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OPPT Document Control Office (DCO)
EPA East Room 6428
1201 Constitution Ave., N.W.
Washington DC, 20460
Attn: 8(d) Health and Safety Reporting Rule (Notification/Reporting)

Re : Submission of TSCA 8(d) Health and Safety Study reports – BASF Corporation

Dear 8(d) Coordinator:

In compliance with 40 CFR 716, BASF hereby submits requested Health and Safety Study reports for substances recently added to the list of subject chemicals (71 FR 47130).

This submission contains information for the following list of substances:

62-56-6	121-69-7	1738-25-6
83-41-0	127-68-4	3039-83-6
84-69-5	131-57-7	4316-73-8
96-22-0	137-20-2	61788-76-9
104-93-8	645-62-5	68188-18-1
110-18-9	939-97-9	68609-05-2
111-44-4	1111-78-0	68909-77-3

Should you have questions regarding this submission, please do not hesitate to contact me at 734-324-6593 or email kara.sparks@basf.com .

Sincerely,

BASF Corporation

Kara Sparks
Manager, North America
Product Regulatory Centre of Expertise

CONTAINS NO CBI

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302148

I U C L I D

D a t a S e t

Existing Chemical	ID: 62-56-6
CAS No.	62-56-6
EINECS Name	thiourea
EC No.	200-543-5
Molecular Weight	76.12 g/mol
Molecular Formula	C H4 N2 S

Producer Related Part

Company:	BASF AG
Creation date:	18-OCT-2006

Substance Related Part

Company:	BASF AG
Creation date:	18-OCT-2006

Memo:	master
Printing date:	17-JAN-2007
Revision date:	
Date of last Update:	**17-JAN-2007**
Number of Pages:	**22**
Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: TSCA 8d

1.0.1 Applicant and Company Information

-

1.0.2 Location of Production Site, Importer or Formulator

-

1.0.3 Identity of Recipients

-

1.0.4 Details on Category/Template

-

1.1.0 Substance Identification

-

1.1.1 General Substance Information

-

1.1.2 Spectra

-

1.2 Synonyms and Tradenames

-

1.3 Impurities

-

1.4 Additives

-

1.5 Total Quantity

-

1.6.1 Labelling

-

1.6.2 Classification

-

1.6.3 Packaging

-

1.7 Use Pattern

-

1.7.1 Detailed Use Pattern

-

1.7.2 Methods of Manufacture

-

1.8 Regulatory Measures

-

1.8.1 Occupational Exposure Limit Values

-

1.8.2 Acceptable Residues Levels

-

1.8.3 Water Pollution

-

1.8.4 Major Accident Hazards

-

1.8.5 Air Pollution

-

1.8.6 Listings e.g. Chemical Inventories

-

1.9.1 Degradation/Transformation Products

-

1.9.2 Components

-

1.10 Source of Exposure

-

1.11 Additional Remarks

-

1.12 Last Literature Search

-

1.13 Reviews

-

2.1 Melting Point

-

2.2 Boiling Point

-

2.3 Density

-

2.3.1 Granulometry

-

2.4 Vapour Pressure

-

2.5 Partition Coefficient

-

2.6.1 Solubility in different media

-

2.6.2 Surface Tension

-

2.7 Flash Point

-

2.8 Auto Flammability

-

2.9 Flammability

-

2.10 Explosive Properties

-

2.11 Oxidizing Properties

-

2.12 Dissociation Constant

-

2.13 Viscosity

-

2.14 Additional Remarks

-

3.1.1 Photodegradation

-

3.1.2 Stability in Water

-

3.1.3 Stability in Soil

-

3.2.1 Monitoring Data (Environment)

-

3.2.2 Field Studies

-

3.3.1 Transport between Environmental Compartments

-

3.3.2 Distribution

-

3.4 Mode of Degradation in Actual Use

-

3.5 Biodegradation

-

3.6 BOD5, COD or BOD5/COD Ratio

-

3.7 Bioaccumulation

-

3.8 Additional Remarks

-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no
NOEC: >= 500
LC0: >= 500
LC50: > 500
LC100: > 500
Limit Test: yes

Method: other
Year: 1980
GLP: no
Test substance: other TS

Method: The study was performed according to "Überprüfung der Durchführbarkeit von Prüfvorschriften und der Aussagekraft des ECHEMG, UBA-Guideline from March 1979, revised 06. Feb 1980.

Result: 48 h-LC50 of the positive control Kaliumdichormate: about 135 mg/L.

During the 48 h exposure to thiourea, mortalities were as follows:

Nominal test concentration (mg/L)	Cumulative mortalitiy (%) after x hours 1/4/24/48
Control	0/0/0/0
500.0	0/0/0/0

Sympotoms of intoxication:

Nominal test concentration (mg/L)	Symptoms of intoxication after x hours 1/4/24/48
Control	-/-/-/-
500.0	-/-/-/-

Definitions of Symptoms:
-: No symptoms
+: All fish dead

All results refer to nominal test concentrations of thiourea. No analytical dose-verification of the test item was carried out.

Behavior of the test item during the test:
No remarkable observations.

Test condition: Test fish: Brachydanio rerio

Supplier: Fa. Eggert, Aquarienhandel, 6700 Ludwigshafen/Rhein, Germany

Body length: 3.0 cm
Body weight: 0.22 g
Corpulence factor of the test fish batch: 0.82

Housing and adpation
Culture conditions: oil-free aerated and charcoal filtered tap water, flow-through system;
Water temperature: 23 +- 1 °C
Duration of housing: about 1 week
Mortality during the last 2 weeks of housing: not indicated
Mortality during the adaption period: not indicated
Medical treatment: none

Diet: "Tetramin" Hauptfutter

Test procedure:
Test water: reconstituted freshwater according to DIN 38412, Part II (draft); prepared from fully demineralised tap water (conductivity: max 10 micro MHO) by adding:
294.0 mg/L $CaCl_2 * 2 H_2O$
123.3 mg/L $MgSO_4 + 7 H_2O$
64.8 mg/L $NaHCO_3$
5.8 mg/L KCl

Continuous aeration with oil-free air

Test water ready for use:

total hardness:	2.5 mmol/L
Acid capacity:	0.8 mmol/L
Ratio Ca/Mg ions:	4 : 1
Ration Na/K ions:	10 : 1
pH:	7.8 +- 0.1

Volume of water: 5 L
No of animals per test concentration and control: 5
Loading rate (g fish/L test water): 0.22
Test vessels: All glass aquaria (30 x 22 x 24 cm)

Test temperature: 23 +- 1 °C
Adaption to test water and test temperature: 1 week
Photoperiod: 16 : 8 hours day-night regime
Aeration: slight
Exposure period: 48 h
pH during the test: 8.1 - 8.2
Oxygen content during the test: 8.4 - 8.9 mg/L
Withdrawal of food: 1 day before and during exposure.

Nominal test concentrations: 500 mg/L. In addition, a control was tested in parallel.

Observation time: 0, 4, 24 and 48 h.
Endpoints investigated: mortality and symptoms of intoxication.

Preparation of the test item:
The test solution was prepared by adding the test item to the test media without any pre-treatment. Then, the fish were placed into the test aquaria.

Statistical evaluation of data:
Probit analysis (Finney 1971); The EC50 value was calculated as the geometrical mean of the LC0 and the LC100 value.

Test substance: Thiourea; CAS 62-56-6; batch No.: no data; purity: p.A.; water solubility: soluble

Conclusion: The 48 h results of p-methylanisole to fish were as follows:
The LC0 and the NOEC were at least 500 mg/L (nominal).
The LC50 and the LC 100 were clearly above 500 mg/L was 68.2 mg/L (nominal).

Reliability: (2) valid with restrictions
Guideline study. Scientifically acceptable, however, test duration lasts 48 h only.

Flag: TSCA 8d
15-NOV-2006 (1)

Species: Leuciscus idus (Fish, fresh water)

Remark: Non-BASF Study.
Flag: TSCA 8d
15-NOV-2006 (2)

Remark: Non-BASF Study.
Flag: TSCA 8d
15-NOV-2006 (3)

4.2 Acute Toxicity to Aquatic Invertebrates

-

4.3 Toxicity to Aquatic Plants e.g. Algae

-

4.4 Toxicity to Microorganisms e.g. Bacteria

-

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Sediment Dwelling Organisms

-

4.6.2 Toxicity to Terrestrial Plants

-

4.6.3 Toxicity to Soil Dwelling Organisms

-

4.6.4 Toxicity to other Non-Mamm. Terrestrial Species

-

4.7 Biological Effects Monitoring

-

4.8 Biotransformation and Kinetics

-

4.9 Additional Remarks

-

5.0 Toxicokinetics, Metabolism and Distribution

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat

Remark: non BASF study
Flag: TSCA 8d
22-NOV-2006 (4)

Type: LD50
Species: rat

Remark: non BASF study
Flag: TSCA 8d
22-NOV-2006 (5)

Type: LD50
Species: rat

Remark: non BASF study
Flag: TSCA 8d
22-NOV-2006 (6)

Type: LD50
Species: rat

Remark: non BASF study
Flag: TSCA 8d
22-NOV-2006 (7)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat

Remark: non BASF study
Flag: TSCA 8d
17-JAN-2007 (8)

Type: LC50
Species: rat

Remark: non BASF study
Flag: TSCA 8d
17-JAN-2007 (9)

5.1.3 Acute Dermal Toxicity

Type: LD50
Sex: female

Remark: non BASF study
Flag: TSCA 8d
17-JAN-2007 (10)

5.1.4 Acute Toxicity, other Routes

-

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

-

5.2.2 Eye Irritation

-

5.3 Sensitization

-

5.4 Repeated Dose Toxicity

Type: Sub-acute
Species: rabbit **Sex:**

Remark: non BASF study
Flag: TSCA 8d
22-NOV-2006 (11)

Type: Sub-acute
Species: rabbit **Sex:**

Remark: non BASF study
Flag: TSCA 8d
17-JAN-2007 (12)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA1535, TA100, TA1537, TA98
Concentration: 3.15; 10, 31.5; 100; 315; 1000; 3000 ug/plate
Cytotoxic Concentration: no
Metabolic activation: with and without
Result: negative

Method: other: Ames et al. 1975
Year: 1979
GLP: no
Test substance: other TS: Thiourea

Method: Ames test, with and without metabolic activation. Standard plate test.
Result: No increase in the number of revertants was noted with TS in any of the tests. In contrast, positive control substances caused increases in the number of revertants as expected, indicating proper test conditions.
Test condition: Bacterial test strains were used in the standard pate test (SPT) in the presence and in the absence of metabolic activation (+S9,-S9, respectively). DMSO was used as solvent. 2 test plates per dose or per control were run in each of the two experiments (second experiment was performed only with TA 100 and without S-9 mix).
Positive controls were included by using 2-aminoanthracenein, Benzo(a)pyrene, 3-Methylcholanthrene incubations without S9, and N-methyl-N'-nitro-N-nitrosoguanidine,
Benzo(a)pyrene-4,5-oxide in incubations with S9.
Test substance: Thiourea, putity: 99%
Conclusion: No mutagenicity was seen with bacterial test strains specific for base substitution and frame shift mutation in the Ames test both with and without metabolic activation
Reliability: (2) valid with restrictions
Only 2 plates/dose and strain were used and only one experiment was performed
No GLP, no guideline study
Flag: TSCA 8d
22-NOV-2006 (13)

Type: Ames test

Remark: non BASF study
Flag: TSCA 8d
17-JAN-2007 (14)

Type: Sister chromatid exchange assay

Remark: non BASF study
Flag: TSCA 8d
17-JAN-2007 (15)

5.6 Genetic Toxicity 'in Vivo'

Type: Micronucleus assay

Remark: non BASF study
Flag: TSCA 8d
22-NOV-2006 (16)

Type: other: genotoxicity and metabolism

Remark: non BASF study
Flag: TSCA 8d
22-NOV-2006 (17)

5.7 Carcinogenicity

-

5.8.1 Toxicity to Fertility

-

5.8.2 Developmental Toxicity/Teratogenicity

-

5.8.3 Toxicity to Reproduction, Other Studies

-

5.9 Specific Investigations

-

5.10 Exposure Experience

-

5.11 Additional Remarks

6.1 Analytical Methods

-

6.2 Detection and Identification

-

7.1 Function

-

7.2 Effects on Organisms to be Controlled

-

7.3 Organisms to be Protected

-

7.4 User

-

7.5 Resistance

-

8.1 Methods Handling and Storing

-

8.2 Fire Guidance

-

8.3 Emergency Measures

-

8.4 Possib. of Rendering Subst. Harmless

-

8.5 Waste Management

-

8.6 Side-effects Detection

-

8.7 Substance Registered as Dangerous for Ground Water

-

8.8 Reactivity Towards Container Material

-

(1) BASF AG (1980). Thioharnstoff: Acute toxicity to fish, zebra fish (Brachydanio rerio Hamm & Buch). Department of Toxicology, unpublished data, Report No. 80/250, 03 Nov 1980.

(2) SKW Werk Trostberg (1977). Thioharnstoff. Acute toxicity to fish, Golden orfe (Leuciscus idus, L., golden variety). 09 Nov 1977.

(3) SKW Werk Trostberg (1977). Thioharnstoff. Acute toxicity to fish, Guppy (Poecilia reticulata, Peters). 09 Nov 1977.

(4) Sueddeutsche Kalkstickstoffwerke AG, Trostberg, Germany, accomplished by TNO Zeist, Netherlands, 29. Dec. 1975, Determination of the acute oral toxicity of thiourea in rats

(5) Sueddeutsche Kalkstickstoffwerke AG, Trostberg, Germany, accomplished by TNO Zeist, Netherlands, 09. Nov.1982, Determination of the acute oral toxicity of thiourea in rats B82.0060/47

(6) Sueddeutsche Kalkstickstoffwerke AG, Trostberg, Germany, accomplished by TNO Zeist, Netherlands, Sep 80, Short term oral toxicity study with thiourea in rats R 6603

(7) Sueddeutsche Kalkstickstoffwerke AG, Trostberg, Germany, accomplished by TNO Zeist, Netherlands, 11 Sep 79, Short term oral toxicity study with thiourea in rats R 6174

(8) Sueddeutsche Kalkstickstoffwerke AG, Trostberg, Germany, accomplished by TNO Zeist, Netherlands, 18 Nov 77, Acute inhalation toxicity study with Thioharnstoff in rats, Report No. R5535

(9) Sueddeutsche Kalkstickstoffwerke AG, Trostberg, Germany, accomplished by TNO Zeist, Netherlands, 31 Oct.79. Acute inhalation toxicity study of a 10% aqueous solution of "Thioharnstoff" with rats.

(10) Sueddeutsche Kalkstickstoffwerke AG, Trostberg, Germany, accomplished by TNO Zeist, Netherlands, 1 May 78, Acute dermal toxicity study with the product "Thioharnstoff" in albino rabbits Report R 5693

(11) Sueddeutsche Kalkstickstoffwerke AG, Trostberg, Germany, accomplished by TNO Zeist, Netherlands, Nov 1979, tudy on the percutaneous absorption of toxicity by the rabbit R6259

(12) Sueddeutsche Kalkstickstoffwerke AG, Trostberg, Germany, accomplished by TNO Zeist, Netherlands, 1 Feb 1980, Study on the percutaneous absorption of toxicity by the rabbit II R6369

(13) BASF AG, Department of toxicology, Ames Test for Thiourea, unpublished report no 77/79. 30 May 1978

(14) Litton Bionics 1977, National Cancer Institut, Bethesda. 12. April 1977. Plate assay for mutagenesis and DNA repair draft report.

(15) Central Institut for Food and Nutrition Research , accomplished by TNO Zeist, Netherlands, 08.Dec.1978. An investigation into the sister chromatid exchange induction in Chinese hamster ovary cells by a sample of Thioharnstoff

(16) Sueddeutsche Kalkstickstoffwerke AG, Trostberg, Germany, accomplished by TNO Zeist, Netherlands, 1979, Evaluation of "Kalkstickstoff" and "Thioharnstoff" in the Micronucleus test R6012

(17) Untersuchungen zum Mechanismus und zur Bedeutung der Genotoxizität von Thioharnstoff in Säugetierzellen in vitro und in vivo. BG Chemie Heidelberg, Germany, 1999 accomplished by GSF Forschungszentrum

10.1 End Point Summary

10.2 Hazard Summary

10.3 Risk Assessment

CAS Number	Product Name	Study Title	Report Date	Laboratory	Comment	Study Report attached?	Report No
62-56-6	Thiourea	Determination of the acute oral toxicity of thiourea in rats B82 0060/47	09-Nov-82	SKW Trostberg,, TNO	Non-BASF report	no	
62-56-6	Thiourea	Short term oral toxicity study with thiourea in rats R 6174	11-Sep-79	SKW Trostberg,, TNO	Non-BASF report	no	
62-56-6	Thiourea	Short term oral toxicity study with thiourea in rats R 6603	01-Sep-80	SKW Trostberg,, TNO	Non-BASF report	no	
62-56-6	Thiourea	Determination of the acute oral toxicity of thiourea in rats	29-Dec-75	SKW Trostberg,, TNO	Non-BASF report	no	
62-56-6	Thiourea	Acute inhalative toxicity study to rats Report 6264	18-Nov-77	SKW Trostberg, TNO	Non-BASF report	no	
62-56-6	Thiourea	Acute inhalative toxicity study of 10% aqueus solution of Thioharnstoff with rats R6264	31-Oct-79	SKW Trostberg, TNO	Non-BASF report	no	
62-56-6	Thiourea	Acute dermal toxicity study with the product "Thioharnstoff" in albino rabbits Report R 5693	01-May-78	SKW Trostberg, TNO	Non-BASF report	no	
62-56-6	Thiourea	An investigation into the sister chromatid exchanges induction in chinese hamster ovary cells by a sample of Thioharnstoff CL/78/120	08-Dec-78	SKW Trostberg, TNO	Non-BASF report	no	
62-56-6	Thiourea	Evaluation of "Kalkstickstoff" and "Thioharnstoff" in the Micronucleus test R6012	01-Feb-79	SKW Trostberg, TNO	Non-BASF report	no	
62-56-6	Thiourea	Study on the percutaneous absorption of toxicity by the rabbit R6259	01-Nov-79	SKW Trostberg, TNO	Non-BASF report	no	
62-56-6	Thiourea	Study on the percutaneous absorption of toxicity by the rabbit II R6369	01-Feb-80	SKW Trostberg, TNO	Non-BASF report	no	
62-56-6	Thiourea	Mechanismus undUntersuchungen zum Mechanismus und zur Bedeutung der Genotoxizität von Thioharnstoff in Saugetierzellen in vitro und in vivo.	22-Nov-99	BG Chemie Heidelberg, Germany, 1999	Non-BASF report	no	
62-56-6	Thiourea	Ames Test for Thiourea 77/79	30-May-78	BASF	BASF	yes	1.1
62-56-6	Thiourea	Plate assay for mutagenesis and DNA repair draft report	12-Apr-77	NTP, Litton bionics	Non-BASF report	no	
62-56-6	Thiourea	Thioharnstoff. Acute toxicity to fish, zebra fish (Brachydanio rerio Hamm & Buch)	03-Nov-80	BASF	BASF	yes	1.2
62-56-6	Thiourea	Thioharnstoff. Acute toxicity to fish, Hongkong Guppy (Poecilia reticulata)	09-Nov-80	SKW Trostberg	Non-BASF report	no	
62-56-6	Thiourea	Thioharnstoff. Acute toxicity to fish, Golden orfe (Leuciscus idus, L., golden variety)	09-Nov-80	SKW Trostberg	Non-BASF report	no	

1.1

Franz Oesch, Ph. D.
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Phone (06131) 19 31 76, 19 31 83, 19 31 72

77/79

Vertraulich

AMES TEST

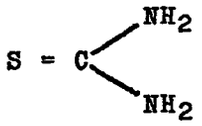
FOR

THIOUREA

Dieser Bericht ist Eigentum der BASF
und darf nur mit deren ausdrücklicher Genehmigung
weitergegeben, vervielfältigt oder veröffentlicht werden

Common name: -

Chemical name: Thiourea

Chemical structure: 

Number of compound: 77/79

Degree of purity: 99 %

INTRODUCTION

The Ames test (1,2) is a short term test for the detection of carcinogens using mutagenicity in bacteria as endpoint. The test considers mammalian metabolism by the use of liver homogenate. A high, but not complete qualitative correlation was found between carcinogenicity and mutagenicity in the Ames test. McCann and Ames (3) found that 90 % of 175 tested carcinogens were mutagenic and 87 % of 94 "non-carcinogens" were not mutagenic. A similar correlation was observed in a study by ICI (4): 91 % of the "known animal or human carcinogens" were positive, 93 % of the "putative non-carcinogens" were negative in the Ames test.

In the Ames test the effect of the test compound is investigated upon the number of backmutations in a battery of histidine auxotrophic Salmonella typhimurium mutants to histidine prototrophy (2,5,6). The strains TA 100 and TA 1535 are derived from prototrophic bacteria by substitution mutations, the strains TA 1537 and TA 98 by frameshift mutations. All four strains lack the DNA excision repair system (uvrB) and show a strong reduction in the hydrophilic polysaccaride layer (rfa), which facilitates the penetration of lipophilic compounds into the bacteria. TA 98 and TA 100 possess a modified post-replication DNA repair system which increases the rate of mutations by error prone repair (6).

Since most carcinogens are not carcinogenic themselves, but only after metabolism (7), the compounds are tested in the Ames test not only directly, but also in the presence of a mammalian metabolizing system. 10,000 g supernatant of liver homogenate from rats treated with Aroclor 1254, and a NADPH generating system were shown to be very favourable for activation (2). The liver represents the most important organ for metabolism of foreign compounds and several drug metabolizing enzymes are induced by Aroclor (8).

In this screening test mutagenicity was studied with S. typhimurium strains TA 98, TA 100, TA 1537 and TA 1535. The compounds were tested in the presence and absence of an activating system. An epoxide hydratase inhibitor and glutathione depleting agent was also used in some experiments.

MATERIAL AND METHODS

Chemicals

The test compounds were stored at 4°C in the dark and dissolved in dimethylsulfoxide (DMSO) or water on the day of the mutagenicity experiment.

Tissue preparations

Male Sprague Dawley rats (200-300 g) received a single intraperitoneal injection of Aroclor 1254 (500 mg/kg body weight; Aroclor was diluted with sun flower oil 1:5 v/v) 6 days before sacrifice. The liver was homogenized in three volumes of sterile, cold KCl (150 mM, buffered with Na phosphate at pH 7.4). The homogenate was centrifuged at 10,000 g for 10 minutes. One volume of the resulting supernatant was mixed with one volume 24 mM $MgCl_2$-100 mM KCl and one volume 12 mM NADP-15 mM glucose-6-phosphate-150 mM Na phosphate pH 7.4.

This preparation is termed S-9 Mix. For all experiments fresh tissue preparations were used from animals which were sacrificed on the day of the experiment.

Bacteria

Bacteria were grown over night in nutrient broth (8 g Bacto Nutrient Broth (DIFCO) + 5 g NaCl/liter). For inoculation stock cultures which were stored at -70°C were used. Before the experiment, bacteria were centrifuged and resuspended in resuspension medium (1.6 g Bacto Nutrient Broth + 5 g NaCl/liter) and adjusted to a titer of $1.7 * 10^9$ bacteria (colony forming units) per milliliter determined by nephelometry.

Mutagenicity experiments

The mutagenicity experiments were performed as described by Ames (2) with minor modifications. The test compound, 500 µl S-9 Mix (or 500 µl 150 mM KCl), 100 µl of the bacterial culture, and 2000 µl top agar (0.55 % agar, 0.55 % NaCl, 50 µM histidine, 50 µM biotin, 25 mM Na phosphate pH 7.4, 45°C) were mixed in a test tube and poured onto a petridish with minimal agar (1.5 % agar, Vogel-Bonner E medium (13) with 2 % glucose). After incubation for 2-3 days in the dark, colonies (his^+ revertants) were counted. The person who performed the counting did not know the specifications of the plates.

Every single experiment contained several different positive controls for checking the activity of the metabolizing system and the mutability of the bacteria as well as negative controls in the form of sterility controls and solvent blanks.

RESULTS AND DISCUSSION

Controls

In the experiments for direct mutagenicity N-methyl-N'-nitro-N-nitrosoguanidine and benzo(a)pyrene 4,5-oxide were used as positive controls, in the experiments with an activating system 3-methylcholanthrene, benzo(a)pyrene and 2-aminoanthracene. All these compounds were strongly mutagenic in our experiments. The mutagenic effects of the positive controls and the numbers of spontaneous revertant colonies per plate were similar to those described by Ames's group (3,5,6).

Thiourea

Thiourea was tested for mutagenicity with Salmonella typhimurium TA 1535, TA 100, TA 1537 and TA 98. Five different concentrations from 100 to 10000 µg per plate were used in the experiments for direct mutagenicity. In the experiments with S-9 Mix seven concentrations from 3.15 to 3000 µg per plate were tested.
The test compound was dissolved under all these conditions and we did not observe any signs of toxicity such as a reduced his^- background lawn.
Therefore the compound could be tested adequadely up to very high doses. But no mutagenicity was observed under all conditions.

Mainz, May 30, 1978

F. Oesch

Prof. Dr. F. Oesch

AMES TEST for Thiourea (purity ≥99 %)

SUMMARIZED RESULTS:
No mutagenicity was observed with thiourea under all experimental conditions.

WITH S-9 MIX (from liver homogenate of Aroclor 1254 treated rats)

Dose (µg/plate)	Solvent (µl DMSO)	TA 1535	TA 100 Experiment 1	TA 100 Experiment 2	TA 1537	TA 98
0	10	9 12	155 137	155 152	16 15	38 37
0	10	21 11	134 137	168 157	15 12	41 38
3.15	10	26 21	155 -	154 145	11 14	48 34
10	10	24 15	158 -	163 158	13 15	36 39
31.5	10	17 14	149 -	155 170	15 11	45 38
100	10	9 11	168 -	152 157	12 11	47 49
315	10	16 17	138 -	149 166	13 10	36 32
1000	10	11 15	131 -	133 150	16 12	41 29
3000	30	17 9	145 -	140 139	15 12	30 34
10 Benzo(a)pyrene	10	56 49	1490 -	2130 3110	158 137	1140 850
10 2-Aminoanthracene	10	1340 1120	5300 -	4700 4900	176 67	4120 3570
90 3-Methylcholanthrene	30	23 13	5700 -	4800 4300	69 75	1050 -

WITHOUT S-9 MIX

Dose (µg/plate)	Solvent (µl DMSO)	TA 1535	TA 100	TA 1537	TA 98
0	10	23 25	133 115	11 10	23 27
0	10	27 29	126 101	8 10	19 25
100	10	24 28	114 108	7 9	26 27
315	10	26 24	105 140	6 8	25 29
1000	10	22 19	122 129	7 7	20 22
3000	30	27 25	128 110	11 7	26 15
10000	100	29 18	102 116	- 5	20 28
1 Benzo(a)pyrene 4,5-oxide	10	25 21	1980 2250	505 627	3010 3310
10 N-Methyl-N'-nitro-N-nitrosoguanidine	10	36000 33000	65000 63000	98 137	82 67

The compounds were tested for mutagenicity as described by Ames et al. (Mut. Res. 31 (1975) 347-364) with only minimal modifications (see "Materials and Methods"). The tables show the number of his^+ revertant colonies of individual plates.

DMSO: Dimethylsulfoxide.

REFERENCES

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Thioharnstoff - Oertraulich

1.2.

80/250 BLATT 1

ZEBRABAERBLING (BRACHYDANIO RERIO HAM.U.BUCH.)

B A S F
AKTIENGESELLSCHAFT
GEWERBEHYGIENE
UND TOXIKOLOGIE
20.10.1980

BERICHT UEBER DIE PRUEFUNG DER AKUTEN TOXIZITAET

SUBSTANZBEZEICHNUNG : THIOHARNSTOFF
(MERCK BEST. NR. 7979)

TIERART : ZEBRABAERBLING (BRACHYDANIO RERIO HAM.U.BUCH.)

SUBSTANZ Nr.: 80/250
AUFTRAG VOM : UBA-RINGTEST 1980

STRUKTURFORMEL : $H_2N-\underset{\underset{S}{\|}}{C}-NH_2$

REINHEITSGRAD : P.A.

LOESLICHKEIT DER REINEN AKTIVSUBSTANZ IN WASSER BEI 20 GRD.C.:

LOESLICH

ZUSAMMENFASSUNG UND BEURTEILUNG :

DIE LC50 NACH

1H	GROESSER	500	(MG/L)	(1 % SIGNIFIKANZLEVEL)
4H	GROESSER	500	(MG/L)	(1 % SIGNIFIKANZLEVEL)
24H	GROESSER	500	(MG/L)	(1 % SIGNIFIKANZLEVEL)
48H	GROESSER	500	(MG/L)	(1 % SIGNIFIKANZLEVEL)

SYMPTOMATIK : KEINE AUFFAELLIGKEITEN

HOECHSTE DOSIS OHNE BEOBACHTETE WIRKUNG : 500 MG/L

Gelbke 13.8. Munk, 03.11.80

DR.MED.HABIL.DR.RER.NAT. H.-P.GELBKE DR.RER.NAT. R.MUNK
VERSUCHSDURCHFUEHRUNG

Dieser Bericht ist Eigentum der BASF
und darf nur mit deren ausdrücklicher Genehmigung
weitergegeben, vervielfältigt oder veröffentlicht werden

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GEWERBEHYGIENE
UND TOXIKOLOGIE
20.10.1980

METHODE : "UEBERPRUEFUNG DER DURCHFUEHRBARKEIT VON PRUEFUNGSVORSCHRIFTEN UND DER AUSSAGEKRAFT DES ECHEMG" NACH UBA-RICHTLINIE VOM MAERZ 79 UND ERGAENZUNGEN VOM 6.2.80
DAS PRODUKT WURDE OHNE VORBEHANDLUNG IN DAS TESTWASSER GEGEBEN.
SCHWACHE BELUEFTUNG DER TESTBECKEN.

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AKTIENGESELLSCHAFT
GEWERBEHYGIENE
UND TOXIKOLOGIE
20.10.1980

TIERART : ZEBRABAERBLING (BRACHYDANIO RERIO HAM.U.BUCH.)

LIEFERANT : FA. EGGERT, AQUARIENHANDEL
6700 LUDWIGSHAFEN/RH., BRD

ZUECHTER : FA. WHITE CRANE
BANKOG, THAILAND

LIEFERUNG VOM : 10.07.1980

KOERPERGEWICHT : 0.22 G

KOERPERLAENGE : 3.0 CM

KORPULENZFAKTOR DER LIEFERUNG : * 0.82

HAELTERUNG : DIE HAELTERUNG ERFOLGT IN UEBER AKTIVKOHLE GEREINIGTEM UND ENTCHLORTEM LEITUNGSWASSER IM KONTINUIERLICHEN DURCHFLUSS BEI DURCHLUEFTUNG MIT OELFREIER LUFT.

WASSERTEMPERATUR : 23 GRD.C. +-1

SAUERSTOFFGEHALT : > 6 MG/L

PH-WERT : 7 - 8

	MVAL/L	MMOL/L	GRD.DH
GESAMTHAERTE :	2.6-5.2	1.3-2.6	7-14.6
KARBONATHAERTE :	2.6-5.2	1.3-2.6	7-14.6
NICHTKARBONATHAERTE :	-	-	-

FUTTER : 'TETRAMIN' ALLEINFUTTER FUER ZIERFISCHE
TETRA-WERKE,D452 MELLE, BRD

MEDIZINISCHE BEHANDLUNG WAEHREND DER HAELTERUNG :
KEINE

* DER KORPULENZFAKTOR K WIRD AUS DEM GEWICHT G (G) UND DER LAENGE L (CM), GEMESSEN VON DER MAULSPITZE BIS ZUM ENDE DER SCHWANZFLOSSE, NACH DER FORMEL K=100*G/L**3 BERECHNET.

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TESTWASSER : SYNTH. SUESSWASSER NACH DIN-ENTWURF 38 412, TEIL 11
HERSTELLUNG AUS GEREINIGTEM, CHLORFREIEM LEITUNGSWASSER
DEMINERALISIERUNG UEBER VOLLENTSALZUNGSPATRONE
'AQUADEM' TYP 42 DF DER FIRMA WTA, KOELN.

DIE AUFSALZUNG ERFOLGT DURCH ZUGABE VON

294.0 MG/L CACL2 . 2H2O
123.3 MG/L MGSO4 . 7H2O
64.8 MG/L NAHCO3
5.8 MG/L KCL

DIE AUFSALZUNG ERFOLGT AUS STAMMLOESUNGEN

TESTWASSER 24 STD. BELUEFTEN UND AUF PH 7.8+-0.1
EINSTELLEN.
GEBRAUCHSFERTIGES TESTWASSER:

GESAMTHAERTE	:	2.5 MMOL/L
KARBONATHAERTE	:	0.8 MMOL/L
VERHAELTNIS CA- ZU MG-IONEN	:	4 : 1
VERHAELTNIS NA- ZU K-IONEN	:	10 : 1

WASSERMENGE : 5 LITER IN GLASAQUARIEN (30 CM * 22 CM * 24 CM)
(FUER 5 FISCHE)

TESTTEMPERATUR : 23 GRD.C. +-1

ADAPTATIONSZEIT : 1 WOCHE

UNTERSUCHUNGEN : BESTIMMUNG DER MORTALITAET
NACH STUNDEN : 1 4 24 48

BESTIMMUNG BZW. BERECHNUNG DER MITTLEREN LETALEN
KONZENTRATION (LC50), DER LC5 UND DER LC95
MIT PROBITANALYSE**
NACH STUNDEN : 1 4 24 48

VERSUCHSBEGINN : 16.07.1980

** FINNEY, D.J., PROBIT ANALYSIS, CAMBRIDGE UNIVERSITY PRESS,
3. AUFL., 1971

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KALIUMDICHROMAT-POSITIVKONTROLLE LC 50:CA. 135 MG/L (48-STD.-WERT)

ANLAGE BLATT 6 : MORTALITAET
SYMPTOME
PH-WERT UND SAUERSTOFFGEHALT
7 : STATISTIK MORTALITAET 1H
8 " " 4H
9 " " 24H
10 " " 48H

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KONZ. (MG/L)	ANZAHL FISCHE BEGINN	TOTE FISCHE NACH 1H	4H	24H	48H
500	5	0	0	0	0
500	5	0	0	0	0
0	5	0	0	0	0
0	5	0	0	0	0

SYMPTOMATIK : KEINE AUFFAELLIGKEITEN

KONZ. (MG/L)	PH-WERT VERSUCHS BEGINN	24H	48H	SAUERSTOFFGEHALT(MG/L) VERSUCHS BEGINN	24H	48H
500	8.2	8.2	8.2	8.4	8.7	8.9
500	8.2	8.2	8.2	8.7	8.8	8.9
0	8.1	8.1	8.1	8.8	8.8	8.9
0	8.1	8.1	8.1	8.8	8.8	8.9

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FISCHTOX : ZEITPUNKT 1H

KONZENTRATION (MG/L)	ANZAHL FISCHE BEGINN	TOTE FISCHE NACH 1H	MORTALITAET (%)	KONZENTRATION VERWENDET
500	10	0	0.	*

LC50-WERT > 500 (1 % SIGNIFIKANZLEVEL)

ZEBRABAERBLING (BRACHYDANIO RERIO HAM.U.BUCH.)

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20.10.1980

FISCHTOX : ZEITPUNKT 4H

KONZENTRATION (MG/L)	ANZAHL FISCHE BEGINN	TOTE FISCHE NACH 4H	MORTALITAET (%)	KONZENTRATION VERWENDET
500	10	0	0.	*

LC50-WERT > 500 (1 % SIGNIFIKANZLEVEL)

ZEBRABAERBLING (BRACHYDANIO RERIO HAM.U.BUCH.)

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FISCHTOX : ZEITPUNKT 24H

KONZENTRATION (MG/L)	ANZAHL FISCHE BEGINN	TOTE FISCHE NACH 24H	MORTALITAET (%)	KONZENTRATION VERWENDET
500	10	0	0.	*

LC50-WERT > 500 (1 % SIGNIFIKANZLEVEL)

ZEBRABAERBLING (BRACHYDANIO RERIO HAM.U.BUCH.)

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UND TOXIKOLOGIE
20.10.1980

FISCHTOX : ZEITPUNKT 48H

KONZENTRATION (MG/L)	ANZAHL FISCHE BEGINN	TOTE FISCHE NACH 48H	MORTALITAET (%)	KONZENTRATION VERWENDET
500	10	0	0.	*

LC50-WERT > 500 (1 % SIGNIFIKANZLEVEL)