

DATA EVALUATION RECORD

STUDY 2

CHEM 122990 Mesotrione §161-2
CAS No. 104206-82-8
FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 44537108

Eya, B. K. 1995. [Carbonyl-¹³C][phenyl-U-¹⁴C]ZA1296 and [cyclohexane-2-¹⁴C]ZA1296 - aqueous photolysis. Laboratory Study No.: PMS-392. Unpublished study performed by ZENECA Inc., Richmond, CA; and submitted by ZENECA Inc., Wilmington, DE.

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REVIEWED BY: D. A. Saccone, B.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

Alex Clem
5/3/01

CONCLUSIONS

Degradation - Photodegradation in Water

1. This study is *acceptable* and provides useful information on the photodegradation of mesotrione in pH 7 aqueous buffer solution. The EPA Subdivision N Guideline requirements for photolysis in water are *satisfied*.

However, the registrant should carefully consider the critical elements in the Comments Section—these may well impact the acceptability of future submissions. Additionally, for future submissions the use of actinometers and the determination of quantum yield is recommended, and will become standard when internationally harmonized guidelines are adopted.

2. Uniformly phenyl ring-labeled [¹⁴C]mesotrione, at a nominal concentration of 2.0 ppm, degraded with a half-life of 86.8 days ($r^2 = 0.99$; equivalent natural sunlight days) in sterile pH 7 aqueous buffer solution which was continuously irradiated with a xenon arc lamp and maintained at $25 \pm 1^\circ\text{C}$ for up to 19 days; however, the half-life was determined beyond the scope of the observed data. In contrast, the parent compound was stable in the dark control solution. Data were reported by the study author as concentrations of the parent compound in solution; all data are reported as reviewer-calculated percentages (mean of two replicates) of the applied radioactivity based on the actual application rate. In the irradiated solution, the parent compound was initially present at 100.0% (2.2 ppm) of the applied radioactivity, decreased to 87.5% (2.0 ppm) by 7 days (17.7 equivalent natural sunlight days) posttreatment, and was 68.3% (1.5 ppm) at 19 days (47.2 equivalent natural sunlight days). Unidentified minor degradates (≥ 8) were each $\leq 6.3\%$ of the applied radioactivity in the irradiated samples. In the dark control samples, the parent compound was present at 97.7-100.0% (2.2 ppm) of the applied radioactivity from 0 to 19 days posttreatment.

Cyclohexane ring-labeled [2-¹⁴C]mesotrione, at a nominal concentration of 2.0 ppm, degraded with a half-life of 80.5 days ($r^2 = 0.98$; equivalent natural sunlight days) in sterile pH 7 aqueous buffer solution which was continuously irradiated with a xenon arc lamp and maintained at $25 \pm 1^\circ\text{C}$ for up to 16 days; however, the half-life was determined beyond the scope of the observed data. In contrast, the parent compound was stable in the dark control solution. Data were reported by the study author as concentrations of the parent compound in solution; all data are reported as reviewer-calculated percentages (mean of two replicates) of the applied radioactivity based on the actual application rate. In the irradiated solution, the parent compound was initially present at 100.0% (2.2 ppm) of the applied radioactivity, decreased to 90.2% (1.9 ppm) by 7 days (17.7 equivalent natural sunlight days) posttreatment, and was 71.2-71.6% (1.5 ppm) of the applied at 14-16 days (40.0 equivalent natural sunlight days). For the irradiated samples, ¹⁴CO₂ accounted for 20.2% of the applied radioactivity at 19 days (40.8 equivalent natural

sunlight days) posttreatment. In the dark control samples, the parent compound was present at 100.0-102.3% (2.2 ppm) of the applied radioactivity from 0 to 14 days posttreatment.

METHODOLOGY

The photolysis of mesotrione {ZA1296; 2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione; p. 14} in pH 7 aqueous buffer solution was examined at $25 \pm 1^\circ\text{C}$ using uniformly phenyl ring-labeled [^{14}C]mesotrione and cyclohexane ring-labeled [2- ^{14}C]mesotrione.

Uniformly phenyl ring-labeled [^{14}C]mesotrione (radiochemical purity 99.1%; specific activity 30.4 mCi/mmol) or cyclohexane ring-labeled [2- ^{14}C]mesotrione (radiochemical purity 99.0%; specific activity 36.6 mCi/mmol), dissolved in acetonitrile:water (1:2, v:v), was added at a nominal rate of 2.0 ppm to 0.0003 M sterile pH 7 (phosphate) aqueous buffer solution (p. 14); the phenyl ring-labeled parent was enriched with ^{13}C (ca. 40%) at the carbonyl position. Solutions contained in sealed autoclaved glass photolysis tubes were placed in a stainless steel chamber covered with a quartz plate and maintained at $25 \pm 1^\circ\text{C}$ using a recirculating water bath (p. 16; Figure 1, p. 38); dark control solutions contained in tubes wrapped with aluminum foil were incubated under similar conditions (p. 19). The temperature was monitored daily using a thermocouple probe inserted into the water bath. Samples were continuously irradiated for up to 19 days (phenyl label) or 16 days (cyclohexane label) with a xenon arc lamp equipped with a filter to remove wavelengths of $<290\text{ nm}$ (Figure 2, p. 39). The spectral distribution and light intensity (300-800 nm) were measured using a spectroradiometer at the initiation and termination of the study (p. 16). One day of continuous irradiation (artificial light source) corresponded to 2.5 California ($37^\circ 56' \text{ N}$) equivalent natural sunlight days (p. 22). Comparison data of artificial and natural sunlight (in tabular form) were provided in Appendix B (Table 1, p. 57); graphical data were provided in Figure 3 (p. 40). Total light intensities for the phenyl and cyclohexane label studies were 528.6 and 529.0 watts/m², respectively (p. 22). To trap volatiles, air was drawn through the system and flushed through two ethyl acetate and two ethanolamine volatile traps (p. 17; Figures 4, 5; pp. 41, 42). Duplicate irradiated samples were removed for analysis at 0, 1, 3, 7, 16, and 19 (phenyl label only) days posttreatment (see Comment #2); dark control samples were removed at 0, 3, 14, and 19 days (phenyl label) or 7 and 15 days posttreatment (cyclohexane label; p. 19). At each sampling interval, the pH of the irradiated samples in the phenyl label study was measured (Table III, p. 33); the pH of the dark control samples was measured at 0, 8, 35, and 47 days posttreatment. The pH remained constant in the phenyl label study; the pH was not monitored in the cyclohexane label study.

At each sampling interval, duplicate aliquots of each sample were analyzed for total radioactivity by LSC (p. 19). Samples were analyzed for the parent and the following

potential degradates: denitro-ZA1296 MBC, ZA1296XanH₄, MNBA and AMBA (Table I, p. 30). Aliquots of each solution were analyzed by reverse-phase HPLC (Alltima C18 column) using a mobile phase gradient of acetonitrile:acidified water (both in 0.1% H₃PO₄; 0:100 to 100:0 or 10:90 to 50:50 to 0:100 or 100:0 to 25:75 to 0:100, v:v) with radioactive flow detection (p. 20). Samples were co-chromatographed with nonradiolabeled reference standards which were visualized by UV light (unspecified wavelength; Figures 6-7, 12-14; pp. 43-44, 49-51). Eluate fractions were collected and analyzed for total radioactivity by LSC (p. 21). Aliquots of samples were further analyzed by TLC on silica gel plates developed in toluene:methanol: triethylamine (12:6:2, v:v:v). Samples were co-chromatographed with nonradiolabeled reference standards which were visualized by UV light (254 nm); radiolabeled residues were quantified by radioimage scanning (p. 21). All samples were analyzed within one week of sampling (p. 25).

Aliquots of the volatile trap solutions were analyzed for total radioactivity by LSC (p. 19). Upon removal from the incubation chamber, the irradiated samples were cooled in an ice bath, opened, re-sealed, and connected to a series of volatile traps as previously described (p. 17). The presence of ¹⁴CO₂ in the ethanolamine traps was confirmed by precipitation with BaCl₂ after transferring the ethanolamine solutions into 1 N NaOH traps (p. 17).

DATA SUMMARY

Uniformly phenyl ring-labeled [¹⁴C]mesotrione

Uniformly phenyl ring-labeled [¹⁴C]mesotrione (radiochemical purity 99.1%), at a nominal concentration of 2.0 ppm (actual rate of 2.2 ppm; p. 18), degraded with a registrant-calculated half-life of 86.8 days ($r^2 = 0.99$; equivalent natural sunlight days; Figure 10, p. 47) in sterile pH 7 aqueous buffer solution which was continuously irradiated with a xenon arc lamp and maintained at $25 \pm 1^\circ\text{C}$ for up to 19 days (p. 23); however, the half-life was determined beyond the scope of the observed data. In contrast, the parent compound was stable in the dark control solution. Data were reported by the study author as concentrations of the parent compound in solution; all data are reported as reviewer-calculated percentages (mean of two replicates) of the applied radioactivity based on the actual application rate. In the irradiated solution, the parent compound was initially present at 100.0% (2.2 ppm) of the applied radioactivity, decreased to 87.5% (2.0 ppm) of the applied by 7 days (17.7 equivalent natural sunlight days) posttreatment, and was 68.3% (1.5 ppm) of the applied at 19 days (47.2 equivalent natural sunlight days) posttreatment (Table V, p. 35). Unidentified minor degradates (≥ 8) were each $\leq 6.3\%$ of the applied radioactivity in the irradiated samples (pp. 24, 27; Figure 12, p. 49; see Comment #4). In the dark control samples, the parent compound was present at 97.7-100.0% (2.2 ppm) of the applied radioactivity from 0 to 19 days posttreatment.

Material balances (based on LSC analysis of individual replicates) were 96.2-101.8% and 97.4-100.8% of the applied radioactivity for the irradiated and dark control samples, respectively (Table IV, p. 34).

Cyclohexane ring-labeled [2-¹⁴C]mesotrione

Cyclohexane ring-labeled [2-¹⁴C]mesotrione (radiochemical purity 99.0%), at a nominal concentration of 2.0 ppm (actual rate of 2.2 ppm; p. 18), degraded with a registrant-calculated half-life of 80.5 days ($r^2 = 0.98$; equivalent natural sunlight days; Figure 11, p. 48) in sterile pH 7 aqueous buffer solution which was continuously irradiated with a xenon arc lamp and maintained at $25 \pm 1^\circ\text{C}$ for up to 16 days (p. 23); however, the half-life was determined beyond the scope of the observed data. In contrast, the parent compound was stable in the dark control solution. Data were reported by the study author as concentrations of the parent compound in solution; all data are reported as reviewer-calculated percentages (mean of two replicates) of the applied radioactivity based on the actual application rate. In the irradiated solution, the parent compound was initially present at 100.0% (2.2 ppm) of the applied radioactivity, decreased to 90.2% (1.9 ppm) of the applied by 7 days (17.7 equivalent natural sunlight days) posttreatment, and was 71.2-71.6% (1.5 ppm) of the applied at 14-16 days (40.0 equivalent natural sunlight days) posttreatment (Table V, p. 35). Unidentified minor degradates (unspecified number) were each present at <5% of the applied radioactivity in the irradiated samples (p. 24). For the irradiated samples, ¹⁴CO₂ accounted for 20.2% of the applied radioactivity at 19 days (40.8 equivalent natural sunlight days) posttreatment (Table VI, p. 36). In the dark control samples, the parent compound was present at 100.0-102.3% (2.2 ppm) of the applied radioactivity from 0 to 14 days posttreatment.

Material balances (based on LSC analysis of individual replicates) were 92.2-99.5% and 99.4-100.6% of the applied radioactivity for the irradiated and dark control samples, respectively (Table IV, p. 34).

COMMENTS

1. Although sterile equipment was used in the experiment and the initial buffered solution was filter-sterilized, sterility was not confirmed at the termination of the study. Subdivision N Guidelines require that sterility of the test systems be confirmed throughout the incubation to ensure that the observed degradation represents photolysis rather than microbial degradation of the test compound.
2. Sampling days (0, 1, 3, 7, 14, 16, and 19 days) reported in this review are "nominal sampling days" and correspond to 0, 2.75, 7.51, 17.67, 34.56, 39.95, and 47.17 equivalent natural sunlight days for the phenyl label study (Table II, p. 32); and 0, 2.68, 7.76, 17.73, 37.92, and 40.90 equivalent natural sunlight days for the cyclohexane label study. The

half-life of the parent was reported by the study author in terms of equivalent natural sunlight days as opposed to the nominal sampling days.

3. The reviewer noted that the registrant-calculated half-life of the parent compound 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.
4. In the phenyl label study, unidentified minor degradates (≥ 8) were each $\leq 6.3\%$ of the applied radioactivity in the irradiated samples (pp. 24, 27; Figure 12, p. 49). The study author stated that the identity of the individual degradates was not determined because the degradates were present at low concentrations.
5. Method detection limits and limits of quantitation were not reported for LSC, HPLC or TLC analyses. Limits of detection and quantitation should be reported to assure the adequacy of the methods for the determination of the parent compound and degradates in the test system.
6. The aqueous solubility of the test compound at 20°C was reported as 15 mg/L (pH 6.9; p. 18).
7. A phosphate buffer solution was used; it is recommended that borate or acetate buffers be utilized to minimize buffer effects. In addition, a 0.0003 M pH 7 buffer solution was used to prepare the test solution. EPA recommends the use of 0.01 M solutions to adequately buffer pH and to minimize catalytic effects of the buffer. The reviewer notes that the pH remained constant in the phenyl label study (Table III, p. 33). However, the pH was not monitored in the cyclohexane label study.
8. The adsorption spectrum (200-800 nm) of the pesticide (at 2.0 ppm and pH 7) is shown in Figure 9 (p. 46).

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