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.

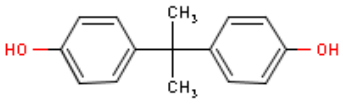
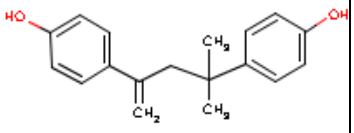
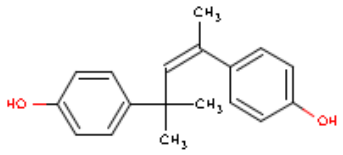
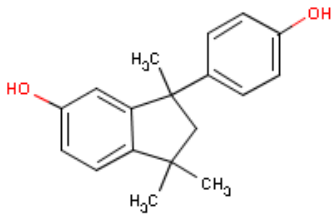
CHEMICAL IDENTITY AND DATA REVIEW

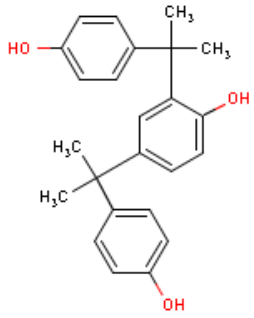
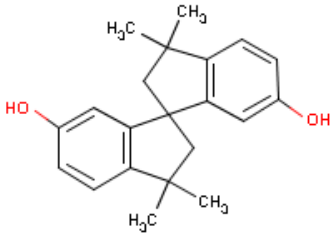
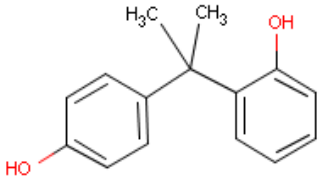
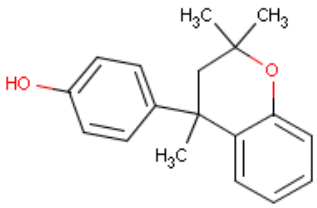
COMPONENTS

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.