

Joint Exhibit 83



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

April 19, 2022

PC Code: 078701

DP Barcode: 437397 and 461052

MEMORANDUM

SUBJECT: Response to Data Waiver Requests for Ecological Effects Related Data for Dimethyl 2,3,5,6-Tetrachloroterephthalate (DCPA) and Its Degradate Tetrachlorophthalic Acid (TPA)

FROM: Christina Wendel, Biologist
Environmental Risk Branch 2
Environmental Fate and Effects Division

Christina M. Wendel

Digitally signed by
CHRISTINA WENDEL
Date: 2022.04.19 14:42:21
-04'00'

THROUGH: Michael Wagman, Senior Scientist
Karen Milians, Ph.D., Risk Assessment Process Leader
Rochelle Bohaty, Ph.D., Acting Branch Chief
Environmental Risk Branch 2
Environmental Fate and Effects Division

MICHAEL
WAGMAN

Digitally signed by MICHAEL
WAGMAN
Date: 2022.04.19 16:28:24 -04'00'

Rochelle
Bohaty

Digitally signed by
Rochelle Bohaty
Date: 2022.04.19
20:49:42 -04'00'

Karen Milians
Digitally signed
by Karen Milians
Date: 2022.04.19
16:31:56 -04'00'

TO: James Douglass, Chemical Review Manager
Jill Bloom, Team Leader
Cathryn Britton, Branch Chief
Risk Management and Implementation Branch 5
Pesticide Re-evaluation Division

The Environmental Fate and Effects Division (EFED) reviewed the following waiver requests from the registrant, AMVAC. The waiver requests pertain to 1) ecological toxicity testing with Tetrachlorophthalic Acid (TPA) (degradate of DCPA) for multiple aquatic animal and plant and terrestrial plant tests, and 2) for DCPA, chronic sediment toxicity testing on the estuarine/marine amphipod *Leptocheirus plumulosus*. All studies were required under the DCPA Generic Data Call-In (GDCI) for Registration Review (GDCI-078701-1140, USEPA, 2013).

- MRID 51398103. Freedlander, D. (2020) Tetrachlorophthalic Acid (TPA): Selected Ecological Study Waiver Request. Project Number: 100-REV-049. Unpublished study prepared by AMVAC Chemical Corporation. 11p.
- MRID 49865803. Freedlander, D. (2016) Proposed Waiver for Dacthal (DCPA) Chronic Study Testing on *Leptocheirus plumulosus*. Project Number: 100/AQU/028, 246A/115, 246A/116A. Unpublished study prepared by AMVAC Chemical Corporation. 10p.

The arguments set forth in the waiver requests are summarized below, followed by a response from EFED. Based on this response, EFED **does** recommend granting the waiver requests for additional ecological toxicity testing with TPA for the:

- Oyster Acute Toxicity (shell deposition; Guideline 850.1025),
- Mysid Acute Toxicity (Guideline 850.1035),
- Fish Acute Toxicity Tests on Freshwater and Estuarine/Marine species (Guideline 850.1075),
- Aquatic Vascular Plant Toxicity Test using *Lemna* spp. (Guideline 850.4400)
- Aquatic Non-vascular Plant Toxicity Data with TPA for all species except the marine diatom (Guideline 850.4500; see below), and
- Terrestrial plant toxicity vegetative vigor test with TPA (Guideline 850.4150).

Consistent with EFED's response to previous waiver requests (USEPA, 2014; USEPA, 2016 DP413324+; D432677), EFED maintains that chronic toxicity data with both TPA and DCPA, in addition to aquatic non-vascular plant toxicity data with TPA (marine diatom only), is still necessary for developing a complete risk assessment.

Accordingly, EFED **still does not** recommend granting the waiver requests for ecological toxicity testing with TPA for the:

- Mysid Chronic Toxicity Test (Guideline 850.1350),
- Fish Early Life-Stage Toxicity Test (Guideline 850.1400), for both Freshwater and Estuarine/Marine Species,
- Aquatic Non-Vascular Plant Toxicity Test using the marine diatom (Guideline 850.4500).

Additionally, EFED **still does not** recommend waiving testing with DCPA for:

- Chronic sediment toxicity testing with an estuarine/marine amphipod (Non-Guideline/ EPA Test Method 600/R-01/020; USEPA, 2001)¹.

Further exploration of the rationale for granting or rejecting these waivers is provided below in Sections 1 (TPA data) and 2 (DCPA data) below.

Additionally, the Fish Early Life-Stage (ELS) Toxicity Test (Guideline 850.1400) is still outstanding for DCPA for both freshwater and estuarine/marine fish. The registrant indicated that work would be initiated sometime in 2021 for the outstanding DCPA ELS studies, with an indication that the freshwater test species was bluegill sunfish and the estuarine/marine test species was sheepshead minnow; however, no time frame has been provided to the Agency regarding the submission of these two outstanding studies.

¹ Per Agency recommendations for chronic sediment testing, the submission of a protocol for this test is needed prior to test initiation.

Waiver Request Summary:

Background:

EPA issued a Data Call-In for DCPA on January 31, 2013. Subsequently, AMVAC initiated certain required studies and submitted waiver requests, including rationales, for several required studies. AMVAC's initial response to the DCI was dated April 13, 2013 (MRID's 49115401; Freedlander, 2013a; 49115402; Beavers, 2013; and 49115404; Freedlander, 2013b). Included in that response was a request to waive requirements for the following outstanding studies for TPA:

- Oyster Acute Toxicity (shell deposition; Guideline 850.1025),
- Mysid Acute Toxicity (Guideline 850.1035),
- Fish Acute Toxicity Test on Freshwater and Estuarine/Marine species (Guideline 850.1075),
- Mysid Chronic Toxicity Test (Guideline 850.1350),
- Fish Early Life-Stage Toxicity Test (Guideline 850.1400), Freshwater and Estuarine/ Marine Species
- Terrestrial Plant Toxicity, Tier I (Seedling Emergence; Guideline 850.4100),
- Terrestrial Plant Toxicity, Tier I (Vegetative Vigor; Guideline 850.4150),
- Aquatic Vascular Plant Toxicity Test using *Lemna spp.* (Guideline 850.4400), and
- Aquatic Non-Vascular Plant Toxicity Test using Algal species; (Guideline 850.4500)

Additionally, the following studies were addressed in AMVAC's 2013 waiver request (MRID 49115401) and are still outstanding for DCPA:

- Fish Early Life-Stage Toxicity Test (Guideline 850.1400), Freshwater and Estuarine/ Marine Species
- Chronic Sediment Toxicity Testing (Non-Guideline/ EPA Test Method 600/R-01/020; USEPA, 2001) with DCPA on the Estuarine/Marine Amphipod *Leptocheirus plumulosus*

On March 21, 2014, EPA completed its review of AMVAC's 2013 waiver request (DP413324+; USEPA, 2014). Based on deficiencies in the studies that had been previously submitted for the purpose of fulfilling these requirements, the Agency denied the waiver requests. The response from the Agency stated:

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.

Subsequently, AMVAC submitted a subset of the required data to the Agency in 2020 (MRID 51398103; Freedlander, 2020), as well as a discussion outlining why the remaining required data were not needed for TPA. Specifically, the studies submitted in 2020 were:

- Chronic (Reproduction) Study with Freshwater invertebrates (*Daphnia magna*) (850.1300); TPA (MRID 51235101) and DCPA (MRID 51398104).
- Terrestrial Plant Toxicity, Tier I (Seedling Emergence; 850.4100); TPA (MRID 51235102).
- Fish Acute Toxicity Test on Freshwater species (*Oncorhynchus mykiss*) (850.1075); Dacthal W-75 – a DCPA formulated product (MRID 51398105).
- Aquatic Non-Vascular Plant Toxicity Test using Green Algae; (850.4500); TPA and Dacthal W-75 – a DCPA formulated product (MRID 51499401 and 51499402).

As characterized by AMVAC MRID 51398103 includes AMVAC’s review of previously submitted DCPA ecotoxicological data as well as a limited set of TPA ecotoxicological data from studies conducted under the DCI. AMVAC compared their estimated-endpoints using TPA to their estimated-endpoints from comparable studies conducted with the parent compound DCPA. AMVAC asserts “that the great distinction in toxicological effects between the parent compound and its degradates [(e.g., TPA)] provides EPA with the information it is seeking and demonstrates that TPA is not of risk to terrestrial and[/or] aquatic species and as such the focus of ecological risk assessments should focus solely on DCPA.” AMVAC asserted that TPA demonstrates a lower toxicity than the parent compound DCPA across a number of species and meets the Agency’s criteria for adopting the limited TPA data set represented by previously conducted studies. AMVAC asserted that the already-submitted TPA data are adequate for fulfilling the ecotoxicological study requirements without submission of new data. On that basis, in its 2020 waiver request (MRID 51398103), AMVAC requested that the additional studies with TPA be waived. See **Attachment 1** for a summary of the submitted information and the data still considered outstanding.

Additional discussion of AMVAC’s rationale for requesting the waiver for DCPA study on an estuarine/marine amphipod is included in Section 2 below.

EFED Response to Waiver Requests for TPA:

Section 1 below discusses EFED’s conclusions for the waiver requests for studies with the DCPA degradate TPA.

1. Overall EFED Conclusions for Waivers for Ecological Toxicity Testing with TPA (degradate of DCPA)

Since the initial response to a waiver request for these studies was completed in 2014 (DP413324+; USEPA, 2014), EFED has reviewed the additional information provided in the document submitted by AMVAC (MRID 51398103; Freedlander, 2020) and reviewed the TPA and DCPA Technical-Grade Active Ingredient (TGAI) product and formulated product toxicity studies cited below in **References**, on pages 20-23. See **Attachment 1** for a summary of the submitted information and the data still considered outstanding.

Table 1 compares toxicity endpoints from studies in the same test species exposed to DCPA and TPA. Based on these comparisons and toxicity data from other species, TPA generally appears to be at most equally toxic, and generally less toxic than DCPA. However, as noted in EFED’s review of the waiver requests for TPA fate data (USEPA, 2022; D461053), available empirical data indicate that TPA is stable in the environment, and the Agency is assuming stability where fate data are missing for TPA. Furthermore, based on this documented and assumed stability, concentrations of TPA in water are predicted to increase over time with repeated application of DCPA and could potentially exceed estimated concentrations of DCPA. On this basis, EFED reconfirms that TPA is still considered an ecological residue of concern, along with the parent DCPA.

The limited available data indicate that TPA is less toxic than DCPA and that TPA may be present in the environment in higher concentrations than DCPA. While EFED could use DCPA endpoints (generally at the limit of solubility) to represent the toxicity of TPA itself, doing so could overestimate the potential hazard. The stability of TPA (and assumptions about stability of TPA due to a lack of data) suggest the potential for this degradate to accumulate to high concentrations in water bodies although not likely at concentrations that would result in acute risk (see Appendix A of USEPA, 2022). Because of these two potentially offsetting factors, TPA toxicity data are still needed in some cases (especially chronic toxicity data) to improve our understanding of the potential risks to aquatic organisms and reduce the uncertainty in the risk assessment.

Table 1. Comparison of DCPA and TPA Ecological Studies which used the Same Test Species

Category	Species	Endpoint	TPA Endpoint* (µg a.i./L or lb ai/A)	DCPA Endpoint (µg a.i./L or lb ai/A)	Factor TPA/DCPA
Aquatic Invertebrate	<i>Daphnia magna</i>	Acute 48 hr EC50	>112,476 MRID 49307519	>550 ^a MRID 49307514	N/A
Aquatic Invertebrate	<i>D. magna</i>	Acute 48 hr NOAEC	≥112,476 MRID 49307519	≥550 ^a MRID 49307514	N/A
Aquatic Invertebrate	<i>D. magna</i>	Chronic 21 day NOAEC	2,763 ^a MRID 51235101	270 ^a MRID 49307510	10.2
Aquatic Invertebrate	<i>D. magna</i>	Chronic 21 day LOAEC	5,416 ^a MRID 51235101	540 ^a MRID 49307510	10.0
Freshwater Fish	<i>Oncorhynchus mykiss</i>	Acute 96 hr LC50	>101,993 ^b MRID 49307518	>500 ^b MRID 41054826	N/A
Freshwater Fish	<i>O. mykiss</i>	Acute 96 hr NOAEC	25,900 ^b MRID 49307518	>500 ^b MRID 41054826	<14.7
Seedling Emergence	<i>Beta vulgaris</i>	IC25	9.77 ^c MRID 51235102	0.548 ^c MRID 49307513	17.8
Seedling Emergence	<i>Beta vulgaris</i>	NOAEC	0.34 ^c MRID 51235102	0.27 ^c MRID 49307513	1.26
Seedling Emergence	<i>Lolium perenne</i>	IC25	>9.94 ^c MRID 51235102	0.277 ^c MRID 49307513	>35.9
Seedling Emergence	<i>Lolium perenne</i>	NOAEC	9.94 ^c MRID 51235102	0.23 ^c MRID 49307513	43.2
Seedling Emergence	<i>Lycopersicon esculentum</i>	IC25	8.47 ^c MRID 51235102	1.07 ^c MRID 49307513	7.91

Category	Species	Endpoint	TPA Endpoint* (µg a.i./L or lb ai/A)	DCPA Endpoint (µg a.i./L or lb ai/A)	Factor TPA/DCPA
Seedling Emergence	<i>Lycopersicon esculentum</i>	NOAEC	2.4 ^c MRID 51235102	0.23 ^c MRID 49307513	10.4
Seedling Emergence	<i>Triticum aestivum</i>	IC25	>9.94 ^c MRID 51235102	5.64 ^c MRID 49307513	>1.76
Seedling Emergence	<i>Triticum aestivum</i>	NOAEC	9.94 ^c MRID 51235102	2.3 ^c MRID 49307513	1.04

* Expressed in terms of DCPA based on the difference between the molecular weights of DCPA and TPA, in which the TPA toxicity endpoint (e.g., LD50 value) is multiplied by the ratio of the molecular weight of DCPA to the molecular weight TPA (331.97 g/mol ÷ 303.91 g/mol = 1.092).

^a For more details see Section 1.1 for acute aquatic invertebrates and Section 1.2 for chronic aquatic invertebrates.

^b For more details see Section 1.3 for acute fish.

^c For more details see Section 1.6 for terrestrial Plants.

1.1 Oyster Acute Toxicity (shell deposition; Guideline 850.1025), and Mysid Acute Toxicity (Guideline 850.1035)

To evaluate whether additional acute estuarine/marine toxicity data is needed, all the available acute aquatic toxicity data for both DCPA and TPA were compared and are summarized below in **Table 2**.

Some of the submitted DCPA toxicity studies had technical deficiencies, resulting in reduced confidence in the endpoints selected for aquatic invertebrates. Overall, however, these studies support the conclusion that DCPA is not acutely toxic to aquatic invertebrates at least up to the limit of solubility limit (0.5 mg/L). TPA is classified as practically non-toxic to freshwater invertebrates on an acute exposure basis. As stated above, although there is potential for this degradate (TPA) to accumulate to high concentrations in water bodies it will not likely be at concentrations that would result in acute risk. As a result, EFED considers it unlikely that TPA exposures would result in acute risks to aquatic invertebrates. Therefore, EFED *does* recommend granting the waiver request for ecological toxicity testing with TPA for both the Oyster Acute Toxicity (shell deposition; Guideline 850.1025), and the Mysid Acute Toxicity (Guideline 850.1035) tests.

Table 2. Available Acute DCPA and TPA Aquatic Invertebrate Toxicity Data

Test Species	Endpoint (µg a.i./L)	MRID/ Classification	Comments
DCPA			
Waterflea (<i>Daphnia magna</i>) (TGAI)	48-h LC ₅₀ >550 ^a Observational NOAEC = 550	49307514 ^N Acceptable	No effects (mortality/ immobility or sublethal) observed at the solubility limit. Observational NOAEC determined by visual interpretation of the data.
Waterflea (<i>D. magna</i>) (TGAI)	48-h LC ₅₀ > 500 ^b	40098001 Supplemental	No effects at observed at the solubility limit.
Midge (<i>Chironomus plumosus</i>) (TGAI)	48-hour EC ₅₀ >500 ^b	40098001 Supplemental	No effects observed at the solubility limit.

Test Species	Endpoint ($\mu\text{g a.i./L}$)	MRID/ Classification	Comments
Amphipod (<i>Gammarus pseudolimnaeus</i>) (TGAI)	96-hour $\text{EC}_{50} > 500^{\text{b}}$	40098001 Supplemental	No effects observed at the solubility limit.
Mysid (<i>Americamysis bahia</i>) (TGAI)	96-h $\text{LC}_{50} > 396^{\text{a}}$ Observational $\text{NOAEC} = 24.9$	49307505 ^N Supplemental	No effects (mortality) $\geq 10\%$ were observed at the solubility limit. No sublethal effects observed in any treatment or control. Observational NOAEC determined by visual interpretation of the mortality data. May be used for risk characterization only.
Eastern oyster (<i>Crassostrea virginica</i>) (TGAI)	96-h $\text{LC}_{50} > 410^{\text{a}}$	49500701 ^N Supplemental	No effects on shell growth were greater than 50% at the solubility limit (maximum % effect was 27%). Growth results are highly variable (using the standard deviations, the confidence intervals for the mean individual measurements for all test concentrations would overlap), but only visual comparisons could be made due to the lack of replication. May be used for risk characterization only.
Eastern oyster (<i>C. virginica</i>) (TGAI)	96-h $\text{EC}_{50} > 500^{\text{e}}$	40228401 Supplemental	No effects $\geq 20\%$ observed at the solubility limit
Brown shrimp (<i>Penaeus aztecus</i>) (TGAI)	96-h $\text{LC}_{50} > 500^{\text{e}}$	40228401 Supplemental	No effects $\geq 20\%$ observed at the solubility limit
TPA			
Water flea (<i>D. magna</i>) (TGAI)	48-hr $\text{EC}_{50} > 103,000^{\text{d}}$ ($> 112,476$) ² Observational $\text{NOAEC} = 103,000^{\text{f}}$ ($112,476$) ^e	49307519 ^N Acceptable	No effects (mortality/ immobility or sublethal). Observational NOAEC determined by visual interpretation of the data.

a.i. = active ingredient

^N Studies submitted since the Problem Formulation was completed are designated with an N after the MRID number. "Greater than" (>) values represent non-definitive endpoints where no effects were observed even at the highest dose tested, or effects did not reach 50% at the highest concentration tested (USEPA, 2011).

^a The highest nominal test concentration was at or above the solubility limit of DCPA (0.5 mg/L).

^b Test solutions were not reported to be centrifuged or filtered to remove any potential precipitates, so the actual bioavailable concentration may be less than the reported nominal concentration which introduces uncertainty, but still indicates little to no effects up to solubility.

^c Could not determine actual exposure concentration, concentrations were not measured, however the concentrations are likely at least the solubility limit (0.5 mg/L).

^d Expressed in terms of Tetrachloroterephthalic Acid (TPA)

^e Expressed in terms of DCPA based on the difference between the molecular weights of DCPA and TPA, in which the TPA toxicity endpoint (e.g., LD50 value) is multiplied by the ratio of the molecular weight of DCPA to the molecular weight of TPA ($331.97 \text{ g/mol} \div 303.91 \text{ g/mol} = 1.092$).

1.2 Mysid Chronic Toxicity (Guideline 850.1350)

To evaluate whether additional chronic estuarine/marine toxicity data is needed, all the available chronic aquatic toxicity data for both DCPA and TPA were compared and are summarized below in **Table 3**. Some DCPA toxicity studies had technical deficiencies which resulted in reduced confidence in the study endpoint for taxa including aquatic invertebrates; they did not factor strongly in the weight of evidence when considering the waiver request. However, overall, the results of these studies support the conclusion that DCPA exhibits toxic effects on a chronic exposure basis to aquatic invertebrates below the limit of solubility.

The data indicate that on a chronic basis, DCPA is at least an order of magnitude more toxic to daphnids than TPA. However, mysids appear to be more sensitive to DCPA than daphnids on a chronic exposure basis, with effects occurring even at the lowest test concentration. Furthermore, as noted above, TPA may be present in high concentrations in the water-column and concentrations may increase over time with repeated applications of DCPA. Therefore, EFED **does not** recommend granting the waiver request for ecological toxicity testing with TPA for the Mysid Chronic Toxicity Test (Guideline 850.1350) test.

Due to the lack of definitive acute and chronic endpoints, an acute to chronic ratio (ACR) approach cannot be used to quantify the chronic toxicity of TPA to mysids. In the absence of TPA chronic mysid toxicity data, the Agency will rely on the submitted data for DCPA for chronic mysid toxicity (summarized in **Table 3**) to characterize potential chronic risks to estuarine/marine invertebrates from both DCPA and TPA. Using DCPA toxicity data may overestimate the toxicity of TPA and therefore, the potential risks. Furthermore, since some of these DCPA data include an unbounded LOAEC (*i.e.*, effects were observed at all test concentrations) and no definitive NOAEC, estimates have the potential to underestimate risks for both DCPA and TPA. These uncertainties are exacerbated by the fate properties of TPA since, as noted previously, TPA concentrations may increase in the water-column over time with repeated use of DCPA.

Table 3. Available Chronic DCPA and TPA Aquatic Invertebrate Toxicity Data

Test Species (TGAI)	Endpoint (µg a.i./L)	MRID/ Classification	Comments
DCPA			
Waterflea (<i>Daphnia magna</i>) (TGAI)	21-day NOAEC = 140 LOAEC = 270	49307510 ^N Acceptable	The LOAEC is based on a 16% reduction on dry weight.
Waterflea (<i>D. magna</i>) (TGAI)	21-day NOAEC = Could not be determined LOAEC = 13	51398104 ^N Supplemental	The LOAEC is based on 22% reduction of number of live offspring, 27% reduction of successful birthrate and a 34% increase on time to first brood. Mortality in the negative control was reported to be 30%, which exceeds the validity requirement of 20%, and there were concerns with solubility and stability of the test substance. The analytical measurements indicate that test organisms in the two lowest doses may not have been exposed to any bioavailable DCPA during part of the study, and the third dose is the LOAEC

Test Species (TGAI)	Endpoint (µg a.i./L)	MRID/ Classification	Comments
			which exhibited reproductive effects. Therefore, a NOAEC could not be determined, and there is considerable uncertainty as to the actual doses the test organisms were exposed to. However, reproductive effects were observed at low doses including the LOAEC. Study may be used for risk characterization only.
Mysid (<i>Americamysis bahia</i>) (TGAI) ^a	28-day NOAEC < 10 LOAEC = 10	49307512 ^N Supplemental	A definitive NOAEC could not be established in the study as effects were observed at all treatment levels, with reduction in F0 Male dry weight and length being the most sensitive endpoint (12 and 19% reduction respectively). Although no significant differences were observed between the solvent and negative controls, there was a potential slight interaction with the solvent and the test substance for the F0 male dry weight endpoint and the number of offspring per surviving female endpoint, resulting in a potential uncertainty and a chance the solvent had an impact on the effects. Study may be used for risk characterization only.
TPA			
Water flea (<i>D. magna</i>) (TGAI)	NOAEC = 2,530 ^a LOAEC = 4,960 ^a (2,763/5,416) ^b	51235101 ^N Acceptable	26% effect on Survival at the LOAEC.

a.i.=active ingredient

^N Studies submitted since the Problem Formulation was completed are designated with an N after the MRID number.

“Less than” (<) values represent non-definitive endpoints where growth, reproductive, and/or mortality effects are observed even at the lowest tested concentrations.

^a In the EFED DER transmittal memo (dated January 21, 2022) the chronic mysid DCPA study (MRID 49307512) was mislabeled and listed under OCSPP guideline 850.1300, and not OCSPP guideline 850.1350; otherwise, the DER and other documents associated have this guideline number listed correctly as OCSPP 850.1350.

^b Expressed in terms of TPA

^c Expressed in terms of DCPA based on the difference between the molecular weights of DCPA and TPA, in which the TPA toxicity endpoint (e.g., LD₅₀ value) is multiplied by the ratio of the molecular weight of DCPA to the molecular weight of TPA (331.97 g/mol ÷ 303.91 g/mol = 1.092).

1.3 Fish Acute Toxicity with Freshwater and Estuarine/Marine Species (Guideline 850.1075):

To evaluate whether additional acute freshwater and estuarine/marine toxicity data is needed, EPA compared all of the available acute fish toxicity data for both DCPA (TGAI and TEP) and TPA, which are summarized below in **Table 4**.

The available acute fish toxicity data for DCPA suggest that on an acute exposure basis, DCPA is not acutely toxic to fish at least up to the limit of solubility of DCPA (0.5 mg/L). TPA is classified as practically non-toxic to rainbow trout, a freshwater fish, on an acute exposure basis. Additionally, AMVAC submitted a newer acute toxicity test (MRID 51398105) with rainbow trout and a DCPA formulated product (Dacthal W-75; 74.6% a.i.) that showed low toxicity;

however, there were technical issues in the conduct of the study, so it did not factor as heavily into EPA’s consideration of the waiver request. As stated above, although there is potential for this degradate (TPA) to accumulate to high concentrations in water bodies it will not likely be at concentrations that would result in acute risk. As a result, EFED has concluded that acute risks to fish from DCPA and/or TPA are unlikely. Therefore, EFED *does* recommend granting the waiver request for ecological toxicity testing with TPA for the Fish Acute Toxicity Test on Freshwater and Estuarine/Marine species (Guideline 850.1075) tests.

Table 4. Available DCPA and TPA Acute Fish Toxicity Data

Test Species (TGAI)	Endpoint (µg a.i./L)	MRID/ Classification	Comments
DCPA			
Bluegill (<i>Lepomis macrochirus</i>) (TGAI)	96-h LC ₅₀ > 500 ^a Observational NOAEC = 500	41054827 Supplemental	Only one exposure level tested. One mortality out of 30 fish (3 replicates of 10 fish each). Observational NOAEC determined by visual interpretation of the data.
Rainbow trout (<i>Oncorhynchus mykiss</i>) (TGAI)	96-h LC ₅₀ > 500 ^a Observational NOAEC = 500	41054826 Supplemental	No effects (mortality or sublethal). Observational NOAEC determined by visual interpretation of the data.
Sheepshead minnow (<i>Cyprinodon variegatus</i>) (TGAI)	96-h LC ₅₀ > 440 ^a Observational NOAEC = 440	49307511 ^N Acceptable	No effects (mortality or sublethal). Observational NOAEC determined by visual interpretation of the data.
Sheepshead minnow (<i>C. variegatus</i>) (TGAI)	96-h LC ₅₀ > 500 ^a	40228401 Supplemental	No effects ≥20% observed at the solubility limit
Rainbow trout (<i>O. mykiss</i>) (TEP; Dacthal W-75; 74.6%)	96-h LC ₅₀ > 23,800 Observational NOAEC = 2630	51398105 ^N Supplemental	Test material was both unstable and insoluble in all treatment levels. Sublethal effects classified as ‘mild’ (e.g., increased cough frequency or a swimming position different than the control) ranged from 10 to 79% in the three highest test levels at test termination. Observational NOAEC determined by visual interpretation of the data.
TPA			
Rainbow trout (<i>O. mykiss</i>) (TGAI)	96-hr EC ₅₀ > 93,400 ^b (>101,993) ^c Observational NOAEC 23,800 ^b (25,900) ^c	49307518 ^N Acceptable	Mortality was 21% at the LOAEC (50,669 µg/L), the second highest concentration. Observational NOAEC determined by visual interpretation of the data.

TEP = Typical end-use product; a.i.=active ingredient

^N Studies submitted since the Problem Formulation was completed are designated with an N associated with the MRID number.

“Greater than” (>) values represent non-definitive endpoints where no effects were observed even at the highest level tested, or effects did not reach 50% at the highest concentration tested (USEPA, 2011).

“Less than” (<) values represent non-definitive endpoints where growth, reproductive, and/or mortality effects are observed at the lowest tested concentration.

^a The highest nominal test concentration was at or above the solubility limit of DCPA (500 µg/L).

^b Expressed in terms of TPA

^c Expressed in terms of DCPA based on the difference between the molecular weights of DCPA and TPA, in which the TPA toxicity endpoint (e.g., LD50 value) is multiplied by the ratio of the molecular weight of DCPA to the

molecular weight of TPA ($331.97 \text{ g/mol} \div 303.91 \text{ g/mol} = 1.092$).

1.4 Fish Early Life-Stage Toxicity Test (Guideline 850.1400), Freshwater and Estuarine/Marine Species

To evaluate whether additional chronic freshwater and estuarine/marine toxicity data is needed, all of the available chronic fish and aquatic vertebrate toxicity data for DCPA (including the *Xenopus laevis* 21-day Amphibian Metamorphosis Assay) were considered and are summarized below in **Table 5**. There are no chronic estuarine/marine fish data available for DCPA. There are no chronic fish data (either freshwater or estuarine/marine) available for TPA.

Based on the available chronic fish toxicity data for DCPA, from studies not conducted according to OCSPP guidelines, EPA determined that additional DCPA chronic freshwater and estuarine/marine fish toxicity data were required and they were included in the DCI. AMVAC notified the Agency that those studies would be initiated in 2021, and the data are still needed for a comprehensive risk assessment.

AMVAC requested a waiver of chronic fish toxicity data for TPA. In reconsidering AMVAC's rationale for the waiver request, EFED reviewed the sole available chronic fish DCPA toxicity study (MRID 49307520). The study was classified as supplemental because it included measurement endpoints for survival and growth only (as per the OECD 215 guideline) and did not include the endpoints recommended by the OCSPP guideline. The OCSPP guideline includes early life stage endpoints such as hatching success, time to swim up, and larval survival. These missing endpoints represent potentially sensitive life-stages, and without them, the reported results of this study may underestimate potential toxicity. Those uncertainties aside, chronic growth effects were observed at concentrations below DCPA's solubility limit.

EFED also considered other chronic aquatic vertebrate data available for DCPA, including a 21-day Amphibian Metamorphosis Assay (AMA) study with the African clawed frog (*Xenopus laevis*) (MRID 48670304), and a 21-day short-term reproduction assay (FSTRA) with fathead minnows (*Pimephales promelas*) (MRID 48670303), which were conducted in response to a Tier 1 EDSP Data Call-in. In the AMA study, there were significant increases in growth measurements (wet weight and snout-vent length) as compared to the negative control at all test concentrations (7.1 - 580 ug/L). In the FSTRA, male body weight was significantly reduced (17-22%) at all treatment levels (7.4 - 580 ug/L), and there was a slight but significant reduction in fertility of 1.3% at the highest treatment level.

Based on the observed effects in the supplemental chronic freshwater fish study with DCPA (MRID 49307520) and the aquatic vertebrate data for DCPA submitted under the EDSP Data Call-in, and because no chronic aquatic vertebrate data are available for TPA, EFED has reconfirmed the need for chronic freshwater and estuarine/marine fish toxicity studies for TPA. EFED **does not** recommend granting the waiver request for testing with TPA for the fish ELS study (Guideline 850.1400), for both freshwater and estuarine/marine species.

Due to the lack of definitive acute and chronic endpoints, an acute to chronic ratio (ACR) approach cannot be used to approximate the chronic toxicity of TPA in fish species. Therefore, in the absence of these data, EFED will need to use either the available supplemental data in

some fashion for freshwater fish as cited (imparting uncertainty to the risk assessment) in **Table 5** or, depending on when they become available, the DCPA freshwater and/or estuarine/marine ELS data (OCSPP 850.1400) that AMVAC has not yet submitted to characterize potential chronic risks from exposure to TPA in fish. If only the current supplemental chronic fish study plus the EDSP data are available, we could conduct a risk assessment, but it will not be known whether the conclusions would under- or over-estimate potential risks and therefore EPA's ability to make decisions that meet either FIFRA-based unreasonable adverse effects or ESA-based effects determinations will be compromised.

Table 5. Available Chronic DCPA and TPA Aquatic Vertebrate Toxicity Data

Test Species (TGAI)	Endpoint (µg a.i./L)	MRID/ Classification	Comments
DCPA			
Rainbow trout (<i>O. mykiss</i>) (TGAI)	28-day NOAEC = 128 LOAEC = 341	49307520 ^N Supplemental	Non-guideline/OECD 215 guideline. There was a 19.5% reduction in Day 28 fork length and 50.8% reduction in 0 – 28 day fork length change; 49.3% reduction in Day 28 wet weight and 70.2% reduction in 0 – 28 day wet weight change at the LOAEC.
African clawed frog (<i>Xenopus laevis</i>) (TGAI)	21-day growth effects at all treatment levels (7.1, 21, & 580)	48670304 ^N Satisfies Tier I EDSP test order requirement	OCSPP 890.1150 guideline, AMA. Significantly increased wet weight (↑8, 28 and 20%) and SVL (↑3 to 9%) relative to the negative control at all treatment levels.
Fathead minnow (<i>Pimephales promelas</i>) (TGAI)	21-day growth effects at all treatment levels (7.4, 22, & 580)	48670303 ^N Satisfies Tier I EDSP test order requirement	OCSPP 890.1350 guideline, FSTRA. Male body weight significantly reduced (18-22%), all treatment levels; (18% at 7.4 µg a.i./L, the lowest concentration tested). Fertility also reduced at highest treatment level.
TPA			
NO DATA			

a.i.=active ingredient

^N Studies submitted since the Problem Formulation was completed are designated with an N after the MRID number.

1.5 Aquatic Vascular Plant Toxicity (Guideline 850.4400), and Aquatic Non-Vascular Plant Toxicity (Guideline 850.4500)

To evaluate whether additional aquatic plant toxicity data (in both vascular and non-vascular plants) is needed, EPA compared all the available aquatic plant toxicity data for both DCPA and TPA, which are summarized below in **Table 6**. The full suite of aquatic plant data with TGAI DCPA is available (except for green algae, for which the test substance was a TEP) while only green algae data are available for TPA (TGAI test substance).

Based on the current database, EFED has concluded that DCPA's effects on vascular and non-vascular plants are limited, with non-definitive IC₅₀s greater than the solubility limit (0.5 mg/L) for all taxa except for marine diatoms. The marine diatoms showed yield inhibition approaching 50% at the solubility limit (MRID 49307504), but there is some uncertainty associated with potential solvent interference and high negative control variability. The available aquatic vascular plant data for DCPA (MRID 49307509), suggest that DCPA is not toxic to aquatic vascular plants at least up to the limit of solubility of DCPA (0.5 mg/L); an IC₅₀ could not be determined because the maximum inhibition for the study endpoints was 15%.

EPA reviewed several other DCPA aquatic plant toxicity studies, but technical issues in those studies resulted in reduced confidence in study endpoints. However, taken together, the results of these studies overall support the conclusion that DCPA is relatively non-toxic to aquatic plant species tested, with the exception of the marine diatom.

The only available data for TPA are from a study in green algae (MRID 51499401), but the highest dose tested did not achieve the IC₅₀. Issues relating to pH impacted EFED's ability to interpret test results at the highest dose, so EFED used the next-to highest dose to estimate the IC₅₀.

EFED has concluded that risks to aquatic vascular plants from exposure to DCPA and TPA are minimal or unlikely. EFED *does* recommend granting the waiver request for toxicity testing with TPA for aquatic vascular plants using *Lemna spp.* (Guideline 850.4400).

EFED also *does* recommend granting the waiver request for TPA testing in aquatic non-vascular plants, except for the marine diatom. The marine diatom was the most sensitive species tested for DCPA. As noted previously, there is potential for TPA concentrations to be present at relatively high concentrations in the environment. In the absence of TPA marine diatom data, EPA will need to use the endpoint from MRID 49307504 for both DCPA and TPA. That approach may overestimate the toxicity of TPA to aquatic plants and yield uncertain risk conclusions, particularly because the other relevant DCPA studies had technical issues which resulted in reduced confidence in the study endpoints. Therefore, EFED *does not* recommend granting the waiver request for ecological toxicity testing with TPA in the marine diatom (Guideline 850.4500).

Table 6. Available DCPA and TPA Aquatic Plant Toxicity Data

Test Species (TGAI/TEP)	Endpoint (µg a.i./L)	MRID/ Classification	Comments
DCPA			
Duckweed (<i>Lemna gibba</i>) (TGAI)	7-day IC ₅₀ >470 ^a NOAEC = 230	49307509 ^N Acceptable	NOAEC based on effects to frond number yield & frond number growth rate, no effects reached 50% (maximum inhibition of 15%).
Marine Diatom (<i>Skeletonema costatum</i>) (TGAI)	96-hr IC ₅₀ =464 ^a NOAEC = 127	49307504 ^N Supplemental	Most Sensitive Endpoint: Yield (with a maximum inhibition of 40%). However, there are uncertainties due to high variability the endpoints for the negative control (CVs up to 29% in cell

Test Species (TGAI/TEP)	Endpoint ($\mu\text{g a.i./L}$)	MRID/ Classification	Comments
			density) and potential solvent interaction (growth promotion). Study may be used for risk characterization only.
Cyanobacteria (<i>Anabaena flos-aquae</i>) (TGAI)	96-hr $\text{IC}_{50} > 535^{\text{a}}$ NOAEC = 535	49307507 ^N Supplemental	Although there are uncertainties due to high variability in the endpoints for the negative control (CVs up to 52% in cell density and AUC), there were no effects at the solubility limit. Study may be used for risk characterization only.
Freshwater diatom (<i>Navicula pelliculosa</i>) (TGAI)	96-hr $\text{IC}_{50} > 514^{\text{a}}$ NOAEC = 116	49307508 ^N Supplemental	All endpoints were significantly affected in the highest test level, but no effects reached 50% (maximum inhibition of 20%).
Green alga (<i>Selenastrum capricornutum</i>) (TEP; Dacthal W-75; 74.6%)	96-hr $\text{IC}_{50} > 61,000$ NOAEC = 6,430	51499402 ^N Supplemental	The yield, growth rate, and area under the curve (AUC) were significantly affected by the test material. Major change in pH over the study duration in control and treatment groups. An increase of 2.3 units in the negative control; and treatment groups beyond the OECD guideline recommendation of 1.5 units. Based on the issues with pH and solubility (poor chemical recovery) the study should only be used for risk characterization.
TPA			
Green alga (<i>S. capricornutum</i>) (TGAI)	96-hr $\text{IC}_{50} > 46,100^{\text{b}}$ (>50,341) ^c NOAEC = 19,700 ^b (21,512) ^c	51499401 ^N Supplemental	All endpoints in this study were significantly affected in the two highest test levels. However, there were issues with low pH in the test in the highest test concentration resulting in no confidence in this treatment level and additionally control and lower treatment groups had pH increases beyond the OECD guideline recommendation of 1.5 units and reached levels of limited environmental relevance (>10). The remaining concentrations were reliable for use in estimating impacts to algae although the IC_{50} is likely somewhere between the second highest and highest test concentration. However, based on the issues with pH the study should only be used for risk characterization.

TEP= Typical end-use product; a.i.=active ingredient

^N Studies submitted since the Problem Formulation was completed are designated with an N associated with the MRID number.

>Greater than values designate non-definitive endpoints where no effects were observed at the highest level tested, or effects did not reach 50% at the highest concentration tested (USEPA, 2011).

^a The highest nominal test concentration was at or above the solubility limit of DCPA (0.5 mg/L).

^b Expressed in terms of TPA

^c Expressed in terms of DCPA based on the difference between the molecular weights of DCPA and TPA, in which the TPA toxicity endpoint (e.g., LD50 value) is multiplied by the ratio of the molecular weight of DCPA to the molecular weight TPA ($331.97 \text{ g/mol} \div 303.91 \text{ g/mol} = 1.092$).

1.6 Terrestrial Plant Toxicity, Tier I (Seedling Emergence; Guideline 850.4100), and Terrestrial Plant Toxicity, Tier I (Vegetative Vigor; Guideline 850.4150)

To evaluate whether additional terrestrial plant toxicity data is needed, EFED compared the available terrestrial plant toxicity data for both DCPA and TPA. These data are summarized below in **Table 7**. AMVAC's 2013 waiver request included a request for waiving the seedling emergence data (OCSPP Guideline 850.4100) for TPA, which EPA denied. Subsequently, AMVAC submitted TPA seedling emergence data in MRID 51235102. EFED reviewed these data (DP460199) and used them in re-considering the waiver request for the TPA vegetative vigor (OCSPP Guideline 850.4150) study as discussed below.

The available seedling emergence data for DCPA and TPA show that for terrestrial plants, TPA is generally less toxic than DCPA, by up to an order of magnitude. The most sensitive species for DCPA were ryegrass (*Lolium perenne*, a monocot) and sugarbeet (*Beta vulgaris*, a dicot). The most sensitive species for TPA was tomato (*Lycopersicon esculentum*, a dicot). There were no significant effects on monocots from exposure to DCPA and no data on monocots for TPA. In general, the IC₂₅ endpoints for TPA approach or exceed the highest concentration tested, suggesting low phytotoxicity.

The seedling emergence studies are intended to capture sub-lethal effects; therefore, survival is not expected to be the most sensitive endpoint. However, for DCPA in ryegrass (*L. perenne*), survival was the most sensitive endpoint among the monocot species (NOAEC = 0.23 lb/A), and there was potentially a strong effect on emergence and survival on ryegrass that may have confounded growth effects (MRID 49307513). The most sensitive dicot was sugarbeet (*B. vulgaris*), based on effects on height (IC₂₅ = 0.548 lb a.i./A; NOAEC = 0.27 lb a.i./A). For TPA, the most sensitive dicot was tomato (*L. esculentum*), based on dry weight (IC₂₅ = 8.47 lb a.i./A; NOAEC = 2.4 lb a.i./A; expressed as DCPA; MRID 51235102). The terrestrial plant toxicity studies are designed to capture sub-lethal effects, and for ryegrass (*L. perenne*), this uncertainty (survival being the most sensitive endpoint) may impact the reliability of the other growth endpoints (e.g., dry weight). However, any effects on ryegrass dry weight did not appear to be dose responsive and therefore do not appear to be treatment related, and therefore there were no significant growth effects on monocots.

Given that TPA forms as a degradation product of DCPA, the exposures to TPA for terrestrial plants are likely limited to runoff (as represented by the test design in seedling emergence studies) and not from spray drift (which is simulated by vegetative vigor studies). Seedling emergence generally was a more sensitive endpoint for DCPA exposures than vegetative vigor. Since seedling emergence was more sensitive and DCPA was less phytotoxic than TPA in seedling emergence testing, EFED has concluded that vegetative vigor data for TPA are not needed to conduct the risk assessment and EFED **does** recommend granting the waiver request for vegetative vigor (Guideline 850.4150).

Table 7. Available DCPA and TPA Terrestrial Plant Toxicity Data for which the same Test Species were Used.

Species	Endpoint	TPA Endpoint ^a (lb a.i./A)	DCPA Endpoint (lb a.i./A)
Seedling Emergence – DCPA (MRID 49307513^N), TPA (MRID 51235102^N) Comparison of same test species			
Sugarbeet <i>Beta vulgaris</i>	IC25	9.77 ^b	0.548 ^b
Sugarbeet <i>B. vulgaris</i>	NOAEC	0.34 ^b	0.27 ^b
Ryegrass <i>Lolium perenne</i>	IC25	>9.94 ^b	0.277 ^b
Ryegrass <i>L. perenne</i>	NOAEC	9.94 ^b	0.23 ^b
Tomato <i>Lycopersicon esculentum</i>	IC25	8.47 ^b	1.07 ^b
Tomato <i>L. esculentum</i>	NOAEC	2.4 ^b	0.23 ^b
Wheat <i>Triticum aestivum</i>	IC25	>9.94 ^b	5.64 ^b
Wheat <i>T. aestivum</i>	NOAEC	9.94 ^b	2.3 ^b
Vegetative Vigor – DCPA only, (MRID 49307506^N) Most sensitive species			
Monocots	IC25	ND	>10.2 ^c
Monocots	NOAEC	ND	10.2 ^c
Soybean <i>Glycine max</i>	IC25	ND	11.9 ^c
Soybean <i>G. max</i>	NOAEC	ND	2.52 ^c

ND = No Data

^N Studies submitted since the Problem Formulation was completed are designated with an N associated with the MRID number.

>Greater than values designate non-definitive endpoints where no effects were observed at the highest level tested, or effects did not reach 50% at the highest concentration tested (USEPA, 2011).

^a Expressed in terms of DCPA based on the difference between the molecular weights of DCPA and TPA, in which the TPA toxicity endpoint (e.g., LD50 value) is multiplied by the ratio of the molecular weight of DCPA to the molecular weight of TPA ($331.97 \text{ g/mol} \div 303.91 \text{ g/mol} = 1.092$).

^b For DCPA, MRID 49307513; classified as acceptable for all species *except* ryegrass and lettuce; see DER memo/DERs for additional details on individual species classifications. For TPA, MRID 51235102; classified as supplemental overall; see DER memo/DER for additional details on individual species classifications.

^c In the DCPA vegetative vigor study, the most sensitive monocot could not be determined due to lack of toxicity (IC25>10.2 lb/A; NOAEC = 10.2 lb/A). The most sensitive dicot was soybean, based on dry weight (a 20% effect at the highest application rate, 10.2 lb a.i./A) (MRID 49307506, classified acceptable).

2. Chronic Sediment Toxicity Testing (Non-Guideline/ EPA Test Method 600/R-01/020; USEPA, 2001) with DCPA on the Estuarine/Marine Amphipod *Leptocheirus plumulosus*

AMVAC offered the following rationale in its request for waiver of chronic sediment testing with the estuarine/marine amphipod (MRID 49865803; Freedlander, 2016):

- In testing with DCPA, minor toxicological effects to aquatic invertebrates were observed only at water concentrations approaching the solubility limit (0.5 mg/L at 25°C). These water concentrations are unlikely to occur in the environment.
- Freshwater amphipods appear to be less sensitive to DCPA than midges, suggesting estuarine/marine amphipods like *L. plumulosus* likely would be less sensitive also. In general, benthic invertebrates like *L. plumulosus* appear to show less sensitivity to DCPA compared to invertebrates inhabiting the water column.
- Testing of *L. plumulosus* has proven difficult due to study validation issues.

EFED reviewed all of the available sediment toxicity data for DCPA in order to evaluate AMVAC’s rationale and to re-evaluate the Agency’s rationale for requiring chronic sediment toxicity data in estuarine/marine invertebrates. These data are summarized **Table 8** below.

No sediment toxicity data are available for TPA. No acceptable acute sediment toxicity data are available for DCPA; the available acute studies for aquatic benthic invertebrates were conducted with DCPA and water column exposures only. In EPA’s 2016 response to AMVAC’s previous waiver request for this study (DP432677, USEPA, 2016), EFED has reviewed two chronic freshwater sediment toxicity studies submitted by AMVAC for DCPA (MRIDs 49865801 and -02).

Table 8. Available DCPA and TPA Benthic Invertebrate Toxicity Data

Test Species (TGAI)	Endpoint (µg a.i./L)	MRID/ Classification	Comments
DCPA			
Freshwater Midge (<i>Chironomus plumulosus</i>) (TGAI)	Acute, Water-column 48-hour EC ₅₀ >500 ^a	40098001 Supplemental	No effects observed at the solubility limit.
Freshwater Amphipod (<i>Gammarus pseudolimnaeus</i>) (TGAI)	Acute, Water-column 96-hour EC ₅₀ >500 ^a	40098001 Supplemental	No effects observed at the solubility limit.
Freshwater Amphipod (<i>Hyalella azteca</i>) (TGAI)	Chronic Sediment 42-day Pore water: NOAEC = 280 LOAEC =360 OC-normalized sediment: NOAEC = 1976 LOAEC = 4405 mg a.i./kg OC	49865801 ^N Acceptable	Both 28 Day survival and length endpoints only had a 4% significant effect at the LOAEC (highest test level), and these effects did not persist at D35 and D42 observations; uncertain if this was actually treatment-related or an artifact of the high power and low variability observed in the study.
Freshwater Midge (<i>Chironomus riparius</i>) (TGAI)	Chronic Sediment 60-day Pore water: NOAEC = 240 LOAEC >240 OC-normalized sediment: NOAEC = 4000 LOAEC >4000 mg a.i./kg OC	49865802 ^N Supplemental	No effects based on solvent control at the highest treatment level. Treatment groups were compared to SC and not the NC due to significant differences between SC and NC for several endpoints. The reviewer determined that the results reported in the treatment groups were in fact the effect of the solvent and not the test substance or could not be ruled

Test Species (TGAI)	Endpoint (µg a.i./L)	MRID/ Classification	Comments
			out to be due to the solvent. Study may be used for risk characterization only.
Estuarine/Marine Amphipod <i>L. plumulosus</i>	NO DATA		
TPA			
NO DATA			

TGAI=Technical Grade Active Ingredient; a.i.=active ingredient

^N Studies submitted since the Problem Formulation was completed are designated with an N associated with the MRID number.

>Greater than values designate non-definitive endpoints where no effects were observed at the highest level tested, or effects did not reach 50% at the highest concentration tested (USEPA, 2011).

^a However, test solutions were not reported to be centrifuged or filtered to remove any potential precipitates, so the actual bioavailable concentration may be less than the reported nominal concentration which introduces uncertainty in the actual EC50 but still indicates little to no effects up to solubility.

EFED generally agrees with AMVAC's rationale that only minor acute toxic effects are observed for aquatic invertebrates at levels approaching the solubility limit of DCPA. However, modeled EECs and monitoring data for DCPA presented in the last risk assessment² conducted by EFED show maximum water concentrations at or above the solubility limit of 0.5 mg/L. Modeled DCPA EECs reached the solubility limit of 0.5 mg/L, the maximum reported concentration of DCPA in surface water monitoring data was 0.1 mg/L, and the maximum reported concentration of DCPA in ground water monitoring data was 0.431 to 0.986 mg/L, indicating that actual concentrations in aquatic environments may approach modeled values². Additionally, based on information from the last assessment², in comparison with the reviewed chronic sediment data summarized in this data waiver response it was determined that chronic EECs would approach/exceed the chronic sediment toxicity endpoints shown in **Table 8**. Therefore, EFED cannot reasonably make the assumption that estuarine/marine invertebrates would not be impacted at concentrations of DCPA expected to occur in the environment.

EFED also agrees that the available chronic sediment studies (see Table 8 above) appear to be less sensitive than the available chronic water-column (see section 1.2 and Table 3, above) studies and that the freshwater sediment amphipod data appears to be less sensitive than the mysid (*A. bahia*; MRID 49307512; see Section 1.2 and Table 3 above). However, based on the results from the water-column chronic invertebrate studies (see Section 1.2 above), estuarine/marine invertebrates (*A. bahia*; MRID 49307512; Claude *et al*, 2014) were found to be more sensitive than freshwater invertebrates (*D. magna*; MRID 49307510; Shaw 2013b). In consideration of the observed increased sensitivity between the tested estuarine/marine and freshwater water-column species on a chronic basis, there is potential for an equivalent increase in sensitivity in estuarine/marine sediment dwelling species.

Finally, regarding the registrant's comment on the challenges of conducting *L. plumulosus* studies, EFED is aware that several studies conducted pursuant to EPA Test Method 600/R-

² U.S. EPA. 2009. Risks of DCPA Use to Federally Threatened California Red-legged Frog (*Rana aurora draytonii*). Environmental Fate and Effects Division, Office of Pesticide Programs, Washington, DC. February 19, 2009. Available at: <https://www3.epa.gov/pesticides/endanger/litstatus/effects/redleg-frog/dcpa/analysis.pdf>

01/020 were found to be acceptable and were used in other risk assessments. These efforts should limit the previously identified issues associated with the conducting of the *L. plumulosus* studies.

Based on the confluence of modeling outputs and monitoring data, the potential for increased toxicity in estuarine/marine amphipods, and improvements in conducting studies with *L. plumulosus*, EFED reiterates that it ***still does not*** recommend waiving chronic sediment toxicity testing with DCPA in an estuarine/marine amphipod (per the non-guideline/EPA Test Method 600/R-01/020, as described in USEPA, 2001). The Agency continues to recommend that the registrant submit a protocol for such a study to the Agency prior to study initiation.

References

- Arnie, J.; Martin, K.; Porch, J. (2013a) Dacthal: A 96-Hour Toxicity Test with the Freshwater Alga (*Anabaena flos-aquae*): Final Report. Project Number: 246P-101. Unpublished study prepared by Wildlife International, Ltd. MRID 49307507.
- Arnie, J.; Martin, K.; Porch, J. (2013b) Dacthal: A 96-Hour Toxicity Test with the Freshwater Diatom (*Navicula pelliculosa*): Final Report. Project Number: 246P-102. Unpublished study prepared by Wildlife International, Ltd. MRID 49307508.
- Arnie, J.; Martin, K.; Porch, J. (2013) Dacthal: a 7-Day Static-Renewal Toxicity Test with Duckweed (*Lemna gibba* G3). Project Number: 246P-104. Unpublished study prepared by Wildlife International, Ltd. MRID 49307509.
- Beavers, J. (2013) (Chlorthal-dimethyl): Avian Reproduction Test: (Northern Bobwhite and Mallard). Project Number: 246/115, 246/116. Unpublished study prepared by Wildlife International, Ltd. 32p. MRID 49115402.
- Claude, M. B.; Martin, K. H.; Gallagher, S. P.; Bodle, E. S.; Krueger, H. O. (2013) A 96-Hour Static Acute Toxicity Test with the Saltwater Mysid (*Americamysis bahia*). Project No. 46A-115, Unpublished report by Wildlife International for AMVAC Chemical Corporation, Newport Beach, CA, MRID 49307505.
- Claude, M. B.; Martin, K. H.; Gallagher, S. P.; Krueger, H. O. (2014) Dacthal: A Flow-Through Life-Cycle Toxicity Test with the Saltwater Mysid (*Americamysis bahia*). Project No. 246A-116A, Unpublished report by Wildlife International for AMVAC Chemical Corporation, Newport Beach, CA, MRID 49307512.
- Freedlander, D. (AMVAC). (2013a) *Residue, Environmental Fate, and Ecotoxicology Responses for Non-Terrestrial Animals*. Project Number AMV-DAC-04-13-13. Unpublished report prepared by Sponsor AMVAC Chemical Corporation. 16p. MRID 49115401.
- Freedlander, D. (AMVAC). (2013b) DCPA: *Avian Acute Inhalation Waiver, Test Guideline SS-1075*. Project Number AMV-DAC-AV-2-04-13. Unpublished report prepared by Sponsor AMVAC Chemical Corporation. 6p. MRID 49115404.
- Freedlander, D. (2016) Proposed Waiver for Dacthal (DCPA) Chronic Study Testing on *Leptocheirus plumulosus*. Project Number: 100/AQU/028, 246A/115, 246A/116A. Unpublished study prepared by Amvac Chemical Corporation. 10p. MRID 49865803.
- Freedlander, D. (2020) Tetrachlorophthalic Acid (TPA): Selected Ecological Study Waiver Request. Project Number: 100-REV-049. Unpublished study prepared by AMVAC Chemical Corporation. MRID 51398103.
- Gourdie, O. J. (2019) 2,3,5,6 -Tetrachlorophthalic acid (TCTPAc): Chronic Toxicity Test with the Cladoceran *Daphnia magna*, Conducted Under Flow-Through Conditions, Study No. 86482, unpublished study performed by Eurofins EAG Agrosience, LLC, Columbia, Missouri. MRID 51235101.

- Manson, P. S. (2003a) Tetrachloroterephthalic Acid (TPA): Acute Toxicity to *Daphnia magna*, Report No. 1708/021-D2149, unpublished study by Covance Laboratories Ltd, Harrogate, North Yorkshire, England, MRID 49307519.
- Manson, P. S. (2003b) Tetrachloroterephthalic Acid (TPA): Acute Toxicity to *Oncorhynchus mykiss*, Report No. 1708/020-D2149, unpublished study by Covance Laboratories Ltd, Harrogate, North Yorkshire, England. MRID 49307518.
- Manson, P. S. (2003c) Tetrachloroterephthalic Acid (TPA): Inhibition of Growth to the Alga *Selenastrum capricornutum*, Report No. 11708/022-D2149, unpublished study by Covance Laboratories Ltd, Harrogate, North Yorkshire, England. MRID 51499401.
- Manson, P. S. (2004a) Chlorthal-dimethyl (DCPA) Reproduction Study with *Daphnia magna*, Report No. 1708/035-D2149, unpublished study by Covance Laboratories Ltd., Harrogate, North Yorkshire, England. MRID 51398104.
- Manson, P. S. (2004b) Dacthal W-75: Acute Toxicity to *Oncorhynchus mykiss*, Report No. 1708/036-D1249, unpublished study by Covance Laboratories Ltd, Harrogate, North Yorkshire, England. MRID 51398105.
- Manson, P. S. (2004c) Dacthal W-75: Inhibition of Growth to the Alga *Selenastrum capricornutum*, Study No. 1708/038-D2149, unpublished study by Covance Laboratories Ltd, Harrogate, North Yorkshire, England. MRID 51499402.
- Manson, P. (2004d) Chlorthal-dimethyl (DCPA): Prolonged Toxicity Test to Juveniles *Oncorhynchus mykiss*. Under Semi-Static Conditions: Final Report. Project Number: 1708/034, 1708/034/D2149. Unpublished study prepared by Covance Laboratories, Ltd. MRID 49307520.
- Martin, K.; Porph, J.; Arnie, J. (2013) Dacthal: A 96-Hour Toxicity Test with the Marine Diatom (*Skeletonema costatum*): Final Report. Project Number: 246P-103A. Unpublished study prepared by Wildlife International, Ltd. MRID 49307504.
- Martin, K.; Porph, J.; Bodle, E.; et al. (2014) Dacthal: A Toxicity Test to Determine the Effects of the Test Substance on Seedling Emergence of Ten Species of Plants: Final Report. Project Number: 246P105. Unpublished study prepared by Wildlife International, Ltd. MRID 49307513.
- Mayer, F. (1986) Acute Toxicity Handbook of Chemicals to Estuarine Organisms: EPA/600/X/86/231. Prepared by US EPA Environmental Research Laboratory, Gulf Breeze, Fl. MRID 40228401.
- Mayer, F.; Ellersieck, M. (1986) Manual of Acute Toxicity: Interpretation and Data Base for 410 Chemicals and 66 Species of Freshwater Animals. US Fish & Wildlife Service, Resource Publication 160. MRID 40098001.

- McKelvey, R.; Arnie, J. R, Sneckenberger, G.; Zhang, L. (2019) TPA: A Toxicity Test to Determine the Effects on Seedling Emergence of Ten Species of Plants, Project No. 246P-111, unpublished report EAG Inc., Easton, Maryland. MRID 51235102.
- Picard, C. R. (2016a) Dacthal Technical -42-Day Toxicity Test Exposing Freshwater Amphipods (*Hyalella azteca*) to a Test Substance Applied to Sediment under Static-Renewal Conditions Following EPA Test Methods, Study No. 11857.6111, Unpublished report by Smithers Viscient for AMVAC Chemical Corporation, Newport Beach, CA. MRID 49865801.
- Picard, C. R. (2016b) Dacthal Technical - Life-Cycle Toxicity Test Exposing Midges (*Chironomus dilutus*) to a Test Substance Applied to Sediment Under Static-Renewal Condition Following EPA Test Methods, Study No. 11857.6110, Unpublished report by Smithers Viscient for AMVAC Chemical Corporation, Newport Beach, CA. MRID 49865802.
- Schneider, S.; Martin, K.; Kendall, T. et al. (2012a) Chlorthal Dimethyl (DCPA): Fish Short-Term Reproduction Assay with the Fathead Minnow (*Pimephales promelas*): Final Report. Project Number: 264A/101A. Unpublished study prepared by Wildlife International, Ltd. MRID 48670303.
- Schneider, S.; Kendall, T.; Krueger, H. (2012b) Chlorthal Dimethyl (DCPA): Amphibian Metamorphosis Assay: Final Report. Project Number: 246A/102. Unpublished study prepared by Wildlife International, Ltd. MRID 48670304.
- Shaw, A. C. (2013a) Dacthal – Acute Toxicity to Water Fleas, *Daphnia magna*, under Static Conditions, Following OCSPP Guideline 850.1010, Study No. 11857-6107, unpublished study by Smithers Viscient, Wareham, Massachusetts. MRID 49307514.
- Shaw, A. C. (2013b), Dacthal – Full Life-Cycle Toxicity Test with Water Fleas, *Daphnia magna* under Static Renewal System, Study No. 11857.6114, unpublished study by Smithers Viscient, Waltham, MA, MRID 49307510.
- Shaw, A. (2013c) Dacthal- Acute Toxicity of Sheepshead Minnow (*Cyprinodon variegatus*) Under Static-Renewal Conditions. Project Number: 11857.6109. Unpublished study prepared by Smithers Viscient Laboratories Waltham, MA. MRID 49307511.
- Shaw, A. (2013d) Dacthal - Acute Toxicity to Eastern Oyster (*Crassostrea virginica*) Under Flow-Through Conditions. Project Number: 11857.6108. Unpublished study prepared by Smithers Viscient Laboratories. MRID 49500701.
- Shelby, D. J. (1995) Adsorption and Desorption of Dimethyl Tetrachloroterephthalate (DCPA) to Soil, Project No. 246A-116A, Unpublished report by Ricerca Inc. for ISK Biosciences Corporation, Mentor. OH, MRID 43661101.

- Shults, S.; Wilson, N. (1985) Static, Acute Toxicity (LC50) Study in Bluegill with Technical DCPA (Dimethyl 2,3,5,6-Tetrachloro- terephthalate): Doc. No. 690-5TX-84-0047-002. Unpublished study prepared by SDS Biotech Corp. MRID 41054827.
- Shults, S.; Wilson, N. (1989) Static, Acute Toxicity (LC50) Study in Rainbow Trout with Technical DCPA (Dimethyl 2,3,5,6-Tetra- chloroterephthalate): Doc. No. 690-5TX-84-0046-002. Unpublished study prepared by SDS Biotech Corp. MRID 41054826.
- Sindermann, A.; Porch, J.; Krueger, H.; et al. (2013) Dacthal: A Toxicity Test to Determine the Effects of the Test Substance on Vegetative Vigor of Ten Species of Plants: Final Report. Project Number: 246P-106. Unpublished study prepared by Wildlife International, Ltd. MRID 49307506.
- Sidermann, A. B.; Porch, J. P.; Martin, K. H.; Bodle, E. S. (2014) Dacthal: A Toxicity Test to Determine the Effects of the Test Substance, Project No. 246P-105, unpublished report by Wildlife International, Easton, Maryland, MRID 41564901.
- USEPA. 2001. “Methods for Assessing the Chronic Toxicity of Marine and Estuarine Sediment-associated Contaminants with the Amphipod *Leptocheirus plumulosus*.” First Edition. E. 600/R-01/020. March 2001. Office of Research and Development. Office of Science and Technology. Office of Water. United States Environmental Protection Agency. Available at: <https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=30002GRK.txt>.
- USEPA. 2008. Memorandum “Health Effects Support Document for Degradates: Tetrachlorophthalic Acid (TPA) and Monomethyl Tetrachlorophthalic Acid (MTP)”, EPA Document No. EPA-822-R-08-0056, May 28.
- USEPA. 2011. Memorandum “Registration Review – Preliminary Problem Formulation for the Ecological Risk Assessment of Dimethyl 2,3,5,6-Tetrachloroterephthalate (DCPA).” DP388337. Dated May 31, 2011. Office of Pesticide Programs, Environmental Fate and Effects Division. Docket ID: EPA-HQ-OPP-2011-0374. <https://www.regulations.gov/search?filter=EPA-HQ-OPP-2011-0374>.
- USEPA. 2014. Memorandum “Response to registrant’s data waiver requests for environmental fate and ecological effects related data for the parent DCPA and degradate TPA.” DP413324+. Dated March 21, 2014. Office of Pesticide Programs, Environmental Fate and Effects Division.
- USEPA. 2016. Memorandum “DCPA: Response to Waiver Request for the Chronic Sediment Toxicity Study with *Leptocheirus plumulosus*.” DP432677. Dated June 27, 2016. Office of Pesticide Programs, Environmental Fate and Effects Division.
- USEPA. 2022. Memorandum “Dimethyl 2,3,5,6-Tetrachloroterephthalate (DCPA): Response to Registrant’s Waiver Requests for Environmental Fate Data for DCPA and It’s Degradate Tetrachlorophthalic Acid (TPA).” DP Barcode 461053. Dated April 19, 2022. Environmental Fate and Effects Division. Office of Pesticide Programs. Washington, D.C.

