

US EPA ARCHIVE DOCUMENT

B. RECOMMENDATIONS:

1. The study authors attributed the incomplete material balance on days 5 and 9 to adsorption onto the glass walls during storage, which was considered an anomaly since there was no previous evidence that parent RH-5287 adsorbed onto glass walls. According to the authors, the problem was corrected by adding acetonitrile to the storage vials in subsequent sampling times. However, it may be possible that at day 5 and 9 photoproducts form that may adsorb stronger onto glass walls than parent and/or other degradation products. The registrant must attempt to characterize/identify the photoproducts/degradates that may form during the first to second week of irradiation.
2. The registrant must address the storage stability of samples during the storage time and conditions prior to analysis.
3. The registrant characterized the degradates according to polarity, but were not able to conclusively identify these degradates, which they associate as being formed by the rapid cleavage of the labile N-S bond followed by subsequent oxidation. Most of the radioactivity (ca 55% at 15 days; ca. 68% at 30 days) associated with degradation products was centered around 4-min retention time and suggest (based on published work) that they are "ring-open structures" and likely to be n-octyl oxalamic and n-octyl malonamic acids. The reviewer agrees that this is likely to be the case. However, since no analyses were performed at sampling times less than 15-days, EFGWB is requesting the registrant to comment about how fast it is believed that ring cleavage would occur.
4. The registrant must submit the electronic absorption spectra (UV-VIS) of RH-5287 at pH 5, 7, and 9.
5. Other comments in the COMMENTS section must also be addressed.

METHODOLOGY:

Ring-labeled [¹⁴C]RH-5287 (labeled in the 3-one position, radiochemical purity >99%, specific activity 55.39 mCi/g, Rohm and Haas) dissolved in acetonitrile, was aseptically added to a sterile Erlenmeyer flask. The acetonitrile was allowed to evaporate, and filter-sterilized (0.22 um) pH 7.0 buffer (0.1 M phosphate) was added to the flask. The solutions were sonicated to insure even mixing; the final concentration of [¹⁴C]RH-5287 was 0.97 ppm. Aliquots of the test solution were aseptically transferred to Pyrex and quartz tubes. The Pyrex tubes were wrapped in aluminum foil to serve as dark controls. The quartz tubes served as irradiation samples. Both sets of tubes were attached to continuous air flow systems, and were immersed (depth of 4 inches) in deionized water in a waterbath which was maintained at 24.7 ± 0.4 C by a constant temperature circulator. The waterbath was located on a rooftop in Lexington, Kentucky (38.05248°N latitude, 84.30°W longitude), and the tubes were oriented

at a 30° angle to the horizon and perpendicular to the path of the sun. Air (uncharacterized) was drawn through the sample vials (flow rate 1-2 mL/min), then sequentially through two sterile foil-wrapped 10% sodium hydroxide trapping solutions to trap carbon dioxide. Sunlight irradiance was measured using a radiometer located near the waterbath and oriented towards the sun at the same angle as the samples. During the 30-day study, the minimum light intensity varied from 75 to 367 uwatts/cm², the maximum light intensity varied from 3776 to 16282 uwatts/cm², and the light energy varied from 1.1 to 6.9 watt·minutes/cm² (Table IV). The average daily light energy was 4.3 ± 1.9 watt·minutes/cm². Duplicate irradiated and dark control tubes of test solution were removed for analysis at 0, 5, 9, 15, 20, and 30 days posttreatment. The gas dispersion tubes were changed at each sampling interval, and aliquots of the sodium hydroxide solution were measured for total radioactivity by LSC.

At each sampling interval, aliquots of the irradiated and dark control solutions were immediately analyzed for total radioactivity using LSC. The remaining test solutions were stored at 4 C for subsequent analysis by HPLC. The test solutions were analyzed on an LC-18 reverse-phase column with a mobile phase of methanol:water (75:25, v:v) to 100% methanol with UV detection (220 nm) and radioactive flow monitoring. Retention times of unknowns were compared to those of reference standards of RH-5287, RH-0244HQ, RH-0245F, RH-0206C, RH-0247R, RH-287 sulfoxide, RH-085 sulfoxide, RH-6810E, RH-16801, RH-893 sulfoxide, SW87-7564, OCPA, RH-893HQ, RH-893-I, [¹⁴C]RH-893HQ, malonamic acid, malonamide, and malonic acid.

DATA SUMMARY:

Ring-labeled [¹⁴C]RH-5287 (labeled in the 3-one position, radiochemical purity >99%), at 0.97 ppm, photodegraded with a registrant-calculated half-life of 13.4 days in sterile aqueous buffer solutions (potassium phosphate, pH 7) that were irradiated with sunlight for 30 days at 24.7 ± 0.4 C (Table IX and Figure 7). The average daily light energy was 4.3 ± 1.9 watts·minutes/cm² (Table IV). In the dark control solutions, RH-5287 comprised 74.7-86.0% of the recovered radioactivity at 30 days posttreatment (Table VIII); the registrant-calculated half-life of RH-5287 in the dark solutions was approximately 80 days.

In the irradiated solutions, RH-5287 declined from 97.7% of the recovered radioactivity immediately posttreatment to 40.3-46.8% at 15 days and 22.1-25.3% at 30 days (Table VIII and Figure 6). The major degradate,

carbon dioxide

totaled 9.2% at 15 days and 14.9% at 30 days (Table V).

Other [¹⁴C]activity increased from approximately 2% of the recovered immediately posttreatment to 76% at 30 days (Table VIII). This [¹⁴C]activity was tentatively characterized as consisting primarily of two ring-opened polar degradates having retention times of 4 and 7 minutes (Peaks 1 and 2, respectively, Figure 6), which reached a maximum of 67.6 and 7.7%, respectively, of the recovered radioactivity at 30 days (Table A). Two additional unidentified degradates each comprised less than 1% of the recovered at 30 days.

The pH of the test solutions was 7.0 or 7.2 over the 30-day test period (Table VII). The material balances for the irradiated solutions were 94.0 to 100.5% of the applied through day 20, and 79.9 and 87.0% on day 30 (Table V). The material balances for the dark control solutions were 91.5 to 105.4% of the applied through day 15, were 72.4 and 76.3% on day 20, and were 31.0 and 46.0% on day 30. The study authors reported that water entering the vials from a storm diluted the solutions prior to the 30-day sampling; there was no apparent explanation for the 20-day samples.

COMMENTS:

1. The first sampling interval for which data were provided was 15 days posttreatment, at which time approximately 56% of the RH-5287 had degraded.

Although samples were collected at 5 and 9 days posttreatment (Table II), data were not provided because the material balances for these intervals were incomplete, which the study authors attributed to adsorption on the glass walls of the containers during storage of the aliquots at 4 C. Since previous research with RH-5287 had not indicated that adsorption was a problem, this loss of activity was thought to be an anomaly that was, in some manner, a function of cold storage and/or adsorption. The problem was reported to have been corrected for subsequent sampling days by adding acetonitrile to the storage vials prior to the addition of the test solution.

2. Based on prior research with isothiazolone-type compounds and comparisons of degradate retention times with those of fourteen potential metabolites of RH-5287 (Table I), the study authors suggested that RH-5287 (when subjected to photodegradation) is hydrolyzed at the N-S bond, resulting in the formulation of carboxylic acid metabolites such as n-octyl oxalmic acid and n-octyl malonamic acid.
3. Storage stability data were not provided. According to the Protocol, samples were required to be kept frozen until analysis; in the Materials and Methods section of the experiment, samples were reported as having been stored at 4 C until analysis. Also, in the Introduction, the study was reported to have been initiated January 1989 and completed December 1990; in the Quality Assurance Report (p. 4), the data for the 20-day samples was reviewed June 15, 1989;

and in the Schedule of Events (Table II), the 20-day samples were reported to have been obtained on May 8, 1990.

4. The absorption spectrum of the pesticide in the test solution was not provided.
5. In order to obtain additional material balance data in the event that some [^{14}C]volatiles were not trapped by the sodium hydroxide solutions, a closed or sealed system was also used to assess the photolysis of RH-5287. Pyrex and quartz tubes filled with test solution were sealed with rubber septa. As before, the Pyrex tubes were wrapped with aluminum foil to serve as dark controls. The samples were incubated as previously described; tubes were collected for analysis at 0, 5, 9, and 30 days posttreatment. At each sampling interval, 1.0 mL of saturated sodium hydroxide was injected through the rubber septum of each tube to convert trapped carbon dioxide into [^{14}C]sodium bicarbonate. Aliquots were obtained for quantification by LSC. The solution in each tube was saturated with barium chloride, vortexed, and centrifuged, and the supernatants were assayed for [^{14}C]residues by LSC. The material balances for the irradiated solutions in sealed systems varied from 87.2 to 103.3% and for the dark controls, from 98.8 to 102.6% (Table VI).
6. Discrepancies also exist concerning the traps. In the Materials and Methods section and Table V, the two carbon dioxide traps were reported to contain 10% sodium hydroxide. In contrast, Figure 2 and a reference in the text indicate that one of the traps contains ethylene glycol.
7. The study authors noted that the percentage of RH-5287 in Table IX (see Footnote 1) used for the half-life calculations were not based on the actual percentages in solution as determined by HPLC and shown in Table VIII. Their calculations were apparently based on the assumption that all non- $^{14}\text{CO}_2$ activity in Table V represented parent and [^{14}C]degradates.
8. The method detection limit was not reported.
9. Analysis of the sample solutions by TLC was mentioned briefly in the methodology provided by the study author; however, details of a TLC analysis were not provided and there was no evidence that this type of analysis was actually conducted.

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