

## DATA EVALUATION RECORD

## STUDY 1

CHEM-030703 *030702* Naptalam §161-1  
 CAS No. 000132-67-2  
 FORMULATION--00--ACTIVE INGREDIENT

## STUDY ID 43647701

Kabler, A. K. and T. Z. Kendall. 1995. N-1-Naphthylphthalamic acid (naptalam): determination of the rate of hydrolysis at pH 5. Toxikon Environmental Sciences Laboratory Project ID: J9501005; and Uniroyal Chemical Company Laboratory Project ID: 9510. Unpublished study performed by Toxikon Environmental Sciences, Jupiter, FL; and submitted by Uniroyal Chemical Company, Inc., Middlebury, CT.

## DIRECT REVIEW TIME = 30 Hours

REVIEWED BY: M. T. Holdsworth, M.S. Signature: *C.A. Sutton for M. Holdsworth*  
 TITLE: Scientist Date: *6/20/00*

EDITED BY: B. S. Perkovich, M.E.M. Signature: *Brenda Perkovich*  
 TITLE: Scientist Date: *6/20/00*

APPROVED BY: P. H. Howard Signature: *Philip H. Howard*  
 TITLE: Project Manager Date: *6/19/00*

ORG: Syracuse Research Corp.  
 Arlington, VA 22202

TEL: 703/413-9369

*Ibrahim Abdel-sabeh*

APPROVED BY: ~~James Breithaupt~~  
 TITLE: Agronomist  
 ORG: ERB II/EFED/OPP  
 TEL: 703/305-5925

*Re-calculated  
 t/2 & plot 10/13/00*

SIGNATURE:



## CONCLUSIONS

### Degradation - Hydrolysis

1. This study is scientifically valid and provides useful information on the hydrolysis of naptalam in pH 5 buffer solution. However, individual test vessels were not prepared for each sampling interval. Instead, two vials (bulk samples) of buffer solution were treated, and duplicate aliquots of solution from each bulk sample were removed for analysis at each sampling interval.
2. This study does not meet Subdivision N Guidelines for the fulfillment of EPA data requirements on hydrolysis for the following reason:
  - (i) the study was not conducted in pH 7 and 9 buffer solutions.
3. Nonradiolabeled plus naphthalene ring-labeled [ $1-^{14}\text{C}$ ]naptalam, at a nominal concentration of 51.9 ppm, degraded with a registrant-calculated half-life of 2.9 days ( $r^2 = 0.97$ ) in sterilized pH 5 aqueous buffer solution incubated in darkness at  $25 \pm 1^\circ\text{C}$  for up to 21 days; however, the observed half-life was approximately 1 day. The parent was initially present at 96.6% of the applied radioactivity, decreased to 48.5% by 1 day, 25.0% by 4 days, and 5.0% by 8 days, and was 1.1% (one replicate) at 21 days posttreatment. The major degradate 1-naphthylamine was a maximum of 86.9% of the applied radioactivity at 21 days posttreatment. The major degradate N-1-naphthylphthalimide was a maximum of 13.5% of the applied radioactivity at 2 days posttreatment and was 3.4% at 21 days. The major degradate (nonradiolabeled) phthalic acid was a maximum of 20.4 ppm at 21 days posttreatment.

## METHODOLOGY

Nonradiolabeled plus naphthalene ring-labeled [ $1-^{14}\text{C}$ ]naptalam {2-[(1-naphthalenylamino)carbonyl]benzoic acid; radiochemical purity >98%, specific activity 24.8 mCi/mmol; p. 10}, dissolved in methanol, was added at a nominal concentration of 51.9 ppm to sterilized pH 5 (acetate) 0.01 M aqueous buffer solution, and the solution was transferred to two autoclaved glass vials (pp. 12, 14). An additional vial containing untreated buffer solution was prepared to serve as a control. The vials were capped, placed on a rotary shaker, and incubated in darkness at  $25 \pm 1^\circ\text{C}$  for up to 21 days. Duplicate aliquots from each test vial were removed for analysis at 0, 1, 2, 4, 8, 15, and 21 days posttreatment.

At each sampling interval, duplicate aliquots were analyzed for total radioactivity by LSC (p. 14). An aliquot from each vial was also analyzed by HPLC (Zorbax  $\text{R}_x\text{-C}_{18}$  column) using a mobile phase gradient of (A)  $\text{CH}_3\text{CN}:\text{water}:\text{CF}_3\text{COOH}$  (5:95:0.1, v:v:v) to (B)

CH<sub>3</sub>CN:water:CF<sub>3</sub>COOH (95:5:0.1, v:v:v; A:B: 90:10 to 50:50, v:v) with UV (280 nm) detection; eluate fractions were collected at one-minute intervals and analyzed by LSC analysis (p. 15). To determine the presence of nonradiolabeled phthalic acid, aliquots from each test vial were analyzed by HPLC (Zorbax R<sub>x</sub>-C<sub>18</sub> column) using a isocratic mobile phase of CH<sub>3</sub>CN:water:CF<sub>3</sub>COOH (14:86:0.1, v:v:v) with UV (280 nm) detection (Table 5, p. 24); the limit of detection was 5.0 ppm.

## DATA SUMMARY

Nonradiolabeled plus naphthalene ring-labeled [1-<sup>14</sup>C]naptalam (radiochemical purity >98%), at a nominal concentration of 51.9 ppm, degraded with a registrant-calculated half-life of 2.9 days ( $r^2 = 0.97$ ) in sterilized pH 5 aqueous buffer solution incubated in darkness at  $25 \pm 1^\circ\text{C}$  for up to 21 days (p. 17; Table 2, p. 21); however, the observed half-life was approximately 1 day. The parent was initially present at 96.6% of the applied radioactivity, decreased to 48.5% by 1 day, 25.0% by 4 days, and 5.0% of the applied by 8 days posttreatment, and was 1.1% (one of two replicates) of the applied at 21 days posttreatment (Table 3, p. 22). The major degradate

### 1-naphthylamine

was initially (day 0) present at 6.6% of the applied radioactivity; increased to 25.7% by 1 day, 41.7% by 2 days, and 77.7% by 8 days posttreatment; and was a maximum of 86.9% of the applied radioactivity at 21 days posttreatment. The major degradate

### N-1-naphthylphthalimide

was initially (day 0) present at 2.2% of the applied radioactivity, increased to a maximum of 13.5% of the applied by 2 days posttreatment, decreased to 8.7% of the applied by 8 days posttreatment, and was 3.4% of the applied at 21 days posttreatment. The major degradate (nonradiolabeled)

### phthalic acid

was present at 15.3 ppm at 1 day posttreatment, increased to 17.3 ppm by 8 days posttreatment, and was a maximum of 20.4 ppm at 21 days posttreatment (data were reported only as concentrations; Table 5, p. 24).

Material balances (based on LSC analysis) were 87.3-100% of the applied radioactivity throughout the incubation period; a clear pattern of decline was not observed (Table 1, p. 21).

COMMENTS

1. Two vials of buffer solution were treated, and duplicate aliquots of solution from each vial were removed for analysis at each sampling interval (p. 14). Scientifically sound laboratory practices dictate that duplicate samples, prepared and incubated for removal at each sampling interval, are necessary in order to accurately determine the decline of the parent and the formation and decline of degradates. The use of bulk samples from which aliquots are drawn repeated over time allows for the possibility of contamination and microbial degradation. However, in this study, the pattern of decline of the parent was similar between the two samples, indicating that microbial degradation of one or the other sample likely did not occur (Table 3, p. 22). In the future, individual duplicate test vessels should be utilized at each sampling interval and sterility of the test solutions should be confirmed throughout the study.
2. The study was conducted only in pH 5 buffer solution. Subdivision N Guidelines require that hydrolysis studies be conducted in solutions of pH 5, 7, and 9.
3. The study was conducted using naphthalene ring-labeled [1-<sup>14</sup>C]naptalam. An additional ring structure (phenyl ring) was not radiolabeled; however, a major degradate (phthalic acid) was detected which contained that ring structure. The major degradate phthalic acid was present at a maximum of 20.4 ppm at 21 days posttreatment (Table 5, p. 24).
4. Method detection limits were not reported for LSC or for one HPLC system. Both limits of detection and quantitation should be reported to allow the reviewer to evaluate the adequacy of the methods for the determination of the test compound and its degradates.
5. Volatiles traps were not used in this study. The reviewer noted that the system was closed, and material balances were reasonable.
6. The solubility of the test compound in the buffer solution was not reported as required by Subdivision N Guidelines. The solubility of the test compound should be reported to allow the reviewer to assess whether the compound was available in solution for hydrolytic degradation. The reviewer notes that the solubility of naptalam in water was reported as 200 mg/L (at 20°C) in *The Pesticide Manual* (11<sup>th</sup> edition, 1997. British Crop Protection Council).
7. The reviewer notes that the major degradate 1-naphthylamine was reported as  $\alpha$ -aminonaphthalene in Table 3 (p. 22).

Table 1. Material Balance of pH 5 Buffered Solutions Treated With [<sup>14</sup>C]-Naptalam and incubated in the dark at 25°C

Sampling Interval (Day)	Mean Total DPM Recovered	<sup>14</sup> C-Naptalam Residues (µg/mL)	% of Applied <sup>14</sup> C-Naptalam Residues Recovered
0	3374	42.5	100
1	3352	42.2	99.3
2	3042	38.3	90.1
4	2947	37.1	87.3
8	3055	38.4	90.4
15	3151	39.6	93.2
21	3043	38.3	90.1

Table 2. Linear Regression Analysis of N-1-Naphthylphthalamic acid (Naptalam) during the definitive hydrolysis study.

Sampling Interval (Day)	Mean Concentration of <sup>14</sup> C-Naptalam (µg/mL)	Percent of Time Zero ( <sup>14</sup> C-Naptalam)	Ln of Percent Time Zero
0	41.0	100	4.61
1	20.4	49.8	3.91
2	13.4	32.7	3.49
4	9.26	22.6	3.12
8	1.92	4.7	1.54 <sup>S</sup>
15	0.71	1.7	0.55 <sup>0.53</sup>
21	0.21	0.51	-0.67

Linear Regression Data (Ln of % Time Zero vs. Sampling Interval)

Constant	4.106054
Std Err of Y Est	0.390746
R Squared	0.965993
No. of Observations	7
Degrees of Freedom	5
X Coefficient	-0.23907 days <sup>-1</sup>
Std Err of Coefficient	0.0201
Correlation	0.9828
t <sub>1/2</sub>	2.90 days

Table 3. HPLC analysis of pH 5 Buffered Solutions Treated With [<sup>14</sup>C]-Naptalam at 51.9 μg/mL and incubated in the dark at 25°C. Data reported as percent of applied radioactivity.

Sampling Interval (Day)	Treatment Replicate	% <sup>14</sup> C-Naptalam	% <sup>14</sup> C-alpha- aminonaphthalene	% <sup>14</sup> C-N-1- naphthyl- phthalimide
0	T1	103.7	5.6	2.2
	T2	89.4	7.6	2.1
	<b>Mean</b>	<b>96.6</b>	<b>6.6</b>	<b>2.2</b>
1	T1	47.7	25.7	8.8
	T2	49.2	25.6	9.7
	<b>Mean</b>	<b>48.5</b>	<b>25.7</b>	<b>9.3</b>
2	T1	33.6	40.0	13.6
	T2	36.6	43.4	13.4
	<b>Mean</b>	<b>35.1</b>	<b>41.7</b>	<b>13.5</b>
4	T1	29.7	59.8	13.4
	T2	20.2	62.7	11.6
	<b>Mean</b>	<b>25.0</b>	<b>61.3</b>	<b>12.5</b>
8	T1	5.7	79.0	8.1
	T2	4.3	76.3	9.3
	<b>Mean</b>	<b>5.0</b>	<b>77.7</b>	<b>8.7</b>
15	T1	1.8	85.1	7.6
	T2	1.8	83.4	9.3
	<b>Mean</b>	<b>1.8</b>	<b>84.3</b>	<b>8.5</b>
21	T1	0.0	87.1	3.8
	T2	1.1	86.7	3.0
	<b>Mean</b>	<b>0.55</b>	<b>86.9</b>	<b>3.4</b>

Table 4. HPLC analysis of pH 5 Buffered Solutions Treated With [<sup>14</sup>C]-Naptalam at 51.9 µg/mL and incubated in the dark at 25°C. Data reported as ppm.

Sampling Interval (Day)	Concentration of Naptalam (µg/mL)	Concentration of α-aminonaphthalene (µg/mL)	Concentration of N-1-naphthylphthalimide (µg/mL)
0	41.0	2.81	0.935
1	20.4	10.8	3.92
2	13.4	16.0	5.17
4	9.26	22.7	4.64
8	1.92	29.8	3.34
15	0.71	33.4	3.37
21	0.21	33.3	1.30

$$\text{Concentration A } (\mu\text{g/mL}) = (\%A \times \text{Naptalam Equivalents} \times 100)$$

where A = Naptalam, α-Aminonaphthalene or N-1-Naphthylphthalimide



Table 5. Quantitation of unlabeled phthalic acid formed during the definitive hydrolysis study with Naptalam.

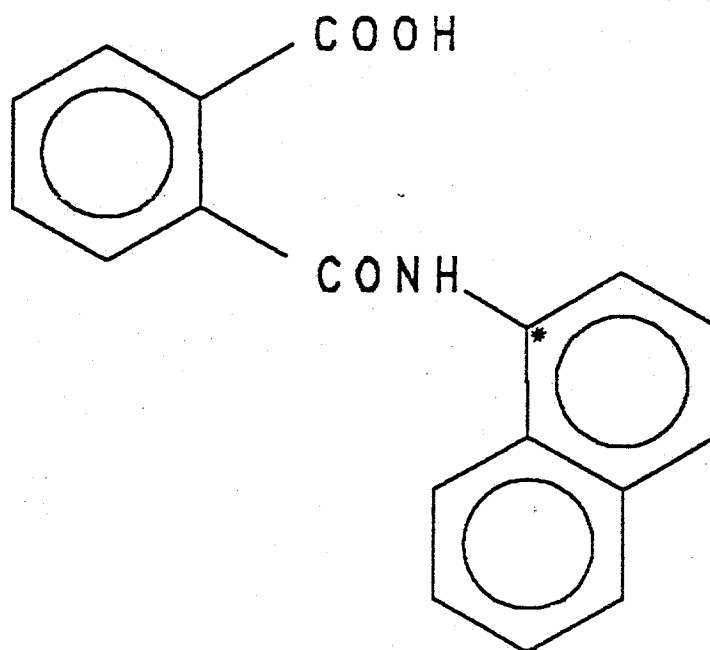
Sampling Interval (Day)	Naptalam Concentration ( $\mu\text{g/mL}$ )	Mean Phthalic Acid* Concentration ( $\mu\text{g/mL}$ )
1	24.6	15.3
8	2.10	17.3
21	0.23	20.4

\* Samples chromatographed isocratically with 14%  $\text{CH}_3\text{CN}$  : 86%  $\text{H}_2\text{O}$  : 0.1%  $\text{CF}_3\text{COOH}$  and detected at 280 nm. The minimum detectable level (MDL) for phthalic acid under these conditions was 5.0  $\mu\text{g/mL}$ .

Table 6. Measurements of pH during the definitive hydrolysis study.

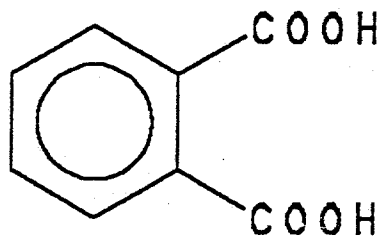
Sampling Interval (Day)	Sample Identification	Measured pH
0	Test Replicate 1	5.01
0	Test Replicate 2	5.01
0	Acetate Buffer Blank	5.01
21	Test Replicate 1	4.34
21	Test Replicate 2	4.36
21	Acetate Buffer Blank	5.11

Figure 1. Structure of N-1-Naphthylphthalamic acid (Naptalam)

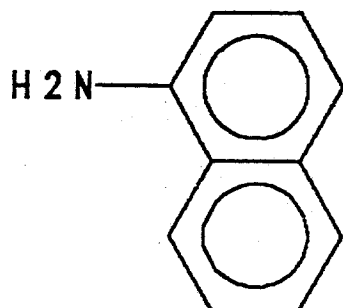


\*Site of radiolabel

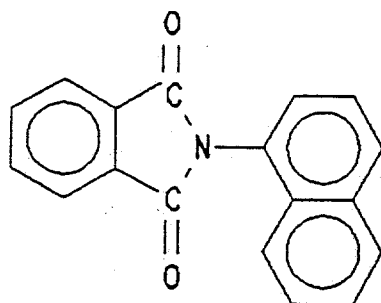
Figure 2. Structures of hydrolysis products of N-1-Naphthylphthalamic acid: phthalic acid, 1-naphthylamine and N-1-naphthylphthalimide



Phthalic Acid



1-Naphthylamine



N-1-Naphthylphthalimide

Figure 3. Graphical representation of the definitive hydrolysis study of [<sup>14</sup>C]-Naptalam at pH 5

