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Chemical Category		
DIMETHYLOCTYLAMINE		

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TABLE 1

Mortality

Test material: Farmin DM08P

Dosage (mg/kg)	Mortality		
	Male	Female	Combined
500	4/5	5/5	9/10
50	0/5	0/5	0/10

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January 23, 1999

To: Document Control Officer
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Please find enclosed with this note, 10 TSCA 8(e) Reports to be forwarded to the Section 8(e) Coordinator.

Hester Kobayashi
Kao Product Safety Manager, N. America

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High Point Chemical
A Kao Group Company
255 Beddington St.
High Point, N.C. 27260
Telephone: (336)878-4210 (direct)
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January 22, 1999

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Document Processing Center
(Attn: Section 8(e) Coordinator) Mail Code 7407
Office of Pollution Prevention and Toxic Substances
U.S. Environmental Protection Agency
401 "M" St., S.W.
Washington, D.C. 20460

Dear Section 8(e) Coordinator:

This letter is to notify the Agency of test data which suggest that the chemical product described below is a poisonous substance.

The substance is described as Dimethyloctylamine with minor impurities in the following mixture:

CASRN	Chemical description	% present (approximate)
7378-99-6	Dimethyloctylamine	97
1120-24-7	Dimethyldecylamine	2
112-18-5	Dimethyllaurylamine	1

The Acute Oral Toxicity (Rat) test data obtained led to a LD50 of 162 mg/kg . The report is attached.

This information was located while reviewing reports of toxicological studies, provided by Kao Corporation, for revision of the U.S. version MSDS for the product. The report was reviewed on January 21, 1999.

The submission of this information is part of Kao Corporation's good faith effort to comply with requirements under TSCA Section 8(e).

Sincerely,

Hester Kobayashi

Hester Kobayashi, Dr.PH
Manager, Kao Product Safety, North America

A 05

Schedule No : KAS/145
Report No : 96/KAS145/0636

DIMETHYLOCTYLAMINE

FARMIN DM08P:
Acute oral toxicity study in the rat

FINAL REPORT

Pharmaco LSR Limited merged with Huntingdon Research Centre Limited on 21 November 1995. With effect from the same date the Company changed its name to Huntingdon Life Sciences Limited.

Study Director

P. B. Rees

To:
Kao Corporation
Tochigi Research Laboratories
2606 Akabane Ichikaimachi, Haga
Tochigi 321-34
Japan

From:
Huntingdon Life Sciences Ltd
Eye
Suffolk IP23 7PX
England

Draft: 6 June 1996
Final: 13 September 1996

FARMIN DM08P:
ACUTE ORAL TOXICITY
STUDY IN THE RAT

FINAL REPORT

Schedule No : KAS/145
Report No : 96/KAS145/0636

I hereby confirm that the work conducted at Huntingdon Life Sciences in respect of this study was in compliance with the Principles of Good Laboratory Practice (GLP) as required by the United Kingdom GLP Compliance Programme (Department of Health, 1989) and that the final report fully and accurately reflects the raw data generated during the conduct of the study.

The United Kingdom Principles of GLP accord with the OECD Principles of GLP (Environmental Monograph No. 45, OCDE/GD (92)32) and conform to and implement the requirements of the directives of the European Council (Directive: 87/18/EEC Directive: 88/320/EEC). The OECD Principles of GLP were reviewed in the relevant policy bodies of the organisation and were formally recommended by the OECD Council in 1981 for use in Member countries, which include Japan and the United States of America.

In line with normal practice in this type of short-term study, the protocol did not require analysis of the dose form.

P. B. Rees, B.Sc., C.Biol., M.I.Biol.
(Study Director)

Date: 13 Sep 1996

FARMIN DM08P:
ACUTE ORAL TOXICITY
STUDY IN THE RAT

FINAL REPORT

Schedule No : KAS/145
Report No : 96/KAS145/0636

The following staff have reviewed this report:

H. A. Cummins, B.Sc.
(Toxicologist)

FARMIN DM08P:
ACUTE ORAL TOXICITY
STUDY IN THE RAT

FINAL REPORT

Schedule No : KAS/145
Report No : 96/KAS145/0636

QUALITY ASSURANCE INSPECTIONS

	Dates (Day.Month.Year)		
	Inspection	Report to Study Director	Report to Management
Protocol check	04.01.96	04.01.96	04.01.96
Audit of the conduct of a study representative of this type	10.01.96		10.01.96
Process-based procedure inspections	09.11.95 20.12.95 10.01.96 07.03.96 23.04.96		09.11.95 20.12.95 10.01.96 07.03.96 23.04.96
Review of the final report	31.05.96	31.05.96	31.05.96

Process-based monitoring of other common procedures and routine inspection of facilities were also conducted and reported.

So far as can be reasonably established, the methods and procedures detailed in this report were found to describe those used during the study and the results to constitute an accurate representation of the data recorded.

A. Jennings, B.Sc., M.Sc., Ph.D.
(Principal Auditor, Quality Assurance)

A Jennings

Date: 9 September 1996

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1. SUMMARY

1.1 The acute oral toxicity of Farmin DM08P was investigated in two groups of five male and five female CD rats. The animals were starved overnight prior to dosing. The test material was administered at dosages of 50 and 500 mg/kg, at a constant volume-dosage of 10 ml/kg in maize oil.

Mortality and signs of reaction to treatment were recorded during a subsequent 14-day observation period; the surviving animals were killed on the following day. All animals were subjected to necropsy.

1.2 The mortality distribution was as follows:

Dosage (mg/kg)	Mortality Males	Mortality Females
500	4/5	5/5
50	0/5	0/5

The deaths occurred on on the day of dosing.

1.3 *Ante mortem* signs comprised prone position.

Signs of reaction in the surviving animal treated at 500 mg/kg comprised underactivity, staggering gait, hunched posture and piloerection. There was no sign of reaction to treatment amongst the animals treated at 50 mg/kg.

1.4 All surviving animals achieved anticipated bodyweight gains.

1.5 Necropsy findings for the decedents were unremarkable. There was no macroscopic abnormality evident amongst animals treated at 50 mg/kg.

1.6 Under the conditions of this study the acute oral median lethal dosage (LD_{50}), of the test material was approximately 162 mg/kg in female animals. Accordingly, Farmin DM08P was assigned to the class 'Toxic'.

2. INTRODUCTION

2.1 Study objective

The objective of this study was to either determine the approximate acute median lethal of the test material or to demonstrate its low toxicity at the maximum practicable dosage (2000 OR 5000 mg/kg, Regulatory Limit test) following a single oral administration to rats; to identify any target organs or systems; to assess the time course of response; and to identify any delayed or irreversible effects resulting from sub-lethal dosages

The study was designed to meet the requirements of Section 4, sub-section 401, of the OECD Guidelines for Testing of Chemicals (1987).

2.2 Study organisation

Location of study	:	Huntingdon Life Sciences Eye Suffolk IP23 7PX England
Study Director	:	P. B. Rees, B.Sc., C.Biol., M.I.Biol.
Study timing	:	The first group of animals arrived on 3 January 1996 and was treated 12 January 1996; the observations were completed on26 January 1996. The second group of animals arrived on 24 January 1996 and was treated on 31 January 1996; the observations were completed on 14 February 1996.
Data storage	:	All raw data pertaining to this study, except those generated or used during Sponsor's or Supplier's analysis, and a copy of the final report are stored in the archives.

3. MATERIALS AND METHODS

3.1 Animals

Young adult rats of the CD strain (remote Sprague-Dawley origin were supplied by Charles River (UK) Limited, Margate, Kent, England. The albino rat was selected for this study as it has been widely accepted as the standard laboratory species for use in acute toxicity tests. The strain has been used for toxicological purposes since its establishment under SPF conditions in 1955.

The animals were housed in stainless steel grid cages (RS Biotech, Northants, England). The grid floor ensured rapid removal of waste material to undertrays which were cleaned as necessary. Five animals of the same sex were accommodated in each cage, unless reduced by mortality. The cages were suspended in mobile stainless steel racks.

3.2 Husbandry

The animals were held in a limited-access facility. All rooms were kept at slight positive pressure relative to the outside and each had its own filtered air supply giving at least 10 complete air changes per hour without re-circulation. Target values for temperature and humidity were 21°C (range 19°-25°C) and 55% R.H (range 40%-70% R.H.), respectively. The achieved values were monitored daily. Electric time-switches regulated a lighting cycle of 12 hours of artificial light per day. An emergency generator was available to maintain the electricity supply in the event of a power failure. All personnel entering the building changed into clean protective clothing and wore an oversuit, gloves, plastic over-shoes and face mask to service animal holding areas.

A commercially-available complete pelleted rodent diet (RM1(E) SQC, from Special Diets Services Limited, Witham, Essex, England) was fed *ad libitum*. The manufacturer supplied analytical data with each batch of diet which included concentrations of nutritional components, aflatoxins and selected heavy metals, pesticides and micro-organisms. The diet contained no added antibiotic or other chemotherapeutic or prophylactic treatment. Samples of diet were taken for analysis at six-monthly intervals to detect potential contaminants by a laboratory independent of the supplier. Results of these analyses are retained in the archives.

Animals had free access to tap water taken from the public supply; in England the supply and quality of this water is governed by Department of the Environment regulations. Certificates of analysis were routinely received from the supplier (Essex and Suffolk Water plc). At approximately six-month intervals water was routinely sampled for analysis, by a laboratory independent of the supplier, for selected chlorinated and organophosphorus pesticides, polychlorinated biphenyls and lead and cadmium contaminants; it was also examined for coliform bacteria. Results of these analyses are retained in the archives.

There was no known information to indicate that normal levels of common contaminants, or any specific contaminants, in the diet or drinking water would influence the outcome of the study.

3.3 Pre-exposure period

On arrival, each animal was inspected before being accepted. All animals were weighed on arrival and the range of bodyweight was recorded. Five animals of the same sex were non-selectively allocated to each cage. Tail tattoos identifying each individual within the cage were made within one day of delivery. The sex of each animal was checked at the same time. An acclimatization period of at least five days was allowed between arrival at the laboratory and administration of the test material. A daily check on the general condition of the animals was made during this time and the record was consulted before each animal was accepted for use in the study.

Food was removed from the hoppers over-night before dosing.

Pre-fasted bodyweight was recorded on the day prior to dosing and was in the range 112 - 153 g for males and 105 - 137 g for females. The animals were approximately five weeks old at this time.

3.4 Treatment

3.4.1 Test material

A consignment of 300 g (net) Farmin DM08P, a clear colourless liquid, was received from the Sponsor on 21 November 1996. The material was further identified by the Batch No. 1318.

It was kept at ambient temperature, in the original container.

The identity, strength and purity of the test material received, and its stability under the storage conditions above, were the responsibility of the Sponsor.

3.4.2 Formulation

The test material was prepared at appropriate concentrations in maize oil to permit administration at a constant volume-dosage of 10 ml/kg bodyweight.

Dosages were calculated and expressed gravimetrically in terms of the material as received. Fresh formulations of the test material were prepared on the morning of administration and any surplus remaining after dosing was disposed of on the same day.

3.4.3 Quality control of dose form

A balance of the calculated amount of test material necessary to prepare the formulation and the quantity actually used was determined. This balance was checked before the formulations were dispensed.

No analyses were undertaken to assess the stability, homogeneity or achieved concentrations of the test material in the vehicle.

3.4.4 Treatment groups and sizes

A preliminary study was carried out using two groups of one male and one female rat given an oral administration of Farmin DM08P at dosages of 500 and 2000 mg/kg, at a constant volume-dosage of 10 ml/kg in maize oil.

The mortality distribution was as follows:

Dosage (mg/kg)	Mortality Males	Mortality Females
2000	1/1	1/1
500	1/1	1/1

No further data on the animals of the preliminary study are reported.

On the basis of this result, the main study was carried out using a single group of five male and five female rats given an oral administration of Farmin DM08P at the dosage of 50 mg/kg, at a constant volume-dosage of 10 ml/kg in maize oil. Since no animal died a further group of five male and five female rats were treated at 500 mg/kg; no further animals were employed

3.4.5 Administration of test material

Dose-volume was determined for each animal according to the fasted bodyweight on the morning of dosing. The dose was administered on Day 1 at a constant volume-dosage of 10 ml/kg bodyweight.

A flexible catheter was passed down the oesophagus allowing instillation of the dose into the lumen of the stomach.

Each animal was returned to its cage and food hoppers were re-filled approximately three hours after dosing.

3.5 Observation period

Three separate recordings of signs were made during the first hour after dosing and two further recordings during the remainder of Day 1. From Day 2 onwards, the animals were inspected twice daily and recordings were made once daily. The circumstances of any death were recorded. Any animal showing severe or enduring signs of pain or distress was humanely killed.

The bodyweight of each animal was recorded on the day before dosing and on Days 1, 8 and 15. The test was terminated on the morning of Day 15.

3.6 Necropsy

Carcases were stored in a refrigerator at approximately 4°C until trained necropsy staff were available. Surviving animals were killed by carbon dioxide inhalation at termination of the study.

All animals were thoroughly examined for abnormality of tissues or organs. All body cavities were opened, larger organs were sectioned and the gastro-intestinal tract was opened at intervals for examination of the mucosal surfaces. All abnormalities were described or the normal appearance of major organs was confirmed.

Macroscopically abnormal tissues were preserved in 4% neutral buffered formaldehyde and retained against future possible histopathological requirements.

3.7 Treatment of data

Probit analysis by the method of Finney (1971) was used to determine the acute median lethal dosage, 95% confidence interval and slope of the dose response curve of the test material for both sexes. The calculations were performed by the GLIM statistics program (Baker and Nelder, 1978) using a special macro program developed by Baker (Baker, 1980).

The classification criteria of the Commission of the European Communities were used in assessing the toxicity rating of the test material. as follows:

LD_{50} (mg/kg)	Classification
$LD_{50} \leq 25$	Very toxic
$25 < LD_{50} \leq 200$	Toxic
$200 \leq LD_{50} \leq 2000$	Harmful

Materials with LD_{50} values in excess of 2000 mg/kg mg/kg are considered to be of 'low oral toxicity'.

4. RESULTS

4.1 Mortality (Tables 1 and 2)

Four male and five female animals treated at 500 mg/kg died on the day of dosing. There was no death amongst the animals treated at 50 mg/kg.

4.2 Signs (Table 2)

Ante mortem signs were restricted to prone posture in one female animal.

The surviving animal treated at 500 mg/kg showed underactivity, staggering gait, hunched posture and piloerection; it was overtly normal after the first over night period.

There was no sign of reaction to treatment amongst animals treated at 50 mg/kg.

4.3 Bodyweight (Table 3)

All surviving animals achieved anticipated bodyweight gains.

4.4 Macroscopic pathology (Table 4)

Necropsy of the decedents revealed areas of fur staining and cases of distension of the small intestine by a yellow viscous fluid.

There was no macroscopic abnormality detected amongst the surviving animals.

5. CONCLUSION

Under the conditions of this study the acute oral median lethal dosage (LD_{50}) and slope of the dose response curve were:

	LD_{50} (mg/kg)	Slope (degrees)
Male	382	72°
Female	162	80°
Combined	342	73°

Accordingly, Farmin DM08P was assigned to the class 'Toxic'.

6. GENERAL REFERENCES

OECD (1987). Acute Oral Toxicity. Section 4, sub-section 401 of the OECD Guidelines for Testing of Chemicals (ISBN 92-64-12900-6).

EEC (1993). General Classification and Labelling Requirements of Dangerous Substances and Preparations; European Communities Council Directive 93/21/EEC. The Official Journal of the European Communities L110A, 4 May 1993 (ISSN 0378-6978).

FINNEY, DJ (1971) Probit Analysis. 3rd ed; Cambridge University Press.

BAKER, RJ and NELDER, JA (1978). The GLIM system; Release 3; Oxford. Numerical Algorithms Group.

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