

Joint Exhibit 66



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OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

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413379, 413381, 413382, 413390, 413392, 413393, and 413399

PC Code: 078701

Date: March 21, 2014

MEMORANDUM

SUBJECT: Response to registrant's data waiver requests for environmental fate and ecological effects related data for the parent DCPA and degradate TPA

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The Environmental Fate and Effects Division (EFED) has completed its reviews of the waiver requests submitted in a response to the generic data call-in (GDCI) associated with initiation of registration review of DCPA (dated April 13, 2013). The Agency issued a data call-in (DCI) notice for environmental fate and ecological effects studies for DCPA and degradate TPA, as a

follow-up to its ecological risk assessment problem formulation for DCPA¹. AMVAC is requesting waivers from the following studies for DCPA: Terrestrial Field Dissipation, Avian Inhalation, and Avian Reproduction; and the following studies for the degradate TPA: Soil Column Leaching, Aerobic Aquatic Metabolism, Anaerobic Aquatic Metabolism, Terrestrial Field Dissipation, 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), Daphnid Chronic Toxicity Test (850.1300), Mysid Chronic Toxicity Test (850.1350), Fish Early Life-Stage Toxicity Test (850.1400), Fish Bioconcentration (850.1730), 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 (850.5400). A summary of the environmental fate and ecological effects data waiver requests are presented in Table 1. EFED's responses are provided below.

Table 1. Disposition of Waiver Requests for DCPA and the degradate TPA¹

Study Number	Study Type	MRID	DP Barcode	Are Additional Data Needed for Risk Assessment?
835.6100	Terrestrial Field Dissipation ²	49115401	413365	Y
DCPA				
SS-1075	DCPA: Avian Inhalation ³	49115404	413324	N (ground spray appl.)/ Y (aerial appl.)
850.2300	DCPA: Avian Reproduction	49115402	413329	N
TPA				
835.1240	TPA: Soil Column Leaching	49115401	413353	N
835.4300	TPA: Aerobic Aquatic Metabolism	49115401	413333	Y
835.4400	TPA: Anaerobic Aquatic Metabolism	49115401	413364	Y
850.1025	TPA: Oyster Acute Toxicity Test (shell deposition)	49115401	413344	Y
850.1035	TPA: Mysid Acute Toxicity Test	49115401	413369	Y
850.1075	TPA: Fish Acute Toxicity Test, Freshwater and Marine Species	49115401	413377	Y
850.1300	TPA: Daphnid Chronic Toxicity Test	49115401	413379	Y
850.1350	TPA: Mysid Chronic Toxicity Test	49115401	413381	Y
850.1400	TPA: Fish Early Life-Stage Toxicity Test	49115401	413382	Y
850.1730	TPA: Fish Bioconcentration	49115401	413399	N
850.4100	TPA: Terrestrial Plant Toxicity, Tier I (Seedling Emergence)	49115401	413390	Y
850.4400	TPA: Aquatic Vascular Plant Toxicity Test, Tiers I/II (<i>Lemna spp.</i>)	49115401	413392	Y

¹ Registration Review – Preliminary Problem Formulation for the Ecological Risk Assessment of Dimethyl 2,3,5,6-Tetrachloroterephthalate (DCPA). EPA-HQ-OPP-2011-0374-0003. Office of Pesticide Programs, U.S. EPA, Washington, D.C. May 31, 2011.

Study Number	Study Type	MRID	DP Barcode	Are Additional Data Needed for Risk Assessment?
850.5400	TPA: Aquatic Non-Vascular Plant Toxicity Test, Tiers I/II (Algal species)	49115401	413393	Y

¹**For the degradate TPA, a more limited testing strategy is still preferred if an acceptable one can be proposed.** One example would be if both an acute and chronic study were submitted, and it both were shown to be is less sensitive than the DCPA data, then additional data would not be needed.

²Only one study is needed as long as all of the degradate information is tracked.

³ Switching to ground applications only, (as proposed), EFED recommends *granting waiver request*; Aerial applications remain on label, EFED recommends *denying waiver request*.

DCPA Environmental Fate Study Requirements:

835.6100: Terrestrial Field Dissipation

AMVAC Comment: “Terrestrial field dissipation: AMVAC proposed to rely upon previously submitted 2003 study, “DCPA (Dacthal® Small-Scale Ground-Water Monitoring Study”, by Cooper, S.C. (MRID 44082601). AMVAC has reviewed the study and believes that it should be considered sufficient for addressing the current guideline requirement. A request for the DER has been made to the Agency.”

EFED Response: Based on the following two points, the dissipation half-life of DCPA cannot be determined with confidence; ***therefore EFED recommends that PRD deny the terrestrial field dissipation study waiver request for DCPA.***

(1) “Addenda to Data Evaluation Records for MRIDs 00114649, 00114652, 4168803, 41508609, and 41508610 for chlorthal dimethyl (PC Code 078701),” dated February 10, 2009. The two terrestrial field dissipation studies (MRIDs 41508609 and 41508610) were upgraded from unacceptable to supplemental because the studies provide useful information on 1) the leaching behavior of chlorthal dimethyl, tetrachloroterephthalic acid (TPA), and monomethyl tetrachloroterephthalic acid (MTP) and 2) on the degradates found in the terrestrial environment after application of chlorthal dimethyl. The deficiencies in the study are still present and the data should only be used with an understanding of the deficiencies. The deficiencies include a large variation in DCPA concentrations with time so that a dissipation half-life could not be calculated. The supplemental studies ***do not fulfill the terrestrial field dissipation guideline requirements.***

(2) “DCPA (Dacthal® Small-Scale Ground-Water Monitoring Study”, by Cooper, S.C. (MRID 44082601). The study design mandated by EPA for small-scale prospective ground-water monitoring studies does not lend itself easily in determining soil half life. Furthermore, although DCPA half-life calculations were made from soil residue samples collected from two study sites, it should be emphasized that the resulting calculations represent only rough estimates of the true half lives for DCPA.

In addition, any new field dissipation studies conducted for DCPA need to include measurements of volatilization of DCPA. DCPA has a vapor pressure ranging from 0.21-

0.33 mPa and estimated Henry's law constants ranging from 0.001042 - 2.2×10^{-6} atm- m^3 /mole, indicating it is semi-volatile. DCPA is considered non-volatile based on criteria described in Corbin *et al.* 2006; however, pesticides with vapor pressures of 0.83 and 0.024 mPa, near the vapor pressure of DCPA, have been found in remote environments, indicating that they underwent atmospheric transport and are semi-volatile (Daly *et al.* 2007; Gouin *et al.* 2004). There is evidence of atmospheric transport with detections far away from use sites, and additional information is needed.

DCPA Ecotoxicology Study Requirements:

SS-1075: Avian Inhalation

AMVAC Comment: "AMVAC is requesting a waiver for the Avian Acute Inhalation study in birds based on a lack of a potential route of exposure to birds and due to the very low toxicity to birds demonstrated for this product. DCPA's primary use is as a pre-emergent herbicide in vegetable crops - primarily onions, some cole crops and some melons. The most likely source of an inhalation exposure in birds would be driven by aerial applications. Aerial applications are currently on the DCPA labels. AMVAC proposes to remove aerial application from the label, if EPA agrees that this action could be the basis for granting a waiver. This action would be taken immediately upon EPA notification."

EFED Response: DCPA is considered to be volatile, and is frequently found at great distances from applied field locations. As such there is the potential for exposure to occur. However, EFED does agree with the proposed removal of the aerial applications from the label. If ground applications only were listed on the label, EFED would recommend that **PRD grant the waiver request for the avian inhalation study with DCPA. However, if aerial applications were to remain on the labels, or the labels did not change, EFED would recommend that PRD deny the waiver request for the avian inhalation study with DCPA.**

850.2300 Avian Reproduction (MRID 49115402; DP413329)

AMVAC Comment: AMVAC provided a written response from the laboratory director of Avian Toxicology, (Wildlife International, Ltd.) who completed the Avian Reproduction studies (MRID 47550001 and 47550002) addressing "the perceived impact of cage size in both studies." Summary tables of the reproductive performance of both control groups were attached, and it is apparent that the performance of both control groups (from both studies) met all criteria. Although there were some clinical observations of slight injury or cage mate aggression, the instances were slight and limited to a few birds and were typically of short duration. Also, the control and treated birds are housed identical, and any minor differences in environmental conditions observed would be uniform across all groups, and would not impact the interpretation of the study. A table was provided in the document that lists a compilation of recommended housing sizes for both bobwhite and mallards from various sources. Bigger may not be better when housing birds that are designed to be "as close to wild type as possible." Birds need sufficient room to stretch, but not attempt flight. Birds that are kept "as close to wild type as possible" may be more "high strung" and may be more prone to injuring themselves or their cage mate.

EFED Response: EFED appreciates the information submitted by Wildlife; it has been reviewed and considered. As per the final OSCPP 850.2300 guideline: “The Agency recognizes that minimum cage size recommendations are evolving over time. The use of a certain cage size, as with any husbandry parameter, should result in control birds with no overt signs of stress (e.g., reproductive results are within test validity elements reported in this guideline). Northern bobwhite and mallards should be housed in breeding pens or cages of adequate size conforming to good husbandry practices (see the most recent standards of good husbandry including, but not limited to, references provided in this guidance document).” Upon review of the submitted information, regarding cage size and the clinical observations of the control pens for both the Northern Bobwhite Quail and Mallard Duck; it was determined that since the control criteria for both species were met and no other major guideline deviations were affected for either species, the studies could be used to meet the guideline requirement for avian reproduction for DCPA. As a result of the submitted information, DER addendums will be created for these two studies (MRID 47550001 - Northern Bobwhite quail and 47550002 - Mallard duck). No additional studies are needed at this time for either species for DCPA. Therefore, **EFED recommends that PRD grant the waiver request for the avian reproduction study with the Northern Bobwhite Quail and Mallard Duck for DCPA.**

TPA Environmental Fate Study Requirements:

835.1240: Soil Column Leaching:

AMVAC Comment: “Soil column leaching: AMVAC proposes to rely upon previously submitted study, “DCPA (Dacthal® Small-Scale Ground-Water Monitoring Study”, by Cooper, S.C. (MRID 44082601). AMVAC has reviewed the study and believes that it should be considered sufficient for addressing the current guideline requirement. A request for the DER has been made to the Agency.”

EFED Response: Adsorption and desorption (*i.e.*, K_d) information and the small-scale ground water study indicating TPA is leaching are both already available for the degradate TPA. Based on the available information, **EFED will rely upon the submitted information, and recommends that PRD grant the waiver request for the soil column leaching study for TPA.**

835.4300: Aerobic Aquatic Metabolism

AMVAC Comment: “Aerobic aquatic metabolism: AMVAC proposes to defer this requirement until the review of this study requirement for DCPA as required by the current DCI and then to perform an ecological risk assessment of the metabolite TPA using the endpoint determined for DCPA.”

EFED Response: TPA, a major degradate, has up to a 100% conversion rate and forms as a major degradate in aerobic and anaerobic metabolism studies. As stated in the problem formulation, TPA will be included as a residue of concern with the parent DCPA for the ecological risk assessment. Given that the formation rate of TPA is up to 100%, it is critical to understand its dissipation pathways. **EFED recommends that PRD deny the waiver request to defer the data collection of TPA until DCPA studies are completed.**

835.4400: Anaerobic Aquatic Metabolism

AMVAC Comment: “Anaerobic aquatic metabolism: In the same manner that EPA has concluded that the anaerobic aquatic metabolism requirement has been fulfilled for the parent compound by relying upon EFED “Guidance for Chemistry and Management Practice Input Parameters for Use in Modeling the Environmental Fate and Transport of Pesticides” dated February 28, 2002, AMVAC proposes to meet this requirement of TPA.”

EFED Response: TPA, a major degradate, has up to a 100% conversion rate and forms as a major degradate in aerobic and anaerobic metabolism studies. As stated in the problem formulation, TPA will be included with the parent DCPA for the ecological risk assessment. Given the high conversion rate, understanding the dissipation of TPA is a critical risk assessment question. Therefore, **EFED recommends that PRD deny the waiver request to defer the data collection of TPA until DCPA studies are completed.**

835.6100: Terrestrial Field Dissipation

AMVAC Comment: “Terrestrial field dissipation: AMVAC proposed to rely upon previously submitted 2003 study, “DCPA (Dacthal® Small-Scale Ground-Water Monitoring Study”, by Cooper, S.C. (MRID 44082601). AMVAC has reviewed the study and believes that it should be considered sufficient for addressing the current guideline requirement. A request for the DER has been made to the Agency.”

EFED Response: Similar to the parent, especially because the metabolite TPA will be the final degradate, the dissipation half-life of DCPA or TPA cannot be determined with confidence from this study; **therefore EFED recommends that PRD deny the terrestrial field dissipation study waiver request for DCPA (as it would inform the TPA environmental fate profile).**

(1) “Addenda to Data Evaluation Records for MRIDs 00114649, 00114652, 4168803, 41508609, and 41508610 for chlorthal dimethyl (PC Code 078701),” dated February 10, 2009. The two terrestrial field dissipation studies (MRIDs 41508609 and 41508610) were upgraded from unacceptable to supplemental because the studies provide useful information on 1) the leaching behavior of chlorthal dimethyl, tetrachloroterephthalic acid (TPA), and monomethyl tetrachloroterephthalic acid (MTP) and 2) on the degradates found in the terrestrial environment after application of chlorthal dimethyl. The deficiencies in the study are still present and the data should only be used with an understanding of the deficiencies. The deficiencies include a large variation in DCPA concentrations with time so that a dissipation half-life could not be calculated. In addition, degradation half lives of TPA could also not be calculated. The supplemental studies **do not fulfill the terrestrial field dissipation guideline requirements.**

(2) “DCPA (Dacthal® Small-Scale Ground-Water Monitoring Study”, by Cooper, S.C. (MRID 44082601). The study design mandated by EPA for small-scale prospective ground-water monitoring studies does not lend itself easily in determining soil half life. Furthermore, although DCPA half-life calculations were made from soil residue samples collected from two study sites, it should be emphasized that the resulting calculations represent only rough estimates of the true half lives for DCPA. In addition, not enough information is gleaned for TPA as it is the final degradation product of DCPA.

TPA Ecotoxicology Study Requirements:

Aquatic Studies: 850.1025: Oyster Acute Toxicity Test (shell deposition); 850.1035: Mysid Acute Toxicity Test; 850.1075: Fish Acute Toxicity Test, Freshwater and Marine; 850.1300: Daphnid Chronic Toxicity Test; 850.1350: Mysid Chronic Toxicity Test; 850.1400: Fish Early Life-Stage Toxicity Test; 850.4400: Aquatic Vascular Plant Toxicity Test, Tiers I/II (*Lemna spp.*); and 850.5400: Aquatic Non-Vascular Plant Toxicity Test, Tiers I/II (Algal species)

AMVAC Comment: “AMVAC proposes to defer this requirement until the review of [these] study requirement[s] for DCPA as required by the current DCI and then to perform an ecological risk assessment of the metabolite TPA using the endpoint[s] determined for DCPA. Further justification provided below.”

“Within [the preliminary problem formulation for DCPA], the Agency describes an ecological risk assessment procedure that would be used in the absence of ecotoxicity data for TPA. EPA has indicated that it would use the highly conservative assumptions in assessing the ecological risk of the metabolite. AMVAC believes this can be accomplished by using the ecotoxicity endpoints associated with DCPA for TPA. The practice of using surrogate data from the parent compound for a metabolite is a practice that has been used by EPA in the past.”

EFED Response: TPA, a major degradate, has up to a 100% conversion rate and forms as a major degradate in aerobic and anaerobic metabolism studies. As stated in the problem formulation, TPA will be included as a residue of concern with the parent DCPA for the ecological risk assessment, and to conduct a risk assessment without these data would result in a highly uncertain risk assessment. 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.***

850.1730: Fish Bioconcentration

AMVAC Comment: “Fish BCF: AMVAC seeks a waiver on this study on the basis of EPA’s Ecological Effects Test Guidelines OPPTS 850.1730 testing criteria. Further justification provided below.”

“Although TPA meets the first criteria concerning its persistence in water, it is a highly water soluble compound and would be expected to predominantly partition into a water phase and demonstrate a log Pow (log of the octanol/water partition coefficient) value significantly greater than 1.0. Evidence for this partitioning behavior is evident in the adsorption/desorption studies where TPA significantly fractionates into the water phases for soils with high organic matter content.”

EFED Response: Based on the review of the information; **EFED recommends that PRD grant the waiver request for the TPA Fish Bioconcentration study.**

Terrestrial Plant Toxicity Study: 850.4100: Terrestrial Plant Toxicity, Tier I (Seedling Emergence)

AMVAC Comment: “AMVAC proposes to defer this requirement until the review of this study requirement for DCPA as required by the current DCI and then to perform an ecological risk assessment of the metabolite TPA using the endpoint determined for DCPA. Further justification provided below.”

“Within [the preliminary problem formulation for DCPA], the Agency describes an ecological risk assessment procedure that would be used in the absence of ecotoxicity data for TPA. EPA has indicated that it would use the highly conservative assumptions in assessing the ecological risk of the metabolite. AMVAC believes this can be accomplished by using the ecotoxicity endpoints associated with DCPA for TPA. The practice of using surrogate data from the parent compound for a metabolite is a practice that has been used by EPA in the past.”

EFED Response: TPA, a major degradate, has up to a 100% conversion rate and forms as a major degradate in aerobic and anaerobic metabolism studies. As stated in the problem formulation, TPA will be included as a residue of concern with the parent DCPA for the ecological risk assessment, and to conduct a risk assessment without these data would result in a highly uncertain risk assessment. EFED indicated in the problem formulation if a limited testing strategy was proposed it would be considered *in lieu* of a comprehensive data submission. To defer 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 the conducting of a limited set of toxicity tests initially for TPA; and depending on the results of these initial studies a full suite of studies may or may not be subsequently required.***

Submissions:

<u>MRID</u>	<u>Citation</u>
49115401	Freedlander, D. (AMVAC). 2013. <i>Residue, Environmental Fate, and Ecotoxicology Responses for Non-Terrestrial Animals</i> . Project Number AMV-DAC-04-13-13. Unpublished report prepared by Sponsor AMVAC Chemical Corporation. 16p.
49115402	<i>AMVAC's Request for Re-Evaluation of the Avian Reproduction Studies in the Mallard (Report Number 246-116) and Bobwhite Quail (Report Number: 246-115) with Chlorthal Dimethyl (DCPA); Wildlife International Project Number: 246-040313. Unpublished report prepared by Wildlife International for Sponsor AMVAC Chemical Corporation. 34p.</i>

49115404 Freedlander, D. (AMVAC). 2013. 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.