

CF98-1-6



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April 20, 1998

Office of the Secretary
Consumer Product Safety Commission
Washington, D.C. 20207

RE: Flame Retardant Chemicals

Dear Sir or Madame:

Enclosed please find written comments in support of the use of flame retardant chemicals that may be suitable for use in upholstered furniture. These comments cover two topics:

- Toxicology of DBDPO, HBCD and Saytex 8010: Three Brominated Flame Retardants Potentially used to Flame Retard Residential Upholstered Furniture in the United States
- and
- Smoke Toxicity and the Influence of Flame Retardants.

These comments supplement those filed by the Fire Retardant Chemicals Association (FRCA).

Sincerely,

Marcia L. Hardy, D.V.M., Ph.D.
Senior Toxicology Advisor
Albemarle Corporation

enclosures

OFFICE OF THE SECRETARY
APR 21 P 2 25

**TOXICOLOGY OF DBDPO, HBCD AND SAYTEX® 8010:
THREE BROMINATED FLAME RETARDANTS POTENTIALLY USED TO FLAME
RETARD RESIDENTIAL UPHOLSTERED FURNITURE IN THE UNITED STATES**

Marcia L. Hardy, D.V.M., Ph.D.
Albemarle Corporation
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INTRODUCTION

Brominated flame retardants (BFRs) are a structurally diverse group of compounds that include aromatic, phenolic, and cyclic compounds. Due to this structural diversity, BFRs major point in common is not their structure, but that of their use as flame retardants. Because of their structural variation, generalized statements regarding the potential health and environmental effects of the entire class of BFRs are inappropriate. BFRs included in this paper are the polybrominated diphenyl oxide, decabromodiphenyl oxide (DBDPO), the cyclic aliphatic, hexabromocyclododecane (HBCD), and a proprietary product of Albemarle Corporation, Saytex® 8010. All three of these flame retardants can be used to back coat textiles for use in upholstered furniture and thereby achieve the desired level of flame retardancy. DBDPO and HBCD flame retardants are currently being used in the United Kingdom for this purpose. In addition, DBDPO and HBCD are likely in use today throughout the United States to meet institutional, commercial and transportation fire safety standards, and in California to meet standards for residential furniture. Saytex 8010 is not currently used in these applications, but its properties allow potential use in textiles for upholstered furniture. This paper will address the toxicology and environmental properties of these three flame retardants, their bioavailability, and the potential for consumer exposure.

I. DECABROMODIPHENYL OXIDE (DBDPO)

A. Inherent Toxicology

1. Mammalian Toxicology

The DBDPO commercial product sold worldwide today is composed of $\geq 97\%$ DBDPO. DBDPO is a very large molecule with a molecular weight of approximately 959 g/m. DBDPO has undergone a wide range of toxicology tests in mammalian and aquatic species and its toxicology is well characterized (TABLE 1; summaries of unpublished studies attached) (*WHO EHC # 162, 1994, Geneva*). DBDPO is not acutely toxic to mammalian (*WHO EHC # 162, 1994, Geneva; Norris et al., 1974, J Fire Flamm Combust Toxicol*) or aquatic species (*MITI, 1992, Data of Existing Chemicals Based on the CSCL Japan; Walsh et al, 1987, Ecotoxicol Environ Saf, 14: 215-222*). DBDPO is not irritating to the skin or eye (*Norris et al., 1974, J Fire Flamm Combust Toxicol*), is not a skin sensitizer (*Norris et al., 1974, J Fire Flamm Combust Toxicol*), and does not induce chloracne (*Norris et al., 1974, J Fire Flamm Combust Toxicol*) or hepatic

enzymes (Carlson, 1980, *Toxicol Lett*, 5:19-25). The soot and char combustion products from a combusted high impact polystyrene/DBDPO/antimony trioxide matrix are also not acutely toxic and are not chloracnegenic (Pinkerton et al, 1989, *Chemosphere*, 18(1-6): 1243-1249). DBDPO is not a reproductive toxicant (Norris et al, 1975, *Environ Health Perspect*, 11: 153-161) and is not teratogenic (Norris et al, 1973, *Appl Polymer Symp*. 22: 195-219; Norris et al., 1974, *J Fire Flamm Combust Toxicol*, 1, 52-77; Norris et al, 1975, *Chem Hum Health Environ*, 1: 100-116).

DBDPO has a low degree of long-term toxicity that can be attributed to its poor absorption, rapid elimination and capacity to be metabolized (NTP, 1986, *Technical Report Series No. 309*; El Dareer et al., 1987, *J Toxicol Environ Health*, 22: 405-415). Pharmacokinetic studies have shown DBDPO has a very low bioavailability and is poorly absorbed from the gastrointestinal tract. Less than 1% of an orally administered dose was absorbed by the rat. DBDPO was rapidly eliminated (primarily in the feces) and its half life was less than 24 hours in the rat. Evidence for metabolism of DBDPO was found.

In repeated dose studies, DBDPO doses of 10% and 5% in the diet were well tolerated with no adverse effects by rats and mice for 14 and 90 days, respectively (NTP, 1986, *Technical Report Series No. 309*). Doses of 5% of the diet were tolerated for two years by rats and mice with no effect on body weight or mortality and only minimal evidence of organ effects (NTP, 1986, *Technical Report Series No. 309*). Two two year carcinogenicity bioassays have been conducted. The first, at a top dose level of 1 mg/kg in rats, produced no evidence of carcinogenicity (Kociba et, 1975, *Combust Toxicol*, 2: 267-285; Norris et al, 1975, *Chem Hum Health Environ*, 1: 100-116; Norris et al, 1975, *Toxicol Appl Pharmacol*, 33(1): 170). The second, conducted at 2.5 and 5% of the diet in rats and mice, produced no, equivocal and some evidence of carcinogenicity depending on genus and sex (NTP, 1986, *Technical Report Series No. 309*). DBDPO is not listed as a carcinogen by IARC, NTP or OSHA.

2. Environmental Toxicology

DBDPO has negligible water solubility (< 0.1 ug/L) and vapor pressure (4.63×10^{-6} Pa) (BFRIP, 1997, *Wildlife International Ltd studies*). DBDPO's measured octanol water partition coefficient is 6.265 (BFRIP, 1997, *Wildlife International Ltd study*). DBDPO did not bioconcentrate in fish when tested in a 6 week study (MITI, 1992, *Data of Existing Chemicals Based on the CSCL Japan, Tokyo*). An earlier study performed over 48 hours and comparing DBDPO's potential fish bioconcentration to that of octabromobiphenyl and tetrachlorobiphenyl found DBDPO and octabromobiphenyl did not bioconcentrate but that tetrachlorobiphenyl concentrated at least 50 times over the initial exposure levels within 4 hours (Norris et al., 1974, *J Fire Flamm Combust Toxicol*, 1, 52-77). DBDPO can undergo photodegradation (at a very slow rate). DBDPO aqueous photodegradation products are not lower brominated diphenyl oxides (Norris et al, 1973, *Appl Polymer Symp*. 22: 195-219; Norris et al., 1974, *J Fire Flamm Combust Toxicol*, 1, 52-77; Norris et al, 1975, *Chem Hum Health Environ*, 1: 100-116). Leaching from polymers is insignificant (Norris et al, 1973, *Appl Polymer Symp*. 22: 195-219; Norris et al., 1974, *J Fire Flamm Combust Toxicol*, 1, 52-77; Norris et al, 1975, *Chem Hum Health Environ*, 1: 100-116).

DBDPO is not widely distributed in the environment, and where found, is largely confined to sediments near point sources (WHO EHC # 162, 1994, Geneva). Due to its physical/chemical properties,

DBDPO is likely to be highly bound to sediment which will limit its bioavailability. DBDPO is unlikely to be toxic to or accumulated by sediment-dwelling species (*WHO EHC # 162, 1994, Geneva*). DBDPO is not being detected in fish and water samples (*WHO EHC # 162, 1994, Geneva*). DBDPO is not likely to present a toxicologic risk to wildlife, based on its low degree of toxicity in multiple studies in mammals. DBDPO does not present a bioaccumulation risk based on its physical/chemical properties, and results of laboratory studies and environmental monitoring.

TABLE 1. DBDPO Toxicology Data.

TEST	RESULTS
Oral LD50 (<i>Norris et al 1974</i>)	> 2,000 mg/kg
Dermal LD50 (<i>WHO EHC # 162, 1994</i>)	> 2,000 mg/kg
Inhalation LC50 (<i>WHO EHC # 162, 1994</i>)	> 48.2 mg/L
Eye Irritation (<i>WHO EHC # 162, 1994</i>)	Not an irritant
Skin Irritation (<i>WHO EHC # 162, 1994</i>)	Not an irritant
Human Skin Sensitization (<i>WHO EHC # 162, 1994</i>)	Not a skin sensitizer
Ames (<i>NTP, 1986</i>)	Not mutagenic
Mouse Lymphoma (<i>NTP, 1986</i>)	Not mutagenic
Sister Chromatid Exchange (<i>NTP, 1986</i>)	Not mutagenic
Chromosome Aberration (<i>NTP, 1986</i>)	Did not induce aberrations
14 Day Rat & Mice Oral (Diet)* (<i>NTP, 1986</i>)	NOEL > 100,000 ppm (10%)
90 Day Rat & Mice Oral (Diet)* (<i>NTP, 1986</i>)	NOEL > 50,000 ppm (5%)
Rat 1 Generation Reproduction** (<i>Norris et al, 1975</i>)	NOEL = 100 mg/kg (highest dose tested)
Rat Teratogenicity ** (<i>Norris et al, 1973</i>)	NOEL > 1,000 mg/kg
Rat & Mouse Carcinogenicity (Diet)* (<i>NTP, 1986</i>)	25,000 (2.5%) or 50,000 (5%) ppm Negative or equivocal evidence of carcinogenicity No effect body weight or mortality Minimal evidence of chronic toxicity
Rat Carcinogenicity (Diet)** (<i>Kociba et al, 1975</i>)	NOEL > 1 mg/kg (highest dose tested)
Rat Hepatic Enzyme Induction (<i>Carlson, 1980</i>)	Did not induce hepatic enzymes
Rabbit Skin Acnegenicity (<i>Pinkerton et al, 1989</i>)	Not acnegenic; Soot and char not acnegenic
Rat Pharmacokinetics (Oral & IV)* (<i>El Dareer et al, 1987</i>)	Low bioavailability Poorly absorbed (<1%) from GI tract Rapidly Eliminated with short half life (< 24 hours)

TABLE 1. Continued.

Ready Biodegradation (<i>MITI, 1992</i>)	Not readily biodegradable
Fish LC50 (<i>MITI, 1992</i>)	> 500 mg/L
Algae EC50 (<i>Walsh et al, 1987</i>)	> 1 mg/L
Fish Bioaccumulation (<i>MITI, 1992</i>)	Not bioaccumulative; BCF<5 (60 ug/L) & <50 (6 ug/L) 6wk
Aqueous Photodegradation (<i>Norris et al, 1973</i>)	Half life >> 90 days; Products not lower BrDPOs
Water Solubility (<i>BFRIP, 1997</i>)	< 0.1 ug/L (ppb)
Vapor Pressure (<i>BFRIP, 1997</i>)	4.63 x 10 ⁻⁶ Pa
Octanol Water Partition Coefficient (<i>BFRIP, 1997</i>)	6.265
Molecular Weight	959 g/m
Polymer Extraction (<i>Norris et al, 1974</i>)	Negligible

* Test article 94-99% DBDPO
 ** Test article only 77% DBDPO

II. HEXABROMOCYCLODODECANE (HBCD)

A. Inherent Toxicology

1. Mammalian Toxicology

HBCD is a cyclic aliphatic compound and is structurally distinct from DBDPO. HBCD's molecular weight is approximately 641 g/m. HBCD has a negligible water solubility (3.4 ug/L) and vapor pressure (6.27 x 10⁻² Pa) (*BFRIP, 1997, Wildlife International Ltd studies*). HBCD's toxicology data is summarized in TABLE 2 (summaries of unpublished studies attached). HBCD is not acutely toxic when administered orally or by inhalation to rats or dermally to rabbits (*Saytex Incorporated, 1978, Consumer Product Testing study*). HBCD was not irritating to the skin or eyes of rabbits (*Saytex Incorporated, 1978, Consumer Product Testing study*). HBCD did not induce skin sensitization when tested in the guinea pig maximization test (*BFRIP, 1997, MA BioServices study*). HBCD did not induce mutations in the *in vitro* Ames *Salmonella* assay (*Saytex Incorporated, 1978, Consumer Product Testing study; BFRIP, 1997, MA BioServices study*) or aberrations in human lymphocytes when tested in the *in vitro* chromosome aberration test (*BFRIP, 1996, MA BioServices study*).

HBCD was well tolerated and had minimal effects in the rat when administered by gavage for 28 days (*BFRIP, 1997, WIL Research Laboratories, Inc. study*). The no adverse effect level (NOAEL) in the rat 28 day study was 1000 mg/kg, the highest dose tested. The only test article related effect seen at the 1000 mg/kg dose was an increase in liver weight at week 4 in males at the high dose and females in the mid and high dose. The male liver weights were statistically comparable to control at the recovery sacrifice. Female liver weights remained increased at the recovery sacrifice, but the

increase was less pronounced than at the 28 day sacrifice. In the absence of test article related liver histopathology and serum chemistry changes, the increases in liver weight were considered to be an adaptive, rather than toxic, response and most likely the result of microsomal induction.

Mice fed diets containing HBCD at 0, 100, 1000 or 10,000 ppm for 18 months showed no evidence of carcinogenicity at any dose level (*Y. Kurokawam et al. Carcinogenesis test of flame retarder Hexabromocyclododecane in mice. Department of Toxicology, National Public Health Research Institute, Biological Safety Test and Research Center*).

HBCD was not teratogenic when administered to pregnant rats at a top dose of 1% of the diet during days 0-20 of gestation (*Murai et al, 1985, Pharmacometrics(Japan), 29:6, 981-986*). HBCD did not affect maternal body weight and caused no significant changes in the number of implants or the number of resorbed, dead, or live fetuses, or in the body weight of live fetuses. HBCD caused no external, visceral or skeletal anomalies. Delivery, nursing behavior, lactation and neonatal development were not affected.

Pharmacokinetics show that HBCD is rapidly absorbed from the gastrointestinal tract of rats, and is rapidly metabolized and excreted. Over 86% of the dose was eliminated within 72 hours (*Velsicol Chemical Corporation, 1980*). In another study, HBCD was administered orally to rats in olive oil at 500 mg/kg for 5 days (*R. Arita et al. Metabolic test of hexabromocyclododecane. Test on chemical substances used in household items. Studies on pharmacodynamics of hexabromocyclododecane (1983)*). Urine and feces were collected daily and organs were collected 24 hours after the last dose. Absorption from the gut was observed as was fecal elimination. Urinary excretion of HBCD was not observed. Among the various organs examined, HBCD was only detected in fatty tissue. Distribution to other organs was not detected.

B. Environmental Toxicology

HBCD has a negligible water solubility (3.4 ug/L) and vapor pressure (6.27×10^{-2} Pa) (*BFRIP, 1997, Wildlife International Ltd study*). These properties will limit HBCD's movement into and in the environment. HBCD's acute LC50 or EC50 values in fish, daphnia, and algae are all greater than HBCD's water solubility (*BFRIP, 1997, Wildlife International Ltd study; Walsh et al, 1987*). In addition, HBCD's no effect level (NOEL) in a chronic 21 day Daphnia study was approximately equivalent to HBCD's water solubility and the maximum accepted toxicant concentration (MATC) was greater than HBCD's water solubility (*BFRIP, 1998 Draft Report, Wildlife International Ltd study*). HBCD's measured octanol water partition coefficient is 5.625 (*BFRIP, 1997 Wildlife International Ltd study*). HBCD is not readily biodegradable (*BFRIP, 1996, Wildlife International Ltd study*). Negligible migration from foam insulation boards, HBCD's major use, was found (*APME, 1997*).

TABLE 2. HBCD Toxicology Data

TEST	RESULTS
Oral LD50 (<i>Saytex Incorporated, 1978</i>)	> 10,000 mg/kg
Dermal LD50 (<i>Saytex Incorporated, 1978</i>)	> 8,000 mg/kg
Inhalation LC50 (<i>Saytex Incorporated, 1978</i>)	> 200 mg/L
Eye Irritation (<i>Saytex Incorporated, 1978</i>)	Not an irritant
Skin Irritation (<i>Saytex Incorporated, 1978</i>)	Not an irritant
Guinea Pig Skin Sensitization (<i>BFRIP 1997</i>)	Did not induce
Ames (<i>Saytex Incorporated, 1978; BFRIP 1997</i>)	Not mutagenic
Chromosome Aberration (<i>BFRIP 1996</i>)	Did not induce
Rat Subchronic 28 Day (Gavage) (<i>BFRIP 1997</i>)	NOAEL = 1,000 mg/Kg body weight
Rat Teratogenicity (Diet) (<i>Murai et al, 1985</i>)	NOEL > 10,000 ppm (1%)
Rat Pharmacokinetics (<i>Velsicol, 1980; Arita 1983</i>)	Rapidly absorbed from GI tract Rapidly metabolized; Fecal elimination primarily Eliminated 86% of dose within 72 hr
Mice Carcinogenicity (Diet) (<i>Kurokawam</i>)	No evidence of carcinogenicity
Chicken Cataractogenicity (Diet)	NOEL > 10,500 ppm (1.5%)
Fish LC50 (<i>BFRIP 1997</i>)	EC50 > water solubility
Daphnia EC50 (<i>BFRIP 1997</i>)	EC50 > water solubility
Bacterial EC50	> 10,000 mg/L
Algae EC50 (<i>Walsh et al 1987; BFRIP 1997</i>)	EC50 > water solubility
Daphnia 21 Day Chronic (<i>BFRIP Draft 1998</i>)	NOEC ~ water solubility
Biodegradation (<i>BFRIP 1996</i>)	Not readily biodegradable
Foam Migration (APME, 1997)	Negligible
Water Solubility (<i>BFRIP 1997</i>)	3.4 ug/L (ppb)
Vapor Pressure (<i>BFRIP 1997</i>)	6.27 x 10 ⁻⁵ Pa
Octanol Water Partition Coefficient (<i>BFRIP 1997</i>)	5.625
Molecular Weight	641 g/m

III. Saytex® 8010

A. Inherent Toxicology

1. Mammalian Toxicology

Saytex® 8010 (S8010) is a proprietary brominated flame retardant of Albemarle Corporation; its structure is being held confidential. (S8010's structure can be provided to the CPSC on a confidential basis upon request.) S8010 is a brominated aromatic with a high molecular weight (approximately 1000 g/m) and large molecular volume. S8010's toxicology data is summarized in TABLE 3 (summaries of unpublished studies attached). S8010 is not acutely toxic to rats or rabbits when administered orally or dermally, respectively (*Ethyl Corporation, 1988, Pharmakon Research International studies*). S8010 was not irritating to the skin or eye in rabbits (*Ethyl Corporation, 1988, Pharmakon Research International studies*). S8010 was not mutagenic in the *in vitro* Ames Salmonella or chromosome aberration (Chinese hamster lung) tests (*Ethyl Corporation, 1988, Pharmakon Research International study; Ethyl Corporation, 1992, Microbiological Associates studies*).

Repeated dose studies of 28 or 90 days in length have shown minimal effects at high dose levels. No effects were seen in rats treated orally with S8010 at doses up to 1250 mg/kg/day for 28 days (*Ethyl Corporation, 1991, Pharmakon Research International study*). No effects were found on body weight, food consumption, body weight gain, hematology and serum chemistry values, urine, ocular exam. No treatment related effects were found on organ weight, gross necropsy or histopathology. Oral dose levels of up to 1000 mg/kg/day for 90 days produced no evidence of systemic toxicity, ocular effects, or alterations in urine, serum chemistry and hematology values in rats (*Ethyl Corporation, 1992, Pharmakon Research International study*). No adverse effect was found on body weights, body weight gain or food consumption. Liver weights were increased in the 1000 mg/kg/day dose group, but not at the 320 mg/kg/day dose group (the next lower dose group). Low grade microscopic liver changes accompanied the increase in liver weights in male rats, but not in female rats. The liver changes resolved without any delayed or long term effect after a 28 day recovery period.

In tests in other organ systems, S8010 did not effect on the development of rats or rabbits at maternal doses of up to 1250 mg/kg/day (*Ethyl Corporation, 1992, Springborn Laboratories studies*). There was no evidence of maternal or developmental toxicity or teratogenicity in rats or rabbits as a result of administration of S8010 doses up to 1250 mg/kg/day administered to pregnant females during the period of major organogenesis.

2. Environmental Toxicology

S8010 has shown minimal effects in environmental tests. A formal water solubility study has not been conducted, but we expect S8010's water solubility to be very low. S8010 is not acutely toxic to fish (*Ethyl Corporation, 1991, CITI study*). The material did not bioconcentrate in fish exposed for an 8 week period (*Ethyl Corporation, 1991, CITI study*). No signs of toxicity were observed in the treated fish during the study. S8010 was not readily biodegradable (*Ethyl Corporation, 1991, CITI study*), but may have potential for inherent biodegradability due to its chemical structure.

TABLE 3. S8010 Toxicology Summary

TEST	RESULTS
Rat Oral LD50 (<i>Ethyl Corporation, 1988</i>)	> 5,000 mg/kg
Rabbit Dermal LD50 (<i>Ethyl Corporation, 1988</i>)	> 2,000 mg/kg
Rabbit Eye Irritation (<i>Ethyl Corporation, 1988</i>)	Not an irritant
Rabbit Skin Irritation (<i>Ethyl Corporation, 1988</i>)	Not an irritant
Ames (<i>Ethyl Corporation, 1988, 1992</i>)	Not mutagenic
Chromosome Aberration (<i>Ethyl Corporation, 1992</i>)	Did not induce aberrations
Rat Teratogenicity (Gavage) (<i>Ethyl Corporation, 1992</i>)	NOEL > 1250 mg/kg/day
Rabbit Teratogenicity (Gavage) (<i>Ethyl Corporation, 1992</i>)	NOEL > 1250 mg/kg/day
Rat Subchronic 28 Day (Gavage) (<i>Ethyl Corporation, 1991</i>)	NOEL > 1250 mg/kg/day
Rat Subchronic 90 Day (Gavage) (<i>Ethyl Corporation, 1992</i>)	NOAEL = 1000 mg/kg/day
Fish LC50 (48 hr) (<i>Ethyl Corporation, 1991</i>)	LC50 > 50 mg/L
Fish Bioaccumulation (<i>Ethyl Corporation, 1991</i>)	Did not accumulate over an 8 wk study
Ready Biodegradation (<i>Ethyl Corporation, 1991</i>)	Did not biodegrade

IV. BIOAVAILABILITY OF DBDPO, HBCD, S8010 UNDER CONDITIONS OF USE

Neither DBDPO, HBCD nor S8010 are expected to exhibit significant bioavailability when used in a backcoating to flame retard upholstery textiles. Both DBDPO and S8010 (by analogy to compounds of similar structure) have, or are expected to have, a low bioavailability. Pharmacokinetic studies have demonstrated DBDPO has a very low bioavailability. DBDPO's low bioavailability is likely a function of its large molecular weight (almost 1000 gm/mole), large molecular volume, and poor water solubility. These properties effectively limit DBDPO's absorption through the skin or following ingestion or inhalation. Further, oral and intravenous pharmacokinetic studies in the rat have shown DBDPO is poorly absorbed from the gastrointestinal tract. Less than 1% of the oral dose was absorbed from the gastrointestinal tract. These studies have also shown that if absorbed, DBDPO is rapidly eliminated and can be metabolized by the mammalian system. The small fraction of the DBDPO dose that was absorbed from the gastrointestinal tract was rapidly eliminated with a half life in the body of < 24 hours.

Any DBDPO inhaled by the consumer as a result of DBDPO textile backcoating is unlikely

to be absorbed. The particle size would likely be so large as to exclude pulmonary absorption. In this event, any inhaled DBDPO would be coughed up, where a portion would be eliminated and a portion swallowed. Again, gastrointestinal absorption would be extremely limited. Skin absorption of DBDPO is extremely unlikely given its physical/chemical properties.

By analogy to compounds of similar structure, S8010 is also expected to have limited bioavailability. S8010 has a high molecular weight and a large molecular volume. Like DBDPO, these properties will limit S8010's availability. Limited bioavailability may be one factor in S8010's minimal effects in repeated dose studies.

HBCD's profile is somewhat different from that of DBDPO and S8010. A pharmacokinetic study in rats has shown HBCD is rapidly absorbed from the gastrointestinal tract. The study also demonstrated that HBCD was rapidly metabolized and excreted from the body. Like DBDPO and S8010, dermal absorption of HBCD is expected to be negligible. Consumer exposure via inhalation is expected to be negligible due to HBCD's encapsulation in the backcoating and the resulting large particle size.

V. POTENTIAL FOR CONSUMER EXPOSURE UNDER CONDITIONS OF USE (INHALATION, INGESTION, DERMAL)

DBDPO, HBCD and S8010 can be used to flame retard upholstery fabrics. In this use, these flame retardants would be applied, encapsulated in a polymer, to the back of the fabric as a backcoating. Potential consumer exposure scenarios include ingestion, inhalation or dermal exposure from sitting, lying or chewing on the furniture. The likelihood of actual consumer exposure to these flame retardants under these potential scenarios is negligible. Encapsulation of the flame retardants within a polymer effectively limits their potential migration and/or release. Further, the flame retardants would have to migrate through the fabric in order to come in contact with the consumer. This provides an additional barrier to exposure.

Wetting the fabric with water, beverages/liquid foods or urine is unlikely to effect these flame retardant's availability. These processes would first have to extract the flame retardant from the polymer in order to create an exposure scenario. Further, these flame retardants have very low solubilities. DBDPO's aqueous solubility is <0.1 ug/L and will not be effected by a change in pH or heat due to DBDPO's chemical structure. Similarly, HBCD's water solubility is also very low - 3.4 ug/L. S8010's water solubility, while not formally measured, is expected to be low based on its chemical structure. These flame retardants are also very unlikely to be extracted by cleaning solvents used by the consumer on furniture due to their chemical/physical properties.

CONCLUSIONS

The inherent toxicity of DBDPO, HBCD and S8010 is minimal. Repeated exposures to very high dose levels produced no to only minimal effects in laboratory animals. The bioavailability of any of these flame retardants by the dermal or respiratory routes is expected to be negligible. Neither DBDPO nor S8010, by analogy, have significant oral bioavailability. HBCD may be absorbed

following oral exposure. However, consumer exposure through use of flame retarded upholstery to any of these flame retardants is expected to be negligible. The hazard to the consumer due to the use of flame retardants in upholstered furniture is negligible and is far outweighed by the very real fire hazard associated with upholstered furniture.

**DECABROMODIPHENYL OXIDE (DBDPO):
SUMMARIES OF UNPUBLISHED STUDIES**

**DECABROMODIPHENYL OXIDE (DBDPO):
DETERMINATION OF THE WATER SOLUBILITY**

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER: 439C-102

**U.S. EPA 40 CFR Ch. 1 § 796.1860 Water Solubility (Generator Column Method)
OECD Guideline 105 Water Solubility (Column Elution Method)**

AUTHORS:

**Joel I. Stenzel
Barbara J. Markley, Ph.D.**

STUDY INITIATION DATE: February 19, 1996

STUDY COMPLETION DATE: June 10, 1997

Submitted to:

**Chemical Manufacturers Association's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, Virginia 22209**



WILDLIFE INTERNATIONAL LTD.

**8598 Commerce Drive
Easton, Maryland 21601
(410) 822-8600**



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SDR23

SUMMARY

SPONSOR:	Chemical Manufacturers Association's Brominated Flame Retardant Industry Panel
SPONSOR'S REPRESENTATIVE:	Hasmukh Shah, Ph.D.
LOCATION OF STUDY, RAW DATA AND A COPY OF THE FINAL REPORT:	Wildlife International Ltd. Easton, Maryland 21601

WILDLIFE INTERNATIONAL LTD.	
PROJECT NUMBER:	439C-102
TEST SUBSTANCE:	Decabromodiphenyl oxide (DBDPO)
STUDY:	Decabromodiphenyl oxide (DBDPO): Determination of the Water Solubility
TEST DATES:	Experimental Start - May 3, 1996 Experimental Termination - September 16, 1996

SUMMARY:	The solubility of DBDPO in water at 25.0°C was determined to be less than 0.1 µg/L (ppb) using a column elution method.
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SUMMARY

SPONSOR:	Chemical Manufacturers Association's Brominated Flame Retardant Industry Panel
SPONSOR'S REPRESENTATIVE:	Hasmukh Shah, Ph.D.
LOCATION OF STUDY, RAW DATA AND A COPY OF THE FINAL REPORT:	Wildlife International Ltd. Easton, Maryland 21601

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER:	439C-115
TEST SUBSTANCE:	Decabromodiphenyl Oxide (DBDPO)
STUDY:	Decabromodiphenyl Oxide (DBDPO): Determination of the Vapor Pressure Using a Spinning Rotor Gauge
TEST DATES:	Experimental Start - June 9, 1997 Experimental Termination - June 13, 1997

SUMMARY:	The vapor pressure of DBDPO was determined to be 4.63×10^{-6} Pa at 21°C using a spinning rotor gauge.
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DECABROMODIPHENYL OXIDE (DBDPO):
DETERMINATION OF n-OCTANOL/WATER PARTITION COEFFICIENT

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER: 439C-101

OPPTS 830.7560 Partition Coefficient (n-Octanol/Water),
Generator Column Method

AUTHORS:

Jon A. MacGregor
Willard B. Nixon, Ph.D.

STUDY INITIATION DATE: March 26, 1997

STUDY COMPLETION DATE: June 16, 1997

Submitted to:

Chemical Manufacturers Association's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, Virginia 22209



WILDLIFE INTERNATIONAL LTD.

8598 Commerce Drive
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CYR13

DECABROMODIPHENYL OXIDE (DBDPO): DETERMINATION OF THE
VAPOR PRESSURE USING A SPINNING ROTOR GAUGE

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER: 439C-115

U.S. EPA OPPTS 830.7950 Vapor Pressure
OECD Guideline 104 Vapour Pressure

AUTHORS:

Joel I. Stenzel
Willard B. Nixon, Ph.D.

STUDY INITIATION DATE: June 9, 1997

STUDY COMPLETION DATE: July 31, 1997

Submitted to

Chemical Manufacturers Association's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, Virginia 22209



WILDLIFE INTERNATIONAL LTD.

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CYR13

SUMMARY

SPONSOR:	Chemical Manufacturers Association's Brominated Flame Retardant Industry Panel
SPONSOR'S REPRESENTATIVE:	Hasmukh Shah, Ph.D.
LOCATION OF STUDY, RAW DATA AND A COPY OF THE FINAL REPORT:	Wildlife International Ltd. Easton, Maryland 21601

WILDLIFE INTERNATIONAL LTD.	
PROJECT NUMBER:	439C-101
TEST SUBSTANCE:	Decabromodiphenyl Oxide (DBDPO)
STUDY:	Decabromodiphenyl Oxide (DBDPO): Determination of n-Octanol/Water Partition Coefficient
TEST DATES:	Experimental Start - March 31, 1997 Experimental Termination - May 5, 1997

SUMMARY:	The log ₁₀ octanol/water partition coefficient (K _{ow}) of DBDPO was determined to be 6.265 at 25 ± 0.05°C using the generator column method.
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化審法の既存化学物質
安全性点検データ集

BIODEGRADATION AND BIOACCUMULATION
DATA
OF EXISTING CHEMICALS
BASED ON THE CSCL JAPAN

通商産業省基礎産業局化学品安全課 監修

COMPILD under the SUPERVISION of
CHEMICAL PRODUCTS SAFETY DIVISION
BASIC INDUSTRIES BUREAU
MINISTRY OF INTERNATIONAL TRADE & INDUSTRY
JAPAN

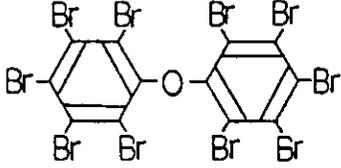
財団法人 化学品検査協会 編集

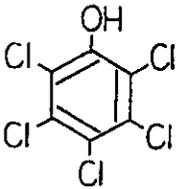
EDITED BY
CHEMICALS INSPECTION & TESTING INSTITUTE
JAPAN

October 1992 ©

社団法人 日本化学物質安全・情報センター 発行

PUBLISHED BY
JAPAN CHEMICAL INDUSTRY ECOLOGY-TOXICOLOGY & INFORMATION CENTER

官報告示番号 CR No.	CAS No.	デカブロモジフェニルエーテル			
3-2846	1163-19-5				
Decabromodiphenylether					
		Physico-chemical			
		M. P.	Soly (Water)		
		285 °C 7	20 mg/l 8		
		B. P.	Hydroly		
		°C			
V. P.	logPow				
Pa					
Biodegradation		Bioaccumulation	Toxicity		
Period	Substance	Sludge	Lipid	Period	48h.LC50 >500 mg/l
2 W	100 mg/l	30 mg/l	— % (Av.)	6 W	
Degree of biodeg.			conc.	BCF	
0 % by BOD		1st	60 mg/l	< 5	
		2nd	6 mg/l	< 50	
Remarks:					

官報告示番号 CR No.	CAS No.	ペンタクロロフェノール			
3-2850	87-86-5				
Pentachlorophenol					
		Physico-chemical			
		M. P.	Soly (Water)		
		190~191 °C 2	77.2 mg/l 8		
		B. P.	Hydroly		
		309~310 °C 2			
V. P.	logPow				
Pa					
Biodegradation		Bioaccumulation	Toxicity		
Period	Substance	Sludge	Lipid	Period	48h.LC50 305 mg/l
4 W	100 mg/l	30 mg/l	5.4 % (Av.)	8 W	
Degree of biodeg.			conc.	BCF	
1 % by BOD		1st	30 mg/l	39~198	
		2nd	3 mg/l	45~224	
Remarks:					

HEXABROMOCYCLODODECANE (HBCD):

SUMMARIES OF UNPUBLISHED STUDIES



FINAL REPORT

VOLUME 1 OF 3
(Text and Summary Tables)

STUDY TITLE

**A 28-DAY REPEATED DOSE ORAL
TOXICITY STUDY OF HBCD IN RATS**

DATA REQUIREMENT

OECD Guideline, Section 407

STUDY DIRECTOR

Christopher P. Chengelis, Ph.D., D.A.B.T.

STUDY INITIATED ON

April 12, 1996

STUDY COMPLETION DATE

February 13, 1997

PERFORMING LABORATORY

WIL Research Laboratories, Inc.
1407 George Road
Ashland, Ohio 44805-9281

LABORATORY STUDY NUMBER

WIL-186004

SPONSOR PROJECT NUMBER

BFRIP 2.0-WIL HBCD

SPONSOR

Chemical Manufacturers Association
Brominated Flame Retardant Industry Panel
1300 Wilson Blvd.
Arlington, Virginia 22209

A 28-Day Repeated Dose Oral
Toxicity Study of HBCD in Rats

I. SUMMARY

The test article, hexabromocyclododecane (HBCD), Lot #3577, in the vehicle, corn oil, was administered orally by gavage to three groups of Sprague-Dawley CrI: CD BR rats for a period of 28 consecutive days. Dose levels were 125 (low), 350 (mid), or 1000 (high) mg/kg/day, administered in a dosage volume of 5 ml/kg. The test groups consisted of 6 males and 6 females in the 125 and 350 mg/kg/day groups and 12 males and 12 females in the 1000 mg/kg/day group. A concurrent control group comprised of 12 males and 12 females received the vehicle, corn oil, for 28 consecutive days at a dosage volume of 5 ml/kg. At the end of the dosing period, 6 animals/sex/group were euthanized and necropsied. The remaining 6 animals/sex in the control and 1000 mg/kg/day groups remained on-test untreated for a 14 day recovery period. At the end of the recovery period, all animals were euthanized and necropsied.

Animals were observed twice daily for mortality and moribundity. Clinical signs were recorded daily. Body weight and food consumption were measured weekly. Functional observational battery and motor activity evaluations were performed during weeks -1 (pretest), 3, and 5 (recovery). Samples for hematology and serum chemistry evaluations were collected at the primary (28 day) and recovery (42 day) necropsies. Complete necropsies were performed on all rats. The brain, liver, kidney, heart, spleen, testes and epididymis or ovaries, adrenal glands, and thymus from all animals were weighed at each necropsy. Approximately 40 tissues were collected and preserved at each necropsy from all animals. The following tissues were examined microscopically from the control and high dose animals: liver, kidney, heart, spleen, testes (males), prostate (males), seminal vesicles (males), epididymis (males), ovaries (females), adrenal glands, thymus, bone with marrow (sternebra), brain, stomach, cecum, duodenum, ileum, jejunum, lymph node, peripheral nerve (sciatic), spinal cord, lung, trachea, uterus (females), urinary

bladder, and all gross lesions.) The lungs, liver, kidneys, stomach, gross lesions and target organs were examined in all dose levels.

Survival was not affected by administration of the test article. All animals survived to the scheduled necropsy. Clinical signs observed during the study were nonspecific, low in incidence, non-dose-related and not considered related to test article.

Body weights, weight gain and food consumption of treated animals were compared statistically by sex and treatment day to their respective control groups ($p < 0.05$ or $p < 0.01$). Body weight, weight gain and food consumption was not affected by treatment. No statistically significant differences in body weight between control and treated animals were detected with the exception of an increase in mean female body weight in the 350 mg/kg/day during week 2 of treatment. Mean female body weight at that time point was 196 g vs 179 in the control group. No statistically significant differences in body weight gain between control and treated animals were detected with the exception of a decrease in mean male body weight gain in the 1000 mg/kg/day recovery group during week 1 of recovery. Mean male body weight gain at that time point was 21 g vs 31 in the control group; mean male body weight was not statistically different from the control mean. No statistically significant differences in food consumption between control and treated animals were detected with the exception of an increase in mean female food consumption in the 350 mg/kg/day during weeks -1, 1, and 2 of treatment. Mean female food consumption at that those time points were 18, 17 and 17 g vs 16, 15 and 15 g in the control group, respectively.

Functional observation battery and motor activity results from treated animals were compared statistically by sex and treatment day to their respective control groups ($p < 0.05$). These parameters were not affected by treatment with the test article. No statistically significant differences were observed between treated and control animals at any time point.

No statistically significant differences between treated and control animals were found for hematology parameters with the exception of an increase in the mean

activated partial thromboplastin time in the 1000 mg/kg/day males on week 4 and a decrease in the mean prothrombin time in the 1000 mg/kg/day females on week 4. These statistical differences were not of toxicological significance.

No toxicologically significant effects on serum chemistry values related to test article administration were observed at the 28 day primary and 42 day recovery necropsies. Scattered instances of statistically significant differences between treated and control animals were detected for some serum chemistry parameters at the 28 day primary necropsy. These scattered statistical differences were not considered toxicologically significant because the statistical differences occurred: in the absence of a dose response, in the absence of the accompanying clinical chemistry changes expected, in the opposite direction from what occurs in a toxic state, in a direction which is without physiologic significance, or due to potential interference with the laboratory method. No statistically significant differences in serum chemistry parameters were detected between groups at the 42 day recovery necropsy.

No gross lesions which could be attributed to the test article were detected at either necropsy. Gross lesions were nonspecific, low in incidence, non-dose-related and considered incidental.

No microscopic lesion which could be attributed to the test article were detected on histopathologic exam. Microscopic changes were nonspecific, low in incidence, non-dose-related and considered incidental.

No statistical significant differences in organ weight or organ to body weight ratios were detected between control and treated animals with one exception. Absolute liver weights were statistically significantly increased with respect to control means at the 28 day necropsy in males in the high dose and females in the mid and high dose. Liver to body weight ratios in mid and high dose males and low, mid and high dose females were statistically significantly increased at the 28 day necropsy. At the recovery necropsy, male absolute and liver to body weight ratio were statistically comparable to the control mean whereas female absolute liver weights and liver to body weight ratio were statistically significantly increased with respect to control mean. The difference in absolute liver weight between control and treated

WIL-186004
CMA BFRIP

females was less pronounced at the end of the recovery period, indicating the increase in liver weight was reversible in females as well as males. In the absence of test article related histopathologic and serum chemistry changes, increases in liver weight are considered an adaptive, rather than a toxic response, are not uncommon in the rat, and are most likely the result of microsomal induction.

In conclusion, no systemic toxicity was observed at any dose level. Based on the results of this study, the NOAEL (No Observed Adverse Effect Level) of HBCD administered orally to male and female rats for 28 consecutive days was 1000 mg/kg/day.

FINAL REPORT

Study Title

CHROMOSOME ABERRATIONS IN
HUMAN PERIPHERAL BLOOD LYMPHOCYTES

Test Article

Hexabromocyclododecane

Authors

Ramadevi Gudi, Ph.D.
Elizabeth H. Schadly, B.S.

Study Completion Date

November 12, 1996

Performing Laboratory

Microbiological Associates, Inc.
9630 Medical Center Drive
Rockville, Maryland 20850

Laboratory Study Number

G96AO61.342

Sponsor

Chemical Manufacturers Association
1300 Wilson Boulevard
Arlington VA 22209

Page 1 of 34

SUMMARY

The test article, Hexabromocyclododecane, was tested in the *in vitro* mammalian cytogenetic test using human peripheral blood lymphocytes (HPBL) both in the absence and presence of metabolic activation. The assay was performed in two phases. The first phase, the initial chromosome aberration assay, was conducted to establish the dose range for testing and to evaluate the clastogenic potential of the test article. The second phase, the independent repeat chromosome aberration assay, was performed to confirm the test system response to the test article seen in the initial assay.

Dimethylsulfoxide (DMSO) was the solvent of choice based on information provided by the Sponsor, the solubility of the test article and compatibility with the target cells. The test article was soluble in DMSO at approximately 500 mg/ml, the maximum concentration tested.

In the initial chromosome aberration assay, the maximum dose tested was 2500 µg/ml. This dose was achieved using a stock concentration of 250 mg/ml, and a 100 µl dosing aliquot added to 10 ml fresh complete medium or S9 reaction mix. Dose levels greater than 2500 µg/ml were insoluble in treatment medium and not tested in the assay. Visible precipitate was observed in treatment medium at dose levels 750 and 2500 µg/ml and was soluble but cloudy (no visible precipitate) at dose levels 75 and 250 µg/ml. The test article was soluble in treatment medium at all other dose levels tested. In the non-activated portion of the initial assay HPBL cells were exposed to the test article continuously for 20 hours; in the S9-activated portion of the initial chromosome aberration assay, HPBL cells were exposed to the test article for 4 hours. Metaphase cells were collected for microscopic evaluation at 20 hours after the initiation of treatment. Dose levels of 2500 µg/ml in the non-activated study and 750 and 2500 µg/ml in the S9-activated study were not analyzed for chromosome aberrations due to complete mitotic inhibition. Toxicity (mitotic inhibition) of approximately 56% was observed at the highest dose level (750 µg/ml) evaluated for chromosome aberrations, in the non-activated study. In the S9-activated study, 13% toxicity was observed at the highest dose level (250 µg/ml) evaluated for chromosome aberrations. No statistically significant increases in chromosome aberrations were observed in either the non-activated or S9-activated test systems relative to the solvent control group regardless of dose level ($p > 0.05$, Fisher's exact test).

Based on the results of the initial assay, an independent repeat chromosome aberration assay was conducted in the absence and presence of an Aroclor-induced S9 metabolic activation system at dose levels of 10, 19, 38, 75, 150, 300, and 600 µg/ml. The test article was soluble but cloudy at dose level 75 µg/ml and was workable in treatment medium at dose levels 150 µg/ml and higher. The test article was soluble in treatment medium at all other concentrations tested. In the independent repeat assay, HPBL cells were exposed to the test article continuously for 20 or 44 hours in the non-activated test system and for 4 hours in the S9-activated test system. Metaphase cells were collected for microscopic evaluation in both the non-activated and S9-activated studies at 20 and 44 hours after the initiation of treatment. Toxicity, measured by mitotic inhibition, was

approximately 55% and 94% at the 20 and 44 hour harvests, respectively, at the highest dose levels (600 and 300 $\mu\text{g/ml}$) evaluated for chromosome aberrations in the non-activated studies. In the S9-activated studies, toxicity was approximately 71% and 69% at the 20 and 44 hour harvests, respectively, at the highest dose levels (300 and 600 $\mu\text{g/ml}$) evaluated for chromosome aberrations. Dose level 600 $\mu\text{g/ml}$ in the non-activated 44 hour harvest and in the S9-activated 20 hour harvest was not analyzed for chromosome aberrations due to an insufficient number of scorable metaphase cells. No statistically significant increases in structural chromosome aberrations were observed in either the non-activated or S9-activated studies, regardless of dose level or harvest time ($p > 0.05$, Fisher's exact test). No statistically significant increases in numerical chromosome aberrations were observed in either the non-activated or S9-activated studies at the 44 hour harvest time, regardless of dose level ($p > 0.05$, Fisher's exact test).

Based on the findings of this study, Hexabromocyclododecane was concluded to be negative for the induction of structural and numerical chromosome aberrations in human peripheral blood lymphocytes.

HEXABROMOCYCLODODECANE (HBCD):
DETERMINATION OF THE WATER SOLUBILITY

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER: 439C-105

U.S. EPA 40 CFR Ch. 1 § 796.1860 Water Solubility (Generator Column Method)
OECD Guideline 105 Water Solubility (Column Elution Method)

AUTHORS:

Joel I. Stenzel
Barbara J. Markley, Ph.D.

STUDY INITIATION DATE: February 19, 1996

STUDY COMPLETION DATE: June 13, 1997

Submitted to:

Chemical Manufacturers Association's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, Virginia 22209



WILDLIFE INTERNATIONAL LTD.

8598 Commerce Drive
Easton, Maryland 21601
(410) 822-8600



Page 1 of 55

CYR11

SUMMARY

SPONSOR:	Chemical Manufacturers Association's Brominated Flame Retardant Industry Panel
SPONSOR'S REPRESENTATIVE:	Hasmukh Shah, Ph.D.
LOCATION OF STUDY, RAW DATA AND A COPY OF THE FINAL REPORT:	Wildlife International Ltd. Easton, Maryland 21601

WILDLIFE INTERNATIONAL LTD.	
PROJECT NUMBER:	439C-105
TEST SUBSTANCE:	Hexabromocyclododecane (HB CD)
STUDY:	Hexabromocyclododecane (HB CD): Determination of the Water Solubility
TEST DATES:	Experimental Start - May 3, 1996 Experimental Termination - March 12, 1997

SUMMARY:	The solubility of HB CD in water at 25.0°C was determined to be 3.4 µg/L (ppb) using a column elution method.
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HEXABROMOCYCLODODECANE (HBCD): DETERMINATION OF THE
VAPOR PRESSURE USING A SPINNING ROTOR GAUGE

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER: 439C-117

U.S. EPA OPPTS 830.7950 Vapor Pressure
OECD Guideline 104 Vapour Pressure

AUTHORS:

Joel I. Stenzel
Willard B. Nixon, Ph.D.

STUDY INITIATION DATE: May 20, 1997

STUDY COMPLETION DATE: July 23, 1997

Submitted to

Chemical Manufacturers Association's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, Virginia 22209



WILDLIFE INTERNATIONAL LTD.

8598 Commerce Drive
Easton, Maryland 21601
(410) 822-8600



Page 1 of 44

SUMMARY

SPONSOR:	Chemical Manufacturers Association's Brominated Flame Retardant Industry Panel
SPONSOR'S REPRESENTATIVE:	Hasmukh Shah, Ph.D.
LOCATION OF STUDY, RAW DATA AND A COPY OF THE FINAL REPORT:	Wildlife International Ltd. Easton, Maryland 21601

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER:	439C-117
TEST SUBSTANCE:	Hexabromocyclododecane (HBCD)
STUDY:	Hexabromocyclododecane (HBCD): Determination of the Vapor Pressure Using a Spinning Rotor Gauge
TEST DATES:	Experimental Start - May 20, 1997 Experimental Termination - May 21, 1997

SUMMARY:	The vapor pressure of HBCD was determined to be 6.27×10^{-5} Pa at 21°C using a spinning rotor gauge.
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HEXABROMOCYCLODODECANE (HBCD):
A 96-HOUR FLOW-THROUGH ACUTE TOXICITY TEST
WITH THE RAINBOW TROUT (*Oncorhynchus mykiss*)

FINAL REPORT

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER: 439A-101

TSCA Title 40 of the Federal Code of Regulations
Part 797, Section 1400
and
Organisation for Economic Cooperation and Development
OECD Guideline 203

AUTHORS:

William C. Graves
James P. Swigert, Ph.D.

STUDY INITIATION DATE: May 15, 1996

STUDY COMPLETION DATE: June 3, 1997

Submitted to

Chemical Manufacturers Association's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, Virginia 22209



WILDLIFE INTERNATIONAL LTD.

8598 Commerce Drive
Easton, Maryland 21601
(410) 822-8600



SUMMARY

SPONSOR:	Chemical Manufacturers Association's (CMA) Brominated Flame Retardant Industry Panel
SPONSOR'S REPRESENTATIVE:	Dr. Hasmukh Shah
LOCATION OF STUDY, RAW DATA AND A COPY OF THE FINAL REPORT:	Wildlife International Ltd. Easton, Maryland 21601

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER:	439A-101
TEST SUBSTANCE:	Hexabromocyclododecane (HBCD)
STUDY:	Hexabromocyclododecane (HBCD): A 96-Hour Flow-Through Acute Toxicity Test with the Rainbow Trout (<i>Oncorhynchus mykiss</i>)
NOMINAL TEST CONCENTRATIONS:	Negative Control, Solvent Control, 1.5, 2.2, 3.2, 4.6 and 6.8 $\mu\text{g/L}$
MEAN MEASURED TEST CONCENTRATIONS:	Negative Control, Solvent Control, 0.75, 1.5, 2.3, 2.3 and 2.5 $\mu\text{g/L}$
TEST DATES:	Experimental Start - April 7, 1997 Biological Termination - April 11, 1997 Experimental Termination - April 23, 1997
LENGTH OF TEST:	96 Hours

TEST ORGANISM:	Rainbow Trout (<i>Oncorhynchus mykiss</i>)
SOURCE OF TEST ORGANISMS:	Troutlodge, Inc. P. O. Box 1290 Sumner, WA 98390
AGE OF TEST ORGANISMS:	Juveniles
MEASUREMENTS OF 10 NEGATIVE CONTROL FISH:	
WEIGHT (g):	Mean = 2.4; Range = 1.6 to 3.6
TOTAL LENGTH (mm):	Mean = 55; Range = 50 to 61

96-HOUR LC50:	>6.8 $\mu\text{g/L}$ (nominal, 2X HBCD's water solubility of 3.4 $\mu\text{g/L}$) (>2.5 $\mu\text{g/L}$ mean measured concentration)
NO MORTALITY CONCENTRATION:	6.8 $\mu\text{g/L}$ (nominal, 2X HBCD's water solubility of 3.4 $\mu\text{g/L}$) (>2.5 $\mu\text{g/L}$ mean measured concentration)
NO-OBSERVED-EFFECT-CONCENTRATION:	6.8 $\mu\text{g/L}$ (nominal, 2X HBCD's water solubility of 3.4 $\mu\text{g/L}$) (>2.5 $\mu\text{g/L}$ mean measured concentration)

HEXABROMOCYCLODODECANE (HBCD)
A 96-HOUR TOXICITY TEST WITH THE
FRESHWATER ALGA (*Selenastrum capricornutum*)

FINAL REPORT

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER: 439A-103

TSCA, Title 40 of the Code of Federal Regulations
Part 797, Section 1050
and
Organisation for Economic Cooperation and Development
OECD Guideline 201

AUTHORS:

Cindy A. Roberts
James P. Swigert, Ph.D.

STUDY INITIATION DATE: February 16, 1996

STUDY COMPLETION DATE: June 3, 1997

Submitted to

Chemical Manufacturers Association's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, VA 22209



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8598 Commerce Drive
Easton, Maryland 21601
(410) 822-8600



- 7 -

SUMMARY

SPONSOR:	Chemical Manufacturers Association's Brominated Flame Retardant Industry Panel
SPONSOR'S REPRESENTATIVE:	Dr. Hasmukh Shah
LOCATION OF STUDY, RAW DATA AND A COPY OF THE FINAL REPORT:	Wildlife International Ltd. Easton, Maryland 21601

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER:	439A-103
TEST SUBSTANCE:	Hexabromocyclododecane (HBCD)
STUDY:	Hexabromocyclododecane (HBCD): A 96-Hour Toxicity Test with the Freshwater Alga (<i>Selenastrum capricornutum</i>)
NOMINAL TEST CONCENTRATIONS:	Negative Control; Solvent Control, (0.1 mL DMF/L) 1.5, 2.2, 3.2, 4.6 and 6.8 µg HBCD/L
MEAN MEASURED TEST CONCENTRATIONS:	Negative Control; Solvent Control and 3.7 µg HBCD/L
SOLUBILITY µg HBCD/L IN WELL WATER AT 25°C)	3.4 µg HBCD/L
TEST DATES:	Experimental Start - April 10, 1997 Exposure Termination - April 14, 1997 Experimental Termination - April 26, 1997
LENGTH OF TEST:	96 Hours

TEST ORGANISM:	Freshwater Alga (<i>Selenastrum capricornutum</i>)
SOURCE OF TEST ORGANISMS:	Wildlife International Ltd. Easton, Maryland 21601

HEXABROMOCYCLODODECANE (HBCD):
A 48-HOUR FLOW-THROUGH ACUTE TOXICITY TEST
WITH THE CLADOCERAN (*Daphnia magna*)

FINAL REPORT

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER: 439A-102

TSCA Title 40 of the Federal Code of Regulations
Part 797, Section 1300
and
Organisation for Economic Cooperation and Development
OECD Guideline 202, Part I

AUTHORS:

William C. Graves
James P. Swigert, Ph.D.

STUDY INITIATION DATE: May 15, 1996

STUDY COMPLETION DATE: May 21, 1997

Submitted to

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1300 Wilson Boulevard
Arlington, Virginia 22209



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(410) 822-8600



- 7 -

SUMMARY

SPONSOR:	Chemical Manufacturers Association's (CMA) Brominated Flame Retardant Industry Panel
SPONSOR'S REPRESENTATIVE:	Dr. Hasmukh Shah
LOCATION OF STUDY, RAW DATA AND A COPY OF THE FINAL REPORT:	Wildlife International Ltd. Easton, Maryland 21601

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER:	439A-102
TEST SUBSTANCE:	Hexabromocyclododecane (HBCD)
STUDY:	Hexabromocyclododecane (HBCD): A 48-Hour Flow-Through Acute Toxicity Test with the Cladoceran (<i>Daphnia magna</i>)
NOMINAL TEST CONCENTRATIONS:	Negative Control, Solvent Control, 1.5, 2.2, 3.2, 4.6 and 6.8 $\mu\text{g/L}$
MEAN MEASURED TEST CONCENTRATIONS:	Negative Control, Solvent Control, 2.4, 1.8, 2.1, 2.3 and 3.2 $\mu\text{g/L}$
TEST DATES:	Experimental Start - April 4, 1997 Biological Termination - April 6, 1997 Experimental Termination - April 10, 1997
LENGTH OF TEST:	48 Hours

TEST ORGANISM:	Neonate Cladocerans (<i>Daphnia magna</i>)
SOURCE OF TEST ORGANISMS:	Wildlife International Ltd. cultures Easton, Maryland 21601
AGE OF TEST ORGANISMS:	< 24 hours at test initiation

48-HOUR EC50:	>6.8 $\mu\text{g/L}$ (nominal) (3.2 $\mu\text{g/L}$ mean measured concentration) (2 x HBCD's water solubility of 3.4 $\mu\text{g/L}$)
NO MORTALITY/IMMOBILITY CONCENTRATION:	6.8 $\mu\text{g/L}$ (nominal) (3.2 $\mu\text{g/L}$ mean measured concentration) (2 x HBCD's water solubility of 3.4 $\mu\text{g/L}$)
NO-OBSERVED-EFFECT-CONCENTRATION:	6.8 $\mu\text{g/L}$ (nominal) (3.2 $\mu\text{g/L}$ mean measured concentration) (2 x HBCD's water solubility of 3.4 $\mu\text{g/L}$)

HEXABROMOCYCLODODECANE (HBCD):
DETERMINATION OF n-OCTANOL/WATER PARTITION COEFFICIENT

WILDLIFE INTERNATIONAL LTD. PROJECT NUMBER: 439C-104

OPPTS 830.7560 Partition Coefficient (n-Octanol/Water),
Generator Column Method

AUTHORS:

Jon A. MacGregor
Willard B. Nixon, Ph.D.

STUDY INITIATION DATE: March 11, 1997

STUDY COMPLETION DATE: May 23, 1997

Submitted to:

Chemical Manufacturers Association's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, Virginia 22209



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Easton, Maryland 21601
(410) 822-8600



SUMMARY

SPONSOR:	Chemical Manufacturers Association's Brominated Flame Retardant Industry Panel
SPONSOR'S REPRESENTATIVE:	Hasmukh Shah, Ph.D.
LOCATION OF STUDY, RAW DATA AND A COPY OF THE FINAL REPORT:	Wildlife International Ltd. Easton, Maryland 21601

WILDLIFE INTERNATIONAL LTD.	
PROJECT NUMBER:	439C-104
TEST SUBSTANCE:	Hexabromocyclododecane (HBCD)
STUDY:	Hexabromocyclododecane (HBCD): Determination of the n-Octanol/Water Partition Coefficient
TEST DATES:	Experimental Start - March 11, 1997 Experimental Termination - March 18, 1997

SUMMARY:	The \log_{10} octanol/water partition coefficient (K_{ow}) of HBCD was determined to be 5.625 at $25 \pm 0.05^\circ\text{C}$ using the generator column method.
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HEXABROMOCYCLODODECANE (HBCD): CLOSED BOTTLE TEST

WILDLIFE INTERNATIONAL LTD. PROJECT NO.: 439E-102

AUTHORS:
Edward C. Schaefer
Doug Haberlein

STUDY INITIATION DATE: June 11, 1996

STUDY COMPLETION DATE: November 11, 1996

Submitted to

Chemical Manufactures Association's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, Virginia 22209



WILDLIFE INTERNATIONAL LTD.
8598 Commerce Drive
Easton, Maryland 21601
(410) 822-8600



SUMMARY

SPONSOR:	Chemical Manufacturers Association's Brominated Flame Retardant Industry Panel
CONTACT:	Hasmukh Shah, Ph.D.
LOCATION OF STUDY, RAW DATA AND A COPY OF THE FINAL REPORT:	Wildlife International Ltd. Easton, MD 21601

WILDLIFE INTERNATIONAL LTD.	
PROJECT NUMBER:	439E-102
STUDY:	Hexabromocyclododecane (HBCD): Closed Bottle Test
TEST CONCENTRATION:	7.7 mg/L
TEST DATES:	Experimental Start - June 18, 1996 Experimental Termination - July 16, 1996
LENGTH OF EXPERIMENTAL PHASE:	28 Days

TEST SUBSTANCE:	PERCENT BIODEGRADATION:
Hexabromocyclododecane (HBCD)	0.0

SAYTEX® 8010:
SUMMARIES OF UNPUBLISHED STUDIES

1403234-N12-2

PHARMAKON RESEARCH INTERNATIONAL, INC.
WAVERLY, PENNSYLVANIA 18471

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Acute Exposure Oral Toxicity

[Handwritten symbols]

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SEP 29 1988

HEALTH & ENVIRONMENT
INFORMATION CENTER

Submitted to

Ethyl Corporation
Baton Rouge, Louisiana

[Signature]
Victor T. Mallory, B.S., PLAT
Study Director

[Signature]
Date September 14, 1988

[Signature]
Richard S. Matthews
Test Facility Management

[Signature]
Date September 9, 1988

Acute Exposure Oral Toxicity

[]
In a Limit Test, test article, []
was orally administered to one group of ten animals at a single dose level of
5000 mg/kg. No signs were observed during the study. None of the animals
died at the 5000 mg/kg dose level. No visible lesions were observed in any
animal upon terminal necropsy.

Based upon the results from the Acute Exposure Oral Toxicity Study, the
estimated acute oral LD₅₀ for [] was
determined to be greater than 5000 mg/kg.

3234 A

PHARMAKON RESEARCH INTERNATIONAL, INC.
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Primary Eye Irritation



Submitted to

Ethyl Corporation
Baton Rouge, Louisiana

Victor T. Mallory
Victor T. Mallory, B.S., RLAT
Study Director

August 26, 1988
Date

Richard W. Mattheis
Test Facility Management

August 25, 1988
Date

3201 110 ✓

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Primary Dermal Irritation Study in Rabbits



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Submitted to

Ethyl Corporation
Baton Rouge, Louisiana

Victor T. Mallory
Victor T. Mallory, B.S., RLAT
Study Director

August 27, 1988
Date

Richard Vitellano
Test Facility Management

August 27, 1988
Date

Primary Dermal Irritation Study in Rabbits

[]
SUMMARY

In order to assess the dermal irritant and/or corrosive effects on the skin of rabbits, [] was applied to one intact skin site on each of six rabbits (three males and three females). No signs of erythema or edema were observed during the study. The study was terminated following the 72 hour observation period.

Based upon the results of the Primary Dermal Irritation Study in Rabbits, [] was determined not to be a dermal irritant.

~~FILED~~
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TK03234-NB-2

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Acute Exposure Dermal Toxicity

[] }
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SEP 29 1988

HEALTH & ENVIRONMENT
INFORMATION CENTER

Submitted to

Ethyl Corporation
Baton Rouge, Louisiana

Victor T. Mallory
Victor T. Mallory, B.S., RLAT
Study Director

September 14, 1988
Date

Richard J. Matthews
Test Facility Management

September 24, 1988
Date

Acute Exposure Dermal Toxicity/Rabbit

SUMMARY

In a 2000 mg/kg Limit Test, ten rabbits (five males and five females) were dermally administered [] Diarrhea was observed in one animal during the study. No other signs were observed through the study. None of the animals died during the course of the study. No visible lesions were observed in any animal at terminal necropsy.

Based upon the observations made in the Acute Exposure Dermal Toxicity Study in Rabbits, the estimated dermal LD₅₀ for [] was determined to be greater than 2000 mg/kg.

PHARMAKON RESEARCH INTERNATIONAL, INC.
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28 Day Oral Toxicity Study in Rats

Handwritten initials or marks, possibly "C" and "M".

Submitted to:

Ethyl Corporation
Baton Rouge, Louisiana

Dennis J. Margitich
Dennis J. Margitich, B.S., RLAT
Study Director

6/19/91
Date

Alvin B. Cizala
Test Facility Management

6/19/91
Date

28 Day Oral Toxicity Study - Rat

SUMMARY

The test article Saytex [] Flame Retardant, [] was administered orally by gavage in corn oil to four groups of rats at dose levels of 0 (control, n=12/sex), 125 (low, n=6/sex), 400 (mid, n=6/sex) and 1250 (high, n=12/sex) mg/kg seven days per week for 28 days. At the end of the 28 day treatment period all animals in the low and mid dose groups and six randomly selected rats/sex in the control and high dose groups were sacrificed. The remaining rats in the control and high dose groups were continued on test untreated for a 14 day recovery period prior to sacrifice.

Animals were observed daily throughout the study and any clinical signs were recorded. Body weights and food consumption were measured weekly. Blood was collected at each sacrifice for hematology and serum chemistry measurements. Urine was collected prior to each sacrifice for urinalysis. Ocular exams were performed prior to study initiation and each termination. All animals were necropsied and the liver, brain, spleen, thymus, kidneys, adrenals and gonads weighed. Approximately 40 organs or tissues/animal were collected and preserved. Paraffin sections of selected tissues from the control and high dose groups were examined under the light microscope. Statistical comparisons by sex and treatment day were made between the control and treated animals where indicated ($p \leq 0.05$).

No rats died prior to scheduled sacrifice. Clinical signs were non-specific, low in incidence, non-dose-related and not related to test article administration. No test-article-related ocular lesions were detected on ophthalmic exam.

No statistically significant differences were observed at any time point in mean body weight, body weight gain or food consumption between the control and low, mid and high dose groups or between the recovery control and recovery high dose groups. Body weight, body weight gain and food consumption of the treated and recovery animals were compared statistically by sex and treatment day to their respective control groups ($p \leq 0.05$).

No biologically or toxicologically significant differences in hematology and serum chemistry values were observed between the control and treated groups. A few scattered instances of non-dose-related statistically significant differences were detected between control and treated animals ($p \leq 0.05$). These changes are not considered biologically or toxicologically significant because the statistical differences occurred without pattern, were non-dose-related and occurred in animals which exhibited no evidence of toxicity.

No biologically or toxicologically significant differences in quantitative or qualitative urinalysis parameters were observed between the control and treated groups. A single statistically significant difference (a decrease in urine specific gravity, $p \leq 0.05$) between the female high dose recovery and control recovery

28 Day Oral Toxicity Study - Rat

SUMMARY (continued)

groups was detected in urine collected at the recovery group sacrifice. All other quantitative urinalysis parameters in the treated groups were statistically comparable to the control values.

No gross lesions attributable to the test article or vehicle control were detected at either sacrifice. No biologically or toxicologically significant differences in absolute organ weight, organ to body weight or organ to brain weight were found at either sacrifice between treated and control groups. No statistical differences in organ weights of treated animals compared to control animals were found with the exception of an increase in the liver to body weight ratio (female high dose on day 28) and a decrease in the thymus to brain weight ratio (male high dose recovery group on Day 42, $p \leq 0.05$). These differences were coincidental and, in the absence of any lesions detected by light microscopy, are not considered related to the administration of test article.

No treatment-related microscopic changes were found in any of the tissues evaluated from rats in the high dose group (adrenals, heart, kidneys, liver, mesenteric lymph node, parathyroids, spleen, and thyroid). A few spontaneous and incidental findings occurred in the vehicle controls and rats receiving the high dose. These were of the usual number, type and frequency observed in this age and strain of rats.

The no-observed-effect level following the administration of Saytex Flame Retardant to rats for 28 days was ≥ 1250 mg/kg/day. This is based on the absence of toxicity at this dose level as measured by: body weight, food consumption, body weight gain, hematology and serum chemistry values, urinalysis, ocular exam, gross necropsy results, organ weight, and light microscopic exam of selected tissues.

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Subchronic 90 Day Oral Toxicity Study in Rats

[]
Saytex []
[]

Submitted to:

Ethyl Corporation
Baton Rouge, Louisiana

Dennis J. Margitich
Dennis J. Margitich, B.S., RLAT
Study Director

9/1/92
Date

J.M. Morgan
Test Facility Management

9/1/92
Date

022792

Subchronic 90 Day Oral Toxicity Study in Rats

SUMMARY

The test article, Saytex [] Flame Retardant, [] was administered orally by gavage once daily in corn oil to four groups of rats at dose levels of 0 (control, n=20/sex), 100 (low, n=10/sex), 320 (mid, n=10/sex) and 1000 (high, n=20/sex) mg/kg/day seven days per week for 90 days. At the end of the 90 day treatment period all animals in the low and mid dose groups and ten randomly selected rats/sex in the control and high dose groups were sacrificed. The remaining rats in the control and high dose groups continued on test untreated for a 28 day recovery period prior to sacrifice.

Animals were observed daily throughout the study and clinical signs were recorded. Body weights and food consumption were measured weekly. Blood was collected on approximately Day 30 and at each sacrifice for hematology and serum chemistry measurements. Urine was collected prior to each sacrifice for urinalysis. Ocular exams were performed prior to study initiation and prior to each sacrifice. Approximately 40 organs or tissues/animal were collected and preserved. Paraffin sections of selected tissues from the control and high dose groups and the kidneys, liver, lungs and gross lesions from all animals were examined under the light microscope. Statistical comparisons by sex and treatment day were made between the control and treated animals where indicated ($p \leq 0.05$).

No rats died prior to scheduled sacrifice. Clinical signs were non-specific, low in incidence, non-dose-related and not related to test article administration. No test-article-related ocular lesions were detected on ophthalmic exam.

Throughout the study, mean male body weights in the low and high dose groups tended to be greater than the control male body weight mean. Statistical significance was reached in several instances ($p \leq 0.05$). Mean body weight of the male high dose group was statistically greater than the control mean on study Days 42, 77 and 84. The mean body weights of high dose males were 452.4, 534.0, and 547.7 g on Days 42, 77 and 84 vs control means of 425.1, 500.9, and 513.2 g, respectively. A statistical increase in the mean body weight of low dose males compared to the control value was also found on Days 63, 70, 77 and 84. The mean body weights of low dose males on these days were 514.8, 528.7, 541.2, 555.5 vs control means of 474.6, 483.4, 500.9, and 513.2 g, respectively.

Mean female body weights in all treated groups were statistically comparable to the control mean throughout the treatment period. On recovery Days 91, 105, 112 and 118, the

Subchronic 90 Day Oral Toxicity Study in Rats

SUMMARY (continued)

female high dose recovery group mean body weight was statistically lower than the female control mean body weight. The mean body weight of the female high dose recovery group was 278.3, 279.9, 280.8, 288.5, and 288.1 g vs 298.3, 299.2, 307.2, 311.4, and 308.8 g in the control females on Days 91, 98, 105, 112 and 118, respectively. These statistical differences in female body weight were considered coincidental as they occurred during the recovery period without treatment in animals with no evidence of toxic effects (clinical chemistry, histomorphometry).

Daily weight gain between treated and control animals was statistically comparable except in a few instances ($p \leq 0.05$). Mean daily weight gain was statistically greater than control weight gain in mid and high dose males on study Days 42 (mid) and 7 and 42 (high). Female daily weight gain in the treated groups was comparable to control weight gain throughout the majority of the study. On Days 14, 35, 42 and 105, mean daily weight gain in the high dose female group was statistically less than the control mean.

Mean food consumption of control and treated animals was generally statistically comparable throughout the study; statistical increases in food consumption were found in the high dose males on study Days 7, 28, 42, 56, 70, 77, 84 and 118 ($p \leq 0.05$). No significant differences were found in food consumption between treated and control females.

A few scattered instances of statistically significant differences in hematology or serum chemistry values were detected between control and treated animals ($p \leq 0.05$). These statistical differences did not appear to be of clinical significance as the changes occurred in otherwise healthy animals, were not correlated with histologic or gross lesions, did not persist during the recovery period, occurred in only one sex and/or were not dose-related.

No treatment-related effect was found on urinalysis (specific gravity, ph, color, transparency, protein, glucose, ketone, bilirubin, blood).

No statistical differences in organ weights were found between male control and treated animals ($p < 0.05$). A statistical difference in absolute liver weight was found between female high (8.41 g) and control (7.43 g) groups on Day 91. No statistical differences in organ weights were found between female groups on Day 119.

The relative organ to body weight ratio was 2.91 in the control males for liver and 3.14 in the high dose males for liver on Day 91. This difference was statistically significant ($p < 0.05$). In females on Day 91, the relative

Subchronic 90 Day Oral Toxicity Study in Rats

SUMMARY (continued)

organ to body weight ratio was 2.65 in the control group for liver and 2.92 in the high dose group. This difference was also statistically significant ($p < 0.01$). There were no statistical differences between control and treated animals of both sexes for other organ to body weight ratios on Day 91. Similarly, no statistical differences in relative organ to body weight ratios were found between control and high dose groups of both sexes on Day 119.

Gross necropsy observations were low in incidence. Only minor changes were found on histopathological exam. Findings in treated animals included low grade liver changes in the high, and possibly mid, dose male rats. No treatment-related changes were found in the liver of female rats. The liver changes were characterized by minimal to slight hepatocellular vacuolation (high dose males) and minimal to slight centrilobular hepatocytomegaly (high and possibly mid dose males). By the end of the 28-day recovery period, the liver changes had resolved without any delayed or long term toxic effects. Histologic evidence of aspirated test article was found in individual mid and high dose rats. No-treatment-related histomorphologic changes were present in any of the other tissues examined in either sex.

CONCLUSIONS

Based on the results of the Subchronic 90 Day Oral Toxicity Study in Rats with Saytex [] Flame Retardant [] dose levels of 0, 100, 320 and 1000 mg/kg/day, produced no compound-related clinical signs of systemic toxicity, ocular lesions, or alterations in urinalysis, clinical chemistry and hematology values in the treated or recovery groups. No biologically or toxicologically significant differences were observed in body weights, body weight gains and food consumption. Statistically significant differences were found between control and high dose animals in mean liver absolute or relative organ weights. Histomorphological evaluation revealed an increased incidence of low grade liver changes in male rats consisting of minimal to slight hepatocellular vacuolation (high dose males) and minimal to slight centrilobular hepatocytomegaly (high and

Subchronic 90 Day Oral Toxicity Study in Rats

[]
SUMMARY (continued)

possibly mid dose males). By the end of the 28-day recovery period, the liver changes had resolved without any delayed or long term toxic effects. No treatment-related changes were found in the livers of female rats. Histologic evidence of aspirated test article was found in individual mid and high dose rats. No treatment-related histomorphologic changes were present in any of the other tissues examined in either sex.

SUMMARY

This study was performed to detect and evaluate the potential embryotoxic or teratogenic effects of Saytex[®] when administered orally to pregnant rats during the period of major organogenesis. The study design consisted of a vehicle control and three treatment groups. Each group contained twenty-five mated female Sprague-Dawley rats. The test article was suspended in corn oil and administered at dosage levels of 125, 400 and 1250 mg/kg/day from gestation day 6 through gestation day 15. All doses were given at a constant volume of 5 ml/kg. Control animals were administered corn oil under the same experimental conditions and at an equivalent dose volume. The animals were observed daily for clinical signs of toxicity. Body weights and food consumption were measured on gestation days 0, 6, 9, 12, 16 and 20. All females were sacrificed on gestation day 20 and subjected to cesarean section. Fetuses were individually weighed, sexed and examined for external, visceral and skeletal abnormalities.

No maternal mortality or clinical signs of toxicity were observed during the study. No treatment-related differences were noted among the groups with respect to maternal body weights, food consumption, necropsy or cesarean section data. In addition, no treatment-induced malformations or developmental variations occurred in the study.

Based on the results of this study, no evidence of maternal or developmental toxicity or teratogenicity was observed in rats treated with Saytex[®] at dosage levels up to 1250 mg/kg/day.

DEVELOPMENTAL TOXICITY (TERATOLOGY)
STUDY IN RABBITS WITH SAYTEX® []

FINAL REPORT

Author

Michael D. Mercieca, B.S.

Study Completed on

June 24, 1992

Performing Laboratory

Springborn Laboratories, Inc. (SLS)
Life Sciences Division
553 North Broadway
Spencerville, OH 45887

SLS Study No.

[]

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JUN 25 1992

Submitted to:

**HEALTH & ENVIRONMENT
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Ethyl Corporation
Ethyl Tower
451 Florida
Baton Rouge, LA 70801

Page 1 of 225

Springborn
Laboratories

SUMMARY

This study was performed to detect and evaluate the potential embryotoxic or teratogenic effects of Saytex[®] when administered orally to pregnant rabbits during the period of major organogenesis. The study design consisted of a vehicle control and three treatment groups. Each group contained twenty artificially inseminated female New Zealand White rabbits. The test article was suspended in 0.5% methylcellulose and administered at dosage levels of 125, 400 and 1250 mg/kg/day on gestation day 6 through gestation day 18. All doses were given at a constant volume of 2 ml/kg. Control animals were administered 0.5% methylcellulose under the same experimental conditions and at an equivalent dose volume. The animals were observed daily for clinical signs of toxicity. Body weights were recorded on gestation days 0, 6, 9, 12, 15, 19, 24 and 29 and food consumption was measured daily. Surviving animals were sacrificed on gestation day 29 and subjected to cesarean section. Fetuses were weighed individually, sexed and examined for external, visceral and skeletal abnormalities.

No treatment-related mortality, abortions or clinical signs of toxicity were observed during the study. Maternal body weights, weight gain, food consumption, necropsy observations and cesarean section data were generally comparable among the groups. No treatment-related malformations or developmental variations were observed.

Based on the results of the study, no evidence of maternal toxicity, developmental toxicity or teratogenicity was observed in rabbits treated with Saytex[®] at dosage levels up to 1250 mg/kg/day on gestational days 6-18.

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Ames/Salmonella Plate
Incorporation Assay

[] []
[] []
[] []

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AUG - 5 1988

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Submitted to

Ethyl Corporation
Baton Rouge, Louisiana

Leon F. Stankowski, Jr.
Leon F. Stankowski, Jr., Ph.D.
Study Director

10 August 1988
Date

Shirley Matthews
Test Facility Management

August 10, 1988
Date

Ames/Salmonella Plate Incorporation Assay

SUMMARY

[] was evaluated in the Ames/Salmonella Plate Incorporation Assay to determine its ability to induce reverse mutations at selected histidine loci in five tester strains of Salmonella typhimurium in the presence and absence of an exogenous metabolic activation system (S9). Toxicity of [] was first evaluated in a prescreen by treating duplicate cultures of strains TA1538 and TA100 with five doses of [] in the absence of S9. Results of the prescreen indicated [] was not toxic to either strain at doses of 50.0, 167, 500, 1670 and 5000 ug/plate. However, the test article was found to precipitate from solution at doses ≥ 167 ug/plate.

Based upon these findings, [] was evaluated in triplicate cultures in strains TA1535, TA1537, TA1538, TA98 and TA100 in the presence and absence of S9 at doses of 50.0, 167, 500, 1670, 3330 and 5000 ug/plate. Six dose levels of [] were evaluated with and without S9 in the event of unacceptably high toxicity and/or precipitation at the highest dose level. The S9 mixture included 6% (v/v) Aroclor 1254-induced male Sprague-Dawley rat liver homogenate with the appropriate buffer and cofactors. The test article was again found to precipitate at doses ≥ 167 ug/plate. Revertant frequencies for all doses of [] in all strains approximated or were less than those observed in the concurrent negative control cultures. All positive and negative control values were within acceptable limits.

Therefore, the results for [] were negative in the Ames/Salmonella Plate Incorporation Assay under the conditions, and according to the criteria, of the test protocol.

3234



**MICROBIOLOGICAL
ASSOCIATES, INC.**

Life Sciences Center
9900 Blackwell Road • Rockville • Maryland 20850
(301) 738-1000 • Fax (301) 738-1036

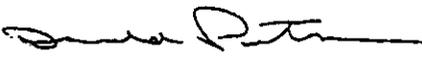
March 9, 1992

Marcia Hardy, D.V.M., Ph.D.
Ethyl Corporation
451 Florida Street
Baton Rouge, LA 70801

Dear Dr. Hardy:

This letter will verify that MA study [Chromosome Aberrations in Chinese Hamster Lung (CHL) Cells using your test article Saytex® was indeed performed using CHL cells. Any reference in earlier reports to CHO cells or to F-12 medium used to support growth of the-test system was in error. These errors have been corrected by final report amendments.

Should you need any additional information, please feel free to contact me.

Sincerely,

Donald L. Putman, Ph.D.
Study Director

SUMMARY

The test article, Saytex® [] was tested in the chromosome aberration assay using Chinese hamster lung cells. The test system was exposed to Saytex® [] for 24 and 48 hours in the absence of an exogenous source of metabolic activation and for 6 hours both in the absence and presence of an S-9 reaction mixture. Metaphase cells were collected for microscopic evaluation immediately after the 24 and 48 hour treatments and at 18 hours after the completion of the 6 hour pulse treatments.

The initial assay was conducted both in the absence and presence of an Aroclor-induced S-9 activation system at dose levels of 78.5, 157, 313 and 625 ug/ml. Dose selection was limited due to excessive test article precipitation which interfered with the analysis of metaphase cells at dose levels exceeding 625 ug/ml. Precipitation was evident at test concentration 625 ug/ml, but a sufficient number of unobscured metaphase spreads were obtained for the evaluation of structural and numerical chromosome aberrations. Toxicity at the highest test concentration was measured by cell growth inhibition and was approximately 13% in the 6 hour non-activated treatment; 52% in the 24 and 48 hour non-activated treatments; and 33% in the 6 hour S-9 activated treatment. No significant increase in structural or numerical chromosome aberrations was observed in either the non-activated or S-9 activated test system regardless of the length of exposure.

In order to test up to 5000 ug/ml, a repeat assay was conducted using the following changes in procedure to minimize test article precipitate interference with microscopic analysis: the test article was suspended in 1% carboxymethyl cellulose and the treatment medium was washed off at the time of Colcemid treatment. The repeat assay was conducted both in the absence and presence of an Aroclor-induced S-9 activation system at dose levels of 625, 1250, 2500 and 5000 ug/ml. Test article precipitation was evident at all concentrations tested, but a sufficient number of unobscured metaphase spreads were obtained for the evaluation of structural and numerical chromosome aberrations at all dose levels for the 6 hour pulse treatments and the 24 hour non-activated treatment. Test article precipitation obscured many metaphase cells located for evaluation and, thereby, limited the number scored at dose levels 2500 and 5000 ug/ml in the 48 hour non-activated treatment. Toxicity at the highest test concentration evaluated for chromosome aberrations was measured by cell growth inhibition and was approximately 49% in the 6 hour non-activated treatment; 34% in the 24 hour non-activated treatment; 47% in the 48 hour non-activated treatment; and 27% in the 6 hour S-9 activated treatment. No significant increase in structural or numerical chromosome aberrations was observed in either the non-activated or S-9 activated test system regardless of the length of exposure. Saytex® [] was concluded to be negative in the CHL cytogenetics assay.

AMENDED FINAL REPORT

Study Title

SALMONELLA/MAMMALIAN-MICROSOME PLATE INCORPORATION
MUTAGENICITY ASSAY (AMES TEST) AND ESCHERICHIA COLI WP2 uvrA
REVERSE MUTATION ASSAY

Test Article

Saytex® []

Authors

Richard H.C. Sah, Ph.D.
Valentine O. Wagner, III, M.S.

Study Report Date

12/19/91

Performing Laboratory

Microbiological Associates, Inc.
9900 Blackwell Road
Rockville, MD 20850

Laboratory Study Number

[]

Submitted To

Ethyl Corporation
451 Florida Blvd.
Baton Rouge, LA 70801

Page 1 of 68

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ASSOCIATES, INC.

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FEB 15 1991

**TOXICOLOGY & REGULATORY
AFFAIRS**

Accepted number	
Test number	

FINAL REPORT

Test on biodegradability of SAYTEX- by microorganisms.

FILE COPY

Kurume Research Laboratories
Chemical Biotesting Center
Chemicals Inspection & Testing Institute, Japan

SUMMARY

1. Title of the test

Test on biodegradability of SAYTEX- by microorganisms.

2. Biodegradability test

2.1 Test conditions

(1) Concentration of test substance	100 mg/L
(2) Concentration of activated sludge (as the concentration of suspended solid)	30 mg/L
(3) Volume of test solution	300 mL
(4) Cultivating temperature	25±1 °C
(5) Cultivating duration	28 days

2.2 Measurement and analysis

- (1) Measurement of biochemical oxygen demand (BOD) by closed system oxygen consumption measuring apparatus
- (2) Measurement of the test substance by weighing

3. Test results

(1) Percentage biodegradation by BOD	1 %, 0 %, 0 %	mean 0 %
(2) Percentage biodegradation by weighing	6 %, 0 %, 1 %	mean 2 %

4. Stability of the test substance

It was confirmed that the test substance was stable under the storage condition.

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**TOXICOLOGY & REGULATORY
AFFAIRS**

Accepted number	C 3
Test number	[]

FINAL REPORT

Test on bioaccumulation of SAYTEX- [] in carp.

FILE COPY

Kurume Research Laboratories
Chemical Biotesting Center
Chemicals Inspection & Testing Institute, Japan

SUMMARY

1. Title of the test

Test on bioaccumulation of SAYTEX-[] in carp.

2. Test conditions

2.1 Acute toxicity test

(1) Test fish	Orange-red killifish (<u>Oryzias latipes</u>)
(2) Duration of exposure	48 hrs
(3) Exposing method	Semi static system (Renewal of test water, at every 8~16 hrs)

2.2 Bioaccumulation test

(1) Test fish	Carp (<u>Cyprinus carpio</u>)
(2) Exposing level	Level 1 0.5 mg/L Level 2 0.05 mg/L
(3) Duration of exposure	8 weeks
(4) Exposing method	Continuous flow system
(5) Analytical method	Ion chromatography

3. Test results

(1) 48-hr LC50 value	>50.0 mg/L
(2) Bioconcentration factor	Level 1 <2.5 Level 2 <25 ~ 34

4. Stability of the test substance

It was confirmed that the test substance was stable under the storage and testing circumstances.

SMOKE TOXICITY AND THE INFLUENCE OF FLAME RETARDANTS

Marcia L. Hardy, D.V.M., Ph.D.
Albemarle Corporation
Baton Rouge, LA

AFIRE'S PROGRESSION. A fire begins with the ignition of combustible matter; a match ignites discarded paper in a waste basket, for example. This initially small fire generates heat that ignites nearby objects, perhaps curtains. The heat builds and radiates, spreads the fire to surrounding objects, (chairs and carpeting), and evolves a mix of flammable gases. The flammable gas mixture ignites and spreads the fire over the entire room almost instantaneously. Called "flashover", this is the point where the fire's extremely hot atmosphere causes all combustible matter in the room to burst into flame simultaneously. Flashover typically occurs very rapidly after the fire's ignition and can happen in as little as 3-7 minutes. Once flashover occurs, the fire is fully developed, the room temperature exceeds 1000 degrees C, and the fire spreads to adjacent rooms until it peaks. The fire then diminishes.

CAUSE OF FIRE DEATHS. Most fire deaths are not due to burns, a fact not widely recognized outside the fire safety field. Most fire deaths in the U.S. are due to smoke inhalation and the majority of smoke inhalation deaths are due primarily or entirely to carbon monoxide (CO) poisoning (*J. Hall, "Burns, Toxic Gases, and Other Hazards Associated with Fires: Deaths and Injuries in Fire and Non-Fire Situations, NFPA, Quincy, MA, December 1996; G. Nelson, "Carbon Monoxide and Fire Toxicity", BCC Conference on Fire Retardancy, 1995*). Most U.S. fire victims die in post- flashover fires where the role of CO in fire hazard is maximized and the role of HCN and other gases is less than predicted by bench scale tests (*G. Nelson, BCC Conference on Fire Retardancy, 1995*).

CO is produced when any substance burns, whether flame retarded or not. The amount of CO produced is determined by the rate of heat release from the burning material. Faster burning materials have a greater rate of heat release and generate more CO than slower burning materials.

A review of almost 5,000 fire fatalities found (*Debanene et al. 1992 and Hirschler et al. 1993, as reported by Hirschler in "Smoke Toxicity How Important is it for Fire Safety?", BCC Conference on Flame Retardancy, 1995*):

- The toxicity of fire atmospheres was determined almost solely by the amount of CO evolved.
- Blood carboxyhemoglobin (COHb) values > 20 % may be lethal depending on the age and physical condition of the victim. The lethal CO threshold was previously thought to be 50% COHb.
- Victims of fire and non-fire CO exposures were different. Fire victims were much older, much younger, and/or suffering from more preexisting disease than non-fire-CO victims. Thus, fire victims were more sensitive to CO poisoning than those in non-fire CO exposures.
- A comparison of fire fatalities before and after the plastics era indicated the use of

man-made materials in household goods made no difference to fire atmosphere toxicity.

FIRE VICTIMS. Fire victims tend to be the very old, the very young or the infirm (C. Conley and R. Fahu, "Who dies in Fires in the United States?", *NFPA Journal*, May/June 1994, 99-106). In home fires, the death rate of preschool children age 5 and under is more than twice the national average. Adults age 65 and older die in home fires at a rate twice the national average. Those age 75 and older die at a rate almost three times the national average. And those over age 85 die at four times the national average.

FIRES INVOLVING FLAME RETARDED VS NON-FLAME RETARDED MATERIALS. It has been speculated that toxicity of smoke involving flame retarded materials is of greater hazard than that of non-flame retarded materials. This speculation is not borne out by research, however. Research has demonstrated that a fire's toxic hazard is determined primarily by its burning rate.

The U.S. National Institute of Standards and Technology (NIST) tested five product categories in full-scale room fires (Brabrauskas et al., *Fire Hazard Comparison of Fire-Retarded and Non-Fire-Retarded Products*, NBS Special Publication 749, National Bureau of Standards, Gaithersburg, MD, 1988). The results showed a fire's toxic hazard is a direct function of the fire's rate of heat release. Fire retarded polymers were compared to the same base polymers without fire retardants. The fire retarded polymers had a 4-fold decrease in rate of heat release, a three-fold decrease in smoke toxicity, and a 10-fold increase in tenability time. Considerable improvement in toxicity was obtained by a decrease in the rate of heat release. The decrease in toxicity was almost irrespective of the actual toxic potency of the materials/products involved.

Morikawa et al. ("*Toxicity of Gases from Full-Scale Room Fires Involving Fire Retardant Contents*", *Journal of Fire Sciences*, Vol 13, 1995, page 23-42) studied the toxicity of gases from full-scale room fires involving fire retarded contents. He found that "There was no case where fires involving fire retardant materials were more dangerous in toxicity than those of non-fire retardant ones." In this study, fire experiments were conducted in a 2 story fire resistant house using one of the first floors as the burn room with various fire retardant or non-fire retardant items. The toxicity of the fire effluents was determined both by chemical analysis and bioassay techniques. Hydrogen cyanide (HCN) and CO were the two major toxicants. The hydrogen chloride (HCL) level was generally and unexpectedly low in terms of toxicity. Calculated incapacitation times were in roughly good agreement with the actual incapacitation times for rabbits when the toxicants were limited to HCN and CO.

FIRES INVOLVING PRODUCTS FLAME RETARDED WITH BROMINATED FLAME RETARDANTS (BFRs). Speculation has also arisen about the potential role of hydrogen bromide (HBr) which may be produced when substances containing brominated flame retardants burn. Research has shown that any HBr produced does not adversely influence the toxicity of smoke.

Cullis (1987) reported brominated flame retardants may produce HBr during a fire. HBr is believed to contribute to the brominated flame retardants mechanism of action and reacts with free radicals in the fire. Cullis further stated "In a fire situation, however, it is almost always toxic combustion gases, such as carbon monoxide and hydrogen cyanide (HCN), rather than irritants (*such as hydrogen bromide, explanatory comment added*) which cause rapid incapacitation. Indeed, due to its high reactivity, hydrogen bromide (HBr) is unlikely to reach dangerously high concentrations."

Claims that halogen-containing flame retardants increase both the quantity of smoke and its toxicity led Clarke to investigate the effect of brominated flame retardants on two aspects of fire hazard: smoke density and toxicity (F. Clarke, "The Life Safety Benefits of Brominated Flame Retardants in the United States" Prepared for the CMA Brominated Flame Retardant Industry Panel, April 1997). A careful examination of BFRs in fire revealed no evidence that BFRs adversely affected any aspect of fire hazard. Smoke density and toxicity were either reduced or unaffected by the brominated flame retardants. This study also found no evidence that of an increase in toxic smoke hazard due to HBr produced by BFR-treated material upon burning. HBr, a potential component of fire gasses when brominated flame retardants are present, did not contribute to the toxic hazard of full scale fires involving BFR-treated products. Previously-reported increases in CO cause by the flame retardant action of BFR's were found to be largely artifacts of small-scale smoke toxicity testing which disappear when real fires of any threatening size are considered.

Clarke found that the net overall effect of BFRs was a decrease in smoke hazard. BFRs reduced ignitability which in turn reduced flame spread. The reduction in flame spread reduced the fire's burning rate. The reduced burning rate reduced the quantity of smoke and CO produced.

The rate of heat release is critically important to fire hazard because the rate of heat release determines the amount of CO produced and CO is responsible for the majority of fire deaths. CO is generated when any substance burns whether the substance is flame retarded or not. The real risk to human life is the probability that a fire occurs at all with the subsequent endangerment of life from CO poisoning. Flame retardants diminish the likelihood of fire and with it, the major cause of fire deaths.

CONCLUSIONS. Research comparing the relative toxicity of the combustion products of flame retarded materials (slow burning) to nonflame retarded material (fast burning) demonstrates:

- The majority of fire deaths are due to carbon monoxide (CO) poisoning;
- Fire hazard is a function of several fire properties with the rate of heat release from the materials or products involved the most important;
- The importance of the rate of heat release in determining fire hazard exceeds that of smoke toxic potency; and
- Flame retarded materials do not produce more toxic combustion products than those which are not flame retarded.
- Flame retardants diminish the likelihood of fire and with it, the major cause of fire deaths.