SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

SPONSORED CHEMICAL

Acetylene (CAS No. 74-86-2)
[9th CI Name: Ethyne]

SUPPORTING CHEMICAL

Propyne (CAS No. 74-99-7)
[9th CI Name: 1-Propyne]

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INTERIM

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SCREENING-LEVEL HAZARD CHARACTERIZATION
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The High Production Volume (HPV) Challenge Program[1] is a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsor chemicals; sponsorship entails the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data do not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to "SIDS" (Screening Information Data Set[1,2]) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency's Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals. OPPT is using a hazard-based screening process to prioritize review of the submissions. The hazard-based screening process consists of two tiers described below briefly and in more detail on the Hazard Characterization website[3].

Tier 1 is a computerized sorting process whereby key elements of a submitted data set are compared to established criteria to "bin" chemicals/categories for OPPT review. This is an automated process performed on the data as submitted by the sponsor. It does not include evaluation of the quality or completeness of the data.

In Tier 2, a screening-level hazard characterization is developed by EPA that consists of an objective evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. The evaluation is performed according to established EPA guidance[2,4] and is based primarily on hazard data provided by sponsors. EPA may also include additional or updated hazard information of which EPA, sponsors or other parties have become aware. The hazard characterization may also identify data gaps that will become the basis for a subsequent data needs assessment where deemed necessary. Under the HPV Challenge Program, chemicals that have similar chemical structures, properties and biological activities may be grouped together and their data shared across the resulting category. This approach often significantly reduces the need for conducting tests for all endpoints for all category members. As part of Tier 2, evaluation of chemical category rationale and composition and data extrapolation(s) among category members is performed in accord with established EPA[2] and OECD[5] guidance.

The screening-level hazard characterizations that emerge from Tier 2 are important contributors to OPPT's existing chemicals review process. These hazard characterizations are technical documents intended to support subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and provide information previously not readily available to the public. The public, including sponsors, may offer comments on the hazard characterization documents.

The screening-level hazard characterizations, as the name indicates, do not evaluate the potential risks of a chemical or a chemical category, but will serve as a starting point for such reviews. In 2007, EPA received data on uses of and exposures to high-volume TSCA existing chemicals, submitted in accordance with the requirements of the Inventory Update Reporting (IUR) rule. For the chemicals in the HPV Challenge Program, EPA will review the IUR data to evaluate exposure potential. The resulting exposure information will then be combined with the screening-level hazard characterizations to develop screening-level risk characterizations[4,6]. The screening-level risk characterizations will inform EPA on the need for further work on individual chemicals or categories. Efforts are currently underway to consider how best to utilize these screening-level risk characterizations as part of a risk-based decision-making process on HPV chemicals which applies the results of the successful U.S. High Production Volume Challenge Program and the IUR to support judgments concerning the need, if any, for further action.

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[1] U.S. EPA. High Production Volume (HPV) Challenge Program; http://www.epa.gov/chemrtk/index.htm.
[2] U.S. EPA. HPV Challenge Program – Information Sources; http://www.epa.gov/chemrtk/pubs/general/guidocs.htm.
[3] U.S. EPA. HPV Chemicals Hazard Characterization website (http://www.epa.gov/hpvis/abouthc.html).
[4] U.S. EPA. Risk Assessment Guidelines; http://cfpub.epa.gov/ncea/raf/rafguid.cfm.
[5] OECD. Guidance on the Development and Use of Chemical Categories; http://www.oecd.org/dataoecd/60/47/1947509.pdf.
[6] U.S. EPA. Risk Characterization Program; http://www.epa.gov/osa/spc/2riskchr.htm.

SCREENING-LEVEL HAZARD CHARACTERIZATION
Acetylene (CAS No. 74-86-2)

Introduction

The sponsor, American Chemistry Council Acetylene Panel, submitted a Test Plan and Robust Summaries to EPA for acetylene (CAS No. 74-86-2; 9th CI name: ethyne) on December 30, 2003. EPA posted the submission on the ChemRTK HPV Challenge website on February 26, 2004 (http://www.epa.gov/chemrtk/pubs/summaries/acetylen/c15005tc.htm). EPA comments on the original submission were posted to the website on May 16, 2005. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on November 16, 2005 and March 13, 2007, which were posted to the ChemRTK website on January 26, 2006 and July 20, 2007, respectively.

This screening level hazard characterization is based primarily on the review of the test plan and robust summaries of studies submitted by the sponsor(s) under the HPV Challenge Program. In preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor's responses to comments and revisions made to the submission. A summary table of SIDS endpoint data with the structure(s) of the sponsored chemical(s) is included in the Appendix. The screening-level hazard characterization for environmental and human health effects is based largely on SIDS endpoints and is described according to established EPA or OECD effect level definitions and hazard assessment practices.

Since acetylene is a gas that partitions to air and rapidly evaporates from the aqueous environment, EPA agreed with the sponsor that ecotoxicity testing is not considered relevant. Therefore, the ECOSAR estimated values address the endpoints for the purposes of the HPV Challenge Program.

Justification for Supporting Chemical

The sponsor submitted data for the supporting chemical, propyne (CAS No. 74-99-7), also known as methylacetylene. Propyne is the most closely related chemical to acetylene in molecular structure, size and functionality. EPA considers propyne to be a reasonable supporting chemical for acetylene.

Summary-Conclusion

Acetylene is a gas that forms explosive mixtures in air. The lower explosive limit is 2.5% (25,000 ppm).

The log K_{ow} of acetylene indicates that its potential to bioaccumulate is expected to be low. Biodegradation is not a relevant endpoint for acetylene.

The evaluation of estimated toxicity data for fish, aquatic invertebrates and aquatic plants indicate that the potential acute hazard of acetylene to aquatic organisms is low.

Acute inhalation toxicity of acetylene in humans is low. The major clinical signs observed are mild intoxication, and increased aggressiveness (at high dose levels). Repeated inhalation exposure to rats resulted in mortality, intoxication or anesthesia related toxicity, and capillary hyperemia in the liver, kidneys and spleen. Mortality was also observed in mice, guinea pigs and rabbits. Rats repeatedly exposed to the supporting chemical, propyne, showed ataxia, gross tremors of head and extremities; recovery occurring after exposure termination. Discoloration and increased pulmonary irritation in the lungs were seen histopathologically. In dogs, exposure to propyne resulted in marked salivation, excitability, muscular fasciculation, ataxia, mydriasis and tonic convulsions, and signs of intoxication. Histopathological examination showed no abnormalities. No data were provided for the reproductive/developmental toxicity endpoints. Acetylene did not induce gene mutation in *bacteria* or chromosomal aberrations in mammalian cells *in vitro.* The supporting chemical, propyne, induced gene mutation in bacteria *in vitro*.

The potential health hazard of acetylene is low.

Data gaps for the reproductive and developmental toxicity endpoints were identified under the HPV Challenge Program.

1. Physical-Chemical Properties and Environmental Fate

A summary of physical-chemical and environmental fate data submitted is provided in the Appendix. For the purpose of the screening-level hazard characterization, the review and summary of these data were limited to the octanol-water partition coefficient and biodegradation endpoints as indicators of bioaccumulation and persistence, respectively.

Acetylene is a gas that forms explosive mixtures in air. The lower explosive limit is 2.5% (25,000 ppm).

Octanol-Water Partition Coefficient

Acetylene (CAS No. 74-86-2)
Log K_{ow}: 0.37 (estimated)

Biodegradation

Acetylene (CAS No. 74-86-2)
Biodegradation is not a relevant endpoint for acetylene since this substance exists as a gas in the environment.

Conclusion: The log K_{ow} of acetylene indicates that its potential to bioaccumulate is expected to be low. Biodegradation is not a relevant endpoint for acetylene.

2. Environmental Effects – Aquatic Toxicity

Since acetylene is a gas that partitions to air and rapidly evaporates from the aqueous environment, EPA agrees with the sponsor that ecotoxicity testing is not considered relevant. Therefore, the ECOSAR estimated values address the endpoints for the purposes of the HPV Challenge Program.

Acute Toxicity to Fish

Acetylene (CAS No. 74-86-2)
96-h EC_{50} = 496.15 mg/L (ECOSAR)

Acute Toxicity to Aquatic Invertebrates

Acetylene (CAS No. 74-86-2)
48-h EC_{50} = 479.30 mg/L (ECOSAR)

Toxicity to Aquatic Plants

Acetylene (CAS No. 74-86-2)
96-h EC_{50} (growth) = 274.86 mg/L (ECOSAR)

Conclusion: The evaluation of estimated toxicity data for fish, aquatic invertebrates and aquatic plants indicate that the potential acute hazard of acetylene to aquatic organisms is low.

3. Human Health Effects

Acute Inhalation Toxicity

Acetylene (CAS No. 74-86-2)

(1) Humans (number and gender were not listed) were administered acetylene 10 – 50% (~ 106.5 to 532.5 mg/L) from a Douglas bag in the sitting position. No re-breathing was allowed. Inhalation of 10% acetylene for 1 hour caused feelings of mild intoxication with parethesia (numbness) and had a slight effect on reaction time. Fifteen percent acetylene caused distinct intoxication with talkativeness, sleepiness and inability to walk a straight line, but did not include symptoms of marked intoxication (even after a 1 hour inhalation period). After inhalation of 20% acetylene for 4 minutes marked intoxication was evident. Slight incoordination of head movements was noticed after 20% had been inhaled for 18 minutes. Twenty-five percent acetylene caused similar, but more marked, symptoms. General incoordination and aggressive behavior were noted after inhalation of 30% acetylene for 13 minutes. Inhalation of 33 or 35% caused unconsciousness within 7 or 5 minutes, respectively. Inhalation of 50% acetylene produced feelings of intense intoxication within 35 seconds and an unbearable feeling of suffocation within 70 seconds (after which the experiment was stopped).

(2) In rats a concentration of 780,000 ppm produced anesthesia in 15 minutes and at 900,000 ppm, respiratory failure was seen in approximately 2 hours. (No additional information is available.)

Repeated-Dose Toxicity

Acetylene (CAS No. 74-86-2)

Rats, mice, guinea pigs, rabbits and dogs (number/sex unspecified) were exposed to acetylene in oxygen at concentrations of 250,000, 500,000 or 800,000 ppm (equivalent to 25, 50 or 80% or approximately 266.3, 532.5 or 852 mg/L) daily. Numbers of animals, exposures, durations of exposure and deaths were as follows:

Animal	Concentration (percent)	Daily exposure time (h)	Number of days exposed	Total exposure time (h)	Deaths/total animals
Rat	25	1	7 – 93	7 – 93	6/16
Rat	50	2	1 – 8	2 – 16	9/10
Guinea pig	50	2	1 – 9	2 – 18	7/7
Mouse	50	2	1 – 6	2 – 12	5/5
Rat	80	½	2 – 36	1 – 18	36/47
Rat	80	1	14	14	0/8
Guinea pig	80	1	10	10	0/6
Rabbit	80	1	6 – 10	6 – 10	3/4
Dog	80	1	12	12	1/2

Animals were exposed to the acetylene/oxygen mix in air-tight glass cages. Mortality was observed in most treatment groups, including the lowest exposure for the shortest duration. (The study suggests that the deaths were mostly caused by pneumonia, which was also found in the control animals.) At the lower concentrations (concentrations were not stated) the animals appeared slightly sleepy. At higher concentrations (70-80%), the majority of animals fell asleep after 15-20 minutes. The rats, rabbits, guinea pigs and dogs generally recovered from narcosis in a short time. The mice did not survive treatment. Treated animals that survived to termination, showed no evidence of cellular injury to the parenchymatous cells of the heart, lungs, liver, kidneys, or spleen. Capillary hyperemia was observed in the liver, kidneys and spleen of rats exposed to 250,000 ppm (the number was not stated). This effect was observed until at least the second day after the last exposure to the gas and was not observed in animals sacrificed 5 or 14 days after the last exposure.

LOAEL (rat) = 266.3 mg/L (250,000 ppm) (based on increased mortality and capillary hyperemia in liver, kidney and spleen)

NOAEL = Not established

Propyne (CAS No. 74-99-7, supporting chemical)
(1) Albino rats (20 males, species not stated) were exposed to propyne at an average concentration of 28,700 ppm (approximately 30.6 mg/L) for 6 hours/day, 5 days/week for 6 months. Eight deaths occurred from exposure day 21 – 103. Signs of toxicity included ataxia, gross tremors of head and extremities; recovery occurring after exposure termination. Body-weight gain was reduced. Treatment-related effects on the lungs included discoloration, purulent empyema, cysts and pulmonary irritation. Remaining organs appeared to be normal.
LOAEL = 30.6 mg/L (28,700 ppm) (based on mortality and pulmonary irritation of the lungs)
NOAEL = Not established

(2) Dogs (one/sex) were exposed to propyne at an average concentration of 28,700 ppm (approximately 30.6 mg/L) for 6 hours/day, 5 days/week for 6 months. No deaths occurred during the study. Signs of toxicity during exposure included marked salivation, excitability and muscular fasciculations within 7 minutes of exposure. After 13 minutes, the dogs exhibited ataxia and mydriasis, within 15 minutes of exposure, dogs appeared to be intoxicated (similar to alcohol) and after 30 minutes, one dog showed effects of anesthesia. Throughout the remaining exposures, similar signs of toxicity were observed. Excitability and occasionally staggering and falling on the floor were also seen. Tonic convulsions occurred in at least one of the dogs on days 22, 110, 123 and 137. Body weights were reduced up to the first 6 weeks of the study and increased overall by study completion. No treatment-related effects were observed on any hematological, urinalysis or biochemical indices of toxicity or during the gross pathological examinations of the lungs, liver, kidney, heart, spleen and gastrointestinal tract.
LOAEL = 30.6 mg/L (28,700 ppm) (based on clinical signs)
NOAEL = No established

Reproductive Toxicity

Data gap

Developmental Toxicity

Data gap

Genetic Toxicity – Gene Mutation

In vitro
Acetylene (CAS No. 74-86-2)
Salmonella typhimurium strains TA97, TA98 and TA100 were exposed to acetylene in acetone at concentrations of 0.3, 1, 3, 10 or 31 µg/plate in the presence and absence of metabolic activation. Positive controls produced an appropriate response. Cytotoxicity was not determined.
Acetylene was not mutagenic in this assay.

Propyne (CAS No. 74-99-7, supporting chemical)
Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 and *Escherichia coli* WP2uvrA were exposed to propyne at concentrations of 0, 5, 10, 21 or 50% in the presence and absence of metabolic activation. Cytotoxicity was not determined. Propyne did not induce genetic mutation in any of the *S. typhimurium* strains tested at any concentration in the presence or absence of metabolic activation, but did cause a dose-dependent increase in the number of mutations in *E. coli* WP2uvrA in the presence and absence of metabolic activation (positive at concentrations ≥ 21% without S9 mix and ≥ 5% with S9 mix).
Propyne was mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro
Acetylene (CAS No. 74-86-2)
Chinese Hamster lung (CHL) cells were exposed to acetylene at concentrations up to 1.25% for 6 or 24 hours. Positive controls produced an appropriate response. Acetylene did not induce any dose-related increases in the frequency of cells with structural or numerical chromosome aberrations either in the presence or absence of metabolic activation.
Acetylene did not induce chromosomal aberrations in this assay.

Conclusion: Acute inhalation toxicity of acetylene in humans is low. The major clinical signs were from mild intoxication to incoordination, effect on reaction time, memory, writing, inability to walk straight and aggressiveness. In rats and dogs, at high concentrations, respiratory failure was noted. Repeated inhalation exposure to rats resulted in mortality, intoxication or anesthesia related toxicity, and capillary hyperemia in the liver, kidneys and spleen. Mortality was also observed in mice, guinea pigs and rabbits. Rats repeatedly exposed to the supporting chemical, propyne, showed ataxia, rats lying down on the abdomen or on the side with gross tremors of head and extremities; recovery occurring after exposure termination. Body-weight gain was reduced. Discoloration and increased pulmonary irritation in the lungs were seen histopathologically. In dogs, exposure to propyne resulted in marked salivation, excitability, muscular fasciculations, ataxia, mydriasis, and tonic convulsions, signs of intoxication. Histopathological examination showed no abnormalities. No data were provided for the reproductive/developmental toxicity endpoints. Acetylene did not induce gene mutation in *bacteria* or chromosomal aberrations in mammalian cells *in vitro.* The supporting chemical, propyne, induced gene mutation in bacteria *in vitro*.

The potential health hazard of acetylene is low.

4. Hazard Characterization

Acetylene is a gas that forms explosive mixtures in air. The lower explosive limit is 2.5% (25,000 ppm).

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The potential health hazard of acetylene is low.

5. Data Gaps

Data gaps for the reproductive and developmental toxicity endpoints were identified under the HPV Challenge Program.

APPENDIX

Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program		
Endpoints	**SPONSORED CHEMICAL Acetylene (74-86-2)**	**SUPPORTING CHEMICAL Propyne (74-99-7)**
Structure	HC≡CH	CH3C≡CH
Summary of Physical-Chemical Properties and Environmental Fate Data		
Melting Point (°C)	-80.8	-101.5
Boiling Point (°C)	-84 (sublimes)	-23.2
Vapor Pressure (hPa at 25°C)	6969.2 (extrapolated)	5155 (20 °C)
Log K_{ow}	0.37 (20 °C) (estimated)	0.94 (estimated)
Water Solubility (mg/L at 25ºC)	1230 (20 °C)	3,640
Indirect (OH^-) Photodegradation Half-life ($t_{1/2}$)	13.1 d (estimated)	–
Stability in Water (Hydrolysis) ($t_{1/2}$)	No hydrolysable functional groups	–
Fugacity (Level III Model) **Air (%)** **Water (%)** **Soil (%)** **Sediment (%)**	 99.9 0.104 0.0101 1.77×10^{-4}	–
Biodegradation at 28 days (%)	Biodegradation is not a relevant endpoint for acetylene.	
Summary of Environmental Effects – Aquatic Toxicity Data		
Fish 96-h LC_{50} (mg/L)	496.15 (estimated)	–
Aquatic Invertebrates 48-h EC_{50} (mg/L)	479.30 (estimated)	–
Aquatic Plants 72-h EC_{50} (mg/L) (growth) (biomass)	274.86 (96-h, estimated)	–

Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program		
Endpoints	**SPONSORED CHEMICAL Acetylene (74-86-2)**	**SUPPORTING CHEMICAL Propyne (74-99-7)**
Summary of Human Health Data		
Acute Inhalation Toxicity LC_{50} (mg/L)	> 106.50 (1-h)	–
Repeated-Dose Toxicity NOAEL/LOAEL Inhalation (mg/L/day)	266.3	~ 30.6 (6-mo)
Reproductive Toxicity NOAEL/LOAEL Inhalation (mg/L/day)	Data gap	–
Developmental Toxicity NOAEL/LOAEL Inhalation (mg/L/day)	Data gap	–
Genetic Toxicity – Gene Mutation *In vitro*	Negative	Positive
Genetic Toxicity – Chromosomal Aberrations *In vitro*	Negative	–

– Indicates that endpoint was not addressed for this chemical.