citoxlab
Safety and Health Research

FINAL REPORT

6-methoxy-harmalan:
Acute Dermal Toxicity Study in Rats

Study code: 18/068-002P

Study Director:

10 December 2018

GENERAL INFORMATION

STUDY TITLE:	6-methoxy-harmalan: Acute Dermal Toxicity Study in Rats
TEST ITEM:	6-methoxy-harmalan
SPONSOR:	SODEVAL S.A.S. Address: 3 boulevard de Verdun, 86000 Poitiers, France
STUDY MONITOR:	Jean-Bernard Fourtillan E-mail: jb.fourtillan@gmail.com
TEST FACILITY:	Citoxlab Hungary Ltd. Address: H-8200 Veszprém, Szabadságpuszta Hungary Phone: +36 88-545-300 Fax: +36 88-545-301
STUDY DIRECTOR:	
TEST FACILITY MANAGEMENT:	
QUALITY ASSURANCE*:	
RESPONSIBLE PERSONS*:	

* *Other trained, competent personnel may have worked on the study as required.*

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study has been performed in accordance with the Study Plan, OECD Guidelines for Testing of Chemicals (No.: 402, 24th Feb. 1987), Commission Regulation (EC) No 440/2008, B.3 (L142, 30 May 2008), OPPTS 870.1200 (EPA 712-C-98-192, August 1998), and the Principles of Good Laboratory Practice (Hungarian GLP Regulations: 42/2014. (VIII. 19.) EMMI decree of the Ministry of Human Capacities which corresponds to the OECD GLP, ENV/MC/CHEM (98) 17.).

I, the undersigned, declare that this report constitutes a true record of the actions undertaken and the results obtained in the course of this study.

Signature: Date: 10 December 2018

STATEMENT OF THE MANAGEMENT

According to the conditions of the research and development agreement between SODEVAL S.A.S. (as Sponsor) and Citoxlab Hungary Ltd. (as Test Facility), the study titled "6-methoxy-harmalan: Acute Dermal Toxicity Study in Rats" was performed in compliance with the Principles of Good Laboratory Practice.

Signature: Date: 10 Dec 2018

QUALITY ASSURANCE STATEMENT

Study Code: 18/068-002P

Study Title: 6-methoxy-harmalan:
Acute Dermal Toxicity Study in Rats

Test Item: 6-methoxy-harmalan

This study has been inspected, and this report audited by the Quality Assurance Unit in compliance with the Principles of Good Laboratory Practice. As far as it can be reasonably established the methods described and the results incorporated in this report accurately reflect the raw data produced during this study.

All inspections, data reviews and the report audit were reported in written form to the Study Director and to Management. The dates of such inspections and of the report audit are given below:

Date of Inspection	Phase(s) Inspected/Audited	Date of report to	
		Management	Study Director
22 August 2018	Study Plan	22 August 2018	22 August 2018
28 August 2018	Treatment	28 August 2018	28 August 2018
20 October 2018	Draft Report	20 October 2018	20 October 2018
10 December 2018	Final Report	10 December 2018	10 December 2018

Signature: Date: 10 December 2018

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1.0 SUMMARY

An acute dermal toxicity study was performed with the test item 6-methoxy-harmalan in male and female Crl:WI Wistar rats, in compliance with OECD Guideline No.: 402 (1987), Commission Regulation (EC) No 440/2008, B.3 and OPPTS 870.1200 [1-3].

A limit test was carried out at 2000 mg/kg body weight (bw) in both sexes (5 rats/sex). The test item was applied as a single dermal 24-hour exposure followed by a 14-day observation period.

Clinical observations were performed on all animals at 1 and 5 hours after dosing and daily for 14 days thereafter. Body weight was measured on Day 0 (prior to dosing) and on Days 7 and 14 (before necropsy). Gross macroscopic examination was performed on all animals at necropsy at the end of the 2-week observation period (Day 14).

The results of the study were summarised as follows:

Mortality

Test item did not cause mortality at the dose level of 2000 mg/kg bw.

Systemic clinical signs

There were no adverse systemic clinical signs noted in any animal throughout the 14-day observation period.

Local dermal signs

No adverse local dermal signs were observed after treatment with the test item or during the 14-day observation period. Coloured skin (yellowish, in the treated area) was noted for all animals from Day 1 up to Day 7, which was related to the test item and was not identified as a local dermal sign.

Body weight and body weight gain

There were no treatment related effects on body weight or body weight gain during the observation period.

Necropsy

There was no evidence of any macroscopic changes at a dose level of 2000 mg/kg bw.

Conclusions

The acute dermal median lethal dose (LD_{50}) of the test item 6-methoxy-harmalan was found to be greater than 2000 mg/kg body weight in male and female Crl:WI rats.

According the GHS and the GHS-EU (CLP) criteria [4, 5], classification of 6-methoxy-harmalan can be ranked as "Not classified" for acute dermal exposure.