

DATA EVALUATION RECORD

STUDY 1

§161-1

CHEM 067710 DPX-MP062 CAS No. 144171-61-9 FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 44477301

Ferraro, P. and S. McEuen. 1996. Hydrolysis of DPX-JW062 (a racemic mixture of DPX-KN128 and DPX-KN127) in buffer solutions of pH 5, 7, and 9. Laboratory Project ID: AMR 2789-93. Unpublished study performed and submitted by E. I. du Pont de Nemours and Co., Wilmington, DE.

| DIRECT REVIEW TIME = 57 hours | | | | | |
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CONCLUSIONS

Degradation - Hydrolysis

1. This study provides supplemental data on the hydrolysis of DPX-JW062. The data are deemed as supplemental because 1.) there was inadequate buffering in the pH 5 and 9 buffer solution (0.5 pH unit change), 2.) degradate identification and rate studies were conducted under different environmental conditions (e.g., cosolvent concentration), 3.) polar degradates in pH 9 buffer solution were not identified, 4.) there was incomplete

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degradate identification in the pH 7 buffer solution, 5.) the limit of quantification (LOQ) and limit of detection (LOD) for the analytical methods were not reported. To satisfy the data requirement, the registrant should provide additional hydrolysis data on degradate identification and degradation rate analysis of DPX-JW062 in pH 7 and 9 buffer solution. Since DPX-JW062 was stable (t1/2 > 1 year) in the pH 5 buffer solutions, EFED believes that repeating a study in pH 5 solution should not yield additional information. Additionally, the registrant should report the LOD and LOQ for the analytical methods.

2. Radiolabeled DPX-JW062, at a nominal concentration of 0.15 mg/L, was hydrolytically stable in pH 5 aqueous buffer solution (mean half-life = 519 days), and hydrolyzed with nonlinear first-order half-lives of 36 days ($r^2 = 0.95$, indanone label; $r^2 = 0.97$, phenyl label) and 24 hours ($r^2 = 0.98$, indanone label; $r^2 = 0.83$, phenyl label) in pH 7 and pH 9 aqueous buffer solutions incubated in darkness at 25 °C for up to 30 days. Similar degradation patterns were observed for the indanone and phenyl labeled DPX-JW062. The major degradate for indanone and phenyl labeled DPX-JW062 in both pH 7 and 9 buffer solutions was IN-KT413. However, unidentified minor degradates were detected in the pH 7 and 9 buffer solutions.

METHODOLOGY

Indanone ring-labeled [1-14C]DPX-JW062 {(R,S)-methyl 7-chloro-2,5-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2e][1,3,4]oxadiazine-4a(3H)-carboxylate; radiochemical purity 98.6%, specific activity 55.49 μ Ci/mg} or uniformly phenyl ring-labeled [¹⁴C]DPX-JW062 {radiochemical purity 99.8%, specific activity 54.034 μ Ci/mg}, dissolved in acetonitrile (1% by volume), was added at a nominal concentration of 0.15 mg/L to autoclaved borosilicate glass vials containing pH 5 (acetate), pH 7 (phosphate), and pH 9 (borate) 0.001 M aqueous buffer solutions (p. 10). Buffer solutions were filter-sterilized (0.02 μ m) and tested for sterility in tubes of trypticase soy broth. The vials were capped and incubated at 25 °C in darkness for up to 30 days. An individual test vial (for each label) was removed for analysis from the pH 5 test system at 0, 1, 3, 8, 15, 22, and 30 days posttreatment; from the pH 7 test system at 0, 1, 3, 5, 7, 9, 12, 15, 18, 21, 25, and 30 days posttreatment; and from the pH 9 test system at 0, 3, 6, 8, 10, 12, 24, 48, 72 and 120 hours, and at 15 and 30 days posttreatment. To generate sufficient degradates for characterization, an additional set of samples was prepared at an application rate of 1 ppm using acetonitrile at 5% by volume (p. 14).

At each sampling interval, triplicate aliquots of each solution were analyzed for total radioactivity by LSC; aliquots of two vial rinsates were also analyzed to determine material balances from the samples used to determine parent compound degradation. Aliquots of each solution were analyzed by HPLC (Zorbax RX-C8 column) using a mobile phase gradient of acetonitrile:water (20:80 to 100:0) with fraction collection followed by LSC analysis (pp. 12-13). To characterize degradates, eluent fractions from the 1 ppm treatment system were additionally analyzed by LC/MS (Zorbax C18 Column) using a

mobile phase gradient of 0.1% formic acid:acetonitrile (98:2, v:v; System A): acetonitrile:0.1% formic acid (95:5, v:v; System B; A:B 80:20 to 10:90) with mass selective detection in the negative ion mode (p. 39).

DATA SUMMARY

Radiolabeled DPX-JW062 (radiochemical purities of indanone and phenyl labels, respectively, 98.6% and 99.8%) at a nominal concentration of 0.15 mg/L, was hydrolytically stable in pH 5 aqueous buffer solution, and hydrolyzed with respective registrant-calculated half-lives of 38 days ($r^2 = 0.95$, indanone label; $r^2 = 0.97$, phenyl label) and 24 hours ($r^2 = 0.98$, indanone label; $r^2 = 0.83$, phenyl label) in pH 7 and pH 9 aqueous buffer solutions incubated in darkness at 25°C for up to 30 days (p. 15). In the pH 5 buffer solution, the parent was initially present at 98.1-98.7% of the applied radioactivity, and was 94.0-94.3% of the applied at 30 days posttreatment (Table II, p. 18). In the pH 7 buffer system, the parent was initially present at 98.4-98.6% of the applied radioactivity, decreased to 70.8-69.7% by 15 days posttreatment, and was present at 57.2-57.7% of the applied at 30 days (Table III, p. 19). The major degradate

sodium 7-chloro-2,5,-dihydro-2-[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2-e][1,3,4]oxidiazine-4a(3H)carboxylic acid (IN-KT413)

was present in pH 7 buffer solution at approximately 25-26% of the applied radioactivity (both labels) at 30 days posttreatment (p. 15). Additional unidentified degradates were found in the indanone label system at 6% and in the phenyl label system at 8% of the applied radioactivity at 30 days posttreatment; data for these degradates were not reported for other sampling intervals (p. 16). In the pH 9 buffer system, the parent was initially present in the indanone label system at 97.0% of the applied radioactivity, decreased to 67.2 and 40.8% at 12 and 24 hours posttreatment, respectively, and was 10.3-15.7% of the applied from 120 hours to 30 days. In the phenyl label pH 9 buffer system, the parent was initially present at 96.2% of the applied, decreased to 60.7% and 27.0% by 12 and 24 hours, respectively, and was 12.1-16.0% of the applied from 120 hours to 30 days (Table IV, p. 20). The major degradate

IN-KT413

was present at 43-48% of the applied radioactivity (both labels) at 30 days posttreatment (p. 16). Multiple minor unidentified degradates were observed in the phenyl label system at 30 days posttreatment. Unidentified polar degradates were present in the indanone label system at a total of \geq 20% of the applied radioactivity at 30 days posttreatment. Additional analysis indicated that the unidentified polar compounds were minor degradates (< 10% of applied).

Material balances, as total radioactivity for each solution as determined by LSC analysis prior to residue characterization, were 89.0-104%, 98.6-106%, and 95.4-108% for the pH 5, 7, and 9 test systems (both labels), respectively, throughout the incubation. Material balances as a sum of the parent and degradates in solution were not determined for either the 1% or the 5% cosolvent systems (see Comment # 2).

COMMENTS

- 1. Replicate test vials were not utilized in the study. Individual test vials were prepared and analyzed at each sampling interval for each radiolabel. The use of single test samples is generally not considered to be good laboratory practice; at a minimum duplicate test vials are necessary for each label in order to accurately determine the formation and decline of the degradates. In future studies, the registrant should use treatment replication to assess variability of the data.
- 2. Complete degradate characterization and identification data were not provided. Additional data on the major degradate and other unidentified degradates at day 30 only are mentioned in the text (pp. 15-16); data were not reported for other sampling intervals. It is necessary that the registrant report and summarize the data for all degradates in solution at every sampling interval. In addition, parent compound data at each sampling interval should be included, with summations of parent and degradates reported as material balances for each label/pH combination. The reviewer notes, however, that material balances must be determined using a single system; separate systems cannot be used for kinetics studies and degradate characterization studies, with data combined for the determination of material balances. If separate studies are performed, individual material balances must be reported.
- 3. Degradate characterization data were determined using buffer systems with acetonitrile as a cosolvent at 5% by volume. According to Subdivision N guidelines, cosolvents should be used at ≤1% by volume. The reviewer notes that in the aqueous photolysis study (MRID 44477302; p. 19), the use of acetonitrile at 50% by volume altered the patterns of decline of the degradates by increasing the stability time of intermediate degradates (which were not observed in the kinetic rate study). It is unclear whether the same effect would be observed at a lower concentration for the cosolvent. Additionally, in the aerobic aquatic study (MRID 44477306), the study authors stated that the degradate IN-KT413 was "inherently unstable in acetonitrile" in reference to its degradation in the mobile phase (20:80 or 65:35 acetonitrile:water, v:v) during HPLC analysis (p. 21).
- 4. The pH of each test solution was not constant. In the pH 9 buffer system (both labels), the pH was initially 8.98 and decreased to 8.30-8.34 by 30 days (Table I, p. 17). The reviewer notes that the concentration of the buffers was 0.001 M (p. 10). Subdivision N Guidelines recommend a buffer concentration of 0.01 M in order to keep pH constant.

- 5. Unidentified polar degradates were present in the pH 9 indanone label system at a total of >20% of the applied radioactivity at 30 days posttreatment. The study author stated that none of the polar degradates were present at $\ge 10\%$ of the applied; however, numerical data were not submitted.
- 6. A phosphate buffer system was utilized to study the test compound at pH 7 in water (p.10); it is recommended that borate or acetate buffers be utilized to minimize buffer effects.
- 7. Method detection limits were not reported. Method detection limits and limits of quantitation should be reported to assure the adequacy of the methods for determination of parent and metabolite in the test system.
- 8. The maximum water solubility of the test compound was reported in the study as 300 mg/L at various pH levels when acetonitrile was used as a cosolvent at 1% (p. 12).
- 9. The parent DPX-JW062 is a racemic mixture of {(R,S)-methyl 7-chloro-2,5-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2-e] [1,3,4]oxadiaxine-4a(3H)-carboxylate}. The (S)-enantiomer is the insecticidally active enantiomer and is also called DPX-KN128 (CAS No. 173584-44-6). The (R)-enantiomer is the insecticidally inactive enantiomer and is also called IN-KN127. The compound DPX-MP062 is a formulation containing 75% of DPX-KN128 and 25% of IN-KN127 (MRID 44477309) and is also referred to as DPX-JW062EL.

| · · · · · · · · · · · · · · · · · · · | Nominal pH: 5 | | Nominal pH: 7 | | Nominal pH: 9 | |
|---------------------------------------|------------------|------|---------------|------|---------------|------|
| Experimental Day | IND | TMP | IND | TMP | IND | TMP |
| 0 | 5.19 | 5.19 | 7.07 | 7.07 | 8.98 | 8.98 |
| 15 | n/a ¹ | n/a | n/a | n/a | 8.60 | n/a |
| 30 | 5.64 | 5.57 | 7.16 | 7.16 | 8.34 | 8.30 |

TABLE IPH OF TEST SYSTEMS DURING HYDROLYSIS

| | IND- | IND-JW062 | | TMP-JW062 | |
|---------|--|-----------------------|--------------------------------|-----------------------|--|
| Sample | Total ¹⁴ C (%AR ²) | % Parent Remaining | Total ¹⁴ C (%AR) | % Parent Remaining | |
| 0 Hour | 98.2 | 98.7 | 104 | 98.1 | |
| 1 Day | 104 | 99.5 | 101 | 97.2 | |
| 3 Day | 100 | 99.0 | 102 | 98.4 | |
| 8 Day | 90.7 | 98.4 | 101 | 96.5 | |
| 15 Day | 89.0 | 96.9 | 100 | 97.5 | |
| 22 Day | 91.2 | 96.0 | 97.2 | 95.7 | |
| 30 Day | 100 | 94.0 | 96.6 | 94.3 | |
| Average | 96.2 | | 100 | | |

TABLE IIPH 5 Hydrolysis:Material Balance and Percent of Parent
Remaining

² AR = applied radioactivity

| | IND- | IND-JW062 | | TMP-JW062 | |
|---------|--------------------------------|-----------------------|--------------------------------|-----------------------|--|
| Sample | Total ¹⁴ C (%AR) | % Parent Remaining | Total ¹⁴ C (%AR) | % Parent Remaining | |
| 0 Hour | 103 | 98.4 | 103 | 98.6 | |
| 1 Day | 104 | 95.4 | 101 | 96.8 | |
| 3 Day | 101 | 92.4 | 102 | 91.1 | |
| 5 Day | 100 | 87.9 | 101 | 86.8 | |
| 7 Day | 98.6 | 79.0 | 105 | 82.9 | |
| 9 Day | 101 | 77.7 | 104 | 78.0 | |
| 12 Day | 101 | 74.8 | 103 | 72.4 | |
| 15 Day | 102 | 70.8 | 105 | 69.7 | |
| 18 Day | 103 | 67.3 | 106 | 65.7 | |
| 21 Day | 101 | 60.8 | 106 | 64.1 | |
| 25 Day | 102 | 63.7 | 103 | 61.0 | |
| 30 Day | 104 | 57.2 | 104 | 57.7 | |
| Average | 102 | | 104 | | |

TABLE IIIPH 7 Hydrolysis:Material Balance and Percent of ParentRemaining

TABLE IVPH 9 Hydrolysis:Material Balance and Percent of ParentRemaining

| | IND- | IND-JW062 | | TMP-JW062 | |
|----------|--------------------------------|---------------------------------------|--------------------------------|-----------------------|--|
| Sample | Total ¹⁴ C (%AR) | % Parent Remaining | Total ¹⁴ C (%AR) | % Parent Remaining | |
| 0 Hour | 95.4 | 97.0 | 99.2 | 96.2 | |
| 3 Hour | 98.9 | 88.2 | 101 | 85.2 | |
| 6 Hour | 101 | 79.0 | 104 | 80.7 | |
| 8 Hour | 100 | 75.2 | 105 | 74.2 | |
| 10 Hour | 103 | 73.0 | 106 | 68.1 | |
| 12 Hour | 101 | 67.2 | 103 | 60.7 | |
| 24 Hour | 102 | 40.8 | 107 | 27.0 | |
| 48 Hour | 104 | 26.2 | 104 | 26.8 | |
| 72 Hour | 103 | 16.0 | 104 | 24.8 | |
| 120 Hour | 104 | 10.4 | 107 | 12.1 | |
| 15 Day | 104 | 15.7 | 104 | 16.0 | |
| 30 Day | 105 | 10.3 | 108 | 13.8 | |
| Average | 102 | · · · · · · · · · · · · · · · · · · · | 104 | 444, | |

TABLE VNATURAL LOG-CONVERTED DATA AND BEST-FIT LINE PARAMETERS OFDPX-JW062 Hydrolysis

| Hydrolysis pH S: % parent remaining time (days) ND natural log IND TMP natural log TMF 0 98.7 4.59 98.1 4.59 1 99.5 4.60 97.2 4.58 3 99.0 4.60 98.4 4.59 8 98.4 4.59 96.5 4.56 30 94.0 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 r/2 r/2 = 0.96 0.77 4.60 98.1 4.59 pH 7: % parent remaining intercept = 99.4 4.60 98.1 4.59 intercept = 99.4 4.59 98.6 4.59 1 95.4 4.59 98.6 4.59 1 95.4 4.56 96.8 4.57 3 92.4 4.53 91.1 4.51 5 87.9 4.48 <t< th=""><th>hydrolysis pH 5: % parent remaining time (days) ND natural log IND NP 0 98.7 4.59 98.1 4.59 1 99.5 4.60 97.2 4.58 3 99.0 4.60 98.4 4.59 8 98.4 4.59 96.5 4.57 15 96.9 4.57 97.5 4.58 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 -1.5E-03 r^2 = 0.96 0.77 4.55 slope = 99.4 4.60 98.1 4.59 intercept = 99.4 4.60 98.1 4.59 1 95.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 12 74.8</th><th></th><th></th><th></th><th></th><th></th></t<> | hydrolysis pH 5: % parent remaining time (days) ND natural log IND NP 0 98.7 4.59 98.1 4.59 1 99.5 4.60 97.2 4.58 3 99.0 4.60 98.4 4.59 8 98.4 4.59 96.5 4.57 15 96.9 4.57 97.5 4.58 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 -1.5E-03 r^2 = 0.96 0.77 4.55 slope = 99.4 4.60 98.1 4.59 intercept = 99.4 4.60 98.1 4.59 1 95.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 12 74.8 | | | | | |
|---|---|----------------|---------|-------------------|---------|-----------------|
| time (days) IND natural log IND IMP natural log IMP 0 98.7 4.59 98.1 4.59 1 99.5 4.60 97.2 4.58 3 99.0 4.60 98.4 4.57 15 96.9 4.57 97.5 4.58 22 96.0 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 0.77 tit/2 (days) = 400.86 604.21 0.77 time (days) ND natural log IND TMP natural log TMF 0 98.5 4.59 98.6 4.59 1 95.4 4.56 96.8 4.57 3 92.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 12 74.8 4.31 72.4 4.28 < | time (days) IND natural log IND INP natural log IMP 0 98.7 4.59 98.1 4.59 1 99.5 4.60 98.4 4.59 3 99.0 4.60 98.4 4.59 8 98.4 4.59 96.5 4.57 15 96.9 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 77 1/2 (days) = 400.86 604.21 604.21 intercept = 99.4 4.60 98.1 4.59 1 95.4 4.59 98.6 4.59 1 95.4 4.56 96.8 4.57 3 92.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 15 70.8 4.26 69.7 4.24 15 70.8 4.26 69.7 4.24 15 | hydrolysis | pH 5: % | parent remaining | | |
| $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ | time (days) | IND | natural log IND | IMP | natural log IMP |
| 1 99.5 4.60 97.2 4.58 3 99.0 4.60 98.4 4.59 8 98.4 4.59 96.5 4.57 15 96.9 4.57 97.5 4.58 22 96.0 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 77 11/2 (days) = 400.86 604.21 604.21 intercept = 99.4 4.60 98.1 4.59 Time (days) ND natural log IND TMP natural log TME 0 98.5 4.59 98.6 4.59 1 95.4 4.56 96.8 4.57 3 92.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 12 74.8 4.21 65.7 4.19 21 | 1 99.5 4.60 97.2 4.58 3 99.0 4.60 98.4 4.59 8 98.4 4.59 96.5 4.57 15 96.9 4.57 97.5 4.58 22 96.0 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 slope -1.73E-03 -1.15E-03 -1.5E-03 r^2 = 0.96 0.77 112 (days) -0.96 0.77 11/2 (days) 90.8 604.21 -1.5E-03 -1.55 -1.59 p pH 7: % parent remaining | 0 | 98.7 | 4.59 | 98.1 | 4.59 |
| 3 99.0 4.60 98.4 4.59 8 98.4 4.59 96.5 4.57 15 96.9 4.57 97.5 4.58 22 96.0 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 -77 r ² = 0.96 0.77 112 (days) = 400.86 604.21 intercept = 99.4 4.60 98.1 4.59 98.6 4.59 1 95.4 4.56 98.6 4.59 1 14.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 12 74.8 4.31 72.4 4.28 15 70.8 4.26 69.7 4.24 18 67.7 4.16 25 63.7 4.15 61.0 4.11 30 57.2 4.05 57.7 4.05 12 74.8 | 3 99.0 4.60 98.4 4.59 8 98.4 4.59 96.5 4.57 15 96.9 4.57 97.5 4.58 22 96.0 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 sigpe = -1.73E-03 -1.15E-03 0.77 th/2 = 0.96 0.77 11/2 (days) = 4.60 98.1 4.59 pH 7: % parent remaining | 1 | 99.5 | 4.60 | 97.2 | 4.58 |
| 8 98.4 4.59 96.5 4.57 15 96.9 4.57 97.5 4.58 22 96.0 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 0.77 r ² 2 = 0.96 0.77 115E-03 intercept = 99.4 4.60 98.1 4.59 intercept = 99.4 4.60 98.1 4.59 ime (days) ND natural log IND TMP natural log TMF 0 98.5 4.59 98.6 4.59 1 95.4 4.56 96.8 4.57 3 92.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 12 74.8 4.31 72.4 4.28 15 70.8 4.26 69.7 4.24 18 </td <td>8 98.4 4.59 96.5 4.57 15 96.9 4.57 97.5 4.58 22 96.0 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 0.77 thereight 99.4 4.60 98.1 4.59 pH 7: % parent remaining memaining memaining time (days) ND natural log IND TMP natural log TMP 0 98.5 4.59 98.6 4.59 1 95.4 4.56 96.8 4.57 3 92.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 12 74.8 4.31 72.4 4.28 15 70.8 4.26 69.7 4.24 18 67.3 4.21 65.7 4.19</td> <td>3</td> <td>99.0</td> <td>4.60</td> <td>98.4</td> <td>4.59</td> | 8 98.4 4.59 96.5 4.57 15 96.9 4.57 97.5 4.58 22 96.0 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 0.77 thereight 99.4 4.60 98.1 4.59 pH 7: % parent remaining memaining memaining time (days) ND natural log IND TMP natural log TMP 0 98.5 4.59 98.6 4.59 1 95.4 4.56 96.8 4.57 3 92.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 12 74.8 4.31 72.4 4.28 15 70.8 4.26 69.7 4.24 18 67.3 4.21 65.7 4.19 | 3 | 99.0 | 4.60 | 98.4 | 4.59 |
| 15 96.9 4.57 97.5 4.58 22 96.0 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 0.77 t1/2 (days) = 400.86 604.21 604.21 intercept = 99.4 4.60 98.1 4.59 pH 7: % parent remaining matural log IND TMP natural log TMF 0 98.5 4.59 98.6 4.59 1 95.4 4.56 96.8 4.57 3 92.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 15 70.8 4.26 69.7 4.24 18 67.3 4.21 65.7 4.19 21 60.8 4.11 64.1 4.16 25 63.7 4.15 61.0 4.11 | 15 96.9 4.57 97.5 4.58 22 96.0 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 slope -1.73E-03 -1.15E-03 -1.15E-03 r^2 = 0.96 0.77 1 intercept = 99.4 4.60 98.1 4.59 PH 7: % parent remaining time (days) IND natural log IND TMP natural log TMP 0 98.5 4.59 98.6 4.59 1 95.4 4.56 96.8 4.57 3 92.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 12 74.8 4.31 72.4 4.28 15 70.8 4.26 69.7 4.24 16 67.3 4.21 65.7 4.19 21 60.8 4.11 61. | 8 | 98.4 | 4.59 | 96.5 | 4.57 |
| $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ | 22 96.0 4.56 95.7 4.56 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 0.77 th/2 = 0.96 0.77 th/2 = 99.4 4.60 98.1 4.59 pH 7: % parent remaining matural log IND TMP natural log TMP 0 98.5 4.59 98.6 4.59 1 95.4 4.56 96.8 4.57 3 92.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 12 74.8 4.31 72.4 4.28 15 70.8 4.26 69.7 4.24 18 67.3 4.21 65.7 4.19 21 60.8 4.11 64.1 4.16 25 63.7 4.15 61.0 4.11 30 57.2 | 15 | 96.9 | 4.57 | 97.5 | 4.58 |
| 3094.04.5494.34.55slope = r^2 =-1.73E-03 0.96-1.15E-03 0.77t1/2 (days) = intercept =99.44.6098.14.59pH 7: % parent remainingtime (days)IND 0natural log IND natural log INDTMP natural log TMF 098.54.59098.54.5998.64.59195.44.5696.84.57392.44.5391.14.51587.94.4886.84.46779.04.3782.94.42977.74.3578.04.361274.84.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05slope = 0.950.974.5896.24.5711/2 (days) = 3038.2037.52intercept =94.74.5595.04.55PH 9: % parent remainingtime (days)IND natural log INDTMP natural log TMP097.04.5896.24.570.12588.24.4885.24.450.2579.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.111< | 30 94.0 4.54 94.3 4.55 slope = -1.73E-03 -1.15E-03 r ² = 0.96 0.77 til/2 (days) = 99.4 4.60 98.1 4.59 pH 7: % parent remaining time (days) ND natural log IND TMP natural log TMP 0 98.5 4.59 98.6 4.59 1 95.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 12 74.8 4.31 72.4 4.28 15 70.8 4.26 69.7 4.24 18 67.3 4.21 65.7 4.19 21 60.8 4.11 64.1 4.16 25 63.7 4.15 61.0 4.11 30 57.2 4.05 57.7 4.05 -1.81E-02 -1.85E-02 752 | 22 | 96.0 | 4.56 | 95.7 | 4.56 |
| $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ | slope =-1.73E-03-1.15E-03r^2 =0.960.77t1/2 (days) =99.44.6098.14.59 PH 7: % parent remainingtime (days)NDnatural log INDTMPnatural log TMP098.54.5998.64.59195.44.5696.84.57392.44.5391.14.51587.94.4886.84.46779.04.3782.94.42977.74.3578.04.361274.84.2669.74.241570.84.2669.74.241867.34.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05stops0.97t1/2 (days) =-1.81E-02-1.85E-02r^2 =0.950.97t1/2 (days) =38.2037.52intercept =94.74.5595.0H 9:% parent remainingtime (days)INDnatural log INDnatural log INDnatural log TMP097.04.3780.70.12588.24.4885.24.450.2579.04.3780.70.33375.34.3274.21440.83.7127.03.16.02.773.30 <td>30</td> <td>94.0</td> <td>4.54</td> <td>94.3</td> <td>4.55</td> | 30 | 94.0 | 4.54 | 94.3 | 4.55 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{split} & \text{slope} = & -1.73 \text{E-03} & -1.15 \text{E-03} \\ & \text{r}^2 = & 0.96 & 0.77 \\ & \text{tl/2} (days) = & 400.86 & 604.21 \\ & \text{intercept} = & 99.4 & 4.60 & 98.1 & 4.59 \\ \hline \text{pH 7: % parent remaining} \\ \hline \text{time (days)} & \text{IND} & \text{natural log IND} & \text{TMP} & \text{natural log TMP} \\ & 0 & 98.5 & 4.59 & 98.6 & 4.59 \\ & 1 & 95.4 & 4.56 & 96.8 & 4.57 \\ & 3 & 92.4 & 4.53 & 91.1 & 4.51 \\ & 5 & 87.9 & 4.48 & 86.8 & 4.46 \\ & 7 & 79.0 & 4.37 & 82.9 & 4.42 \\ & 9 & 77.7 & 4.35 & 78.0 & 4.36 \\ & 12 & 74.8 & 4.31 & 72.4 & 4.28 \\ & 15 & 70.8 & 4.26 & 69.7 & 4.24 \\ & 18 & 67.3 & 4.21 & 65.7 & 4.19 \\ & 21 & 60.8 & 4.11 & 64.1 & 4.16 \\ & 25 & 63.7 & 4.15 & 61.0 & 4.11 \\ & 30 & 57.2 & 4.05 & 57.7 & 4.05 \\ \hline \text{slope} = & -1.81 \text{E-02} & -1.85 \text{E-02} \\ & r^2 = & 0.95 & 0.97 \\ & \text{tl/2} (days) = & 38.20 & 37.52 \\ \hline \text{intercept} = & 94.7 & 4.55 & 95.0 & 4.55 \\ \hline \text{o.25 } & 79.0 & 4.37 & 80.7 & 4.39 \\ & 0 & 97.0 & 4.58 & 96.2 & 4.57 \\ & 0.125 & 88.2 & 4.48 & 85.2 & 4.45 \\ & 0.25 & 79.0 & 4.37 & 80.7 & 4.39 \\ & 0 & 333 & 75.3 & 4.32 & 74.2 & 4.31 \\ & 0.417 & 73.0 & 4.29 & 68.1 & 4.22 \\ & 0.5 & 67.2 & 4.21 & 60.7 & 4.11 \\ & 1 & 40.8 & 3.71 & 27.0 & 3.30 \\ & 2 & 26.2 & 3.27 & 26.8 & 3.29 \\ & 3 & 16.0 & 2.77 & 24.8 & 3.21 \\ & 5 & 10.5 & 2.35 & 12.1 & 2.49 \\ & 15 & 15.7 & 2.75 & 16.0 & 2.77 \\ & 30 & 10.3 & 2.33 & 13.8 & 2.62 \\ \hline \text{slope} (0-2 \text{ day}) = & -6.73 \text{E-01} & -7.10 \text{E-01} \\ & r^2 = & 0.98 & 0.83 \\ & 11/2 (\text{ days}) = & 1.03 & 0.98 \\ \hline \text{tl/2} (\text{ days}) = & -6.73 \text{E-01} & -7.10 \text{E-01} \\ \hline \text{r}^2 = & 0.98 & 0.83 \\ & 11/2 (\text{ days}) = & -6.73 \text{E-01} & -7.10 \text{E-01} \\ \hline \text{r}^2 = & 0.98 & 0.83 \\ & 11/2 (\text{ days}) = & -6.73 \text{E-01} & -7.10 \text{E-01} \\ \hline \text{r}^2 = & 0.98 & 0.83 \\ & 11/2 (\text{ days}) = & -6.73 \text{E-01} & -7.10 \text{E-01} \\ \hline \text{r}^2 = & 0.98 & 0.83 \\ & 11/2 (\text{ days}) = & -6.73 \text{E-01} & -7.10 \text{E-01} \\ \hline \text{r}^2 = & 0.98 & 0.83 \\ \hline \text{r}^2 = & 0.98 & 0.98 \\ \hline \text{r}^2 = & 0.98 & 0.83 \\ \hline \text{r}^2 = & 0.98 & 0.98 \\ \hline \text{r}^2 = & 0$ | | | · · · · · · · · · | м. С | , |
| $\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | slope = | | -1.73E-03 | ۲, | -1.15E-03 |
| 11/2 (days) = 400.86 604.21 intercept = 99.4 4.60 98.1 4.59 time (days) IND natural log IND TMP natural log TMF 0 98.5 4.59 98.6 4.59 1 95.4 4.56 96.8 4.57 3 92.4 4.53 91.1 4.51 5 87.9 4.48 86.8 4.46 7 79.0 4.37 82.9 4.42 9 77.7 4.35 78.0 4.36 12 74.8 4.31 72.4 4.28 15 70.8 4.26 69.7 4.24 18 67.3 4.21 65.7 4.19 21 60.8 4.11 64.1 4.16 25 63.7 4.15 61.0 4.11 30 57.2 4.05 57.7 4.05 sibpe = -1.81E-02 -1.85E-02 7.52 1172 rt1/2 (days) = 94.7 4.55 95.0 4.55 | $\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$ | r^2 = | | 0.96 | | 0.77 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | intercept =99.44.6098.14.59pH 7: % parent remainingtime (days)INDnatural log INDTMPnatural log TMP098.54.5998.64.59195.44.5696.84.57392.44.5391.14.51587.94.4886.84.46779.04.3782.94.42977.74.3578.04.361274.84.3172.44.281570.84.2669.74.241867.34.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05stops0.97t1/2 (days) =38.2037.52intercept =94.74.5595.04.55PH 9: % parent remainingtime (days)INDnatural log INDTMP097.04.5896.24.570.12588.24.4885.24.450.2579.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.77 <td>t1/2 (days) =</td> <td></td> <td>400.86</td> <td></td> <td>604.21</td> | t1/2 (days) = | | 400.86 | | 604.21 |
| PH 7: % parent remainingtime (days)INDnatural log INDTMPnatural log TMF098.54.5998.64.59195.44.5696.84.57392.44.5391.14.51587.94.4886.84.46779.04.3782.94.42977.74.3578.04.361274.84.3172.44.281570.84.2669.74.241867.34.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05stopspH 9: % parent remainingtime (days)NDnatural log IND097.04.5896.24.550.12588.24.4885.24.450.2579.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.7724.83.21510.52.3512.12.491515.72.7516.02.773010.32.3313.8 </td <td>pH 7: % parent remainingtime (days)INDnatural log INDTMPnatural log TMP098.54.5998.64.59195.44.5696.84.57392.44.5391.14.51587.94.4886.84.46779.04.3782.94.42977.74.3578.04.361274.84.3172.44.281570.84.2669.74.241867.34.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05stope = -1.81E-02-1.85E-02r^2 = 0.950.97tit/2 (days) =38.2037.52intercept =94.74.5595.04.55pH 9: % parent remainingtime (days)INDnatural log INDTMP097.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.7724.83.21510.52.3512.12.491515.72.7516.0<t< td=""><td>intercept =</td><td>99.4</td><td>4.60</td><td>98.1</td><td>4.59</td></t<></td> | pH 7: % parent remainingtime (days)INDnatural log INDTMPnatural log TMP098.54.5998.64.59195.44.5696.84.57392.44.5391.14.51587.94.4886.84.46779.04.3782.94.42977.74.3578.04.361274.84.3172.44.281570.84.2669.74.241867.34.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05stope = -1.81E-02-1.85E-02r^2 = 0.950.97tit/2 (days) =38.2037.52intercept =94.74.5595.04.55pH 9: % parent remainingtime (days)INDnatural log INDTMP097.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.7724.83.21510.52.3512.12.491515.72.7516.0 <t< td=""><td>intercept =</td><td>99.4</td><td>4.60</td><td>98.1</td><td>4.59</td></t<> | intercept = | 99.4 | 4.60 | 98.1 | 4.59 |
| time (days)INDnatural log INDTMPnatural log TMF098.54.5998.64.59195.44.5696.84.57392.44.5391.14.51587.94.4886.84.46779.04.3782.94.42977.74.3578.04.361274.84.3172.44.281570.84.2669.74.241867.34.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05r^2 =0.950.950.97t1/2 (days) =38.2037.52intercept =94.74.5595.04.5896.24.570.12588.24.4885.24.4885.24.450.2579.04.3780.70.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.7316.02.7724.83.29316.02.773.010.32.3313.82.623.2726.83.29316.02.773.01515.72.7516.02.773010.32.3313.82.62 </td <td>time (days)INDnatural log INDTMPnatural log TMP098.54.5998.64.59195.44.5696.84.57392.44.5391.14.51587.94.4886.84.46779.04.3782.94.42977.74.3578.04.361274.84.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05slope =-1.81E-02-1.85E-02r^2 =0.950.974.5595.04.55intercept =94.74.5595.04.55intercept =94.74.5595.04.55intercept =94.74.5595.04.550.12588.24.4885.24.450.2579.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.7724.83.21510.52.3512.12.491515.72.7516.02.773010.32.3313.82.62slope (0-2 day) =</td> <td></td> <td>pH 7: %</td> <td>parent remaining</td> <td></td> <td></td> | time (days)INDnatural log INDTMPnatural log TMP098.54.5998.64.59195.44.5696.84.57392.44.5391.14.51587.94.4886.84.46779.04.3782.94.42977.74.3578.04.361274.84.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05slope =-1.81E-02-1.85E-02r^2 =0.950.974.5595.04.55intercept =94.74.5595.04.55intercept =94.74.5595.04.55intercept =94.74.5595.04.550.12588.24.4885.24.450.2579.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.7724.83.21510.52.3512.12.491515.72.7516.02.773010.32.3313.82.62slope (0-2 day) = | | pH 7: % | parent remaining | | |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ | time (days) | IND | natural log IND | TMP | natural log TMP |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 0 | 98.5 | 4.59 | 98.6 | 4.59 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 1 | 95.4 | 4.56 | 96.8 | 4.57 |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 3 | 92.4 | 4.53 | 91.1 | 4.51 |
| 779.04.3782.94.42977.74.3578.04.361274.84.3172.44.281570.84.2669.74.241867.34.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05slope =-1.81E-02-1.85E-02r^2 =0.950.950.950.950.97time (days)INDnatural log INDTMPnatural log TMI097.04.5896.24.570.12588.24.4885.24.450.2579.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.7724.83.21510.52.3512.12.491515.72.7516.02.773010.32.3313.82. | 779.04.3782.94.42977.74.3578.04.361274.84.3172.44.281570.84.2669.74.241867.34.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05sign colspan="4">sign colspan="4" sign colspan="4">sign colspan="4" sign colspan="4" sign colspan="4 | 5 | 87.9 | 4.48 | 86.8 | 4.46 |
| 977.74.3578.04.361274.84.3172.44.281570.84.2669.74.241867.34.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05slope =-1.81E-02-1.85E-02r^2 =0.950.950.950.950.950.950.97time (days)NDnatural log INDTMPnatural log TMi097.04.5896.24.570.12588.24.4885.24.450.2579.04.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.7724.83.21510.52.3512.12.491515.72.7516.02.773010.32.3313.82.62 | 977.74.3578.04.361274.84.3172.44.281570.84.2669.74.241867.34.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05slope =-1.81E-02-1.85E-02 r^2 =0.950.97t1/2 (days) =38.2037.52intercept =94.74.5595.04.5595.04.55pH 9:% parent remainingtime (days)INDnatural log INDTMP097.04.5896.24.570.12588.24.4885.24.450.2579.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.7724.83.21510.52.3512.12.491515.72.7516.02.773010.32.3313.82.62slope (0-2 day) =-6.73E-01-7.10E-01 $r^2 =$ 0.980.830.98 | 7 | 79.0 | 4.37 | 82.9 | 4.42 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 9 | 77.7 | 4.35 | 78.0 | 4.36 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 1570.84.2669.74.241867.34.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05slope =-1.81E-02-1.85E-02 r^2 =0.950.97t1/2 (days) =38.2037.52intercept =94.74.5595.091097.04.5896.291197.04.5896.291288.24.4885.291373.34.3274.291373.04.2968.1913316.02.7724.89226.23.2726.89316.02.7724.89316.02.7724.89310.32.3313.8942.623.279316.02.779310.32.3312515.72.7516.02.773010.32.3313.82.621515.79316.094-7.10E-01 r^2 =0.980.831.030.98 | 12 | 74.8 | 4.31 | 72.4 | 4.28 |
| 1867.34.2165.74.192160.84.1164.14.162563.74.1561.04.113057.24.0557.74.05slope =-1.81E-02-1.85E-02 r^2 =0.950.97t1/2 (days) =38.2037.52intercept =94.74.5595.04.55PH 9: % parent remainingtime (days)INDnatural log INDTMPnatural log TMi097.04.5896.24.570.12588.24.4885.24.450.2579.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.7724.83.21510.52.3512.12.491515.72.7516.02.773010.32.3313.82.62 | 18 67.3 4.21 65.7 4.19 21 60.8 4.11 64.1 4.16 25 63.7 4.15 61.0 4.11 30 57.2 4.05 57.7 4.05 slope = -1.81E-02 -1.85E-02 -1.85E-02 r^2 = 0.95 0.97 t1/2 (days) = 38.20 37.52 intercept = 94.7 4.55 95.0 4.55 pH 9: % parent remaining | 15 | 70.8 | 4.26 | 69.7 | 4 24 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 21 60.8 4.11 64.1 4.16 25 63.7 4.15 61.0 4.11 30 57.2 4.05 57.7 4.05 $slope =$ $-1.81E-02$ $-1.85E-02$ $r^2 =$ 0.95 0.97 $t1/2$ (days) = 38.20 37.52 intercept = 94.7 4.55 95.0 4.55 95.0 4.55 pH 9: % parent remainingtime (days)INDnatural log IND 0 97.0 4.58 96.2 4.57 0.125 88.2 4.48 85.2 4.48 85.2 4.45 0.25 79.0 4.37 80.7 4.39 0.333 75.3 4.32 74.2 4.31 0.417 73.0 4.29 68.1 4.22 0.5 67.2 4.21 60.7 4.11 1 40.8 3.71 27.0 3.30 2 26.2 3.27 26.8 3.29 3 16.0 2.77 24.8 3.21 5 10.5 2.35 12.1 2.49 15 15.7 2.75 16.0 2.77 30 10.3 2.33 13.8 2.62 slope (0-2 day) = $-6.73E-01$ $-7.10E-01$ r^42 = 0.98 0.83 0.98 | 18 | 67.3 | 4 21 | 65 7 | 1 19 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 21 | 60.8 | A 11 | 6/ 1 | 4.15 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 25 | 63.7 | 7.11 | 61.0 | 4.10 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 30 37.2 4.05 57.7 4.05 $slope =$ $-1.81E-02$ $-1.85E-02$ $r^2 =$ 0.95 0.97 $t1/2$ (days) = 38.20 37.52 intercept = 94.7 4.55 95.0 $pH 9:$ % parent remainingtime (days)INDnatural log INDTMP 0 97.0 4.58 96.2 4.57 0.125 88.2 4.48 85.2 4.45 0.25 79.0 4.37 80.7 4.39 0.333 75.3 4.32 74.2 4.31 0.417 73.0 4.29 68.1 4.22 0.5 67.2 4.21 60.7 4.11 1 40.8 3.71 27.0 3.30 2 26.2 3.27 26.8 3.29 3 16.0 2.77 24.8 3.21 5 10.5 2.35 12.1 2.49 15 15.7 2.75 16.0 2.77 30 10.3 2.33 13.8 2.62 $slope$ $(0-2 day) =$ $-6.73E-01$ $-7.10E-01$ $r^{A} =$ 0.98 0.83 0.98 | 20 | 57.0 | 4.15 | 67.7 | 4.11 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | slope =-1.81E-02-1.85E-02 $r^2 =$ 0.950.97t1/2 (days) =38.2037.52intercept =94.74.5595.04.5595.04.55pH 9: % parent remainingtime (days)INDnatural log INDTMP097.04.5896.24.570.12588.24.4885.24.450.2579.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.7724.83.21510.52.3512.12.491515.72.7516.02.773010.32.3313.82.62slope (0-2 day) =-6.73E-01-7.10E-01 $r^2 =$ 0.980.83t1/2 (days) =1.030.98 | 30 | 57.2 | 4.05 | 57.7 | 4.05 |
| Intervent of 1000 of 10000 of 1000 of 10000 of 1000 of 10 | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | slope = | | -1.81E-02 | | -1.85E-02 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | r^2 = | | 0.95 | | 0.97 |
| $\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$ | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ | t1/2 (days) - | | 38.20 | | 37 52 |
| $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | 1.33pH 9: % parent remainingtime (days)INDnatural log INDTMPnatural log TMF097.04.5896.24.570.12588.24.4885.24.450.2579.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.7724.83.21510.52.3512.12.491515.72.7516.02.773010.32.3313.82.62slope (0-2 day) =-6.73E-01-7.10E-01 $r^2 =$ 0.980.83t1/2 (days) =1.030.98 | intercept = | 94 7 | 4 55 | 95.0 | J7.JZ A 55 |
| INDnatural log INDTMPnatural log TMI097.04.5896.24.570.12588.24.4885.24.450.2579.04.3780.74.390.33375.34.3274.24.310.41773.04.2968.14.220.567.24.2160.74.11140.83.7127.03.30226.23.2726.83.29316.02.7724.83.21510.52.3512.12.491515.72.7516.02.773010.32.3313.82.62 | The part of part of part of the part | | pH 9: % | parent remaining | 33.0 | 4.33 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | time (davs) | ND | natural log IND | TMP | natural log TMP |
| 0.125 88.2 4.48 85.2 4.45 0.25 79.0 4.37 80.7 4.39 0.333 75.3 4.32 74.2 4.31 0.417 73.0 4.29 68.1 4.22 0.5 67.2 4.21 60.7 4.11 1 40.8 3.71 27.0 3.30 2 26.2 3.27 26.8 3.29 3 16.0 2.77 24.8 3.21 5 10.5 2.35 12.1 2.49 15 15.7 2.75 16.0 2.77 30 10.3 2.33 13.8 2.62 | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 0 | 97.0 | 4 58 | 96.2 | 4 57 |
| 0.125 79.0 4.37 80.7 4.39 0.25 79.0 4.37 80.7 4.39 0.333 75.3 4.32 74.2 4.31 0.417 73.0 4.29 68.1 4.22 0.5 67.2 4.21 60.7 4.11 1 40.8 3.71 27.0 3.30 2 26.2 3.27 26.8 3.29 3 16.0 2.77 24.8 3.21 5 10.5 2.35 12.1 2.49 15 15.7 2.75 16.0 2.77 30 10.3 2.33 13.8 2.62 slope $(0-2 day) =$ $-6.73E-01$ $-7.10E-01$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 0 125 | 88.2 | 4 48 | 85.2 | 4.57 A AE |
| 0.100 75.0 4.37 60.7 4.39 0.333 75.3 4.32 74.2 4.31 0.417 73.0 4.29 68.1 4.22 0.5 67.2 4.21 60.7 4.11 1 40.8 3.71 27.0 3.30 2 26.2 3.27 26.8 3.29 3 16.0 2.77 24.8 3.21 5 10.5 2.35 12.1 2.49 15 15.7 2.75 16.0 2.77 30 10.3 2.33 13.8 2.62 slope $(0-2 day) =$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 0.25 | 79.0 | 4.40 | 80.Z | 4.40 |
| 0.333 73.3 4.32 74.2 4.31 0.417 73.0 4.29 68.1 4.22 0.5 67.2 4.21 60.7 4.11 1 40.8 3.71 27.0 3.30 2 26.2 3.27 26.8 3.29 3 16.0 2.77 24.8 3.21 5 10.5 2.35 12.1 2.49 15 15.7 2.75 16.0 2.77 30 10.3 2.33 13.8 2.62 slope (0-2 day) = -6.73E-01 | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 0.23 | 75.0 | 4.07 | 74.0 | 4.39 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 0.000 | 70.0 | 4.02 | 14.2 | 4.31 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 0.417 | 73.0 | 4.29 | 68.1 | 4.22 |
| 1 40.8 3.71 27.0 3.30 2 26.2 3.27 26.8 3.29 3 16.0 2.77 24.8 3.21 5 10.5 2.35 12.1 2.49 15 15.7 2.75 16.0 2.77 30 10.3 2.33 13.8 2.62 slope (0-2 day) = -6.73E-01 | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 0.5 | 67.2 | 4.21 | 60.7 | 4.11 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 1 | 40.8 | 3.71 | 27.0 | 3.30 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 2 | 26.2 | 3.27 | 26.8 | 3.29 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 3 | 16.0 | 2.77 | 24.8 | 3.21 |
| 1515.72.7516.02.773010.32.3313.82.62slope (0-2 day) = $-6.73E-01$ $-7.10E-01$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 5 | 10.5 | 2.35 | 12.1 | 2.49 |
| 30 10.3 2.33 13.8 2.62 slope (0-2 day) = $-6.73E-01$ $-7.10E-01$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 15 | 15.7 | 2.75 | 16.0 | 2.77 |
| slope (0-2 day) = -6.73E-01 -7.10E-01 | slope $(0-2 \text{ day}) =$ -6.73E-01-7.10E-01 $r^2 =$ 0.980.83 $t1/2 \text{ (days)} =$ 1.030.98 | 30 | 10.3 | 2.33 | 13.8 | 2.62 |
| slope $(U-2 \text{ day}) = -6.73\text{E}-01 -7.10\text{E}-01$ | slope $(0-2 \text{ day}) =$ -6.73E-01-7.10E-01 $r^2 =$ 0.980.83 $t1/2 \text{ (days)} =$ 1.030.98 | | | | - | |
| 4 | $r^{2} = 0.98 	0.83 	1/2 	(days) = 1.03 	0.98$ | slope (0-2 day | () = | -6.73E-01 | | -7.10E-01 |
| r^2 = 0.98 0.83 | t1/2 (days) = 1.03 0.98 | r^2 = | | 0.98 | | 0.83 |
| t1/2 (days) = 1.03 0.98 | | t1/2 (days) = | | . 1.03 | | 0.98 |
| intercept = 93.8 4.54 88.9 4.49 | Intercept = 93.8 4.54 88.9 4.49 | intercept = | 93.8 | 4.54 | 88.9 | 4.49 |

FIGURE 1 STRUCTURES AND NAMES OF RADIOLABELED TEST SUBSTANCE AND THE MAJOR HYDROLYSIS PRODUCT

TEST SUBSTANCE



¹Denotes site of ¹⁴C label in Test Substance Label 1 ²Denotes site of ¹⁴C label in Test Substance Label 2

> Label 1: [Indanone-1-¹⁴C]DPX-JW062 HOTC file # 421 Specific activity: 55.49 µCi/mg Radiochemical purity: 98.6%

Label 2: [Trifluoromethoxyphenyl-ring-¹⁴C]DPX-JW062 HOTC file # 423 Specific activity: 54 .034 µCi/mg Radiochemical purity: 99.8%

DPX Number:

JW062

Chemical Name:

(R,S)-methyl 7-chloro-2,5-dihydro-2-[[(methoxycarbonyl)]4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2e][1,3,4]oxadiazine-4a(3H)-carboxylate

CAS Registry No.: 144171-61-9 Solubility in water: 16 ppb (µg/liter) at 25°C Molecular Weight: 527.84

FIGURE 1 (CONTINUED)

ACTIVE INGREDIENT



DPX Number:

KN128

CAS Name:

DOCUME

.

EPA ARCHI

(S)-methyl 7-chloro-2,5-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2e][1,3,4]oxadiazine-4a(3H)-carboxylate

CAS Registry No.: 173584-44-6

MAJOR HYDROLYSIS PRODUCT



IN Code:

KT413

Chemical Name:

sodium 7-chloro-2,5,-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2e][1,3,4]oxadiazine-4a(3H)-carboxylic acid

Molecular Weight: 513.82 (free acid)





EPA ARCHIVE DOCUMEN

DuPont Report No. AMR 2789-93

30

25



10

15

Time (Days)

20

FIGURE 3 HYDROLYSIS OF DPX-JW062: PH 7

10 -

0

5



FIGURE 4 HYDROLYSIS OF DPX-JW062: PH 9



DuPont Report No. AMR 2789-93

FIGURE 7 TIME COURSE OF FORMATION OF IN-KT413 AT PH 7 (TOP) AND PH 9 (BOTTOM)

