

201-14952A

HIGH PRODUCTION VOLUME (HPV) CHALLENGE PROGRAM

REVISED TEST PLAN

FOR

HYDROQUINONE bis(2-HYDROXYETHYL)ETHER

CAS NO. - 104-38-1

PREPARED BY:

ARCH CHEMICALS, INC.

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December 19, 2003

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OVERVIEW

Arch Chemicals, Inc. (Arch) hereby submits for review and public comment the revised test plan for hydroquinone bis(2-hydroxyethyl)ether (HQEE; CAS # 104-38-1) under the Environmental Protection Agency's High Production Volume Chemical Challenge Program. It is the intent of Arch to use existing data, data from proposed studies and estimated values using predictive computer models acceptable to EPA to adequately fulfill the Screening Information Data Set (SIDS) for the physicochemical endpoints, environmental fate, ecotoxicity and human health-related toxicology.

HQEE is produced using hydroquinone and ethylene oxide and is used for polyurethane reactions as a chain extender. Chain extenders are low molecular weight substances that are capable of reacting with isocyanate groups to produce polyurethanes. HQEE has attained commercial significance for cast polyurethane elastomers as well as in thermoplastic elastomers to produce polyurethanes. These polyurethanes are very resistant to mechanical abrasion. The reaction using HQEE to produce polyurethanes is performed under temperature-controlled conditions in a polyurethane mixing and metering unit. This unit feeds components into the mixing head where the reaction between the isocyanate and HQEE begins. The reaction is completed in a closed mold to prevent reaction with atmospheric moisture. This unit is a sealed system because any exposure to moisture would compromise the reaction between HQEE and the isocyanate. The nature of this operation allows for very tight control of the HQEE; thus employee exposure to this material is low.

This chemical is not sold to the individual consumer. Its uses are in the industrial workplace where exposures are tightly controlled.

TEST PLAN SUMMARY

Hydroquinone bis(2-hydroxyethyl)ether CAS # 104-38-1	Information	OECD Study	Other	Estimation	GLP	Acceptable	New Testing Required
STUDY	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICOCHEMICAL DATA							
Melting Point	Y	-	-	N	N	Y	N
Boiling Point	Y	-	-	Y	N	Y	N
Vapor Pressure	N	-	-	-	-	-	Y
Partition Coefficient	Y	-	-	Y	N	Y	N
Water Solubility	Y	-	-	Y	N	Y	N
ENVIRONMENTAL FATE DATA							
Photodegradation	Y	-	-	Y	N	Y	N
Stability in Water	Y	Y	-	-	Y	Y	N
Biodegradation	N	-	-	-	-	-	Y
Transport between Environmental Compartments (Fugacity)	N	-	-	-	-	-	Y
ECOTOXICOLOGICAL DATA							
Acute Toxicity to Fish	Y	Y	-	-	Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	Y	-	-	Y	Y	N
Toxicity to Aquatic Plants	N	-	-	-	-	-	Y
MAMMALIAN TOXICOLOGICAL DATA							
Acute Toxicity	Y	N	-	-	Y	Y	N
Genetic Toxicity							
Mutation	N	-	-	-	-	-	Y
Chromosome Aberration	N	-	-	-	-	-	Y
Repeated Dose Toxicity	Y	Y	-	-	Y	Y	N
Toxicity to Reproduction	N	-	-	-	-	-	Y
Developmental Toxicity	N	-	-	-	-	-	Y

TEST PLAN DESCRIPTION FOR EACH SIDS ENDPOINT

A. Physicochemical Endpoints

Melting Point – A value for this endpoint was obtained from published data (Pirrung and Nunn, 1996).

Boiling Point – A value for this endpoint was obtained using a computer estimation model (EPIWIN, Version 3.10.).

Vapor Pressure – This endpoint has not been satisfied. The data requirement for this endpoint will be satisfied using a study that will be conducted according to OECD (TG 104) and GLP guidelines.

Partition Coefficient – A value for this endpoint was obtained using a computer estimation model (EPIWIN, Version 3.10.).

Water Solubility – A value for this endpoint was obtained from published data (Molyneux and Vekavakayanondha, 1986).

Conclusion – All endpoints except vapor pressure have been satisfied by the utilization of data obtained from published data or from computer estimation models. The results from the utilization of these computer modeling programs are recognized by EPA as acceptable in lieu of actual data or values obtained from literature references.

B. Environmental Fate Endpoints

Photodegradation – A value for this endpoint was obtained using a computer estimation model (EPIWIN, Version 3.10.).

Stability in Water – This endpoint has been satisfied by a study (Ward et al., 2003) that was conducted according to OECD (TG 111) and GLP guidelines.

Biodegradation – This endpoint has been partially satisfied by data generated according to the Zahn-Wellens/EMPA test for inherent biodegradability (OECD guideline number 302B) (Lawrence and Ruffing, 1995). This testing was conducted according to GLP assurances. Further investigation will be conducted using a protocol (OECD 301B) for ready biodegradation in which the inoculum is not acclimated to the test chemical.

Fugacity – A value for this endpoint will be calculated when all pertinent physicochemical data are available.

Conclusion – The endpoints for photodegradation and stability in water have been satisfied and the endpoint for biodegradation has been partially satisfied using actual data or through the use of EPA-acceptable estimation models. A study to

determine the ready biodegradability of HQEE will be conducted. Also, the endpoint for fugacity will be calculated when all pertinent physicochemical data are available.

C. Ecotoxicity Endpoints

Acute Toxicity to Fish – This endpoint was satisfied by data generated in a 96-hour bioassay using the fathead minnow (Lawrence and Hirsch, 1995a). The concentrations of the test material were analytically measured at the start and end of the study. The study was conducted according to OECD (TG 203) and GLP guidelines.

Acute Toxicity to Aquatic Invertebrates – This endpoint was satisfied by data generated in a 48-hour bioassay using the species, *Daphnia magna* (Lawrence and Hirsch, 1995b). The concentrations of the test material were analytically measured at the start and end of the study. The study was conducted according to OECD (TG 202) and GLP guidelines.

Toxicity to Aquatic Plants – This endpoint has not been satisfied. The data requirement for this endpoint will be satisfied using a study that will be conducted according to OECD (TG 201) and GLP guidelines.

Conclusion – All endpoints except for toxicity to algae have been satisfied using actual data.

D. Mammalian Toxicological Endpoints

Acute Toxicity – This endpoint was satisfied by data generated via two routes of exposure, oral gavage and dermal administration (Shepard, 1989). One study per exposure route was performed and each was conducted as a limit test. Both studies were conducted according to currently accepted scientific methodology and GLP guidelines.

Repeat Dose Toxicity – This endpoint was satisfied using data generated in a 28-day study via the oral (feed incorporation) route of exposure (Hosefeld and Hankinson, 1988). The study was conducted according to OECD (TG-407) and GLP guidelines.

Genetic Toxicity – These endpoints for mutation and chromosome aberration have not been satisfied. The data requirement for these two endpoints will be satisfied using studies conducted according to OECD (TG 471 and TG 474) and GLP guidelines.

Reproductive and Developmental Toxicity – The endpoints for reproductive performance and fetal development have not been satisfied. The data requirement for these two endpoints will be satisfied using a study conducted according to OECD (TG 421) and GLP guidelines.

SIDS DATA SUMMARY

Data to assess the various physicochemical properties (boiling point, melting point, partition coefficient and water solubility) for HQEE were obtained from published data or EPA-acceptable computer estimation modeling programs found in EPIWIN. These data indicate that HQEE is a solid at room temperature. It has a low estimated octanol to water partition coefficient and is moderately soluble in water. The use of published data and modeled data meet the requirements of the above endpoints. Vapor pressure will be determined as previously stated above according to OECD and GLP guidelines.

Data to address endpoints for environmental fate of photodegradation and biodegradation were obtained from actual studies or EPA-acceptable computer estimation modeling programs found in EPIWIN. Computer modeling predicts that HQEE would be expected to rapidly degrade in the atmosphere. Results from an inherent biodegradation study indicate that HQEE undergoes rapid biodegradation and would not be expected to be persistent in the environment. This endpoint will be further investigated using a study to determine its ready biodegradability according to OECD and GLP guidelines. The data to define the acid/base-catalyzed hydrolysis indicate that HQEE is hydrolytically stable with a $t_{1/2}$ greater than 1 year.

The data for aquatic toxicity endpoints were obtained from actual studies. HQEE is of low toxicity to fish and daphnids and is expected to have low toxicity to algae. The LC_{50} to fish (96 hours) is >1044 mg/l and the EC_{50} (immobility) to *Daphnia* (48 hours) is >100 mg/l. The EC_{50} (96 hours) to algae is 1672 mg/l as estimated using computer modeling. The toxicity to algae will be determined as stated above according to OECD and GLP guidelines.

The data to determine acute toxicity and repeated dose toxicity are from studies that were conducted according to acceptable scientific methodology (acute toxicity) or an OECD test guideline (TG-407). The oral LD_{50} and dermal LD_{50} are greater than 5 g/kg and 2 g/kg, respectively.

HQEE was administered to rats in the diet at concentrations of 0.1, 0.3 or 1.0 % for 28 days. Following exposure no treatment-related clinical signs of toxicity were observed. There were no statistical body weight differences between any of the treated animals and control animals. The mean blood platelet count for the high-dose males was slightly less than for the control group. No other abnormalities in hematology were noted in the males. No hematological abnormalities were observed in any of the female animals. The clinical chemistry findings in all treated animals were comparable to controls. Relative kidney weights in low- and mid-dose females were lower ($p=0.02$), but not different from controls in the high-dose females. Absolute kidney weights for all treated female animals were similar to controls. No other organ weight differences were seen in

any dose group for either sex. No compound related histopathological change was observed in any organs. The NOAEL in this study was 0.3 % in the diet (249 mg/kg) for male rats and 1.0 % (851 mg/kg) for females.

The endpoints for reproductive performance and fetal development have not been satisfied. The data requirement for these two endpoints will be satisfied using a study conducted according to OECD and GLP guidelines.

EVALUATION OF DATA FOR QUALITY AND ACCEPTABILITY

The collected data were reviewed for quality and acceptability following the systematic approach described by Klimisch et al. (1997). The codification described by Klimisch specifies four categories of reliability for describing data adequacy. They are:

1. **Reliable without restriction:** Includes studies or data complying with Good Laboratory Practices (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.
2. **Reliable with restrictions:** Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.
3. **Not reliable:** Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.
4. **Not assignable:** Includes studies or data in which insufficient detail is reported to assign a rating, e.g., listed in abstracts or secondary literature.

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