

201-14994A

HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM

TEST PLAN FOR

METHYL ACETOACETATE
CAS NO. 105-45-3

PREPARED BY:
COLOR PIGMENTS MANUFACTURERS ASSOCIATION, INC.
DIKETENE DERIVATIVES TASK FORCE

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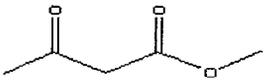
December 29, 2003

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OVERVIEW

The Diketene Derivatives Task Force (DDTF) of the Color Pigments Manufacturers Association (CPMA) and its member companies hereby submit for review and public comment the test plan for Methyl acetoacetate (MAA) under the U. S. Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program. It is the intent of the DDTF and its member companies to use, existing data, data from structurally similar compounds, and predictive computer models. These data will adequately fulfill the Screening Information Data Set (SIDS) for physical-chemical endpoints, environmental fate endpoints, ecotoxicity test data, and toxicological and human health effects. The DDTF believes that adequate data exists. There is no need to conduct of any additional animal tests.

I. <u>CAS No. 105-45-3</u> 	INFORMATION	OECD STUDY	OTHER	ESTIMATION	GLP	ACCEPTABLE	NEW TESTING REQUIRED
STUDY							
PHYSICAL – CHEMICAL DATA							
Melting Point	Y	-	Y			Y	N
Boiling Point	Y	-	Y			Y	N
Vapor Pressure	Y	-	Y			Y	N
Partition Coefficient	Y	-		Y		Y	N
Water Solubility	Y	-	Y			Y	N
ENVIRONMENTAL FATE ENDPOINTS							
Photodegradation	Y			Y		Y	N
Stability in Water	Y			Y		Y	N
Biodegradation	Y		Y			Y	N
Transport between Environmental Compartments (Fugacity)	Y			Y		Y	N
ECOTOXICITY DATA							
Acute Toxicity to Fish	Y	Y			Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	Y			Y	Y	N
Toxicity to Aquatic Plants	Y	Y			Y	Y	N
TOXICOLOGICAL DATA							
Acute Toxicity	Y	Y			Y	Y	N
Repeated Dose Toxicity	Y	Y			Y	Y	N
Genetic Toxicity – Mutation	Y	Y			Y	Y	N
Genetic Toxicity – Chromosomal Aberration	Y	Y			Y	Y	N
Combined Reproductive/Developmental Toxicity	Y	Y			Y	Y	N

TEST PLAN FOR METHYL ACETOACETATE

I. Background

Methyl acetoacetate (MAA) is a clear colorless liquid of very high purity. It is a chemically stable substance. The manufacture and transport of MAA is via a closed-systems process. Only a limited number of customers purchase this material and they too handle this material in closed systems. The primary use of this chemical intermediate is in the production of color pigments. There is no known direct or consumer uses of this chemical, where exposure to the general population may occur. To minimize employee exposure a closed-systems and good industrial hygiene practices are in place. Exposure to the environment is unlikely except under conditions of an accidental release during manufacture or transport.

II. Description of the Test Plan for Each SIDS Endpoint

A. Physical –Chemical Data

Melting point –	Values for this endpoint was obtained from National Institute of Standards and Technology, NIST Chemistry WebBook(1), reputable textbook and information from company product literature.
Boiling point -	Values for this endpoint was obtained from reputable textbook and information from company product literature.
Vapor pressure -	Values for this endpoint were obtained from reputable textbooks and information from company product literature.
Partition coefficient -	A value for this endpoint was obtained using KOWIN, a computer estimation program (2).
Water solubility -	Values for this endpoint were obtained from a reputable textbook and information from company product literature.
Conclusion:	All endpoints satisfied by, either actual data or accepted estimation models, and are of sufficient quality to conclude that no additional testing is required.

B. Environmental Fate Endpoints

Photodegradation -	A value for this endpoint was obtained using AOPWIN, a computer estimation program (2).
Stability in Water -	A value for this endpoint was obtained using EPIWIN, a computer estimation program (2).
Biodegradation -	This endpoint was satisfied with existing data that included evaluation of chemical, biological and total oxygen demand, as well as a multi-day biodegradation assessment using a Modified OECD TG-302B Zahn-Wellens test.
Transport between Environmental Compartments (Fugacity) –	Transport between environmental compartments was determined using EPIWIN:EQC, a Level III Fugacity computer modeling system(1).
Conclusion:	All endpoints are satisfied using data or estimation models that are of sufficient quality to conclude that no additional testing is necessary. The principle use of this substance is a chemical intermediate and because the

substance is handled in closed-systems, it is highly unlikely to enter into the environment.

C. Ecotoxicity Data

- Acute Toxicity to Fish - This endpoint was fulfilled by data from an OECD TG-203 study conducted under GLP assurances.
- Acute Toxicity to Aquatic Invertebrates – This endpoint was fulfilled by data from an OECD TG-202 study conducted under GLP assurances.
- Toxicity to Aquatic Plants - This endpoint was fulfilled by data from an OECD TG-201 study conducted under GLP assurances.
- Conclusion: All endpoints have been satisfied using data that are of sufficient quality to conclude that no additional testing is necessary. The principle use of this substance is a chemical intermediate and because the substance is handled in closed-systems, it is highly unlikely to enter into the environment.

C. Toxicity Data

- Acute Toxicity - This endpoint was fulfilled by data from two studies. The first study was conducted in accordance with OECD TG-401 study protocol under GLP assurances. The other study was conducted in accordance with the Federal Hazardous Substance Act regulations, FHSA, and is a well documented acute oral toxicity study.
- Repeated Dose Toxicity - This endpoint was fulfilled by data from two studies conducted under GLP assurances. The first was a 4 Week toxicity study with 2 week recovery similar to an OECD TG-407, while the second was part of the combined repeat dose and reproductive/developmental toxicity screening Test (OECD TG-422).
- Genetic Toxicity Mutation - This endpoint was fulfilled by two studies conducted under GLP assurances. One study followed OECD TG-471, while the other study was conducted in accordance with the Guidelines for Screening Mutagenicity Testing of Chemicals (Japan) and OECD TG-471 and 472.
- Genetic Toxicity Chromosomal Aberration - This endpoint was fulfilled with data conducted in accordance with Guidelines for Screening Mutagenicity Testing of Chemicals (Japan) and OECD TG- 473.
- Developmental Toxicity - This endpoint was fulfilled with data obtained from a combined repeat dose and reproductive/developmental toxicity screening Test (OECD TG-422).
- Reproductive Toxicity - This endpoint was filled with data obtained from a combined repeat dose and reproductive/developmental toxicity screening Test (OECD TG-422).
- Conclusion: All endpoints have been satisfied using data that are of sufficient quality to conclude that no additional testing is necessary. The principle use of this substance is as a chemical intermediate and exposure to the general population is not anticipated. The employee exposure is minimized through use of good industrial hygiene practices as well as through its manufacture and handling in closed-systems.

III. Evaluation of Data for Quality and Acceptability

The collected data were reviewed for quality and acceptability following the general US EPA guidance (3) and the systematic approach described by Klimisch *et al* (5). These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. This scoring system was only applied to ecotoxicity and human health endpoints per US EPA recommendations (3). The codification described by Klimisch *et al* (4) specifies four categories of reliability for describing data adequacy.

These are:

- (1) Reliable without Restriction: Includes studies or data complying with Good Laboratory Practice (GLP) procedures or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.
- (2) Reliable with Restrictions: Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.
- (3) Not Reliable: Includes studies or data in which there are interferences, or that non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or were insufficiently documented.
- (4) Not assignable: Includes studies or data in which insufficient detail to assign a rating, *e.g.*, listed in abstracts or secondary literature.

References:

1. *NIST Chemistry WebBook*, NIST Standard Reference Database 69 – March 2003 Release.
2. EPI™ Suite. Version 3.11. U.S. Environmental Protection Agency, Washington, DC 20460.
3. USEPA, 1999b, Determining the Adequacy of Existing of Existing Data. Guidance for the HPV Challenge Program. Draft dated 2/10/1999.
4. Klimisch, H.-J., Andreae, M., and Tillmann, U. (1997). A systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. *Regul. Toxicol. Pharmacol.* 25:1-5.