DATA EVALUATION RECORD

STUDY 6

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REVIEWED BY:	M. T. Holdsworth, M.S.	Signature:
TITLE:	Scientist	Date:
	M. K. Mahoney, M.S.	
	Scientist	
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

5/3/01

CONCLUSIONS

Metabolism - Aerobic Soil

1. This study is ***acceptable*** and ***partially satisfies data requirements*** for aerobic soil metabolism. It provides useful information on metabolism in 13 soils covering six textural classifications: clay loam, silty clay loam, silt loam, loamy sand, loam, and sandy loam. However, the presence of high concentrations of unextracted [^{14}C]residues by day 7 (for each soil except the silty clay loam soil #742 from IL) and by day 14 for all soils (including soil #742) indicates that the analytical method, specifically extraction, may not have been adequate (see comment 1 in the Comments section); thus, without other data, the apparent half-lives would be open to interpretation, and there is a degree of uncertainty about the nature and identity of some transformation products. In spite of this and other discrepancies noted in the Comments section of this report, this study, in conjunction with several other aerobic metabolism studies (and other fate studies) submitted for mesotrione, is part of a consistent picture of metabolic behavior in aerobic soil. ***In combination with results from other studies, data requirements for aerobic soil metabolism are satisfied.***

2. The registrant should carefully consider the critical elements in the Comments section. There were *numerous* unnecessary departures from standard Guideline practices which, in many instances, would vitiate future study results. For example, the reviewer could not confirm that the samples were incubated in darkness (comment 5). Additionally, only single samples were incubated and removed for analysis at each sampling interval for each soil (comment 2). However, in this case, single values at each interval for 13 soils far outweighs duplicate analysis for the minimally required one soil. ***The Agency applauds the use of 13 test soils.***

3. Uniformly phenyl ring-labeled [^{14}C]mesotrione, at a nominal application rate of 0.6 ppm (wet-weight basis; rates varied from 0.60 to 0.85 ppm on a dry-weight soil basis), degraded with calculated first-order half-lives of **22.0 days** ($r^2 = 0.98$) in clay loam soil (#721) from Iowa; **10.6 days** ($r^2 = 1.0$) in silty clay loam soil (#722) from Iowa; **16.6** days ($r^2 = 0.98$) in silt loam soil (#723) from Illinois; **25.9 days** ($r^2 = 0.96$) in loamy sand soil (#724) from Nebraska; **8.0 days** ($r^2 = 0.97$) in loam soil (#725) from Kansas; **24.1** days ($r^2 = 0.92$) in clay loam soil (#727, there is no #726) from Indiana; **8.5 days** ($r^2 = 0.98$) in sandy loam soil (#728) from Indiana; **12.9 days** ($r^2 = 1.0$) in silt loam soil (#729) from Wisconsin; **19.1 days** ($r^2 = 0.91$) in clay loam soil (#730) from Ohio; **14.4 days** ($r^2 = 1.0$) in silty clay loam soil (#731) from Missouri; **15.8 days** ($r^2 = 0.97$) in silty clay loam soil (#732) from South Dakota; **31.5 days** ($r^2 = 0.94$) in silty clay loam soil from Illinois ("low" pH soil #741); and **8.2 days** ($r^2 = 0.99$) in silty clay loam soil from Illinois ("high" pH soil #742) adjusted to 100% of 0.33 bar moisture content and incubated at 25 ± 2°C for up to 42 days. However, the presence of high concentrations of unextracted [^{14}C]residues by day 7 (for each soil except the silty clay loam soil from IL, soil #742)

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and by day 14 (for soil #742) indicates that the analytical method may not have been adequate; therefore, without data from other studies, the half-lives would be subjective. Also, the half-life of the parent in the Illinois silty clay loam soil (soil #741) is of questionable validity since it was determined beyond the scope of the observed data.

All data designated below as percentages of the applied represent percentages of the nominal application. Degradate data are reported in parent equivalents.

In the clay loam soil from Iowa (soil #721), the parent compound was initially present at 86.4% of the applied radioactivity, decreased to 49.8% by 14 days and 41.0% by 21 days, and was 35.1% at 28 days posttreatment. The *minor degradate MNBA* was a maximum of 1.7% of the applied radioactivity at 7 days posttreatment. *Unextracted [^{14}C]residues* were initially (day 0) 3.1% of the applied radioactivity, increased to 19.2% by 7 days, and were 29.2-29.4% at 21-28 days posttreatment. *Evolved $^{14}CO_2$* initially (day 7) accounted for 1.5% of the applied radioactivity and was 7.4% at 28 days posttreatment.

In the silty clay loam soil from Iowa (soil #722), the parent compound was initially present at 90.3% of the applied radioactivity, decreased to 52.1% by 7 days and 37.4% by 14 days, and was 14.3% at 28 days posttreatment. The *minor degradate MNBA* was a maximum of 3.5% of the applied radioactivity at 7 days posttreatment. *Unextracted [^{14}C]residues* were initially (day 0) 1.5% of the applied radioactivity, increased to a 21.7% by 7 days and 36.2% by 14 days, and were 35.4% at 28 days posttreatment. *Evolved $^{14}CO_2$* accounted for 5.2% of the applied radioactivity at 14 days posttreatment and was 10.4% at 28 days.

In the silt loam soil from Illinois (soil #723), the parent compound was initially present at 89.3% of the applied radioactivity, decreased to 51.1% by 14 days and 42.7% by 21 days, and was 26.7% at 28 days posttreatment. The *minor degradate MNBA* was a maximum of 2.4% of the applied radioactivity at 14 days posttreatment. *Unextracted [^{14}C]residues* were initially (day 0) 1.2% of the applied radioactivity, increased to 13.0% by 7 days, 22.7% by 14 days and 30.7% by 21 days, and were 37.2% at 28 days posttreatment. *Evolved $^{14}CO_2$* accounted for 3.8% of the applied radioactivity at 14 days posttreatment and was 10.1% at 28 days.

In the loamy sand soil from Nebraska (soil #724), the parent compound was initially present at 89.4% of the applied radioactivity, decreased to 55.8% by 14 days and 46.0% by 21 days, and was 41.7% at 28 days posttreatment. The *minor degradate MNBA* was a maximum of 1.5% of the applied radioactivity at 28 days posttreatment. *Unextracted [^{14}C]residues* were initially (day 0) 0.5% of the applied radioactivity, increased to 13.1-13.2% by 7-14 days, and were 21.0-23.1% at 21-28 days posttreatment. *Evolved $^{14}CO_2$* accounted for 5.6% of the applied radioactivity at 28 days posttreatment.

In the loam soil from Kansas (soil #725), the parent compound was initially present at

89.0% of the applied radioactivity, decreased to 35.4% by 7 days, and was 7.6% at 28 days posttreatment. The *minor degradate MNBA* was a maximum of 3.2% of the applied radioactivity at 7 days posttreatment. *Unextracted [^{14}C]residues* were initially (day 0) 2.0% of the applied radioactivity, increased to 23.7% by 7 days, and were 41.6% at 28 days posttreatment. *Evolved $^{14}CO_2$* initially (day 7) accounted for 7.1% of the applied radioactivity, increased to 13.8% by 14 days, and was 20.7% at 28 days posttreatment.

In the clay loam soil from Indiana (soil #727), the parent compound was initially present at 91.3% of the applied radioactivity, decreased to 51.1% by 14 days, and was 40.8% at 28 days posttreatment. The *minor degradate MNBA* was a maximum of 1.4% of the applied radioactivity at 14 days posttreatment. *Unextracted [^{14}C]residues* were initially (day 0) 1.9% of the applied radioactivity, increased to 18.6% by 7 days, and were 29.1-29.2% at 21-28 days posttreatment. *Evolved $^{14}CO_2$* initially (day 7) accounted for 1.2% of the applied radioactivity and was 4.3% at 28 days posttreatment.

In the sandy loam soil from Indiana (soil #728), the parent compound was initially present at 91.8% of the applied radioactivity, decreased to 43.6% by 7 days, and was 8.8% at 28 days posttreatment. The ***major** degradate MNBA* was initially (day 0) present at 1.9% of the applied radioactivity, was a maximum of 13.7% at 7 days, and was 0.63% at 28 days posttreatment. *Unextracted [^{14}C]residues* were initially (day 0) 1.3% of the applied radioactivity, increased to 12.6% by 7 days and 21.6% by 14 days, and were a maximum of 40.0% at 28 days posttreatment. *Evolved $^{14}CO_2$* accounted for 7.8% of the applied radioactivity at 14 days and was 15.0% at 28 days posttreatment.

In the silt loam soil from Wisconsin (soil #729), the parent compound was initially present at 91.6% of the applied radioactivity, decreased to 60.5% by 7 days and 43.5% by 14 days, and was 20.5% at 28 days posttreatment. The *minor degradate MNBA* was a maximum of 3.6% of the applied radioactivity at 7 days posttreatment. *Unextracted [^{14}C]residues* were initially (day 0) 1.2% of the applied radioactivity, increased to 19.0% by 7 days and 29.0% by 14 days, and were a maximum of 40.4% at 28 days posttreatment. *Evolved $^{14}CO_2$* initially (day 7) accounted for 1.6% of the applied radioactivity, increased to 4.4% by 14 days, and was 11.5% at 28 days posttreatment.

In the clay loam soil from Ohio (soil #730), the parent compound was initially present at 92.7% of the applied radioactivity, decreased to 44.0-46.0% by 14-21 days, and was 29.3% at 28 days posttreatment. The *minor degradate MNBA* was a maximum of 2.2% of the applied radioactivity at 7 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 1.2% of the applied radioactivity, were 21.0-25.3% from 7 to 21 days, and were a maximum of 34.8% at 28 days posttreatment. *Evolved $^{14}CO_2$* initially (day 7) accounted for 1.1% of the applied radioactivity and was 6.9% at 28 days posttreatment.

In the silty clay loam soil from Missouri (soil #731), the parent compound was initially present at 92.1% of the applied radioactivity, decreased to 45.3% by 14 days, and was

23.5% at 28 days posttreatment. The ***major*** *degradate MNBA* was initially (day 0) present at 1.4% of the applied radioactivity, increased to 9.8% by 7 days and a maximum of 14.2% by 21 days, and was 13.2% at 28 days posttreatment. *Unextracted [^{14}C]residues* were initially (day 0) 1.4% of the applied radioactivity, increased to 12.2% by 7 days, 19.0% by 14 days and 24.2% by 21 days, and were a maximum of 25.8% at 28 days posttreatment. *Evolved $^{14}CO_2$* initially (day 7) accounted for 1.9% of the applied radioactivity, increased to 3.7% by 14 days, and was 12.5% at 28 days posttreatment.

In the silty clay loam soil from South Dakota (soil #732), the parent compound was initially present at 90.3% of the applied radioactivity, decreased to 58.2% by 7 days and 40.2% by 14 days, and was 25.8% at 28 days posttreatment. The *minor degradate MNBA* was a maximum of 1.2% of the applied radioactivity at day 0. *Unextracted [^{14}C]residues* were initially (day 0) 1.7% of the applied radioactivity, increased to 17.2% by 7 days and 27.1-27.4% by 14-21 days, and were a maximum of 32.0% at 28 days posttreatment. *Evolved $^{14}CO_2$* initially (day 7) accounted for 1.9% of the applied radioactivity, increased to 2.2-4.4% by 14-21 days, and was 7.4% at 28 days posttreatment.

In the silty clay loam soil from Illinois (soil #741), the parent compound was initially present at 90.3% of the applied radioactivity and decreased to 48.0% by 28 days posttreatment. The *minor degradate MNBA* was a maximum of 1.6% of the applied radioactivity at 28 days posttreatment. *Unextracted [^{14}C]residues* were initially (day 0) 1.9% of the applied radioactivity, increased to 11.7% by 7 days, and were a maximum of 26.4% by 28 days posttreatment. *Evolved $^{14}CO_2$* initially (day 7) accounted for 0.6% of the applied radioactivity and was 2.5% at 28 days posttreatment.

In the silty clay loam soil from Illinois (soil #742), the parent compound was initially present at 92.0% of the applied radioactivity, decreased to 60.9% by 7 days and 36.2% by 14 days, and was 8.7% at 28 days posttreatment. The ***major*** *degradate MNBA* was initially (day 0) present at 1.5% of the applied radioactivity, increased to 21.2% by 7 days, and was a maximum of 57.2% at 28 days posttreatment. *Unextracted [^{14}C]residues* were initially (day 0) 2.3% of the applied radioactivity, increased to 7.8% by 7 days and 11.9% by 14 days, and were a maximum of 14.5% at 28 days posttreatment. *Evolved $^{14}CO_2$* initially (day 7) accounted for 0.5% of the applied radioactivity and was 5.0% at 28 days posttreatment.

METHODOLOGY

Samples (59 g) of sieved (2 mm) Iowa clay loam, Iowa silty clay loam, Illinois silt loam, Nebraska loamy sand, Kansas loam, Indiana clay loam, Indiana sandy loam, Wisconsin silt loam, Ohio clay loam, Missouri silty clay loam, South Dakota silty clay loam, Illinois (soil #741) silty clay loam, and Illinois (soil #742) silty clay loam soils (Table III, pp. 41-42) were weighed into centrifuge bottles and adjusted to 100% of the soil moisture

content at 0.33 bar (p. 20); samples were pre-incubated for 2-3 days prior to treatment. Soil samples were treated by pipette with uniformly phenyl ring-labeled [^{14}C]mesotrione {2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione; radiochemical purity ≥96.6%, specific activity 30.4 mCi/mmol; pp. 15, 19}, dissolved in phosphate buffer (pH 7.5) and acetonitrile, at a nominal application rate of 0.6 ppm (wet-weight basis; rates varied from 0.60 to 0.85 ppm on a dry-weight soil basis; see Comment #8); parent was enriched with ^{13}C at the carbonyl position. The treated soil samples were incubated in a desiccator at 25 ± 2°C for up to 42 days; a diagram of the incubation apparatus was not provided. Each desiccator (one for each soil type) was equipped with inlet and outlet tubes for volatile collection; humidified air was passed through the chamber and into a 1 M NaOH volatile trap. Sample bottles were weighed during the incubation period to verify that the soil moisture content was maintained at 100% of 0.33 bar moisture content (p. 22); water was added as necessary (see Comment #4). Single samples were removed for analysis at 0, 7, 14, 21, and 28 days posttreatment for all thirteen soils; samples collected at 42 days posttreatment were not analyzed. Volatile trap solutions were collected for analysis and replaced with 1 M NaOH at each sampling interval (p. 23).

At each sampling interval, soil samples were extracted three times by shaking with 0.05 M NH_4OH followed a single extraction with acetone, and then centrifuged (p. 23). The supernatant was decanted, acidified to pH 1 (HCl), centrifuged, and decanted again. The soil pellet was extracted by shaking and ultrasonic treatment with acetonitrile, and centrifuged. The supernatant was partitioned three times with ethyl acetate and the ethyl acetate extracts were combined with the acetonitrile extract. The combined extracts were concentrated by evaporation under a stream of nitrogen and analyzed by TLC on silica gel plates developed in at least one of thirteen solvent systems (Table II, p. 40). Samples were co-chromatographed with nonradiolabeled reference standards of the parent and the degradates MNBA and 5-hydroxy-ZA1296 which were visualized with UV (254 nm) light. Radioactive residues on TLC plates were quantified by radioimage scanning (p. 18). It was not reported whether a confirmatory method of analysis was used. Post-extracted soil samples were analyzed by LSC following combustion.

In an attempt to characterize bound [^{14}C]residues, selected post-extracted soil samples (day 21, soils #721, 727, 728) were refluxed with 2 *N* HCl for 2 hours and filtered, and the acid hydrolysate was partitioned three times with ethyl acetate (p. 24). The organic fraction was concentrated by rotary evaporation and analyzed by TLC on silica gel plates developed with toluene:1,4-dioxane:ethanol:triethylamine (3:3:3:1, v:v:v:v); toluene:1,4-dioxane:formic acid (20:20:1, v:v:v); and chloroform: tetrahydrofuran:formic acid (20:20:1, v:v:v). Samples were co-chromatographed with nonradiolabeled reference standards. The organic fraction from selected samples (Indiana sandy loam soil) was oxidated with hydrogen peroxide and analyzed by two-dimensional TLC on silica gel plates developed in the three solvent systems described previously for bound residue characterization (p. 25). Extracted soil samples were mixed with 0.2 M $KMnO_4$ in a water bath at 50°C for 2 hours. The mixture was acidified to pH 1 (HCl), filtered and

partitioned three times with ethyl acetate. The organic fraction was concentrated by rotary evaporation and analyzed by TLC on silica gel plates developed in solvent systems of chloroform:methanol:water: formic acid (20:7:1:1, v:v:v:v) and chloroform:tetrahydrofuran:formic acid (20:20:1, v:v:v). The post-extracted soil samples were analyzed by LSC following combustion.

DATA SUMMARY

Uniformly phenyl ring-labeled [^{14}C]mesotrione, at a nominal application rate of 0.6 ppm (wet-weight basis; rates varied from 0.60 to 0.85 ppm on a dry-weight soil basis; see Comment #8), degraded with calculated first-order half-lives of 22.0 days ($r^2 = 0.98$) in clay loam soil from Iowa; 10.6 days ($r^2 = 1.0$) in silty clay loam soil from Iowa; 16.6 days ($r^2 = 0.98$) in silt loam soil from Illinois; 25.9 days ($r^2 = 0.96$) in loamy sand soil from Nebraska; 8.0 days ($r^2 = 0.97$) in loam soil from Kansas; 24.1 days ($r^2 = 0.92$) in clay loam soil from Indiana; 8.5 days ($r^2 = 0.98$) in sandy loam soil from Indiana; 12.9 days ($r^2 = 1.0$) in silt loam soil from Wisconsin; 19.1 days ($r^2 = 0.91$) in clay loam soil from Ohio; 14.4 days ($r^2 = 1.0$) in silty clay loam soil from Missouri; 15.8 days ($r^2 = 0.97$) in silty clay loam soil from South Dakota; 31.5 days ($r^2 = 0.94$) in silty clay loam soil from Illinois (soil #741); and 8.2 days ($r^2 = 0.99$) in silty clay loam soil from Illinois (soil #742) adjusted to 100% of 0.33 bar moisture content and incubated at 25 ± 2°C for up to 42 days (Table VI, pp. 49-51; Figure 5, pp. 63-66). However, the presence of high concentrations of nonextracted [^{14}C]residues by day 7 (for each soil except the silty clay loam soil from IL, soil #742) and by day 14 (for soil #742) indicates that the analytical method may not have been adequate; therefore, the validity of the half-lives is questionable. Also, the half-life of the parent in the Illinois silty clay loam soil (soil #741) is of questionable validity since it was determined beyond the scope of the observed data.

All data designated below as percentages of the applied, represent percentages of the nominal application. Degradate data are reported in parent equivalents.

Clay loam soil from Iowa (soil #721)

The parent compound was initially present at 86.4% of the applied radioactivity, decreased to 49.8% by 14 days and 41.0% by 21 days, and was 35.1% of the applied at 28 days posttreatment (Table VII, pp. 52-54). The minor degradate 4-(methylsulfonyl)-2-nitrobenzoic acid (MNBA) was initially (day 0) 1.0% of the applied radioactivity, was a maximum of 1.7% of the applied at 7 days, and was 0.96% of the applied at 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 3.1% of the applied radioactivity, increased to 19.2% of the applied by 7 days posttreatment, and were 29.2-29.4% of the applied at 21-28 days posttreatment (Table IV, pp. 43-45). Evolved $^{14}CO_2$ initially (day 7) accounted for 1.5% of the applied radioactivity and was 7.4% of the

applied at 28 days posttreatment.

Material balances (based on LSC analysis) were initially 98.4% of the applied radioactivity, decreased to 90.7% of the applied by 21 days posttreatment, and were 87.1% of the applied at 28 days posttreatment (Table IV, pp. 43-45).

Silty clay loam soil from Iowa (soil #722)

The parent compound was initially present at 90.3% of the applied radioactivity, decreased to 52.1% by 7 days and 37.4% by 14 days, and was 14.3% of the applied at 28 days posttreatment (Table VII, pp. 52-54). The minor degradate MNBA was initially (day 0) 0.97% of the applied radioactivity, was a maximum of 3.5% of the applied at 7 days posttreatment, and was 0.92% of the applied at 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 1.5% of the applied radioactivity, increased to 21.7% by 7 days and a maximum of 36.2% by 14 days, and were 35.4% of the applied at 28 days posttreatment (Table IV, pp. 43-45). Evolved $^{14}CO_2$ accounted for 5.2% of the applied radioactivity at 14 days posttreatment and was 10.4% of the applied at 28 days posttreatment.

Material balances (based on LSC analysis) were initially 100.9% of the applied radioactivity, decreased to 87.3% of the applied by 21 days posttreatment, and were 82.3% of the applied at 28 days posttreatment (Table IV, pp. 43-45).

Silt loam soil from Illinois (soil #723)

The parent compound and was initially present at 89.3% of the applied radioactivity, decreased to 51.1% by 14 days and 42.7% by 21 days, and was 26.7% of the applied at 28 days posttreatment (Table VII, pp. 52-54). The minor degradate MNBA was initially (day 0) 2.2% of the applied radioactivity, was a maximum of 2.4% of the applied at 14 days posttreatment, and was 1.1% of the applied at 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 1.2% of the applied radioactivity, increased to 13.0% by 7 days, 22.7% by 14 days and 30.7% by 21 days, and were a maximum of 37.2% of the applied at 28 days posttreatment (Table IV, pp. 43-45). Evolved $^{14}CO_2$ accounted for 3.8% of the applied radioactivity at 14 days posttreatment and was 10.1% of the applied at 28 days posttreatment.

Material balances (based on LSC analysis) were 92.9-99.4% of the applied radioactivity throughout the incubation period, with no obvious pattern of decline (Table IV, pp. 43-45).

Loamy sand soil from Nebraska (soil #724)

The parent compound was initially present at 89.4% of the applied radioactivity,

decreased to 55.8% by 14 days and 46.0% by 21 days, and was 41.7% of the applied at 28 days posttreatment (Table VII, pp. 52-54). The minor degradate MNBA was initially (day 0) 1.3% of the applied radioactivity and was a maximum of 1.5% of the applied at 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 0.5% of the applied radioactivity, increased to 13.1-13.2% of the applied by 7-14 days posttreatment, and were 21.0-23.1% of the applied at 21-28 days posttreatment (Table IV, pp. 43-45). Evolved $^{14}CO_2$ accounted for 1.6% of the applied radioactivity at 7 days and was 5.6% of the applied at 28 days posttreatment.

Material balances were 89.6-99.1% of the applied radioactivity throughout the incubation period, with no observed pattern of decline (Table IV, pp. 43-45).

Loam soil from Kansas (soil #725)

The parent compound was initially present at 89.0% of the applied radioactivity, decreased to 35.4% of the applied by 7 days, and was 7.6% of the applied at 28 days posttreatment (Table VII, pp. 52-54). The minor degradate MNBA was initially (day 0) 2.1% of the applied radioactivity, was a maximum of 3.2% of the applied at 7 days posttreatment, and was 0.61% of the applied at 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 2.0% of the applied radioactivity, increased to 23.7% of the applied by 7 days posttreatment, and were a maximum of 41.6% of the applied at 28 days posttreatment (Table IV, pp. 43-45). Evolved $^{14}CO_2$ initially (day 7) accounted for 7.1% of the applied radioactivity, increased to 13.8% of the applied by 14 days posttreatment, and was 20.7% of the applied at 28 days posttreatment.

Material balances (based on LSC analysis) were initially 100.0% of the applied radioactivity and decreased to 83.8-88.5% of the applied by 7-28 days posttreatment (Table IV, pp. 43-45).

Clay loam soil from Indiana (soil #727)

The parent compound was initially present at 91.3% of the applied radioactivity, decreased to 51.1% of the applied by 14 days posttreatment, and was 40.8% of the applied at 28 days posttreatment (Table VII, pp. 52-54). The minor degradate MNBA was initially (day 0) 1.1% of the applied radioactivity, was a maximum of 1.4% of the applied at 14 days posttreatment, and was 0.41% of the applied at 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 1.9% of the applied radioactivity, increased to 18.6% of the applied by 7 days posttreatment, and were 29.1-29.2% of the applied at 21-28 days posttreatment (Table IV, pp. 43-45). Evolved $^{14}CO_2$ initially (day 7) accounted for 1.2% of the applied radioactivity and was 4.3% of the applied at 28 days posttreatment.

Material balances (based on LSC analysis) were initially 100.7% of the applied

radioactivity and generally decreased to 89.3-90.2% of the applied by 14-28 days posttreatment (Table IV, pp. 43-45).

Sandy loam soil from Indiana (soil #728)

The parent compound was initially present at 91.8% of the applied radioactivity, decreased to 43.6% of the applied by 7 days posttreatment, and was 8.8% of the applied at 28 days posttreatment (Table VII, pp. 52-54). The major degradate

4-(methylsulfonyl)-2-nitrobenzoic acid (MNBA)

was initially (day 0) present at 1.9% of the applied radioactivity, was a maximum of 13.7% of the applied at 7 days posttreatment, and was 0.63% of the applied at 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 1.3% of the applied radioactivity, increased to 12.6% by 7 days and 21.6% by 14 days, and were a maximum of 40.0% of the applied at 28 days posttreatment (Table IV, pp. 43-45). Evolved $^{14}CO_2$ accounted for 7.8% of the applied radioactivity at 14 days posttreatment and was 15.0% of the applied at 28 days posttreatment.

Material balances (based on LSC analysis) were initially 100.0% of the applied radioactivity and were 76.9-88.0% of the applied at 7-28 days posttreatment; an obvious pattern of decline was not observed from 7 to 28 days. (Table IV, pp. 43-45).

Silt loam soil from Wisconsin (soil #729)

The parent compound was initially present at 91.6% of the applied radioactivity, decreased to 60.5% by 7 days and 43.5% by 14 days, and was 20.5% of the applied at 28 days posttreatment (Table VII, pp. 52-54). The minor degradate MNBA was initially (day 0) 1.2% of the applied radioactivity, was a maximum of 3.6% of the applied at 7 days posttreatment, and was 1.1% of the applied at 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 1.2% of the applied radioactivity, increased to 19.0% by 7 days and 29.0% by 14 days, and were a maximum of 40.4% of the applied at 28 days posttreatment (Table IV, pp. 43-45). Evolved $^{14}CO_2$ initially (day 7) accounted for 1.6% of the applied radioactivity, increased to 4.4% of the applied by 14 days posttreatment, and was 11.5% of the applied at 28 days posttreatment.

Material balances (based on LSC analysis) were initially 101.0% of the applied radioactivity and decreased to 90.0-90.8% of the applied by 21-28 days posttreatment (Table IV, pp. 43-45).

Clay loam soil from Ohio (soil #730)

The parent compound was initially present at 92.7% of the applied radioactivity,

decreased to 44.0-46.0% of the applied by 14-21 days posttreatment, and was 29.3% of the applied at 28 days posttreatment (Table VII, p. 52-54). The minor degradate MNBA was initially (day 0) 0.51% of the applied radioactivity, was a maximum of 2.2% of the applied at 7 days posttreatment, and was 1.4% of the applied at 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 1.2% of the applied radioactivity, were 21.0-25.3% of the applied from 7 to 21 days, and were a maximum of 34.8% of the applied at 28 days posttreatment (Table IV, pp. 43-45). Evolved $^{14}CO_2$ initially (day 7) accounted for 1.1% of the applied radioactivity and was a maximum of 6.9% of the applied at 28 days posttreatment.

Material balances (based on LSC analysis) were 96.7-99.4% of the applied radioactivity from 0 to 7 days posttreatment and were 88.2%-89.8% of the applied from 14 to 28 days (Table IV, pp. 43-45).

Silty clay loam soil from Missouri (soil #731)

The parent compound was initially present at 92.1% of the applied radioactivity, decreased to 45.3% of the applied by 14 days posttreatment, and was 23.5% of the applied at 28 days posttreatment (Table VII, pp. 52-54). The major degradate

4-(methylsulfonyl)-2-nitrobenzoic acid (MNBA)

was initially (day 0) present at 1.4% of the applied radioactivity, increased to 9.8% by 7 days and a maximum of 14.2% by 21 days, and was 13.2% of the applied at 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 1.4% of the applied radioactivity, increased to 12.2% by 7 days, 19.0% by 14 days and 24.2% by 21 days, and were a maximum of 25.8% of the applied at 28 days posttreatment (Table IV, p. 43-45). Evolved $^{14}CO_2$ initially (day 7) accounted for 1.9% of the applied radioactivity, increased to 3.7% of the applied by 14 days posttreatment, and was 12.5% of the applied at 28 days posttreatment.

Material balances (based on LSC analysis) were 92.7-99.6% of the applied radioactivity at 0-14 days posttreatment and decreased to 84.8-88.8% of the applied by 21-28 days posttreatment (Table IV, pp. 43-45).

Silty clay loam soil from South Dakota (soil #732)

The parent compound was initially present at 90.3% of the applied radioactivity, decreased to 58.2% by 7 days and 40.2% by 14 days, and was 25.8% of the applied at 28 days posttreatment (Table VII, pp. 52-54). The minor degradate MNBA was initially (day 0) present at a maximum of 1.2% of the applied radioactivity and was 1.0-1.1% of the applied from 7 to 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 1.7% of the applied radioactivity, increased to 17.2% by 7 days and 27.1-27.4%

by 14-21 days, and were a maximum of 32.0% of the applied at 28 days posttreatment (Table IV, p. 43-45). Evolved $^{14}CO_2$ initially (day 7) accounted for 1.9% of the applied radioactivity, increased to 2.7-4.4% of the applied by 14-21 days posttreatment, and was 7.4% of the applied at 28 days posttreatment.

Material balances (based on LSC analysis) were initially 99.8% of the applied radioactivity and decreased to 81.6-87.9% of the applied by 14-28 days posttreatment (Table IV, pp. 43-45).

Silty clay loam soil from Illinois ("low" pH soil #741)

The parent compound was initially present at 90.3% of the applied radioactivity, decreased to 58.2% by 14 days and 52.2% by 21 days, and was 48.0% of the applied at 28 days posttreatment (Table VII, pp. 52-54). The minor degradate MNBA was initially (day 0) 1.1% of the applied radioactivity and was 1.5-1.6% of the applied from 7 to 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 1.9% of the applied radioactivity, increased to 11.7% of the applied by 7 days, and were a maximum of 26.4% of the applied by 28 days posttreatment (Table IV, pp. 43-45). Evolved $^{14}CO_2$ initially accounted for 0.6% of the applied radioactivity and was 2.5% of the applied at 28 days posttreatment.

Material balances (based on LSC analysis) were 91.4-98.2% of the applied radioactivity throughout the incubation period, with no observed pattern of decline (Table IV, p. 44).

Silty clay loam soil from Illinois ("high" pH soil #742)

The parent compound was initially present at 92.0% of the applied radioactivity, decreased to 60.9% by 7 days and 36.2% by 14 days, and was 8.7% of the applied at 28 days posttreatment (Table VII, pp. 52-54). The major degradate

4-(methylsulfonyl)-2-nitrobenzoic acid (MNBA)

was initially (day 0) present at 1.5% of the applied radioactivity, increased to 21.2% of the applied by 7 days posttreatment, and was a maximum of 57.2% of the applied at 28 days posttreatment. Unextracted [^{14}C]residues were initially (day 0) 2.3% of the applied radioactivity, increased to 7.8% by 7 days and 11.9% by 14 days, and were a maximum of 14.5% of the applied at 28 days posttreatment (Table IV, pp. 43-45). Evolved $^{14}CO_2$ initially (day 7) accounted for 0.5% of the applied radioactivity and was 5.0% of the applied at 28 days posttreatment.

Material balances (based on LSC analysis) were initially 101.4% of the applied radioactivity and decreased to 93.6% of the applied by 28 days posttreatment (Table IV, pp. 43-45).

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COMMENTS

1. Unextracted [^{14}C]residues were high (≥10% of the applied radioactivity; range of 11.7-23.7%) by 7 days post-treatment for all soils except the silty clay loam soil from Illinois (soil #742; Table IV, pp. 43-45); unextracted [^{14}C]residues accounted for 11.9% of the applied in soil #742 by 14 days post-treatment. The presence of high concentrations of unextracted residues by the first sampling interval after time 0 (day 7) for each soil except soil #742 indicates that the analytical method, specifically extraction, may have been inadequate for the determination of the parent. Without the appropriate extraction procedures to ensure quantitative recovery of the compounds of interest, the validity of the reported half-lives is questionable. Additionally, the patterns of formation and decline of the degradate MNBA are questionable. Following preliminary extractions, selected soil samples (day 21, soils #721, 727, and 728) were subjected to acid hydrolysis followed by partitioning with ethyl acetate and oxidation with hydrogen peroxide and/or potassium permanganate (p. 24). The reviewer noted that the parent, MNBA, and two unidentified degradates were detected in the organic extracts (p. 33; Table VIII, p. 55); therefore, the initial extraction method was inadequate for quantitative extraction of the parent and its degradates. Based on the levels of radioactivity remaining in the soil following the additional extractions (Table VIII, p. 55), it is possible that acid hydrolysis followed by oxidation was also inadequate for the recovery of the compounds of interest. Additionally, organic matter fractionation was not performed. Subdivision N Guidelines require that a reasonable attempt be made to extract and identify all degradates present at ≥10% of the applied radioactivity. Unless appropriate extraction procedures are utilized, it cannot be confirmed that additional parent material or degradates were not present in the fraction of the applied radioactivity that was classified as "nonextractable" [^{14}C]residues (labeled "unextracted" in the data tables).

2. Duplicate samples were not utilized at each sampling interval for each soil type tested in the study. The use of single test samples is generally not considered to be good laboratory practice; at a minimum, duplicate samples should be utilized for each sampling interval and each treatment. *However, the use of 13 soils is to be applauded* and certainly superior to duplicate analysis for the minimally required one soil.

3. The test compound was applied at an exaggerated rate. This study was conducted at a nominal application rate of 0.6 ppm (wet-weight basis); the application rates on a dry-weight soil basis varied from 0.73 to 0.85 ppm (with the exception 0.60 ppm for the loamy sand soil from Nebraska, soil #724; Appendix B, Table B-I, p. 80; also see Comment #8). The reviewer noted that additional aerobic soil metabolism studies (MRIDs 44373531 and 44505130) were conducted at nominal application rates of 0.31-0.35 ppm (10% greater than the proposed maximum label rate of 280 g a.i./ha; MRID 44373531, p. 13); therefore, the application rate (dry-weight basis) in the current study was greater than the maximum label rate. The use of exaggerated dose rates may effect

the degradation rate of the chemical relative to the degradation rate that would occur under normal use rates. While exaggerated dose rates may be used to facilitate residue identification, EPA requires that kinetic studies be performed using the proposed maximum application rate (US EPA. 1993. *Pesticide Reregistration Rejection Rate Analysis: Environmental Fate*. EPA 738-R-93-010, p. 67). However, the maximum application rate given in the currently proposed label is 482 g a.i./ha (0.43 lb/acre) which corresponds approximately to 0.2 ppm with 6-inch soil incorporation.

4. Soil moisture was not maintained at 75% of 0.33 bar. The study author stated that the soil moisture content of all samples was maintained at 91-110% of 0.33 bar throughout the incubation period with the exception of the loamy sand soil from Nebraska which was 183-204% of 0.33 bar moisture content (p. 22). Subdivision N Guidelines require that aerobic soil metabolism studies be performed at 75% of the soil moisture content at 0.33 bar in order to ensure aerobic conditions and soil viability.

5. The reviewer could not confirm that the samples were incubated in darkness as required by Subdivision N Guidelines. Clarification by the registrant is appropriate.

6. The material balances for ten of the thirteen soils declined with time (Table IV, pp. 43-45); material balances for six of the thirteen soils were outside the acceptable range of 90-110% of the applied radioactivity by the end of the study. Material balances for the loam soil from KS, and the sandy loam soil from IN, were 83.8-88.5% and 76.9-88.0% of the applied radioactivity, respectively, from 7 to 28 days posttreatment. Material balances for the clay loam soil from OH, and the silty clay loam soil from SD, were 88.2-89.8% and 81.6-87.9% of the applied radioactivity, respectively, from 14 to 28 days posttreatment. Material balances for the silty clay loam soil from IA, and the silty clay loam soil from MO, were 82.3-87.3% and 84.8-88.8% of the applied radioactivity, respectively, from 21 to 28 days posttreatment. Subdivision N Guidelines require that material balances be 90-110% of the applied radioactivity. The study author stated that material loss was most likely due to leakage of $^{14}CO_2$ from the test systems or inefficiency of the method for the collection of volatiles (p. 26).

7. The half-life of the parent (31.5 days; Table VI, p. 50) in the Illinois silty clay loam soil (soil #741) was estimated assuming the continuation of the apparent degradation pattern beyond the scope of the observed data. However, data which appear linear may become curvilinear with time and half-life estimations based on extrapolated data may be inaccurate. The study author stated that data collected up to 28 days posttreatment established the decline of the parent in all of the soil test systems and, therefore, analysis of the samples incubated for removal at 42 days posttreatment was not necessary (p. 22). However, the parent was initially present in soil #741 at 90.3% of the applied radioactivity was still present at 48.0% of the applied at 28 days posttreatment (Table VII, pp. 52-54).

8. Residue concentrations of the parent and degradates were not reported. In future studies submitted to the EPA, it is necessary that data also be reported in units of concentration, such as ppm. The reviewer did not calculate these values for the current study because the actual application rate on a dry-weight basis varied between soil types and, therefore, concentration data (in ppm) determined based on the actual rate would not provide a valid comparison between data for the different soils. The reviewer notes that the half-lives reported in this study may not be directly comparable between soils due to the different treatment rates (range of 0.60 to 0.85 ppm on a dry-weight soil basis) utilized for each soil type.

9. Sterilized test systems were not prepared and incubated along with the treated test systems as controls. Sterile controls would have helped to quantify the extent of abiotic degradation occurring in the test systems.

10. The incubation temperature was not held constant at ± 1°C as required by Subdivision N Guidelines. The study author reported that the soils were incubated at 25 ± 2°C (p. 21); raw temperature data were not reported.

11. Method detection limits were not reported for TLC or LSC analyses. Limits of detection and quantitation should be reported to allow the reviewer to evaluate the adequacy of the methods for the determination of parent compound and its metabolites.

12. The soil series names of the soils were not reported. Instead, the soils were referred to by their geographic source (Table III, p. 41). The two silty clay loam soils from Champaign, IL, were distinguished by their laboratory identification numbers.

13. The study author stated that MNBA accounted for 1-2% of the total radioactivity present in the treatment solution (p. 19).

14. Soil viability was not confirmed throughout the incubation period. Generally, metabolism studies include data demonstrating the viability of the soil microbial population at the start and termination of the study. This would be of particular importance in the case of the loamy sand soil from Nebraska, which was maintained at 183-204% of 0.33 bar moisture content.

    Measurement of soil respiration and/or use of benchmark compounds are recommended as indicators of soil viability. Such measurements, in effect, normalize results among various metabolism studies, and allow for meaningful comparisons of relative persistence among various chemicals and soils.

15. The study was conducted using uniformly phenyl ring-labeled [^{14}C]mesotrione; the compound contained an additional ring structure that was not radiolabeled. The reviewer notes that additional aerobic soil metabolism studies were also submitted (MRIDs

44373531, 44505130, 44505208 and 44901714).

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