Walter Cybulski/DC/USEPA/US
11/22/2006 09:01 AM

To NCIC HPV@EPA
cc
bcc
Subject Fw: Question on HPV Challenge Submission

---- Forwarded by Walter Cybulski/DC/USEPA/US on 11/20/2006 08:48 AM ----

"John P. Van Miller" <jvanmiller@toxregserv.com>

11/20/2006 08:22 AM

To Walter Cybulski/DC/USEPA/US@EPA
cc
Subject RE: Question on HPV Challenge Submission

Mr. Cybulski

Thank you very much for the assistance. The Chemical is **"2-Propanone, Reaction Products with Phenol (CAS RN 72162-28-8)"**. I have attached the submission as sent which includes the cover letter and the data. I received a delivery notice but no notice that the file was "read".

Again, many thanks for your assistance.

John

-----Original Message-----
From: Cybulski.Walter@epamail.epa.gov
[mailto:Cybulski.Walter@epamail.epa.gov]
Sent: Monday, November 20, 2006 8:15 AM
To: John P. Van Miller
Subject: Question on HPV Challenge Submission

Hello, Mr. Van Miller.

I received your voicemail with your question asking whether our document control office received a submission that you provided to the Agency on November, 15, on behalf of GE.

I can check items that have come through, and also check with the document control office. Can you tell me a little more information about the submission -- e.g., chemical/category it dealt with; CAS#(s) to which it pertained -- that may help me determine if they received that specific submission?

Thank you.

Walt Cybulski

Walter J. Cybulski III, Ph.D.
U.S. Environmental Protection Agency
Office of Pollution Prevention and Toxics
Chemical Control Division
EPA East -- Room 4410-G, Mail Code 7405M
1200 Penn Ave NW, Washington, DC 20460
Tel (202) 564-2409, Fax (202) 564-4775
cybulski.walter@epa.gov

----- Message from "John P. Van Miller" <jvanmiller@toxregserv.com> on Wed, 15 Nov 2006 16:27:03 -0500 -----

To: <oppt.ncic@epa.gov>, <chem.rtk@epa.gov>

cc: "Stephen Dimond \(stephen.dimond@ge.com\)" <stephen.dimond@gep.ge.com>

Please find the attached submission.

John


72162-28-8 BPA Tars Transmittal Letter Nov 15 06.pdf 72162-28-8 BPA Tars Test Plan November 15 2006.pdf

TRS
TOXICOLOGY/REGULATORY SERVICES, INC.

November 15, 2006

HPV Coordinator
US Environmental Protection Agency
PO Box 1473
Merrifield, VA 22116

Attention: Chemical Right-to-Know Program, AR-201

Re: Test Plan for 2-Popanone, Reaction Products with Phenol (CAS RN 72162-28-8)

Toxicology/Regulatory Services (TRS) is submitting the Test Plan/Robust Summaries on behalf of General Electric Plastics for 2-Popanone, Reaction Products with Phenol (CAS RN 72162-28-8) as notified in their commitment letter dated August 28, 2006. Please address any questions to:

Stephen S. Dimond
Staff Toxicologist
General Electric Company
One Plastics Avenue
Pittsfield, MA 01201
Phone: (603) 860-5056
EMAIL: stephen.dimond@ge.com

Thank you,

John P. Van Miller

Digitally signed by John P. Van Miller
DN: cn=John P. Van Miller, c=US, o=TRS, email=jvanmiller@toxregserv.com
Date: 2006.11.15 14:43:46 -05'00'

John P. Van Miller, Ph.D., DABT
Vice President/Principal
Toxicology/Regulatory Services, Inc.
Charlottesville, VA 22911
PH: 434-977-5957
EMAIL: jvanmiller@toxregserv.com

U.S. HIGH PRODUCTION VOLUME (HPV)

CHEMICAL CHALLENGE PROGRAM

ROBUST SUMMARY

2-Propanone, Reaction Products with Phenol (CAS RN 72162-28-8)

Prepared By:
General Electric Company
One Plastics Avenue
Pittsfield, MA 01201

Prepared for:
U.S. Environmental Protection Agency
Washington, D.C., USA

November 15, 2006

Table of Contents

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TEST PLAN

2-Propanone, Reaction Products with Phenol **CAS RN: 72162-28-8**		Information	OECD Study	GLP	Other Study	Estimation Method	Acceptable	SIDS Testing Required
STUDY		**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**
PHYSICAL AND CHEMICAL DATA								
1.0	Melting Point	Y	N	N	Y	N	Y	N
2.0	Boiling Point	Y	N	N	Y	N	Y	N
3.0	Vapor Pressure	Y	N	N	Y	N	Y	N
4.0	Partition Coefficient	Y	N	N	Y	N	Y	N
5.0	Water Solubility	N	N	N	N	N	N	Y
ENVIRONMENTAL FATE AND PATHWAY								
6.0	Photodegradation	Y	N	N	Y	Y	Y	N
7.0	Stability in Water	Y	Y	N	N	N	Y	N
8.0	Transport and Distribution	Y	N	N	Y	Y	Y	N
9.0	Biodegradation	N	N	N	N	N	N	Y
ECOTOXICITY								
10.0	Acute Toxicity to Fish	Y	Y	Y	N	N	Y	N*
11.0	Toxicity to Algae	Y	Y	Y	N	N	Y	N
12.0	Acute Toxicity to Daphnia	Y	Y	Y	N	N	Y	N
TOXICITY								
13.0	Acute Toxicity	Y	N	N	Y	N	Y	N
14.0	Genotoxicity *In Vitro or In Vivo* (Chromosome Aberration Test)	Y	N	N	N	N	Y	Y**
15.1	Genotoxicity *In Vitro* (Bacterial Test)	Y	N	N	N	N	Y	Y**
15.2	Genotoxicity *In Vitro* (Mammalian Cells)	Y	N	N	N	N	Y	Y**
16.0	Repeated Dose Toxicity	Y	N	N	Y	N	Y	N
17.0	Reproductive Toxicity	Y	Y	Y	N	N	Y	N
18.0	Developmental Toxicity / Teratogenicity	Y	N	Y	Y	N	Y	N

* As indicated below, a toxicity study in fish will be conducted if the water solubility study indicates measurable components of BPA Tars in solution.

** As indicated below, studies to verify lack of mutagenic activity will be conducted.

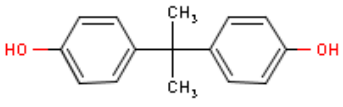
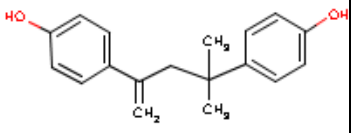
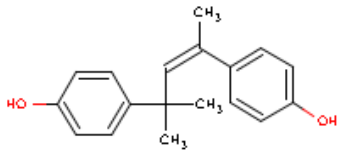
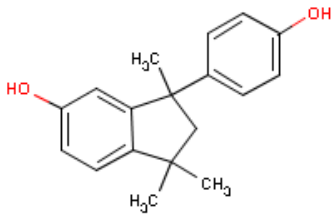
CHEMICAL IDENTITY AND DATA REVIEW

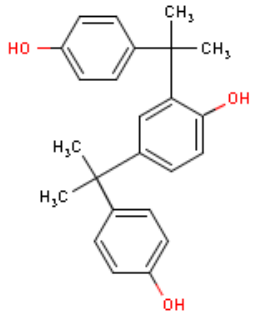
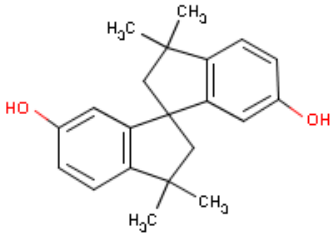
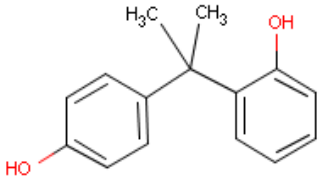
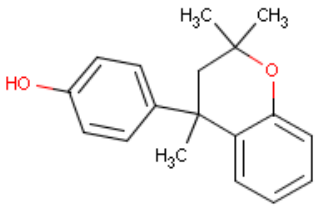
COMPONENTS

2-Propanone, Reaction Products with Phenol (hereafter called "BPA Tars") is a mixture of residual chemicals from the production of Bisphenol A. The table below includes the major components of BPA Tars along with a typical percentage for each component. Please note that the exact percentage of each component varies pending upon the process operating parameters.

CAS No.	Name	Category	Chemical Name	Percent
80-05-7	p,p-BPA	Bisphenol	4,4-(1-Methylethylidene)-Bisphenol	50
13464-24-9	Linear Dimer I	Bisphenol	4,4-(1,1,3-trimethyl-1,3-propenediyl)bisphenol	33
57244-54-9	Linear Dimer II	Bisphenol	4,4-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisphenol	
10527-11-4	Cyclic Dimer and Isomer of Cyclic Dimer	Bisphenol	2,3-dihydro-3-(4-hydroxyphenyl)1-1,3-trimethyl 1H-inden-5-ol	
2300-15-4	BPX-I - Linear Trimer of Isopropenyl Phenol and Isomers	Trisphenol	2,4-bis(1-(4-hydroxyphenyl)-1-methylethyl) phenol	4.5
287110-79-6	BPX-II and Isomers	Trisphenol	Acetone adduct of BPX-I	6.5
1568-80-5	Sprirobiindane and Isomers	Bisphenol	2,2',3,3'-Tetrahydro-3,3,3',3'-Tetramethyl-1,1'-Spirobi-1H-Indene-6,6'-Diol	3.5
837-08-1	o,p-BPA	Bisphenol	2,4-(1-Methylethylidene)-Bisphenol	< 0.1
472-41-3	Chroman I	Bisphenol	Phenol, 4-(3,4-dihydro-2,2,4-trimethyl-2H-1-benzopyran-4-yl)-	2.0
Not defined	High molecular weight unknowns	Bisphenol and Trisphenol	Not defined	0.5

STRUCTURE, MOLECULAR FORMULA, MOLECULAR WEIGHT

CAS No.	Chemical Name	Structure	Molecular Formula	Molecular Weight
80-05-7	4,4-(1-Methylethylidene)-Bisphenol		$C_{15}H_{16}O_2$	228.289
13464-24-9	4,4-(1,13-trimethyl-1,3-propenediyl)bisphenol		$C_{18}H_{20}O_2$	268.354
57244-54-9	4,4-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisphenol		$C_{18}H_{20}O_2$	268.354
10527-11-4	2,3-dihydro-3-(4-hydroxyphenyl)1-1,3-trimethyl 1H-inden-5-ol		$C_{18}H_{20}O_2$	268.354

CAS No.	Chemical Name	Structure	Molecular Formula	Molecular Weight
2300-15-4	2,4-bis(1-(4-hydroxyphenyl)-1-methylethyl) phenol		$C_{24}H_{26}O_3$	362.466
287110-79-6	Acetone adduct of BPX-I	No Structure Available	$C_{27}H_{30}O_3$	~ 402
1568-80-5	2,2',3,3'-Tetrahydro-3,3,3',3'-Tetramethyl-1,1'-Spirobi-1H-Indene-6,6'-Diol		$C_{21}H_{24}O_2$	308.419
837-08-1	2,4-(1-Methylethylidene)-Bisphenol		$C_{15}H_{16}O_2$	228.289
472-41-3	Phenol, 4-(3,4-dihydro-2,2,4-trimethyl-2H-1-benzopyran-4-yl)-		$C_{18}H_{20}O_2$	268.354

OVERVIEW

BPA Tars (CAS RN 72162-28-8) is a residual mixture resulting from the production of bisphenol A (p,p-BPA; CAS RN 80-05-7). NOTE: throughout this document, "BPA" refers to p,p-BPA. For the purposes of the HPV Chemical Challenge Program, an evaluation of toxicity and environmental fate and effects for this mixture is based on the known or predicted effects of BPA to make predictions about the effects of other substances with similar chemical structures in the mixture. BPA is chemically reactive, a requirement for its use in the production of polymers, and is the lowest molecular weight and highest percentage by weight component of BPA Tars. The other components of BPA Tars are higher molecular weight bisphenols and trisphenols that are expected to have similar or lower chemical and biological reactivity.

Based on the chemical nature of BPA Tars as noted above, the data for BPA is considered to define the toxicity of BPA Tars. BPA has been extensively evaluated in all HPV required studies for environmental and human health. A Risk Assessment, including review of more than 300 references, has been completed by the European Union and is available (European Chemicals Bureau, Existing Substances, 3rd Priority List, Volume 37, 2003). This review is used, herein, to support the data for BPA and BPA Tars.

USE PATTERN AND EXPOSURE

BPA Tars is sold to a limited number of companies in the US. In all cases, the end use is such that the product is expected to be ultimately and completely consumed in the manufacture of articles. No residual BPA, bisphenolics or trisphenolics are expected. The greatest potential risk to workers is associated with the high temperature at which the material is maintained while loading or unloading trucks, rather than any toxicity unique to the material. Thus, worker exposure must be managed through a combination of engineering and personal protective equipment (PPE) to prevent burns. The GE-established exposure limit of 3.5 mg/m^3 for BPA is enforced when BPA Tars is handled at room temperature as a solid.

Based on the use pattern and relatively limited distribution and the life cycle of BPA Tars is of short duration; therefore, only a few locations exist where environmental releases could occur. Releases to the air may occur during loading of trucks since the material is hot with potential loss via the vent pipe. However, based upon the low vapor pressure, even at this temperature (estimated to be less than 0.1 mm Hg) and with the transfer methods used, any releases to the atmosphere are expected to be very low.

Since residual monomers, dimers, etc. do not exist in final products, exposure to end users is essentially non-existent.

PHYSICAL/CHEMICAL PROPERTIES

MELTING POINT

As a result of the mixture of chemicals, BPA Tars has no defined melting point. Above 250°C, an exothermic decomposition begins with subsequent boiling. Measured or estimated melting points for various components are provided below.

CAS No.	Name	Melting Point*
80-05-7	BPA	150-157 °C
13464-24-9	Linear Dimer I	149.8 °C**
57244-54-9	Linear Dimer II	151.2 °C**
10527-11-4	Cyclic Dimer	164.2 °C**
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	215.3 °C**
287110-79-6	BPX-II	
1568-80-5	Spirobiindane	178.0 °C**
837-08-1	o,p-BPA	131.8 °C**
472-41-3	Chroman I	141.5 °C**

*Empty cells indicate that data are unavailable for that chemical/endpoint.
** Value obtained from the EPISuite Model.

Robust Summaries have been prepared for BPA and are included below. These data are considered adequate to meet the HPV Chemical Challenge requirements.

BOILING POINT

As a result of the mixture of chemicals, BPA Tars has no defined boiling point. Above 250°C, an exothermic decomposition begins with subsequent boiling. Measured or estimated boiling points for various components are provided below.

CAS No.	Name	Boiling Point*
80-05-7	BPA	250-252°C at 17 hPa; 360.5°C
13464-24-9	Linear Dimer I	394.3°C**
57244-54-9	Linear Dimer II	398.8°C**
10527-11-4	Cyclic Dimer	396.3°C**
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	505.7°C**
287110-79-6	BPX-II	
1568-80-5	Sprirobiindane	425.9°C**
837-08-1	o,p-BPA	363.5°C**
472-41-3	Chroman I	377.3°C**

*Empty cells indicate that data are unavailable for that chemical/endpoint.
** Value obtained from the EPISuite Model.

Robust Summaries have been prepared for BPA and are included below. These data are considered adequate to meet the HPV Chemical Challenge requirements.

VAPOR PRESSURE

As a result of the mixture of chemicals, BPA Tars has no defined vapor pressure. The major component, BPA has a very low vapor pressure, calculated to be 5.3×10^{-8} hPa at 25°C. The other components are primarily larger dimers/trimers of BPA and would have even lower vapor pressures. Overall, therefore, BPA Tars is considered to be non-volatile. Measured or estimated vapor pressure values for various components are provided below.

CAS No.	Name	Vapor Pressure at 25°C*
80-05-7	BPA	5.3×10^{-8} hPa
13464-24-9	Linear Dimer I	4.45×10^{-8} hPa**
57244-54-9	Linear Dimer II	3.21×10^{-8} hPa**
10527-11-4	Cyclic Dimer	2.69×10^{-8} hPa**
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	4.81×10^{-12} hPa**
287110-79-6	BPX-II	
1568-80-5	Sprirobiindane	2.70×10^{-9} hPa**
837-08-1	o,p-BPA	5.08×10^{-7} hPa**
472-41-3	Chroman I	5.98×10^{-7} hPa**

*Empty cells indicate that data are unavailable for that chemical/endpoint.
** Value obtained from the EPISuite Model

Robust Summaries have been prepared for BPA and are included below. These data are considered adequate to meet the HPV Chemical Challenge requirements.

PARTITION COEFFICIENT (LOG K_{ow})

As a result of the mixture of chemicals, BPA Tars has no definable partition coefficient. The major component, BPA has low water solubility and has a log Kow of 3.4. The other components are primarily larger dimers/trimers of BPA be expected to be less water soluble and have high octanol/water partition coefficients. Because of the limited potential for environmental exposure, these high partition coefficients do not present a concern for the environment. Measured or estimated octanol water partition coefficients for various components are provided below.

CAS No.	Name	Partition Coefficient (Log Kow)*
80-05-7	BPA	3.4
13464-24-9	Linear Dimer I	5.6**
57244-54-9	Linear Dimer II	5.5**
10527-11-4	Cyclic Dimer	5.0**
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	5.8**
287110-79-6	BPX-II	
1568-80-5	Sprirobiindane	6.3**
837-08-1	o,p-BPA	3.6**
472-41-3	Chroman I	5.0**

*Empty cells indicate that data are unavailable for that chemical/endpoint.
** Value obtained from the EPISuite Model and modeled at 25°C.

Robust Summaries have been prepared for BPA and are included below. These data are considered adequate to meet the HPV Chemical Challenge requirements.

WATER SOLUBILITY

As a result of the mixture of chemicals, BPA Tars has no readily definable water solubility. The major component, BPA has a low water solubility of 300 mg/L. The other components are primarily larger dimers/trimers of BPA and would be expected to be less water soluble. Because of the importance of water solubility to behavior of BPA Tars in the environment, a water solubility determination is proposed. Since BPA Tars is a mixture, following OECD Guideline 105 is not feasible (the Guideline states: *"This guideline addresses the determination of the solubility in water of essentially pure substances which are stable in water and not volatile."*). The goal of this test will be to determine whether any components other than BPA will be soluble in water at concentrations that can be measured. The results of this testing will be used to determine whether aquatic testing beyond that available for BPA is needed; that is, whether the toxicity data for BPA adequately represent potential toxicity of BPA Tars (see below).

Measured or estimated water solubility values for various components are provided below. The estimated values are consistent with the assumption that the higher molecular weight components are less water soluble than BPA.

CAS No.	Name	Water Solubility (mg/L)*
80-05-7	BPA	300
13464-24-9	Linear Dimer I	1.3**
57244-54-9	Linear Dimer II	1.5**
10527-11-4	Cyclic Dimer	4.2**
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	0.2**
287110-79-6	BPX-II	
1568-80-5	Sprirobiindane	0.2**
837-08-1	o,p-BPA	91.5**
472-41-3	Chroman I	4.1**

*Empty cells indicate that data are unavailable for that chemical/endpoint.
** Value obtained from the EPISuite Model and modeled at 25°C.

Robust Summaries have been prepared for BPA and are included below.

ENVIRONMENTAL FATE

PHOTODEGRADATION

As a result of the mixture of chemicals, BPA Tars has no definable photodegradation half life. The major component, BPA is estimated to be rapidly degraded. Estimated rate constants and half lives for various components are summarized below.

CAS No.	Name	Overall OH Rate Constant (cm3/molecule•sec)*	Half-Life (Hours)*
80-05-7	BPA	80.58×10^{-12}	1.59
13464-24-9	Linear Dimer I	124.48×10^{-12}	1.03
57244-54-9	Linear Dimer II	159.00×10^{-12}	0.81
10527-11-4	Cyclic Dimer	129.75×10^{-12}	0.99
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	129.02×10^{-12}	1.00
287110-79-6	BPX-II		
1568-80-5	Sprirobiindane	178.93×10^{-12}	0.72
837-08-1	o,p-BPA	80.58×10^{-12}	1.59
472-41-3	Chroman I	71.06×10^{-12}	1.81

*Empty cells indicate that data are unavailable for that chemical/endpoint.
** Value obtained from the EPISuite Model

Robust Summaries have been prepared for BPA and the other modeled values and are included below. These data are considered adequate to meet the HPV Chemical Challenge requirements.

STABILITY IN WATER

BPA has no hydrolyzable groups and is, therefore, considered to be hydrolytically stable. Similarly, the derivatives of BPA contained in BPA Tars are anticipated to not hydrolyze.

TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS, INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

As a result of the mixture of chemicals, BPA Tars has no definable transport and distribution pattern in the environment. The values presented below are modeled for various components and are based upon equal distribution to air, water and soil (1000 kg/hr). The models were run based physical chemical properties estimated by the program; no additional data were entered.

CAS No.	Name	Mass Amount (%)*			
		Air	Water	Soil	Sediment
80-05-7	BPA	<0.01	11.9	87.5	0.57
13464-24-9	Linear Dimer I	<0.01	5.19	58.3	36.5
57244-54-9	Linear Dimer II	<0.01	5.63	60.4	33.9
10527-11-4	Cyclic Dimer	<0.01	8.38	74.4	17.2
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	<0.01	3.05	54.6	42.3
287110-79-6	BPX-II				
1568-80-5	Sprirobiindane	<0.01	1.9	46.8	51.3
837-08-1	o,p-BPA	<0.01	11.4	87.4	1.15
472-41-3	Chroman I	<0.1	6.87	73.9	19.2

*Empty cells indicate that data are unavailable for that chemical/endpoint.

Robust Summaries have been prepared for BPA and the other modeled values and are included below.

BIODEGRADATION

BPA is readily biodegradable based on results from an OECD 301F study. A Robust Summary for this study is included below. Due to the higher molecular weight of the non-BPA components, a biodegradation study with BPA Tars will be conducted. The appropriate OECD Guideline will be determined based on the results of the water solubility testing.

ECOTOXICOLOGICAL DATA

ACUTE/PROLONGED TOXICITY TO FISH

A substantial database for acute and prolonged toxicity to fish exists for BPA and is summarized in the EU Risk Assessment. For the purposes of the BPA Tars HPV program, a 96-hour LC_{50} value of 4.6 mg/L is considered the most representative of the major component, BPA. It is anticipated that the other components of BPA will have lower water solubility (see Water Solubility discussion above) and, therefore, the majority of the BPA Tars in solution will be BPA itself.

As noted in the discussion on Water Solubility above, a determination of the water solubility of BPA Tars is planned. It is anticipated that the principle soluble component of the BPA Tars will be BPA itself. If other components of BPA Tars are identified at measurable quantities in the water solubility test, a confirmatory aquatic toxicity study (to show comparable toxicity to the above referenced values for BPA) will be performed for BPA Tars. If it is considered useful to conduct an aquatic toxicity study, it is proposed that a study with the fathead minnow be conducted. This decision is based on the following: 1) the LC_{50} value for the minnow is similar to the EC_{50} values for invertebrates and plants and, therefore, is representative of the toxicity of BPA to aquatic organisms; and 2) because of the complex nature of the BPA Tars, it is anticipated that a study with fish will be technically more feasible and, therefore, will provide a higher level of confidence in the results. If the study shows, as expected, that the toxicity of BPA Tars is similar to BPA, then no additional testing is proposed.

ACUTE TOXICITY TO AQUATIC INVERTEBRATES (E.G. DAPHNIA)

Several studies examining BPA toxicity to *Daphnia magna* are summarized in the EU Risk Assessment. For the purposes of the BPA Tars HPV program, a 48-hour EC_{50} value of 10.2 mg/L is considered the most representative of the major component, BPA. It is anticipated that the other components of BPA will have lower water solubility (see water solubility discussion) and, therefore, the majority of the BPA Tars in solution will be BPA itself. Therefore, it is reasonable to consider the 10.2 mg/L value representative of BPA Tars. This conclusion will be reevaluated pending the results of the water solubility testing and the potential fish toxicity study.

TOXICITY TO AQUATIC PLANTS (E.G. ALGAE)

Several studies examining BPA toxicity to algae are summarized in the EU Risk Assessment. For the purposes of the BPA Tars HPV program, a 96-hour EC_{50} value of 2.7 – 3.1 mg/L is considered the most representative of the major component, BPA. It is anticipated that the other components of BPA will have lower water solubility (see water solubility discussion) and, therefore, the majority of the BPA Tars in solution will be BPA itself. Therefore, it is reasonable to consider the 2.7 – 3.1 mg/L value representative of

BPA Tars. This conclusion will be reevaluated pending the results of the water solubility testing and the potential fish toxicity study.

HUMAN HEALTH-RELATED DATA

GENERAL COMMENTS

As noted above, the extensive database for toxicity evaluation of BPA is summarized in the EU Risk Assessment. Key studies for HPV endpoints are included in the Robust Summary below (because of the large database, only one study is provided for endpoints where the study is sufficient to meet the HPV requirements). Overall, it is appropriate to consider the data for BPA to be representative of the toxicity of BPA Tars since the other components, of higher molecular weight, are expected to be less bioavailable and less chemically and biologically reactive. Further evidence that the bisphenolic components of BPA Tars would yield similar or lesser results in toxicology studies comes from acute toxicity studies and an Ames test done on one of the bisphenolic impurities, spirobiindane (CAS No. 1568-80-5). The data for spirobiindane are also included in the Robust Summary below. The acute oral and dermal LD_{50} values for spirobiindane were >5000 mg/kg and >2000 mg/kg, respectively. Spirobiindane was also negative in the Salmonella Reverse Mutation assay. In addition, the section on Additional Testing below discusses approaches to confirmatory data.

OVERVIEW OF BPA TOXICITY STUDIES FOR HPV ENDPOINTS

Following oral administration absorption of BPA is rapid and extensive while dermal absorption is limited. Extensive first pass metabolism occurs following absorption from the gastrointestinal tract with glucuronide conjugation being the major metabolic pathway. Bisphenol A is of low acute toxicity (rodent oral LD_{50} values from 3300-4100 mg/kg, a rabbit oral LD_{50} value 2230 mg/kg and a rat acute inhalation 6-hour LC_{50} value >170 mg/m^3). Bisphenol A is not a skin irritant, however, it is severely irritating to the eyes. BPA was negative in gene mutation and clastogenicity assays in cultured mammalian cells, as well as in a micronucleus test for clastogenicity *in vivo*; therefore, BPA is considered not to present a genotoxic concern for human health. BPA results in minimal effects on the liver and kidney (LOAEL from chronic exposure in the diet was 50 mg/kg/day). For reproductive toxicity, data from a three-generation study in the rat, BPA was not a selective reproductive toxicant at doses ranging from 0.001 to 500 mg/kg/day. BPA is not a developmental toxicant in rats or mice.

ADDITIONAL TESTING

As noted above, BPA is not considered to be genotoxic based on a large number of studies. The higher molecular weight components of BPA Tars are not anticipated to be mutagenic. However, due to the chemical reactivity of BPA (i.e. in its use in the production of polymers), it is considered useful to confirm the lack of mutagenic activity for BPA Tars mixture to allow direct comparison of biological reactivity. Therefore, testing BPA Tars in bacterial cells (Bacterial Reverse Mutation Assay) and mammalian cells (Chromosomal Aberration and Mouse Lymphoma Assays) will be conducted. Assuming the expected, negative results are obtained, no further testing in experimental animals is warranted for the HPV Chemical Challenge Program for BPA Tars.

ROBUST SUMMARY

PHYSICAL AND CHEMICAL DATA

1.0 MELTING POINT

1.0.1

Value:	150-157 °C
Decomposition:	Yes [ ] No [X] Ambiguous [ ]
Sublimation:	Yes [ ] No [X] Ambiguous [ ]
Method:	Not specified
GLP:	Yes [ ] No [ ] ? [X]
Test Substance:	Bisphenol A (CAS RN 80-05-7)
References:	As cited in the EU Risk Assessment: Sax, N.I. and Lewis, R.J. 1996. Sax's Dangerous Properties of Industrial Materials, 9th Edition. New York. London. Van Nostrand Reinhold. Pohanish, R.P. and Greene, S.A. 1996. Hazardous Materials Handbook. New York. London. Van Nostrand Rheinhold. IPCS. 1993. Bisphenol-A; International Chemical Safety Cards, 8th Series prepared by IPCS. International Programme on Chemical Safety (IPCS). Merck Index. 1989. The Merck Index. an Encyclopedia of Chemicals Drugs and Biologicals. 11th Edition. Budavari, S. et al. (eds), Rahway, N.J. Merck & Co. Hubbard, N.W. et al. 1948. J. Am. Chem. Soc.70:3259-3261. Bayer Leverkusen. 1989. Ullmann's Encyclopedia of Industrial Chemistry. 1991. Encyclopedia of Industrial Chemistry. 5th completely revised edition. Gerhartz, W. (ed), Weinheim. VCH.
Reliability:	(Klimisch Code 2) Valid with restrictions.

1.0.2

Value:	See Below
Decomposition:	Yes [ ] No [ ] Ambiguous [ ] Not Applicable [X]
Sublimation:	Yes [ ] No [ ] Ambiguous [ ] Not Applicable [X]
Method:	Estimated
GLP:	Yes [ ] No [X] ? [ ]
Test Substance:	See Below
Remarks:	The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used.

CAS No.	Name	Melting Point*
80-05-7	BPA	131.8 °C
13464-24-9	Linear Dimer I	149.8 °C
57244-54-9	Linear Dimer II	151.2 °C
10527-11-4	Cyclic Dimer	164.2 °C
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	215.3 °C
287110-79-6	BPX-II	
1568-80-5	Sprirobiindane	178.0 °C
837-08-1	o,p-BPA	131.8 °C
472-41-3	Chroman I	141.5 °C

*Empty cells indicate that data are unavailable for that chemical/endpoint.

Reference: U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; MPBPWIN Program, Version 1.41; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).
Reliability: (Klimisch Code 2) Valid with restrictions.

2.0 BOILING POINT

2.0.1
Value: 250-252°C
Pressure: 17 kPa
Decomposition: Yes [ ] No [ ] Ambiguous [X]
Method: Not specified
GLP: Yes [ ] No [ ] ? [X]
Test Substance: Bisphenol A (CAS RN 80-05-7)
Reference: Von Braun. 1925. ANN. 472:65.
Reliability: (Klimisch Code 2) Valid with restrictions.

2.0.2
Value: 360.5°C
Pressure: 101.3 kPa
Decomposition: Yes [X] No [ ] Ambiguous [ ]
Method: Not specified
GLP: Yes [ ] No [ ] ? [X]
Test Substance: Bisphenol A (CAS RN 80-05-7)
Reference: DIPPR. 1994. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Taylor and Francis.
Reliability: (Klimisch Code 2) Valid with restrictions.

2.0.3
Value: See below
Pressure: 760 mm Hg
Decomposition: Yes [ ] No [ ] Ambiguous [ ] Not Applicable [X]
Method: Estimated
GLP: Yes [ ] No [X] ? [ ]
Test Substance: See below

Remarks: The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used.

CAS No.	Name	Boiling Point*
80-05-7	BPA	363.5°C
13464-24-9	Linear Dimer I	394.3°C
57244-54-9	Linear Dimer II	398.8°C
10527-11-4	Cyclic Dimer	396.3°C
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	505.7°C
287110-79-6	BPX-II	
1568-80-5	Sprirobiindane	425.9°C
837-08-1	o,p-BPA	363.5°C
472-41-3	Chroman I	377.3°C

*Empty cells indicate that data are unavailable for that chemical/endpoint.

Reference: U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; MPBPWIN Program, Version 1.41; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).
Reliability: (Klimisch Code 2) Valid with restrictions.

3.0 VAPOR PRESSURE

3.0.1
Value: 5.3×10^{-8} hPa @ 25°C
Decomposition: Yes [ ] No [ ] Ambiguous [ ] Not Applicable [X]
Method: Calculated [X] Measured [ ]
GLP: Yes [ ] No [ ] ? [X]
Test Substance: Bisphenol A (CAS RN 80-05-7)
Reference: Bayer AG. 1988. Manufacturers Safety Data Sheet.
Reliability: (Klimisch Code 2) Valid with restrictions

3.0.2
Value: See below
Decomposition: Yes [ ] No [ ] Ambiguous [ ] Not Applicable [X]
Method: Calculated [X] Measured [ ]
GLP: Yes [ ] No [X] ? [ ]
Test Substance: See below
Remarks: The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used.

CAS No.	Name	Vapor Pressure at 25°C*
80-05-7	BPA	3.0×10^{-7} hPa
13464-24-9	Linear Dimer I	4.45×10^{-8} hPa
57244-54-9	Linear Dimer II	3.21×10^{-8} hPa
10527-11-4	Cyclic Dimer	2.69×10^{-8} hPa
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	4.81×10^{-12} hPa
287110-79-6	BPX-II	
1568-80-5	Sprirobiindane	2.70×10^{-9} hPa
837-08-1	o,p-BPA	5.08×10^{-7} hPa
472-41-3	Chroman I	5.98×10^{-7} hPa

*Empty cells indicate that data are unavailable for that chemical/endpoint.

Reference: U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; MPBPWIN Program, Version 1.41; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).
Reliability: (Klimisch Code 2) Valid with restrictions.

4.0 PARTITION COEFFICIENT (LOG10POW)

4.0.1
Log K_{ow}: 3.4
Temperature: Not reported
Method: Measured; method not specified
GLP: Yes [ ] No [ ] ? [ ] Not applicable [X]
Test Substance: Bisphenol A (CAS RN 80-05-7)
Reference: Bayer AG. 1993. Material Safety Data Sheet.
Reliability: (Klimisch Code 2) Valid with restrictions.

4.0.2
Log K_{ow}: See below
Temperature: 25°C
Method: Estimated
GLP: Yes [ ] No [X] ? [ ]
Test Substance: See below
Remarks: The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used.

CAS No.	Name	Partition Coefficient (Log Kow) at 25°C*
80-05-7	BPA	3.6
13464-24-9	Linear Dimer I	5.6
57244-54-9	Linear Dimer II	5.5
10527-11-4	Cyclic Dimer	5.0
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	5.8
287110-79-6	BPX-II	
1568-80-5	Sprirobiindane	6.3
837-08-1	o,p-BPA	3.6
472-41-3	Chroman I	5.0

*Empty cells indicate that data are unavailable for that chemical/endpoint.

Reference: U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; KOWWIN Program, Version 1.67; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).
Reliability: (Klimisch Code 2) Valid with restrictions.

5.0 WATER SOLUBILITY

5.1 SOLUBILITY

5.1.1
Value: 300 mg/L
Temperature: Room temperature
Description: Miscible [ ]; Of very high solubility [ ]; Of high solubility [ ]; Soluble [ ]; Slightly soluble [ ]; Of low solubility [ ]; Of very low solubility [X]; Not soluble [ ]
Method: Not specified
GLP: Yes [ ] No [ ] ? [X] Not applicable [ ]
Test Substance: Bisphenol A (CAS RN 80-05-7)
Reference: Bayer AG. 1988. Manufacturers Safety Data Sheet.
Reliability: (Klimisch Code 2) Valid with restrictions.

5.1.2
Value: See below
Temperature: 25°C
Description: Miscible [ ]; Of very high solubility [ ]; Of high solubility [ ]; Soluble [ ]; Slightly soluble [ ]; Of low solubility [ ]; Of very low solubility [ ]; Not soluble [ ]; Not Applicable [X]
Method: Estimated
GLP: Yes [ ] No [ ] ? [ ] Not applicable [X]
Test Substance: See below
Remarks: The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used.

CAS No.	Name	Water Solubility (mg/L)*
80-05-7	BPA	173
13464-24-9	Linear Dimer I	1.3
57244-54-9	Linear Dimer II	1.5
10527-11-4	Cyclic Dimer	4.2
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	0.2
1568-80-5	Sprirobiindane	0.2
287110-79-6	BPX-II	
837-08-1	o,p-BPA	91.5
472-41-3	Chroman I	4.1

*Empty cells indicate that data are unavailable for that chemical/endpoint.

Reference: U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; WSKOWWIN Program, Version 1.41; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).
Reliability: (Klimisch Code 2) Valid with restrictions.

5.2. pH VALUE, pKa VALUE

No studies were found.

ENVIRONMENTAL FATE AND PATHWAYS

6.0 PHOTODEGRADATION

6.0.1
Method: Calculated [X] Measured [ ]
GLP: Yes [ ] No [X] ? [ ]
Test Substance: Bisphenol A (CAS RN 80-05-7)
Concentration: Not applicable
Temperature °C: Not stated
Direct photolysis: Not applicable
Indirect photolysis: Not applicable
Breakdown products: Not applicable
Value: Overall OH Rate Constant (k_{phot}) = 80.577 x 10^{-12} cm^3/molecule●sec
Half-life ($t_{1/2}$) = 1.593 Hrs (12-hour day; 1.5 x 10^6 OH/cm^3)
Remarks: The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used.
Atmospheric photo-oxidation potential, mediated by reaction with hydroxyl radicals, was estimated using the submodel, Atmospheric Oxidation Potential for Windows (AOPWIN v.1.91, EPIWIN v3.12, US EPA, 2005). The SAR methods rely on structural features of the subject molecule. The model calculates a second-order half-life with units of cm^3/molecules-sec. A pseudo-first order photo-degradation rate is in

turn based on the second order rate of reaction (cm^3/molecules-sec) with hydroxyl radicals (HO•), assuming first-order kinetics and an HO• concentration of 1.5×10^6 molecules/cm^3 and 12 hours of daylight. Pseudo-first order half-lives ($t_{1/2}$) were then calculated as follows:

$$t_{1/2} = 0.693 / [k_{phot} \times HO\bullet \times 12\text{-hr} / 24\text{-hr}].$$

Reference: U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; AOPWIN Program, Version 1.91; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Reliability: (Klimisch Code 2) Valid with restrictions.

6.0.2

Method: Calculated [X] Measured [ ]
GLP: Yes [ ] No [X] ? [ ]
Test Substance: See below
Concentration: Not applicable
Temperature °C: Not stated
Direct photolysis: Not applicable
Indirect photolysis: Not applicable
Breakdown products: Not applicable
Value: See below
Remarks: The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used.

CAS No.	**Name**	**Overall OH Rate Constant (cm^3/molecule•sec)***	**Half-Life (Hours)***
80-05-7	BPA	80.58×10^{-12}	1.59
13464-24-9	Linear Dimer I	124.48×10^{-12}	1.03
57244-54-9	Linear Dimer II	159.00×10^{-12}	0.81
10527-11-4	Cyclic Dimer	129.75×10^{-12}	0.99
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	129.02×10^{-12}	1.00
287110-79-6	BPX-II		
1568-80-5	Sprirobiindane	178.93×10^{-12}	0.72
837-08-1	o,p-BPA	80.58×10^{-12}	1.59
472-41-3	Chroman I	71.06×10^{-12}	1.81

*Empty cells indicate that data are unavailable for that chemical/endpoint.

Reference: U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; AOPWIN Program, Version 1.91; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Reliability: (Klimisch Code 2) Valid with restrictions.

7.0 STABILITY IN WATER

Type:	Abiotic (hydrolysis) [X]; biotic (sediment) [ ]
Half life:	Not applicable
Degradation:	Not applicable
Method:	Not applicable
GLP:	Yes [ ] No [X] ? [ ]
Test Substance:	Bisphenol A (CAS RN 80-05-7)
Remarks:	Bisphenol A has no hydrolyzable groups and, therefore, does not undergo hydrolysis.
Reference:	None – conclusion based on chemistry of Bisphenol A.
Reliability:	(Klimisch Code 2) Valid with restrictions.

8.0 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS, INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

8.1 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

8.1.1

Type:	Fugacity model level III
Media:	Other: air, water, soil, sediment
Method:	Calculated [X] Measured [ ]
GLP:	Yes [ ] No [X] ? [ ]
Test Substance:	Bisphenol A (CAS RN 80-05-7)
Value:	Air < 0.01% Water = 11.9% Soil = 87.5% Sediment = 0.6%
Remarks:	The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used. Default values were assumed for environmental compartment descriptions, dimensions, and properties, advective and dispersive properties. Emissions were assumed to be equally to air, water and soil (Model run with 1000 kg/hr emissions each to air, water and soil.). Air: $t_{1/2}$ = 3.185 hr Water: $t_{1/2}$ = 900 hr Soil: $t_{1/2}$ = 1800 hr Sediment: $t_{1/2}$ = 8100 hr
Reference:	U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Reliability: (Klimisch Code 2) Valid with restrictions, calculated value.

8.1.2
Type: Fugacity model level III
Media: Other: air, water, soil, sediment
Method: Calculated [X] Measured [ ]
GLP: Yes [ ] No [X] ? [ ]
Test Substance: See below
Value: See below
Remarks: The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used. Model run with 1000 kg/hr emissions each to air, water and soil.

CAS No.	Name	Mass Amount (%)*			
		Air	Water	Soil	Sediment
80-05-7	BPA	<0.01	11.9	87.5	0.57
13464-24-9	Linear Dimer I	<0.01	5.19	58.3	36.5
57244-54-9	Linear Dimer II	<0.01	5.63	60.4	33.9
10527-11-4	Cyclic Dimer	<0.01	8.38	74.4	17.2
2300-15-4	BPX-I - Linear Trimer of isopropenyl phenol	<0.01	3.05	54.6	42.3
287110-79-6	BPX-II				
1568-80-5	Sprirobiindane	<0.01	1.9	46.8	51.3
837-08-1	o,p-BPA	<0.01	11.4	87.4	1.15
472-41-3	Chroman I	<0.1	6.87	73.9	19.2

*Empty cells indicate that data are unavailable for that chemical/endpoint.

Reference: U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).
Reliability: (Klimisch Code 2) Valid with restrictions.

8.1.3
Type: Fugacity model level III
Media: Other: air, water, soil, sediment
Method: Calculated [X] Measured [ ]
GLP: Yes [ ] No [X] ? [ ]
Test Substance: Bisphenol A (CAS RN 80-05-7)
Value: Air < 0.01%
Water = 3.06%
Soil = 96.8%
Sediment = 0.145
Remarks: The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used.

Default values were assumed for environmental compartment descriptions, dimensions, and properties, advective and dispersive properties.

Emissions were assumed to be equally to air, water and soil (Model run with 1000 kg/hr emissions to air.).

Air: $t_{1/2}$ = 3.185 hr
Water: $t_{1/2}$ = 900 hr
Soil: $t_{1/2}$ = 1800 hr
Sediment: $t_{1/2}$ = 8100 hr

Reference: U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Reliability: (Klimisch Code 2) Valid with restrictions.

8.1.4

Type: Fugacity model level III
Media: Other: air, water, soil, sediment
Method: Calculated [X] Measured [ ]
GLP: Yes [ ] No [X] ? [ ]
Test Substance: Bisphenol A (CAS RN 80-05-7)
Value: Air < 0.01%
Water = 95.5%
Soil < 0.1%
Sediment = 4.53
Remarks: The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used. Default values were assumed for environmental compartment descriptions, dimensions, and properties, advective and dispersive properties.

Emissions were assumed to be equally to air, water and soil (Model run with 1000 kg/hr emissions to air.).

Air: $t_{1/2}$ = 3.185 hr
Water: $t_{1/2}$ = 900 hr
Soil: $t_{1/2}$ = 1800 hr
Sediment: $t_{1/2}$ = 8100 hr

Reference: U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Reliability: (Klimisch Code 2) Valid with restrictions.

8.1.5

Type:	Fugacity model level III
Media:	Other: air, water, soil, sediment
Method:	Calculated [X] Measured [ ]
GLP:	Yes [ ] No [X] ? [ ]
Test Substance:	Bisphenol A (CAS RN 80-05-7)
Value:	Air < 0.01% Water = 0.676% Soil < 99.3% Sediment = 0.03
Remarks:	The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used. Default values were assumed for environmental compartment descriptions, dimensions, and properties, advective and dispersive properties. Emissions were assumed to be equally to air, water and soil (Model run with 1000 kg/hr emissions to soil). Air: $t_{1/2}$ = 3.185 hr Water: $t_{1/2}$ = 900 hr Soil: $t_{1/2}$ = 1800 hr Sediment: $t_{1/2}$ = 8100 hr
Reference:	U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).
Reliability:	(Klimisch Code 2) Valid with restrictions.

8.1.6

Type:	Fugacity model level III
Media:	Other: air, water, soil, sediment
Method:	Calculated [X] Measured [ ]
GLP:	Yes [ ] No [X] ? [ ]
Test Substance:	Bisphenol A (CAS RN 80-05-7)
Value:	Air < 0.01% Water = 21.7% Soil = 77.3% Sediment = 1.03
Remarks:	The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used. Default values were assumed for environmental compartment descriptions, dimensions, and properties, advective and dispersive properties.

Emissions were assumed to be equally to air, water and soil (Model run with 1000 kg/hr emissions to air and water).

Air: $t_{1/2}$ = 3.185 hr
Water: $t_{1/2}$ = 900 hr
Soil: $t_{1/2}$ = 1800 hr
Sediment: $t_{1/2}$ = 8100 hr

Reference: U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Reliability: (Klimisch Code 2) Valid with restrictions.

8.1.7

Type: Fugacity model level III
Media: Other: air, water, soil, sediment
Method: Calculated [X] Measured [ ]
GLP: Yes [ ] No [X] ? [ ]
Test Substance: Bisphenol A (CAS RN 80-05-7)
Value: Air < 0.01%
Water = 1.82%
Soil = 98.1%
Sediment = 0.09
Remarks: The EPIWIN model was not run with any physico-chemical property input values. The CAS Numbers were entered for the individual chemicals below and the model data used.Default values were assumed for environmental compartment descriptions, dimensions, and properties, advective and dispersive properties.

Emissions were assumed to be equally to air, water and soil (Model run with 1000 kg/hr emissions to air and soil).

Air: $t_{1/2}$ = 3.185 hr
Water: $t_{1/2}$ = 900 hr
Soil: $t_{1/2}$ = 1800 hr
Sediment: $t_{1/2}$ = 8100 hr

Reference: U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Reliability: (Klimisch Code 2) Valid with restrictions.

8.1.8

Type: Fugacity model level III
Media: Other: air, water, soil, sediment
Method: Calculated [X] Measured [ ]

GLP:	Yes [ ] No [X] ? [ ]
Test Substance:	Bisphenol A (CAS RN 80-05-7)
Value:	Air < 0.01% Water = 18.6% Soil = 80.6% Sediment = 0.881
Remarks:	Default values were assumed for environmental compartment descriptions, dimensions, and properties, advective and dispersive properties. Emissions were assumed to be equally to air, water and soil (Model run with 1000 kg/hr emissions to water and soil). Air: $t_{1/2}$ = 3.185 hr Water: $t_{1/2}$ = 900 hr Soil: $t_{1/2}$ = 1800 hr Sediment: $t_{1/2}$ = 8100 hr
Reference:	U.S. EPA (Environmental Protection Agency). 2005. EPI Suite™, Version 3.12; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).
Reliability:	(Klimisch Code 2) Valid with restrictions.

9.0 BIODEGRADATION

Type:	Aerobic [X]; Anaerobic [ ]
Inoculum:	Adapted [ ]; Non-adapted [X]
Concentration of the chemical:	2.52 mg O_2/mg as ThOD
Medium:	Water [X]; Water-sediment [ ]; Soil [ ]; Sewage treatment [ ]; Other [ ]:
Contact time:	28 days at 27.1 °C
Degradation:	73.0 – 80.1%
Result:	Readily biodeg. [X]; Inherently biodeg. [ ]; Other [ ]
Kinetic of test substance:	See below
Reference substance:	Information not stated in EU Risk Assessment
Degradation Products:	Yes [ ] No [ ] Not measured [X]
Method (Year):	OECD Test Guideline 301F
GLP:	Yes [ ] No [ ] ? [X]
Test Substance:	Bisphenol A (99.7% purity)
Remarks:	The theoretical oxygen demand (ThOD) of bisphenol A was calculated as 2.52 mg O2/mg. The inoculum used in the experiment consisted of activated sludge mixed liquor collected from a municipal sewage treatment plant. The experimental details followed the procedures detailed in the OECD 301F test to Good Laboratory Practice (GLP) standards. However, the temperature used in the experiment was 27.1°C, which is 2.1°C above the range of temperatures quoted in the OECD guidelines. The initial concentrations of bisphenol A used in the

	experiment were 7 mg/l and 25 mg/l. Oxygen consumption and CO2 evolution were measured over 28 days and removal of dissolved organic carbon (DOC) from the biodegradation reactions was determined after 28 days. The time required for achieving 10% degradation for the bisphenol A ranged from 5.6 days (7 mg/l bisphenol A) to 6.1 days (25 mg/l bisphenol A) with biodegradation exceeding the 60% degradation level after an additional 3.5 days (7 mg/l bisphenol A) and 5.0 days (25 mg/l bisphenol A). Ten days following the defined lag periods biodegradation averaged 77.6% and 73.7% for the 7 mg/l and 25 mg/l reactions. The maximum degradation levels averaged 84.6% and 81.7% of the ThOD for the 7 mg/l and 25 mg/l reactions respectively after 28 days. The rate and extent of bisphenol A mineralisation observed indicate that bisphenol A can be classified as "readily biodegradable". Evolution of CO2 resulting from mineralisation of bisphenol A closely followed biodegradation of the compound as measured from oxygen consumption. Maximum yields of CO2 ranged from 73.0% to 80.1% of ThCO2 indicating nearly complete conversion of the added organic carbon to CO2.
Reference:	West, R.J. and Goodwin, P.A. 1997. Evaluation of Ready Biodegradability of Bisphenol A Using the OECD 301F: Manometric Respirometry Test. Dow Company Report. Study ID 971108A. As cited in the EU Risk Assessment.
Reliability:	(Klimisch Code 1) Valid without restrictions.

ECOTOXICOLOGICAL DATA

10.0 ACUTE/PROLONGED TOXICITY TO FISH

Type of Test:	Static [X] Semi-static [ ] Flow-through [ ] Other [ ] Open-system [ ] Closed-system [ ]
Species:	Fathead minnow
Exposure Period:	96 hours
Results:	LC_{50} (96h) 4.6 mg BPA/L NOAEC = Not reported LOAEC = Not reported
Analytical Monitoring:	Yes [ ] No [ ] ? [X]
Method:	ASTM E-35 21 (1992)
GLP:	Yes [ ] No [ ] ? [X]
Test Substance:	Bisphenol A (CAS RN 80-05-7)
Remarks:	Test conditions: The reported test conditions are summarized below:

Parameter	Test Condition
Test type	Flow
Duration	96 hours
Test organism	Fathead minnow (*Pimephales promelas*)
Average weight ± SD & range	0.41 g
Average fork length ± SD & range	3.0 cm
Temperature	16.1 to 17.9 ºC
Dissolved oxygen	>81% saturation
pH	7.6-8.0
Criterion for Effect	Death
Toxicity Endpoints	96-hour LD_{50}

Results: LC_{50} = 4.6 mg BPA/L
Reference: Alexander, H.C., Bartlett, E.A. and Boggs, G.U. 1985. Bisphenol A: Flow-Through Acute Toxicity to the Fathead Minnow. Dow Company Report: ES-764. As cited in the EU Risk Assessment.
Alexander, H.C., Dill, D.C., Smith, L.W., Guiney, P.D. and Dorn, P. 1988. Bisphenol A: Acute aquatic toxicity. Environmental Toxicology and Chemistry 7**:**19-26. As cited in the EU Risk Assessment.
Reliability: (Klimisch Code 1) Valid without restrictions.

11.0 ACUTE TOXICITY TO AQUATIC INVERTEBRATES (E.G. DAPHNIA)

Type of Test: Static [X] Semi-static [ ] Flow-through [ ] Other [ ]
Open-system [ ] Closed-system [ ]
Species: *Daphnia magna*
Exposure Period: 48 hours
Results: EC_{50} (96h) 10.2 mg/L
NOEC = Not reported
LOEC > Not reported
Analytical Monitoring: Yes [X] No [ ] ? []
Method: ASTM E-35.21
GLP: Yes [ ] No [ ] ? [X]
Test Substance: Bisphenol A (CAS RN 80-05-7)

Remarks: The reported test conditions are summarized below:

Parameter	Test Condition
Test type	Static
Duration of test	48 hours
Test organism	*Daphnia magna*
Age at Test Initiation	First instar
Test Solution Temperature	19.8-20.4ºC
Dissolved Oxygen Concentration	>96%
pH	8.0-8.3
Criterion for effect	Immobilization
Calculated toxicity values	EC_{50} at 48-h

Results: 24-hr EC_{50}(immobilization) = 15.5 mg BPA/L (measured)
48-hr EC_{50}(immobilization) = 10.2 mg BPA/L (measured)

Reference: Alexander, H.C., Milazzo, D.P. and Boggs, G.U. 1985. Bisphenol A: Daphnid Static Acute Toxicity Test. Dow Company Report. ES-763. As cited in the EU Risk Assessment.
Alexander, H.C., Dill, D.C., Smith, L.W., Guiney, P.D. and Dorn, P. 1988. Bisphenol A: Acute aquatic toxicity. Environmental Toxicology and Chemistry 7**:**19-26. As cited in the EU Risk Assessment.

Reliability: (Klimisch Code 1) Valid without restrictions.

12.0 TOXICITY TO AQUATIC PLANTS (E.G. ALGAE)

Species: Green algae (*Selenastrum capricornutum*)
End-point: Biomass [X] Growth rate [ ] Other [ ]
Exposure Period: 96 hours
Results: Growth:
EC_{50}(96h) = 2.7-3.1 mg/L
Analytical Monitoring: Yes [ ] No [ ] ? [X]
Method: Not reported
GLP: Yes [ ] No [ ] ? [X]
Test Substance: Bisphenol A (CAS RN 80-05-7)
Remarks: Test conditions were not reported. The percentage inhibition of cell count and cell volume was reported for the concentrations tested. From these data, it was possible to derive the EC_{1-} using probit analysis.
Results: 96-hr EC_{50} = 2.7-3.1 mg BPA/L
Calculated EC_{10} (By the EU RAR) = 1.36 mg BPA/L (cell count) and 1.68 mg BPA/L (cell volume)
Reference: Alexander, H.C., Dill, D.C., Milazzo, D.P. and Boggs, G.U. 1985. Bisphenol A: Algal Toxicity Test. Dow Company Report: ES-762. As cited in the EU Risk Assessment.
Alexander, H.C., Dill, D.C., Smith, L.W., Guiney, P.D. and Dorn, P. 1988. Bisphenol A: Acute aquatic toxicity. Environmental Toxicology and Chemistry 7**:**19-26. As cited in the EU Risk Assessment.
Reliability: (Klimisch Code 1) Valid without restrictions.

HUMAN-HEALTH RELATED DATA

13.0 ACUTE TOXICITY

13.1 ACUTE ORAL TOXICITY

13.1.1

Type: LD_0 [ ] LD_{100} [ ] LD_{50} [X] LD_{L0} [ ] Other [ ]
Species/Strain: Rat/F344
Sex: Male and female
Animals: 5/sex
Vehicle: Not reported
Value: LD_{50} (males) = 4100 mg/kg
LD_{50} (females) = 3300 mg/kg
Method: Not reported
GLP: Yes [ ] No [ ] ? [X]
Test Substance: Bisphenol A (CAS RN 80-05-7)
Remarks: Rats (5 per sex per group) were given 2,150, 3,160, 4,640 or 6,810 mg/kg of bisphenol A.
Results:

Dose Level (mg/kg)	Male Mortality	Female Mortality
2150	0/5	1/5
3160	1/5	4/5
4640	3/5	2/5
6810	5/5	5/5

The calculated LD_{50} values were 4,100 mg/kg in males and 3,300 mg/kg in females. No other aspects of the study were reported.

Reference: NTP. 1982. Carcinogenesis Bioassay of Bisphenol A (CAS No. 80-05-7) in F344 Rats B6C3F1 Mice (Feed Study). National Toxicology Program. Technical Report No. 215, Order No. PB82-184060 (NTIS), 1-116. As cited in the EU Risk Assessment.
Reliability: (Klimisch Code 2) Valid with restrictions.

13.1.2

Type: LD_0 [ ] LD_{100} [ ] LD_{50} [X] LD_{L0} [ ] Other [ ]
Species/Strain: Rabbit
Sex: Not reported
Animals: Not reported
Vehicle: Not reported
Value: LD_{50} = 2230 mg/kg
Method: Not reported
GLP: Yes [ ] No [X] ? [ ]
Test Substance: Bisphenol A (CAS RN 80-05-7)
Remarks: A rabbit LD_{50} value was obtained. No other details are reported.
Results: LD_{50} = 2230 mg/kg

Reference:	Mellon Institute of Industrial Research. 1948. The Acute and Subacute Toxicity of Diphenylol Propane. Study No. 11-13. Union Carbide Corporation Unpublished Report. As cited in the EU Risk Assessment.
Reliability:	(Klimisch Code 2) Valid with restrictions.

13.1.3

Type:	LD_0 [ ] LD_{100} [ ] LD_{50} [X] LD_{L0} [ ] Other [ ]
Species/Strain:	Rat/Crl:CD®(SD)BR
Sex:	Male and female
# Animals:	5/sex
Vehicle:	Corn oil
Value:	LD_{50} > 5000 mg/kg
Method:	Not reported
GLP:	Yes [ ] No [ ] ? [X]
Test Substance:	Spirobiindane (CAS RN 1568-80-5)
Remarks:	Test article was administered once orally via gastric intubation to a single group of 5/sex Crl:CD®(SD)BR rats (221-245g) at a dose of 5000 mg/kg. Mortality, clinical observations, body weight changes and day 14 gross necropsy findings were evaluated.
Results:	There were no deaths, body weight changes or test article-related gross necropsy findings. Seven rats had red and/or yellow external matting. Abnormal excreta was noted for four animals. One female was hypoactive. All animals were normal by day 8 or earlier. The oral LD_{50} was found to be >5000 mg/kg.
Reference:	Kern[1], T., Hurley[1], J., Wilmot[1], A. and Dimond, S. 1997. Acute Toxicity Studies with Spirobiindane. General Electric Plastics, Pittsfield, MA, USA and [1]WIL Research Laboratories, Inc. Ashland, OH, USA.
Reliability:	(Klimisch Code 1) Valid without restrictions.

13.2 ACUTE INHALATION TOXICITY

Type:	LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain:	Rat/Fischer F344
Sex:	Males and females
# animals:	10/sex
Value:	>170 mg/L
Method (Year):	Not reported.
GLP:	Yes [ ] No [ ] ? [X]
Test substance:	Bisphenol A (CAS RN 80-05-7)
Remarks:	Groups of 10 male and female Fischer F344 rats were exposed, whole body, to Bisphenol A dust at concentrations of 0 or 170 mg/m^3.
Results:	The mass median aerodynamic diameter (MMAD) of the test substance was 3.9 micrometers (μm), and the exposure concentration used was the highest attainable by the investigators with the test system used. Half the animals were necropsied on the day following exposure and the rest on day 14. Microscopic examination was limited to the respiratory tract (nasal turbinates, larynx, trachea and lungs) and associated tissues. No

	deaths occurred and therefore the LD50 value for rats is >170 mg/m^3 for 6 hours. No gross signs of toxicity were observed. At necropsy, "slight" inflammation of the epithelium lining of the anterior portion of the nose and "slight ulceration" of the oronasal duct were reported in 5/5 males and 4/5 females exposed to 170 mg/m^3 and sacrificed on day 2. No exposure-related effects were observed in animals necropsied on day 14.
Reference:	Nitschke, K.D., Quast, J.F. and Wolfe, E.L. 1985. Bisphenol A: Acute Aerosol Toxicity Study with Fischer 344 Rats. Dow Chemical Company Unpublished Report. As cited in the EU Risk Assessment.
Reliability:	(Klimisch Code 2) Valid with restrictions.

13.3 ACUTE DERMAL TOXICITY

13.3.1

Type:	LD_0 [ ] LD_{100} [ ] LD_{50} [X] LD_{L0} [ ] Other [ ]
Species/Strain:	Rats/Crl:CD®(SD)BR
Value:	>2000 mg/kg
Method:	Not reported
GLP:	Yes [ ] No [X] ? [ ]
Test Substance:	Spirobiindane (CAS RN 1568-80-5)
Remarks:	Test article was administered once dermally at a dose of 2000 mg/kg to the clipped, intact skin of 5/sex Crl: CD®(SD)BR rats (224-247g) for a 24-hour period under semi-occlusive dressing. Mortality, clinical observations, dermal findings, body weight changes and day 14 gross necropsy findings were evaluated.
Results:	There were no deaths, test article-related clinical findings, body weight changes or gross necropsy findings. Two and seven rats had very slight to slight erythema and desquamation, respectively. The dermal LD_{50} and the No-Observable-Effect Level (NOEL) for systemic toxicity were found to be >2000 mg/kg.
Reference:	Kern[1], T., Hurley[1], J., Wilmot[1], A. and Dimond, S. 1997. Acute Toxicity Studies with Spirobiindane. General Electric Plastics, Pittsfield, MA, USA and [1]WIL Research Laboratories, Inc. Ashland, OH, USA.
Reliability:	(Klimisch Code 1) Valid without restrictions.

14.0 GENETIC TOXICITY *IN VITRO* OR *IN VIVO*

14.1 BACTERIAL *IN VITRO* TEST

14.1.1

Type:	Bacterial reverse mutation assay (Ames test)
System of testing:	*Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537
Concentrations:	0 to 333 µg/plate
Metabolic activation:	With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:	Negative
Cytotoxicity conc.:	With and without metabolic activation: 333 µg/plate
Genotoxic effects:	With metabolic activation: positive [ ]; ambiguous [ ];

	Negative [X]
	Without metabolic activation: positive [ ]; ambiguous [ ]; Negative [X]
Year:	1983
GLP:	Yes [ ] No [ ] ? [X]
Test substance:	Bisphenol A (CAS RN 80-05-7)
Remark:	The pre-incubation method with *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 was used at bisphenol A concentrations up to 333 µg/plate in the presence and absence of metabolic activation (Aroclor induced rat and hamster liver S9). At 333 µg/plate, slight and complete clearance of the background lawn was observed in all strains with (rat and hamster liver S9) and without metabolic activation, respectively. No increase in the number of revertants was seen in any of the tested cultures. Controls gave results that confirmed the validity of this test. The negative result was confirmed by independent experiment.
Conclusion:	The test substance did not exhibit mutagenic activity in this assay.
Reference:	Haworth, S., Lawlor, T., Mortelmans, K., Speck, W. and Zeiger, E. 1983. Salmonella mutagenicity test results for 250 chemicals. Environ. Mutagen. **1:**3-142. As cited in the EU Risk Assessment.
Reliability:	(Klimisch Code 2) Valid with restrictions.

14.1.2

Type:	Bacterial reverse mutation assay (Ames test)
System of testing:	*S. typhimurium* TA 1538 and *E. coli* strains WP2 and WP2*uvr*A
Concentrations:	0 to 1.0 mg/mL (concentrations in µg/plate not reported)
Metabolic activation:	With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:	Negative
Cytotoxicity conc.:	With and without metabolic activation: 1.0 mg/ml
Genotoxic effects:	With metabolic activation: positive [ ]; ambiguous [ ]; Negative [X]
	Without metabolic activation: positive [ ]; ambiguous [ ]; Negative [X]
Year:	1983
GLP:	Yes [ ] No [ ] ? [X]
Test substance:	Bisphenol A (CAS RN 80-05-7)
Remark:	*S. typhimurium* TA 1538 and *E. coli* strains WP2 and WP2*uvr*A were exposed in a pre-incubation assay to bisphenol A at concentrations up to 1.0 mg/mL in the presence and absence of metabolic activation. Cytotoxicity, as evidenced by a >50% decrease in the number of spontaneous revertants, was observed at 0.5 mg/ml in WP2*uvra* with and without metabolic activation and TA 1538 without metabolic activation. No cytotoxicity was observed in WP2 with and without metabolic activation. No increase in the number of revertants was seen in any of the tested cultures. An independent experiment using a plate incorporation protocol and the performance of the controls confirmed the validity of this test.
Conclusion:	The test substance did not exhibit mutagenic activity in this assay.

Reference:	Dean, B.J. and Brooks, T.M. 1978. Toxicity Tests with Diphenylol Propane (DPP): *In vitro* Mutation Studies. Shell Research Report TLGR.0111.78. As cited in the EU Risk Assessment.
Reliability:	(Klimisch Code 2) Valid with restrictions.
14.1.3	
Type:	Bacterial reverse mutation assay (Ames test)
System of testing:	*S. typhimurium* TA98, TA100, TA1535 and TA1537 and *E. coli* strain WP2*uvr*A
Concentrations:	0 - 5000 μg/plate
Metabolic activation:	With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:	Negative
Cytotoxicity conc.:	≥150 μg/plate
Genotoxic effects:	With metabolic activation: positive [ ]; ambiguous [ ]; Negative [X] Without metabolic activation: positive [ ]; ambiguous [ ]; Negative [X]
Year:	1997
GLP:	Yes [ ] No [ ] ? [X]
Test substance:	Spirobiindane (CAS RN 1568-80-5)
Remark:	*S. typhimurium* tester strains TA98, TA100, TA1535 and TA1537 and *E. coli* tester strain WP2 *uvr*A were exposed using the plate incorporation method to Spirobiindane at concentrations up to 5000 μg/plate in the presence and absence of metabolic activation (Aroclor-induced rat liver S9). The test substance was dissolved in DMSO at a concentration of 500 mg/ml.
Results:	In the first phase, the preliminary toxicity assay, the maximum dose tested was 5000 μg/ plate; this dose was achieved using a concentration of 100 mg/ml and a 50 μl plating aliquot. Precipitate was observed at ≥333 μg/plate. Toxicity was observed at ≥267 to ≥333, μg/plate, except for tester strain TA98 in the presence of S9 activation, in which toxicity was not observed. Based on the findings of the toxicity assay, the doses plated in the initial mutagenicity assay were 3.3-450 μg/plate without metabolic activation and 3.3-750 μg/plate with metabolic activation. In the mutagenicity assay, no positive response was observed. Precipitate was observed at ≥150 to 450 μg/plate and toxicity was observed at ≥150 to 750 μg/plate. This result was confirmed in an independent repeat assay.
Conclusion:	The test substance did not exhibit mutagenic activity in this assay.
Reference:	Wagner, V. 1997. Unpublished Report No. G97AH81.5020 entitled "Bacterial Reverse Mutation Assay with an Independent Repeat Assay", dated April 3, 1997 for General Electric Company, Plastics Business Operations, Pittsfield, MA, USA; from BioReliance, Inc., Rockville, MD, USA
Reliability:	(Klimisch Code 1) Valid without restriction

14.2 NON-BACTERIAL *IN VITRO* TEST (MAMMALIAN CELLS)

Type:	*In vitro* mammalian cell gene mutation test (Chromosomal aberration assay)
System of testing:	CHO cells
Concentration:	30 - 50 μg/mL with activation 20 - 40 μg/mL without activation
Metabolic activation:	With [ ]; Without [ ]; With and Without [X]; No data [ ]
Results:	Negative with and without metabolic activation.
Cytotoxicity conc.:	With metabolic activation: 50 μg/mL Without metabolic activation: None reported

Genotoxic effects:	+	?	-
With metabolic activation:	[ ]	[ ]	[X]
Without metabolic activation:	[ ]	[ ]	[X]

GLP:	Yes [ ] No [] ? [X]
Test Substance:	Bisphenol A
Remarks:	In a chromosome aberration study in Chinese hamster ovary (CHO) cells were exposed in two separate experiments to 30-50 μg/mL bisphenol A for 2 hours with metabolic activation and 20-40 μg/mL for 8 hours without metabolic activation. Cells were harvested at 11 hours with metabolic activation and 21 hours without metabolic activation. In the first test with metabolic activation, an increase in the percentage of metaphases with chromosome aberrations from bisphenol A treated cultures was observed only at the top dose in the presence of cytotoxicity; 14% at 50 μg/mL compared to 3% in controls. In these high-dose cultures, it was stated that cell confluence was reduced by approximately 70%. In the second test, no significant increases were observed in with metabolic activation; only 3% of cells at the highest dose had aberrations. No significant increases in aberrations were observed without metabolic activation with bisphenol A evidently being tested up to "toxic levels." The positive controls produced clear increases in chromosome aberrations.
Conclusions:	This study was judged to have given a negative result, since the observed increase in the first experiment was not reproducible.
Reference:	Ivett, J.L., Brown , B.M., Rodgers, C., Anderson, B.E., Ressnick, M.A. and Zeiger, E. 1989. Chromosomal aberrations and sister chromatid exchange tests in Chinese hamster ovary cells *in vitro*. IV. Results with 15 chemicals. Environ. Mol. Mutagen. **14**:165-187. As cited in the EU Risk Assessment.
Reliability:	(Klimisch Code 2) Valid with restrictions.

15.0 REPEATED DOSE TOXICITY

Species/Strain:	Rat/F344
Sex:	Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration:	Oral, Dietary feed
Exposure Period:	103 weeks
Frequency of Treatment:	Daily

Post Exposure Observation Period:	None
Dose:	0, 1000 or 2000 ppm (approximately 50 and 100 mg/kg/day)
Control Group:	Yes [X] No [ ] No data [ ] Concurrent no treatment [X] Concurrent vehicle [ ] Historical [ ]
NOAEL:	None established
LOAEL:	1000 ppm
Method:	Chronic study protocol from NTP
Year:	1982
GLP:	Yes [ ] No [X] ? [ ]
Test Substance:	Bisphenol A
Remark:	The following was summarized for the IRIS Risk Assessment: In this 103-week dietary study, groups of 50 rats/sex were fed diets containing 0, 1000, or 2000 ppm bisphenol A. All treated groups of rats had reduced body weights, compared with controls, evident from the 5th week of exposure. Food consumption was also reduced, compared with controls, but this effect was not observed until the 12th week of treatment. Reduced body weights in rats, therefore, was considered a direct adverse effect of exposure to bisphenol A.
Results:	The LOAEL for BPA was considered to be 50 mg/kg/day. The Oral RfD was established at 0.05 mg/kg/day by IRIS.
Reference:	Integrated Risk Information System (IRIS Document); Bisphenol A. CASRN: 80-05-7. 1993.
Reliability:	(Klimisch Code 2) Valid with restrictions.

16.0 REPRODUCTIVE TOXICITY

Type:	Fertility [ ] One generation study [ ] Two generation study [ ] Other [X]
Species/Strain:	Rat/CD® (Sprague-Dawley)
Sex:	Female [ ] Male [ ] Male/Female [X] No data [ ]
Route of Administration:	Dietary
Exposure Period:	F0 males: 15 weeks; F0 females: 18 weeks F1 & F2 males: 18 weeks; F1 & F2 females: 21 weeks F3 males & females: 13 weeks
Premating Exposure Period:	10 weeks
Dose:	0, 0.15, 0.3, 4.5, 75, 750 or 7500 ppm (0, 0.001, 0.02, 0.3, 5, 50 or 500 mg/kg/day)
Control Group:	Yes [X]; No [ ]; No data [ ]; Concurrent no treatment [ ] Concurrent vehicle [X] Historical [ ]
NOAEL Parental:	75 ppm (5 mg/kg/day)
NOAEL Reproduction:	750 ppm (50 mg/kg/day)
NOAEL F1 Offspring:	750 ppm (50 mg/kg/day)
Method:	OECD Test Guideline 416 (modified)
GLP:	Yes [X] No [ ] ? [ ]
Test Substance:	Bisphenol A (99.5% pure)
Remark:	Test procedure: Exposure to bisphenol A began for the F0 generation at about 7 weeks of age and continued throughout a 10-week pre-breed exposure period, a 2-week mating period (when F0 animals were mated [one male and one female] within each dose group) and gestation. F0 males were sacrificed after the F1 delivery period. Exposure of F0 females to bisphenol A continued throughout lactation until weaning (post-natal day 21) when F0 animals were sacrificed. Selected F1 animals were similarly mated to produce the F2 generation and selected F2 animals were mated to produce the F3 generation. The same exposure regime was used for F1 and F2 animals with direct exposure to bisphenol A in the diet commencing approximately at post-natal day 21. Selected F3 animals were exposed to bisphenol A only for a 10-week period from weaning as they were not mated. For the F0 generation and retained F1, F2 and F3 animals, clinical signs of toxicity, body weights and food consumption were reported. Estrous cycles were monitored in the last 3 weeks of the pre-breed exposure period and during the mating period for all generations. At the necropsy of adult animals, sperm samples were taken for analysis of epididymal sperm number, motility (using a computer assisted sperm motion analysis system) and morphology, testicular-resistant spermatid head counts, daily sperm production, and efficiency of daily sperm production, a number of organs were weighed and selected organs were examined histopathologically. Parameters assessed in the young offspring included litter size, body weights, survival, gross appearance, anogenital distance (AGD) (in F2 and F3 offspring only), sexual development and, for animals killed at weaning, gross appearance of organs at necropsy with attention given to reproductive organs.

Results

7500 ppm (approximately 500 mg/kg/day). Adult systemic toxicity (F0, F1, F2, and F3) was expressed as consistent and persistent reduced body weights and weight gains, typically greater than 15%, occasional reductions in feed consumption as g/day, and occasional increases in feed consumption as g/kg/day. Food efficiency was occasionally reduced. For non-reproductive organs, absolute organ weights were consistently reduced in both sexes, while relative organ weights were commonly increased. Histopathologic findings on non-reproductive organs included increased incidence of renal tubular degeneration and chronic hepatic inflammation only in F0, F1, and F2 females (but not F3). There were no treatment- or dose-related direct effects on reproductive organ weights, histopathology, or function. Consistent with the reduced body weights and body weight gains in this group, paired ovarian weights were significantly reduced for F0, F1, and F2 females (absolute and relative weights) and for F3 females (absolute weights only). Paired ovarian follicle counts (ten females each at 0 and 7500 ppm) were significantly increased at 7500 ppm in F0 females but were unaffected in F1, F2, and F3 females. There were no effects of treatment on any andrological parameters at any dose in any generation (except for significantly reduced epididymal sperm counts only in F1 males at 7500 ppm, and for significantly reduced daily sperm production per testis, but not efficiency of daily sperm production only in F3 males at 7500 ppm). The only reproductive effect was a significant decrease in total and live pups per litter (with no significant increase in prenatal postimplantation loss per litter) on pnd 0 and 4 (precull) for F1, F2, and F3 litters at 7500 ppm, associated with reduced uterine weight in parental F0, F1, and F2 females. There were no effects on mating, fertility, or gestational indices, on precoital interval, gestational length, offspring sex ratios, or on nipple and/or areola retention in preweanling F1, F2, and F3 male pups. The only offspring effects at 7500 ppm included statistically significant reductions in pup body weights per litter, beginning on pnd 7 for F1, F2, and F3 offspring, and statistically significant delayed acquisition of both vaginal patency and preputial separation for F1, F2, and F3 postweanling pups. Anogenital distance (measured in F2 and F3 offspring on pnd 0) was unaffected for F2 and F3 males and for F3 females. Only F2 female anogenital distance was significantly increased by 0.03 mm at 0.015, 0.3, and 4.5 ppm, and by 0.04 mm at 750 ppm versus the control value. Although statistically significant, these variations were only 0.03 to 0.04 mm and were considered to be due to the extremely precise measurement technique used and were not considered to be of biological or toxicological significance. These changes (referring to preputial separation, vaginal patency, and anogenital distance) did not affect reproductive function in the animals exhibiting them. The effects observed on reproductive function or postnatal toxicity were present in a clearly toxic dose (adult systemic toxicity) and were not observed at doses below 7500 ppm.

750 ppm (approximately 50 mg/kg/day). Adult systemic toxicity was present for F0, F1, F2, and F3 generations, expressed only as reduced

	body weights for F0 females (but not males) during prebreed, gestation, and lactation; F1 females (but not males) during gestation and lactation (but not prebreed); F2 males (but not females) only during prebreed, but not for F3 males or females. Feed consumption in g/day or g/kg/day and food efficiency were not consistently or persistently affected. In males, absolute liver weight was significantly reduced in all generations, absolute pituitary weight was significantly reduced in the F1 generation, and absolute kidney and spleen weights were significantly reduced in the F2 generation. In females, absolute and relative non-reproductive organ weights were not affected in any generation. There were no treatment-related gross or histopathologic findings. Reproductive organ weights, histopathology, and reproductive function were all unaffected in both males and females. There were no effects on reproductive, gestational, or offspring parameters, on pre- or postnatal survival, anogenital distance (F2 and F3 offspring, except for a significant increase of 0.04 mm for F2 female anogenital distance), or onset of puberty (except for a small delay in acquisition of preputial separation in F1 males, but not in F2 or F3 males) **75 ppm - 0.015 ppm (approximately 5 - 0.001 mg/kg/day).** There were no consistent or persistent treatment-related effects in F0, F1, F2, or F3 animals, nor in F1, F2, or F3 offspring.
Conclusion:	Exposure to dietary BPA for three generations, one litter per generation, resulted in adult systemic toxicity only at 750 and 7500 ppm. Because of the lack of adverse effects below these doses, the adult systemic toxicity NOAEL (no observable adverse effect level) was established at 75 ppm (equivalent to approximately 5 mg/kg/day) in CD® (Sprague-Dawley) rats, under the conditions of this study. Similarly, because there were no treatment- or dose-related reproductive or postnatal toxicity effects below 7500 ppm, the reproductive and postnatal toxicity NOAELs were concluded to be 750 ppm (equivalent to approximately 50 mg/kg/day) in CD® (Sprague-Dawley) rats, under the conditions of this study. There were no effects of BPA dietary exposure on any adult or offspring parameter at 0.015, 0.3, 4.5, or 75 ppm (resulting in BPA intakes of approximately 0.001, 0.02, 0.3, or 5 mg/kg/day, respectively).
Reference:	R.W. Tyl, Ph.D., DABT, C.B. Myers, M.S, M.C. Marr, B.A., LATG. 2000. Three-Generation Reproductive Toxicity Study of Dietary Bisphenol A in CD Sprague-Dawley Rats. RTI Report #: 65C-07036-000.
Reliability:	(Klimisch Code 1) Valid without restrictions.

17.0 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species/Strain:	Rat; Sprague-Dawley CD
Sex:	Female [X]; Male [ ]; Male/Female [ ]; No data [ ]
Route of Administration:	Oral (gavage)
Duration of Test:	20 days
Exposure Period:	Days 6 through 15 of gestation
Frequency of Treatment:	Daily
Dose:	0, 160, 320, 640 or 1280 mg/kg/day
Control group:	Yes [X] No [ ] No data [ ] Concurrent no treatment [ ] Concurrent vehicle [X] Historical [ ]
NOEL Maternal Toxicity:	None Established; LOAEL = 160 mg/kg/day.
NOEL Teratogenicity:	> 640 mg/kg/day
GLP:	Yes [X] No [ ] ? [ ]
Test Substance:	Bisphenol A
Method:	Not stated.
Remark:	Range-finding study: groups of 8 time-mated CD rats were gavaged with 0, 500, 1000, 1500, 2000, 2500 or 3000 mg BPA/kg/day in corn oil on days 6 to 15 of gestation. Animals were sacrificed on day 20 of gestation and the fetuses were examined for gross morphological abnormalities only. Deaths were observed in 1, 5, 3 and 5 rats at 1,500, 2,000, 2,500 and 3,000 mg/kg, respectively. Clinical signs of toxicity were observed at all doses and included diarrhea, lacrimation, lethargy, rough coat, wheezing, wet urogenital area, arched back, dyspnea, bloody nose, disorientation, alopecia, piloerection and vaginal bleeding. A statistically significant decrease in maternal body weight gain (24%) was observed at 1000 mg/kg and above during the gestation period, and during the treatment period a decrease in maternal body weight was observed at 1500 mg/kg and above. In the main study, two tests were performed and the data from both tests combined. Thus in total, groups of 27-29 time-mated CD rats were gavaged with 0, 160, 320, 640 or 1280 mg BPA/kg/day in corn oil on days 6 to 15 of gestation. Animals were sacrificed on day 20 of gestation and the fetuses were subjected to routine external, visceral and skeletal examination.
Results:	No deaths were observed in the 0, 160, 320 and 640 mg/kg dose groups. At 1280 mg/kg, deaths were observed in 7/27 females and, because of this high mortality rate, the top dose group was not included in statistical analysis. Outward signs of toxicity observed in BPA treated animals included rough coat, piloerection, alopecia, pica, excess salivation, wet urogenital area, dyspnea, chromodacryorrhea, tremors, red-stained coat, wheezing and vocalization. A statistically significant decrease in mean maternal body weight gain was observed in dams at all dose levels for the treatment period (35-54%) and the gestation period (11-14%). No effect was observed on gravid uterine weights. When maternal body weight gain was corrected for gravid uterine weight, a statistically significant decrease was still apparent at all dose levels (26-34%). At necropsy, no

	effect was observed on mean relative liver weight in dams. Pregnancy rates were not affected by treatment with BPA, nor was there any effect on the number of implantation sites per litter, % resorptions per litter, number of live fetuses per litter, sex ratio, mean fetal body weight per litter, % fetuses malformed per litter and % litters with malformed fetuses.
Conclusion:	No evidence of developmental toxicity in the rat was evident at exposure levels which are toxic to the mother. A maternal no effect level could not be identified; the LOAEL of 160 mg/kg based on clinical signs of toxicity and a statistically significant decrease (26%) in body weight gain was identified. No fetal effects were seen at the highest dose level evaluated, 640 mg/kg.
Reference:	Morrissey, R.E., George, J.D., Price, C.J., Tyl, R.W., Marr, M.C. and Kimmel, C.A. 1987. The developmental toxicity of bisphenol A in rats and mice. Fundam. Appl. Toxicol. **8**:571-582. As cited in the EU Risk Assessment.
Reliability:	(Klimisch Code 1) Reliable without restrictions.