

## SCREENING-LEVEL HAZARD CHARACTERIZATION

### SPONSORED CHEMICAL

#### **Methyl 3,3-dimethyl-4-pentenoate (CASRN 63721-05-1)**

The High Production Volume (HPV) Challenge Program<sup>1</sup> 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<sup>1,2</sup>) 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<sup>2,3</sup> 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

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<sup>1</sup> U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

<sup>2</sup> U.S. EPA. HPV Challenge Program – Information Sources; <http://www.epa.gov/chemrtk/pubs/general/guidocs.htm>.

<sup>3</sup> U.S. EPA. Risk Assessment Guidelines; <http://cfpub.epa.gov/ncea/raf/rafguid.cfm>.

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.

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.

<b>Chemical Abstract Registry Number (CASRN)</b>	<b>63721-05-1</b>
<b>Chemical Abstract Index Name</b>	<b>Methyl 3,3-dimethyl-4-pentenoate</b>
<b>Structural Formula</b>	
<b>Summary</b>	
<p>Methyl 3,3-dimethyl-4-pentenoate is a liquid with moderate water solubility and high vapor pressure. It is expected to have high mobility in soil. Volatilization of methyl 3,3-dimethyl-4-pentenoate from water and moist soil is considered moderate based on its Henry's Law constant. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered moderate. Methyl 3,3-dimethyl-4-pentenoate is expected to have low persistence (P1) based on the rapid biodegradation of a structurally similar ester and low bioaccumulation potential (B1).</p> <p>Acute oral toxicity of methyl 3,3-dimethyl-4-pentenoate to rats is low. Acute inhalation toxicity to rats and acute dermal toxicity to rabbits of methyl 3,3-dimethyl-4-pentenoate is low. The test substance was described as minimally irritating to rabbit skin. Requirements for repeated dose and reproductive toxicity testing were waived under the HPV Challenge Program because the sponsored substance is a closed-system intermediate. No data were provided for the developmental toxicity endpoint. Methyl 3,3-dimethyl-4-pentenoate did not induce gene mutations in bacteria <i>in vitro</i>. There are no data for the chromosomal aberrations endpoint.</p> <p>For the acute hazard of CASRN 137-26-8, the estimated 96-hour LC<sub>50</sub> to fish is 9.0 mg/L, the estimated 48-hour EC<sub>50</sub> to aquatic invertebrates is 17.2 mg/L, and the estimated 96-hour EC<sub>50</sub> to aquatic plants is 6.9 mg/L.</p> <p>Data gaps remain under the HPV Challenge Program for developmental toxicity and chromosomal aberrations endpoints for human health hazard evaluation, and acute toxicity to fish, aquatic invertebrates, and aquatic plants in the environment.</p>	

The sponsor, FMC Corporation, submitted a Test Plan and Robust Summaries to EPA for methyl 3,3-dimethyl-4-pentenoate (CASRN 63721-05-1; CA Index name: 4-pentenoic acid, 3,3-dimethyl-, methyl ester) on December 30, 2002. EPA posted the submission on the ChemRTK HPV Challenge website on January 28, 2003 (<http://www.epa.gov/chemrtk/pubs/summaries/methyl33/c14190tc.htm>). EPA comments on the original submission were posted to the website on May 28, 2003. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on July 23, 2003, which were posted to the ChemRTK website on August 20, 2003.

The Agency reviewed the information in the HPV test plan and determined that the HPV chemical met the HPV Challenge Program guidance for a closed-system intermediate. The chemical is manufactured and processed in systems that are expected to reduce the potential for worker exposure and environmental releases that could lead to other human and environmental exposure.

## 1 Chemical Identity

### 1.1 Identification and Purity

There is no discussion of the identity or purity of this chemical in the sponsor's Test Plan.

### 1.2 Physical-Chemical Properties

The physical-chemical properties of CASRN 63721-05-1 are summarized in Table 1.

<b>Table 1. Physical-Chemical Properties of Methyl 3,3-dimethyl-4-pentenoate<sup>1</sup></b>	
<b>Property</b>	<b>Value</b>
CASRN	63721-05-1
Molecular Weight	142.20 <sup>2</sup>
Physical State	Liquid <sup>2</sup>
Melting Point	Not applicable
Boiling Point	73°C at 50 mm Hg (measured); 95–99°C at 140 mm Hg (measured); 70°C at 60 mm Hg (measured)
Vapor Pressure	50 mm Hg at 73°C (measured)
Water Solubility	512 mg/L at 25°C (estimated) <sup>3</sup>
Dissociation Constant (pK <sub>a</sub> )	Not applicable
Henry's Law Constant	5.39×10 <sup>-4</sup> atm·m <sup>3</sup> /mole (estimated) <sup>3</sup>
Log K <sub>ow</sub>	2.58 (estimated) <sup>3</sup>

<sup>1</sup>FMC Corporation. 2003. Revised Robust Summary for Methyl 3,3-dimethyl-4-pentenoate.

<http://www.epa.gov/chemrtk/pubs/summaries/methyl33/c14190tc.htm>.

<sup>2</sup>Aldrich Handbook of Fine Chemicals. 2007–2008.

<sup>3</sup>U.S. EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v 3.20. U.S. Environmental Protection Agency, Washington, DC, USA. <http://www.epa.gov/opptintr/exposure/pubs/episuite.htm>.

## **2 General Information on Exposure**

### **2.1 Production Volume and Use Pattern**

This HPV chemical did not have any IUR submissions in 2006. Prior IUR data indicates that this chemical had aggregated annual production and import volumes in the United States of less than 500,000 pounds in 2002, 1 to 10 million pounds in 1998 and 1990, and 500,000 to 1 million pounds in 1994, respectively. The High Production Volume (HPV) submission states that the chemical is used as a chemical intermediate.

### **2.2 Environmental Exposure and Fate**

No quantitative information is available on releases of this chemical to the environment.

The environmental fate properties are provided in Table 2. Methyl 3,3-dimethyl-4-pentenoate is expected to have high mobility in soil. No biodegradation data was provided by the sponsor for this chemical; however, a structurally similar ester, methyl methacrylate (CASRN 80-62-6), achieved 94.3% of its theoretical BOD using an activated sludge inoculum and the modified MITI test (OECD 301C) over a 2-week incubation period.<sup>4</sup> Volatilization of methyl 3,3-dimethyl-4-pentenoate is considered moderate based on its Henry's Law constant. The persistence of methyl 3,3-dimethyl-4-pentenoate is expected to be low (P1). Methyl 3,3-dimethyl-4-pentenoate is expected to have low bioaccumulation potential (B1).

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<sup>4</sup>National Institute of Technology and Evaluation Biodegradation and Bioconcentration of the Existing Chemical Substances. [http://www.safe.nite.go.jp/english/kizon/KIZON\\_start\\_hazkizon.html](http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html).

<b>Property</b>	<b>Value</b>
Photodegradation Half-life	4.7 hours (estimated; assumes 12-hour day and $5 \times 10^5$ hydroxyl radicals/cm <sup>3</sup> ) <sup>3</sup>
Hydrolysis Half-life	5.4 years at pH 8 and 25°C (estimated); 54 years at pH 7 and 25°C (estimated)
Biodegradation	94.3% in 14 days (data for structural analog methyl methacrylate) <sup>4</sup>
Bioconcentration	BCF = 19.38 (estimated) <sup>3</sup>
Log K <sub>oc</sub>	1.7 (estimated) <sup>3</sup>
Fugacity (Level III Model)	Air = 2.86% Water = 34.9% Soil = 62.1% Sediment = 0.206%
Persistence	P1(low) <sup>5</sup>
Bioaccumulation	B1 (low) <sup>5</sup>

<sup>1</sup>FMC Corporation. 2003. Revised Robust Summary for Methyl 3,3-dimethyl-4-pentenoate.

<http://www.epa.gov/chemrtk/pubs/summaries/methyl33/c14190tc.htm>.

<sup>2</sup>Aldrich Handbook of Fine Chemicals. 2007–2008.

<sup>3</sup>U.S. EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v 3.20. U.S. Environmental Protection Agency, Washington, DC, USA. <http://www.epa.gov/opptintr/exposure/pubs/episuite.htm>.

<sup>4</sup>National Institute of Technology and Evaluation Biodegradation and Bioconcentration of the Existing Chemical Substances. Accessed July 7, 2008. [http://www.safe.nite.go.jp/english/kizon/KIZON\\_start\\_hazkizon.html](http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html).

<sup>5</sup>Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. Federal Register 64, Number 213 (November 4, 1999) pp. 60194–60204.

**Conclusion:** Methyl 3,3-dimethyl-4-pentenoate is a liquid with moderate water solubility and high vapor pressure. It is expected to have high mobility in soil. Volatilization of methyl 3,3-dimethyl-4-pentenoate from water and moist soil is considered moderate based on its Henry's Law constant. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered moderate. Methyl 3,3-dimethyl-4-pentenoate is expected to have low persistence (P1) based on the rapid biodegradation of a structurally similar ester and low bioaccumulation potential (B1).

### **3 Human Health Hazard**

#### ***Acute Oral Toxicity***

Sprague-Dawley rats (5/sex/dose) were administered methyl 3,3-dimethyl-4-pentenoate via an unspecified oral route at 4000, 5000 and 6000 mg/kg-bw and were observed for up to 14 days following dosing. No data on number of deaths per dose group were provided. The conclusions of robust summary for an LD<sub>50</sub> for males does not make sense with the reported doses tested.

**LD<sub>50</sub> (males) > 5000 mg/kg-bw**

**LD<sub>50</sub> (females) = 5498 mg/kg-bw**

### *Acute Inhalation Toxicity*

Sprague-Dawley rats (5/sex) were exposed to vapors of methyl 3,3-dimethyl-4-pentenoate at 2000 ppm (approximately 11.6 mg/L) for 6 hours and observed for up to 14 days following exposure. No deaths occurred.

**LD<sub>50</sub> > ~ 11.6 mg/L** (only dose tested)

### *Acute Dermal Toxicity*

New Zealand White rabbits (5/dose, sex not specified) were administered methyl 3,3-dimethyl-4-pentenoate via the dermal route at 20 or 300 mg/kg-bw under occluded conditions for 24 hours. Animals were observed for up to 14 days following exposure. No deaths occurred. Slight erythema was observed in both groups during the first 48 hours, which resolved within 72 hours following exposure. Four days after dosing, redness reappeared on four animals in the 300 mg/kg-bw group that persisted to day 7. Additionally, one animal exhibited desquamation on day 7. At termination, slight redness persisted on two animals. The test substance was described as minimally irritating.

**LD<sub>50</sub> > 300 mg/kg-bw**

### *Repeated-Dose Toxicity*

The requirement for repeated-dose toxicity testing was waived because methyl 3,3-dimethyl-4-pentenoate is a closed system intermediate.

### *Reproductive Toxicity*

The requirement for reproductive toxicity testing was waived because methyl 3,3-dimethyl-4-pentenoate is a closed system intermediate.

### *Developmental Toxicity*

No data provided.

### *Genetic Toxicity – Gene Mutation*

#### *In vitro*

*Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 were exposed to methyl 3,3-dimethyl-4-pentenoate in DMSO at concentrations ranging from 100 to 10,000 g/plate in the presence and absence of metabolic activation. All samples were run in triplicate. No data on cytotoxicity or precipitation were provided. Positive and negative controls were tested concurrently, but data on control responses were not provided.

**Methyl 3,3-dimethyl-4-pentenoate was not mutagenic in this assay.**

### *Genetic Toxicity – Chromosomal Aberrations*

No data provided.

**Conclusion:** Acute oral toxicity of methyl 3,3-dimethyl-4-pentenoate to rats is low. Acute inhalation toxicity to rats and acute dermal toxicity to rabbits of methyl 3,3-dimethyl-4-pentenoate is low. The test substance was described as minimally irritating to rabbit skin. Requirements for repeated dose and reproductive toxicity testing were waived under the HPV Challenge Program because the sponsored substance is a closed-system intermediate. No data were provided for the developmental toxicity endpoint. Methyl 3,3-dimethyl-4-pentenoate did not induce gene mutations in bacteria *in vitro*. There are no data for the chromosomal aberrations endpoint.

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

#### **4 Hazards to the Environment**

##### ***Acute Toxicity to Fish***

EPA considered the submitted data inadequate due to the high volatility of methyl 3,3-dimethyl-4-pentenoate, the absence of analytical monitoring of test substance and the use of an open and static test system. A 96-hour LC<sub>50</sub> for fish, estimated by ECOSAR, was 9.0 mg/L.  
96-h LC<sub>50</sub> = 9.0 mg/L (estimated)

##### ***Acute Toxicity to Aquatic Invertebrates***

No measured data were available. A 48-hour EC<sub>50</sub> for Daphnia, estimated by ECOSAR, was 17.2 mg/L.  
48-h EC<sub>50</sub> = 17.2 mg/L (estimated)

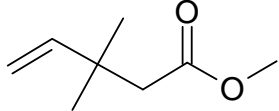
##### ***Toxicity to Aquatic Plants***

No measured data were available. A 96-hour EC<sub>50</sub> for green algae, estimated by ECOSAR, was 6.9 mg/L.  
96-h EC<sub>50</sub> = 6.9 mg/L (estimated)

**Conclusion:** For acute hazard of CASRN 137-26-8, the estimated 96-hour LC<sub>50</sub> to fish is 9.0 mg/L, the estimated 48-hour EC<sub>50</sub> to aquatic invertebrates is 17.2 mg/L, and the estimated 96-hour EC<sub>50</sub> to aquatic plants is 6.9 mg/L.

Data gaps for acute toxicity to fish, aquatic invertebrates, and aquatic plants were identified under the HPV Challenge Program.

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

Endpoints	SPONSORED CHEMICAL Methyl 3,3-dimethyl-4-pentenoate (63721-05-1)
Structure	
<b>Summary of Human Health Data</b>	
Acute Oral Toxicity LD <sub>50</sub> (mg/kg-bw)	> 5000
Acute Inhalation Toxicity LC <sub>50</sub> (mg/L)	> ~ 11.6
Acute Dermal Toxicity LD <sub>50</sub> (mg/kg-bw)	> 300
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	Requirement waived for closed system intermediate.
Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	Requirement waived for closed system intermediate.
Developmental Toxicity NOAEL/LOAL Oral (mg/kg-bw/day)	No Data
Genetic Toxicity – Gene Mutation <i>In vitro</i>	Negative
Genetic Toxicity – Chromosomal Aberrations	No Data
<b>Summary of Environmental Effects – Aquatic Toxicity Data</b>	
Fish 96-h LC <sub>50</sub> (mg/L)	9.0 (estimated)
Aquatic Invertebrates 48-h EC <sub>50</sub> (mg/L)	17.2 (estimated)
Aquatic Plants 72-h EC <sub>50</sub> (mg/L) (growth)	6.9 (estimated)