Supporting Documents for Initial Risk-Based Prioritization of High Production Volume Chemicals

2,3-Dihydro-2,2-dimethyl-7-benzofuranol (CASRN 1563-38-8) (9th CI and CA Index Name: 7-Benzofuranol, 2,3-dihydro-2,2-dimethyl-)

Contents:

BACKGROUND

Screening-level hazard, exposure and risk characterizations for high production volume chemicals (HPV) are important contributions to the chemicals cooperation work being done in North America[1] through the EPA Chemical Assessment and Management Program (ChAMP)[2]. These screening-level characterizations are developed by EPA for individual chemicals or chemical categories to support initial Risk-Based Prioritizations (RBPs) for HPV chemicals. These screening-level characterizations are technical documents intended primarily to inform the Agency's internal decision-making process. Accordingly, they are written for assessment professionals and assume a degree of technical understanding. Each of the support documents is described below.

The Risk-Based Prioritizations are found in an accompanying document and are written for a general audience. They present EPA's initial thinking regarding the potential risks presented by these chemicals and future possible actions that may be needed.

Hazard Characterizations for HPV Chemicals

EPA's screening-level hazard characterizations are based primarily on the review of the summaries of studies and other information submitted by the chemical sponsor(s) under the HPV Challenge Program[3]. These studies included in the scope of the HPV Challenge comprise the Screening Information Data Set (SIDS) of the Organization for Economic Cooperation and Development (OECD)[4], an internationally recognized battery of tests that provides the basic data necessary to make an initial evaluation of a chemical's hazards and fate. In preparing the initial hazard characterizations, EPA also consulted a variety of reliable sources[5] for additional relevant information and 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 an HPV submission, EPA also searched publicly available databases[6] for information entered from one year prior to the HPV submission through May 2008. The screening-level hazard characterization is performed according to established EPA guidance[7]. A more detailed description of the hazard characterization process is available on the EPA website[8].

With respect to chemicals for which internationally-accepted OECD SIDS Initial Assessment Profiles (SIAP) and Initial Assessment Reports (SIAR) were available, EPA did not generate its own screening-level hazard characterization, but did check for and incorporate updated information in the risk characterization.

Exposure Characterizations for HPV Chemicals

EPA recently received exposure-related data on chemicals submitted in accordance with the requirements of Inventory Update Reporting (IUR)[9]. The 2006 IUR submissions pertain to chemicals manufactured in

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[1] U.S. EPA – U.S. Commitments to North American Chemicals Cooperation: http://www.epa.gov/hpv/pubs/general/sppframework.htm.
[2] U.S. EPA – ChAMP information: http://www.epa.gov/champ/.
[3] U.S. EPA – HPV Challenge Program information: http://www.epa.gov/hpv.
[4] U.S. EPA – Technical Guidance Document, OECD SIDS Manual Sections 3.4 and 3.5: http://www.epa.gov/chemrtk/pubs/general/sidsappb.htm.
[5] U.S. EPA – Public Database Hazard Information: http://www.epa.gov/hpvis/hazardinfo.htm.
[6] U.S. EPA – Public Database Update Information: http://www.epa.gov/chemrtk/hpvis/updateinfo.htm.
[7] U.S. EPA – Risk Assessment Guidelines: http://cfpub.epa.gov/ncea/raf/rafguid.cfm.
[8] U.S. EPA – About HPV Chemical Hazard Characterizations: http://www.epa.gov/hpvis/abouthc.htm.
[9] U.S. EPA – Basic IUR Information: http://www.epa.gov/opptintr/iur/pubs/guidance/basic-information.htm.

(including imported into) the U.S. during calendar year 2005 in quantities of 25,000 pounds or more at a single site. The reports include the identity, the quantity, and the physical form of the chemical manufactured or imported, and the number of workers reasonably likely to be exposed during manufacture of the chemical. For chemicals manufactured or imported in quantities of 300,000 pounds or more at a single site, additional reported information includes: the industrial processing and uses of the chemical; the number of industrial processing sites and workers reasonably likely to be exposed to the chemical at those sites; the consumer and commercial uses of the chemical; and an indication whether the chemical was used in products intended for use by children under 14 years of age.

EPA's screening-level exposure characterizations are based largely on the information submitted under the IUR reporting, although other exposure information submitted to the Agency (for example, in HPV submissions) or readily available through a limited set of publicly accessible databases[10] was also considered. The screening-level Exposure Characterizations identify a potential (high, medium, or low) that each of five populations – the environment, the general population, workers, consumers, and children – might be exposed to the chemical. In most cases, this potential doesn't address the quantity, frequency, or duration of exposure, but refers only to the likelihood that an exposure could occur.

In many instances EPA is not able to fully disclose to the public all the IUR exposure-related data reviewed or relied upon in the development of the screening-level documents because some of the material was claimed as confidential business information (CBI) when it was submitted to the Agency. These CBI claims do limit the Agency's ability to be completely transparent in presenting some underlying exposure and use data for chemicals in public documents. EPA does consider all data, including data considered to be CBI, in the screening-level exposure and risk characterization process, and endeavors whenever possible to broadly characterize supporting materials claimed as confidential in ways that do not disclose actual CBI.

Risk Characterizations for HPV Chemicals

EPA combines the information from the screening-level exposure characterization with the screening-level hazard characterization to develop a qualitative screening-level risk characterization, as described in the Agency's guidance on drafting risk characterizations[11]. These screening-level risk characterizations are technical documents intended to support subsequent priority-setting decisions and actions by OPPT. The purpose of the qualitative screening-level risk characterization is two-fold: to support initial risk-based decisions to prioritize chemicals, identify potential concerns, and inform risk management options; and to identify data needs for individual chemicals or chemical categories.

These initial characterization and prioritization documents do not constitute a final Agency determination as to risk, nor do they determine whether sufficient data are available to characterize risk. Recommended actions reflect EPA's relative judgment regarding this chemical or chemical category in comparison with others evaluated under this program, as well as the uncertainties presented by gaps that may exist in the available data.

[10] U.S. EPA – Summary of Public Databases Routinely Searched: http://www.epa.gov/chemrtk/hpvis/pubdtsum.htm.
[11] U.S. EPA – Risk Characterization Program: http://www.epa.gov/osa/spc/2riskchr.htm.

QUALITATIVE SCREENING-LEVEL RISK CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

SPONSORED CHEMICAL

2,3-Dihydro-2,2-Dimethyl-7-Benzofuranol (CAS No. 1563-38-8)
[9th CI Name: 7-Benzofuranol, 2,3-Dihydro-2,2-Dimethyl-]

September 2008

Prepared by

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QUALITATIVE SCREENING-LEVEL RISK CHARACTERIZATION FOR 2,3-Dihydro-2,2-Dimethyl-7-Benzofuranol (CAS No. 1563-38-8)

1. Physical-Chemical Properties and Environmental Fate

2,3-Dihydro-2,2-dimethyl-7-benzofuranol is a liquid at room temperature with a moderate vapor pressure and high water solubility. In the environment, it is expected to partition primarily to soil and water. In soil, it is moderately mobile and volatilization from moist soil and water is considered low. 2,3-Dihydro-2,2-dimethyl-7-benzofuranol in water is subject to slow direct photolysis and the rate of hydrolysis is considered negligible. If present in the atmosphere, it exists primarily as a vapor and the rate of photodegradation by reaction with photochemically generated hydroxyl radicals is moderate. 2,3-Dihydro-2,2-dimethyl-7-benzofuranol is expected to have moderate persistence (P2) and low bioaccumulation potential (B1).

2. Hazard Characterization

Aquatic Organism Toxicity: Acute toxicity of 2,3-dihydro-2,2-dimethyl-7-benzofuranol to fish, aquatic invertebrates and aquatic plants is low.

Human Health Toxicity: The acute oral and inhalation toxicity of 2,3-dihydro-2,2-dimethyl-7-benzofuranol to rats is low. The acute dermal toxicity to rabbits is low. In an oral combined repeated-dose reproductive/development toxicity study of 2,3-dihydro-2,2-dimethyl-7-benzofuranol in rats, there was low systemic toxicity in the parental animals, and low developmental and reproductive toxicity. In an oral prenatal developmental toxicity study in rats, there was low maternal and developmental toxicity. 2,3-Dihydro-2,2-dimethyl-7-benzofuranol was mutagenic when tested *in vitro* in bacteria and mammalian cells. However, it did not induce chromosomal aberrations in an *in vivo* mouse micronucleus assay.

3. Exposure Characterization

2,3-Dihydro-2,2-dimethyl-7-benzofuranol (CAS # 1563-38-8) has an aggregated production and/or import volume in the United States of 10 million to 50 million pounds. According to the IUR submissions, the industrial uses were claimed as confidential business information (CBI). There are no reported commercial/consumer uses of this chemical.

Potential Exposures to the General Population and the Environment: Based on the information considered—uncertainty about this chemical's industrial releases, persistence in the environment, and the Agency's expert judgment—EPA identifies, for the purposes of risk-based prioritization, a medium potential that the general population and the environment might be exposed.

Potential Exposure to Workers: Based on the information considered including Inventory Update Reporting (IUR) data and in combination with the Agency's professional judgment, EPA identifies, for the purposes of risk-based prioritization, a low relative ranking for potential worker exposure. This low relative ranking is based on the moderate vapor pressure of 0.009

mm Hg and use information, potential inhalation exposure to vapor, limited industrial uses, and no known commercial uses. This chemical does not have an OSHA Permissible Exposure Limit.

Potential Exposures to Consumers: EPA identifies, for the purposes of risk-based prioritization, a low potential that consumers might be exposed. No uses of this chemical in consumer products are reported in the IUR, nor other data sources.

Potential Exposures to Children: EPA identifies, for the purposes of risk-based prioritization, a low potential that children might be exposed. No uses in products intended to be used by children are reported in the IUR, nor other data sources.

5. Risk Characterization

The statements and rationale provided below are intended solely for the purpose of this screening-level and qualitative risk characterization and will be used for prioritizing substances for future work in the Chemical Assessment and Management Program (ChAMP).

Risk Statement and Rationale

Potential Risk to Aquatic Organism from Environmental Release: (LOW CONCERN) EPA identifies a medium potential that aquatic organisms might be exposed from environmental releases. 2,3-Dihydro-2,2-dimethyl-7-benzofuranol has a low potential for bioaccumulation. These characteristics in combination with low toxicity to fish, aquatic invertebrates and plants indicate a low concern for potential risk to fish, aquatic invertebrates and plants.

Potential Risk to the General Population from Environmental Releases: (LOW CONCERN) EPA identifies a medium potential that the general population might be exposed from environmental releases. The potential human health hazard is low. Therefore, taken together, the available information indicates a low concern for potential risk to the general population from environmental releases.

Potential Risk to Workers: (LOW CONCERN) EPA identifies a low relative ranking for potential worker exposure. The potential human health hazard is low. Therefore, taken together, the available information suggests a low concern for potential risks to workers.

Potential Risk to Consumers: (LOW CONCERN) EPA identifies a low potential that consumers might be exposed. There are no reported commercial/consumer uses of this chemical. The potential human health hazard is low. Therefore, taken together, the available information suggests a low concern for potential risks to consumers.

Potential Risk to Children: (LOW CONCERN) EPA identifies a low potential that children might be exposed. No uses in products intended to be used by children were reported in the IUR, or in other data sources. In rats, exposure during early life stages showed low toxicity. Therefore, taken together, the available information suggests a low concern for potential risks to children.

SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

SPONSORED CHEMICAL

2,3-Dihydro-2,2-Dimethyl-7-Benzofuranol (CAS No. 1563-38-8)
[9th CI Name: 7-Benzofuranol, 2,3-Dihydro-2,2-Dimethyl-]

September 2008

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SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS 2,3-Dihydro-2,2-Dimethyl-7-Benzofuranol (CAS No. 1563-38-8)

Introduction

The sponsor, FMC Corporation, submitted a Test Plan and Robust Summaries to EPA for 2,3-dihydro-2,2-dimethyl-7-benzofuranol (CAS No. 1563-38-8; 9th CI name: 7-benzofuranol, 2,3-dihydro-2,2-dimethyl-) on January 5, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on February 19, 2001 (http://www.epa.gov/chemrtk/pubs/summaries/7benz/c12874tc.htm). EPA comments on the original submission were posted to the website on June 14, 2001. Public comments were also received and posted to the website. The sponsor submitted final updated/revised documents on January 5, 2004, which were posted to the ChemRTK website on August 20, 2004.

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. 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 2003 to May 2008: the NLM databases (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, EXTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. 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 toxicity is based largely on SIDS endpoints and is described according to established EPA or OECD effect level definitions and hazard assessment practices.

Hazard Characterization

2,3-Dihydro-2,2-dimethyl-7-benzofuranol is a liquid at room temperature with a moderate vapor pressure and high water solubility. In the environment, it is expected to partition primarily to soil and water. In soil, it is moderately mobile and volatilization from moist soil and water is considered low. 2,3-Dihydro-2,2-dimethyl-7-benzofuranol in water is subject to slow direct photolysis and the rate of hydrolysis is considered negligible. If present in the atmosphere, it exists primarily as a vapor and the rate of photodegradation by reaction with photochemically generated hydroxyl radicals is moderate. 2,3-Dihydro-2,2-dimethyl-7-benzofuranol is expected to have moderate persistence (P2) and low bioaccumulation potential (B1).

The acute toxicity of 2,3-dihydro-2,2-dimethyl-7-benzofuranol to fish, aquatic invertebrates and aquatic plants is low.

The acute oral and inhalation toxicity of 2,3-dihydro-2,2-dimethyl-7-benzofuranol to rats is low. The acute dermal toxicity to rabbits is low. In an oral combined repeated-dose/reproductive/development toxicity study of 2,3-dihydro-2,2-dimethyl-7-benzofuranol in rats, there was low systemic toxicity in the parental animals, and low developmental and reproductive toxicity. In an oral prenatal developmental toxicity study in rats, there was low maternal and developmental toxicity. 2,3-Dihydro-2,2-dimethyl-7-benzofuranol was mutagenic when tested *in vitro* in bacteria and mammalian cells. However, it did not induce chromosomal aberrations in an *in vivo* mouse micronucleus assay.

Ready biodegradation has been identified as a data gap under the HPV Challenge Program.

1. Physical-Chemical Properties and Environmental Fate

The physical-chemical properties of 2,3-dihydro-2,2-dimethyl-7-benzofuranol are summarized in Table 1a, while its environmental fate properties are given in Table 1b. The structure of the compound is provided in the Appendix.

Physical-Chemical Properties Characterization

2,3-Dihydro-2,2-dimethyl-7-benzofuranol is a liquid at room temperature. It has a moderate vapor pressure and high water solubility.

Table 1a. Physical-Chemical Properties of 2,3-Dihydro-2,2-dimethyl-7-benzofuranol[1]

Property	Value
CAS No.	1563-38-8
Molecular Weight	164.21
Physical State	Liquid
Melting Point	<0°C (measured)
Boiling Point	76°C at 1 mm Hg (measured)
Vapor Pressure	27.2 Pa at 20°C (measured) 1.14 Pa at 25°C (measured)
Henry's Law Constant	4.6×10^{-7} atm-m^3/mol (estimated)[2,3]
Water Solubility	7.9 g/L at 25°C (measured)
Log K_{ow}	2.13 (measured)

[1]FMC Corporation. 2004. Robust Summary for 2,3-Dihydro-2,2-dimethyl-7-benzofuranol. http://www.epa.gov/chemrtk/pubs/summaries/7benz/c12874tc.htm.
[2]US EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v 3.20. United States Environmental Protection Agency, Washington, DC, USA. http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.
[3]Data not provided in robust summary.

Environmental Fate Characterization

2,3-Dihydro-2,2-dimethyl-7-benzofuranol is expected to partition primarily to soil and water, according to the results of a Level III fugacity model that assumes equal emission to air, water, and soil. In soil, it is moderately mobile and the rate of volatilization from moist soil and water is considered low. 2,3-Dihydro-2,2-dimethyl-7-benzofuranol in water is subject to slow direct photolysis and the rate of hydrolysis is considered negligible. If present in the atmosphere, it exists primarily as a vapor and the rate of photodegradation by reaction with photochemically generated hydroxyl radicals is moderate.

Ready biodegradation data for the substance was not submitted and is considered a data gap under the HPV Challenge Program. However, several studies on the biodegradation of a chemical analog, carbofuran, in soil and water were identified by EPA (see references). These studies suggested that under environmental conditions, 2,3-dihydro-2,2-dimethyl-7-benzofuranol (carbofuran phenol) was moderately persistent. The estimated BCF for 2,3-dihydro-2,2-dimethyl-7-benzofuranol is 8.7. 2,3-Dihydro-2,2-dimethyl-7-benzofuranol is expected to have moderate persistence (P2) and low bioaccumulation potential (B1).

Table 1b. Environmental Fate Characteristics of 2,3-Dihydro-2,2-dimethyl-7-benzofuranol[1]	
Property	**Value**
Photodegradation Half-life	OH reaction half-life = 5.1 hours (estimated)[2] Direct aqueous photolysis: half-life = 9.9 days (measured)
Biodegradation	Data gap
Hydrolysis Half-life	277 days at pH 9 and 20°C, 74 days at pH 9 and 37°C, stable at pH 4 and 7 (measured)
Bioconcentration	BCF = 8.7 (estimated)[2]
Log K_{oc}	3.0 (estimated)[2]
Fugacity (Level III Model)[2]	Air = 0.26% Water = 37.5% Soil = 62.1% Sediment = 0.156%
Persistence[3]	P2 (moderate)
Bioaccumulation[3]	B1 (low)

[1]FMC Corporation. 2004. Robust Summary for 2,3-Dihydro-2,2-dimethyl-7-benzofuranol. http://www.epa.gov/chemrtk/pubs/summaries/7benz/c12874tc.htm.
[2]US EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v 3.20. United States Environmental Protection Agency, Washington, DC, USA. http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.
[3]FR. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) Page 60194–60204.

Conclusion: 2,3-Dihydro-2,2-dimethyl-7-benzofuranol is a liquid at room temperature with a moderate vapor pressure and high water solubility. In the environment, it is expected to partition primarily to soil and water. In soil, it is moderately mobile and volatilization from moist soil and water is considered low. 2,3-Dihydro-2,2-dimethyl-7-benzofuranol in water is subject to slow direct photolysis and the rate of hydrolysis is considered negligible. If present in the atmosphere, it exists primarily as a vapor and the rate of photodegradation by reaction with photochemically generated hydroxyl radicals is moderate. 2,3-Dihydro-2,2-dimethyl-7-benzofuranol is expected to have moderate persistence (P2) and low bioaccumulation potential (B1).

2. Environmental Effects – Aquatic Toxicity

Acute Toxicity to Fish

Rainbow trout (*Oncorhynchus mykiss*) were exposed to 2,3-dihydro-2,2-dimethyl-7-benzofuranol at measured concentrations of 0, 2.9, 7.0, 13, 21, 33 and 50 mg/L for 96 hours under static conditions.
96-h LC_{50} = 37 mg/L

Acute Toxicity to Aquatic Invertebrates

Daphnia magna were exposed to 2,3-dihydro-2,2-dimethyl-7-benzofuranol at nominal concentrations of 0, 13, 22, 36, 59 and 100 mg/L (measured concentrations of 0, 13, 21, 35, 57 and 97 mg/L) for 48 hours under static conditions.
48-h EC_{50} = 33 mg/L

Toxicity to Aquatic Plants

Green algae (*Pseudokirchneriella subcapitata*) were exposed to 2,3-dihydro-2,2-dimethyl-7-benzofuranol at nominal concentrations of 0, 6.4, 13, 26, 52 and 100 mg/L (measured concentrations of < 2.9 (control), 6.2, 13, 25, 50 and 99 mg/L) for up to 120 hours under static conditions.
96-h EC_{50} (biomass) = 50 mg/L
96-h EC_{50} (growth) > 99 mg/L

Conclusion: The acute toxicity of 2,3-dihydro-2,2-dimethyl-7-benzofuranol to fish, aquatic invertebrates and aquatic plants is low.

3. Human Health Effects

Acute Oral Toxicity

Sprague-Dawley rats (10/sex/group) were administered undiluted 2,3-dihydro-2,2-dimethyl-7-benzofuranol by gavage to at doses of 1800, 2300 and 3000 mg/kg-bw for males and 1000, 1400, 1800 and 2300 mg/kg-bw for females. Prostration, recumbency, tremors, decreased activity and nasal, ocular and oral discharges were observed.
LD_{50} (males) = 2450 mg/kg-bw
LD_{50} (females) = 1743 mg/kg-bw

Acute Dermal Toxicity

New Zealand White rabbits (5 males/dose) were exposed to 20 and 300mg/kg-bw 2,3-dihydro-2,2-dimethyl-7-benzofuranol dermally in contact with intact skin for 24 hours under an occlusive wrap. Slight erythema was seen on day 4 in one rabbit treated with 300 mg/kg-bw.
LD_{50} (dermal) > 300 mg/kg-bw

Acute Inhalation Toxicity

Sprague-Dawley rats (5/sex/group) were exposed in a dynamically-operated whole-body inhalation chamber for 6 hours to a normal vapor concentration of 2,3-dihydro-2,2-dimethyl-7-benzofuranol (4.5 ppm or 0.03 mg/L, nominal; 18 ppm or 0.12 mg/L, measured; the maximum attainable saturated vapor concentration). A control group of rats was sham-exposed to room air only. There were no deaths or changes in body weight due to treatment during the study. The only clinical sign noted was red periocular fur in one male upon removal from the chamber and at the one-hour post-exposure observation. All other animals remained healthy during the study.
LC_{50} > 0.12 mg/L

Repeated-Dose Toxicity

In a combined repeated-dose/reproductive/developmental toxicity screening test, rats (10/sex/group) were administered 2,3-dihydro-2,2-dimethyl-7-benzofuranol in the diet at concentrations of 100, 1000, 5000, 10,000 and 20,000 ppm (~ 5.9/9, 59.2/89.6, 296.5/448.3, 592/896 and 1184/1792 mg/kg-bw/day for females and males, respectively). A concurrent control group and a 2-week recovery (high dose) group were included in the study. The experimental groups were dosed prior to mating, during mating, post-mating (males and females), during pregnancy and up to lactation day 4 (females). Concentrations of 100, 1000 and 5000 ppm did not have any adverse effects on general health. At 10,000 ppm, maternal body weight was decreased during gestation. At 20,000 ppm, decreases were seen in body weight, food consumption, maternal body weight and food consumption during gestation and lactation period, and terminal fasting body weights. Relative liver weights were increased. Histopathology data were not reported.
LOAEL ~ 896 and 1792 mg/kg-bw/day for males and females, respectively (based on decreased body weight)
NOAEL ~ 448.3 and 592 mg/kg-bw/day for males and females, respectively

Reproductive Toxicity

In the combined repeated–dose/reproductive/developmental toxicity screening test described above, concentrations of 100, 1000 and 5000 ppm did not have adverse effects on general health. At 10,000 ppm, maternal body weight during gestation and litter size were decreased. At 20,000 ppm, body weight, maternal body weight during gestation and lactation periods, litter size, mean viable litter size, mean number of corpora lutea, mean number of implantations and terminal fasting body weights were decreased. Relative liver weights were increased.
LOAEL (systemic toxicity) ~ 896 and 1792 mg/kg-bw/day for males and females, respectively (based on decreased body weights)
NOAEL (systemic toxicity) ~ 448.3 and 592 mg/kg-bw/day for males and females, respectively
LOAEL (reproductive toxicity) ~ 896 for females (based on decreased litter size)
NOAEL (reproductive toxicity) ~ 448.3 and 1792 mg/kg-bw/day for females and males, respectively

Developmental Toxicity

(1) In the combined repeated–dose/reproductive/developmental toxicity screening test described above, concentrations of 100, 1000 and 5000 ppm did not have adverse effects on general health. At 10,000 ppm, maternal body weight during gestation and litter size were decreased. At 20,000 ppm, body weight, maternal body weight during gestation and lactation period, litter size, mean viable litter size, mean number of corpora lutea, mean number of implantations and terminal fasting body weights were decreased. Liver weights were increased.
LOAEL (maternal/developmental toxicity) ~ 896 mg/kg-bw/day (based on decreased body weights and developmental parameters related to litters)
NOAEL (maternal/developmental toxicity) ~ 448.3 mg/kg-bw/day

(2) In another developmental toxicity study, groups of pregnant Sprague-Dawley rats were administered 2,3-dihydro-2,2-dimethyl-7-benzofuranol orally via gavage at dose levels of 0, 100, 500 or 1000 mg/kg-bw/day from days 6 through 19 of gestation. Maternal toxicity was observed at the all doses, and included clinical signs of toxicity and reduced body weight. The fetal body weights were decreased in the top two dose groups.
LOAEL (maternal toxicity) = 100 mg/kg-bw/day (based on clinical signs and body weight)
NOAEL (maternal toxicity) = Not established
LOAEL (developmental toxicity) = 500 mg/kg-bw/day (based on decreased fetal body weight)
NOAEL (developmental toxicity) = 100 mg/kg/day

Genetic Toxicity – Gene Mutation

In vitro
(1) An Ames assay was performed using *Salmonella typhimurium,* strains TA98, TA100, TA1535, TA1537 and TA1538, with and without metabolic activation and at 2,3-dihydro-2,2-dimethyl-7-benzofuranol concentrations of 61–10,000 μg/plate. The test material did not induce an increase in mutant frequency in tester strains TA98, TA100, TA1537 or TA1538, in the presence or in the absence of metabolic activation. In TA1535, the test material induced a marked positive response without metabolic activation. The mutant frequency was approximately 2.5–3 times the solvent control. Appropriate positive and negative controls responses were observed in the study.
2,3-Dihydro-2,2-dimethyl-7-benzofuranol was mutagenic in this assay.

(2) 2,3-Dihydro-2,2-dimethyl-7-benzofuranol was tested in an *in vitro* mouse lymphoma mutagenicity assay, in the presence and absence of metabolic activation at concentrations of 0.001 – 100 μL/mL. DMSO was used as a solvent control and appropriate positive and negative controls were included and showed appropriate responses. Mean mutant frequencies for the highest four doses was markedly increased compared to the solvent control in absence of metabolic activation and the two highest doses showed positive results in the presence of metabolic activation.
2,3-Dihydro-2,2-dimethyl-7-benzofuranol was mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vivo
In an *in vivo* mouse micronucleus assay, 2,3-dihydro-2,2-dimethyl-7-benzofuranol (in corn oil) was administered to male mice via a single intraperitoneal injection at 25, 50 or 100 mg/kg-bw. Bone marrow cells were examined 24 and 48 hours after exposure for micronucleated polychromatic erythrocytes. No significant increase ($p > 0.05$) in micronucleated polychromatic erythrocytes was seen, indicating that 2,3-dihydro-2,2-dimethyl-7-benzofuranol did not induce a notable increase in micronucleated polychromatic erythrocytes in male mice.
2,3-Dihydro-2,2-dimethyl-7-benzofuranol did not induce chromosomal aberrations in this assay.

Conclusion: The acute oral and inhalation toxicity of 2,3-dihydro-2,2-dimethyl-7-benzofuranol to rats is low. The acute dermal toxicity to rabbits is low. In an oral combined repeated-dose/reproductive/development toxicity study of 2,3-dihydro-2,2-dimethyl-7-benzofuranol in rats, there was low systemic toxicity in the parental animals, and low developmental and reproductive toxicity. In an oral prenatal developmental toxicity study in rats, there was low maternal and developmental toxicity. 2,3-Dihydro-2,2-dimethyl-7-benzofuranol was mutagenic when tested *in vitro* in bacteria and mammalian cells. However, it did not induce chromosomal aberrations in an *in vivo* mouse micronucleus assay.

4. **References**

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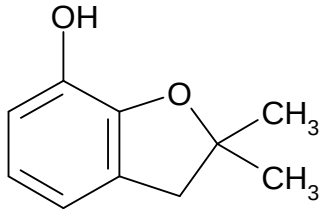
APPENDIX

Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program	
Endpoints	**SPONSORED CHEMICAL 2,3-Dihydro-2,2-Dimethyl-7-Benzofuranol (1563-38-8)**
Structure	
Summary of Environmental Effects – Aquatic Toxicity Data	
Fish 96-h LC_{50} (mg/L)	37
Aquatic Invertebrates 48-h EC_{50} (mg/L)	33
Aquatic Plants 72-h EC_{50} (mg/L)	
(growth)	50
(biomass)	> 99
Summary of Human Health Data	
Acute Oral Toxicity LD_{50} (mg/kg-bw)	1743 (female) 2450 (male)
Acute Dermal Toxicity LD_{50} (mg/kg-bw)	> 300
Acute Inhalation Toxicity LC_{50} (mg/L)	> 0.12 (6 h)
Repeated-Dose Toxicity NOAEL/LOAEL (mg/kg-bw/day)	
(male)	NOAEL = 592 LOAEL = 1792
(female)	NOAEL = 448.3 LOAEL = 896
Reproductive Toxicity NOAEL/LOAEL (mg/kg-bw/day)	
(Systemic toxicity)	NOAEL = 448.3 and 592 for females and males, respectively LOAEL = 896 and 1792 for females and males, respectively
(Reproductive toxicity)	NOAEL = 448.3 and 1792 for females and males, respectively LOAEL = 896 for females

Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program	
Endpoints	**SPONSORED CHEMICAL 2,3-Dihydro-2,2-Dimethyl-7-Benzofuranol (1563-38-8)**
Developmental Toxicity **NOAEL/LOAEL (mg/kg-bw/day)** **(Maternal/Developmental toxicity)** **(Maternal toxicity)** **(Developmental toxicity)**	 NOAEL = 448.3 LOAEL = 896 NOAEL = Not established LOAEL = 100 NOAEL = 100 LOAEL = 500
Genetic Toxicity – Gene Mutation ***In vitro***	Positive
Genetic Toxicity – Chromosomal Aberrations ***In vivo***	Negative

Screening Level Exposure Characterization for HPV Challenge Chemical

2,3-Dihydro-2,2-Dimethyl-7-Benzofuranol

CAS # 1563-38-8

September 2008

Prepared by

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Screening Level Exposure Characterization
2,3-Dihydro-2,2-Dimethyl-7-Benzofuranol
(CAS# 1563-38-8)

Non-CBI Executive Summary

2,3-Dihydro-2,2-dimethyl-7-benzofuranol (CAS # 1563-38-8) has an aggregated production and/or import volume in the United States of 10 million to 50 million pounds. According to the IUR submissions, the industrial uses were claimed as confidential business information (CBI). There are no reported commercial/consumer uses of this chemical.

Potential Exposures to the General Population and the Environment: Based on the information considered—uncertainty about this chemical's industrial releases, persistence in the environment, and the Agency's expert judgment—EPA identifies, for purposes of risk-based prioritization, a medium potential for exposure to the general population and the environment.

Potential Exposure to Workers: Based on the information considered including Inventory Update Reporting (IUR) data and in combination with the Agency's professional judgment, EPA identifies, for the purposes of risk-based prioritization, a low relative ranking for potential worker exposure. This low relative ranking is based on the moderate vapor pressure of 0.009 mm Hg and use information, potential inhalation exposure to vapor, limited industrial uses, and no known commercial uses. This chemical does not have an OSHA Permissible Exposure Limit.

Potential Exposures to Consumers: EPA identifies, for the purposes of risk-based prioritization, a low potential for exposures to consumers from products containing this chemical. No uses of this chemical in consumer products are reported in the IUR, nor other data sources.

Potential Exposures to Children: EPA identifies, for the purposes of risk-based prioritization, a low potential for exposures to children. No uses in products intended to be used by children are reported in the IUR, nor other data sources.

This characterization was completed using both public, non-confidential sources, and one or more IUR submissions that were available as of this writing.

<u>Volume and Use Information</u>

2,3-Dihydro-2,2-dimethyl-7-benzofuranol (CAS # 1563-38-8) has an aggregated production and/or import volume in the United States of 10 million to 50 million pounds.[12] The IUR data indicate that chemical manufacturing/import sites were claimed confidential.

Persons submitting IUR information for 2005 asserted that some or all of the information was confidential. Only non-confidential IUR data are included in this summary.

[12] USEPA, 2006 Partial Updating of TSCA Chemical Inventory.

According to the IUR submissions, the chemical's industrial processing and uses were claimed as CBI, and there are no reported commercial/consumer uses of this chemical.

Publicly available data sources searched for this report did not have any information on use.

Exposures to Workers

Based on the information considered, including IUR data and in combination with the Agency's professional judgment, EPA identifies, for the purposes of risk-based prioritization, a low relative ranking for potential worker exposure. The low relative ranking is based on the potential for inhalation exposure to vapor, the moderate vapor pressure, limited industrial uses, and no known commercial uses. The following is a summary of relevant information affecting worker exposure.

Summary of Parameters affecting Worker Exposure

Parameter	
Volume*	10 million to 50 million pounds
Physical Form(s)*	Liquid
Vapor Pressure	0.009 mm Hg (measured) @ 25°C
Concentration*	Claimed CBI
Number of Potentially Exposed Workers	<100 (including those in manufacturing, processing and use)
Uses	Claimed CBI
Key MSDS Info	Use Government approved respirator. Wear appropriate protective gloves to prevent skin exposure. Wear chemical safety goggles.
Other hazard characteristics	Causes skin irritation. May be harmful by inhalation, ingestion, or skin absorption. Vapor or mist is irritating to eyes, mucous membranes, and upper respiratory tract.

*Only non-confidential IUR data are included in this summary.

Based on IUR data, the maximum total number of workers reasonably likely to be exposed to this chemical during manufacturing and industrial processing and use may be less than 100. This estimate does not include potentially exposed commercial workers, although no commercial use was reported for this chemical under IUR. The National Occupational Exposure Survey (NOES) has no data for the total number of workers potentially exposed to this chemical.[13]

Based on IUR data, the chemical is manufactured in liquid form, and worker exposures are possible for this chemical. There may be other physical forms that are claimed confidential. Also, the maximum concentration is claimed confidential. This chemical has a vapor pressure of

[13] NIOSH, 1983. National Occupational Exposure Survey (NOES, 1981-1983). Accessed, 5/14/08. http://www.cdc.gov/noes/srch-noes.html.

0.009 mm Hg which may result in worker exposures to vapors if workers are proximal to the liquid.[14]

This chemical does not have OSHA Permissible Exposure Limits (PELs).[15]

Environmental Releases

Environmental releases may impact general population and environmental exposures. Factors affecting releases include volumes produced, processed and used; numbers of sites; and, processes of manufacture, processing, and use.

Based on IUR data, the number of manufacturing, industrial processing and use sites is confidential.

The chemical is not on the Toxics Release Inventory.[16] No additional data on releases were found from other sources.

Experience has shown that air releases due to volatilization have not been an issue for chemicals with vapor pressures below 0.01 mm Hg. The vapor pressure for this chemical of 0.009 mm Hg is a level at which air releases are not expected to be significant.

Exposures to the General Population and the Environment

Based on the lack of information in the IUR—limited use information and some unaccounted-for production/import volume—it is likely that there would be some releases to the environment during manufacturing, processing, and use. A search of additional relevant databases did not provide any further information on releases of this chemical. EPA assumes that the potential for environmental release and subsequent exposure to the general population and the environment is likely. The IUR ranking for general population and the environment is medium based on the uncertainty of the limited use information and unaccounted-for volume.

The persistence rating for this chemical is P2; the bioaccumulation rating for this chemical is low (B1). These ratings suggest that this chemical is persistent in the environment; and it is not bioaccumulative.

Based on the information considered—uncertainty in this chemical's industrial uses, persistence in the environment, and the Agency's expert judgment—EPA identifies, for purposes of risk-based prioritization, a medium potential that the general population and the environment might be exposed.

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[14] USEPA, 2008. SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS, SPONSORED CHEMICAL: 2,3-Dihydro-2,2-Dimethyl-7-Benzofuranol (CAS No. 1563-38-8). July 2008.

[15] NIOSH, 1988. OSHA PEL Project Documentation. http://www.cdc.gov/niosh/pel88/npelcas.html. Accessed, 5/20/08.

[16] USEPA, 2006. Toxic Release Inventory. Accessed, 5/14/08. http://www.epa.gov/tri/.

Exposures to Consumers

Consumer uses were not reported in the IUR data, as seen in Table 2 at the end of this summary.

Based on the IUR data, EPA identifies, for the purposes of risk-based prioritization, a low potential that consumers might be exposed from products containing this chemical.

Exposures to Children

No uses in products intended to be used by children were reported in the IUR, nor were any found in other data sources. Therefore, EPA identifies, for the purposes of risk-based prioritization, a low potential that children might be exposed.

Non Confidential IUR Data Summary: 2,3-Dihydro-2,2-dimethyl-7-benzofuranol (CAS # 1563-38-8)

Manufacturing/ Import Information

Production (includes import volume):	10 million to 50 million pounds
List of non-CBI companies/ sites:	Confidential
Maximum number of exposed workers:	less than 100 (including those in manufacturing, processing and use)
Highest non-CBI maximum concentration:	Confidential
Non-CBI physical forms*:	Liquid

* There may be other physical forms that are claimed confidential.

Table 1
Industrial Processing and Use Information
Reported in 2006 IUR

Processing Activity	Industrial Sector	Function in Industrial Sector
Claimed as CBI		

Table 2
Commercial/ Consumer Uses
Reported in 2006 IUR

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
None reported		