

HIGH PRODUCTION VOLUME (HPV) CHALLENGE PROGRAM

TEST PLAN
FOR
N,N-DIMETHYLACETOACETAMIDE
(CAS NO.: 2044-64-6)

201-14993A

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DIKETENE DERIVATIVES TASK FORCE

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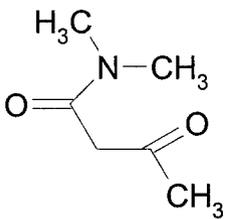
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OVERVIEW

The Diketene Derivatives Task Force (DDTF) of the Color Pigment Manufacturers Association (CPMA) and its member companies hereby submits for review and public comment the test plan for N,N-dimethylacetoacetamide (DMAA; CAS No.: 2044-64-6) under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Challenge Program. It is the intent of the DDTF and its member companies to use existing data, data to be generated, and predictive computer models to adequately fulfill the Screening Information Data Set (SIDS) for the various physicochemical, environmental fate, ecotoxicity test, and human health effects endpoints.

N,N-Dimethylacetoacetamide is a yellow liquid manufactured in closed-systems to a high degree of purity. At the present time, DMAA is utilized solely as a co-promoter in the production of unsaturated polyester resins used in coating materials and as an industrial intermediate in the synthesis of an insecticide.

TEST PLAN SUMMARY

CAS No. 2044-64-6	Information	OECD Study	Other	Estimation	GLP	Acceptable	New Testing Required
	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
STUDY	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL-CHEMICAL DATA							
Melting Point	Y	-	-	Y	N	Y	N
Boiling Point	Y	-	-	Y	N	Y	N
Vapor Pressure	Y	-	-	Y	N	Y	N
Partition Coefficient	Y	-	-	Y	N	Y	N
Water Solubility	Y	-	-	Y	N	Y	N
ENVIRONMENTAL FATE ENDPOINTS							
Photodegradation	Y	-	-	Y	N	Y	N
Stability in Water	N	-	-	-	-	-	Y
Biodegradation	Y	N	Y	-	Y	Y	N
Transport between Environmental Compartments (Fugacity)	Y	-	-	Y	N	Y	N
ECOTOXICITY							
Acute Toxicity to Fish	Y	Y	-	-	Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	Y	-	-	Y	Y	N
Toxicity to Aquatic Plants	N	-	-	-	-	-	Y
TOXICOLOGICAL DATA							
Acute Toxicity	Y	N	Y	-	N	Y	N
Repeated Dose Toxicity	N	-	-	-	-	-	Y
Genetic Toxicity – Mutation	N	-	-	-	-	-	Y
Genetic Toxicity – Chromosomal Aberrations	N	-	-	-	-	-	Y
Developmental Toxicity	N	-	-	-	-	-	Y
Toxicity to Reproduction	N	-	-	-	-	-	Y

TEST PLAN DESCRIPTION FOR EACH SIDS ENDPOINT

A. Physicochemical

- Melting point - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN (1).
- Boiling Point - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN.
- Vapor Pressure - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN.
- Partition Coefficient - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN.
- Water Solubility - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN.

Conclusion: All end points have been satisfied by utilizing data obtained from the various physical chemical data modeling programs within EPIWIN. The results of the various computer estimation models within EPIWIN have been noted by the Agency as acceptable in lieu of actual data or values identified from textbooks. No new testing is required.

B. Environmental Fate

- Photodegradation - A value for this endpoint was obtained using AOPWIN, a computer estimation-modeling program within EPIWIN (1).
- Stability in Water - No data are available. A new study is needed to complete this endpoint.
- Biodegradation - This endpoint was satisfied through the use of a study that is similar to an OECD-301C Modified MITI Test. The study was conducted under GLP assurances.
- Fugacity - A value for this endpoint was obtained using the EQC Level III partitioning computer estimation model within EPIWIN.

Conclusion: Except water stability all endpoints have been filled with data utilizing acceptable methodologies and of sufficient quality to fulfill these endpoints. The DDTF proposes to conduct a water hydrolysis study following OECD test guideline 111 to complete the missing endpoint.

C. Ecotoxicity Data

- Acute Toxicity to Fish - This endpoint is filled by data from a study that followed OECD TG-203 and was conducted under GLP assurances. The study quality was deemed to be “reliable without restrictions”.
- Acute Toxicity to Aquatic Invertebrates - This endpoint is filled by data from a study that followed OECD TG-202 and was conducted under GLP assurances. The study quality was deemed to be “reliable without restrictions”.
- Toxicity to Aquatic Plants - No data are available. A new study is needed to complete this endpoint.

Conclusion: All endpoints, but algal toxicity, have been satisfied with data from studies that were conducted using established OECD guidelines and GLP assurances. In total, these currently available studies are of sufficient quality to conclude that no additional testing is needed for those endpoints. The DDTF proposes to conduct an algal toxicity study following OECD test guideline 201 to complete the missing endpoint.

D. Toxicological Data

Acute Toxicity - This endpoint is filled by oral exposure data from a study completed in 1962 and did not follow an established protocol. Nevertheless, there was sufficient documentation to deem the quality of the study as “reliable with restrictions”. This endpoint is filled by data from two studies utilizing two different species with similar results.

Repeat Dose Toxicity - No data are available. A new study is needed to complete this endpoint.

Genetic Toxicity
Mutation - No data are available. A new study is needed to complete this endpoint.

Aberration - No data are available. A new study is needed to complete this endpoint.

Developmental
Toxicity - No data are available. A new study is needed to complete this endpoint.

Reproductive
Toxicity - No data are available. A new study is needed to complete this endpoint.

Conclusion: Currently only data assessing acute toxicity are available. While these data are somewhat old (1962, pre-GLP) they are nonetheless still believed reliable enough to fulfill this endpoint. All other missing endpoints will be completed through the conduct of new studies. To assess genotoxicity the DDTF proposes to conduct mutation and aberration studies following OECD test guidelines 471 and 473, respectively. To fulfill the missing data needs for the assessment of toxicity following repeated exposure and to understand its potential to induce developmental and reproductive toxicity the task forces is proposing to conduct a study following OECD test guideline 422.

SIDS DATA SUMMARY

Data assessing the various physicochemical properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility) for DMAA were obtained from estimations using the models within EPIWIN. These data indicate that DMAA is a liquid at room temperature with a low vapor pressure. It has a relatively low estimated octanol to water partition coefficient ($K_{ow} = -0.58$) and accordingly is very soluble in water (288 g/L).

The assessment of the environmental fate endpoints photodegradation and biodegradation indicate the material is capable of being degraded by photochemical reactions but appears to not be readily degraded using biological processes. Fugacity predictions indicate a very limited amount of partitioning into the air, with 99% estimated to be distributed into the soil and water in roughly equal amounts. Water stability data still need to be generated.

The potential toxicity of DMAA to fish and Daphnia indicate the material is of very low toxicity to these organisms with LC_{50} and EC_{50} concentrations close to 1,000 mg/L. Studies assessing toxicity to algae are being proposed.

The potential to induce toxicity in mammalian species following acute oral exposure is low as the LD_{50} value in both rats and mice was $>3,200$ mg/kg. Data from the other mammalian toxicity endpoints are still needed.

In conclusion, data that are currently available suggest this chemical likely constitutes a low risk to workers and the environment. Due to its only current known use as an industrial intermediate and no known direct applications

within consumer products, exposure to the general public is not anticipated and exposure to workers is managed through prudent industrial hygiene practices.

EVALUATION OF DATA FOR QUALITY AND ACCEPTABILITY

The collected data were reviewed for quality and acceptability following the general US EPA guidance (2) and the systematic approach described by Klimisch *et al.* (3). 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 ecotoxicology and human health endpoint studies per EPA recommendation (4). The codification described by Klimisch 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 use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.
4. **Not Assignable:** Includes studies or data in which insufficient detail is reported to assign a rating, e.g., listed in abstracts or secondary literature.

REFERENCES

1. EPIWIN, Version 3.10, Syracuse Research Corporation, Syracuse, New York.
2. USEPA (1998). 3.4 Guidance for Meeting the SIDS Requirements (The SIDS Guide). Guidance for the HPV Challenge Program. Dated 11/2/98.
3. 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.
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