

**SUBMISSION REVIEW PROCESS  
AND  
HEALTH RISK ASSESSMENT**

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# **SUBMISSION COMPONENTS**

## **NEW ACTIVE INGREDIENT \* FORMULATION**

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### **ADMINISTRATIVE PART**

**Covering letter, application forms, fees forms,  
Product Specifications Form**

### **LABEL**

**Guarantees, contents, names; Use Directions;  
Warnings; Health information; Environmental  
information; Commerce class**

### **CHEMISTRY STUDIES**

**Product identity, product composition  
Physical/chemical properties, manufacturing  
methods, microcontaminants, analytical  
methodology**

### **EFFICACY/VALUE STUDIES**

**Effectiveness, economics, sustainability**

### **ENVIRONMENTAL STUDIES**

**Environmental chemistry and fate - soil, water  
Environmental toxicology - plants, aquatic and  
terrestrial organisms**

### **HEALTH EFFECTS STUDIES**

**Toxicology  
Exposure - Occupational, bystander  
- Food residues, drinking water**

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# **SUBMISSION CATEGORIES**

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## **Approach:**

- C Submissions sorted to 5 categories**
  - C Descending complexity for number of components and review resources required**
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**A New technical active ingredient/ major new use**

**B Amendments/ changes to registered use**

**C Minor changes/no change to registered use**

**D Variable types**

**Import for manufacture and export**

**User requested minor use label expansion**

**Own use import**

**E Research Permits**

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# **SUBMISSION PROCESS**

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<b>ACTIVITIES</b>
<b>VERIFICATION</b>
<b>SCREENING</b>
<b>PRELIMINARY REVIEW</b>
<b>EVALUATION</b>
<b>INTEGRATION OF REVIEWS</b>
<b>PROPOSED REGULATORY DECISION DOCUMENT (PRDD)</b>
<b>PRDD CONSULTATION</b>
<b>FINAL DECISION INCORPORATING CONSULTATION</b>
<b>LABEL - Final</b>

# **HEALTH EFFECTS ASSESSMENT**

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## **COMPONENTS**

### **TOXICOLOGY**

**Defining the hazard**  
**Risk assessment decisions**

### **EXPOSURE**

#### **FOOD RESIDUES**

**Exposure from food sources and water**  
**Risk assessment**  
**Risk management**

#### **OCCUPATIONAL/BYSTANDER**

**Exposure to workers and bystanders**  
**Risk assessment**  
**Risk Management**

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# **TOXICOLOGY EVALUATION**

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## **OBJECTIVE:**

- **Identify inherent hazard**
  - range of toxicity studies
  - acute effects, chronic effects
- **Identify potential for effects on human health**
  - dietary
  - occupational
  - bystander
- **Determine acceptable levels for humans exposure**

## **ASSESSMENT OF:**

**technical active ingredient  
formulation**

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# **TYPES OF TOXICOLOGY STUDIES**

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**TOXICOKINETICS - absorption, distribution, metabolism, excretion**

**ACUTE TOXICITY - oral, dermal, inhalation, sensitization, eye/skin irritation**

**REPEATED DOSE, SHORT TERM 2-4 wks., 3-6 mos., 1 year**

**REPEATED DOSE, CHRONIC/ONCOGENICITY - 2 years**

**REPRODUCTIVE TOXICITY - 2 generations**

**DEVELOPMENTAL TOXICITY - birth defects**

**GENOTOXICITY - interaction with DNA**

**NEUROTOXICITY - effects on nervous system**

**SPECIAL STUDIES - mechanistic, target organs**

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# **RISK ASSESSMENT TOXICOLOGY EFFECTS**

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- C Identify adverse effects (hazard) local and systemic, target organs**
- C Assess relevance to humans**
- C Identify most sensitive/relevant species**
- C Identify most relevant endpoints and the lowest NOEL for that effect**
- C Assess formulant toxicity when assessing formulation**
- C Determine Acceptable Daily Intake (ADI)\***

$$\frac{\text{NOEL (mg/kg bw/d)}}{\text{Uncertainty Factor (100x minimum)}} = \text{ADI*}$$

- C Determine Acceptable Margin of Exposure for Occupational Exposure**

$$\frac{\text{NOEL (mg/kg bw/d from most relevant study)}}{\text{Margin of Exposure (100x minimum)}} = \text{dose limit exposure}$$

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# FOOD RESIDUE ASSESSMENT

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- C Product chemistry (LSD); analytical methods - detect chemical in food sources**
  - C Use pattern and food crops to be treated (label)**
  - C Metabolism - animals, plants, soil (EAD), rat (Toxicology) - identify residues of concern**
  - C Residue trials - data for crops and/or animal products at maximum label rates (MRL) - worst case scenerio**
  - C Processed food residues**
  - C Storage stability**
  - C Livestock feeding studies - meat, milk, eggs**
  - C Crop rotation data**
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# **RISK ASSESSMENT FOOD RESIDUE EXPOSURE**

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- C Maximum Residue Limits (MRLs) for all crops and food animals; include processing considerations**
  
  - C Using MRL**
    - + Canadian dietary intake of products**
    - + drinking water residues****calculate Potential Daily Intake (PDI) for adults and children**
  
  - C Compare PDI to ADI established from toxicology review**
  
  - C PDI must be less than ADI**
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# **RISK MANAGEMENT FOOD RESIDUES**

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**Risk Management Trigger:  
PDI greater than ADI**

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**Options:**

- C Remove crops from label**
  - C No treated crops as animal feed**
  - C Increase post application intervals**
  - C Obtain definitive residue data for crops based on actual use (use not always maximum label rates or frequency)**
  - C Reduce label rates**
  - C Reduce application frequency**
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# OCCUPATIONAL/BYSTANDER EXPOSURE ASSESSMENT

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## Objective:

**Determine systemic dose from labelled use**

- amount breathed in**
  - amount deposited on skin**
  - amount absorbed through skin**
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## Mixer/Loader/Applicator

- C Modelling - Pesticide Handlers Exposure Database**
- C Studies of Mixer/Loader/Applicator**
  - Passive dosimetry (dermal, inhalation)**
  - Biological monitoring**
- Dermal Absorption Studies**

## Post Application (re-entry)

- C Studies of workers, bystanders**
    - Passive dosimetry**
    - Biological monitoring**
  - C Dislodgeable Residues - foliar, soil, surfaces**
  - C Ambient air samples**
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# **RISK ASSESSMENT OCCUPATIONAL/BYSTANDER EXPOSURE**

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**NOEL (mg/kg bw/d from animal studies) \_\_\_\_\_ = Margin of Exposure**  
**Exposure (mg/kg bw/d from studies or model)**

## **Typical Scenarios for Exposure Assessment**

### **Occupational**

#### **Mixer/Loader/Applicator**

- agricultural (ground, aerial)
- greenhouses
- industrial
- Pest Control Operators

### **Residential**

- home/garden

### **Post application**

- worker settings
  - commercial, residential - including children
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# **RISK MANAGEMENT OCCUPATIONAL/BYSTANDER EXPOSURE**

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## **RISK MANAGEMENT TRIGGER:**

**Margin of Exposure less than determined necessary from toxicology review**

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## **ADMINISTRATIVE CONTROLS**

- C Re-entry intervals**
- C Application rate; limit number of applications**
- C Training**
- C Classification - restricted, commercial, domestic**
- C Monitoring**
- C Label Improvement**

## **ENGINEERING CONTROLS**

- C Personal protective equipments**
  - C Closed systems**
  - C Ventilation**
  - C Packaging**
  - C Reformulation**
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