MEERUT INSTITUTE OF ENGINEERING & TECHNOLOGY

(MIET Meerut)

CPCSEA Registration Number: 711/PO/Re/S/02/CPCSEA
(Ministry of Environment, & Forest, Government of India)

ACUTE ORAL TOXICITY OF MIROR REVIVE TABLETS

(OECD Test No. 423: Acute Oral toxicity)

SPONSOR

MIROR THERAPEUTICS PVT LTD
VASANTHA NAGAR
BANGALORE, KARNATAKA

CLINICAL RESEARCH ORGANIZATION

MITTAL GLOBAL CLINICAL TRIAL SERVICES (MGCTS)

DATA REQUIREMENTS

OECD Test No. 423: Acute Oral toxicity

TEST LABORATORY

PHARMACOLOGY DEPARTMENT, DEPARTMENT OF PHARMACEUTICAL TECHNOLOGY, MIET Meerut
NH-58, Delhi-Roorkee Highway, Baghpat Bypass Road Crossing, Meerut, U.P. – 250005

PROJECT NO : 2024-07-246
REPORT NO. : MIET/DPT/2024-07/246/AST
DATE : 30-08-2024

MEERUT INSTITUTE OF ENGINEERING & TECHNOLOGY

Test Compound : MIROR REVIVE TABLETS
SPONSOR : Miror Therapeutics Pvt Ltd
CRO : Mittal Global Clinical Trial Services (MGCTS)
STUDY : ACUTE ORAL TOXICITY
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1. STATEMENT OF COMPLIANCE

I, the undersigned hereby declare that Project No. 2024-07-246/ Report No. MIET/DPT/2024-07/246/AST; entitled "***Acute Oral Toxicity of Miror Revive Tablets***" was performed in accordance to the standard procedure of Pharmacology Department, Department of Pharmaceutical Technology, MIET Meerut, UP, as well as the approved study plan.

I hereby attest the authenticity of the study and guarantee that this report is a true and accurate record of the results obtained and shall not be reproduced except in full, without the written approval of the Sponsor.

The study was conducted in compliance with the OECD Test No. 423: Acute Oral toxicity. This study was conducted in accordance to the Good Laboratory Practices (GLP).

All original raw data including documentation, the draft report, a copy of the final report and the representative test sample are archived at the Pharmacology Department, Department of Pharmaceutical Technology, MIET Meerut, UP. There were no circumstances that may have affected the quality and integrity of the study.

The sponsor of the study is responsible for the necessary evaluation of the test sample concerning the chemicals, purity, identity, stability and other required data.

Principal Investigator **30-08-2024**
Ms Rashi Faujdar (M. Pharm.) Date

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2. STATEMENT BY TEST FACILITY MANAGEMENT

Management of the test facility has made available all the resources to the Principal Investigator necessary for conduct of the present study in compliance with the principles of GLP.

I, the undersigned, take overall responsibility for the reliability of the work described in the report with accordance to GLP.

Vipin

Laboratory In-charge
Dr. Vipin Kumar Garg (M.Pharm, PhD)

30-08-2024
Date

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3. QUALITY ASSURANCE REPORT

This **Project No. 2024-07-246**, **Report No. MIET/DPT/2024-07/246/AST** entitled "***Acute Oral Toxicity of Miror Revive***" (OECD Test No. 423: Acute Oral toxicity) was subjected to inspection by Quality Assurance Unit.

This report had been audited by the Quality Assurance Unit, and is considered to be an accurate account of the data generated and of the procedures followed. In each case, the outcome of the QA evaluation is reported to the Principal Investigator and Management on the day of evaluation. Audits of study documentation, and process inspections appropriate to the type and schedule of this study were as follows:

Standard Test Method Compliance Audit	: 10-07-2024
Animal Preparation	: 01-08-2024
Test Material Preparation	: 06-08-2024
Application of test compound	: 06-08-2024
Assessment of Response	: 14 Days (06-08-2024 to 19-08-2024)
Draft Report Audit	: 25-08-2024
Final Report Date	: 30-08-2024

QUALITY ASSURANCE OFFICER **30-08-2024**
Ms. Garima Agarwal (M.Pharm) Date

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4. STUDY PERSONNEL

Principal Investigator : Ms Rashi Faujdar (M. Pharm)

Co – Investigators : Ms Falguni Goel

Veterinarian : Dr. Sonia Sharma

Study Managers **:** Ms. Garima Agarwal (M.Pharm)

: Mr. Ankit Chaudhary (M.Pharm)

5. SUMMARY

The study was conducted in accordance to the OECD Guideline for the testing chemical No. 423 to evaluate the acute oral toxicity of Miror Revive Tablets.

The test sample was dissolved in the purified water, and four pre specified fixed-doses (5, 50, 300, and 2000 mg/kg body weight) was orally administered in female Wistar rats (8-12 weeks) by oral gavage. The body weight of animals was measured at day 0 (before the drug administration) and on days 1, 7, and 14 of the study. The rate of mortality and general behavior of the animals were observed continuously for the initial 1, 4, and 24 h after the drug administration and then daily for 14 days. Cage side observations included variations in the skin and fur, eyes, and mucous membranes. Particular attention was directed to observations of tremor, convulsions, salivation, diarrhea, lethargy, sleep, and coma. Also, respiratory, circulatory, autonomic, and central nervous systems and somatomotor activity were examined.

In the study, no mortality was observed up to 14 days. No toxic symptoms were found in rats in all four doses. No abnormalities were been observed in general clinical observations or gross necropsy. The rats were found to behave normally with no variation in locomotors, behavioral, neurological, or secretary patterns. No significant changes were observed in the body weight of rats in all four treated doses.

Considering the data obtained from the study, the Miror Revive Tablet is not found to be lethal up to a dose of 2000 mg/kg. According to the GHS (Globally Harmonized Classification System), the test sample Miror Revive was classified into Category 4.

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6. INTRODUCTION

A. Purpose of the Study:

The test article identified below was extracted and evaluated to determine if the test substance provided would cause acute systemic toxicity following oral administration to rats.

B. Testing Guidelines:

The study was conducted based on the OECD Guidelines 423-Acute Toxic Class Method.

7. MATERIALS

Sample Details

The test article provided by the sponsor was identified and handled as follows:

Test Compound	: Miror Revive Tablets
Batch No	: EC269
Mfg Date	: 03/2024
Physical Appearance	: Yellow colored oblong tablets
Expiry Date	: 08/2025
Storage Condition	: Room Temperature
Control Article	: NA
Control Article Stability Testing	: NA

Sample Preparation:

The sample was dissolved in the purified water just before its administration in rats.

Test System

Species	: Wistar rats
Source	: Lala Lajpat Rai University
Strain	: Albino
Sex	: Female
Body Weight Range	: 160-220 gm
Acclimatization	: Minimum 5 days
No. of Animals	: 12 Rats

Identification Method: Marked with tattoo ink on the tail

Animal Management Husbandry:
The conditions conformed to MIET Standard Operating System that are based on "*Guide for the Care and Use of Experimental Animals*"

Food:
A commercially available Rat feed was provided daily

Water:
Portable water was provided *ad libitum* through species appropriate water container or delivered through an automatic watering system.

Environmental conditions:
Air-conditioned rooms with 10-15 air changes per hour, Temperature between 22 ± 3°C, relative humidity 40 – 60% and illumination cycle set to 12 hours artificial fluorescent light and 12 hours dark.

Selection:
Only healthy previously unused animals were selected.

Personnel:
Associates involved were appropriately qualified and well trained.

Veterinary Care:
Standard veterinary medical care was provided in the study.

IAEC:
This procedure has been approved by MIET's Institutional Animal Ethical Committee and is reviewed at least half-yearly by the same committee.

8. METHODS

Preparation of Animals:

Female rats were randomly selected, weighed, and marked individually for identification. A total of four groups were formed containing three rats in each group. The animals were kept in the cages for five days before dosing to allow for acclimatization to the laboratory conditions.

Preparation of test drug:

Test drug was dissolved in the purified water just prior to the dose administration.

Drug administration:

Animals were kept on overnight fasting before the drug administration and three to four hours post drug administration. During the time, the animals had free access to the water. Prior to the drug administration, the animals were weighed. The drug in fixed-dose (5, 50, 300, and 2000 mg/kg body weight) was administered through oral gavage in the respective groups.

Mortality observation:

The numbers of animal deaths were observed at 1, 4, 24 h, and upto 14 days after drug administration.

General Clinical observation:

Post drug administration, the animals were continuously observed for the muscle activity (Locomotion, muscle coordination, catatonia, tremor and convulsive episode), reflex activity (Visual place response, writhing response, Tail pinch response, piloerection), and secretory activity (Lacrimation, salivation, sniffing and defecation). Also, respiratory and heart rate were examined.

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Body weight Measurement:

The body weight was measured on day 0 (prior to drug administration) and day 1, 7, and 14 of the drug administration using electric balance.

Gross Necropsy:

At the end of the observation period the survived animals were sacrificed by an over dosage of pentobarbital and were subjected to gross necropsy. All gross pathological changes were recorded.

9. Acceptance Criteria and Statistical Analysis

According to the OECD Guidelines 423, the number of animal mortalities and evident toxicity, the hazard class of acute oral toxicity was classified to the category of Globally Harmonized Classification System.

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10. RESULTS & DISCUSSION

Mortality :
No mortality was observed in any animals until 14 days post drug administration.

Clinical signs:
No abnormalities were observed in any animals until 14 days after the drug administration.

Body Weight:
No significant variation has been observed. Weight gain or weight loss in the study cannot be considered a sign of evident toxicity as no abnormalities were observed in clinical and gross necropsy findings.

Macroscopic Findings:
No abnormalities were observed in any animals at 5, 50, 300, and 2000 mg/kg dose.

Table:

Dose (mg/kg)	Animals No.	Mortality Observed	Initial Body weight	Body weight post-drug administration			Macroscopic Findings (Abnormalities detected)
			Day 0	Day 1	Day 7	Day 14	
5 mg/kg	1	No	218.2	219.4	223.6	225.7	None
	2	No	220.1	221.0	224.5	226.9	None
	3	No	217.2	217.9	220.9	224.4	None
50 mg/kg	1	No	218.5	219.2	224.1	227.8	None
	2	No	215.6	216.1	219.8	223.3	None
	3	No	221.3	222.5	227.7	231.4	None
300 mg/kg	1	No	224.1	224.9	227.0	231.1	None
	2	No	210.9	210.2	204.6	207.2	None
	3	No	212.6	213.0	216.5	220.4	None
2000 mg/kg	1	No	220.3	221.2	225.1	228.9	None
	2	No	219.4	220.3	224.2	227.5	None
	3	No	217.7	218.3	221.6	225.8	None

11. ARCHIVE

On completion of the study, the raw data and other material, a sample of the test substance, and the study report are being retained for 09 years at the Pharmacology Department, Department of Pharmaceutical Technology, MIET Meerut, UP.

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12. CERTIFICATE

This is to certify that the "***Acute Oral Toxicity of Miror Revive Tablets***" sponsored by **Miror Therapeutics Pvt Ltd** and the testing material for the study was provided by Clinical Research Organization: **MITTAL GLOBAL CLINICAL TRIAL SERVICES (MGCTS) and Fare Labs** was performed according to the OECD Test No. 423: Acute Oral toxicity. **The test sample was found to be non-lethal up to dose of 2000 mg/kg.**

Note: Results and conclusions apply only to the test article tested. Any extrapolation of these data to other samples is the sponsor's responsibility.

Principal Investigator
Ms Rashi Faujdar (M.Pharm)

30-08-2024
Date

13. ANNEXURE – I: REFERENCES

- OECD Test No. 423: Acute Oral toxicity

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14. ANNEXURE –II: SAMPLE PHOTO

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15. QAI CERTIFICATE

Quality And Accreditation Institute
Centre for Laboratory Accreditation

Certificate of Accreditation

MIET Animal House Facility & MIET Cell Culture Lab
(Meerut Institute of Engineering & Technology, City Educational and Social Welfare Society)
A Block, N.H. 58, Delhi-Roorkee Highway, Baghpat Road Bypass Crossing, Meerut-250005, Uttar Pradesh, India

has been assessed and accredited in accordance with the Standard
ISO/IEC 17025:2017
"General Requirements for the Competence of Testing and Calibration Laboratories"
In the field of
Testing

This certificate remains valid for the Scope of Accreditation as specified in the annexure subject to continued compliance to the above standard & any other requirements specified by QAI.

QAI/CLA/TL/2023/0028

Valid from: 10 October 2023 Valid until: 09 October 2025

Dr. Bhupendra Kumar Rana
Chief Executive Officer

Prof. Vikram Kumar
Chair, CLA

User is advised to verify the current scope of accreditation by visiting our website: www.qai.org.in