## Section A6.1.1 — Acute Oral Toxicity - Rat

**Annex Point IIA 6.1** — **Rat, cypermethrin, oral LD50**

| | | | Official use only |
|---|---|---|---|
| | | **1 REFERENCE** | |
| **1.1** | **Reference** | [redacted]; Acute oral toxicity study (acute toxic class method) with cypermethrin in Wistar rats; [redacted], report no. [redacted].<br>Dates of work: 29th March 2005 – 22nd April 2005 | |
| **1.2** | **Data protection** | Yes | |
| 1.2.1 | Data owner | Agriphar s.a. | |
| 1.2.2 | | | |
| 1.2.3 | Criteria for data protection | Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I authorisation | |
| | | **2 GUIDELINES AND QUALITY ASSURANCE** | |
| **2.1** | **Guideline study** | Yes, OECD guideline 423 (17th December 2001) | |
| **2.2** | **GLP** | Yes | |
| **2.3** | **Deviations** | No | |
| | | **3 MATERIALS AND METHODS** | |
| **3.1** | **Test material** | Cypermethrin technical (cypermethrin cis:trans/40:60) | |
| 3.1.1 | Lot/Batch number | CMN92T1197AN | |
| 3.1.2 | Specification | Certificate of Analysis supplied with study report verified the batch was within accepted specification | |
| 3.1.2.1 | Description | Viscous liquid | |
| 3.1.2.2 | Purity | 94.0% w/w | |
| 3.1.2.3 | Stability | Stable – expiry date August 2006 | |
| **3.2** | **Test Animals** | | |
| 3.2.1 | Species | Rat | |
| 3.2.2 | Strain | Wistar | |
| 3.2.3 | Source | [redacted] | |
| 3.2.4 | Sex | Female | |
| 3.2.5 | Age/weight at study initiation | 9-10 weeks, 132-152g | |
| 3.2.6 | Number of animals per group | 3 | |
| 3.2.7 | Control animals | No | |
| **3.3** | **Administration/ Exposure** | Oral | |
| 3.3.1 | Post exposure period | 15 days | |

## Section A6.1.1 — Acute Oral Toxicity - Rat

**Annex Point IIA 6.1** — **Rat, cypermethrin, oral LD50**

| | | |
|---|---|---|
| | | **Oral** |
| 3.3.2 | Type | Gavage |
| 3.3.3 | Concentration | 300 mg/kg bodyweight (G1F first and second treatment step) and 2000 mg/kg bodyweight (G2F first treatment step) |
| 3.3.4 | Vehicle | Refined groundnut oil |
| 3.3.5 | Concentration in vehicle | 60 mg/ml (GF1 300 mg/kg group) and 400 mg/ml (GF2 2000 mg/kg group) |
| 3.3.6 | Total volume applied | 5 ml/kg bw |
| 3.3.7 | Controls | Not applicable |
| **3.4** | **Examinations** | Toxic signs and mortality observed 5 times during day 1 (at 30 mins and 4 times at hourly intervals) and once daily during days 2-15. Bodyweights recorded pre-administration (day 1) and 8, 15 days post treatment/death. Gross necropsy at death and all survivors at the end of the observation period. |
| **3.5** | **Method of determination of $LD_{50}$** | According to Annex 2c of guideline 423 |
| **3.6** | **Further remarks** | - |
| | | **4 RESULTS AND DISCUSSION** |
| **4.1** | **Clinical signs** | No toxic signs/pre-terminal deaths in the G1F (300 mg/kg) group. In the G2F (2000 mg/kg) group, toxic signs observed were slight/severe salivation, tremors, lethargy, ataxia and perineum wet with urine. |
| **4.2** | **Pathology** | In the G2F group, one rat died on day 2 and no abnormality was detected at necropsy. The other 2 rats died on day 3, lung congestion was detected in both rats at necropsy. No abnormalities detected in remaining rats at necropsy. |
| **4.3** | **Other** | In the G1F group, all rats gained bodyweight during the observation period. In the G2F group, all dead rats lost weight compared to their initial bodyweight. |
| **4.4** | **$LD_{50}$** | LD50 was found to be **500 mg/kg bw** as per LD50 cut-off value of Annex 2c of the guideline.<br>Category 4 as per Globally harmonized classification system of Annex 2c of the guideline. |

## Section A6.1.1 — Acute Oral Toxicity - Rat

**Annex Point IIA 6.1** — **Rat, cypermethrin, oral LD50**

| | | |
|---|---|---|
| | | **5 APPLICANT'S SUMMARY AND CONCLUSION** |
| **5.1** | **Materials and methods** | Acute oral administration in rat (acute toxic class method) with 15 day post-treatment observation based on OECD guideline 423. A dose of 300 mg/kg bw (G1F group) was administered to 3 female rats on day1. Three further animals were treated at the same dose 3 days later. Based on the results, the next upper dose of 2000 mg/kg bw was administered to 3 animals to determine the LD50 cut-off value. |
| **5.2** | **Results and discussion** | An LD50 of 500 mg/kg was determined based on the acute toxic class method. |
| **5.3** | **Conclusion** | Acute oral LD50 = 500 mg/kg bw |
| 5.3.1 | Reliability | 1 |
| 5.3.2 | Deficiencies | No |

| **Evaluation by Competent Authorities** | |
|---|---|
| | Use separate "evaluation boxes" to provide transparency as to the comments and views submitted |
| | **EVALUATION BY RAPPORTEUR MEMBER STATE** |
| **Date** | April, 2011. |
| **Materials and Methods** | The applicant's version is acceptable. |
| **Results and discussion** | The applicant's version is adopted with the following amendment:<br>4.1 Clinical signs:<br>G1F (300 mg/kg) group: tremors observed in one rat on day 1. No toxic signs were observed in the remaining rats. |
| **Conclusion** | The applicant's version is adopted.<br>**Acute oral LD50 = 500 mg/kg bw** |
| **Reliability** | 1 |
| **Acceptability** | Acceptable |
| **Remarks** | |

## Section A6.1.1 Acute Oral Toxicity - Rat

**Annex Point IIA 6.1**

**Rat, cypermethrin, oral LD50**

| | **COMMENTS FROM ...** |
|---|---|
| **Date** | *Give date of comments submitted* |
| **Materials and Methods** | *Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.*<br>*Discuss if deviating from view of rapporteur member state* |
| **Results and discussion** | *Discuss if deviating from view of rapporteur member state* |
| **Conclusion** | *Discuss if deviating from view of rapporteur member state* |
| **Reliability** | *Discuss if deviating from view of rapporteur member state* |
| **Acceptability** | *Discuss if deviating from view of rapporteur member state* |
| **Remarks** | |

## Table A6_1_1. Table for Acute Oral Toxicity

| *Dose [mg/kg]* | *Number of dead / number of investigated* | *Time of death (range)* | *Observations* |
|---|---|---|---|
| G1F<br>1st treatment 300 mg/kg | 0/3 | - | Tremors observed in 1 animal on day 1. |
| G1F<br>2nd treatment 300 mg/kg | 0/3 | - | No toxic sign |
| G2F<br>2000 mg/kg | 3/3 | Day 2 or 3 | Slight/severe salivation, tremors, lethargy, ataxia and perineum wet with urine |
| $LD_{50}$ value | 500 mg/kg bw | | |