SCREENING-LEVEL HAZARD CHARACTERIZATION

2-Pentanone
(CASRN 107-87-9)

The High Production Volume (HPV) Challenge Program[1] was conceived as 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 sponsored chemicals; sponsorship entailed the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data did 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 by developing hazard characterizations (HCs). These HCs consist of an evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. They are not intended to be definitive statements regarding the possibility of unreasonable risk of injury to health or the environment.

The evaluation is performed according to established EPA guidance[2,3] and is based primarily on hazard data provided by sponsors; however, 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. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. OPPT's focus on these specific sources is based on their being of high quality, highly relevant to hazard characterization, and publicly available.

OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment Profiles (SIAP) are available. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

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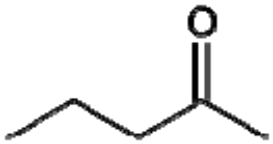
[1] U.S. EPA. High Production Volume (HPV) Challenge Program; http://www.epa.gov/chemrtk/index.htm.
[2] U.S. EPA. HPV Challenge Program – Information Sources; http://www.epa.gov/chemrtk/pubs/general/guidocs.htm.
[3] U.S. EPA. Risk Assessment Guidelines; http://cfpub.epa.gov/ncea/raf/rafguid.cfm.

These hazard characterizations are technical documents intended to inform 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.

Chemical Abstract Service Registry Number (CASRN)	**107-87-9**
Chemical Abstract Index Name	**2-Pentanone**
Structural Formula	

Summary

CASRN 107-87-9 is a colorless liquid with high water solubility and high vapor pressure at room temperature. It is expected to have high mobility in soil. Volatilization is considered moderate based on its Henry's Law constant. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered slow. CASRN 107-87-9 is expected to be readily biodegradable. CASRN 107-87-9 is expected to have low persistence (P1) and low bioaccumulation potential (B1).

The acute toxicity of CASRN 107-87-9 is low in rats by the oral route and moderate in rats by the inhalation route. No effects were seen in a repeated-dose toxicity study in rats exposed to CASRN 107-87-9 via the drinking water up to 13 months at doses up to 454 mg/kg/day, the highest dose tested; the NOAEL for systemic toxicity is 454 mg/kg/day. No effects were observed in a combined inhalation reproductive/developmental toxicity screening test in rats at doses up to 5 mg/L, the highest dose tested; the NOAEC for parental, maternal, reproductive, and developmental toxicity is 5mg/L. CASRN 107-87-9 did not induce gene mutations or chromosomal aberrations *in vitro*.

For CASRN 107-87-9, the 96-hour acute fish LC_{50} value is 1240 mg/L, the acute aquatic invertebrate 48-hour EC_{50} value is >1000 mg/L, and the 72-hour aquatic plants EC_{50} values on growth rate and biomass are and 308.8 and 174.5 mg/L, respectively.

There are no data gaps identified under the HPV Challenge Program.

The sponsor, the Eastman Chemical Company, submitted a Test Plan and Robust Summaries to EPA for 2-pentanone (CAS No. 107-87-9) [2-pentanone] dated October 12, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on December 3, 2001 (http://www.epa.gov/chemrtk/pubs/summaries/2pentano/c13231tc.htm). EPA comments on the original submission were posted to the website on April 16, 2002. The sponsor submitted updated/revised documents on May 21, 2002, which were posted to the ChemRTK website (posting date not indicated).

1. Chemical Identity

1.1. Identification and Purity

The following description is taken from the revised 2002 Test Plan:

Although not mentioned in the Test Plan, several studies in the Robust Summary indicate the purity of CASRN 107-87-9 as > 97%.

1.2. Physical-Chemical Properties

CASRN 107-87-9 is a colorless liquid with high water solubility and high vapor pressure at room temperature.

The physical-chemical properties of CASRN 107-87-9 are summarized in Table 1.

Table 1. Physical-Chemical Properties of 2-Pentanone[1]

Property	Value
CASRN	107-87-9
Molecular Weight	86.13
Physical State	Colorless liquid
Melting Point	-78°C (measured)
Boiling Point	101.7°C (measured)
Vapor Pressure	35.4 mm Hg at 25°C (measured)
Water Solubility	43,000 mg/L at 25°C (measured)
Dissociation Constant (pK_a)	Not applicable
Henry's Law Constant	8.36×10^{-5} atm-m^3/mole at 25°C (measured)[2]
Log K_{ow}	0.91 (measured)

[1] Eastman Chemical Company. May 30, 2002. Revised Test Plan and Robust Summary for 2-Pentanone. Available online from: http://www.epa.gov/chemrtk/pubs/summaries/2pentano/c13231tc.htm as of March 29, 2010.
[2] SRC. 2010. The Physical Properties Database (PHYSPROP). SRC: Syracuse, NY. Available online from http://www.srcinc.com/what-we-do/free-demos.aspx as of March 29, 2010.

2. General Information on Exposure

2.1. Production Volume and Use Pattern

According to the 2006 IUR submissions, CASRN 107-87-9 had an aggregated production and/or import volume in the United States between 10 and 50 million pounds.

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing as solvents (which become part of product formulation or mixture); other basic organic chemical manufacturing as solvents (for cleaning or degreasing). Non-confidential commercial and consumer uses of this chemical include paints and coatings.

2.2. Environmental Exposure and Fate

CASRN 107-87-9 is expected to have high mobility in soil. 2-Pentanone was readily biodegradable using a method similar to the modified MITI test (OECD 301C), and in the closed bottle test (OECD 301D). In the modified MITI test, 2-pentanone achieved roughly 69% of its theoretical biochemical oxygen demand (BOD) after 20 days and the 5-day BOD/COD ratio was greater than 0.5, indicating the substance is readily biodegradable. In the closed bottle test, 2-pentanone achieved 70% of its theoretical BOD after 14 days. The rate of volatilization is considered moderate based on the Henry's Law constant of this substance. The rate of hydrolysis is considered negligible. CASRN 107-87-9 is expected to have low persistence (P1) and low bioaccumulation potential (B1). The environmental fate properties are provided in Table 2.

Table 2. Environmental Fate Characteristics of 2-Pentanone[1]	
Property	**Value**
Photodegradation Half-life	2.2 days (estimated)[2]
Hydrolysis Half-life	Stable
Biodegradation	BOD/COD = 0.77 after 5 days (readily biodegradable); 70% after 14 days (readily biodegradable)
Bioaccumulation Factor	BAF = 1.5 (estimated)[2]
Log K_{oc}	0.91 (estimated)[2]
Fugacity (Level III Model)[2]	
Air (%)	7.9
Water (%)	40.5
Soil (%)	51.5
Sediment (%)	0.1
Persistence[3]	P1 (low)
Bioaccumulation[3]	B1 (low)

[1] Eastman Chemical Company. May 30, 2002. Revised Test Plan and Robust Summary for 2-Pentanone. Available online from: http://www.epa.gov/chemrtk/pubs/summaries/2pentano/c13231tc.htm as of March 29, 2010.
[2] U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm as of March 22, 2010
[3] Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

Conclusions: CASRN 107-87-9 is a colorless liquid with high water solubility and high vapor pressure at room temperature. It is expected to have high mobility in soil. Volatilization is considered moderate based on its Henry's Law constant. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered slow. CASRN 107-87-9 is expected to be readily biodegradable. 2-Pentanone is expected to have low persistence (P1) and low bioaccumulation potential (B1).

3. Human Health Hazard

A summary of health effects data submitted for SIDS endpoints is provided in Table 3.

Acute Oral Toxicity

(1) Male rats (2/dose; strain not specified) were fasted overnight and then administered a single dose of 200, 400, 800, 1600 or 3200 mg/kg-bw by oral gavage. During a 14-day observation period, both rats at 3200 mg/kg-bw died.
LD_{50} 1600 - 3200 mg/kg-bw

(2) Male mice (2/dose; strain not specified) were fasted overnight and then administered a single dose of 200, 400, 800, 1600 or 3200 mg/kg-bw by oral gavage. Following a 14-day observation period, one mouse at each dose of 1600 and 3200 mg/kg-bw died.
LD_{50} = 1600 mg/kg-bw

Acute Inhalation Toxicity

Charworth Wistar rats (6 rats/sex; dose not specified) were exposed to a nominal concentration of the test substance at 2000 and 4000 ppm. Time periods extended from 15 minutes to 8 hours, until the LC_{50} was defined. After 4 hours at 2000 ppm (~7.05 mg/L), 1/6 rats died; after 4 hours at 4000 ppm (~14.1 mg/L), 6/6 rats died.
LC_{50} 7.05 - 14.1 mg/L

Repeated-Dose Toxicity

Oral
Sprague-Dawley male rats (10/dose) were administered 2-pentanone at 0, 144 mg/kg/day for 10 months, and 250 mg/kg/day and 454 mg/kg/day for 13 months continuously in drinking water. The drinking water was measured every other day to determine exposure. Animals were observed daily for body weight changes and neurological examinations. At termination, animals were divided into two groups and processed for histological and nervous system tissue examinations. Only the liver, kidney and testes were weighed; microscopically 35 different organs and tissues were examined. Mortalities were observed at 0 (1/10), 250 (1/10) and 454 (1/10) mg/kg/day. It was unclear if these deaths were treatment related. Necropsy examinations were unremarkable. No effects on neurotoxicity were observed (specifics of what was assessed was not provided).
NOAEL (systemic toxicity) = 454 mg/kg/day (highest dose tested)

Reproductive/Developmental Toxicity

Inhalation
A combined reproductive/developmental toxicity screening test was performed in Sprague-Dawley rats (12/sex/dose) via vapor inhalation at 0, 1.0, 2.5 or 5.0 mg/L for 6 hours/day, 7 days/week, for 51 days (males) and 35 to 48 days (females; through gestation day 19). Reproductive and fetal parameters were examined along with sperm count and motility at necropsy. Organs that were histologically examined included the ovaries, vagina, uterus, fallopian tubes, testes, epididymis, and male accessory sex organs. The testes and epididymis were also weighed. No mortalities were reported. There were no effects on food consumption or body weight in either sex. There were no effects on any of the litter parameters or reproductive performance. There were no effects seen on any of the selected organs that were weighed, or examined grossly or histologically. An increase in mean absolute (but not relative) epididymal weight was seen in high-concentration males, but there were no histopathological changes observed. There was reduced activity in the high dose animals during the exposure period only.
NOAEC (reproductive toxicity) = 5 mg/L (highest concentration tested)
NOAEC (developmental toxicity) = 5 mg/L (highest concentration tested)
NOAEC (maternal toxicity) = 5 mg/L (highest concentration tested)

Genetic Toxicity -- Gene Mutation

In vitro
Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 and *E. coli* strain WP2*uvr*A pKM101 were treated with 2-pentanone at concentrations up to 5000 µg/plate in the presence or absence of metabolic activation. Positive and negative controls were used. The cytotoxic concentration was reportedly >5000 µg/plate (no evidence of cytotoxicity observed and the highest dose tested). The positive controls were responded appropriately.
2-Pentanone was not mutagenic in this assay.

In a NTP study, *Salmonella typhimurium* strains TA97, TA98, TA100, TA1535 and TA1537 were treated with 2-pentanone at concentrations of 0 up to 5 mL in the presence of metabolic activation using SD9 rat liver or S9 hamster liver cells via vapor from liquid. A positive control was used and responded appropriately. All strains were negative for genetic mutations.
2-Pentanone was not mutagenic in this assay.

Genetic Toxicity -- Chromosomal Aberrations

In vitro
Chinese Hamster Ovary (CHO) cells were treated with 2-pentanone at concentrations up to 900 µg/mL with and without metabolic activation. Positive and negative controls were used and responded appropriately. No evidence of cytotoxicity was observed. The test material was shown to be non-clastogenic.
2-Pentanone did not induce chromosomal aberrations in this assay.

Additional Information:

Repeated-Dose Toxicity

Neurotoxicity

Inhalation
Charles River CD male rats (5/dose) were exposed to 2-pentanone at 305 ppm (~ 1.07 mg/L) for 17.5 weeks via inhalation for two 16-hour periods and two 20-hour periods for four consecutive days. Methyl n-butyl ketone was used as a positive control. The use of a negative control was not mentioned. Nervous tissue was harvested and processed for histological examination. There were no clinical or histopathological neurotoxic effects reported.
2-Pentanone was not neurotoxic in this assay.
NOAC = ~1.07 mg/L (highest concentration tested)

Conclusions: The acute toxicity of CASRN 107-87-9 is low in rats by the oral route and moderate in rats by the inhalation route. No effects were seen in a repeated-dose toxicity study in rats exposed to CASRN 107-87-9 via the drinking water up to 13 months at doses up to 454 mg/kg/day, the highest dose tested; the NOAEL for systemic toxicity is 454 mg/kg/day. No effects were observed in a combined reproductive/developmental toxicity screening test in rats at doses up to 5 mg/L, the highest dose tested; the NOAEC for

parental/maternal/reproductive/developmental toxicity is 5mg/L. CASRN 107-87-9 did not induce gene mutations or chromosomal aberrations *in vitro*.

Table 3: Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program: Human Health

Endpoints	**SPONSORED CHEMICAL 2-Pentanone (107-87-9)**
Acute Oral Toxicity LD_{50} **(mg/kg-bw)**	**1600**
Acute Inhalation Toxicity LC_{50} **(mg/L)**	**~7.05**
Repeated-Dose Toxicity **NOAEL/LOAEL** **Oral (mg/kg/day)** **Drinking Water** **NOAEC/LOAEC** **Inhalation (mg/L)** **Reproductive Toxicity** **Developmental Toxicity** **Maternal Toxicity**	**LOAEL = 454 (13-month)** **NOAEC = ~ 5.0** **NOAEC = ~ 5.0** **NOAEC = ~ 5.0** **(highest concentration tested; 17.5 weeks)**
Genetic Toxicity – Gene Mutation ***In vitro***	**Negative**
Genetic Toxicity – Chromosomal Aberrations ***In vitro***	**Negative**
Additional Information Neurotoxicity	 **Negative**

4. Hazard to the Environment

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 4.

Acute Toxicity to Fish

Fathead minnow (*Pimephales promelas*) were exposed to nominal concentrations of 100 or 1000 mg/L for 96 hours in a static toxicity test. Test concentrations were not measured. No effects were seen at any test concentration.
96-h LC_{50} > 1000 mg/L

Fathead minnow (*Pimephales promelas*) were exposed to measured concentrations of 0, 455, 669, 1042, 1512, 2396 mg/L for 96 hours. Test was conducted under flow-through conditions. (ref.1)
96-h LC_{50} = 1240 mg/L

Acute Toxicity to Aquatic Invertebrates

Daphnia magna were exposed to nominal concentrations of 100 or 1000 mg/L for 96 hours in a static toxicity test. Test concentrations were not measured. No effects were seen at any test concentration.
96-h EC_{50} > 1000 mg/L

QSAR prediction for aquatic invertebrates was conducted on 2-pentanone using ECOSAR version 1.000a. The predicted value was estimated using neutral organic equation for 48-h was done with log Kow of 0.91.
48-h EC_{50} = 290 mg/L

Toxicity to Aquatic Plants

Green algae *(Pseudokirchneriella subcapitata)* were exposed to measured geometric mean concentrations of 0, 9.27, 17.81, 35.98, 73.77 or 150.27 mg/L for 72 hours. Nominal concentrations were 0, 15.6, 31.2, 62.5, 125 or 250 mg/L. Information on growth inhibition at each concentration was not provided.
72-h EC_{50} (biomass) = 174.5 mg/L
72-h EC_{50} (growth rate) = 308.8 mg/L

Conclusions: For CASRN 107-87-9, the 96-hour acute fish LC_{50} value is 1240 mg/L, the acute aquatic invertebrate 48-hour EC_{50} value is >1000 mg/L, and the 72-hour aquatic plants EC_{50} values on growth rate and biomass are 308.8 and 174.5 mg/L, respectively.

Table 4: Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program: Aquatic Toxicity Data	
Endpoints	**SPONSORED CHEMICAL 2-Pentanone (107-87-9)**
Fish 96-h LC_{50} (mg/L)	**1240** [1]
Aquatic Invertebrates 48-h EC_{50} (mg/L)	**>1000 (96-h)**
Aquatic Plants 72-h EC_{50} (mg/L) (growth rate) (biomass)	**308.8 174.5**

Bold = test data; 1= see reference; e = estimated

5. Reference

Brooke LT, Call DJ, Acute Toxicities of Organic Chemicals to Fathead Minnows (*Pimephales promelas*). Vol III. Superior, Wisconsin: University of Wisconsin-Superior 1986. p.91.