

Ciba Specialty Chemicals Corporation
USA

Additives

8EHQ-1498-14319

RECEIVED
OPPT/CBIC

98 NOV 20 AM 11:28



Ciba

Via Federal Express
Confidential

MR 12551

November 17, 1998

Document Control Office (7407)
Room G99 East Tower
Attention: Section 8(e)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street, SW
Washington, DC 20460-0001



8EHQ-98-14319

Subject: TSCA 8(e) Notice - CG36-1573

Dear Section 8(e) Coordinator:

In accordance with EPA's March 16, 1978 Policy Statement on Section 8(e) reporting under the Toxic Substances Control Act (TSCA), the EPA's June, 1991 TSCA Section 8(e) Reporting Guide, Ciba Specialty Chemicals Corporation wishes to bring to the attention of the Environmental Protection Agency results observed in an oral dosage study conducted in Japan with sodium salt of 3-(2-hydroxy-3,5-dimethylphenyl)butanoic acid, called CG36-1573. CG36-1573 was detected in the liquid chromatographic analysis of the product generated in the biodegradation study by microorganisms for the parent compound, 2,4-Dimethyl-6-(1-methylpentadecyl)-phenol, also known as CGX AO 145.

We are enclosing a copy of the document entitled "Summary of Toxicological Studies for CG36-1573". This describes a subacute toxicity (28-day study) in rats and is the only information available in English. The substance produced histopathological and organ weight changes similar to the parent compound that was previously reported to the EPA as an 8(e). At the high dose (800 mg/kg), possible neurotoxic effects occurred as well.

Please call the undersigned if you have any questions concerning this submittal.

Respectfully,

Ciba Specialty Chemicals Corporation

Naeem Mady, Director,
Regulatory Compliance

D:\Mady\TSCA8(e)Notice.doc

Contains No CBI



88990000038

540 White Plains Road
P.O. Box 2005
Tarrytown, NY 10591-9005

Tel. 914 785 2000

98 DEC 28 PM 2:57

RECEIVED
OPPT/CBIC

Value beyond chemistry

Summary of Toxicological Studies
CG36-1573

Subacute toxicity (28-day-study)

Species/strain: Rat/Crj:CD(SD)

Route of administration: oral

Dosing vehicle: distilled water

Dose regime (5 or 7 days/week): 7 days/week

Number of animals, doses (concentrations) and group numbers:

Sex	Number of animals	Dose level
males	6	8, 40, 200, 800 mg/kg
females	6	8, 40, 200, 800 mg/kg

Results (in relation to dose levels/concentrations)

1) Clinical observations:

Decreased spontaneous locomotion was observed in both sexes of the 800 mg/kg. Decreased respiration rate, lacrimation, salivation, and staining and moist hair around the nose and mouth were observed in the females of the 800 mg/kg.

2) Laboratory findings:

Hematology data indicated decreases in hemoglobin conc. and hematocrit value in the males of the 800 mg/kg.

Biochemical examinations detected increases in GPT, total cholesterol and total protein levels in the males of the 200 mg/kg and above.

Albumin and calcium levels were increased in the males of the 800 mg/kg.

Increases in GPT and glucose levels, and a decrease in chloride level were noted in the females of the 800 mg/kg.

3) Effects on organs:

Absolute and relative liver weights were increased in both sexes of the 200 mg/kg and above.

Relative kidney weights were increased in the males of the 800 mg/kg.

Absolute and relative kidney weights were increased in the females of the 800 mg/kg.

Swelling of the liver was observed in the males of the 200 mg/kg and above, and in the females of the 800 mg/kg.

Elevation of the limiting ridge of the forestomach was observed in both sexes of the 800 mg/kg.

Centrilobular swelling of the hepatocytes, increased eosinophilic bodies in the kidney and focal hyperplasia of the squamous epithelium in the forestomach were observed in the males of the 200 mg/kg and above.

Centrilobular swelling of the hepatocytes and focal hyperplasia of the squamous epithelium in the forestomach were observed in the females of the 800 mg/kg.

Dose of concentration at which no toxic effects were observed: 40 mg/kg/day

Method: 28-day Repeated Dose Toxicity Study in Mammalian Species in Notification on Partial Revision of Testing Methods Relating to the New Chemical Substances (Notification No. 700 of the Planning and Coordination Bureau, EA, No. 1039 of the Pharmaceutical Affairs Bureau, MHW & No. 1014 of the Basic Industries Bureau, MITI, December 5, 1986) and Section 407, Repeated Dose Oral Toxicity-Rodent: 28-day or 14-day Study in the OECD Guidelines for Testing of Chemicals (May 12, 1981)

GLP Status: Concerning Testing Facilities Stipulated in Article 4 of the Order Prescribing the Items of the Test Related to the New Chemical Substances and of the Toxicity Investigations Related to the Designated Chemical Substances (Notification No. 39 of the Planning and Coordination Bureau, EA, No. 229 of the Pharmaceutical Affairs Bureau, MHW & No. 85 (1984) of the Basic Industries Bureau, MITI, March 31, 1984 Notification No. 233 of the Planning and Coordination Bureau, EA, No. 38 of the Pharmaceutical Affairs Bureau, MHW & No. 823 (1988) of the Basic Industries Bureau, MITI, revised on November 18, 1988) and OECD Principles of Good Laboratory Practice (May 12, 1981)

Body/responsible for test Performing Laboratory: Hita Research Laboratories,
Chemical Biotesting Center
Chemicals Inspection & Testing
Institute, Japan

Study director: Masakuni Sawaki, M.S., D.V.M.

Test period: from June 9, 1997 to January 9, 1998

Test on Biodegradability of 2,4-Dimethyl-6-(1-methylpentadecyl)phenol

(Abbreviation: CGX A0 145) by Microorganisms

Rep. No. G4-9623 · D122 · CP

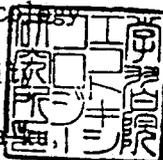
(December 10, 1996)

Institute of Ecotoxicology

Gakushuin University

1-5-1 Mejiro, Toshima

Tokyo, 171 Japan



T i t l e Test on biodegradability of 2,4-Dimethyl-6-(1-methyl
pentadecyl)phenol (Abbreviation: CGX A0 145) by micro-
organisms

S p o n s o r Ciba Specialty Chemicals Ltd.

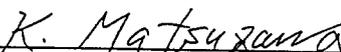
T e s t I n s t i t u t e

Name Institute of Ecotoxicology
Address 1-5-1 Mejiro, Toshima-ku, Tokyo, 171 Japan
Telephone +81 3 5992 1019
Director Prof. Dr. Tadayoshi Kan

T e s t P e r s o n n e l

Personnel engaged in
conduct of the study

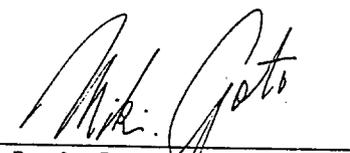

Aiko Suzuki


Kaori Matsuzawa

Study Director


Mitsuko Takamatsu

Quality Assurance Person

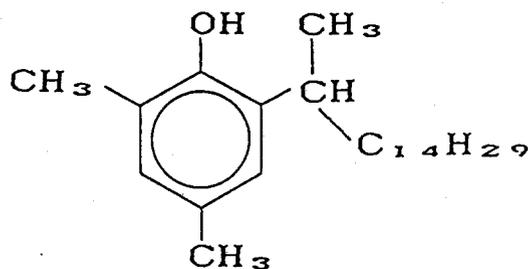

Prof. Dr. Mikiyasu Goto

1. Test Substance

Chemical name: 2,4-Dimethyl-6-(1-methylpentadecyl)phenol

Abbreviation: CGX AO 145 or TK13267(CG 27-145)

Structural formula:



Molecular formula: C₂₄H₄₂O (M.W. 346.59)

Purity: 98.05 %

2. Purpose

To acquire information on the biodegradability of 2,4-dimethyl-6-(1-methylpentadecyl)phenol by microorganisms

3. Outline of the test

The sludge was collected from different places in Japan, combined and cultivated for one month and then used for testing. The test substance (100mg ℓ⁻¹) was incubated with the sludge (30mg ℓ⁻¹) for 4 weeks at 25°C and the compound analyzed by HPLC. The oxygen consumption was also measured and the biodegradability determined.

4. Test method and conditions

4.1 Test method

The test was conducted in accordance with OECD Test Guidelines for Testing of Chemicals, "Ready Biodegradability: Modified MITI Test(I)" (No. 301C, adopted 12 May 1981).

4.2 Ready biodegradability

Percent degradation after 28 days was determined.

Reference substance: aniline

Start concentration of test substance: 100mg l^{-1}

Start concentration of sludge: 30mg l^{-1}

Incubation temperature: $25\text{ }^{\circ}\text{C}$

5. Test period

Initiated: October 17, 1996

Completed: December 10, 1996

6. Results

6.1 Percent biodegradability based on oxygen consumption

Test substance (CGX A0 145)		Reference substance (aniline)	
No. (day)	%	day	%
No.1 (28)	37	28	69
No.2 (28)	27	(7)	(52)
No.3 (28)	35		

6.2 Percent biodegradability based on HPLC analyses

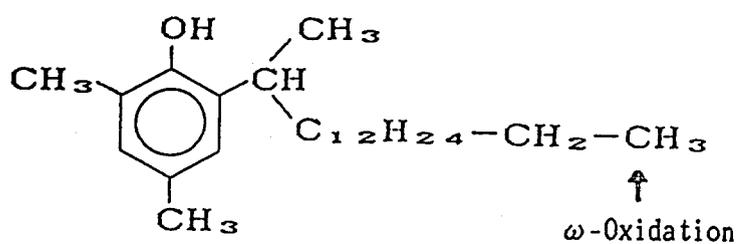
The concentrations of CGX A0 145 and its metabolite, 3-(2-hydroxy-3,5-dimethyl-phenyl)butanoic acid (5MPBA) in test mediums after 28 days were determined by HPLC. The biodegradation ratios of CGX A0 145 is shown in the Table below and the biodegradation pathway in the Figure (see, next page); the molar ratio (%) of the residual compounds are given in parentheses.

Degradation ratios of CGX A0 145	
No. (day)	%
No.1 (28)	94
No.2 (28)	80
No.3 (28)	91

7. Conclusion

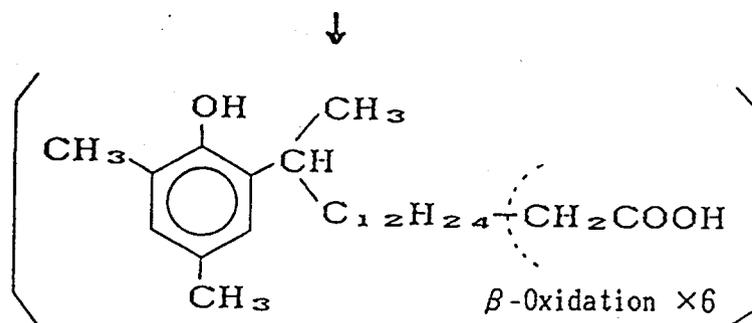
Test substance, CGX A0 145 was mostly biodegraded to 3-(2-hydroxy-3,5-dimethyl-phenyl)butanoic acid; no other metabolites were detected in the cultured medium.

BIODEGRADATION OF CGX AO 145 BY MICROORGANISMS

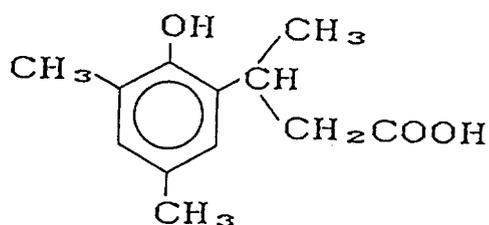


2,4-Dimethyl-6-(1-methylpentadecyl)phenol (Abbr. CGX AO 145)

5.7%, 20.2%, 8.9%



↓
↓



3-(2-Hydroxy-3,5-dimethylphenyl)butanoic acid (Abbr. 5MPBA)

93.5%, 78.2%, 90.5%