DATA EVALUATION RECORD

STUDY 15

CHEM 122990 Mesotrione §164-1
CAS No. 104206-82-8
FORMULATION--SC--SOLUBLE CONCENTRATE

STUDY ID 44505207
Graham, D. G., D. J. Elvira, and L. A. Wiebe. 1997. ZA1296: residue levels after treatment of bare soil - North Carolina, 1995-1996. Study Number: 1296-95-SD-01. Report Number: RR 96-083B. Unpublished study performed by Zeneca Inc., Richmond, CA; and submitted by ZENECA, Inc., Wilmington, DE.

STUDY ID 44505125
Wiebe, L. A. 1995. ZA1296: Extractability of residues from soil. Report No.: TMR 0606B. Unpublished study performed by ZENECA Inc., Richmond, CA; and submitted by ZENECA Inc., Wilmington, DE.

DIRECT REVIEW TIME = 65 Hours

REVIEWED BY:	M. K. Mahoney, M.S.	Signature:
TITLE:	Scientist	Date:
EDITED BY:	C. A. Sutton, Ph.D.	Signature:
TITLE:	Sr. Scientist/Asst. Project Manager	Date:
APPROVED BY:	P. H. Howard, Ph.D.	Signature:
TITLE:	Project Manager	Date:
ORG:	Syracuse Research Corp. Arlington, VA 22202	
TEL:	703/413-9369	

EDITED, MODIFIED AND APPROVED BY:	Alex Clem, Environmental Scientist	
ORG:	ERB III/EFED/OPP	
TEL:	703/305-5773	Richard Clem 5/03/01

CONCLUSIONS

Field Dissipation - Terrestrial

1. This study did not adequately account for the field dissipation of mesotrione on a bare ground plot of sandy loam soil in North Carolina. It does, however, provide ***supplemental*** aspects which are consistent with the laboratory findings of a relatively short residency time for mesotrione in soil.

   Although parent mesotrione "disappeared" fairly rapidly, 1) no degradates, including MNBA and AMBA which were found in laboratory studies, were detected at any sampling interval, and 2) mesotrione was not observed to leach. Furthermore, because there was no water balance during the study (or even pan evaporation data), it could not be determined if and when conditions were favorable for leaching and whether potential leached amounts of parent or degradates could have escaped detection by leaching below the maximum depth sampled during the time between sampling intervals and/or by insufficiently low detection limits in the sampled soil profile. Thus, this study presents an unresolved account of the terrestrial field dissipation of mesotrione.

2. In addition to the fundamental problems cited above, this study does not meet Subdivision N Guidelines for the partial fulfillment of EPA data requirements on terrestrial field dissipation for reasons given in the Comments section of this report. In brief, some of these reasons are the following:

   (i) application rates were not verified;

   (ii) the reported disappearance half-life of parent mesotrione was calculated incorrectly on a soil sample wet-weight basis;

   (iii) samples were excessively composited;

   (iv) the soil extraction method was most likely insufficient;

   (v) detection limits (not reported) and limits of quantitation (reported) were probably inadequate for tracking parent and degradates in the soil profile;

   (vi) storage stability data may have been inadequate.

   In spite of the many shortcomings in this and two other similarly conducted terrestrial field dissipation studies (MRIDs 44505205 and 4450206), taking all the environmental fate and ecotoxicological studies as a whole, there would be little value added to satisfactory performance of definitive dissipation studies. Therefore, ***EFED is not requiring additional terrestrial field dissipation studies at this time.*** However, the

registrant should consider the critical elements cited above and in the Comments section of this document, as these would almost always prohibit the acceptability of future study submissions and elicit requirements for new studies.

3. Mesotrione (ZA1296 4SC), broadcast applied twice (55-day interval) as a spray at nominal application rates of 0.3 lb a.i./acre and 0.2 lb a.i./acre, disappeared with an apparent registrant-calculated half-life of 2 days following the second application on a bare ground plot of Norfolk sandy loam soil located near Whitakers, NC. However, this half-life is subject to the limitations cited above and in the Comments section.

Following the *first application*, the parent compound was initially detected in the 0- to 6-inch depth at 0.089 mg/kg, decreased to 0.060 mg/kg by 7 days, and was last detected at 0.014 mg/kg at 21 days. The *parent compound was not detected below the 0- to 6-inch depth. The degradates MNBA and AMBA were not detected at any sampling interval or depth.* Following the *second application*, the parent compound was initially detected at 0.050 mg/kg, decreased to 0.012 mg/kg by 4 days, and was not detected at 6, 12, or 26 days posttreatment. The *parent compound was not detected below the 0- to 6-inch depth. The degradates MNBA and AMBA were not detected at any sampling interval or depth.*

METHODOLOGY

Mesotrione (ZA1296 4SC) was broadcast applied twice as a spray at nominal application rates of 0.3 lb a.i./acre and 0.2 lb a.i./acre (at a 55-day interval; total nominal application of 0.5 lb a.i./acre) onto a bare ground plot (66.5 × 100 ft, with three equivalent size subplots of 13.3 × 100 ft; ≤1% slope; pp. 10, 12; Appendix A, p. 29) of Norfolk sandy loam soil (0-8 inch depth, 71.9% sand, 17.8% silt, 10.2% clay, 0.87% organic matter, pH 5.8, CEC 2.3 meq/100 g; p. 11) near Whitakers, NC (Nash County). An untreated bare ground plot (13.3 × 100 ft) was located 20 feet from the treated plot. Applications were made using a tractor-mounted boom sprayer (Appendix A, pp. 37, 38). After the first application, the test compound was incorporated into the soil to a depth ≤3 inches using a rotovator. A three-year plot history indicated no prior pesticide use (p. 12). Bare ground conditions were maintained throughout the study period using three applications of paraquat (0.75-1.25 lb a.i./acre; Appendix A, p. 39). The mean depth to the water table was >5 feet (p. 10). Precipitation was supplemented with irrigation; total water input (21.8 inches) was 137% of the 30-year mean annual precipitation for the months April through July (reviewer-calculated; Appendix A, p. 36; see Comment #10). Environmental data were collected on-site (p. 11). Pan evaporation data were not reported. There was no water balance.

Soil samples from the treated and control plots were collected prior to the first application; at 0, 3, 6, 20, and 54 (one day prior to the second application) days after the first application; and at 0, 4, 6, 12, and 26 days following the second application (Table

III, p. 23; see Comment #9). At each sampling interval, five soil cores were collected from each treated subplot (total of 15 cores) and 10 soil cores were collected from the control plot (p. 13). A three-phase sampling was performed using a tractor-mounted hydraulic probe fitted with plastic butyrate liners to collect a 0- to 6-inch depth sample (2-inch i.d.; Appendix A, p. 30, 33), a 6- to 24-inch depth sample (1.3-inch i.d.; Appendix A, p. 31), and a 24- to 42-inch depth sample (1.3-inch i.d.; Appendix A, p. 32); samples collected at 0 days posttreatment were to depth of 6 inches and samples collected at 4 and 7 days posttreatment were taken only to a depth of 24 inches. Samples were shipped frozen to the analytical lab (p. 14; Appendix A, p. 44). Samples were stored frozen for 42-96 days prior to analysis (p. 16; Appendix B, pp. 56-58). Soil samples were sectioned into 6-inch increments and composited by depth and subplot (see Comment #4). Samples collected from the 36- to 42-inch depth were discarded.

Soil samples were analyzed for the parent mesotrione and the degradates 4-(methylsulfonyl)-2-nitrobenzoic acid (MNBA) and 2-amino-4-(methylsufonyl)-benzoic acid (AMBA; p. 9). The soil samples were extracted by shaking with 0.05 M NH_4OH and then centrifuged (p. 15; Appendix C, pp. 60-68). The supernatant was decanted and acidified to pH 3.5-4.0 by shaking with formic acid. The samples were centrifuged and the supernatant was filtered (0.2 or 0.45 µm) and analyzed for the degradate AMBA by reverse-phase HPLC (Phenomenex Prodigy C18 column) using a mobile phase of 6 mM ammonium acetate:formic acid (100:0.30, v:v; System A):acetonitrile:water (95:5, v:v; System B); OR by reverse-phase HPLC (Keystone Prism RP column) using a mobile phase of 50 mM ammonium acetate:formic acid (100:0.30, v:v; System A): acetonitrile:water (95:5, v:v; system B); OR by reverse-phase HPLC (Phenomenex Ultracarb C18 column) using a mobile phase of water:formic acid (100:0.1, v:v; System A):acetonitrile:formic acid (95:5, v:v; system B) with fluorescence (424 nm) detection; the mobile phase gradient in all cases was 100:0 to 30:70 to 5:95 (v:v, A:B; Appendix C, p. 65). The limit of quantitation for HPLC was 0.01 µg/g. Samples were co-chromatographed with a reference standard of AMBA. Separate eluate fractions containing the parent and the degradate MNBA were collected during HPLC analysis. The eluate fractions were evaporated to dryness and the parent and MNBA were converted to AMBA for quantitation by shaking and heating with $SnCl_2$ in 2 *N* HCl. The solutions were cleaned by solid phase extraction (SPE; C18 Column) and analyzed for AMBA by HPLC as previously described; samples were co-chromatographed with a reference standard of the parent and a reference standard of MNBA that was converted to AMBA as previously described for the test samples. A confirmatory method was not utilized.

The application rate was not confirmed using monitoring pads or a similar method. The concentration of the parent in soil immediately following the first and second applications was 65% and 66% of the expected, respectively, based on the nominal application rates (p. 18; Figures 1-2, p. 24).

In a concurrent recovery study, respective mean recoveries (± CV; p. 16) of the parent compound, MNBA, and AMBA from untreated control soil fortified at 0.01-0.20 ppm, 0.01-0.05 ppm, and 0.01 ppm, respectively, were 94.3 ± 11.6%, 94.7 ± 9.4%, and 97.0 ± 5.3%, respectively (Table I, p. 21).

In a frozen storage stability study, soil samples were fortified separately at 0.1 ppm with the parent, MNBA and AMBA, and placed in frozen storage for up to 6 months (Table II, p. 22; see Comment #7). Mean corrected recoveries (reviewer-calculated; see Comment #8) of the parent were 109-153% following 0-1 month of frozen storage, decreased to 80% after 3 months of storage, and were 88% after 6 months of frozen storage. Mean corrected recoveries of MNBA were 87-92% following 0 to 6 months of frozen storage, with no clear pattern of decline. Mean corrected recoveries of AMBA were 91% following 0-1 month of frozen storage, decreased to 83% after 3 months of storage, and were 76% after 6 months of frozen storage.

MRID 44505125 Soil Extraction Method

In an extraction efficiency study, soil samples from a field dissipation study (1296-93-SD-02; MRID not reported) containing residues of mesotrione were extracted one, two, or three times with 0.05 M NH_4OH, followed by centrifugation (p. 8). Control samples and samples fortified with the parent at 0.2 ppm were extracted as described above. The extracts were acidified (formic acid) and analyzed for the degradate AMBA by HPLC (method not reported); eluent fractions were collected at times that corresponded to the retention times of mesotrione and MNBA. Eluent fractions were analyzed for mesotrione and MNBA following conversion to AMBA. Mean recoveries of mesotrione from soil samples subject to one, two, and three extractions were 87%, 96%, and 100% of the amounts recovered from soils following three extractions, respectively (Table I, p. 12; see Comment #11). Mean recoveries of MNBA from soil samples subject to one, two, and three extractions were 101%, 107%, and 100% of the of the amounts recovered from soils following three extractions, respectively. Mean recoveries of AMBA from soil samples subject to one, two, and three extractions were 86%, 98%, 100% of the amounts recovered from soils following three extractions, respectively. In a separate method validation study, control soil samples were fortified with the parent compound, MNBA, and AMBA at 0.005-0.2 ppm, respectively; respective recoveries were 82%, 76%, and 95% following three extractions.

DATA SUMMARY

Mesotrione (ZA1296 4SC), broadcast applied twice (55-day interval) as a spray at nominal application rates of 0.3 lb a.i./acre and 0.2 lb a.i./acre, disappeared with a registrant-calculated half-life of 2 days following the second application on a bare ground plot of Norfolk sandy loam soil located near Whitakers, NC (p. 17; Figure 2, p. 24; see

Comment #9). However, the half-life was calculated using data reported on a wet-weight basis and such data cannot be validly compared over time (see Comment #2). Following the first application, the parent compound was initially detected in the 0- to 6-inch depth at 0.089 mg/kg, decreased to 0.060 mg/kg by 7 days, and was last detected at 0.014 mg/kg at 21 days (p. 8; Table III, p. 23). The parent compound was not detected below the 0- to 6-inch depth. The degradates MNBA and AMBA were not detected at any sampling interval or depth.

Following the second application, the parent compound was initially detected at 0.050 mg/kg, decreased to 0.012 mg/kg by 4 days posttreatment, and was not detected at 6, 12, or 26 days posttreatment (p. 8; Table III, p. 23). The parent compound was not detected below the 0- to 6-inch depth. The degradates MNBA and AMBA were not detected at any sampling interval or depth.

COMMENTS

1. The study failed to adequately demonstrate the field dissipation of the test compound. Although the parent disappeared/dissipated fairly rapidly, the putative degradates from laboratory studies, MNBA and AMBA, were not detected at any sampling intervals and the parent was not observed to leach. MNBA was a major degradate (>10% of the applied radioactivity) detected at maximums of 0.049 ppm in an aerobic soil metabolism (sandy loam) study (MRID 44505208); AMBA was a minor degradate. The reviewer noted, however, that in an aerobic soil metabolism study of cyclohexanedione ring-labeled [2-^{14}C]mesotrione (MRID 44373730), evolved $^{14}CO_2$ accounted for 2.1% of the applied radioactivity at 1 day, 38.9% at 15 days, and 82.6% at 180 days posttreatment.

   It is further noted, however, that the analytical methods utilized in several of the submitted aerobic soil metabolism studies (e.g. MRID 44373731) were considered to be inadequate for the determination of the parent and degradates, as concentrations of unextracted residues were high and parts of the analytical method, as reported, were of questionable validity. It is likely that similar methodology problems hindered the demonstration of the dissipation of the parent in the current study; especially since there was but one extraction step and only with 0.05M NH_4OH in this study, whereas in numerous lab studies it was demonstrated with aged samples that more extraction steps combined with the use of organic solvents significantly increased yields of parent and degradates. (Also see Comment #11). The issue of adequacy of extraction will be discussed further in the EFED fate assessment of the new chemical review document for mesotrione.

2. The reported half-life was determined using data that were reported on a wet-weight basis and were obtained from soil samples which were excessively composited prior to analysis (p. 17; also see Comments #4, 9). Because the moisture in the soil samples would not likely be constant between samples, the resulting concentration data may not be validly

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compared over time, as a dilution or concentration effect may occur. All data should be reported on a dry-weight basis (corrected for moisture content). The study authors stated that "measured moisture contents of the 0- to 6-inch samples ranged from 8 to 14%" (p. 17). With these relatively small differences in soil moisture, the reviewer notes that failure to correct for moisture has only a minor effect on final results.

The reviewer also notes that the half-life appeared to be calculated using two data points; generally, at least four points (over time) are necessary for a valid calculation of the half-life, and replicate data should be utilized. The important point, however, is that the degradation of the parent was very rapid, with a reported half-life of only 2 days.

3. Water balance data (or even pan evaporation data) were not provided. Such data are necessary to assess whether daily fluctuations in soil moisture were sufficient to facilitate leaching of the test substance. For interpretative purposes, these daily data should be plotted on the same graph as chemical dissipation data. The reviewer noted that total water input during June, 1995 (the period 15 days prior to the second application through 15 days posttreatment) was approximately 299% of the 30-year mean annual precipitation for the month of June (11.6 inches *vs.* 3.9 inches; Appendix A, p. 36).

4. Soil samples were excessively composited prior to analysis, precluding a determination of variability between replicates. At each sampling interval, five soil cores were collected from each of the three treated subplots (total of 15 cores), sectioned into 6-inch increments, and composited by depth and subplot (three composites per depth). Immediately following the first and second applications and at 3 days following the first application, each of the three composites was analyzed for the parent and degradates. For all other sampling intervals, the three composites were combined into a larger single composite for analysis (p. 14; Table III, p. 23). Subdivision N Guidelines require that a minimum of fifteen soil cores with a minimum of three composites be analyzed in order to provide a measure of the statistical variability of the treated subplots. Irrespective of Guidelines requirements/recommendations, it is scientifically appropriate to determine the size of the surface area to be sampled in relation to the number of samples and replications necessary to capture the inherent sample variability in all studies.

5. Samples were not collected randomly. Soil cores were collected from transects extending diagonally across the subplots in a systematic fashion (p. 13). The study authors stated that this sampling plan was designed to minimize variability between subplots at each sampling interval. Although Subdivision N Guidelines require that soil cores be collected randomly in order to accurately represent variability in the test plots and to minimize variability among the data points, this reviewer agrees with the study authors, and believes that the judicious use of such transects tends to eliminate application artifacts and more efficiently captures sample variability.

6. The application rate was not verified by monitoring pads or, preferably, by collection of a

sufficiently large number of large area surface soil samples (see also related Comment 5 above). Recoveries of the parent from soil, were 65% and 66% of the expected (based on the target application rate) immediately following the first and second applications, respectively (p. 18; Figures 1, 2, p. 24).

7. Frozen storage stability data may not have been adequate. It was unclear whether the soil samples utilized were from the test site; the reviewer noted that storage stability data were identical to data reported in terrestrial field dissipation studies conducted in Illinois, and Mississippi (MRIDs 44505205 and 44505206). Subdivision N Guidelines require that storage stability studies be conducted with samples from the test site which have been fortified separately with the parent compound and its degradates and stored for a duration equal to the longest interval for which the test samples were stored. Clarification by the registrant is appropriate.

8. The study authors reported frozen storage stability data in Table II (p. 22); however, data were not corrected for concurrent recoveries. Therefore, the reviewer calculated corrected storage stability data by dividing individual storage stability recoveries by their respective concurrent recoveries. The reviewer reported mean corrected recoveries (reviewer-calculated) in the Data Summary section of this DER. The reviewer used the concurrent recovery values (designated "0^2 day") that preceded the storage stability data for the respective intervals. For time 0, the first value (of the three reported as "0 day") was assumed to be the corresponding "0^2" value for that interval; the reviewer assumed that the apparently incorrect entry was a typographical error. Clarification by the registrant may be necessary.

9. The reviewer noted a discrepancy between the results reported in the text and those reported in the half-life graphs. The parent was detected in the soil at only two sampling intervals following the second application (0 and 4 days; Table III, p. 23). The sampling interval (day 5) corresponding to the second data point in Figure 2 does not agree with the sampling interval for which data were reported (p. 24). It is unclear which values (for days) were utilized in the half-life calculation. Clarification by the registrant is necessary. The nominal sampling intervals were reported as 0, 4, 7, 21, and 55 days after the first application and 0, 5, 7, 13, 27, and 91 days following the second application (p. 8). The actual sampling intervals were 0, 3, 6, 20, and 54 days after the first application and 0, 4, 6, 12, and 26 days following the second application (Table III, p. 23). The reviewer reported the actual sampling intervals in the test of this DER.

10. The study authors stated that rainfall and irrigation were 32.2 inches and 0.5 inches, respectively (p. 11), and that rainfall plus irrigation were 137% of the 30-year mean annual precipitation (pp. 11, 19); however, the reviewer noted that total water input was determined by the study authors for the months April through August, 1995, and compared to the long-term precipitation data for the same months (Appendix A, p. 36). The reviewer-calculated total water input (21.8 inches) for the months when the study

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was actually conducted (April through July, 1995; p. 8) was approximately 139% of the 30-year mean annual precipitation during those months.

11. Method validation data were presented in MRIDs 445058126, 44505127, and 44505210; results indicated that the method was adequate for the determination of *freshly spiked* mesotrione, MNBA, and AMBA in soil. In the extraction efficiency study (MRID 44505125), recoveries of the parent, MNBA, and AMBA from soils subject to one, two, or three extractions were calculated as percentages of the amount of each respective compound recovered after three extractions (Table I, p. 12); hence, recoveries of each compound were designated "100%" following three extractions. However, this method was inadequate for the determination of extraction efficiency since the amount of each compound initially present in the samples was unknown and, therefore, it can not be concluded that three extractions were adequate for removal of each compound for subsequent quantitation. The reviewer notes that in the extraction efficiency study (MRID 44505125), recoveries of the parent and AMBA from soils subject to one extraction were only 87% and 86%, respectively, of the amounts recovered from the soils following three extractions (Table I, p. 12); recoveries of MNBA following one extraction were 101%. Additionally, method validation data included in the extraction efficiency study indicated that the analytical method utilizing three extractions only resulted in recovery of 82% of the applied from samples fortified with the parent; recoveries of MNBA and AMBA from separately fortified samples were 76% and 95%, respectively. In the current study, a single extraction was utilized. Comment 1 also addresses the issue of the inadequacy of extraction.

12. Terrestrial field dissipation studies of mesotrione were also conducted on bare ground plots in Illinois (MRID 44505205) and Mississippi (MRID 44505206).

13. The total application rate utilized (0.5 lb a.i./acre) was stated to be the maximum label rate for multiple applications. The study authors stated that the first pesticide application (0.3 lb a.i./acre) was applied to represent a pre-plant incorporated application; the second application (0.2 lb a.i./acre) was applied to represent a post-emergence application (p. 9). These values compare with the currently proposed maximum total rate of 0.43 lb a.i./acre.

14. The study authors inadvertently reported the first application rate as 3.0 lb a.i./acre on page 9; the first application of mesotrione was at the nominal concentration of 0.3 lb a.i./acre (p. 12; Appendix A, p. 37). This was also evident from the total application rate (0.5 lb a.i./acre) reported on page 9.

15. The limit of quantitation was reported for HPLC; but the limit of detection was not. Both limits of detection and quantitation should be reported to allow the reviewer to evaluate the adequacy of the method for the determination of the test compound and its degradates at potentially very low concentrations deeper in the soil profile and at later times.

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16. The reviewer noted that the treated subplots were true replicate plots separated by 13.3-foot buffer zone (Appendix A, p. 29).

17. The reviewer noted a discrepancy between reported application recovery values. The concentrations of the parent in soil immediately following the first and second applications were 65% and 66% of the expected, respectively, based on the nominal application rates (Figures 1, 2, p. 24); recoveries were inadvertently reported as 65% and 69%, respectively, in Appendix B (p. 47).

18. The study authors did not report the mean parent concentration at each sampling interval in the results section of the study; instead, mean data were included only in the summary (p. 8). All data (including individual replicate data and their means) should be reported in the results section (i.e., in the main text) of the study.

MP 44505207

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