Petitioner AMVAC Exhibit 45

STUDY TITLE

Tetrachlorophthalic Acid (TPA): Selected Ecological Study Waiver Request

TEST GUIDELINE:

None

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STUDY COMPLETION DATE:

December 13, 2020

PERFORMING COMPANY:

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AMVAC Report 100-REV-049

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GOOD LABORATORY PRACTICE COMPLIANCE

This study does not fall under EPA FIFRA Good Laboratory Practice (GLP) Standards set forth in Title 40, Part 160 of the Code of Federal Regulations.

Submitter:

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EXECUTIVE SUMMARY

Tetrachlorophthalic acid (TPA) is highly polar with little binding propensity or partitioning capability for absorption or absorption into or onto biological matrices. These physicochemical properties may in part explain the relatively innocuous effect of this chemical in aquatic and terrestrial environments.

Mammalian studies conducted with TPA when compared with its parent diester dacthal (DCPA) demonstrate a toxicity that is significantly less potent (USEPA, 2008). Therefore, the deesterification of DCPA can be considered a very effective detoxifying mechanism.

Exposure to the sensitive freshwater aquatic invertebrate *Daphnia magna* for a 48-hour period yielded no effects on mobility at the highest tested dose of 100 mg/L (Manson, 2003a). Testing on the higher-level aquatic species, *Oncorhynchus mykiss* not surprisingly yielded these same results (Manson, 2003b). As a diacid, TPA did not present the same phytotoxicity effects as DCPA. Its effect on the growth of a unicellular green alga, *Selenastrum capricornutum* supports an EC50 of greater than 100 mg/L (Manson, 2003c). The phytotoxicity effects of TPA on terrestrial plants through seed germination inhibition also demonstrates the higher potency of DCPA compared with TPA.

TABLE OF CONTENTS

I. INTRODUCTION

Background

EPA issued a Data Call-In for DCPA on January 31, 2013. At that time, AMVAC commenced with the conduct of certain required studies and submitted rationale for waiver requests for other studies, including the ecological fate study requirements for TPA. AMVAC's initial response to EPA occurred on April 13, 2013. Included in that submission was a request to waive the requirement for a list of TPA ecological studies. Specifically, AMVAC has requested waivers for the following outstanding studies: Oyster Acute Toxicity (shell deposition; Guideline 850.1025), Mysid Acute Toxicity (850.1035), the Fish Acute Toxicity Test on Freshwater and Marine species (850.1075), Mysid Chronic Toxicity Test (850.1350), Fish Early Life-Stage Toxicity Test (850.1400), Terrestrial Plant Toxicity, Tier I (Seedling Emergence; 850.4100), Aquatic Vascular Plant Toxicity Test using *Lemna spp.* (850.4400), and Aquatic Non-Vascular Plant Toxicity Test using Algal species (850.4500).

On March 21, 2014, EPA responded to our waiver request, but that memorandum was not received by AMVAC until March 17, 2017. The Agency's rationale for the denial was based on a brief description of the deficiencies for studies that had been previously submitted for the purpose of fulfilling these requirements. That response is provided in below:

> EFED indicated in the problem formulation if a limited testing strategy was proposed it would be considered *in lieu* of a comprehensive data submission. EPA would still consider a more limited testing strategy if proposed by the registrant. However, deferring all toxicity testing of the degradate TPA until DCPA studies are completed, is not an acceptable alternative strategy; therefore, EFED recommends that PRD ***denies request to defer the data collection of TPA until DCPA studies are completed with the intention of using DCPA toxicity data in lieu of TPA toxicity data. Toxicity data is needed for TPA, therefore one possible solution is conducting a limited set of toxicity tests initially for TPA (for example, an acute and chronic toxicity study in daphnids); and depending on the results of these initial studies, a full suite of studies may or may not be subsequently required.***

In response, on February 22, 2018, AMVAC provided additional information that is in keeping with the Agency's. Therefore, the purpose of this document is to review the ecotoxicological data that AMVAC has provided to the Agency and compare derived study endpoints with that developed in comparable studies with the parent compound DCPA. AMVAC believes that the great distinction in toxicological effects between the parent compound and its degradates provides EPA with the information it is seeking and demonstrates that TPA is not of risk to terrestrial and aquatic species and as such the focus of ecological risk assessments should focus solely on DCPA.

II. Comparison of DCPA and TPA Ecological Studies

A comparative table of DCPA and TPA endpoints is provided below, followed by a brief summary of the underlying data. Based on AMVAC's technical assessment, TPA demonstrates a lower toxicity than the parent compound DCPA and would meet the Agency's criteria for adopting this limited data set for fulfilling the ecotoxicological study requirements for TPA.

Category	Species	Study	TPA Endpoint	DCPA Endpoint	Factor TPA/DCPA
Aquatic Invertebrate	*Daphnia magna*	NOEC Acute 48 hrs	>0.55 mg/L	>0.55 mg/L	1.0
Aquatic Invertebrate	*Daphnia magna*	NOEC Chronic Reproductive 21 days	0.297 mg/L	0.031 mg/L	9.6
Freshwater Fish	*Oncorhynchus mykiss*	NOEC Acute 96 hrs	12.5 mg/L	9.33 mg/L	1.3
Unicellular Alga	*Selenastrum capricornutum*	Means Specific Growth Rate 96 hrs	46.1 mg/L	11.2 mg/L	4.1
Seedling Emergence	*Beta vulgaris*	NOER	1.25 lb/A	0.278 lb/A	4.5
Seedling Emergence	*Lolium perenne*	NOER	10 lb/A	0.278 lb/A	36
Seedling Emergence	*Glycine max*	NOER	1.25 lb/A	7.5 lb/A	0.17

1. Aquatic Invertebrate Testing of TPA and DCPA

Acute Studies

An acute study with TPA was conducted on the test species *Daphnia magna* at the mean measured concentration 104 mg/L with control, using a static test system (Manson, 2003a). Effect concentrations after 48 hours yielded a NOEC of 0.55 mg/L, the highest concentration tested.

An acute study with DCPA was conducted on the test species *Daphnia magna* at the mean measured concentrations of 0.032, 0.066, 0.13, 0.27, and 0.55 mg/L with control, using a static renewal test system (Shaw, 2013a). Effect concentrations after 48 hours yielded a NOEC of 0.55 mg/L, the highest concentration tested.

Chronic Studies

A chronic study with TPA was conducted on the test species *Daphnia magna* at the mean measured concentrations of 0.296, 0.596, 1.23, 2.53, and 4.96 mg/L with control, using a flow through test system (Gourdie, 2019b). Effect concentrations after 21 days yielded a NOEC of 2.53 mg/L, the highest concentration tested. Reproductive effects on length and 1st brood production yielded NOECs of 4.96 mg/L, the highest rate tested.

A chronic study with DCPA was conducted on the test species *Daphnia magna* at the mean measured concentrations of 0.0272, 0.0842, 0.246, 0.679, and 1.73 mg/L with control, using a semi-static test system design (Manson, 2004a). Effect concentrations after 21 days yielded a NOEC of 0.246 mg/L, the highest concentration tested. Reproductive effects on length and 1st brood production yielded NOECs of 0.031 mg/L. This study yielded some measurements that did not demonstrate a consistent trend that questioned some of the findings; therefore, the work was repeated to provide a better comparison.

The second chronic study with DCPA was conducted on the test species *Daphnia magna* at the measured concentrations of 0.031, 0.065, 0.14, 0.27, and 0.54 mg/L with control, using a static renewal test system (Shaw, 2013b). Effect concentrations after 21 days yielded a NOEC of 0.54 mg/L, the highest concentration tested. Reproductive effects on length and 1st brood production yielded NOECs of 0.297 mg/L.

<u>2. Fish Testing of TPA and DCPA</u>

<u>Acute</u>

An acute study with TPA was conducted on the test species *Oncorhynchus mykiss* at the mean measured concentrations of 6.72, 12.7, 23.8, 46.4, and 93.4 mg/L with control, using a static test system (Manson, 2003b). Effect concentrations after 96 hours yielded an LC50 >93.4 mg/L and a reported NOEC of 12.5 mg/L.

An acute study with DCPA formulated product was conducted on the test species *Oncorhynchus mykiss* at the mean measured concentration of solubilized active ingredient of 4.66, 9.33, 18.7, 37.3, and 74.6 mg/L with control, using a static test system (Manson, 2004b). Effect concentrations after 96 hours yielded an LC50 >74.6 mg/L and a reported NOEC of 9.33 mg/L.

<u>3. Algal Testing of TPA and DCPA</u>

An alga study with TPA was conducted on the unicellular green algal test species *Selenastrum capricornutum* at the mean measured concentrations of 8.9, 19.7, 46.1, and 103 mg/L with control (Manson, 2003c). Effect concentrations yielded a NOEC for mean area under the growth curve and means specific growth rate after 72 and 96 hours of 19.7 and <3.99mg/L and 103 and 46.1 mg/L.

An alga study with DCPA formulated product was conducted on the unicellular green algal test species *Selenastrum capricornutum* at the geometric mean measured concentration of solubilized active ingredient of 2.56, 6.42, 11.2, 31.2, and 60.7 mg/L with control (Manson, 2004c). Effect concentrations yielded a NOEC for mean area under the growth curve and means specific growth rate after 72 and 96 hours of <2.56 and <2.56 mg/L and 11.2 and 11.2 mg/L.

4. Terrestrial Seedling Emergence Testing of TPA and DCPA

Testing was conducted with TPA on the monocots: *Allium cepa* (Onion), *Lolium perenne* (Ryegrass), *Triticum aestivum* (Wheat), *Zea mays* (Corn) and the dicots: *Beta vulgaris* (Sugarbeet), *Brassica napus* (Oilseed Rape), *Brassica oleracea* (Cabbage), *Glycine max* (Soybean), *Helianthus annuus* (Sunflower), *Lycopersicon esculentum* (Tomato) at the nominal test levels for all species: 0.313, 0.625, 1.25, 2.5, 5.0 and 10 lbs. a.i./A (McKelvey, 2019). NOERs were established for onion, ryegrass, wheat, corn, oilseed rape, cabbage, and sunflower at the highest rate of 10 lbs. a.i./A. For tomato and lettuce, the NOER was 5.0 lbs. a.i./A based on shoot height. For sugar beet, the NOER was 1.25 lbs. a.i./A based on emergence. For soybean, the NOER was 1.25 lbs. a.i./A based on shoot height.

Testing was conducted with Dacthal Flowable herbicide product (0.75 lbs. ai/pint) on the monocots: *Allium cepa* (Onion), *Lolium perenne* (Ryegrass), *Triticum aestivum* (Wheat), *Zea mays* (Corn) and the dicots: *Beta vulgaris* (Sugarbeet), *Brassica na pus* (Oilseed Rape), *Brassica oleracea* (Cabbage), *Glycine max* (Soybean), *Helianthus annuus* (Sunflower), *Lycopersicon esculentum* (Tomato) at the nominal test levels for lettuce ranged from 0.00345 – 0.825 lbs. a.i./A, for onion ranged from 0.0375 – 7.5 lbs. a.i./A, and for remaining crops ranged from 0.09 – 7.5 lbs. a.i./A (Sidermann, 2014). NOERs were established for oilseed rape, cabbage, and soybeans at the highest rate of 7.5 lbs. a.i./A. For onion, corn, and wheat, the NOER was 2.48 lbs. a.i./A based on emergence for onion, and height/dry weight for corn and wheat. For tomato and lettuce, the NOER was 0.825 lbs. a.i./A, based on emergence/height/weight for tomatoes and height/weight for lettuce. For ryegrass and sugar beet, the NOER was 0.278 lbs. a.i./A based on emergence/height/weight for ryegrass and height/weight for sugar beet.

III. CONCLUSIONS

Based on AMVAC's technical assessment, TPA demonstrates a lower toxicity than the parent compound DCPA and would meet the Agency's criteria for adopting the currently available TPA data set for fulfilling the ecotoxicological study requirements for this chemical.

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