Toxicology Assessment of Fire Suppressant Agents

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Toxicity Programs

Time	Traditional Program	Expedited Program
1st quarter	Inhalation screen	Inhalation Screen, Mouse Micronucleus
2nd quarter	Cardiac sensitivity, Acute toxicity Ames & Micronucleus.	Cardiac sensitivity, Acute toxicity Ames & Chromosome Aberration
3rd & 4th quarter	Cardiac sensit. Complete Environ. (Fish, Daphnia, Algae) Chromosome aberration Initiate 4-week inhalation tox.	Cardiac sensit. Complete Environ. (Fish, Daphnia, Algae) Initiate 4- & 13 wk inhal. Tox. Initiate Subchronic genetics Initiate metabolism Initiate carcinogenicity screen
5th & 6th quarter PMN & E.U. registration	Complete 4-week inhalation tox. Initiate 13- week inhalation tox.	Complete 4- & 13- week inhalation Complete Subchronic genetics Initiate Developmental tox. (rat) Continue Metabolism Continue Carcinogenicity screen
7th & 8th quarter	Developmental tox. (rat) Complete 13-week inhalation tox. Initiate Metabolism Initiate Reproduction study Optional Rabbit Developmental	Complete Developmental toxicity Complete Carcinogenicity screen Continue Metabolism Initiate Reproduction study Optional Rabbit Developmental
3rd year	Initiate Chronic Inhalation. Study Complete Metabolism study Complete 13 Week Inhalation tox.	Continue Metabolism Complete Reproduction tox. Complete Rabbit Developmental toxicity
4th – 6th year	Complete Reproduction study Complete Carcinogenicity study	

Toxicology Program Description

- **Acute Toxicity: 4-hr $LC_{50:}$ How toxic is a single exposure (>100,000 ppm)**
- **Cardiac Sensitization to Adrenalin: dog study to assess potential to sensitize heart to adrenalin (> 50,000 ppm) Key Study**
- **Repeat Exposure Toxicity:**
  - **2-week study: preliminary indicatory of toxicity (NOEL ≥ 50,000)**
  - **4-week study:, minimum requirement for evaluation (NOAEL ≥25,000 ppm)**
  - **13-week study: Comprehensive evaluation ~ equal to working lifetime (NOAEL ≥ 10,000 ppm)**

Reproduction/Developmental Toxicity

- **Reproduction: Not required forfire supressant agents since exposures are limited and effects on reproductive organs will be seen in repeat toxicity studies**
- **Developmental toxicity study (rat) : Desirable for applications in occupied spaces**

Toxicology Program Description

- **Metabolism**
  - **Identifies metabolic products that could be toxic and gives indication of biological activity**
- **Mutagenicity gives an indication of potential carcinogenicity**
  - **Ames Assay: Preliminary mutagenicity assay**
  - **In vivo mouse micronucleus: Uses intact animal**
  - **In vitro chromosome aberration w. human lymphocytes: human cells**
  - **In vivo UDS w 4-wk exposure: optional**
  - **In vivo rat micronucleus w 4-week exposure: optional**

Example HFC-134a

134a

- **Acute lethality**
  - **LOEL 567,000 ppm**
- **Cardiac sensitization**
  - **NOEL 50,000 ppm & LOEL 75,000 ppm**
- **4-week toxicity**
  - **NOEL >50,000 ppm**
- **13 week toxicity**
  - **NOEL 50,000 ppm**
- **Developmental toxicity**
  - **Rat NOAEL ~300,000 ppm**
  - **Rabbit NOAEL 10,000 ppm**

- **Metabolism > 0.1%**
- **Mutagenicity**
  - **Ames not active**
  - **Chromosome Aberration not active**
  - **Micronucleus (mouse) not active**

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