CODING FORMS FOR SRC INDEXING

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Date Produced	Date Received	TSCA Section
09/12/88	05/15/97	8E

Submitting Organization
BAYER CORP

Contractor
BAYER AG - WUPPERTAL

Document Title	INITIAL SUBMISSION: ACUTE TOXICITY OF (2,3,5,6-TETRAFLUOROPHENYL)-METHYL-(1R-TRANS)-3-(2,2-DICHLORO-ETHENYL)-2, 2-DIMETHYLCYCLOPROPANE CARBOXYLATE W/TSCA COVER SHEET DATED 05/08/97
Chemical Category	(2,3,5,6-TETRAFLUOROPHENYL)-METHYL-(1R-TRANS)-3-(2,2-DICHLORO-

TSCA HEALTH & SAFETY STUDY COVER SHEET

TSCA CBI STATUS:

-CHECK IF THIS PAGE CONTAINS CONFIDENTIAL BUSINESS INFORMATION (CBI)

Clearly mark the confidential information with bracketing and check the box in the appropriate section (☐*Contains CBI*).
Submit a sanitized cover sheet with CBI deleted. Mark the sanitized copy, "Public Display Copy" in the heading.

1.0 SUBMISSION TYPE - *Contains CBI* 8EHQ-0597-14045

☐ 8(d) **X 8(e)** ☐ FYI ☐ 4 ☐ OTHER: Specify

X- Intial Submission -Follow-up Submission -Final Report Submission

Previous EPA Submission Number or Title if update or follow-up: Docket Number, if any: #

☐ continuation sheet attached

2.1 SUMMARY/ABSTRACT ATTACHED (may be required for 8(e): optional for §4, 8(d) & FYI)	**2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID**	**2.3 FOR EPA USE ONLY**
- YES X -NO	Cert# P 917006688 97-2-12(f)	STUDY 6 OF 6

3.0 CHEMICAL/TEST SUBSTANCE IDENTITY -*Contains CBI*

Reported Chemical Name (specify nomenclature if other than CAS name):

CAS#: N/A (2,3,5,6-tetrafluorophenyl)-methyl-(1R-trans)-3-(2,2-dichloroethenyl)-2,

Purity 94.5 % 2-dimethylcyclopropane carboxylate

☐ - Single Ingredient
X - Technical Active Ingredient
☐ -Mixture *Trade Name:* NAK 4455 *Common Name:*

8EHQ-97-14045

4.0 REPORT/STUDY TITLE - *Contains CBI*

NAK 4455 Technical - Study for Acute Intraperitoneal Toxicity to Rats, Report # 17139

☐ Continuation sheet attached

5.1 STUDY/TSCATS INDEXING TERMS

[CHECK ONE]

HEALTH EFFECTS (HE): X ENVIRONMENTAL EFFECTS (EE): ENVIRONMENTAL FATE (EF):

5.2 STUDY/TSCATS INDEXING TERMS (see instructions for 4 digit codes)

STUDY TYPE: ATOX	SUBJECT ORGANISM (HE, EE only): RATS	ROUTE OF EXPOSURE (HE only): INTP	VEHICLE OF EXPOSURE (HEonly)
Other:	*Other:*	*Other:*	*Other:*

6.0 REPORT/STUDY INFORMATION ☐*Contains CBI* ☐ Study is GLP

Laboratory Bayer AG -Wuppertal Report/Study Date: 9/12/88

Source of Data/Study Sponsor (if different than submitter) Bayer AG Number of pages 52

☐ continuation sheet attached

7.0 SUBMITTER INFORMATION ☐*Contains CBI*

Submitter: Donald W. Lamb, Ph.D Title: V. P., Prod. Safety & Reg. Affrs Phone: 412-777-7431

Company Name: Bayer Corporation Company Address: 100 Bayer Road

Pittsburgh, PA 15205-9741 Submitter Address (if different):

Technical Contact: Donald W. Lamb, Ph.D Phone: (412)777-7431

☐ continuation sheet attached

8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS ☐*Contains CBI*

Substance is a developmental pyrethroid and the report indicates some impact on neurotoxicity.

Contains No CBI

☐ continuation sheet attached

Submitter Signature: Donald W Lamb **Date:** 5/8/97

EVEN PAGES WERE NOT SENT BY SUBMITTER

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BAYER AG
Fachbereich Toxikologie
(Toxicology Division)
Friedrich-Ebert-Str. 217 - 333
D-56 Wuppertal 1

Report no. 17139

Date 12.09.1988

NAK 4455 techn.

STUDY FOR ACUTE INTRAPERITONEAL TOXICITY TO RATS

by

Dr. F. Krötlinger

Study number: T 2025122

Until they are published, the findings contained in this report may only be used with the approval of BAYER AG. Further reproduction of all or part of this report is not permissible.

1. QUALITY ASSURANCE/GLP DECLARATIONS

Test substance: NAK 4455 techn.

Study no.: T 2025122

1.1. Quality assurance declaration

The study was inspected by Quality Assurance on the dates given below. The results of the checks and inspections are conveyed in writing to the study director and, if necessary, also the Head and Director of the Institute, or other persons affected.

Date of check/inspection	Date of issue of inspection report
25.03.1987	25.03.1987
25.03.1987	30.03.1987

The results of the study and the methods used have been correctly reported.

Quality Assurance
PH-AQ-S/GLP, Bayer AG

Date: 07.09.88 Responsible: (Dr. H. P. Schulz)

1.2. Study director's GLP declaration

The study conformed to the OECD principles of Good Laboratory Practice (GLP) of 4.2.1983, published in Bundesanzeiger No. 42a of 2.3.1983.

Dr. F. Krötlinger
(Study director) Date 11.04.1988

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3. SUMMARY

A study for acute intraperitoneal toxicity to the rat was conducted with the active ingredient NAK 4455 techn.

The test compound was formulated with polyethylene glycol E 400.

LD50 intraperitoneal

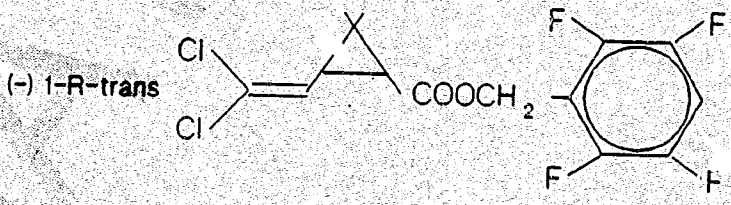
Rat male: 2413 (2022 - 2881) mg/kg bw
Rat female: 1496 (1340 - 1670) mg/kg bw

Assessment

The test compound proved to be slightly toxic to rats after acute intraperitoneal administration. The symptoms observed pointed to an action on the nervous system, as is familiar after dosage of pyrethroids of this class.

6. MATERIAL AND METHODS

6.1. Test compound

Test compound designation:	NAK 4455 technical active ingred.
Manufacturer:	Bayer AG
Batch no.:	130187
Purity:	94.5 % (analytical finding, APF of 27.01.87, see Appendix, page 52)
Approval:	until 27.07.1987
State of aggregation:	solid/liquid (melting point 50° C)
Appearance:	dark brown
pH	4.4 (2 % in water)
Storage:	in laboratory cabinet at 20.5° C to 24° C
Chemical name:	(2,3,5,6-tetrafluorophenyl)-methyl-(1R-trans)-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylate (CA)
Structural formula:	
Molar mass:	371.2 g/mol
Molecular formula:	$C_{15}H_{12}Cl_2F_4O_2$

6.3. Animal husbandry

6.3.1. Accommodation of animals

During the acclimatisation period the animals were conventionally kept in Makrolon(R) cages type III (five per cage/sex), and during the test period individually in Makrolon(R) cages type II (SPIEGEL, A., GÖNNERT, R., Zschr. Versuchstierkunde 1, 38, 1961, and MEISTER, G., Zschr. Versuchstierkunde 7, 144 - 153, 1965). The cages were replaced at least once a week with cages containing clean litter.

The litter used was low-dust wood granules (manufacturer: Bogner GmbH, Solingen-Ohligs). The granules were spot-checked for contaminants. The documentation on the results of the checks is filed at BAYER AG. The analytical results did not provide any indications of an effect on the objective of the study.

6.3.2. Rooms

All the animals in this study were in one room. Rats in other toxicological studies were temporarily kept in the same room. Adequate spatial separation and suitable organisation of procedures ensured that the animals were not confused. The animals were not treated in the room, but in a separate laboratory.

6.3.3. Cleaning, disinfection

The animal room was cleaned and disinfected once weekly. It was ensured that the food was not contaminated and there was no contact with the animals.

6.3.4. Climatic conditions

The room climate was set as follows.

Room temperature:	22° ± 2° C
Humidity (relative):	approx. 50 %
Light/dark rhythm:	12-hour, from 6 to 18 hrs CET artificial lighting
Air throughput:	approx. 10 times per hour

Occasional variations from this standard, for instance due to room cleaning, occurred. They had no apparent effect on the course of the study.

6.4.2. Grouping and identification of animals

All the animals were allocated to the treatment groups before administration with the aid of random number tables (van der Gulden, Dr. W.J.I. et al.: Versuchstiere und Versuchstechnik, Band II, 325-327, 1975). The animals were identified by individual marks using aqueous picric acid solution, and also by cage cards giving test compound, animal number, dose, sex and study number. Five animals were used per dose and sex.

6.4.3. Administration and dosage

The test compound was injected once into the abdominal cavities of male and female rats.

The volume administered was 5 ml/kg or 10 ml/kg body weight.

In addition to the test compound groups, a control group was also used, in which the animals were administered 5 ml/kg bw polyethylene glycol E 400.

6.4.4. Examinations

6.4.4.1. Clinical observation

Appearance and behaviour were recorded several times on the day of administration, and then at least once per day. If symptoms occurred, their type, duration and intensity were compiled as group findings. In the case of mortalities the time of death was registered. The times given refer to the administration day (first test day) at administration. For clearer presentation these times may be adjusted by five and ten minutes, and to quarter, half and full hours. The figures in days represent test days. If symptoms no longer occur after an observation-free period between two test days (e.g. overnight), it is assumed that they were present for the full previous test day. If symptoms occur for the first time after such an observation-free period, it is assumed that they were already present on the previous test day.

Similarly mortalities occurring in this observation-free period (e.g. overnight) are allocated to the previous test day.

6.4.4.2. Observation period

The observation period lasted fourteen days.

7. RESULTS

7.1. Acute intraperitoneal toxicity (rat)

7.1.1. Dose-effect table (LD50)

The results of the tests for acute intraperitoneal toxicity to the rat, stating the LD50, are compiled in the following Table 1. The graphs for the LD50 determination are shown on page 20 in the Appendix.

Table 1

Dosis (mg/kg Kgw.) / Dose (mg/kg b.w.)	Toxikol. Ergebnis* / Toxicol. results*	Symptomdauer / Duration of signs	Todeszeitpunkt / Time of death	Mortalitaet(%) / Mortality (%)
	Ratte/rat - ♂			
0.0	0/ 5/ 5	50´-1d	--	0
1.0	0/ 5/ 5	25´-1d	--	0
10.0	0/ 5/ 5	175´-1d	--	0
100.0	0/ 5/ 5	40´-2d	--	0
1000.0	0/ 5/ 5	55´-7d	--	0
1600.0	0/ 5/ 5	20´-5d	--	0
2000.0	1/ 5/ 5	50´-4d	2d	20
2500.0	4/ 5/ 5	20´-9d	1d-2d	80
3550.0	4/ 5/ 5	15´-5d	1d-2d	80
5000.0	5/ 5/ 5	20´-2d	1h30´-2d	100
5000.0 **	3/ 5/ 5	45´-4d	2h38´-4d	60

LD50 = 2413 mg/kg Kgw.
Vertrauensbereich (95%) = 2021.9 - 2880.9 mg/kg Kgw.
Steigung = 3.31

	Ratte/rat - ♀			
0.0	0/ 5/ 5	45´-1d	--	0
1.0	0/ 5/ 5	20´-1d	--	0
10.0	0/ 5/ 5	175´-4d	--	0
100.0	0/ 5/ 5	50´-2d	--	0
1000.0	0/ 5/ 5	55´-7d	--	0
1400.0	2/ 5/ 5	55´-8d	2d-6d	40
1600.0	3/ 5/ 5	45´-8d	1d-4d	60
1800.0	4/ 5/ 5	20´-7d	1d-3d	80
2000.0	5/ 5/ 5	50´-2d	2d	100
2500.0 **	5/ 5/ 5	15´-2d	2d	100

LD50 = 1496 mg/kg Kgw.
Vertrauensbereich (95%) = 1340.4 - 1669.7 mg/kg Kgw.
Steigung = 5.49

Vertrauensbereich - confidence range

7.1.4. Gross pathological findings

- Animals dying during observation: lung patchy, distended, in isolated cases up to dark red and with fluid in tissue; liver sometimes patchy; liver lobes adherent to each other and to diaphragm and other abdominal organs; whitish to yellowish deposits on all abdominal organs; in isolated cases spleen patchy, pale, covered with whitish skin; in isolated cases kidneys patchy; sometimes ulceroid foci in glandular stomach; yellowish brownish to almost black mucous contents in gastro-intestinal tract.

- Animals sacrificed at end of observation: liver swollen, liver lobes fused or adherent to each other and to abdominal wall and abdominal organs; spleen covered with whitish skin. These findings were also made for the controls, and are attributed to the local effect of the vehicle polyethylene glycol E 400.

The individual autopsy findings are listed in the Appendix on pages 37 to 49.

9. REFERENCES

BLISS, C.I.
The determination of the dosage-mortality curve from small numbers.
Q.J. Pharm. Pharmacol. 11, 192-216 (1938).

PAULUHN, J.
Über die computergestützte Abschätzung der LD50/LC50
BAYER AG, Bericht-Nr.: 11835 vom 18.5.1983
(unveröffentlicht).

ROSIELLO, A.P., J.M. ESSIGMANN und G.N. WOGAN
Rapid and accurate determination of the median lethal dose (LD50) and its error with small computer.
J. Tox. and Environ. Health 3, 797-809 (1977).

10. KEY TO ABBREVIATIONS

Kgw /bw	body weight
Nr./no.	number
Toxikol. Ergebnis/ toxicol. results	toxicological results
ip	intraperitoneal