TEST PLAN FOR PROPANOIC ACID, 3-HYDROXY-2,2-DIMETHYL-,3-HYDROXY-2,2-DIMETHYLPROPYL ESTER (CAS NO. 1115-20-4)

November 28, 2006

OVERVIEW

BASF Corporation has agreed to sponsor propanoic acid, 3-hydroxy-2,2-dimethyl-, 3-hydroxy-2,2-dimethylpropyl ester (CAS No. 1115-20-4) in the U.S. EPA High Production Volume Chemical Program. The sponsor hereby submits a test plan for this substance. It is the sponsor's intent to use existing and modeled data for the material of interest and data from related materials (as proposed in the test plan) to fulfill the Screening Information Set (SIDS) endpoints.

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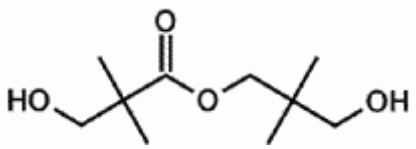
1. Introduction

The BASF Corporation has agreed to supply screening information under the U.S. EPA High Production Volume Chemical Program for propanoic acid, 3-hydroxy-2,2-dimethyl-, 3-hydroxy-2,2-dimethylpropyl ester (CAS No. 1115-20-4). For this test plan, the test substance will be referred to as hydroxypivalyl hydroxypivalate (HPHP).

2. Designation of Test Substance

The IUPAC designation for the test substance presented in this test plan is propanoic acid, 3-hydroxy-2,2-dimethyl-, 3-hydroxy-2,2-dimethylpropyl ester (CAS No. 1115-20-4). The substance is a Class 1 organic compound. Its chemical formula, molecular structure and SMILES notation are as follows:

$C_{10}H_{20}O_4$ or $HOCH_2C(CH_3)_2C(=O)OCH_2C(CH_3)_2CH_2OH$



O=C(OCC(CO)(C)C)C(CO)(C)C

Synonyms:

Esterdiol 204
3-Hydroxy-2,2-dimethylpropyl hydroxypivalate
Hydroxyneopentyl hydroxypivalate
Hydroxypivalic acid neopentyl glycol ester
3-(Hydroxypivaloyloxy)-2,2-dimethylpropanol
Hydroxypivalyl hydroxypivalate
HPHP
Neopentyl glycol monohydroxypivalate

3. General Use and Exposure Information

Uses of Test Substance
HPHP is used as an intermediate in the manufacture of binding agents and coatings (coil coatings or powder coatings) (BASF AG, 2005). It is also used as a monomer in the manufacture of polymers. HPHP is not known to be present in consumer products. Exposure to this substance is most likely to occur in the workplace during manufacture or use as an intermediate. Possible routes of exposure (from most to least likely) are dermal, inhalation, and oral. Since HPHP has low volatility (0.03 hPa at 20 degrees C) and because manufacture of HPHP and use in synthesis

as an intermediate take place in closed systems, the opportunity for significant worker exposures is low. Workplace exposure is most likely to take place during sampling.

4. Criteria for Determining Adequacy of Data

All available studies were reviewed and assessed for adequacy according to the standards of Klimisch et al. (1997). Studies receiving a Klimisch rating of 1 or 2 were considered to be adequate.

5. Test Plan Approach

The test plan makes use of existing studies and modeling for HPHP, combined with additional studies for the analog propanoic acid, 2-methyl-, 2-methylpropyl ester (CAS No. 97-85-8) to address the screening information data set endpoints. This substance is also known as isobutyl isobutyrate (IBIB). The test plan also makes use of the expected rapid hydrolysis of HPHP to hydroxy pivalic acid and neopentyl glycol (NPG, CAS No. 126-30-7). IBIB and NPG have already been reviewed by OECD/SIDS. The robust summary dossiers for the SIDS submissions of CAS Nos. 97-85-8 and 126-30-7 (that are available at http://www.chem.unep.ch/irptc/sids/OECDSIDS/97858.pdf and http://cs3-hq.oecd.org/scripts/hpv, respectively) have been appended to this test plan submission. Additional information from a European Commission IUCLID document for CAS No. 126-30-7 (available at http://ecb.jrc.it/IUCLID-Data-Sheet/126307.pdf) also has been added to the data set.

Support for the use of the analog and metabolism considerations

Data rich Analog

Isobutyl Isobutyrate (IBIB) (analog): This substance is very similar in molecular structure to HPHP. Both are aliphatic esters with a high degree of branching. HPHP has a neopentyl structure with five carbon atoms for both the acid and alcohol portions. IBIB has an isobutyl structure with four carbon atoms for both the acid and alcohol portions. A difference is that the test substance also has terminal hydroxy (alcohol) groups in both the acid and alcohol portions of the molecule. These are not present in the IBIB molecule. The comparative molecular structures are shown below.

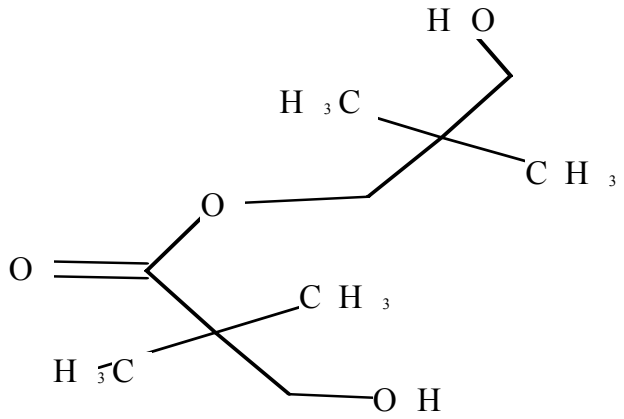
Metabolism considerations

Metabolism of the analog IBIB to isobutanol and isobutyric acid in animals occurs rapidly (via enzymatic hydrolysis) (Deisinger, 2003). Similarly, HPHP is expected to undergo rapid hydrolysis to hydroxypivalic acid and NPG. As isobutanol is further oxidized to isobutyric acid, NPG will be metabolized to hydroxypivalic acid. Similar to other acids, hydroxypivalic acid can be further metabolized or conjugated (e.g., glucuronides, sulfates, etc.) to polar products that are excreted in the urine (Bevan, 2001; Cragg , 2001; Thurman,1992).

The molecular structures of the above substances and the test substance are shown below for comparison:

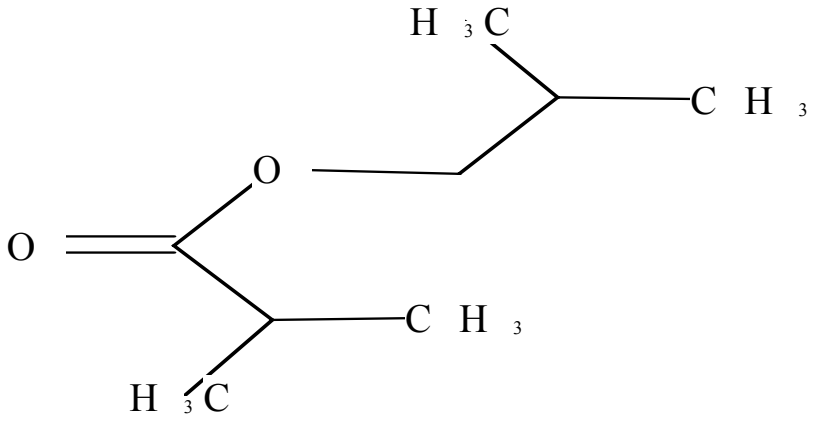
Test Substance: Propanoic acid, 3-hydroxy-2,2-dimethyl-, 3-hydroxy-2,2-dimethylpropyl ester (CAS No. 1115-20-4)

$HOCH_2C(CH_3)_2C(=O)OCH_2C(CH_3)_2CH_2OH$ or:



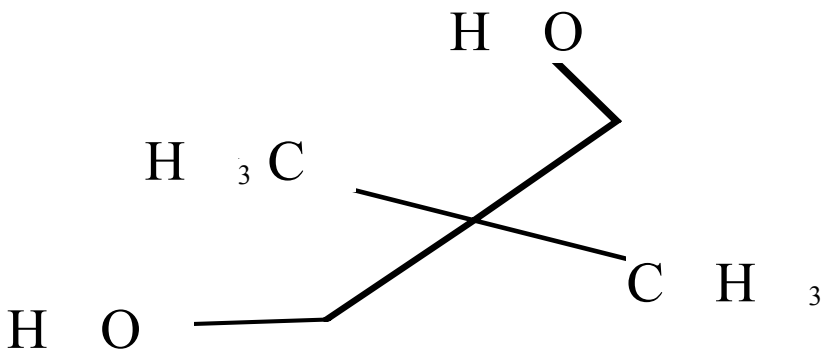
Analog: Propanoic acid, 2-methyl-, 2-methylpropyl ester (CAS No. 97-85-8)

$CH_3CH(CH_3)C(=O)OCH_2CH(CH_3)CH_3$ or



Neopentyl glycol (CAS No. 126-30-7)

$HOCH_2C(CH_3)_2CH_2OH$ or



The HPHP test plan matrix (as shown in Table 1) was constructed after a careful evaluation of all existing data (see below). This matrix is arranged by study type (columns) and screening data endpoints (rows), and indicates if data are provided for each end point in the sets of robust summaries.

Table 1. Test Plan Matrix for Propanoic acid, 3-hydroxy-2,2-dimethyl-, 3-hydroxy-2,2-dimethylpropyl ester CAS No. 1115-20-4)

CAS No. 1115-20-4	Information	Measured	Estimated	Analog/ Metabolite	New Testing Required
ENDPOINT	Y/N	Y/N	Y/N	Y/N	Y/N
PHYS/CHEM PROPERTIES					
Melting Point	Y	Y	N	N	N
Boiling Point	Y	Y	E	N	N
Vapor Pressure	Y	Y	E	N	N
Partition Coefficient	Y	Y	Y	N	N
Water Solubility	Y	Y	E	N	N
ENVIRONMENTAL FATE					
Photodegradation	Y	N	Y	N	N
Stability in Water	Y	N	Y	N	N
Biodegradation	Y	Y	N	N	N
Transport between Environmental Compartments (Fugacity)	Y	N	Y	N	N
ECOTOXICITY					
Acute Toxicity to Fish	Y	Y	N	N	N
Acute Toxicity to Aquatic Invertebrates	Y	Y	N	N	N
Toxicity to Aquatic Plants	Y	Y	N	N	N
Acute Toxicity to Bacteria (NR)	Y	Y	N		
TOXICOLOGICAL DATA					
Acute Toxicity	Y	Y	N	N	N
Repeated Dose Toxicity	N	N	N	Y	N
Genetic Toxicity-Mutation	Y	Y	N	N	N
Genetic Toxicity-Chromosomal Aberrations	N	N	N	Y	N
Toxicity to Reproduction	N	N	N	Y	N
Developmental Toxicity	N	N	N	Y	N
OTHER TOXICITY DATA					
Skin Irritation (NR)	Y	Y	N	N	N
Eye Irritation (NR)	Y	Y	N	N	N

Y = yes; N = no; NR = not required

5.1 Chemical and Physical Properties

The results of chemical/physical property testing are shown in Table 2.

Table 2. Chemical/physical properties of HPHP

Endpoint	Measured Data	Estimated Data (EPIWIN)
Molecular weight (g/mol)	204.27	None available
Melting point	48.0 - 54.9 ºC	80.89 ºC
Boiling point	283.2ºC at 1013 hPa	303.7 ºC at 1013 hPa
Relative density	1.015 at 67 ºC	None available
Vapor pressure	0.03 hPa at 20 °C	.00012 hPa at 20 °C
Partition coefficient (Log Pow or Kow)	0.858 at 25 °C	1.07
Water solubility (mg/l)	270,000 at 25 °C	18,400 at 25 °C

5.1.1 Melting Point

A measured melting point of 48.0-54.9 ºC was obtained from a standard test procedure (BASF AG, 1981). Additional studies performed by BASF AG and Union Carbide indicate a melting point of approximately 50 ºC (BASF AG, 1974a; 1987a, Union Carbide, 1997)

5.1.2 Boiling Point

A measured boiling point of 283.2 ºC at 1013 hPa has been reported by BASF AG (1987b). No study documentation is given, but the boiling point was run by a scientifically acceptable BASF AG standard procedure using a highly pure test sample. A boiling point of 303.7ºC at 1013 hPa was estimated by EPIWIN MPBPWIN.

5.1.3 Vapor Pressure

BASF AG reports a vapor pressure of 0.03 hPa at 20 ºC on its MSDS (2006). A vapor pressure of 0.00012 hPa at 20 ºC was estimated by EPIWIN MPBPWIN.

5.1.4 Octanol/Water Partition Coefficient

An OECD Guideline 107 “Shake Flask” study provides a measured value of Log Pow = 0.858 (BASF AG, 1988a). This value is in rough agreement with an EPIWIN KOWWIN program estimation of log Kow = 1.07.

5.1.5 Water Solubility

A measured water solubility value of 270,000 mg/l at 25ºC has been determined by BASF AG (1999). A water solubility of 18,400 mg/l at 25ºC was estimated by EPIWIN WSKOW

5.1.6 Summary/Test Plan for Physical Properties

Measured and calculated values are available for boiling point, vapor pressure, octanol/water partition coefficient and water solubility. A measured value is available for melting point. These values are considered to be sufficient to characterize these endpoints.

5.2 Environmental Fate/Pathways

Results of environmental fate modeling and studies are summarized in Table 3.

Table 3. Environmental fate parameters for HPHP

Endpoint	Value
Indirect Photolysis (OH sensitizer) (Hydroxyl Radical Rate Constant)[b] (Atmospheric $T_{1/2}$) [b]	 10.829 E-12 cm3/(molecule*sec) 11.9 hours
Stability in Water[a]	$T_{1/2}$ = 113.7 year at 20 ºC at pH=7
Henry's Law Constant[b]	1.70 E-9 atm-m^3/mol
Koc[b]	10
Environmental transport (Fugacity Level III mass percentages)[b]	Air = 0.424 Water = 37.1 Soil = 62.4 Sediment = 0.073
Biodegradation[a]	Readily Biodegradable

[a]measured; [b] Estimated using EPIWIN

5.2.1 Photodegradation

Photodegradation with hydroxyl radical sensitizer was estimated using EPIWIN/AOP (v1.90). An overall OH rate constant of 10.829 E-12 cm^3/(molecule*sec) was calculated. A half-life of 11.9 hours was calculated assuming a constant concentration of OH radical and pseudo first order kinetics.

5.2.2 Stability in Water

EPIWIN HYDROWIN (v1.67) estimates a hydrolysis half-life of 113.7 years under neutral ambient abiotic conditions, and in the absence of catalysts.

5.2.3 Fugacity

Level III fugacity modeling has been conducted on HPHP using the EPIWIN model. Measured inputs to the program are the melting point, boiling point, vapor pressure, partition coefficient and water solubility values listed in Tables 2 and 3. Emission rates inputted into the program were air: 1000 kg/hr, water: 1000 kg/hr, soil: 1000 kg/hr and sediment: 0 kg/hour. The following half-lives were calculated: T ½ air = 23.7 hr, water = 360 hr, soil = 720 hr, and sediment = 3240 hr. A Henry's Law Constant of 1.70 E -9 atm-m^3/mol and a soil sediment

partition constant (Koc) of 10 were estimated using the EPIWIN/HENRY and PCKOC Programs, respectively.

5.2.4 Biodegradation

Results of an OECD Test Guideline 301 A, Ready Biodegradability: DOC Die Away Test show that HPHP is readily biodegradable (99 % after 21 days) (BASF, 2003a). Additionally, an OECD Guideline 302 B, Inherent biodegradability: Modified Zahn-Wellens Test shows 100% biodegradation after 28 days (Lawrence and Ruffing, 1995).

5.2.5 Summary/Test Plan for Environmental Fate Parameters

Measured data are available for biodegradation and partition coefficient. Estimation data are available for atmospheric photodegradation, rate of hydrolysis and for environmental transport. No additional studies are needed.

5.3 Ecotoxicity

5.3.1 Acute Toxicity to Fish

A static OECD Test Guideline 203 study (with analytical confirmation of test concentrations) has been performed in Pimephales promelas (fathead minnows) with HPHP of approximately 98% purity (Hinkson and Hirsch, 1995a). The 96-hr no observable effect concentration (NOEC) and LC_{50} value were 1024 mg/l and > 1024 mg/l, respectively. An additional, reliable study performed in Leuciscus idus (golden orfe), reports NOEC and LC_{50} values of 1000 mg/l and 3160 mg/l, respectively (BASF AG, 1987c).

5.3.2 Acute Toxicity to Aquatic Invertebrates

A static OECD Test Guideline 202 study in Daphnia (with analytical confirmation of test concentrations) was performed with nominal concentrations of up to 1000 mg/l HPHP of 98% purity (Hinkson and Hirsch, 1995b). The study was performed in duplicate. The 48-hour no observable effect concentration (NOEC) and effective concentration in 50% of the organisms (EC_{50}) in the first series were 1125.8 mg/l and > 1125.8 mg/l, respectively. In the second replicate, the respective values were 559.6 mg/l and > 559.6 mg/l. The most conservative EC_{50} value (> 559.6 mg/l) is the value that will be used for this assessment. An additional, reliable study in which concentrations were not analytically measured reports a 48-hr EC_{50} value of > 500 mg/l (BASF AG, 1988b).

5.3.3 Acute Toxicity to Aquatic Plants

HPHP of unknown purity was tested in Desmodesmus subspicatus (formerly Scenedesmus), according to German Industrial Standard DIN 38412, Part 9 (BASF, 1989b). The 72 hour EC_{50} values determined for biomass (the more sensitive indicator) and growth rate were 1600 mg/l. and 2000 mg/l, respectively.

5.3.4 Acute Toxicity to Bacteria

An OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test" conducted with HPHP of 98.7% purity reports 30-minute EC_{20}, EC_{50} and EC_{80} values of > 1000 mg/l (BASF AG, 2003b).

5.3.5 Summary/Test Plan for Ecotoxicity

LC_{50} and EC_{50} toxicity values for HPHP towards fish, Daphnia, algae and bacteria have been determined in Guideline studies. The LC_{50}/EC_{50} values in all three species are all greater than 559 mg/l. No additional testing is necessary.

5.4 Human Health Data

5.4.1 Toxicokinetics and Metabolism

Metabolism/toxicokinetic studies have been conducted with the related material isobutyl isobutyrate (IBIB) using intravenous injections (femoral vein) with simultaneous intravenous (jugular vein) sampling (Deisinger, 2003). The following comments were excerpted from the IBIB SIAR presented at SIAM 20. “Isobutyl isobutyrate levels within the first seconds had mean values of 1045 µM and rapidly decreased thereafter. The calculated $T_{1/2}$ by one-compartment modeling was 11.1 seconds. Isobutanol and isobutyric acid levels increased rapidly up to peak levels of 218 and 304 µM, respectively. Isobutyric acid levels were consistently higher than isobutanol levels, suggesting further metabolism of the isobutanol metabolite to isobutyric acid. Both isobutanol and isobutyric acid levels remained increased throughout the 240 second sampling period.” These results indicate rapid metabolism of IBIB to isobutanol and isobutyric acid in vivo, followed by oxidation of isobutanol to isobutyric acid. Based on similarities in structure, HPHP is therefore expected to undergo rapid hydrolysis to NPG and hydroxypivalic acid, with further oxidation of NPG to hydroxypivalic acid.

Data from IBIB and isobutanol toxicity studies (as well as the HPHP metabolite NPG) have been included in the human health section. Data from these substances are useful when assessing the hazards associated with the systemic toxicity of HPHP due to the structural similarities between HPHP and IBIB.

5.4.2 Acute Mammalian Toxicity

This endpoint is filled by a sufficient oral toxicity study with HPHP in Sprague-Dawley rats. The study was similar to and OECD 401 Guideline study, but was given a reliability rating of 2 (valid with restrictions) because the observation period was 7 (rather than 14) days. In this study, the LD_{50} value for HPHP of 100% purity is 8000 mg/kg (BASF Ag, 1974b). Deaths (1/10 animals dosed with 4640 mg/kg and 7/10 dosed with 10000 mg/kg) occurred within 4 hours of dosing. No signs of toxicity were seen in low dose animals. Signs in high dose animals included dyspnea, abdominal and lateral posture, apathy, cyanosis, red encrusted noses.

The acute oral LD_{50} value of IBIB in rats is >6,400 mg/kg bw (Eastman Kodak Co., 1956). Weakness, ataxia, and death were noted at 12,800 mg/kg bw. As show in the table below, data from isobutanol acute oral toxicity studies (Christopher, 1993) are in agreement with the IBIB (as well as HPHP data).

Table 4. Oral LD50 values in rats for HPHP, NPG, IBIB and isobutanol

Material	HPHP	NPG	IBIB	isobutanol
LD_{50} value (mg/kg)	8000	3200*	> 6400	> 2830 mg/kg (males) 3350 (females)

* questionable reliability

An Inhalation Hazard Test has also been performed with 100% pure HPHP. Twelve Sprague-Dawley rats were exposed for 8 hours to a saturated atmosphere (estimated concentration of 0.04 mg/l). None of the animals died and no symptoms of toxicity were noted over the 7 day observation period (BASF Ag, 1974b).

5.4.3 Repeated Dose Mammalian Toxicity

In an OECD Test Guideline 422 study, Sprague-Dawley rats were administered 0, 100, 300 or 1000 mg/kg/day of the HPHP metabolite NPG (99% pure) by gavage (MHW, date unknown). Males were exposed for 14 days prior to mating and during mating (total of 42 days), and females were exposed for 14 days prior to mating, and during mating, gestation and three days of lactation. The no observable effect limit (NOAEL) for systemic toxicity was 100 mg/kg/day. Effects observed at 300 mg/kg/day (in males only) were increased total protein, bilirubin and albumin in blood and increased absolute and relative kidney and liver weights. Additional findings at 1000 mg/kg/day were hypertrophy of the liver of two males (without evidence of histological lesions) and a high incidence of protein casts, hyaline droplets and basophilic changes in the renal tubules of males. Systemic toxicity was not observed in females.

As stated in the SIAR for CAS No. 97-85-8, an 18-week subchronic oral gavage toxicity study has been done in rats using dose levels of 0, 10, 100, or 1,000 mg/kg bw/day (Drake, et al., 1978). The NOAEL was 1000 mg/kg bw/day in rats. Oral gavage studies with isobutanol support these findings (Toxicology Research Laboratories, Ltd, 1987).

Table 4. Oral. Repeated Dose Toxicity for NPG, IBIB and isobutanol

Material	NPG	IBIB	isobutanol
Study Duration (days)	42+	126	90
NOAEL value (mg/kg)	100	1000	316
LOAEL value (mg/kg)	300		1000

5.4.4 Genetic Toxicity

5.4.4.1 Mutagenicity

A study similar to an OECD Test Guideline 471 test was performed with 4 to 2500 µg/plate HPHP (> 97.5% purity) in 5 strains of *S. typhimurium* (TA98, TA100, TA1535, TA1537 and TA1538) (BASF AG, 1979). The test substance did not increase the number of revertants in any test strain, with or without metabolic activation. The study was given a reliability rating of 2 (valid with restrictions) since the material was not tested into the cytotoxic range and the highest dose used (2500 µg/plate) was less than that recommended by the current OECD 471 test guideline (5000 µg/plate). However, these inadequacies are not considered to invalidate the study. Ames tests and mammalian cell gene mutation assays performed with the similar materials NPG and IBIB are also negative (Hatano Research Institute, date unknown; MHW, 1993; SafePharm, 2003)

5.4.4.2 Chromosomal aberration

An in vitro cytogenicity assay has been performed with NPG (0.25, 0.50, 1.0 mg/ml) in Chinese Hamster Lung Cells, according to a Japanese guideline (Hatano Research Institute, date unknown). Results of this study were negative.

An oral *in vivo* mouse micronucleus test conducted with isobutanol was described in the SIAR for CAS No. 97-85-8 (Engelhardt and Hoffman, 2000). Isobutanol was administered once orally to male and female NMRI mice at doses up to 2,000 mg/kg/day body weight. Positive and negative controls all produced appropriate responses. Isobutanol did not produce any chromosome-damaging (clastogenic) effect, and there were no indications of any impairment of chromosome distribution in the course of mitosis (spindle poison effect).

5.4.5 Reproductive and Developmental Toxicity

An OECD Test Guideline 422 study, has been conducted with the HPHP metabolite NPG in Sprague-Dawley rats. Rats were administered 0, 100, 300 or 1000 mg/kg/day of NPG (99% pure) by gavage (MHW, date unknown). Males were exposed for 14 days prior to mating and during mating (total of 42 days), and females were exposed for 14 days prior to mating, and during mating, gestation and three days of lactation.

The NOAEL for reproductive effects was the highest dose tested (1000 mg/kg/day). There was no effect of test material on copulation, fertility, estrus cycle or lactation. Delivery was normal with the exception of one control animal. The NOAELs for teratogenicity and fetal toxicity were also 1000 mg/kg/day. Stillborn, dead pups and pups killed on Day for of lactation showed no abnormal findings attributable to administration of the test material. Body weight gain of treated pups (to Day 4 of lactation) was normal. External examination of the pups revealed no increase in abnormalities in exposed groups.

A two-generation reproductive toxicity study has been conducted by inhalation with isobutanol (WIL Research Labs, 2003). Groups of male and female rats were exposed by inhalation (6 hours/day, seven days/week) to 0, 1.52, 3.03, or 7.58 mg/L (500, 1000, or 2500-ppm) isobutanol for two generations. Daily treatments were continuous with the exception of the period between gestation day 21 through postnatal day 4 (removal of the dams from the pups during this period typically causes pup mortality). Exposure to 2500 ppm or 7.58 mg/L isobutanol did not cause any parental systemic, reproductive, or neonatal toxicity when administered for two generations via whole-body exposure.

In two definitive developmental toxicity studies (BASF, 1990; Klimisch, 1990, 1995), groups of pregnant female rats (25/group) or rabbits (15/group) were exposed via inhalation to 0, 0.5, 2.5 or 10 mg/L isobutanol for 6 hours/day during gestation (rats - days 6-15; rabbits – days 7-19). Rabbit dams exposed to 10 mg/L had slight decreases in body weight gain during gestation while exposures in rats had no treatment-related effects. No evidence of developmental or fetotoxicity was reported in either the rats or the rabbits fetuses.

5.4.6 Additional Data

5.4.6.1 Skin Irritation

The results of an occlusive skin irritation study in rabbits performed with an 80% concentration of HPHP in water indicate that the material is not irritating to skin (BASF AG, 1974b). The reliability of the study is questionable due to non-detailed documentation.

5.4.6.2 Eye Irritation

A study that was given a reliability rating of 2 (valid with restrictions) showed that a dose of 0.05 ml of concentrated HPHP was irritating to rabbit eyes. Moderate reddening, edema and corneal opacity developed within 24 hr after eye contact and persisted until day 8 post treatment. Based on the experimental experience, the lesions were not expected to be reversible. Therefore the material was classified as capable of posing a risk of serious damage to eyes (BASF AG, 1974b).

5.4.7 Summary/Test Plan for Mammalian Toxicity

Adequate toxicity studies have been conducted for HPHP with regard to acute toxicity and mutagenicity endpoints. Repeated dose, reproductive and developmental toxicity and chromosome aberration data from the metabolite NPG and the related materials IBIB and

isobutanol are used to fill these endpoints for HPHP since it is expected that HPHP will undergo rapid hydrolysis in vivo to NPG and hydroxypivalic acid (with further oxidation of NPG to hydroxypivalic acid). This expectation is based on data for the analogous chemical IBIB, which is rapidly hydrolyzed to isobutanol and isobutyric acid in vivo.

6. Summary

Physical properties

Measured values are available for melting point, boiling point, vapor pressure, octanol/water partition coefficient and water solubility. These values are considered to be sufficient to characterize these endpoints, without additional testing.

Environmental fate properties

Measured data are available for biodegradation and partition coefficient. Estimation data are available for atmospheric photodegradation, rate of hydrolysis and for environmental transport. Biodegradation testing indicates that the material is readily and inherently biodegradable. No additional environmental fate testing is necessary.

Aquatic toxicity

Results of Guideline studies performed in fish, Daphnia, algae and bacteria indicate LC_{50} and EC_{50} values for HPHP > 559 mg/l. Since adequate studies exist (which characterize the toxicity hazard of HPHP as minimal), no additional testing is necessary.

Mammalian toxicity

Adequate acute and eye toxicity and mutagenicity data are available for HPHP. Acute oral exposure to large amounts of HPHP is required to cause lethality in rats. Irreversible eye injury occurs in rabbits exposed to concentrated HPHP. HPHP is not mutagenic, and the metabolite NPG and related material isobutanol are not clastogenic.. In an OECD Guideline 422 study, there was no effect of treatment with up to 1000 mg/kg/day of NPG on reproduction or development of rats. In this study, male rats exposed to 300 and 1000 mg/kg/day NPG for 43 days exhibited changes in the liver and kidney. No effects were noted at 100 mg/kg/day. Therefore, the NOAELs for repeated dose, reproductive and developmental study for NPG are 100, 1000 and 1000 mg/kg/day, respectively. These are also expected to be the NOAELs for HPHP, since HPHP is rapidly metabolized to NPG in vivo. The related material isobutanol is not a reproductive or developmental toxicant in rats when inhaled at concentrations up to 7.58 or 10 mg/l. respectively.

7. References

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