Hydrolysis of [test compound] at pH [4, 7, and 9, or other values studied]

|  |  |
| --- | --- |
| Report: | [Provide full citation. Provide the MRID (first) if the review is unilateral.] |
| Document No.: | [MRID xxxxxxxx] |
| Guideline: | OCSPP 835.2120  [If the study was conducted under a different guideline, state ‘Conducted by’ and provide the most relevant guideline(s) the study was conducted under. Then state ‘Reviewed by OCSPP 835.2120.’ If this review is multilateral, also provide the guideline numbers under which participating agencies are reviewing the study.] |
| Statements: | [Indicate whether the study was conducted in compliance with FIFRA GLP standards and whether signed and dated Data Confidentiality, GLP Compliance, Quality Assurance, and Authenticity Certification statements were provided. If the study was not conducted in compliance with FIFRA GLP standards, indicate how not or why not.] |
| Classification: | This study is [provide classification and very concise statement of any deficiencies that impacted the classification]. [If multiple classification terminologies are needed for multilateral reviews, list or tabulate them.] |
| PC Code: | [xxxxxx] |
| Reviewer: | [Provide final reviewer(s)’s name Signature:  and title.] Date: [Type date of signature.] |

**Executive Summary**

The abiotic hydrolysis of [type of radiolabel(s)]-labeled [test compound] at [measured concentration] was investigated in sterile aqueous buffered solutions at pH 4, 7, and 9. A pre-test was conducted in the dark at each pH at 50°C for [5 days or other duration] and was followed by additional tests at each pH conducted at 25°C and at [10°C or other temperature] for [duration]. Duplicate test vessels were collected and analyzed using [methods used (*e.g.*, LSC and HPLC-UV].

Table 1. Results Synopsis

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| pH | Observed DT50 (days) | SFO Half-life A (days) | Model Parameters and Statistics | **Transformation Products**  Common Name (maximum %AR B observed, associated interval) | |
| **Major** | **Minor** |
| **50°C [modify table as needed for other temperatures]** | | | | | |
| 4 | [value] | [value] | C0=[#], k=[#], SSFO=[#], r2=[#], p=[#] | [name] (#%, # d) | [name] (#%, # d) |
| 7 | [value] | [value] | C0=[#], k=[#], SSFO=[#], r2=[#], p=[#] | [name] (#%, # d) | [name] (#%, # d) |
| 9 | [value] | [value] | C0=[#], k=[#], SSFO=[#], r2=[#], p=[#] | [name] (#%, # d) | [name] (#%, # d) |
| A The Single First-Order (SFO) kinetics model is used to describe hydrolytic degradation.  B AR means “applied radioactivity.” | | | | | |

**I. Material and Methods**

**A. Materials:**

**1. Test Material:** [[Type of radiolabel]-labeled[test compound]  
Specific radioactivity: [value] MBq/mg

Radiochemical purity: [percentage (HPLC, TLC)]

Chemical purity: [percentage (HPLC)]

Batch number: [value]

Solubility in water: [value] mg/L [If pH-dependent, list available values at each study pH.]

**2. Reference** [List the common name and batch number of each reference

**Compounds:** compound. Provide other chemical information in the structure table.]

**3. Buffer:** 0.01 M sterile aqueous buffer solutions were prepared at pH 4 using [compound(s)], pH 7 using [compound(s)], and pH 9 using [compound(s)].

**B. Study Design:** [Tabulation of these data is encouraged as long as the length of this section is not substantially increased.]

**1. Experimental conditions:** The abiotic hydrolysis of [[type of radiolabel(s)]-labeled[test compound] at [measured concentration] was investigated in sterile aqueous buffered solutions at pH 4, 7, and 9. Equipment was sterilized by [method]. A pre-test was conducted in the dark at each pH at 50°C for [5 days or other duration] and was followed by additional tests at each pH conducted at 25°C and at [10°C or other temperature] for [duration]. The tests were performed at a nominal concentration(s) of [value] in sealed [vessel type] test vessels with [trapping method and type of traps, if any] for volatiles. Measured concentrations were [list values]. The cosolvent used ([(concentration) solvent]) was [percentage v/v] of the sample solutions. [If sterility was checked during the study, indicate the method used.]

**2. Sampling:** Duplicate test vessels [volume] were taken for analysis at [list intervals, per system if different] after application. [Report the sampling interval of any checks on pH, temperature, or sterility.]

**3. Analytical procedures:** Samples were analyzed using [LSC] for determination of total radioactivity. [Reversed-phase HPLC with 14C-flow-through detection techniques and normal phase TLC] were used as primary and confirmatory chromatographic methods for the separation and quantitation of products formed. The limit of detection (LOD) was determined to be [percentage] of the applied radioactivity (%AR), with a limit of quantitation (LOQ) at [percentage]AR).

**II. Results and Discussion**

**A. Mass Balance:** Recoveries ranged from [percentage] to [percentage]AR at pH 4, [percentage] to [percentage]AR at pH 7, and [percentage] to [percentage]AR at pH 9. [Indicate whether there was substantial loss of radioactivity by sorption to glassware or volatilization. Indicate whether a substantial amount of radioactivity was unidentified.]

**B. Findings:** The results including total mass balances and distribution of radioactivity are presented in [table(s)]. [Individual replicate values are reported rather than means and standard deviations.] [Indicate the result of any checks on pH, sterility, or other test condition.]

Table 2. Hydrolysis of [radiolabel-test compound] at pH [value] and [temperature] expressed as percentage of applied radioactivity [Duplicate table as needed for additional pH values, temperatures, and radiolabels.]

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **pH [#], [#]°C** |  |  |  |  |  |  |  |  |  |  |  |  |
| **Sampling Interval (days)** | **[Int. 1]** | **[Int. 1]** | **[Int. 2]** | **[Int. 2]** | **[Int. 3]** | **[Int. 3]** | **[Int. 4]** | **[Int. 4]** | **[Int. 5]** | **[Int. 5]** | **[Int. 6]** | **[Int. 6]** |
| **Replicate Number** | **1** | **2** | **1** | **2** | **1** | **2** | **1** | **2** | **1** | **2** | **1** | **2** |
| [Test compound] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] |
| [Product 1] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] |
| [Product 2] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] |
| Unidentified | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] |
| Volatile organics | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] |
| CO2 | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] |
| Radioactivity at walls of test vessel | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] |
| Mass balance | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] | [#] |
| n.d. = not detected, n.a. = not analyzed | | | | | | | | | | | | |

Table 3. Hydrolysis kinetics of [radiolabel-test compound] in aqueous buffer solutions A

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **pH** | **Observed DT50 (days)** | **Observed DT90 (days)** | **Calculated**  **Half-life** B **(days)** | **SFO Model Parameters** B | **SFO Model Statistics** |
| **50°C** | | | | | |
| 4 | [value] | [value] | [value] | C0=[#], k=[#] | SSFO=[#], r2=[#], p=[#] |
| 7 | [value] | [value] | [value] | C0=[#], k=[#] | SSFO=[#], r2=[#], p=[#] |
| 9 | [value] | [value] | [value] | C0=[#], k=[#] | SSFO=[#], r2=[#], p=[#] |
| **25°C** | | | | | |
| 4 | [value] | [value] | [value] | C0=[#], k=[#] | SSFO=[#], r2=[#], p=[#] |
| 7 | [value] | [value] | [value] | C0=[#], k=[#] | SSFO=[#], r2=[#], p=[#] |
| 9 | [value] | [value] | [value] | C0=[#], k=[#] | SSFO=[#], r2=[#], p=[#] |
| **[10°C or other third temperature]** | | | | | |
| 4 | [value] | [value] | [value] | C0=[#], k=[#] | SSFO=[#], r2=[#], p=[#] |
| 7 | [value] | [value] | [value] | C0=[#], k=[#] | SSFO=[#], r2=[#], p=[#] |
| 9 | [value] | [value] | [value] | C0=[#], k=[#] | SSFO=[#], r2=[#], p=[#] |
| A Data were obtained from [location of data in study report] and calculations in the attached Excel workbook [name(s) of worksheets, if needed]. See Attachment 3 for calculations.  B The Single First-Order (SFO) kinetics model is used to describe hydrolytic degradation. | | | | | |

[Images of kinetics calculation results using the R program may replace **Table 3**. R images should include the model parameters and statistics that are otherwise reported in **Table 3**.]

[Half-lives should be calculated with non-linear regression assuming single first-order (SFO) kinetics and following the NAFTA kinetics guidance (USEPA, 2011). Other half-life calculation methods may be added to the table when needed, such as when degradation is not first-order. Rows may be added for transformation product half-lives and DT50s as needed. If multiple experiments were conducted per study condition using test compound with different radiolabel positions, calculate kinetics values for the combined data rather than for specific radiolabel positions.]

[Indicate whether reviewer-reported half-lives are consistent with study-reported values.]

**Table 4. Hydrolytic Products of [Test Compound]**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| pH | Transformation Product(s) | Maximum %AR Observed | Associated Interval | Final %AR Observed | Final Interval |
| 50°C [modify table as needed for other temperatures] | | | | | |
| 4 | [common name] | [#] | [# d] | [#] | [# d] |
| [common name] | [#] | [# d] | [#] | [# d] |
| 7 | [common name] | [#] | [# d] | [#] | [# d] |
| [common name] | [#] | [# d] | [#] | [# d] |
| 9 | [common name] | [#] | [# d] | [#] | [# d] |
| [common name] | [#] | [# d] | [#] | [# d] |

[If applicable, provide a description of the transformation pathway here, including a schematic as Figure 1.]

**[Figure 1. Hydrolysis Pathway of [radiolabel-test compound]]**

**III. Study Deficiencies and Reviewer’s Comments**

[This section is titled “Conclusions” in the original T2S template.]

[List any deficiencies with the study and any additional salient information. Results and conclusions contained in the Executive Summary are not repeated in this section.]

**IV. References** [List any references cited in the review.]

U.S. Environmental Protection Agency (USEPA). 2011. Guidance for Evaluating and Calculating Degradation Kinetics in Environmental Media. (Interim draft document dated Dec. 21, 2011.)

**Attachment 1: Chemical Names and Structures**

[A table (*i.e.*, structure table) of the chemical names, SMILES strings, CAS numbers, and structures of the test compound, all identified transformation products, and all reference compounds that were not identified in study samples should be either referenced as a separate, associated document or attached to the study review. Multiple versions of structures to show or not show radiolabeling and multiple versions of chemical names and SMILES strings should not be included in the table. Sources of data need not be included. However, formatting the structure table in conformance with the guidance for tabulating transformation product data for EFED ROCKS memoranda is recommended. This formatting includes table columns for MRIDs and associated study data such as maximum and final concentrations of transformation products and their intervals.

For multilateral reviews, chemical names, SMILES strings, structures, and CAS numbers are captured elsewhere in the Monograph[[1]](#footnote-1). Therefore these data are not attached to each study review within the Monograph. When the Monograph is split into individual reviews in EFED’s files, however, the Monograph’s structure table should be either referenced as a separate, associated document or attached to each individual review.]

[Sample structure table with the minimum information needed.]

|  |  |
| --- | --- |
| **[Common name [list other common names] [if the same common name is used in different studies for different compounds, provide in parentheses the MRID associated with the common name for this compound.]]** | |
|  |  |
| IUPAC Name: | [Provide one IUPAC name.] |
| CAS Name: | [Provide one CAS name.] |
| CAS Number: | [Provide if available.] |
| SMILES String: | [Provide one SMILES string.] |
|  | |
| [Paste structure here.] | |
|  | |
|  | |

[Sample EFED ROCKS memorandum format for structure tables.]



Attachment 2: Statistics Spreadsheets and Graphs



[Supporting electronic spreadsheet files should be inserted here; electronic attachment files should be electronically finalized as separate files as well. Electronic attachments should have the same file name as the Microsoft Word study review file with the addition of “Calc” for Excel workbooks and WinZip files, the addition of “Data” for Adobe Acrobat and Document Imaging files, and the addition of brief descriptors as appropriate for SigmaPlot Notebooks. Electronic attachment files should be compressed into a WinZip file when three or more are prepared for a study review.]

[Hard copies of a study review and any attachment sheets from separate electronic files should be printed and finalized together as one hard copy file.]

[The attached Excel file has two example spreadsheets for mass balance and kinetics calculations.]

Attachment 3: Calculations

Calculations were performed by the reviewer using [indicate program(s) used for calculations] and the following equations. [The following equations are anticipated to reflect the NAFTA kinetics guidance as of January, 2012. If these equations are not current, they should be replaced by the applicable equations from current guidance.]

Single First-Order (SFO) Model

(eq. 1)

where,

Ct = concentration at time t (%)

C0 = initial concentration (%)

e = Euler’s number (-)

k = SFO rate constant of decline (d-1)

t = time (d)

The SFO equation is solved [with the Excel Solver] by adjusting *C0* and *k* to minimize the objective function (SSFO) shown in equation 4.

DT50 = natural log (2)/k (eq. 2)

DT90 = ln (10)/k (eq. 3)

(eq. 4)

where,

SSFO = objective function of SFO model fit (%2)

n = number of data points (-)

Cmodel,t = modelled value at time corresponding to Cd,t (%)

Cd,t = experimental concentration at time t (%)

1. A Monograph is a collection of multiple study reviews and data summaries prepared by government agencies into a single document that follows an OECD format. Typically, Tier II Summaries prepared by industry are updated by government agencies based on agency-review and then placed within the Monograph. [↑](#footnote-ref-1)