Pesticides regulation from a human health perspective

By David Pinzon, PhD
Corteva Agriscience


Content
• Introduction
• Current context
• Pesticides regulations in Canada
• Risk vs Hazard
• Human risk assessment
• Conclusions/Questions

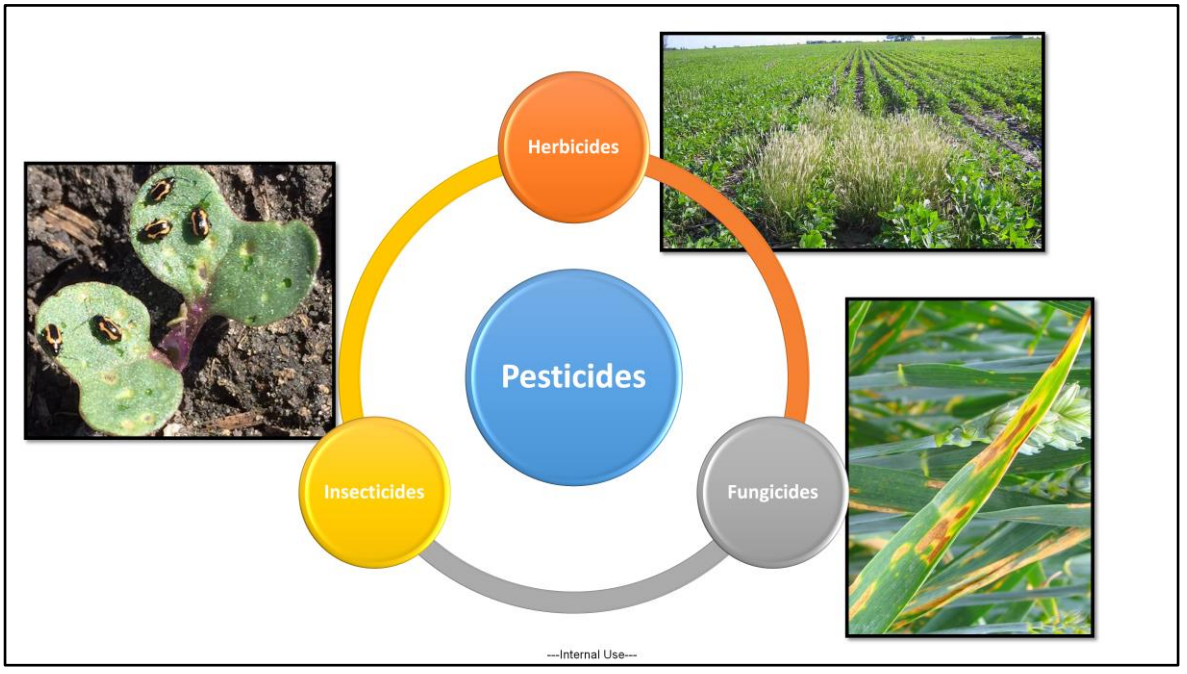
Introduction – about me

- 11 years at Corteva Agriscience
- Regulatory affairs manager – Crop protection and Biotechnology
  - Work with other scientist globally to register best in class pesticides and support customer technical needs.
- Enjoy presenting about agriculture to kids, teachers, universities, IVM applicators, and my family.

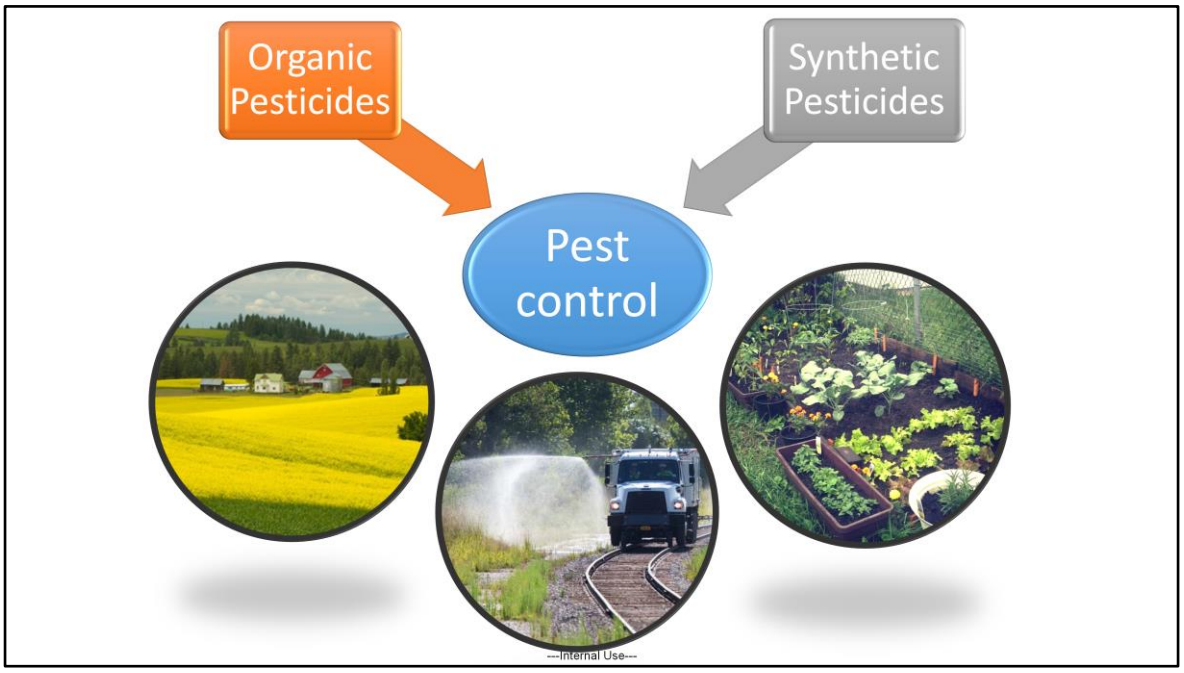
Education

- Ph.D. – Plant Biology – Molecular Biology, University of Alberta, 2014
- M.Sc. – Microbiology - Plant pathology, University Los Andes, 2009
- B.Sc. – Microbiology, University Los Andes, 2007

Pest Management



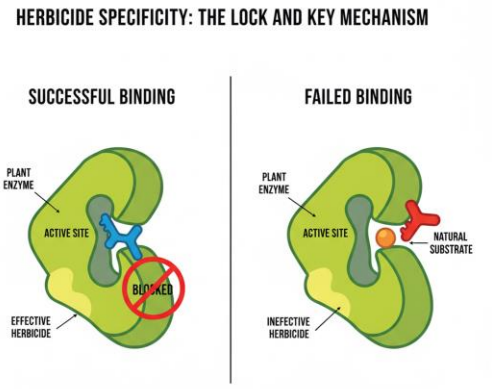
Septoria in wheat.
Flea beetle in Canola


Organic Pesticides
Synthetic Pesticides
Pest control
---Internal Use---


8911
CN
Vegetation management
https://www.cn.ca

How do herbicides work?

1. Herbicides target processes specific to plants (and sometimes just certain plants).
2. When the herbicide binds to a specific site in the plant this function of the plan is negatively affected.
   - The plant is controlled as a result



Why do we use herbicides to control vegetation?

- EFFECTIVE.
  - Effectively control brush and weeds.
- EFFICIENT.
  - Herbicides control the entire plant and often require only one application every few years. This eliminates the need for more frequent mechanical treatments.
- SAFE.
  - Registered for use by the Pest Management Regulatory Agency who is affiliated with Health Canada (we will elaborate on this further).

Waterton Knapweed Rodeo

BY ANNA LEE-CARSWELL
Ecological Integrity Communications Officer, Waterton Lakes National Park

ON A FINE SUMMER DAY, 61 volunteers from local communities and partner organizations (and even Park visitors!) joined with 33 Waterton park staff to contribute 445 hours to roping in Knapweed for the Annual Waterton Knapweed Rodeo held in July, 2009.

The group picked 159 bags of knapweed, which will prevent an estimated 850 million seeds from spreading on the Blakiston fan! By pulling knapweed before the flowers go to seed, this invasive plant can be held in check, both now, and in the future, since knapweed seeds can last for up to 8 years before sprouting.

Volunteer prize draws were made at the end of each shift, with fabulous prizes donated by Waterton businesses being awarded. The prizes were greatly appreciated by the worn out volunteers! Special congratulations to the Kelly Cooley –who won the final draw for a National Parks Canada Pass.

Edwin Knott, in charge of Resource Management and Public Safety for Waterton Park, says the massive effort helps.

"We didn't get it all but it sure helped. We have been back to some of the areas we picked to spray Milestone herbicide on the abundant rosettes. Seems like this was the most amazing year for growth... it just keeps coming!"

Several option to control vegetation. Which one is better?

Pesticide Regulation in Canada

Who regulates pesticides in Canada?

- Pest Management Regulatory Agency (PMRA)
  - Affiliated with Health Canada
- What does the PMRA do?
  - Review applications for the registration of pest control products
  - Conduct science-based health, environmental and value (including efficacy) assessments of each pesticide before deciding if it should be approved for use in Canada

Health Canada Santé Canada

Products registered in Canada must be:

- Non-carcinogenic
- Non-teratogenic
- Non-mutagenic
- Must not bio-accumulate

PMRA FAQ:

What is Health Canada's response to suggestions that pesticides lead to illnesses like cancer and Parkinson's disease?

Health Canada will not register a pesticide that is known to cause cancer or other illnesses when used according to label directions.

Before a pesticide is allowed to be used or sold in Canada, it must undergo a rigorous scientific assessment process to ensure that no harm will occur when pesticides are used according to label directions. All pesticides registered in Canada, including for agricultural, forestry and domestic uses, undergo this level of scrutiny.

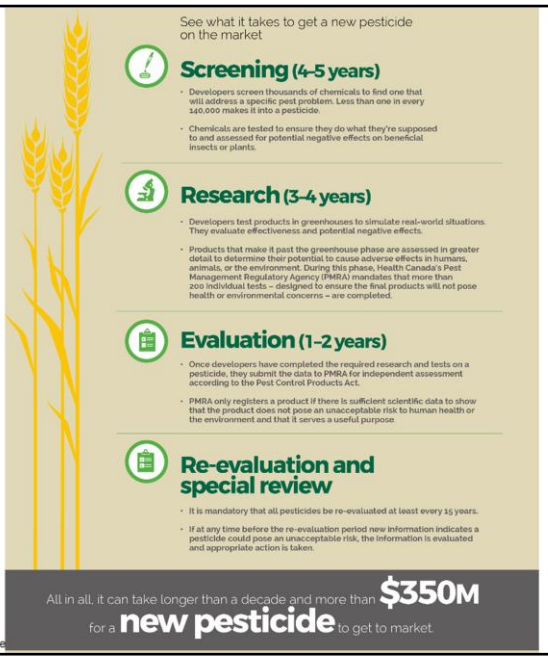
If there is strong evidence that exposure to a pesticide causes Parkinson's disease, cancer, other serious illness or negative environmental effects then regulatory action will be taken.

---Internal Use---

Carcinogenic- Cancer causing
Mutagenic- Causes gene mutations
Teratogenic- Causes birth defects
Bio-accumulate in the food chain- eg DDT- No longer registered in Canada

If the product doesn't meet Health Canada's standards…

Interesting facts about herbicide registration



http://croplife.ca/protecting-people-planet/pesticide-regulations/

Health Canada Santé Canada

Regulatory Sciences

Each pesticide has to go through 120-150 separate health, safety, efficacy, and environmental tests before it can be registered by the PMRA and EPA.

Agencies determine if the products present acceptable risk and value.

Are pesticides toxic?

- Yes, organic and synthetic pesticides are toxic to the **specific** target organism, affecting unique biological processes in that organism

The remedy is obtained with the right dose

- Swiss physician Paracelsus (1493-1541)
  - "The father of modern toxicology."

- The dose dictates the effect of a substance
  - *"All substances have the potential to be poisons: there is none which is not a poison. The right dose differentiates a poison from a remedy."*

Risk = Hazard x Exposure

Risk = Hazard x Exposure

Risk = Hazard x Exposure

Risk = Hazard x Exposure

---Internal Use---

Risk = Hazard x Exposure

Hazard – Natural vs Artificial

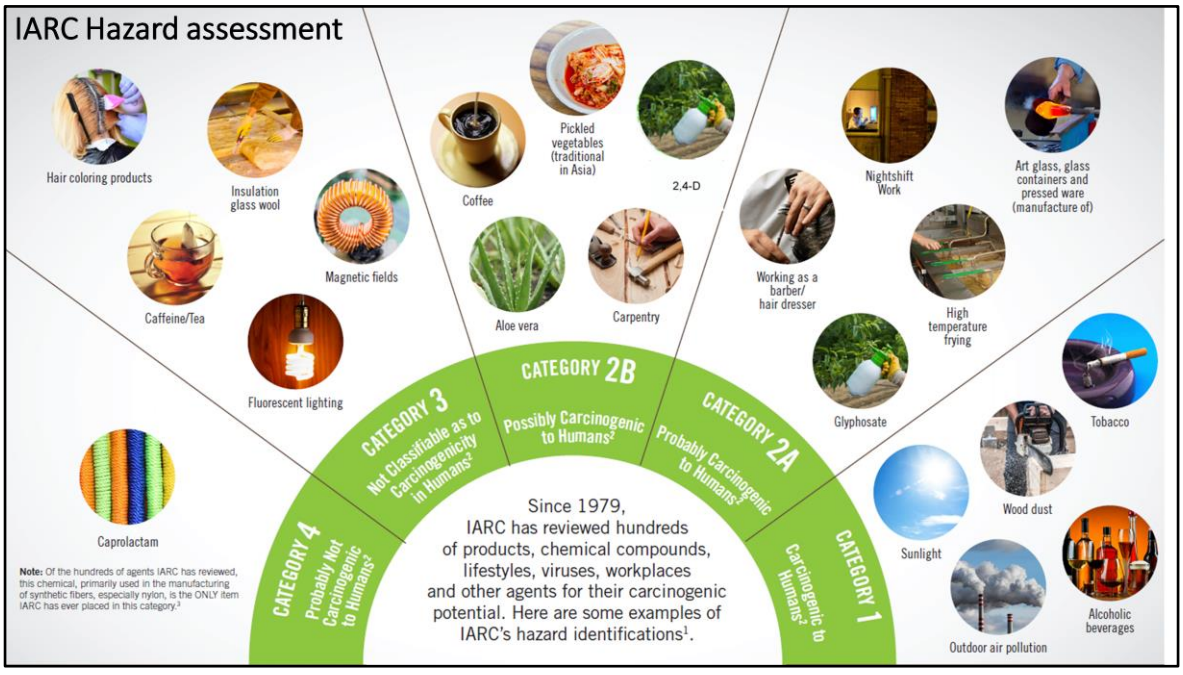
Being natural (organic) or artificial (conventional) doesn't dictate the safety of a compound.

Regulatory assessment

Risk = f(Exposure, Hazard)

Protect the Environments where our products are released and Humans who consume treated commodities or can be subject to exposure

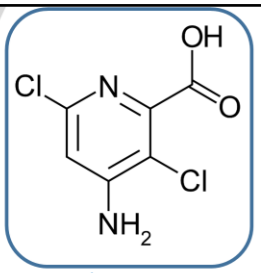




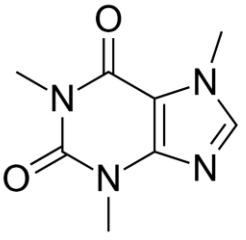
International Agency for Research on Cancer

What is a herbicide?

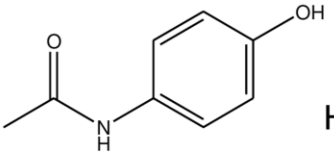
Herbicides are chemical compounds, which are often synthetic mimics of natural plant hormones which interfere with growth of the target plants



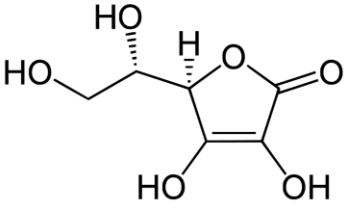
Milestone



Caffeine

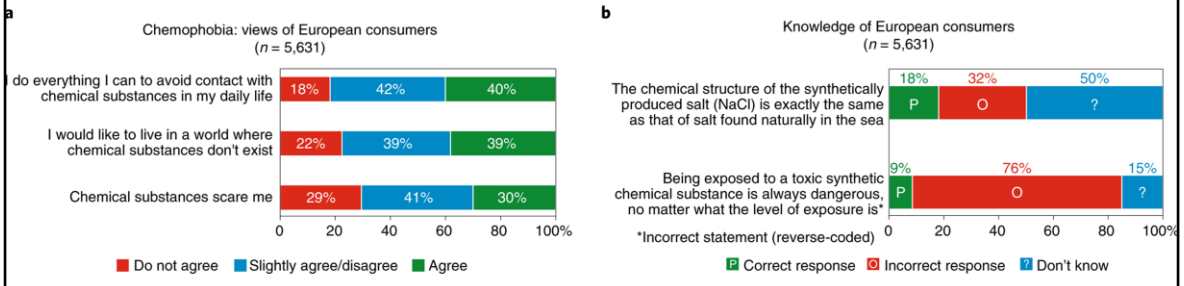


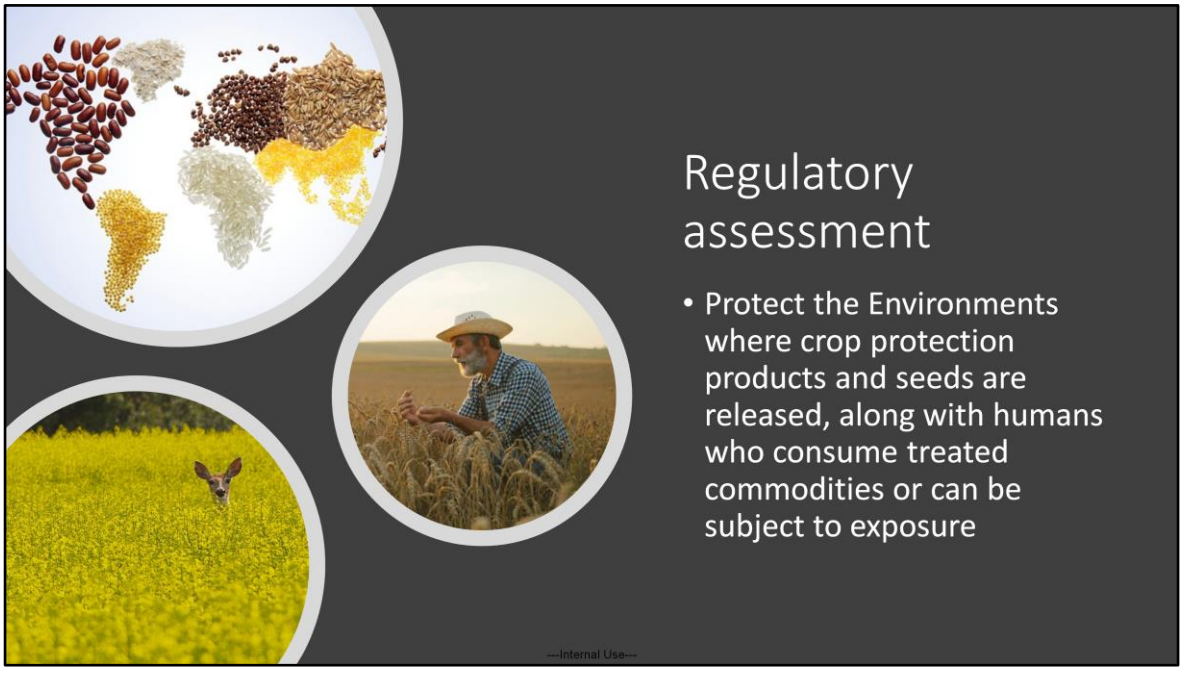
Acetaminophen



Vitamin C – Ascorbic acid

Chemophobia





Risk = f(Exposure, Hazard)

Regulatory Sciences

- Environmental fate
  - Soil
  - Aquatic
  - Air
- Environmental toxicology
- Mammalian toxicity
- Physicochemical and analytical studies
- Crops residues
- Animal feeding
- Biology

Risk Assessment
Human Exposure

- Operator
- Re-entry
- Bystander
- Residential
- Dietary

How can pesticides enter the body?

---Internal Use---

Inhalation
Dermal absorption
Ingestion
Ocular absorption

Toxicity

Acute toxicity

- Adverse effects that occur after a single exposure or multiple exposures within one day
- Effect that manifest immediately or shortly after exposure.
  - Common measurement unit
    - **LD50** (median lethal dose)
    - **NOAEL** (Non-observed adversed effect level)
    - **LOAEL** (Lowest observed adverse effect level)

Chronic toxicity

- Adverse effects caused by long term exposures.
- Not necessarily measured in lethality.
- Non-lethal yet still adverse effects on health
  - Common measurement units
    - **NOAEL** (Non-observed adversed effect level)
    - **LOAEL** (Lowest observed adverse effect level)

NOAEL (*No Observed Adverse Effect Level): the highest level at which no increase in the frequency or severity of adverse effects is observed*
LOAEL *(Lowest Observed Adverse Effect Level): the lowest dose that has been tested or observed to have an adverse effect*
RfD *(Reference Dose): an estimate of the daily exposure to humans that is likely to be without appreciable risk of deleterious effects throughout the entire lifetime.*

Measuring units to study toxicity

NOAEL

- Non-observed adversed effect level
- The highest level at which no increase in the frequency or severity of adverse effects is observed

LOAEL

- Lowest observed adverse effect level
- The lowest dose that has been tested or observed to have an adverse effect

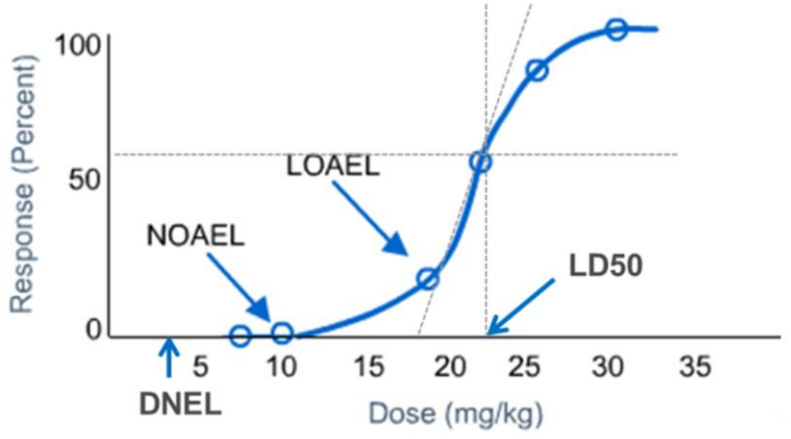
The **LD_{50}** tells how toxic something is (how much causes death). The NOAEL/LOAEL tell at what dose toxicity starts to occur (how sensitive organisms are to lower, nonlethal effects).

Toxicity – even substances such as water can be considered toxic

- What is the LD_{50} of water?
- 90ml/kg
- What does that mean to humans?
  - A 150lb person can consume just over 6L or 13.5 lbs of water before they could potentially die

Substance	Animal, route	LD_{50} (LC_{50})	LD_{50} : g/kg (LC_{50} : g/L) standardised	Reference
Water	rat, oral	90,000 mg/kg		[7]
Sucrose (table sugar)	rat, oral	29,700 mg/kg	29.7	[8]
Glucose (blood sugar)	rat, oral	25,800 mg/kg	25.8	[9]
Monosodium glutamate (MSG)	rat, oral	16,600 mg/kg	16.6	[10]
Stevioside (from stevia)	mice and rats, oral	15,000 mg/kg	15	[11]
Gasoline (Petrol)	rat	14,063 mg/kg	14.0	[12]
Vitamin C (ascorbic acid)	rat, oral	11,900 mg/kg	11.9	[13]
Glyphosate (isopropylamine salt of)	rat, oral	10,537 mg/kg	10.537	[14]
Lactose (milk sugar)	rat, oral	10,000 mg/kg	10	[15]
Aspartame	mice, oral	10,000 mg/kg	10	[16]
Urea	rat, oral	8,471 mg/kg	8.471	[17]
Cyanuric acid	rat, oral	7,700 mg/kg	7.7	[18]
Cadmium sulfide	rat, oral	7,080 mg/kg	7.08	[19]
Ethanol (Grain alcohol)	rat, oral	7,060 mg/kg	7.06	[20]
Sodium isopropyl methylphosphonic acid (IMPA, metabolite of sarin)	rat, oral	6,860 mg/kg	6.86	[21]
Melamine	rat, oral	6,000 mg/kg	6	[18]
Methanol	human, oral	810 mg/kg	0.81	[22]
Taurine	rat, oral	5,000 mg/kg	5	[23]
Melamine cyanurate	rat, oral	4,100 mg/kg	4.1	[18]
Fructose (fruit sugar)	rat, oral	4,000 mg/kg	4	[24]
Sodium molybdate	rat, oral	4,000 mg/kg	4	[25]
Sodium chloride (table salt)	rat, oral	3,000 mg/kg	3	[26]
Paracetamol (acetaminophen)	rat, oral	1,944 mg/kg	1.944	[27]
Delta-9-tetrahydrocannabinol (THC)	rat, oral	1,270 mg/kg	1.27	[28]
Cannabidiol (CBD)	rat, oral	980 mg/kg	0.98	[29]
Metallic Arsenic	rat, oral	763 mg/kg	0.763	[30]
Ibuprofen	rat, oral	636 mg/kg	0.636	[31]

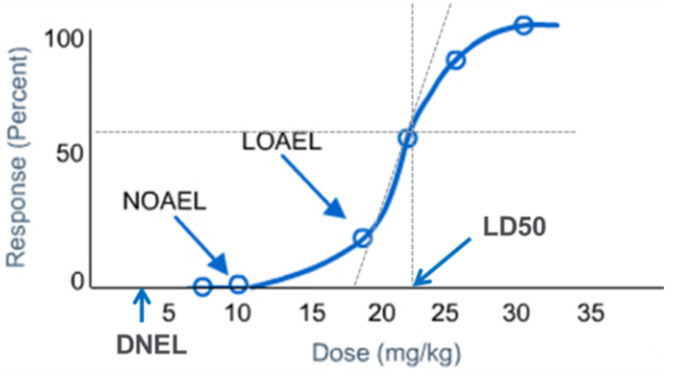
Chronic toxicity



NOAEL - Non-observed adversed effect level

- All existing data regarding the toxicity of the pesticide is reviewed and evaluated to identify the NOAEL.

Dose level (mg/kg/day)	Animals with enlarged Livers
0	0/10 (0%)
10 (NOAEL)	0/10 (0%)
20 (LOAEL)	2/10 (20%)
30	10/10 (100%)



---Internal Use---

DART: [Developmental and Reproductive Toxicology Database]

Reference doses: ARfD and ADI

- Amount of compound to which a person can be safely exposed to on a chronic lifetime exposure **(ADI – acceptable daily intake)** or on a short term acute exposure **(ARfD)**.

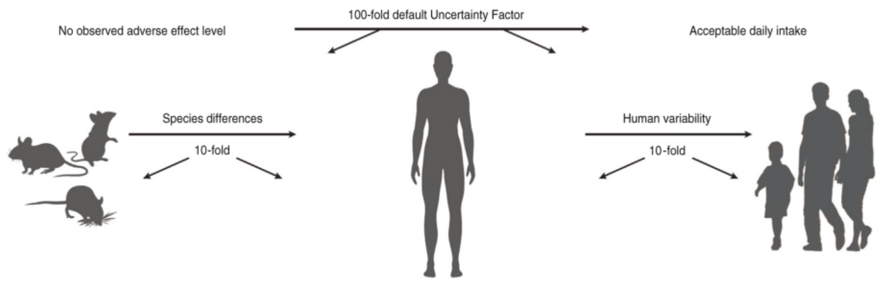
Establishing the reference dose (RfD)

1. Establish the NOAEL: (e.g. 1 mg/kg/day)

Establishing the reference dose (RfD)

1. Establish the NOAEL: 1 mg/kg/day
2. Apply uncertainty factors (10x inter-species, 10x intra-species)
   - From 100x to 3000x, higher if there are substantial concerns regarding the nature of toxicity.

Establishing the reference dose (RfD)



Take into account the potential differences in response, both within the same species (i.e., adults versus children) and between species (i.e., animals versus humans).

---Internal Use---

https://journals.co-action.net/index.php/ijch/article/view/33845/html_112

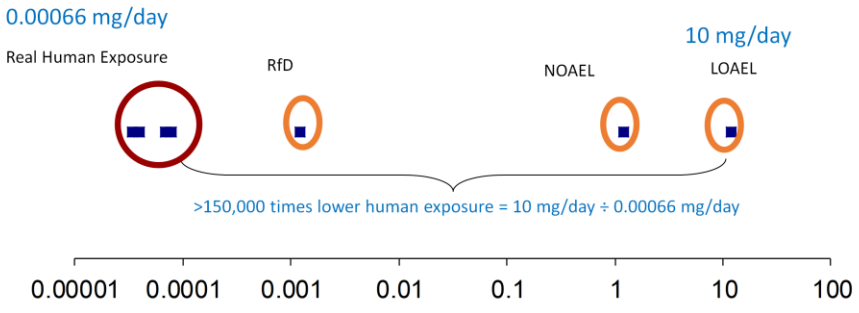
Acceptable Daily Intakes (ADI) -- the amount of a compound that can be consumed daily for a lifetime with no adverse effects

These safety factors are designed to take into account the potential differences in response, both within the same species (i.e., adults versus children) and between species (i.e., animals versus humans).

Establishing the reference dose (RfD)

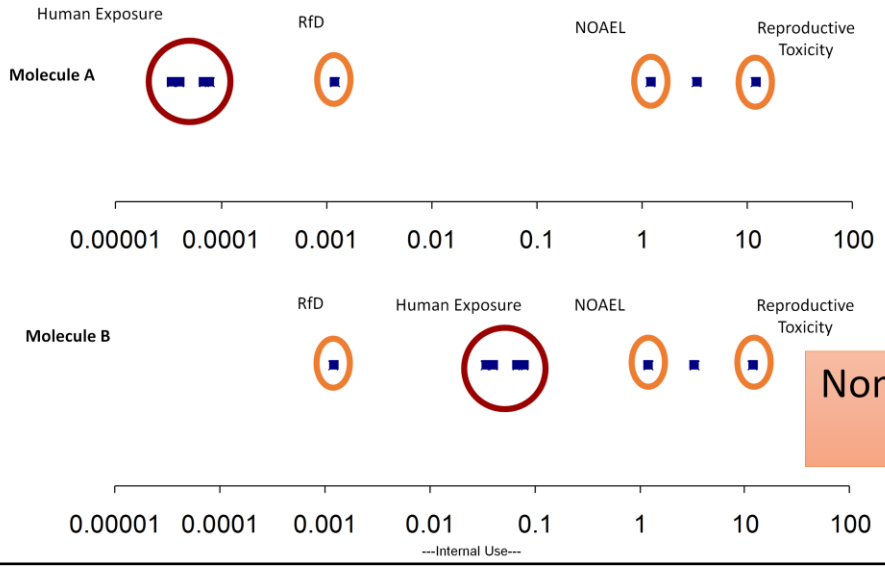
1. Establish the NOAEL: 1 mg/kg/day
2. Apply uncertainty factors (10x inter-species, 10x intra-species)
   - From 100x to 3000x, higher if there are substaintial concerns regarding the nature of toxicity.
3. Calculate the reference dose
   - 1 mg/kg/day ÷ 100 = 0.01 mg/kg/day
4. RfD in a 70 kg person:
   - 0.01 mg/kg/day x 70 kg = 0.7 mg/day
     - Exposure cannot exceed this value

Margin of Exposure Molecule A



Margin of Exposure

Risk = f(Hazard and Exposure)



Acceptable Risk

Non acceptable Risk

45

Glyphosate

- PMRA defined ARfD general population: 1.0 mg/kg bw of glyphosate
  - 70 kg person: 70 mg of glyphosate
- ARfD Females 13-49 years of age: 0.5 mg/kg bw of glyphosate
  - 50 kg person: 25 mg of glyphosate

Amount found on cheerios 497 ppb

= 0.000497 mg/g

One serving of cheerios (28 g) contains 0.01 mg of glyphosate

25 mg ÷ 0.01 mg = 2500 times lower exposure

Mitigate the risk

- Dietary risk assessment:
  - Reduce application rate
  - Increase pre-harvest interval
- Non-dietary risk assessment:
  - Personal Protective Equipment (PPE) e.g., gloves, coverall
  - Closed cabs for tractor-mounted application
  - Respirators
  - Professional application only
  - Reduce application rate

How can you minimize your risk?

- As simple as following the label:
  - Wear and follow PPE requirements
  - Use the type of application that is appropriate for every scenario.
    - i.e. Applying with a spray truck vs. hose & hand gun
  - Frequently wash your application clothing

Drug Facts

Active ingredient — **Purpose**
Aluminum Zirconium Tetrachlorohydrex GLY (15.2%)..... anti-perspirant

Uses
- reduces underarm wetness
- 24 Hour Protection

Warnings

For external use only

Do not use on broken skin

Ask a doctor before use if you have kidney disease

Stop use if rash or irritation occurs

Keep out of reach of children.
If swallowed, get medical help or contact a Poison Control Center right away.

Directions apply to underarms only

Other Information Do not store over 115°F

Inactive ingredients
Cyclopentasiloxane, Stearyl Alcohol, Isopropyl Palmitate, PPG-14 Butyl Ether, Talc, Mineral Oil, Hydrogenated Castor Oil, C12-15 Alkyl Benzoate, Dimethicone, Fragrance (Parfum), PEG-8, BHT.

Drug Facts

Active Ingredient — **Purpose**
Sodium monofluorophosphate 0.76% — Anti-Cavity Toothpaste

Use: Helps prevent against cavities

Warnings: Keep out of reach of children under 6 years of age. If you accidentally swallow more than used for brushing, get medical help or contact a Poison Control Center immediately.

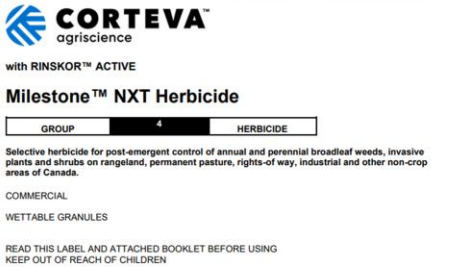
Directions: adults and children 2 yrs. & older: brush teeth thoroughly after meals or at least twice a day or use as directed by a dentist .To minimize swallowing use a -

Drug Facts (continued)

pea sized amount in children under 6. Supervise children's brushing until good habits are established. Children under **2 yrs.: ask a dentist**

Inactive Ingredients: Sorbitol, Silica, Water, Sodium Lauryl Sulfate, Flavor, PEG-32, Mica, Sodium Carboxy Methyl Cellulose, Saccharin, Trisodium Phosphate, FD&C Blue No. 1, Calcium Glycerophosphate

Questions? Call 1-866-373-7374
www.drfresh.com



CORTEVA™ agriscience

with RINSKOR™ ACTIVE

Milestone™ NXT Herbicide

GROUP	4	HERBICIDE

Selective herbicide for post-emergent control of annual and perennial broadleaf weeds, invasive plants and shrubs on rangeland, permanent pasture, rights-of way, industrial and other non-crop areas of Canada.

COMMERCIAL

WETTABLE GRANULES

READ THIS LABEL AND ATTACHED BOOKLET BEFORE USING
KEEP OUT OF REACH OF CHILDREN

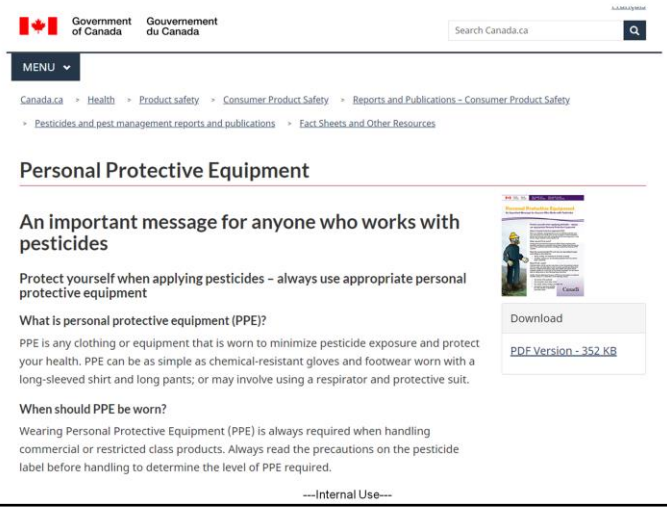
---Internal Use---

What document tells you what PPE you should be wearing?

- Product label
- If unsure, ask
- Wearing more PPE than required is acceptable

- SDS is intended for people working on the manufacturing and transportation of the product. The label has all the necessary precautions to apply the product safely.

How to choose the proper PPE



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Personal Protective Equipment

An important message for anyone who works with pesticides

Protect yourself when applying pesticides – always use appropriate personal protective equipment

What is personal protective equipment (PPE)?

PPE is any clothing or equipment that is worn to minimize pesticide exposure and protect your health. PPE can be as simple as chemical-resistant gloves and footwear worn with a long-sleeved shirt and long pants; or may involve using a respirator and protective suit.

When should PPE be worn?

Wearing Personal Protective Equipment (PPE) is always required when handling commercial or restricted class products. Always read the precautions on the pesticide label before handling to determine the level of PPE required.

Download

PDF Version - 352 KB

---Internal Use---

Conclusions

Vegetation management

- *You are spraying public land, be mindful of people's concerns and try to address them proactively.*
- *Do not be afraid to talk about chemicals and engage in conversations to help others feel comfortable with what you do.*
- *Always think about the alternates to using herbicides and help others understand the pros and cons of those alternatives.*
- *As long as you follow the label you will be protecting yourself, others, and the environment.*
  - *Scientist at Health Canada ensure that the medicines and pesticides you use provide you the greatest benefit with an acceptable risk.*

Questions and Discussion