

DATA EVALUATION RECORD

STUDY 16

CHEM 122990 Mesotrione §164-1
CAS No. 104206-82-8
FORMULATION--15--SOLUBLE CONCENTRATE

STUDY ID 44505206

Graham, D. G., D. J. Elvira, and L. A. Wiebe. 1997. ZA1296: Residue levels after treatment of bare soil - Mississippi, 1995-1996. Study No.: 1296-95-SD-01. Report No.: RR 96-082B. Unpublished study performed by ZENECA Inc., Richmond, CA; and submitted by ZENECA Inc., Wilmington, DE.

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CONCLUSIONS

Field Dissipation - Terrestrial

1. This study did not adequately account for the field dissipation of mesotrione on a bare ground plot of loam¹ soil in Mississippi. 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, precluding a determination of variability between replicates;
 - (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;
 - (vii) storage stability data may have been inadequate for parent and degradates.

In spite of the many shortcomings in this and two other similarly conducted terrestrial field dissipation studies (MRIDs 44505205 and 4450207), taking all the environmental

¹See Comment 12 regarding the textural classification of the Bosket soil.

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 (7-week interval) as a spray at nominal rates of 0.3 lb a.i./acre and 0.2 lb a.i./acre, disappeared with a registrant-calculated, apparent half-life of 14 days ($r^2 = 0.91$) following the second application on a bare ground plot of Bosket loam¹ soil located near Leland, MS. However, the calculated half-life is subject to interpretation based on the limitations cited above and in the Comments section.

Following the *first application*, mesotrione was initially present in the 0- to 6-inch depth at 0.10 mg/kg, was a maximum of 0.13 mg/kg at 6 days posttreatment, decreased to 0.053 mg/kg by 20 days, and was 0.01 mg/kg at 49 days (p. 8); mesotrione was not detected below the 0- to 6-inch depth. The degradates MNBA and AMBA were not detected at any sampling intervals or depths following the first application. Following the *second application*, mesotrione was initially present in the 0- to 6-inch depth at 0.066 mg/kg, was 0.042 mg/kg from 3 to 8 days posttreatment, was 0.032 mg/kg at 20 days, and was not detected by 35 days (the next sampling interval); mesotrione was not detected below the 0- to 6-inch depth. As was the case after the first application, *the degradates MNBA and AMBA were not detected at any sampling intervals or depths following the second application.*

METHODOLOGY

Mesotrione (ZA1296 4SC) was broadcast applied twice (7-week interval) as a spray at nominal rates of 0.3 lb a.i./acre and 0.2 lb a.i./acre (total application rate of 0.5 lb a.i./acre) onto a bare ground plot (66.5 x 100 ft with three subplots of 13.3 x 100 ft; 0.05 to 0.15% slope; pp. 10, 12; Appendix A, p. 30) of Bosket loam soil (51% sand, 36.4% silt, 12.7% clay, 0.63% organic matter, pH 6.0, CEC 6.4 meq/100 g soil; p. 11) near Leland, Mississippi (Washington County). Applications were made using a tractor-mounted sprayer with eight nozzles (Appendix A, pp. 38, 39); the pesticide was incorporated into the soil to a depth of ≤ 3 inches following the first application. An untreated control plot (13.3 x 100 ft) was located 230 feet from the treated plots. Plots were treated four times with Gramoxone Extra[®] (paraquat; 2.0-3.0 pt/acre), once with Gramoxone Extra[®] (3.0 pt/acre) plus Surfoil (1.0%) and once with Select[®] (clethodim, 10.0 oz/acre) to maintain bare ground conditions (Appendix A, p. 40). A three-year plot history indicated no prior pesticide use (p. 12). The seasonal depth to the water table was 8-20 feet (p. 10). Environmental data were collected on-site (p. 11). Precipitation was

supplemented with irrigation; total water input (27.3 inches) was approximately 130% (reviewer-calculated) of the 30-year mean annual precipitation during the study period (Appendix A, p. 37; see Comment #13). Pan evaporation data were not reported. There was no water balance.

Soil samples from the treated and control plots were collected one day prior to the first application; at 0, 3, 6, 20, and 49 days following the first application (the day of the second application); and at 0, 3, 8, 20, 35, and 92 days following the second application (Appendix A, pp. 41-44; see Comment #5). At each sampling interval, five soil cores were collected from each treated subplot (15 total) and ten soil cores were collected from the control plot (p. 13). A 0- to 6-inch depth sample (2-in i.d.), a 6- to 24-inch depth sample (1.25-in i.d.), and a 24- to 42-inch depth sample (1.25-in i.d.) were collected using a tractor-mounted, zero-contamination coring device with a plastic butyrate liner (Appendix A, pp. 31-34); samples collected immediately following the first application were only taken to a depth of 0- to 6-inches and samples collected at 3 and 6 days following the first application were only taken to a depth of 0- to 24-inches. Samples were shipped frozen to the analytical laboratory and stored frozen until processing (p. 14). Soil samples were sectioned into 6-inch increments and composited by depth (see Comment #4). Samples collected from the 36- to 42-inch depth were discarded. Field samples were stored frozen for 48-161 days prior to analysis (p. 16; Appendix B, pp. 55-60).

Soil samples were analyzed for parent mesotrione (ZA1296) and the degradates 4-(methylsulfonyl)-2-nitrobenzoic acid (MNBA) and 2-amino-4-(methylsulfonyl)-benzoic acid (AMBA; pp. 9-10). Subsamples were extracted by shaking with 0.05 M ammonium hydroxide and centrifuged (p. 15; Appendix C, pp. 62-70). An aliquot of the extract was transferred to a centrifuge tube and acidified (pH 3.5-4.0; formic acid). The extract was shaken, centrifuged and syringe filtered (0.2 μm or 0.45 μm). The extract was analyzed for 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 for all systems was 100:0 to 30:70 to 5:95 to 100:0 (A:B; v:v; Attachment 1, p. 67). The limit of quantitation was 0.01 mg/kg. Samples were co-chromatographed with a reference standard of AMBA. Individual fractions of the parent and degradate MNBA were collected based on retention times of standards; parent and MNBA were converted to AMBA prior to HPLC analysis. To convert the parent to AMBA, the eluent was evaporated under nitrogen and reconstituted in 6% H₂O₂. Aliquots of catalase enzyme were added to the eluent until peroxide was no longer detected in the eluent; peroxide test strips were used to measure peroxide. Aliquots of 2

N HCl plus 60 mg/mL of SnCl₂ were added to the eluent. The solution was heated, cooled to room temperature, diluted with distilled water and applied to a C₁₈ solid phase extraction (SPE) column. The column was eluted with 0.2% formic acid in acetonitrile. The eluent was evaporated to dryness and reconstituted with 0.2% formic acid in water prior to analysis by HPLC as previously described. Chromatographs were compared to those of reference standards. To convert MNBA to AMBA, the eluent fraction containing MNBA was diluted with distilled water, 2 *N* HCl plus 60 mg/mL SnCl₂ was added to the eluent fraction and the eluent was heated then cooled; the eluent was diluted with an aliquot of distilled water, cleaned by SPE and analyzed by HPLC as previously described. A confirmatory method of analysis was not performed.

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 85% and 69% of the expected based on the nominal application rates (p. 18; Appendix B; p. 48).

Mean concurrent recoveries (\pm C.V.) from control soil samples fortified with mesotrione (0.01-0.2 ppm), MNBA (0.01-0.05 ppm), and AMBA (0.01 ppm) were $88.9 \pm 11.5\%$, $97.7 \pm 8.6\%$, and $96 \pm 7.2\%$, respectively (Table I, p. 21).

In a frozen storage stability study, soil samples were fortified separately at 0.1 mg/kg with mesotrione, MNBA, and AMBA and placed in frozen storage for up to 12 months (Table II, p. 22; see Comment #7). Reported recoveries are reviewer-calculated means of two replicates (see Comment #8). Mesotrione appeared to be relatively stable in frozen storage, but data were variable and precluded a definitive conclusion of stability; mean corrected recoveries of mesotrione were initially (day 0) 109.5%, were 153% following 1 month, and were 80-89% following 3 to 12 months of storage. The degradate MNBA may have been unstable in frozen storage following 6 months; mean corrected recoveries of MNBA were 87-91.5% following 0 to 6 months and were 77% following 12 months of storage. The degradate AMBA was not stable in frozen storage following 3 months; mean corrected recoveries of AMBA were 90.5-91.5% from 0 to 1 month, decreased to 82.5% following 3 months and 76% following 6 months, and were 64.5% following 12 months of storage.

DATA SUMMARY

Mesotrione (ZA1296 4SC), broadcast applied twice (7-week interval) as a spray at nominal rates of 0.3 lb a.i./acre and 0.2 lb a.i./acre, dissipated with a registrant calculated half-life of 14 days ($r^2 = 0.91$; Figure 2, p. 25; see Comments #1 and 9) following the second application on a bare ground plot of Bosket loam soil located near Leland, MS. However, results of this study are subject to the limitations cited in the Conclusions section above and/or in the Comments section below. The half-life was also calculated

using data reported on a wet-weight basis, and the data cannot be validly compared over time (p. 17).

Following the first application, mesotrione was initially present in the 0- to 6-inch depth at 0.10 mg/kg, was a maximum of 0.13 mg/kg at 6 days posttreatment, decreased to 0.053 mg/kg by 20 days posttreatment, and was 0.01 mg/kg at 49 days posttreatment (p. 8; Table III, pp. 23, 24); mesotrione was not detected below the 0- to 6-inch depth. The degradates MNBA and AMBA were not detected at any sampling intervals or depths following the first application.

Following the second application, mesotrione was initially present in the 0- to 6-inch depth at 0.066 mg/kg, was 0.042 mg/kg from 3 to 8 days posttreatment, was 0.032 mg/kg at 20 days posttreatment, and was not detected by 35 days posttreatment (the next sampling interval; p. 8; Table III, p. 24); mesotrione was not detected below the 0- to 6-inch depth. The degradates MNBA and AMBA were not detected at any sampling intervals or depths following the second application.

COMMENTS

1. The study failed to adequately demonstrate the field dissipation of the test compound. Although the parent dissipated fairly rapidly, the degradates 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 a maximum of 0.049 ppm in an aerobic soil (sandy loam) metabolism study (MRID 44505208); AMBA was a minor degradate. The reviewer noted, however, that in an aerobic soil metabolism study of cyclohexanedione ring-labeled [2-¹⁴C]mesotrione (MRID 44373530), evolved ¹⁴CO₂ accounted for 2.1% of the applied radioactivity at 1 day, 38.9% by 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 44373531) 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 accuracy. (Also see Comment #14.) It is likely that similar methodology problems hinder the interpretation of the dissipation of the parent in the current study; especially since there was but one extraction step and only with 0.05M NH₄OH 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 #14). The issue of adequacy of extraction will be discussed further in the EFED fate assessment of the new chemical review document for mesotrione.

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2. The reported half-life was determined using data which were reported on a wet-weight basis and which 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 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 15%" (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.
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 May, 1995 (the period 16 days prior to the second application through 15 days posttreatment) was only approximately 75% of the 30-year mean annual precipitation for the month of May (4.4 inches vs. 5.9 inches; Appendix A, p. 37).
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. 15; Table III, pp. 23, 24). Subdivision N Guidelines require that a minimum of 15 soil cores with a minimum of three composites be analyzed in order to provide a measure of the statistical variability of the treated plots. 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 85% and 69% of the expected immediately following the first and second applications, respectively (p. 18; Appendix B; p. 48).
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 for terrestrial field dissipation studies conducted in Illinois, and North Carolina (MRID's 44505205 and 44505207, respectively). 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 compounds 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.
 9. The registrant-calculated half-life of the parent compound following the second application (14 days; $r^2 = 0.91$; Figure 2, p. 25) is questionable because sampling intervals may have been inadequate. Following the second application, mesotrione was initially present in the 0- to 6-inch depth at 0.066 mg/kg, was 0.042 mg/kg from 3 to 8 days, was 0.032 mg/kg at 20 days (the next sampling interval), and was not detected by 35 days posttreatment (the next sampling interval). The reviewer noted that the registrant-calculated half-lives (Figures 1, 2; p. 25) are based on an exponential fit of the data.
 10. The total application rate utilized (0.5 lb a.i./acre) was stated to be the highest recommended label rate for multiple applications. This value compares with the currently proposed maximum total rate of 0.43 lb a.i./acre.
 11. The reviewer noted that all data points in Figures 1 and 2 (p. 25) did not appear to correspond to the reported sampling intervals. The study authors indicated throughout the study that samples were collected one day prior to the first application; at 0, 3, 6, 20, and 49 days following the first application (the day of the second application); and at 0, 3, 8, 20, 35, and 92 days following the second application. The study authors did not address the discrepancy between the reported sampling intervals and those presented in the figures. Clarification by the registrant may be necessary.
 12. The study authors stated that the test soil was in the Bosket soil series and is a very fine sandy loam to silt loam over clay (p. 10). However, based on the percentages of sand, silt and clay present in the 0- to 6-inch soil depth, the reviewer determined that the soil at the

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field site was loam; the soil classification determined by the reviewer was reported in this DER.

13. The study authors stated that rainfall and irrigation were 23.4 inches and 3.9 inches, respectively (p. 11), and that rainfall plus irrigation were 103% 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 long-term precipitation data for the months March through August. Additionally, the reviewer noted that "trial irrigation" and "long-term" precipitation sums reported in Appendix A (p. 37) were incorrectly calculated. The reviewer-calculated total water input for the months April through August, 1995 (28.0 inches) was approximately 130% of the 30-year mean annual precipitation during those months. The first pesticide application was applied on March 28, 1995 and the last samples were collected on August 16, 1995.
14. Method validation data were presented in MRID's 44505126, 44505127, and 44505210; results indicated that the method was adequate for the determination of *freshly spiked* mesotrione, MNBA, and AMBA in soil. The reviewer notes, however, that in an extraction efficiency study (MRID 44505125) in which field samples were extracted one to three times, recoveries of the parent and AMBA were only 87% and 86%, respectively, of the amounts recovered from the soils following three extractions; 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 still only resulted in a 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% of the applied. In the current study, only a single extraction was utilized. Comment 1 also addresses the issue of the inadequacy of extraction.
15. The study authors stated that additional terrestrial field dissipation studies were conducted on bare ground plots in Illinois (MRID 44505205) and North Carolina (MRID 44505207; p. 8).
16. 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 test method for the determination of the test compound and its degradates at potentially very low concentrations deeper in the soil profile and at later sampling times.
17. The reviewer noted that the treated subplots were true replicate subplots separated by 13.3-ft buffer zones (Appendix A, p. 30).

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Pages 10 through 19 are not included in this copy.

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