



# Acute Toxicity Testing: Office of Pesticide Programs

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# Acute Toxicity Requirements

- Acute data required for both Technical Grade Active Ingredient (TGAI) and end-use product (EUP)
- Registrants may bridge to existing substantially similar data (Similarity Clinic) or seek waiver (e.g., corrosive)

Guideline	Study Type	Food Use	Non-Food Use
870.1100	Acute oral toxicity – Rat	R	R
870.1200	Acute dermal toxicity – Rat /Rabbit	R	R
870.1300	Acute inhalation toxicity – Rat	R	R
870.2400	Primary eye irritation – Rabbit	R	R
870.2500	Primary dermal irritation – Rabbit	R	R
870.2600	Dermal sensitization – Guinea Pig	R	R

# Acute Testing Determines Pesticide Labelling

- Formulation LD50 studies are used for determining PPE for pesticide handlers
- The dermal LD50 data for the technical active ingredients are often used in eco assessments.
- Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) includes specific requirements for label language

**Table 1. Handler PPE for WPS Products**

Route of Exposure	Toxicity Category by Route of Exposure of End-Use Product			
	I DANGER	II WARNING	III CAUTION	IV CAUTION
Dermal Toxicity or Skin Irritation Potential <sup>1</sup>	Coveralls worn over long-sleeved shirt and long pants	Coveralls worn over short-sleeved shirt and short pants	Long-sleeved shirt and long pants	Long-sleeved shirt and long pants
	Socks	Socks	Socks	Socks
	Chemical-resistant footwear	Chemical-resistant footwear	Shoes	Shoes
	Chemical-resistant Gloves <sup>2</sup>	Chemical-resistant Gloves <sup>2</sup>	Chemical-resistant Gloves <sup>2</sup>	No minimum <sup>4</sup>
Inhalation Toxicity	Respiratory protection device <sup>3</sup>	Respiratory protection device <sup>3</sup>	No minimum <sup>4</sup>	No minimum <sup>4</sup>
Eye Irritation Potential	Protective eyewear <sup>5</sup>	Protective eyewear <sup>5</sup>	No minimum <sup>4</sup>	No minimum <sup>4</sup>

# OPP Method Acceptance Status

The same testing approach is currently considered on a case-by-case basis for other classes of pesticides and pesticide products.

Acute Test	Alternative Test	US	OPP
<b>Eye Irritation</b>	Bovine Corneal Opacity (BCOP) Test	ICCVAM (2007)	Replaces rabbit for antimicrobial cleaning products
	Cytosensor Microphysiometer modified	ICCVAM (2010)	Replaces rabbit for antimicrobial cleaning products
	EpiOcular Assay (EO)		Replaces rabbit for antimicrobial cleaning products
<b>Skin Irritation</b>	Reconstructed Human Epidermis models (various)	ICCVAM 2002	Accepted
<b>Sensitization</b>	Local Lymph Node Assay (LLNA) or reduced LLNA (rLLNA)	ICCVAM (2008)	Accepted
<b>Acute Dermal Toxicity</b>			Opportunities for bridging or waiving
<b>Acute Oral Toxicity</b>			Opportunities for bridging or waiving
<b>Acute Inhalation Toxicity</b>			Opportunities for bridging or waiving

# Acute Toxicity Testing for Pesticides: Canadian Perspective

- Health Canada's Pest Management Regulatory Agency – Responsible Regulatory Authority; Pesticides regulated under the Pest Control Products Act
- Acute toxicity information requirements for technical grade of active ingredient (TGAI), integrated system product (ISP) or end-use product (EP)
  - Oral, dermal, inhalation, primary eye irritation, primary dermal irritation, dermal sensitization
- Testing based on guideline studies conducted to GLP
  - e.g., Acute oral toxicity – OECD TG 420, 423, 425 (OPPTS 870.1100)
- Used to determine pesticide labelling for Hazard/PPE/First Aid according to PMRA classification/labelling system
  - e.g., highly acutely toxic pesticide (dermal LD<sub>50</sub> < 500 mg/kg bw) applied by airblast:

Principal Display Panel  
Hazard Symbol



+

Principal Display Panel  
Hazard Statement

**DANGER  
POISON**

+

Secondary Display Panel  
Precaution Statements

- Fatal or Poisonous if absorbed through the skin
- Do not get on skin or clothing
- Wear chemical resistant coveralls over long sleeved shirt and long pants, chemical resistant gloves, socks and chemical resistant footwear during mixing, loading, application, clean up and repair.

+

First Aid  
Statements

Take off contaminated clothing. Rinse skin immediately with plenty of water for 15–20 minutes. Call a poison control centre or doctor for treatment advice.



# Acute Toxicity Testing for Pesticides: Canadian Perspective

- **Guidance/criteria to applicants/registrants for waiving/bridging acute toxicity data**
  - e.g., Eye irritation study – may be waived if material is corrosive to skin, pH < 2 or > 11.5, highly acutely toxic via the dermal route, design prevents ocular exposure
  - e.g., Bridging – use existing data set for one chemical to characterize hazard of another chemical with little or no existing data (i.e., similar composition products, route specific, use of expert judgement)
  - *Guidance for Waiving or Bridging of Mammalian Acute Toxicity Tests for Pesticides.* Pest Management Regulatory Agency Health Evaluation Directorate December 2013 (published)
  - Current status: PMRA co-lead with US EPA on an OECD technical document that builds upon the Canadian and American guidelines



# Acute Toxicity Testing for Pesticides: Canadian Perspective

- **Globally Harmonized System of Classification and Labelling of Chemicals (GHS) for Pest Control Products**
  - Guiding Principles
    - Alignment with trading partners
    - Builds upon NAFTA and Canadian commitment via Regulatory Cooperation Council (RCC)
    - Align across Canada including HC implementation of GHS for WHMIS
      - HC implemented WHMIS 2015 in February – GHS now applies to workplace chemicals with phased implementation to 2018
  - Phased Approach for Pesticides – start with Safety Data Sheets (SDS)
    - Develop guideline on SDSs for commercial, manufacturing, and restricted class products in consultation with industry
      - Will help industry transition, provide lessons learned for future regulation, and ensure efficient/effective guideline development through industry participation
      - Guideline to be released for voluntary adoption in advance of regulatory change
    - Implementation of GHS for labels considered at a later date; consider implementation for domestic class products with implementation for consumer products in Canada
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