ACUTE TOXICITY FOR THE PRODUCT ABINE (Abamectine 1.8% EC)

Table 1: Acute toxicological data obtained with Abamectin 1.8% EC

| Parameter [Reference] | Species | Result mg/kg or mg/m3 or effect | Classification |
| --- | --- | --- | --- |
| Oral route IIIA 7.1.1/01 Aldrin Joseph (2002a) | Rat | LD50 = 500 - 2000 mg/kg bw | Harmful if swallowed R22  H302 |
| Percutaneous route IIIA 7.1.2/01 Aldrin Joseph (2002b) | Rat | LD50 > 2000 mg/kg bw | None |

Abamectin 1.8% EC caused mortalities at 2000 mg/kg bw upon oral administration. The oral LD50 in rats was 500-2000 mg/kg bw.

No mortalities or signs of toxicity were observed in rats upon treatment with Abamectin 1.8% EC via dermal or inhalation administration.

Abamectin 1.8% EC is not irritating to the skin and but irritating to the eye of the rabbit.

Abamectin 1.8% EC does not require labelling as skin sensitizer based on a maximisation test in guinea pigs.

According to the Directive 2001/59/EC and Regulation 1272/2008, Abamectin 1.8% EC has to be labelled with R22 (Harmful if swallowed) and R41 (Irritating to the eye).

According to Regulation (EC) 1272/2008 labelling with H302 (Harmful if swallowed) and H318 (Causes serious eye damage) is required.

IIIA 1.1 Acute oral toxicity

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| **Report:** | **KIIIA 7.1.1/01,** Aldrin Joseph, S. (2002a) |
| Title: | Acute oral toxicity study of Abine (Abamectina 1.8% p/v) in rats |
| Document No: | JRF 3719 |
| Guidelines: | OECD No. 423 |
| GLP | Yes |

**Executive Summary**

An acute oral toxicity study was performed, in which groups of 3 rats were dosed with Abine (1.8% Abamectina) at a dose levels of 200, 500 and 2000 mg/kg bw in a single dose via gavage.

No mortalities occurred at 200 and 500 mg/kg bw but 5 of six animals died prematurely at 2000 mg/kg bw. The oral LD50 of Abine (1.8% Abamectina) was determined to be between 500 and 2000 mg/kg bw. Abine (1.8% Abamectina) requires labelling as being harmful if swallowed (R22) on the basis of this acute oral toxicity study.

Oral LD50 rats 500 - 2000 mg/kg bw

* + - 1. **MATERIALS AND METHODS**
         1. **MATERIALS**

|  |  |
| --- | --- |
| **1. Test Material:**  **Description:**  **Lot/Batch #:**  **Purity:**  **Stability of test compound:** | Abine (1.8% p/v Abamectina)  Clear yellow liquid  0752  1.79% p/v Abamectin  Stable for the duration of the study |
| **2. Vehicle and/or positive control:** | Distilled water |
| **3. Test animals**  **Species:**  **Sex:**  **Strain:**  **Age:**  **Weight at dosing:**  **Source:**  **Acclimatisation period:**  **Diet:**  **Water:** | Rat  Male and female  Wistar  9-11 weeks  158 - 255 g  Breeding facility, Jai Research foundation, India  5-19 days  Rat pellet (Amrut brand), Pranav Agro Industries Ltd., Pune, India, *ad libitum*  Drinking water filter through Aquaguard filtration system, *ad libitum* |
| **4. Environmental conditions**  **Temperature:**  **Humidity:**  **Air changes:**  **Photoperiod:** | 21 - 23°C  66% mean relative humidity  23 air changes per hour  Alternating 12-hour light and dark cycles |

* + - * 1. **STUDY DESIGN AND METHODS:**

The study was conducted at: Jai Research Foundation; Valvada 396 108; Gujarat; India

**1. In life dates:** 16/05/2002-24/06/2002

**2. Animal assignment and treatment**

Abine (1.8% Abamectina) was suspended in distilled water and orally administered via gastric intubation (10 mL/kg bw) stepwise to groups each consisting of three male or female fasted Wistar rats at dosage levels of 200 mg/kg bw. The animals were observed for treatment-related effects on the day of dosing (before and immediately, 1, 3, 6 and 24 hours after administration) and twice per day for a subsequent 14-day observation period. Mortality, clinical observations, body weights, food consumption and gross necropsy findings were recorded. Since no mortalities occurred at the 200 mg/kg bw dose level a further two groups each consisting of three male or female fasted Wistar rats received dosage levels of 2000 mg/kg bw and were observed as stated above. Since mortalities occurred, two final groups of three male and three female rats received Abine (1.8% Abamectina) at a dose level of 500 mg/kg bw.

**3. Statistics**

The data did not warrant statistical analysis.

* + - 1. **RESULTS AND DISCUSSION**
         1. **Mortality**

No mortalities occurred at 200 mg/kg bw or at 500 mg/kg bw.

Two male animal were found death on day 2 and day 12 and all three females (Day 1, 2 and 9) died prematurely at a dose level of 2000 mg/kg bw.

|  |  |  |  |
| --- | --- | --- | --- |
| **Table 7.1-1 Mortalities** | | | |
| **Dose level (mg/kg bw)** | **Males** | **Females** | **Combined** |
| 200 | 0/3 | 0/3 | 0 |
| 500 | 0/3 | 0/3 | 0 |
| 2000 | 2/3 | 3/3 | 5/6 |

* + - * 1. **CLINICAL OBSERVATIONS**

Clinical signs of toxicity noted during the study included lethargy, tremors, abdominal breathing, nasal discharge, piloerection and salivation.

* + - * 1. **Body Weight**

The body weight gain and food consumption was similar to that expected from untreated animals at 200 and 500 mg/kg bw while for animals treated with 2000 mg/kg bw a reduced body weight was noted at 7 days.

* + - * 1. **NECROPSY**

No external findings were recorded upon necropsy. Internal findings included lesions in the lungs (congestion, emphysema), liver (whitish foci) and intestine (yellowish mucus exudation).

* + - 1. **CONCLUSIONS**

The oral LD50 of Abine (1.8% Abamectina) was determined to be between 500 and 2000 mg/kg bw. Abine (1.8% Abamectina) requires labelling as being *Harmful if swallowed* (R22) on the basis of this acute oral toxicity study.

According to Reg (EC) 1272/2008 labelling with H302, *Harmful if swallowed* is required.

(Aldrin Joseph, 2002a)

IIIA 1.2. Acute percutaneous (dermal) toxicity

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| **Report:** | **KIIIA 7.1.2/01,** Aldrin Joseph, S. **(2002b)** |
| Title: | Acute dermal Toxicity Study of Abine (Abamectina 1.8% p/v) in rats |
| Document No: | JFR 3720 |
| Guidelines: | OECD No. 402 |
| GLP | Yes |

**Executive Summary**

In an acute dermal toxicity study, groups of young adult Wistar rats, 5/sex, were exposed to undiluted Abine (1.8% Abamectina) by the dermal route. Approximately 10% of the body surface was clipped and treated with 2000 mg test substance/kg bw for 24 h. A group of 5 rats per sex served as control group and were treated with distilled water. Animals then were observed for 14 days.

No mortalities, no signs of toxicity and no dermal reactions were observed. At necropsy no substance related effects were noted.

Dermal LD50 males > 2000 mg/kg bw

females > 2000 mg/kg bw

**I. MATERIALS AND METHODS**

**A. MATERIALS**

|  |  |
| --- | --- |
| **1. Test Material:**  **Description:**  **Lot/Batch #:**  **Purity:**  **Stability of test compound:** | Abine (1.8% p/v Abamectina)  Clear yellow liquid  0752  1.79% p/v Abamectina  Stable for the duration of the study |
| **2. Vehicle and/or positive control:** | Distilled water |
| **3. Test animals**  **Species:**  **Sex:**  **Strain:**  **Age:**  **Weight at dosing:**  **Source:**  **Acclimatisation period:**  **Diet:**  **Water:** | Rat  Male and female  Wistar  8-9 weeks  155 - 220 g  Breeding facility, Jai Research Foundation, India  7 days  Rat pellet (Amrut brand), Pranav Agro Industries Ltd., Pune, India, *ad libitum*  Drinking water filter through Aquaguard filtration system, *ad libitum* |
| **4. Environmental conditions**  **Temperature:**  **Mean relative humidity:**  **Air changes:**  **Photoperiod:** | 21 - 23°C  66%  25 air changes per hour  Alternating 12-hour light and dark cycles |

**B. STUDY DESIGN AND METHODS**

The study was conducted at: Jai Research Foundation; Valvada 396 108; Gujarat; India.

**1. In life dates:** 18/06/2002-02/07/2002

**2. Animal assignment, treatment and observations**

The animals were randomly assigned to control and treatment groups and prepared by clipping the backs free of hair, approximately 24 h before application of the test material. The undiluted test material was applied uniformly to an area of shorn skin. At least 10% of the body surface was in contact with the test material under semi-occlusive conditions for 24 h. Control animals were treated similarly but with distilled water. After this application time, the bandages were removed and residual test item was removed using cotton moistened with distilled water. The animals were evaluated for effects at the day of dosing and for a subsequent 14-day observation period. Clinical observations, dermal findings, body weights and gross post mortem examinations were recorded. At the end of the study the animals were killed and necropsied.

**3. Statistics**

The data did not warrant statistical analysis.

**II. RESULTS AND DISCUSSION**

**A. MORTALITY**

No mortalities occurred at 2000 mg/kg bw, the only dose level tested.

**Table 7.1.2-1 Doses, mortality/animals treated**

|  |  |  |  |
| --- | --- | --- | --- |
| **Dose (mg/kg bw)** | **Males** | **Females** | **Combined** |
| 2000 | 0/5 | 0/5 | 0/10 |

**B. CLINICAL OBSERVATIONS**

There were no signs of systemic toxicity.

**C. Dermal Responses**

No dermal responses were observed in the animals.

**D. BODY WEIGHT**

The body weight gains were within the range expected for rats used in this type of study.

**E. NECROPSY**

No abnormalities were found in the animals.

**III. CONCLUSIONS**

The combined dermal LD50 of in female and male rats was determined to be in excess of 2000 mg/kg bw. In accordance with the provisions of Council Directive 67/548/EC Abine (1.8% Abamectina) does not require labelling as being toxic or harmful on the basis of this acute dermal toxicity study.

(Aldrin Joseph, 2002b)