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

Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)- (CASRN 61898-95-1) (9th CI and CA Index Name: Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester)

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

Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester (CAS No. 61898-95-1)

[9th CI Name: Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester]

September 2008

Prepared by

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QUALITATIVE SCREENING-LEVEL RISK CHARACTERIZATION FOR Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester (CAS No. 61898-95-1)

1. Physical-Chemical Properties and Environmental Fate

Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester is a clear, colorless liquid at room temperature. It has moderate solubility and moderate vapor pressure. It has moderate mobility in soil and moderate volatility. The rate of hydrolysis is negligible and biodegradation is judged to be moderate to slow; therefore, its persistence potential is judged to be moderate (P2). Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester's bioaccumulation potential is ranked low (B1).

2. Hazard Characterization

Aquatic Organism Toxicity. The acute toxicity of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-,methyl ester to fish, aquatic invertebrates and plants is moderate.

Human Health Toxicity. In rats, the acute oral and inhalation toxicity of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester is low. Repeated-dose and reproductive toxicity data were not required for the HPV Challenge Program because cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl is a closed system intermediate. A combined reproductive/developmental screening toxicity study in rats showed low maternal and developmental toxicity. Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester did not induce gene mutation in bacteria or chromosomal aberrations *in vitro*.

3. Exposure Characterization

There were no 2006 Inventory Update Rule (IUR) submissions for cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-(CAS # 61898-95-1). The 2002 IUR data indicated that this chemical had an aggregated production and/or import volume in the United States of > 1 million to 10 million pounds. No information on commercial/consumer uses was found in the IUR or any other sources.

Potential for Exposures to Human and the Environment:
Based on the information considered, including 2002 IUR data and information from the HPV Challenge Program, and in combination with the Agency's professional judgment, EPA identifies, for the purposes of risk-based prioritization, a low relative ranking for each of the potentially exposed groups (including workers, general population, consumers and children) and the environment. In 2003, the Agency reviewed the information in the HPV submission and test plan and determined that the HPV chemical satisfied the guidance to demonstrate that the chemical is a closed system intermediate. The chemical was determined to be manufactured and processed in systems which is expected to reduce the potential for worker exposure and environmental releases that could lead to other human and environmental exposure. The

guidance for identifying this chemical substance as a closed-system intermediate was satisfied at all sites reporting this chemical in accordance with IUR requirements.

4. 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

The Agency reviewed the information in the HPV submission and test plan and determined that the HPV chemical satisfied the guidance to demonstrate that the chemical is a closed-system intermediate. Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-,methyl ester was determined to be manufactured and processed in closed systems which are expected to reduce the potential for worker exposure and environmental releases that could lead to other human and environmental exposure. The guidance for identifying this chemical substance as a closed-system intermediate was satisfied at all sites reporting this chemical in accordance with IUR requirements. Therefore, there is a low concern for potential risks to aquatic organisms and the general population from environmental releases, and also to workers, consumers, and children.

SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

SPONSORED CHEMICAL

Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester (CAS No. 61898-95-1)
[9th CI Name: Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester]

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SCREENING-LEVEL HAZARD CHARACTERIZATION
Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester (CAS No. 61898-95-1)

Introduction

The sponsor, FMC Corporation, submitted a Test Plan and Robust Summaries to EPA for Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester (CAS No. 61898-95-1) on December 28, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on February 5, 2002 (http://www.epa.gov/chemrtk/pubs/summaries/cyclopro/c13457tc.htm). The sponsor submitted revised test plans on May 1, 2002 and July 8, 2002, which were posted to the website on May 10, 2002 and July 24, 2002, respectively. EPA comments on the original submission were posted to the website on July 19, 2002. The sponsor submitted updated/revised documents on September 17, 2002, which were posted to the ChemRTK website on September 24, 2002. EPA comments on the updated/revised document were posted to the website on July 2, 2003. The sponsor submitted a second updated/revised document on December 30, 2004, which was posted on the Chem RTK website on February 3, 2005.

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 November 2004 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 effects is based largely on SIDS endpoints and is described according to established EPA or OECD effect level definitions and hazard assessment practices.

The sponsor claimed cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester to be a "closed system intermediate" (CSI) chemical and submitted additional information to support this claim in its revised submissions. The revised documents adequately address the clarifications that EPA requested to support the CSI status for this chemical. Based on the CSI status of this chemical, requirement for repeated-dose toxicity and reproductive toxicity endpoints have been waived under the HPV Challenge Program.

Hazard Characterization

Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester is a clear, colorless liquid at room temperature. It has moderate solubility and moderate vapor pressure. It has moderate mobility in soil and moderate volatility. The rate of hydrolysis is negligible and biodegradation is judged to be moderate to slow; therefore, its persistence potential is judged to be moderate (P2). Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester's bioaccumulation potential is ranked low (B1).

The acute toxicity of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl to fish, aquatic invertebrates and aquatic plants is moderate.

In rats, the acute oral and inhalation toxicity of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester are low. Repeated-dose and reproductive toxicity data were not required for the HPV Challenge Program because cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl is a closed system intermediate. However, a reproductive/developmental screening toxicity study in rats was submitted and showed low maternal and developmental toxicity. Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester did not induce gene mutation in bacteria or chromosomal aberrations *in vitro*.

No data gaps were identified under the HPV Challenge Program.

1. Physical-Chemical Properties and Environmental Fate

The physical-chemical properties of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester 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

Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester is a clear, colorless liquid at room temperature. It has moderate solubility and moderate vapor pressure.

Table 1a. Physical-Chemical Properties of Cyclopropanecarboxylic Acid, 3-(2,2-Dichloroethenyl)-2,2-Dimethyl-, Methyl Ester[1]

Property	Value
CAS No.	61898-95-1
Molecular Weight	223
Physical State	Liquid
Melting Point	28ºC (estimated)[2]
Boiling Point	78ºC (0.6 mm Hg) (measured)
Vapor Pressure	0.03 mm Hg at 25ºC (measured)
Henry's Law Constant	1.7×10^{-4} atm-m^3/mol (estimated)[2]
Water Solubility	53 mg/L at 25ºC (measured)
Log K_{ow}	3.66 (measured)

[1]FMC. 2002. Robust Summary for Cyclopropanecarboxylic Acid, 3-(2,2-Dichloroethenyl)-2,2-Dimethyl-, Methyl Ester. http://www.epa.gov/chemrtk/pubs/summaries/cyclopro/c13457tc.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.

Environmental Fate Characterization

Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester is expected to partition primarily to soil, according to the results of a Level III fugacity model that assumes equal emissions to air, water, and soil. Based on its vapor pressure, cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester will exist in the vapor phase in the atmosphere. The rate of vapor-phase photodegradation of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester with hydroxyl radicals is slow. Volatilization of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester is considered moderate based on its Henry's Law constant. The hydrolysis rate of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester is negligible under environmental conditions. It has moderate mobility in soil. Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl did not degrade in 28 days using a closed bottle OECD 301D biodegradation test. This compound is used as a starting material in the synthesis of pyrethroid insecticides such as permethrin and cypermethrin. Field studies and aerobic biodegradation data obtained from the Hazardous Substance Data Bank suggest that these pesticides biodegrade with half-lives of several days to a few weeks; therefore, the persistence potential of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester is ranked as moderate (P2). Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester's bioaccumulation potential is ranked low (B1) based on an estimated BCF of 3.

Table 1b. Environmental Fate Characteristics of Cyclopropanecarboxylic Acid, 3-(2,2-Dichloroethenyl)-2,2-Dimethyl-, Methyl Ester[1]	
Property	**Value**
Photodegradation Half-Life	2.4 days (estimated)[2]
Aerobic degradation	0% at 28 days (not readily biodegradable); Half-lives of several days to a few weeks in field studies of permethrin and cypermethrin[2]
Hydrolysis Half-Life	17 years at pH 7 (estimated) 1.7 years at pH 8 (estimated)
Bioconcentration	BCF = 3 (estimated)[2]
K_{oc}	285.7 (estimated)[2]
Fugacity (Level III Model)[3]	Air = 3.53% Water = 21.4% Soil = 73.7% Sediment = 1.42%
Persistence[4]	P2 (moderate)
Bioaccumulation[4]	B1 (low)

[1]FMC. 2002. Robust Summary for Cyclopropanecarboxylic Acid, 3-(2,2-Dichloroethenyl)-2,2-Dimethyl-, Methyl Ester. http://www.epa.gov/chemrtk/pubs/summaries/cyclopro/c13457tc.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]HSDB. 2008. Hazardous Substances Data Bank. As cited in record for Permethrin and Cypermethrin, accessed May 28, 2008. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB
[4]Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

Conclusion: Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester is a clear, colorless liquid at room temperature. It has moderate solubility and moderate vapor pressure. It has moderate mobility in soil and moderate volatility. The rate of hydrolysis is negligible and biodegradation is judged to be moderate to slow; therefore, its persistence potential is judged to be moderate (P2). Cyclopropanecarboxylic acid, 3-(2,2-dichloro-ethenyl)-2,2-dimethyl-, methyl ester's bioaccumulation potential is ranked low (B1).

2. Environmental Effects – Aquatic Toxicity

Acute Toxicity to Fish

Rainbow trout (*Oncorhynchus mykiss,* 10/replicate) were exposed to cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester at concentrations of 0, 2.56, 4.09, 6.44, 10.7, or 18.5 mg/L (measured) under static renewal conditions for 96 hours.
96-hr LC_{50} = 3.01 mg/L

Acute Toxicity to Aquatic Invertebrates

Daphnia magna (10/replicate) were exposed to cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester at concentrations of 0, 3.04, 5.13, 9.01, 14.6, and 23.6 mg/L (measured) under static renewal conditions for 48 hours.
48-hr EC_{50} = 6.40 mg/L
48-hr LC_{50} = 7.04 mg/L

Toxicity to Aquatic Plants

Green algae (*Pseudokirchneriella subcapitata*) were as exposed to cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester at concentrations of 0, 2.0, 3.8, 7.6, 15.9, or 31.1 mg/L under static conditions for 120 hours. The 24-hour EC_{25} and EC_{50} could not be calculated because growth at all test concentrations and in the control was less than 10,000 cells/mL.
96-hr EC_{50} (biomass) = 5.2 mg/L
96-hr EC_{50} (growth) = 8.3 mg/L

Conclusion: The acute toxicity of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester to fish, aquatic invertebrates and aquatic plants is moderate.

3. Human Health Effects

Acute Oral Toxicity

Sprague-Dawley rats (5/sex) were administered a single oral dose of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester via gavage at 5000 mg/kg-bw and observed for 14 days. Predominant clinical signs included abdominogenital staining, ataxia, chromodacryorrhea, chromorhinorrhea, cyanosis, diarrhea, exophthalmos, lacrimation, decreased locomotion, oral discharge, prostration and recumbency. One female rat died within three days of dosing. All surviving rats returned to normal by the 5th day of the study.
LD_{50} > 5000 mg/kg-bw

Acute Inhalation Toxicity

Sprague-Dawley rats (5/sex) were exposed (whole body) to vapors of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester for six hours at a nominal concentration of 38.7 ppm (0.353 mg/L) and observed for 14 days. There were no deaths during the study. Treatment related clinical signs included squinting eyes, excessive lacrimation, red perinasal fur and irregular breathing patterns. All rats had recovered by study day 1 and remained healthy until termination. There were no gross treatment-related lesions observed in any animal at necropsy.
LC_{50} > 0.353 mg/L

Repeated-Dose Toxicity

The requirement for repeated dose toxicity testing was waived because cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester is a closed system intermediate.

Reproductive Toxicity

The requirement for reproductive toxicity testing was waived because cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester is a closed system intermediate. However, the sponsor submitted a combined reproductive/developmental toxicity test described below.

Developmental Toxicity

In a reproductive/developmental toxicity screening test, Sprague-Dawley rats (male and female, number per dose was not provided), were administered cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester via gavage at 0, 50, 450 or 900 mg/kg-bw/day. Male rats were administered the test substance from 2 weeks before mating to the end of mating period (28 days total). Females were administered the test substance from 2 weeks before mating through gestation and to day 3 post partum (54 days total). There was a high incidence of salivation in both sexes at 450 and 900 mg/kg-bw/day. Two moribund females were sacrificed at 900 mg/kg-bw. There were no treatment-related changes in body weight, food consumption, necropsy finding, or male reproductive organ weights or histopathological findings. An increase in perinatal deaths, decreased number and body weights of live young at birth, and decreased litter size were observed at 900 mg/kg-bw/day. No treatment-related effect was

seen in gestation length, viability index, sex ratio, number of pups with gross lesions, or pups with abnormally low body weights.
LOAEL (maternal toxicity) = 900 mg/kg-bw/day (based on mortality)
NOAEL (maternal toxicity) = 450 mg/kg-bw/day

LOAEL (developmental toxicity) = 900 mg/kg-bw/day (based on increased perinatal deaths, decreased number and body weights of live young at birth, and decreased litter size)
NOAEL (developmental toxicity) = 450 mg/kg-bw/day

NOAEL (reproductive toxicity) = 900 mg/kg-bw/day (males and females)

Genetic Toxicity – Gene Mutation

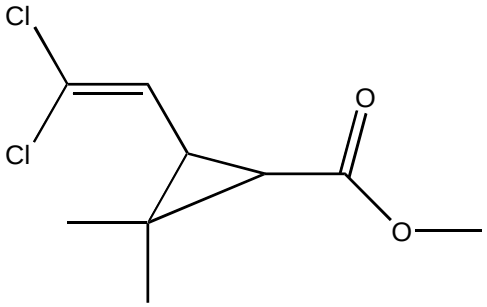
In vitro
Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, and TA1538 were exposed to cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester at 50, 100, 250, 500, or 1000 µg/plate in the presence and absence of metabolic activation. The cytotoxic concentration was determined in the rang-finding study. Positive and negative controls were included in the test and showed appropriate response. The test substance was not mutagenic under the conditions of this test.
Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro
Cultured Chinese hamster lung (CHL) cells were exposed to cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester in the presence and absence of metabolic activation. Cells were exposed in a 6-hour treatment at 0, 100, 300, 500, 700, or 900 µM with metabolic activation and in 6- and 24-hour treatments at 0, 37.5, 75, 150, or 300 µM without metabolic activation. The cytotoxic concentration was determined in the rang-finding study. Positive and negative controls were included in the test and showed appropriate response. The test substance did not induce chromosomal aberrations under the conditions of this study.
Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester did not induce chromosomal aberrations in this assay.

Conclusion: In rats, the acute oral and inhalation toxicity of cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester in rats are low. Repeated-dose and reproductive toxicity data were not required for the HPV Challenge Program because cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl is a closed system intermediate. However, a reproductive/developmental toxicity screening study in rats was submitted and showed low maternal and developmental toxicity. Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, methyl ester did not induce gene mutation in bacteria or chromosomal aberrations in vitro.

APPENDIX

Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program	
Endpoints	**SPONSORED CHEMICAL** **Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2-2-dimethyl-, methyl ester** **(61898-95-1)**
Structure	
Summary of Environmental Effects – Aquatic Toxicity Data	
Fish **96-h LC_{50} (mg/L)**	3.01
Aquatic Invertebrates **48-h EC_{50} (mg/L)**	6.40
Aquatic Plants **72-h EC_{50} (mg/L)** **(biomass)** **(growth)**	 5.22 8.26
Summary of Human Health Data	
Acute Oral Toxicity **LD_{50} (mg/kg-bw)**	> 5000
Acute Inhalation Toxicity **LC_{50} (mg/L)**	> 0.353 (6 hr) (No mortality at saturation)
Repeated-Dose Toxicity **NOAEL/LOAEL** **Oral (mg/kg-bw/day)**	N/A; chemical is a closed system intermediate.
Reproductive Toxicity **NOAEL/LOAEL** **Oral (mg/kg-bw/day)**	NOAEL = 900 (males and females)
Developmental Toxicity **NOAEL/LOAEL** **Oral (mg/kg-bw/day)** **Maternal Toxicity** **Developmental Toxicity**	 NOAEL = 450 LOAEL = 900 NOAEL = 450 LOAEL = 900
Genetic Toxicity – Gene Mutation ***In vitro***	Negative
Genetic Toxicity – Chromosomal Aberrations ***In vitro***	Negative

Screening Level Exposure Characterization for HPV Challenge Chemical

Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-

CAS # 61898-95-1

September 2008

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Screening Level Exposure Characterization

Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)- (CAS # 61898-95-1)

Non-CBI Executive Summary

There were no 2006 Inventory Update Rule (IUR) submissions for cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-(CAS # 61898-95-1). The 2002 IUR data indicated that this chemical had an aggregated production and/or import volume in the United States of > 1 million to 10 million pounds.[12]

Potential for Exposures to Human and the Environment:

Based on the information considered (including 2002 IUR data and information from the HPV Challenge Program), and in combination with the Agency's professional judgment, EPA identifies, for the purposes of risk-based prioritization, a low relative ranking for each of the potentially exposed groups (including workers, general population, consumers and children) and the environment. In 2003, the Agency reviewed the information in the HPV submission and test plan and determined that the HPV chemical satisfied the guidance to demonstrate that the chemical is a closed system intermediate.[13] The chemical was determined to be manufactured and processed in systems which is expected to reduce the potential for worker exposure and environmental releases that could lead to other human and environmental exposure. There were no 2006 IUR submissions for this chemical. No information on commercial/consumer uses was found in the IUR or any other sources.

Non Confidential IUR Data Summary: Cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-(CAS# 61898-95-1)

2002 IUR Data

Manufacturing/Import Information

Production/ import volume:	> 1 million to 10 million pounds
List of non-CBI companies/ sites*:	FMC Corporation

* There may be other companies/ sites that are claimed confidential.

[12] USEPA, 2002. Inventory Update Reporting. http://www.epa.gov/oppt/iur/tools/data/2002-vol.htm. Accessed on June 13, 2008.
[13] USEPA, 2003. EPA Comments on Chemical RTK HPV Challenge Submission. Letter dated June 20, 2003. Accessed June 13, 2008. http://www.epa.gov/chemrtk/pubs/summaries/cyclopro/c13457tc.htm.