Data Evaluation Report on the hydrolysis of iodomethane

PMRA Submission Number {.....} EPA MRID Number 45593705

Data Requirement: PMRA Data Code:
EPA DP Barcode: D280800
OECD Data Point:
EPA Guideline: 161-1

Test material:
Common name: Iodomethane.
Chemical name
IUPAC: N/A.
CAS name: Iodomethane.
CAS No: 74-88-4.
Synonyms: Methyl iodide.
TM-425.
SMILES string: CI

Primary Reviewer: Dana Worcester
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Company Code: [for PMRA]
Active Code: [for PMRA]
Use Site Category: [for PMRA]
EPA PC Code: 000011

CITATION: Wujcik, C.E. 2001. A hydrolysis study of [^{14}C]iodomethane (TM-425) in water. Unpublished study performed by Ricerca, LLC, Metabolism Division, Concord, OH, and submitted by Arvesta Corporation, San Francisco, CA. Project Identificaiton Number 012522; Document Number 012522-1. Study initiation dates were not reported; quality assurance inspections of the experimental portion of the study began in February 2001. Final report issued September 20, 2001.

EXECUTIVE SUMMARY

The hydrolysis of [^{14}C]iodomethane, at 21.1-23.1 mg a.i./L, was studied in the dark at 24.8-25.1 and 49.6-49.8°C in sterile aqueous buffered solutions at pH 4 (acetate), pH 7 (TRIS) and pH 9 (borate) for 30 days. This study was conducted in accordance with USEPA Subdivision N Guideline §161-1 and in compliance with the U.S. EPA GLP standards (40 CFR Part 160, 1989). The test system consisted of amber serum bottles sealed with butyl rubber septa/aluminum crimp caps and maintained in a dark temperature-controlled incubator. Volatiles were not trapped. Duplicate samples of the solutions maintained at 25°C were sampled at 0, 3, 7, 14, 21, 28, and 30 days posttreatment. Duplicate samples of the solutions maintained at 50°C were sampled at 0, 1, 2, 3, 4, 5, 6, and 7 days posttreatment. Aliquots of the buffer solutions were analyzed without manipulation or modification using LSC and HPLC. Identifications were confirmed using GC/MS with EI.

At 25°C, total [^{14}C]residue recovery ranged from 91.3 to 102.6% of the applied (mean 98.38 ± 3.3%) in the pH 4 solution, from 91.7 to 102.7% (97.6 ± 3.6%) in the pH 7 solution, and from 92.6 to 102.7% (98.0 ± 3.0%) in the pH 9 solution. The behavior of iodomethane was independent of pH. In the pH 4, 7, and 9 buffer solutions, iodomethane decreased from an average 97.4-97.8% of the applied at day 0 to 78.6-80.5% at 30 days posttreatment. Methanol was the only transformation product, increasing in all three buffer solutions to averages of 16.3-18.4% of the applied at 30 days posttreatment. Other metabolites (unidentified) totaled ≤0.5% of the applied at all sampling intervals. In the pH 7 solution only, an artifact resulting from the interaction of the TRIS buffer and iodomethane reached 2.3-3.0% of the applied at 28-30 days posttreatment.

At 50°C, total [^{14}C]residue recovery ranged from 93.4 to 105.6% of the applied (mean 101.0 ± 3.1%) in the pH 4 solution, from 94.2 to 103.6% (100.0 ± 2.9%) in the pH 7 solution, and from 91.9 to 102.9% (99.0 ± 3.5%) in the pH 9 solution. In the pH 4 buffer solution, iodomethane decreased from an average 96.6% of the applied at day 0 to 22.2% at 7 days, while methanol increased to a maximum 76.4% at 7 days. In the pH 7 buffer solution, iodomethane decreased from an average 96.2% of the applied at day 0 to 10.8% at 7 days; the study author predicted that the iodomethane concentration in the pH 7 solution at 7 days would have been 19.9% if the interaction with the TRIS buffer was discounted. Methanol averaged a maximum 81.0% of the applied at 7 days. The TRIS artifact averaged a maximum 7.0% of the applied at 5 and 6 days. In the pH 9 buffer solution, iodomethane decreased from an average 95.8% of the applied at day 0 to 16.7% at 7 days, while methanol increased to a maximum 78.0% at 7 days. Other metabolites totaled ≤1.8% of the applied in all buffers at all sampling intervals.

The half-lives for iodomethane in the pH 4, 7, and 9 buffer solutions at 25°C were 105, 94, and 108 days, respectively. The half-lives for iodomethane at 50°C were 2.3-3.34 days.

A transformation pathway was not proposed by the study author. Iodomethane reacts with water to form methanol and iodine.

RESULTS SYNOPSIS:

	Half-life	Major transformation product
25°		
pH 4	0-30 day data: 105.02 days	Methanol
pH 7*	0-30 day data: 93.67 days	Methanol
pH 9	0-30 day data: 108.30 days	Methanol
50°		
pH 4	0-4 day data: 3.34 days	Methanol
pH 7*	0-3 day data: 2.31 days	Methanol
pH 9	0-3 day data: 2.96 days	Methanol

*pH 7 half-lives are based on the measured concentration of iodomethane in the buffer solutions.

Study Acceptability: This study is classified as **acceptable** and satisfies the guideline requirement for a hydrolysis study.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was conducted in accordance with USEPA Subdivision N Guideline §161-1; OECD Guideline for Testing of Chemicals 111; SETAC-Europe: Procedures for assessing the Environmental Fate and Ecotoxicity of Pesticides (March 1995); and Environmental Chemistry and Fate Guidelines for the Registration of Pesticides in Canada 6.2.A.2 (July 1987; p. 17) . No significant deviations from Subdivision N Guideline §161-1 were noted.

COMPLIANCE: This study was conducted in compliance with USEPA GLP Standards (40 CFR Part 160; p. 3). Signed and dated GLP, Quality Assurance, Data Confidentiality, and Certificate of Authenticity statements were provided (pp. 2-3, 6, 8).

A. MATERIALS:

1. Test Material [^{14}C]Iodomethane

Chemical Structure: H_3C^*-I (* location of radiolabel)

Description: Not provided.

Purity: Radiochemical purity: ≥95%. (p.18)
Lot No. 110K9406 for 50°C experiment and 110K9407 for 25°C experiment.
Analytical purity: Not reported.
Specific activity: 6.1 mCi/mMol.
Location of the radiolabel: Methyl carbon.

Storage conditions of test chemicals: The test material was refrigerated at <10°C when not in use (p. 20).

Physico-chemical properties of iodomethane.

Parameter	Values	Comments
Molecular weight	141.94 g/Mol	
Water solubility	14.2 mg/mL at 25°C	
Specific gravity	2.8 at 20°C	Material Safety Data Sheet
Vapor pressure	400 mm/Hg at 25°C 50 kPa at 20°C	Material Safety Data Sheet International Occupational Safety and Health Information Centre
Henry's law K_H	0.22	
UV absorption	Maximum (2.5 absorbance units) at *ca.* 200 nm, with a smaller peak (0.25 au) at *ca.* 250 nm	MRID 45593706
pK_a	Not reported.	
Octanol/Water partition coefficient (log K_{ow})	1.51-1.69	International Occupational Safety and Health Information Centre
Melting point	-66.5°C	International Occupational Safety and Health Information Centre
Boiling point	42.4°C	
Stability of compound at room temperature, if provided	Not reported.	

Data obtained from p. 18 of the study report unless otherwise noted.

2. Buffer Solution: Buffer solutions were made with OPTIMA grade water as follows:

Table 1: Description of buffer solutions.

pH	Type and final molarity of buffer	Composition
4	0.01 M Acetate buffer	0.01 M acetic acid was combined with 0.01 M sodium acetate until a pH of 4 was obtained.
7	0.01 M TRIS buffer	0.01 M TRIS solution was combined with a 1:1 solution of HCl in water until a pH of 7 was obtained.
9	0.01 M Borate buffer	0.01 M boric acid was combined with 0.01 M sodium borate until a pH of 9 was obtained.

Data obtained from p. 21 of the study report.

B. EXPERIMENTAL CONDITIONS

1. Preliminary Studies: Tests were performed using acetate, phosphate and TRIS buffers for the pH 7 buffer solution (p. 16). The acetate could not buffer the system well enough at pH 7 and the phosphate producted artifacts. The TRIS buffer was selected as the best choice, since it buffered well at pH 7 and only produced one minor artifact.

2. Experimental conditions

Table 2: Experimental parameters

Parameters		Details
Duration of the study		25°C: 30 Days. 50°C: 7 Days.
Test concentrations (mg a.i./L) Nominal: Measured:		25 mg a.i./L. 21.7-23.1 mg a.i./L.
No. of replications		2
Preparation of test medium	Volume used/treatment	400 mL of each buffer solution was treated with 3060 or 2830 µL (50°C and 25°C, respectively) of the treatment solution, then 10 mL aliquots were dispensed into the sample bottles.
	Method of sterilization	Treatment solutions and buffer solutions were filter-sterilized (0.22 µm and 0.2 µm, respectively) before use.
	Co-solvent (type/concentration)	None.
Test apparatus (type/material/volume)		Amber serum bottles (10 mL) sealed with 20-mm aluminum crimp-caps with PTFE coated butyl rubber septa.
Details of traps for volatile, if any		Volatiles were not trapped.
If no traps were used, is the test system closed/open?		Closed.
Is there any indication of the test material adsorbing to the walls of the test apparatus?		No.
Experimental conditions Temperature (°C) Lighting		24.8-25.1°C; 49.6-49.8°C. Dark.
Other details, if any		None.

Details obtained from pp. 20-22, 29 of the study report.

3. Supplementary Experiments: No supplementary experiments were conducted.

4. Sampling:

Table 3: Sampling details.

Criteria	Details
Sampling intervals	25°C: 0, 3, 7, 14, 21, 28, and 30 days. 50°C: 0, 1, 2, 3, 4, 5, 6, and 7 days.
Sampling method	Duplicate whole samples.
Sampling methods for the volatile compounds, if any	Volatiles were not determined.
Sampling intervals/times for: pH measurement Sterility check	pH was measured at each sampling interval. Sterility was determined at each sampling interval using Petrifilm plates.
Sample storage before analysis	Samples were processed on the day of collection and analyzed by HPLC within 5 days. Samples were stored at <10°C when not in use.
Other observation, if any:	None.

Details obtained from pp. 22-23; Tables 1-4, pp. 36-39 of the study report.

C. ANALYTICAL METHODS

Extraction/clean up/concentration methods, if used: Samples were analyzed as collected, without manipulation or modification (pp. 22-23).

Volatile residue determination: Volatiles were not trapped.

Total ^{14}C measurement: Aliquots of the buffer solutions were analyzed for total [^{14}C]residues using LSC (pp. 23-24).

Derivatization method, if used: A derivatization method was not employed.

Identification and quantification of the parent: Identification and quantification of [^{14}C]iodomethane was performed by HPLC using the following operating conditions: Aminex HPX 87H column (300 mm x 7.8 mm i.d.); a 60-minute isocratic run with 0.01 N sulfuric acid; flow rate 1.0 mL/minute; column temperature 65°C; and β-ram radioactivity detection (p. 24). Iodomethane was identified by comparison to a reference standard; its HPLC Rt in this system is about 31-33 minutes (p. 19; Figure 1, p. 48). HPLC column recoveries averaged 94.0 ± 4.1% (p. 25).

Confirmation of the identification of iodomethane was done using headspace-GC/MS with Electron Ionization (p. 26).

Identification and quantification of transformation products: Transformation products were isolated and quantified by HPLC as described for the parent compound. Methanol was apparently the only reference standard that was used; its HPLC Rt in this system is about 14 minutes (Figure 1, p. 48). Identification of methanol was confirmed using GC/MS.

Detection limits (LOD, LOQ) for the parent: The Limit of Detection using LSC was two times the average system background, or 0.014-0.034% of the applied (p. 24). The Limit of Detection using HPLC was three times the average background height, or about 0.9% of the applied (p. 25).

Detection limits (LOD, LOQ) for the transformation products: The Limit of Detection using LSC was two times the average system background, or 0.014-0.034% of the applied (p. 24). The Limit of Detection using HPLC was three times the average background height, or about 0.9% of the applied (p. 25).

II. RESULTS AND DISCUSSION

A. TEST CONDITIONS: The incubation temperature was reported to ranged from 24.8 to 25.1°C in the 25°C test and from 49.6 to 49.8°C in the 50°C test; supporting data were not provided (p. 29). In the 25°C test, the pH of the pH 4 buffer solution ranged from 4.01 to 4.07, of the pH 7 buffer solution ranged from 6.96 to 7.03, and of the pH 9 buffer solution ranged from 8.97 to 9.03 (Table 4, p. 39). In the 50°C test, the pH of the pH 4 buffer solution ranged from 3.99 to 4.03, of the pH 7 buffer solution ranged from 6.95 to 7.05, and of the pH 9 buffer solution ranged from 9.01 to 9.06 (Table 3, p. 38). The sterility of the samples was confirmed at each sampling interval (Tables 1-2, pp. 36-37).

B. MASS BALANCE: At 25°C, total [^{14}C]residue recovery ranged from 91.3 to 102.6% of the applied (mean 98.38 ± 3.3%) in the pH 4 solution, from 91.7 to 102.7% (97.6 ± 3.6%) in the pH 7 solution, and from 92.6 to 102.7% (98.0 ± 3.0%) in the pH 9 solution (Table 6, p. 41).

At 50°C, total [^{14}C]residue recovery ranged from 93.4 to 105.6% of the applied (mean 101.0 ± 3.1%) in the pH 4 solution, from 94.2 to 103.6% (100.0 ± 2.9%) in the pH 7 solution, and from 91.9 to 102.9% (99.0 ± 3.5%) in the pH 9 solution (Table 5, p. 40). There was no apparent loss of radioactivity from the solutions.

Table 4: Hydrolysis of [^{14}C]iodomethane, expressed as percentage of the applied radioactivity (mean ± s.d., n = 2), at pH 4 and 25°C.*

Compound	Sampling times (days)						
	0	3	7	14	21	28	30
Iodomethane	97.8 ± 1.8	96.2 ± 0.0	92.2 ± 3.8	90.6 ± 0.4	83.8 ± 5.2	83.6 ± 0.8	78.6 ± 0.4
Methanol	0.9 ± 0.0	2.6 ± 0.1	5.0 ± 0.4	9.0 ± 0.3	11.8 ± 1.0	16.3 ± 0.4	16.0 ± 0.4
Other metabolites	0.0	0.0	0.0	0.2 ± 0.2	0.0	0.2 ± 0.2	0.3 ± 0.1
Volatiles	Volatiles were not measured.						
Total % recovery	100.0 ± 3.7	98.8 ± 0.1	97.6 ± 4.7	100.6 ± 1.6	95.6 ± 6.1	100.5 ± 0.8	94.8 ± 0.6

* Mean and standard deviation calculated by the reviewer using data obtained from Table 6, p. 41, and Table 10, p. 45 of the study report.

Table 5: Hydrolysis of [^{14}C]iodomethane, expressed as percentage of the applied radioactivity (mean ± s.d., n = 2), at pH 7 and 25°C.*

Compound	Sampling times (days)						
	0	3	7	14	21	28	30
Iodomethane	97.5 ± 1.8	94.1± 4.5	92.2 ± 1.1	86.1± 5.4	82.2 ± 4.2	77.7 ± 3.1	78.9 ± 1.0
Methanol	0.9 ± 0.0	2.6 ± 0.3	5.0 ± 0.2	8.7 ± 0.2	12.2 ± 0.7	15.7 ± 0.8	17.5 ± 0.0
Unknown artifact	0.0	0.0	0.6 ± 0.1	1.1 ± 0.1	2.0 ± 0.1	2.6 ± 0.5	2.5 ± 0.0
Other metabolites	0.3 ± 0.1	0.0	0.0	0.2 ± 0.2	0.0	0.0	0.4 ± 0.1
Volatiles	Volatiles were not measured.						
Total % recovery	100.0 ± 3.8	97.1 ± 5.4	97.6 ± 1.0	95.9 ± 5.9	97.1 ± 6.1	96.0 ± 4.4	99.3 ± 0.8

* Mean and standard deviation calculated by the reviewer using data obtained from Table 6, p. 41, and Table 11, p. 46 of the study report.

Table 6: Hydrolysis of [^{14}C]iodomethane, expressed as percentage of the applied radioactivity (mean ± s.d., n = 2), at pH 9 and 25°C.*

Compound	Sampling times (days)						
	0	3	7	14	21	28	30
Iodomethane	97.4 ± 2.0	95.8 ± 1.6	91.0 ± 4.7	86.7 ± 2.1	83.4 ± 3.0	81.2 ± 0.7	80.4 ± 1.6
Methanol	1.0 ± 0.1	2.8 ± 0.2	5.4 ± 0.6	9.2 ± 0.6	13.0 ± 0.5	17.0 ± 0.4	18.4 ± 0.1
Other metabolites	0.4 ± 0.2	0.0	0.0	0.0	0.0	0.0	0.0
Volatiles	Volatiles were not measured.						
Total % recovery	100.0 ± 3.8	98.8 ± 1.8	97.3 ± 6.6	95.8 ± 2.8	96.4 ± 3.5	98.2 ± 0.4	99.2 ± 2.2

* Mean and standard deviation calculated by the reviewer using data obtained from Table 6, p. 41, and Table 12, p. 47 of the study report.

Table 7: Hydrolysis of [^{14}C]iodomethane, expressed as percentage of the applied radioactivity (mean ± s.d., n = 2), at pH 4 and 50°C.*

Compound	Sampling times (days)							
	0	1	2	3	4	5	6	7
Iodomethane	96.6 ± 0.5	78.1± 0.4	63.2 ± 0.2	53.2 ± 0.9	42.1 ± 2.0	32.6 ± 2.8	29.2 ± 0.2	22.2 ± 1.1
Methanol	2.8 ± 0.3	21.0 ± 1.1	35.2 ± 0.8	45.2 ± 0.2	56.6 ± 2.0	63.4 ± 2.0	69.6 ± 0.4	76.4 ± 0.1
Other metabolites	0.6 ± 0.1	0.6 ± 0.8	0.8 ± 0.1	1.0 ± 0.2	1.4 ± 0.1	0.8 ± 0.2	1.1 ± 0.1	1.0 ± 0.2
Volatiles	Volatiles were not measured.							
Total % recovery	100.0 ± 0.3	99.8 ± 0.4	101.8 ± 4.3	101.2 ± 3.5	102.6 ± 1.3	99.2 ± 8.3	101.4 ± 1.2	102.3 ± 4.7

* Mean and standard deviation calculated by the reviewer using data obtained from Table 5, p. 40, and Table 7, p. 42 of the study report.

Table 8: Hydrolysis of [^{14}C]iodomethane, expressed as percentage of the applied radioactivity (mean ± s.d., n = 2), at pH 7 and 50°C.*

Compound	Sampling times (days)							
	0	1	2	3	4	5	6	7
Iodomethane	96.2 ± 1.3	74.0 ± 2.8	57.6 ± 0.8	42.2 ± 0.2	28.4 ± 3.8	24.4 ± 1.6	18.8 ± 2.1	10.8 ± 1.5
Methanol	2.9 ± 0.0	22.2 ± 3.0	35.8 ± 0.1	47.2 ± 0.2	62.6 ± 7.1	67.7 ± 1.4	73.2 ± 3.7	81.0 ± 1.9
Unknown artifact	0.0	2.8 ± 0.4	4.8 ± 0.1	5.8 ± 0.6	5.7 ± 2.0	7.0 ± 0.1	7.0 ± 1.8	4.2 ± 0.6
Other metabolites	0.3 ± 0.4	1.0 ± 0.1	1.2 ± 0.2	1.1 ± 0.0	1.5 ± 0.4	1.0 ± 1.0	1.1 ± 0.1	1.4 ± 0.2
Volatiles	Volatiles were not measured.							
Total % recovery	100.0 ± 1.8	102.0 ± 2.1	100.8 ± 2.3	96.3 ± 3.0	98.2 ± 0.8	101.2 ± 0.8	103.0 ± 0.9	98.6 ± 5.7

* Mean and standard deviation calculated by the reviewer using data obtained from Table 5, p. 40, and Table 8, p. 43 of the study report.

Table 9: Hydrolysis of [^{14}C]iodomethane, expressed as percentage of the applied radioactivity (mean ± s.d., n = 2), at pH 9 and 50°C.*

Compound	Sampling times (days)							
	0	1	2	3	4	5	6	7
Iodomethane	95.8 ± 0.8	71.4 ± 0.9	57.8 ± 2.5	42.2 ± 6.2	33.2 ± 3.2	29.8 ± 0.9	25.6 ± 0.6	16.6 ± 2.9
Methanol	2.75 ± 0.1	27.8 ± 0.3	39.2 ± 0.4	53.8 ± 2.0	61.7 ± 9.0	69.1 ± 0.8	72.6 ± 0.9	78.0 ± 1.8
Other metabolites	1.0 ± 0.1	0.6 ± 0.1	1.2 ± 0.6	1.0 ± 0.1	1.0 ± 0.0	1.0 ± 0.1	0.8 ± 0.1	1.0 ± 0.4
Volatiles	Volatiles were not measured.							
Total % recovery	100.0 ± 1.6	100.8 ± 2.2	99.2 ± 4.1	98.3 ± 6.1	97.4 ± 7.8	101.4 ± 1.0	99.6 ± 2.3	95.6 ± 0.7

* Mean and standard deviation calculated by the reviewer using data obtained from Table 5, p. 40, and Table 9, p. 44 of the study report.

C. TRANSFORMATION OF PARENT COMPOUND: At 25°C, in the pH 4 buffer solution, iodomethane decreased from an average 97.8% of the applied at day 0 to 78.6% at 30 days posttreatment (Table 10, p. 45). In the pH 7 buffer solution, iodomethane decreased from an average 97.5% of the applied at day 0 to 78.9% at 30 days posttreatment (Table 11, p. 46). The study author predicted that the iodomethane concentration in the pH 7 solution at 30 days would have been 81.22% of the applied if the interaction with the TRIS buffer was discounted (Figure 22,

p. 69). In the pH 9 buffer solution, iodomethane decreased from an average 97.4% of the applied at day 0 to 80.5% at 30 days posttreatment (Table 12, p. 47).

At 50°C, in the pH 4 buffer solution, iodomethane decreased from an average 96.6% of the applied at day 0 to 53.2% at 3 days posttreatment and 22.2% at 7 days (Table 7, p. 42). In the pH 7 buffer solution, iodomethane decreased from an average 96.2% of the applied at day 0 to 42.2% at 3 days posttreatment and 10.8% at 7 days (Table 8, p. 43). The study author predicted that the iodomethane concentration in the pH 7 solution at 7 days would have been 19.9% of the applied if the interaction with the TRIS buffer was discounted (Figure 17, p. 64). In the pH 9 buffer solution, iodomethane decreased from an average 95.8% of the applied at day 0 to 42.3% at 3 days posttreatment and 16.7% at 7 days (Table 9, p. 44).

HALF-LIFE: The half-lives for iodomethane in the pH 4, 7, and 9 buffer solutions were determined by the reviewer using linear regression analysis based on first-order kinetics as calculated by Excel 97 SR-2. At 25°C, the respective values were determined to be 105, 94, and 108 days. At 50°C, the half-lives were determined to be 2.3-3.34 days.

Table 10. Calculated Half-lives*

pH	First order linear			DT50	DT90
	Half-life	Regression equation	r^2		
25°C					
4	0-30 day data: 105.0 days	y = -0.0066x + 4.5825	0.8847	ND	ND
7	0-30 day data: 93.7 days	y = -0.0074x + 4.5700	0.8797	ND	ND
9	0-30 day data: 108.3 days	y = -0.0064 + 4.5683	0.8995	ND	ND
50°C					
4	0-7 day data: 3.34 days	y = -0.2077x + 4.5702	0.99313	ND	ND
7	0-7 day data: 2.30 days	y = -0.3001x + 4.6132	0.9794	ND	ND
9	0-7 day data: 3.00 days	y = -0.2339x + 4.5146	0.9632	ND	ND

Half-lives are based on the measured concentration of iodomethane in solution.
ND Not determined.

TRANSFORMATION PRODUCTS: Methanol was the only compound identified in the buffer solutions. It was a major transformation product at all pHs at both 25 and 50°C (Tables 7-12, pp. 42-47).

At 25°C in the pH 4, 7, and 9 buffer solutions, methanol increased steadily to averages of 16.0-18.4% of the applied at 28-30 days posttreatment (Tables 10-12, pp. 45-47). Other metabolites

(unidentified) totaled ≤0.5% of the applied at all sampling intervals. In the pH 7 solution only, an artifact resulting from the interaction of the TRIS buffer and iodomethane reached 2.3-3.0% of the applied at 28-30 days posttreatment (Table 11, p. 46).

At 50°C in the pH 4 buffer solution, methanol averaged a maximum 76.4% of the applied at 7 days posttreatment (Table 7, p. 42). In the pH 7 buffer solution, methanol averaged a maximum 81.0% of the applied at 7 days (Table 8, p. 43). The TRIS artifact averaged a maximum 7.0% of the applied at 5 and 6 days, and was 4.3% at 7 days. In the pH 9 buffer solution, methanol averaged a maximum 78.0% of the applied at 7 days (Table 9, p. 44). Other metabolites totaled ≤1.8% of the applied in all buffers at all sampling intervals.

VOLATILIZATION: Volatiles were not measured.

TRANSFORMATION PATHWAY: A transformation pathway was not proposed by the study author. Iodomethane reacts with water to form methanol, which was measured in this study, and iodine radicals, which were not measured.

Table 1: Chemical name and CAS number for the transformation product of iodomethane.

Applicant's Code Name	CAS Number	Chemical Name	Chemical formula	Molecular weight	SMILES string
Methanol	67-56-1	Methanol	CH_3OH	32.04 g/Mol	

Data obtained from p. 19 of the study report.

D. SUPPLEMENTARY EXPERIMENT-RESULTS: No supplementary experiment was conducted.

III. STUDY DEFICIENCIES: No deficiencies were identified. This study can be used to fulfill the hydrolysis data requirement (§161-1).

IV. REVIEWER'S COMMENTS:

1. Preliminary studies demonstrated that although iodomethane reacted with the TRIS buffer at pH 7, producing a minor artifact, TRIS was superior to either acetate or phosphate as a buffering agent. Acetate did not have sufficient buffering capability and phosphate also produced artifacts. The artifact was not identified, but was reported to degrade to methanol.

   The study author manipulated the study results to subtract out the effect of the formation of the TRIS artifact. This was not done by summing the concentrations of the artifact and iodomethane. The study author determined the concentrations of TRIS artifact that would be observed if the artifact did not degrade to methanol and added that value to the observed

concentration of iodomethane (Figure 17, p. 64; Figure 22, p. 69). The study author determined half-lives for iodomethane as observed and adjusted for the TRIS artifact. At 25°C, the observed and adjusted half-lives were 93.9 and 112.8 days (p. 35, Figure 23, p. 70). At 50°C, the observed and adjusted half-lives were 2.3 and 3.2 days (p. 35; Figure 18, p. 65). Adjusting the half-lives for the TRIS artifact brings the pH 7 half-lives in line with the pH 4 and 9 half-lives, indicating that the rate of hydrolysis is independent of pH within the range pH 4-pH 9.

2. The reviewer-calculated half-lives are similar to those reported by the study author, who used the same statistical software (p. 26; Figures 14-16, pp. 61-63; Figures 19-21, pp. 66-68). Differences between the 25°C half-lives resulted from the number of significant digits used in the Excel calculations. Differences between the 50°C half-lives resulted because the reviewer used the measured concentration of iodomethane in solution for 0 to 7 days.

3. The study author used the Arrhenius equation to calculate the half-lives for iodomethane at 20°C (p. 35, Figures 24-27, pp. 71-74). Based on observed concentrations of iodomethane, the half-lives are 223.9 days at pH 4, 212.7 days at pH 7, and 240.8 days at pH 9. The half-life at pH 7 using adjusted data is 247.1 C.

4. The equipment and operating conditions that were used in the headspace GC/MS analysis were identified, but the headspace analytical procedure was not described.

5. The CAS number provided for methanol on p. 19 is the CAS number for iodomethane.

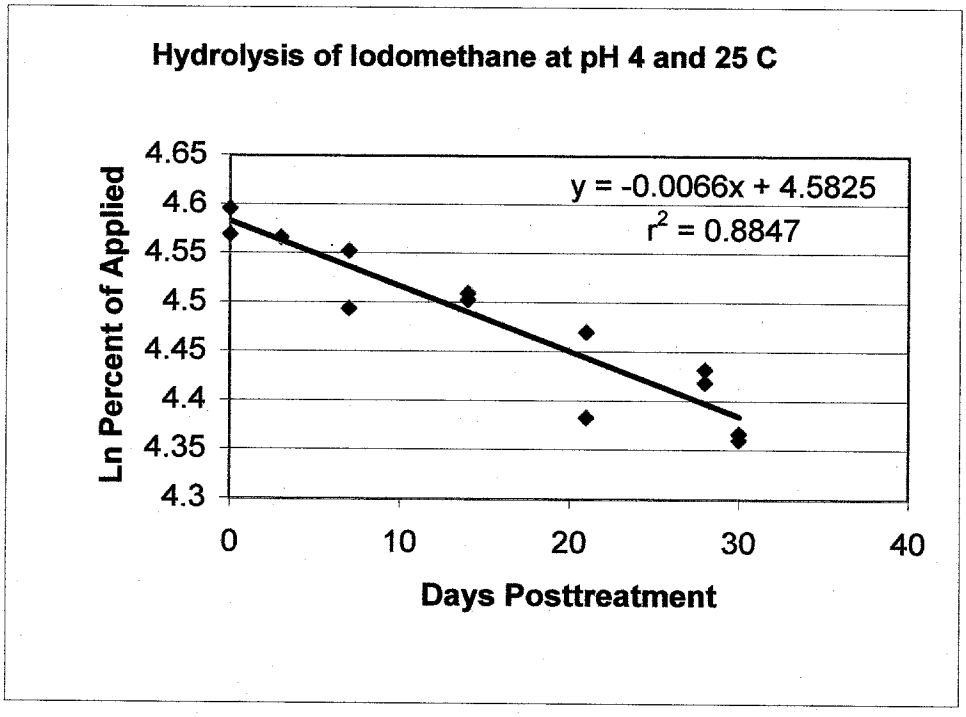
V. REFERENCES: No references were cited in the study.

Attachment 1

Excel Spreadsheets

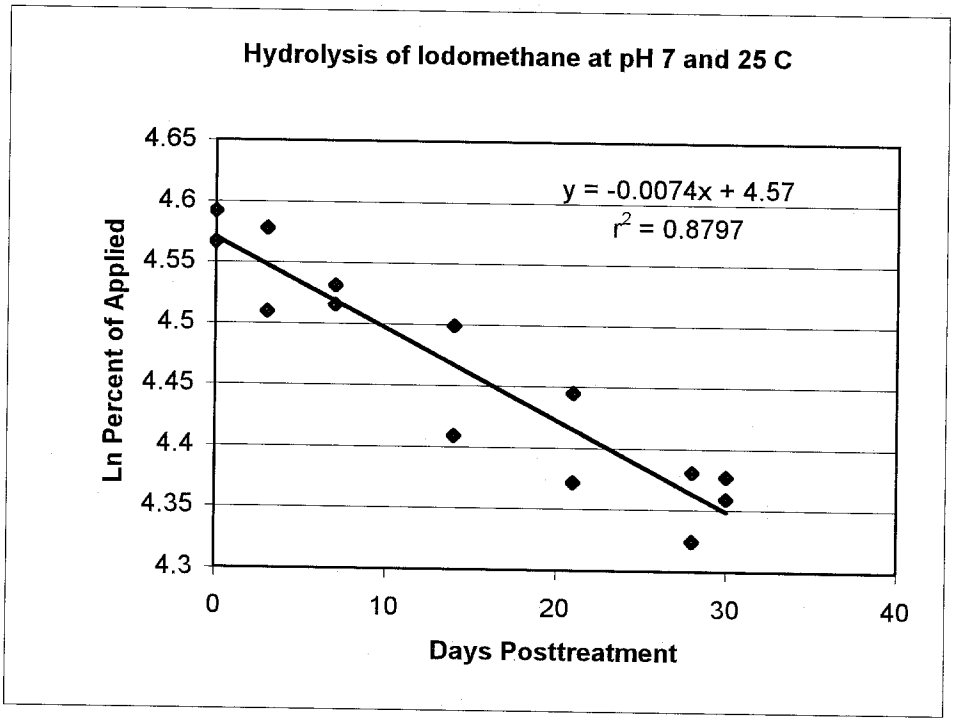
Chemical Name	Iodomethane
MRID	45593705
Guideline No.	161-1
Half-life (days) =	**105.02**
pH	4
Temperature (Celsius)	25

Days Posttreatment	Iodomethane (Percent of Applied)	ln (% of applied)
0	96.5	4.569543008
0	99.1	4.596129441
3	96.2	4.566429358
3	96.2	4.566429358
7	89.5	4.494238625
7	94.9	4.552823706
14	90.3	4.50313746
14	90.9	4.509760001
21	80.1	4.383275854
21	87.4	4.470495283
28	83.0	4.418840608
28	84.1	4.432006567
30	78.3	4.360547603
30	78.8	4.366912997



Chemical Name	Iodomethane
PC Code	30090
MRID	45593705
Guideline No.	161-1
Half-life (days) =	**93.67**
pH	7
Temperature (Celsius)	25

Days Posttreatment	Iodomethane (Percent of Applied)	ln (% of applied)
0	96.2	4.566429358
0	98.7	4.592084946
3	90.9	4.509760001
3	97.3	4.577798989
7	91.4	4.515245478
7	92.9	4.531523646
14	89.9	4.498697941
14	82.2	4.409155302
21	79.2	4.371976299
21	85.2	4.445001434
28	79.9	4.380775853
28	75.5	4.324132656
30	79.6	4.377014093
30	78.2	4.359269648

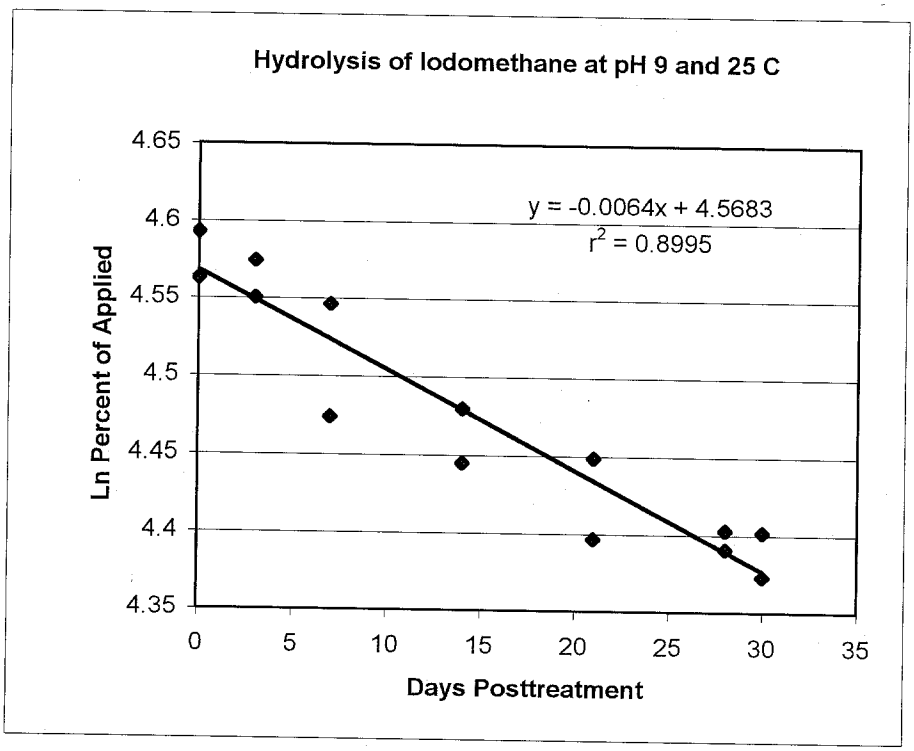


Chemical Name Iodomethane
MRID 45593705
Guideline No. 161-1

Half-life (days) = 108.30

pH 9
Temperature (Celsius) 25

Days Posttreatment	Iodomethane (Percent of Applied)	ln (% of applied)
0	95.9	4.563305982
0	98.8	4.593097605
3	94.7	4.550714
3	97.0	4.574710979
7	87.7	4.473921899
7	94.3	4.54648119
14	88.2	4.479606963
14	85.2	4.445001434
21	85.5	4.448516376
21	81.2	4.396915247
28	80.7	4.390738575
28	81.7	4.403054002
30	79.3	4.373238129
30	81.6	4.401829262

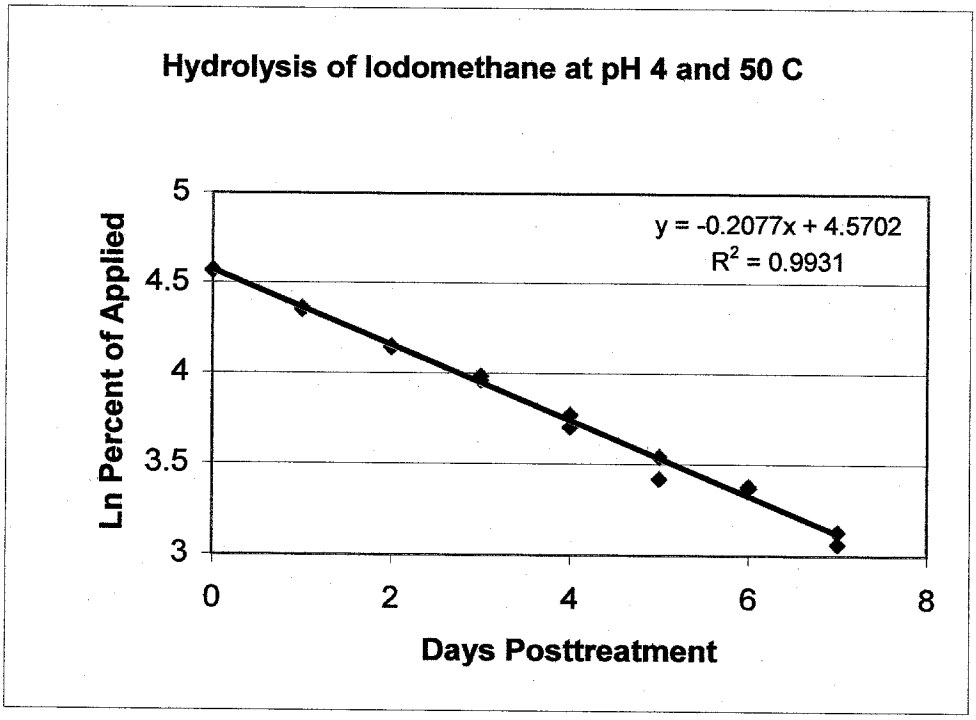


Chemical Name	Iodomethane
MRID	45593705
Guideline No.	161-1

Half-life (days) = 3.34

pH	4
Temperature (Celsius)	50

Days Posttreatment	Iodomethane (Percent of Applied)	ln (% of applied)
0	96.9	4.573679519
0	96.2	4.566429358
1	78.4	4.361823927
1	77.8	4.354141431
2	63.4	4.149463861
2	63.1	4.14472077
3	53.9	3.987130478
3	52.6	3.96271612
4	43.5	3.772760938
4	40.7	3.706228092
5	34.6	3.543853682
5	30.6	3.421000009
6	29.4	3.380994674
6	29.1	3.370738174
7	22.9	3.131136911
7	21.4	3.063390922

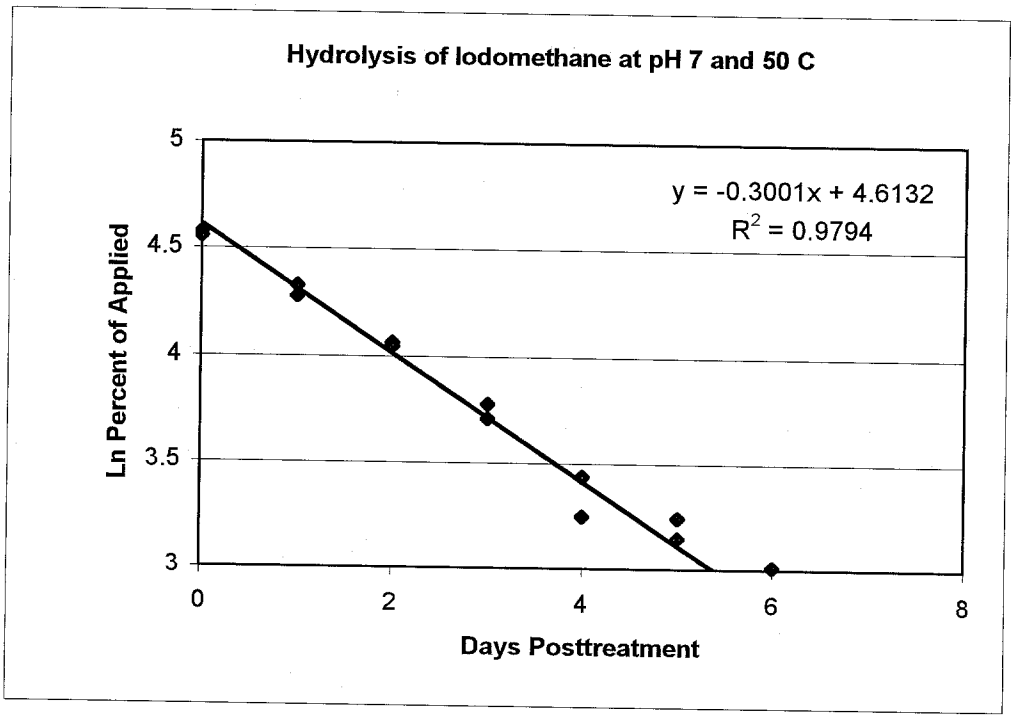


Chemical Name	Iodomethane
PC Code	30090
MRID	45593705
Guideline No.	161-1

Half-life (days) = **2.31**

pH	7
Temperature (Celsius)	50

Days Posttreatment	Iodomethane (Percent of Applied)	ln (% of applied)
0	97.1	4.575741375
0	95.2	4.555979942
1	75.9	4.329416684
1	72.0	4.276666119
2	58.2	4.063885355
2	57.1	4.044804117
3	43.6	3.77505715
3	40.7	3.706228092
4	25.8	3.250374492
4	31.1	3.437207819
5	23.3	3.148453361
5	25.6	3.242592351
6	20.3	3.010620886
6	17.3	2.850706502
7	11.8	2.468099531
7	9.7	2.272125886



Chemical Name	Iodomethane
MRID	45593705
Guideline No.	161-1

Half-life (days) = 2.96

pH	9
Temperature (Celsius)	50

Days Posttreatment	Iodomethane (Percent of Applied)	ln (% of applied)
0	96.3	4.567468319
0	95.2	4.555979942
1	70.7	4.258445573
1	72.0	4.276666119
2	59.6	4.087655574
2	56.1	4.027135813
3	46.6	3.841600541
3	37.9	3.634951112
4	30.9	3.430756184
4	35.5	3.569532696
5	30.5	3.417726684
5	29.2	3.374168709
6	26.0	3.258096538
6	25.2	3.226843995
7	18.7	2.928523524
7	14.6	2.681021529