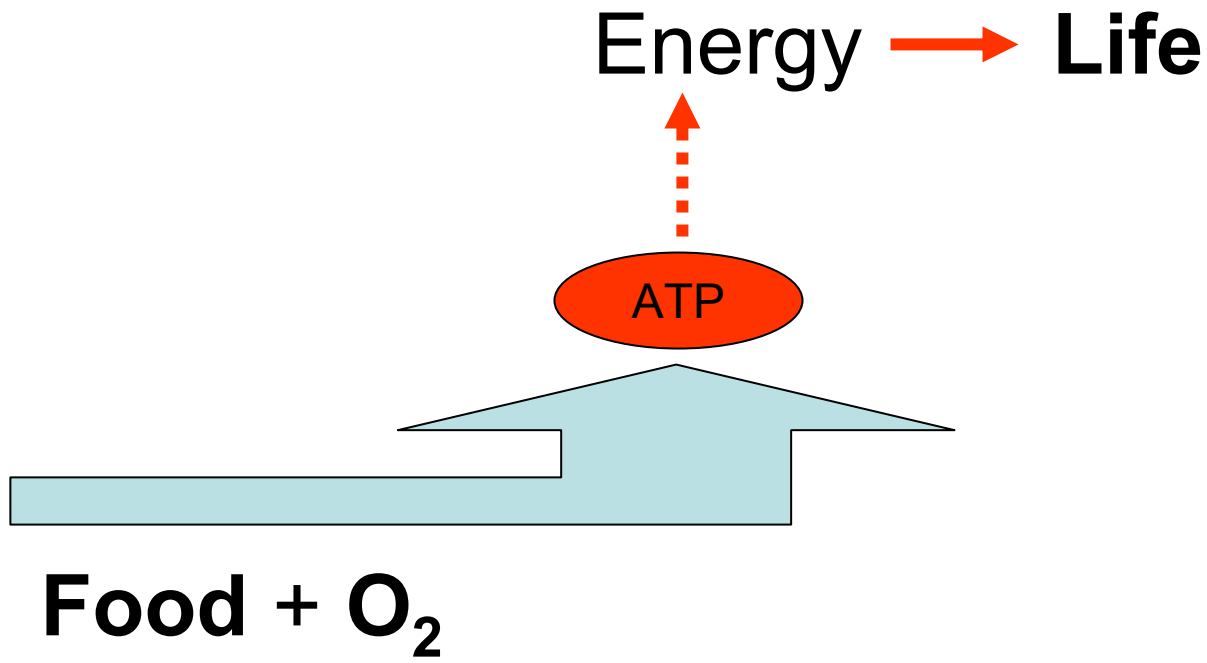
Persistence & Availability

Signal word: DANGER

Signal Word: 6-Pack

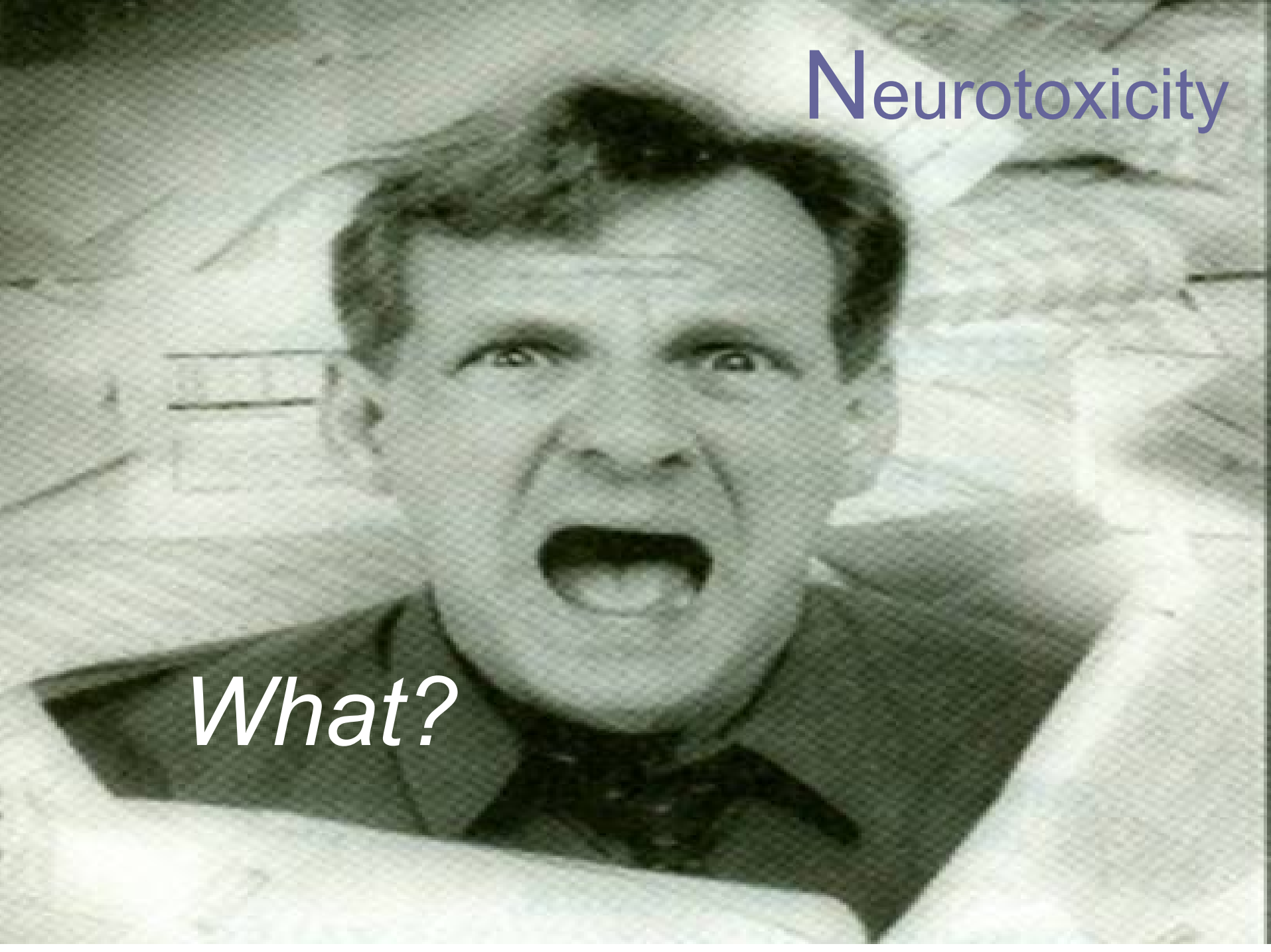
1.	Rat oral LD50	560-7 mg/kg	II _w
	Mouse, oral LD50	45 mg/kg	I _D
2.	Rat, skin LD50	more than 2000	III _c
3.	Rat, inhalation LC50	0.6 mg/l	III _c
4.	Rabbit, eye irritation	slight	III _c
5.	Rabbit, skin irritation	slight	IV
6.	Guinea pig, no skin sensitization		

Energetics: ATP

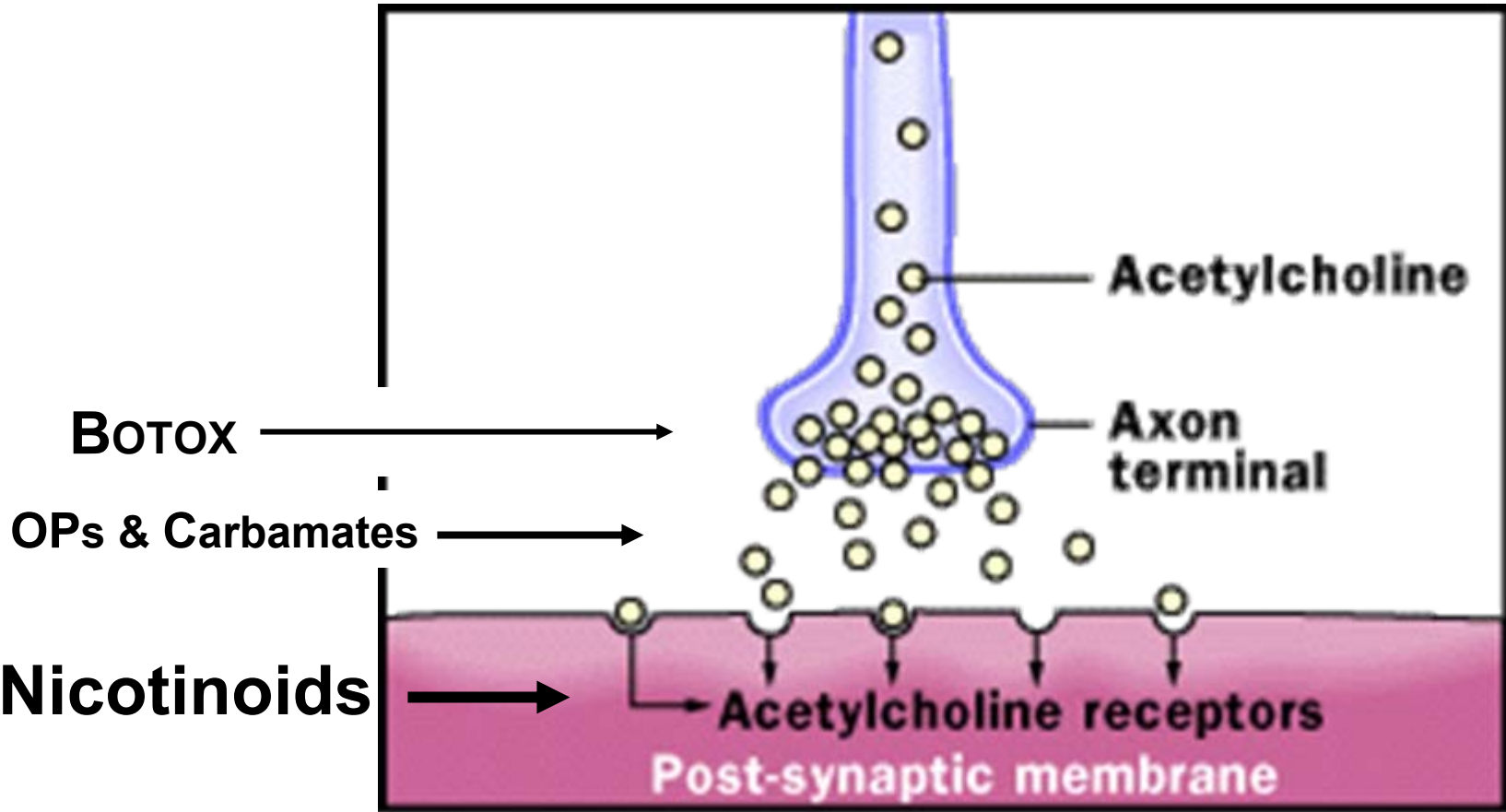


Neurotoxicity

What?

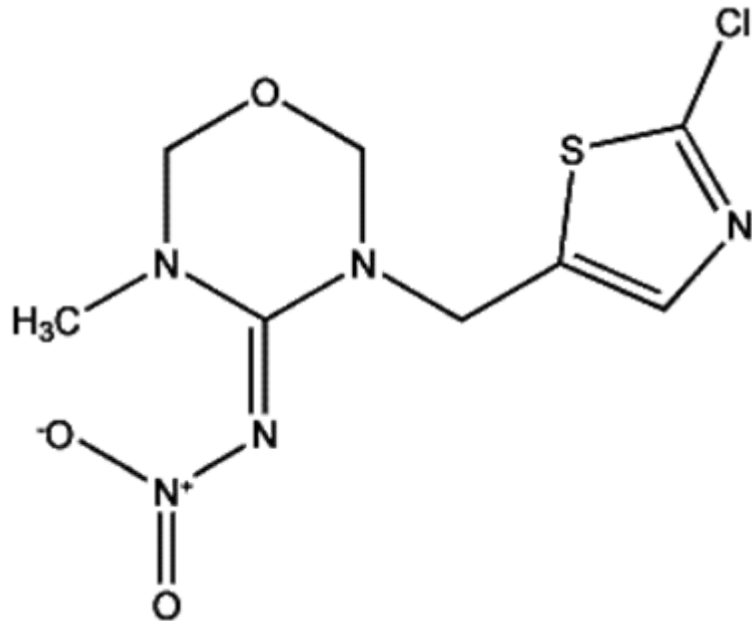


Neurotoxins



Toxicology

Thiamethoxam

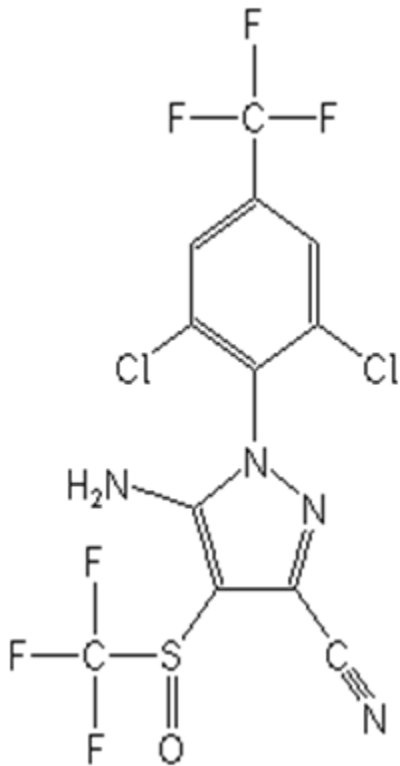


Synonyms

05598 (CA DPR Chem Code) , 060109 (US EPA PC Code) , 153719-23-4 (CAS Number) , 153719234 , 153719234 (CAS Number) , 4H-1,3,5-Oxadiazin-4-imine, 3-(2-chloro-5-thiazolyl)methyltetrahydro-5-methyl-N-nitro- , 4H-1,3,5-Oxadiazin-4-imine, 3-δ(2-chloro-5-thiazolyl)methyl , 4H-1,3,5-Oxadiazin-4-imine, 3-[(2-chloro-5-thiazolyl)methyl]tetrahydro-5-methyl-N-nitro- , 5598 (CA DPR Chem Code) , hiamethoxam , Thiamethoxam , Thiamethoxam (ISO proposed common name) , Thiametoxam , Tiametoxam 05598 (CA DPR Chem Code) , 060109 (US EPA PC Code) , 153719-23-4 (CAS Number) , 153719234 , 153719234 (CAS Number) , 4H-1,3,5-Oxadiazin-4-imine, 3-(2-chloro-5-thiazolyl)methyltetrahydro-5-methyl-N-nitro- , 4H-1,3,5-Oxadiazin-4-imine, 3-δ(2-chloro-5-thiazolyl)methyl , 4H-1,3,5-Oxadiazin-4-imine, 3-[(2-chloro-5-thiazolyl)methyl]tetrahydro-5-methyl-N-nitro- , 5598 (CA DPR Chem Code) , hiamethoxam , Thiamethoxam , Thiamethoxam (ISO proposed common name) , Thiametoxam , Tiametoxam

Toxicology

Fipronil



NOAEL: short term

skin 5 mg/kg

absorption 1%

ingest 0.05 mg/kg

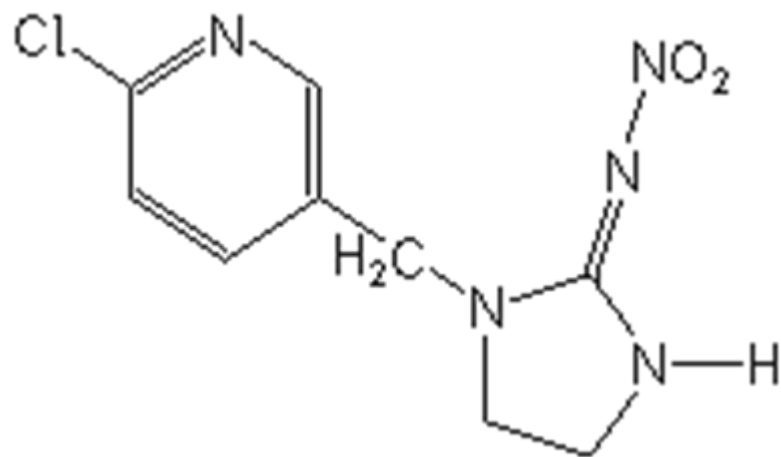
↓ weight gain

↓ food consumption

Neurotoxicity

Toxicology

Imidacloprid



NOAEL: chronic

2-year dietary

5.7 ♀ 7.6♂ mg/kg-d

↓ weight gain

Subchronic (6-16 d)

8 mg/kg

reproductive (↓ pup wgt)

24 mg/kg

developmental (skeletal abs)

Toxicology

Neurotoxin: Nicotinic
Receptor block
↑ Acetylcholine

Signs & Symptoms

- Fatigue
- Twitching
- Cramps
- Muscle weakness
- Difficult breathing

Safety and Evaluation —

Consider Pesticide Effectiveness

Best Guess

Misuse can result in illnesses and deaths.

Check the records...

Health Impact Records

- Occupational: Numbers & Rates
- Causes including poisoning
- California Illnesses and Injuries
- Poison Control Centers

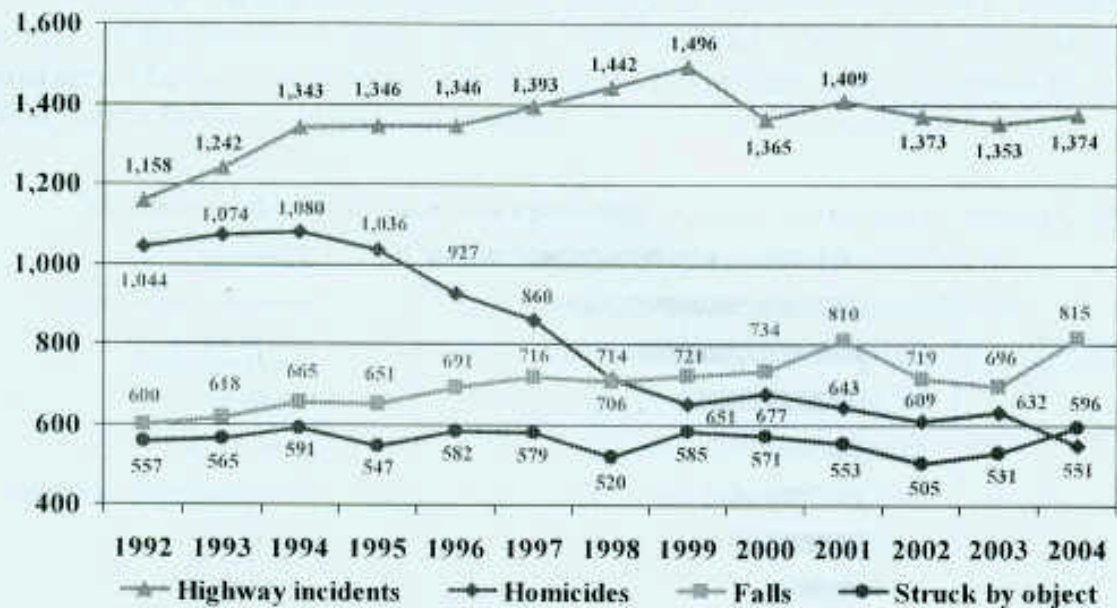
Table 1. Unintentional Injuries at Work by Industry in the U.S.

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

The four most frequent work-related fatal events, 1992-2004

Number of fatalities



NOTE: Data from 2001 exclude fatalities resulting from the September 11 terrorist attacks.

SOURCE: US Department of Labor, Bureau of Labor Statistics, Census of Fatal Occupational Injuries, 2004.

Table 2. Leading Causes of Death in the U.S.: 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 3. 5-Year Summary of California Pesticide Illness and Injury¹

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 3. Five Year Summary of California Pesticide
Illness and Injury Data

Rate Exposures Relationship to Effect

- **Definite**
 - Probable
 - Possible

Table 4-1. Top 5 Substances Most Frequently Involved Children Under 6

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

American Association of Poison Control Centers, 2003

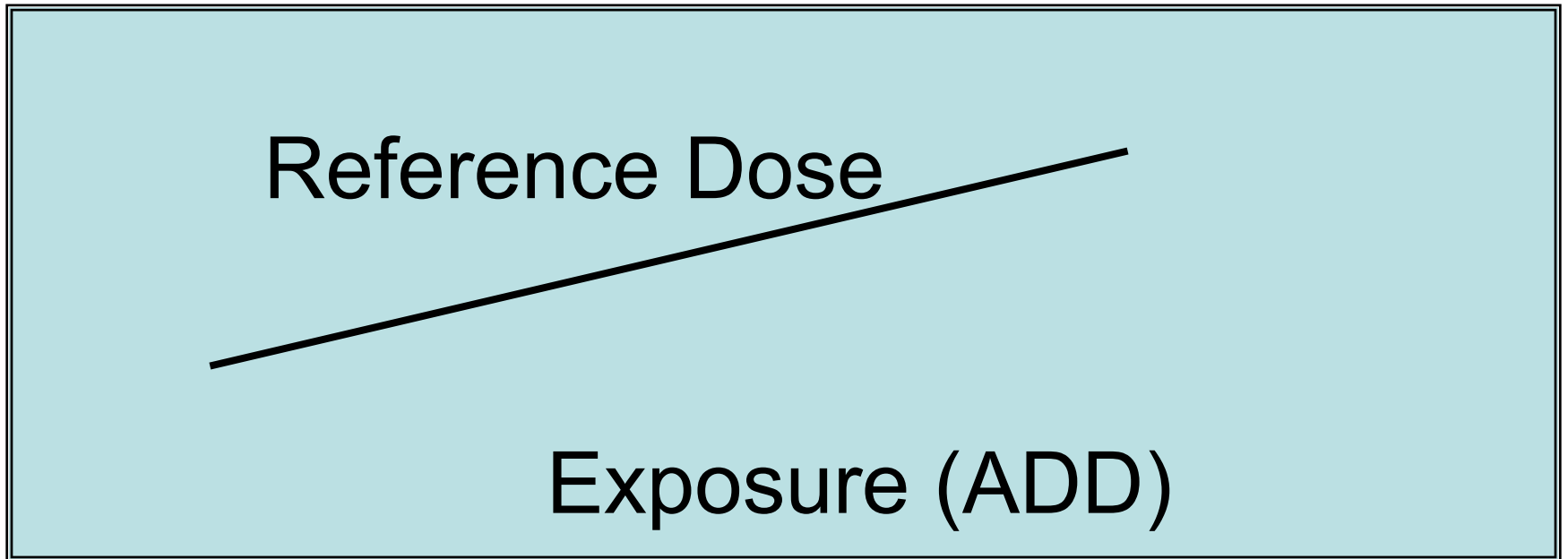
Table 4-2. Next 6-10 Substances Children Under 6

Substance	Number x 10 ⁵	Per Cent
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	--

American Association of Poison Control Centers, 2003



**Primary Regulatory
Strategy
Margin-of-Exposure**





**Environmental Justice
or
Advocate Blackmail?**

Pesticide Regulation

Regulate!

- An alarmed, chemically naïve public
- Extremely low chemical contacts
- NOAELs become illness thresholds!

**Everyone *knows* how
bad *they* are!**

Rachel Carson and followers like EDF,
NRDC, PAN, Jane Seymour, Martin Sheen,
Meryl Streep, Riverside's *Press Enterprise*,
LA Times, *CBS*, *PBS*, etc.

***“Analysts at the Institute have
just announced—***

**“We can now find *a flea* in a line of
100 full-grown, circus elephants!”**

1 Flea ≈ millimeter

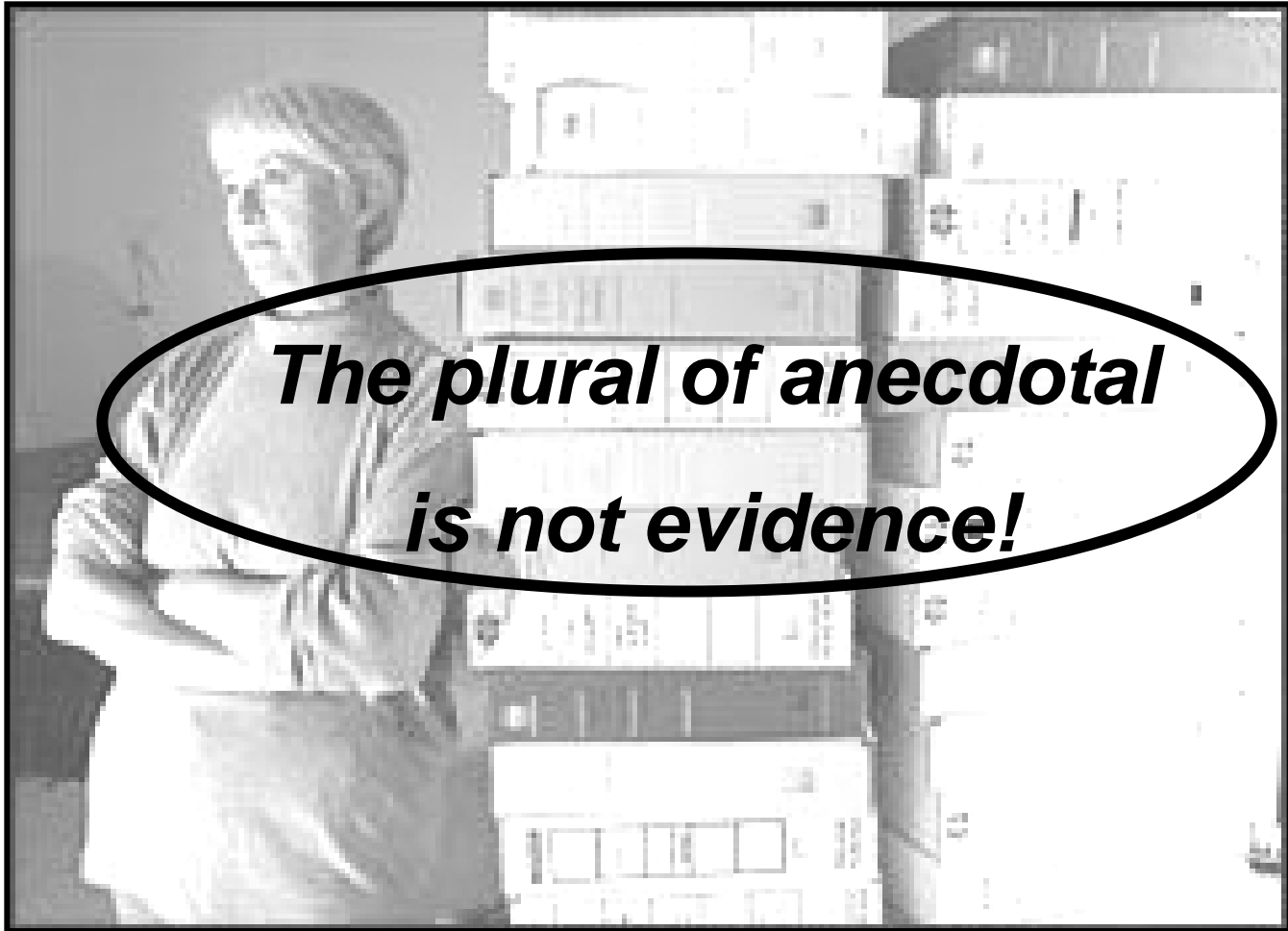
Elephant ≈ 10 meters

Anecdotes Focus Actions

(Good News is not News!)^a

- Birth defects, Collier Co., FL (now NC)
 - “They have to stop spraying!”
 - Moms within 200 ft of field sprays
(in NC it’s early field entry)
 - Phocomelia
 - Deformed jaw
 - 3d Death, deformities
- “That doesn’t rule it out. It’s just that we couldn’t make the link.” Collier Co. Health Dept

^a **60 MINUTES** and Ed Bradley can’t be far behind!



***The plural of anecdotal
is not evidence!***

--the sky is falling!



E P A

Chicken Little

Strive For Balance Safe Use!

Read and Heed Labels

Recognize Realities of Exposure

Use Best Judgment!

Hazards are not *risks*
unless a sensitive population
is exposed and exposure
produces an adverse effect.

Safe Pesticide Use?

- Label developed by scientific studies and effective pest management
- Continuing use in agricultural and residential pest management
- Exposures occur time to time at low levels relative to harmful amounts
- Illness data reveal misconceptions about health impacts of pesticides

**"It's not what we don't know that hurts us,"
said Will Rogers.**

"It's what we know that ain't so."

Safe use?

**Yes, it's up to you!
Just do it!**

*Bob Krieger, Ph. D.
PCEP Entomology
UC Riverside, 2006*

Follow-up Dessert

- Chemicals and Public Perceptions
- General Pesticide Science
- Advanced Pesticide Science
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- Regulate: Margin-of-Exposure
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