Data Evaluation Report on the phototransformation of XDE-742 (pyroxsulam) in water

PMRA Submission Number 2006-4727; EPA MRID Number 47260501; APVMA ATS 40362

Data Requirement:	PMRA DATA CODE:	8.2.3.3.2
	US EPA DP Barcode:	332118
	OECD Data Point:	IIA 2.9.2, IIA 7.6
	US EPA Guideline:	Subdivision N, Section 161-2
Test material:	^{14}C-XDE-742-TP and ^{14}C-XDE-742-PYR (for purity, see: 1. Test Material	
Common name:	XDE-742 (pyroxsulam)	
Chemical name:		
IUPAC:	N-(5,7-dimethoxy[1,2,4]triazolo[1,5-α]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide	
CAS name:	N-(5,7-dimethoxy[1,2,4]triazolo[1,5-α]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide	
CAS No:	422556-08-9	
Synonyms:	DE-742, XR-742	
Smiles string:	c1(c(ccnc1OC)C(F)(F)F)S(Nc2nn3c(n2)nc(cc3OC)OC)(=O)=O	

Primary Reviewer:	J. Catherine Evans (1638) PMRA	**Date:** 6 March 2007
Secondary Reviewer(s):	Peter Takacs (1046) PMRA	**Date:** 14 March, 2007
	Greg Orrick USEPA E Bethel for Greg Orrick	**Date:** 30 May 2007 October 25, 2007
	David McAdam, PhD AUS DEW D. Murphy for David McAdam	**Date:** 30 May 2007 November 2, 2007.
	Émilie Larivière PMRA Émilie Larivière	**Date:** October 22, 2007 October 22, 2007
Company Code:	DWE	
PMRA Active Code:	JUA	
PMRA Use Site Category:	13, 14	
PMRA EPA PC Code:	108702	

2070878

CITATION: Byrne, S. L., Meitl, T. J., , Crabtree, A. B., Linder, S. L., and Balcer, J. L., 2006, Aqueous Photolysis of XDE-742 in pH 7 Buffer Using a Xenon Lamp, Regulatory Laboratories—Indianapolis Lab (Indianapolis, Indiana), Study number 040002, Dow AgroSciences LLC, February 10, 2006.

Data Evaluation Report on the phototransformation of XDE-742 (pyroxsulam) in water

PMRA Submission Number 2006-4727; EPA MRID Number {46908327}; APVMA ATS 40362

EXECUTIVE SUMMARY:

The aqueous phototransformation of radiolabeled XDE-742 (labeled in the 2-C and 6-C position of the pyrimidine ring (PY-label) or in the 2-C position of the triazolopyrimidine portion (TP- label)) was studied at 20 °C in sterile aqueous pH 7 HEPES buffered solution at an initial concentration of 1 mg a.i./L. 15 days of continuous irradiation was employed using a xenon lamp. A supplemental experiment was carried out using pH 7 TRIS buffer as an attempt to circumvent problems arising from the reaction of the HEPES buffer with the 742-ADTP transformation product.

The main experiment was conducted in accordance with the US EPA Subdivision N Section 161-2, SETAC Part 1, Section 10.1, and to meet the US EPA GLP Standards (40 CFR Part 160). Samples were analyzed at 0, 2, 4, 8, and 20 hours, and 2, 4, 7, and 15 days after treatment (DAT), and were analyzed directly by LSC and HPLC. Identification of transformation products was done by LC-MS/MS. Traps for the collection of CO_2 and organic volatiles were not used for the main test samples; a duplicate PY-labeled sample was irradiated for 15 days and used to determine the amount of volatile radioactivity at test termination. A PNAP/pyridine chemical actinometer solution was used to quantify the amount of light that the samples received, such that 1 day of continuous irradiation (DAT) was equated with 4.9 days of irradiation in the summer sun at 40° N latitude for that portion of the spectrum required for the study.

Material balance was 97.5 ± 4.6% of the applied radioactivity for the irradiated samples and 100.5 ± 1.2% applied radioactivity for the dark controls. No significant transformation occurred in the dark samples (100% of the applied radioactivity remained as parent at test termination), and the presence of unidentified products that were detected at low levels throughout the study likely results from (minor) contamination of the test material, not transformation.

In the irradiated samples, the concentration of the parent compound decreased from 99.0% at 0 DAT to 0.6% of the applied amount at 6.8 DAT. The parent compound was not detected at test termination (14.9 DAT). The two major transformation products detected in the irradiated samples were the 742-sulfinic acid (2-methoxy-4-(trifluoromethyl)pyridine-3-sulfinic acid) and 742-ADTP (5,7-dimethoxy[1,2,4]triazolo[1,4-α]pyrimidin-2-amine), with maximum concentrations of 79.2% and 39.8% of the applied amount, respectively, at 3.8 DAT. An additional 7.9% of the radiation was present as a 742-ADTP + HEPES adduct at this time. Both major transformation product concentrations decreased through the remainder of the study, to 45.0% and 23.6% of the applied amount at study termination. The minor transformation products in the irradiated samples were the 742-sulfonic acid (2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonic acid), which formed in the PY-labeled samples at levels too low to be quantified, and multiple unknown minor products. Volatiles were found to be 1.2% of the applied radioactivity in the surrogate test (examined only at 14.9 DAT). The total unidentified radioactivity at test termination was 2.2% and 49-69% of the applied radioactivity in the dark and irradiated samples, respectively.

The photodegradation mechanism of XDE-742 appears to be cleavage of the sulfonamide bridge, yielding the 742-sulfinic acid, which may then oxidize to produce the small quantities of 742-sulfonic acid observed, and the 742-ADTP. The major transformation products are then further transformed to multiple, low level components which could not be separated nor identified in the study.

Data Evaluation Report on the phototransformation of XDE-742 (pyroxsulam) in water

PMRA Submission Number 2006-4727; EPA MRID Number {46908327}; APVMA ATS 40362

The environmental photolytic half-life, derived from the measured half-life in laboratory under artificial lamp, is predicted to be 4.5 days at 40° N latitude in summer sunlight (0.91 days continuous irradiance in the laboratory), and the $t_{9/10}$ is predicted to be 14.7 days (r^2= 0.9957 for first order curve fit of non-zero concentration data).

The concentrations of the two major transformation products peaked at 3.8 DAT and were in decline by the end of the study (14.9 DAT). A supplemental study of the transformation of the 742-ADTP transformation product in three different solutions (pH 7 TRIS buffer, pH 7 HEPES buffer and HPLC-grade water) also gave an excellent fit to first-order kinetics (r^2= 0.9852- 0.9892), but the estimated $t_{1/2}$ for all three were between 22 and 23 days (approx 108-113 equivalent days at 40° N latitude in summer sunlight), which was in excess of the study duration of 15 days.

Results Synopsis

Test medium:	0.01 M HEPES buffer at pH 7
Source of irradiation:	Xenon lamp
Half-life/DT50 for Dark:	no degradation occurred in the dark samples
Half-life/DT50 for phototransformation:	0.91 days (laboratory); 4.5 days (expected at 40°N latitude in summer sunlight)
Major transformation products:	742-ADTP, 742-sulfinic acid
Minor transformation products:	742-sulfonic acid

Study Acceptability: PMRA, US EPA and DEW: This study is classified **acceptable** and satisfies the guideline requirement for a study on phototransformation in water.

Data Evaluation Report on the phototransformation of XDE-742 (pyroxsulam) in water

PMRA Submission Number 2006-4727; EPA MRID Number {46908327}; APVMA ATS 40362

I. MATERIALS AND METHODS

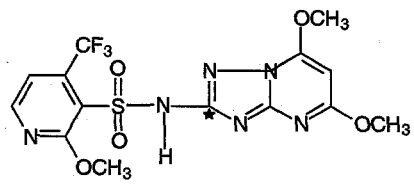
GUIDELINE FOLLOWED: EPA Pesticide Registration Guidelines, Subdivision N, Section 161-2 and SETAC Part 1 Section 10.1

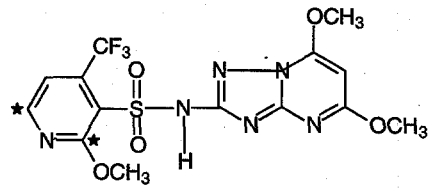
COMPLIANCE: Good Laboratory Practice standards, 40 CFR Part 160

A. MATERIALS:

1. Test Material

Chemical Structure: ^{14}C-XDE-742-TP ^{14}C-XDE-742-PY





(star indicates a radiolabeled carbon)

Description:	technical, solid	
Purity:	^{14}C-XDE-742-TP	^{14}C-XDE-742-PY
Analytical purity:	N/A	N/A
Lot/Batch No.	INV1901	INV1905
Radiochemical purity:	100%	100%
Lot/Batch No.	FA&PC 034003	FA&PC 034005
Specific activity:	36.6 mCi/mmol	43.7 mCi/mmol
Locations of the radio label:	TP ring	PY ring
Storage conditions of test chemicals:	Frozen in the dark.	

Physico-chemical properties of XDE-742 (pyroxsulam) (p. 19)

Parameter	Values	Comments
Water solubility	16.4 mg/L at pH 4 and 20 °C 3.20 x 10^3 mg/L at pH 7 and 20 °C 1.37 x 10^4 mg/L pH 9 and 20 °C 62.6 mg/L at 20 °C (unbuffered)	Very soluble in water. Turner, B. J. "Determination of Water Solubility for XDE-742" NAFST806, unpublished report of Dow AgroSciences LLC, 22-December-2004.

Parameter	Values	Comments
Vapour pressure/ volatility	$< 10^{-7}$ Pa ($<10^{-9}$ torr)	Low volatility Madsen, S. "Determination of the Surface Tension, Density, and Vapour Pressure of the Pure Active Ingredient XDE-742," DERBI 144723, unpublished report of Dow AgroSciences LLC, 09-October-2003.
UV absorption	ε= 8000 $Lmol^{-1}cm^{-1}$, λ = 297 nm (unbuffered neutral solution)	From DACO 8.2.1 Physical Chemical properties (See reviewer comments)
pKa	4.51 (25 °C)	Probe data: Sheets, J. J., Gast, R. E., Hanley, T. R., Krieger, M., Mayes, M. A. "Early Stage Registration Assessment of X666742: Phase I Weed Management Sulfonamide for European and Canadian Cereal Markets," DERBI No 79155, unpublished report of Dow AgroSciences LLC, 28 September 2000.
Log K_{ow}	1.080 at pH 4 -1.010 at pH 7 -1.600 at pH 9	Low potential for bioaccumulation Trend consistent with solubility results. Turner, B. J., "Determination of Octanol/Water Partition Coefficient for XDE-742," NAFST807, 2004, unpublished report of Dow AgroSciences LLC.
Stability of compound at room temperature, if provided	Not available	

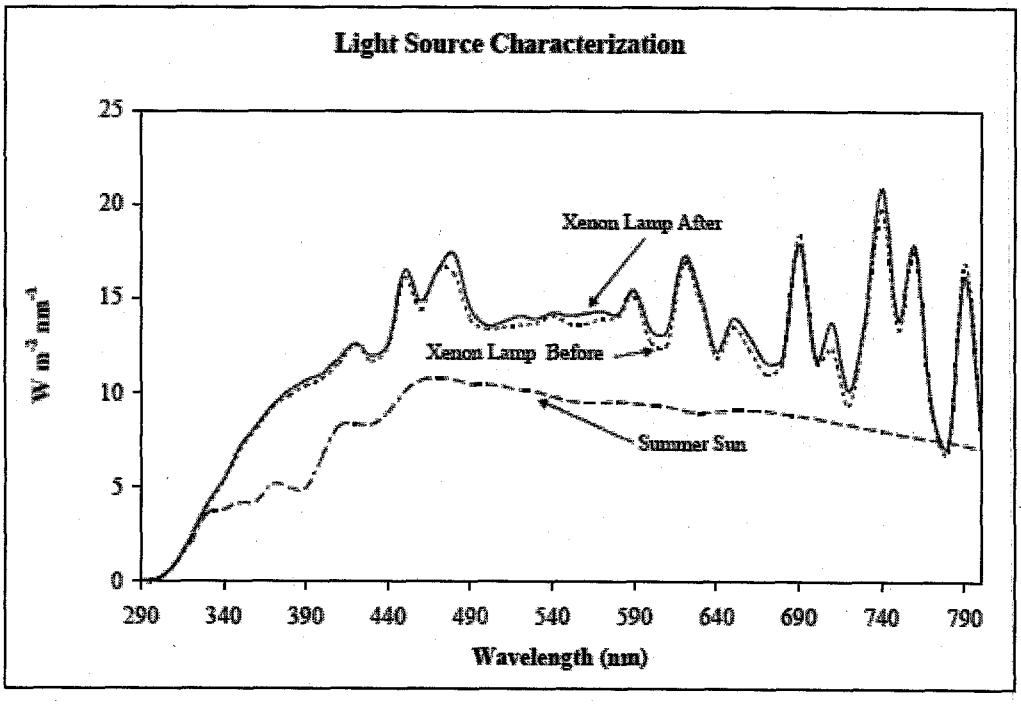
2) Buffer solution: Buffer solutions were made with HPLC grade water as follows:
Table 1: Description of buffer solutions (Table 1, p. 47).

pH	Type of buffer and final molarity	Composition
7.0	0.01 M HEPES (4-(2-hydroxyethyl)-1-piperazineethane sulfonic acid)	2.38g HEPES in 1.0 L HPLC-grade water, adjusted to pH 7.0 using 1.0 N NaOH (additional buffer prepared later using proportional amounts of reagents)
7.0	0.01 M TRIS (tris (hydroxymethyl)amino methane hydrochloride	1.21g TRIS in 1.0 L HPLC-grade water, adjusted to pH 7.0 using 2.0 N HCl (for supplemental experiment)

3) Details of light source:

Table 2: Artificial light source (Table 2, p. 48; Figure 5, p. 67).

Property	Details
Nature of light source	Xenon lamp
Emission wavelength spectrum	Measured using a radiometer. Intensity values similar to those from the Federal Register for 40°N latitude (summer sun, see below)
Light intensity	615 W/m^2 (average)
Filters used	Quartz with infrared coating, soda-lime.
Relationship to natural sunlight	Determination was attempted using radiometry and chemical actinometer values. However, reported radiometry values may be incorrect (Table E2, p. 122-124). Good agreement with natural light over the relevant portion of the spectrum.



B. EXPERIMENTAL CONDITIONS:

1) Preliminary Study: Not applicable

2) Experimental Conditions

Table 3: Experimental Parameters (Table 3; p. 49).

Parameters		Details
Duration of the study		0 to 15 days after treatment (DAT)
Test concentrations (mg a.i./L) nominal: measured:		 1 mg/L 1.06 mg/L (TP label, HEPES study) 0.97 mg/L (PY label HEPES study)
Dark controls used (Yes/No)		Yes
Replication	Dark:	2
	Irradiated:	2
Preparation of the test medium:	Volume used/treatment:	6.5 mL of the bulk solution
	Method of sterilization:	Autoclave
	Co-solvent:	Acetonitrile, 0.75- 0.85% v/v

Parameters		Details
Test material preparation (bulk solution)	Volume of application solution used/treatment:	1.5 mL in 200 mL buffer (TP-label) 1.7 mL in 200 mL buffer (PY-label)
	Application method	glass serological pipette
	Co-solvent:	Acetonitrile
Test apparatus (Type/Material/Volume)		Irradiated samples: 10-ml inverted quartz tubes with glass beads used to keep solution above cap level Dark samples: amber vials Constant temperature room
Details of traps for volatile compounds, if any		None
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; Duration of light/darkness:		Xenon lamp 20 ± 1 °C Continuous irradiance
Other details, if any		Actinometer solution: PNAP/pyridine pH 7 HEPES buffer used for kinetics study

3) Supplementary experiments: A similar study using 10 mg/L TRIS buffer was performed to attempt to confirm the rate of transformation while avoiding the possible confounding effect discovered during the main experiment, where the HEPES buffer used formed an adduct with the 742-ADTP transformation product. All experimental conditions other than the buffer and sampling times were identical to that for the main study, however, the pH in the irradiated samples dropped from 6.97 to 5.41 by 14 DAT, so the data are considered to be supplemental.

Since the HEPES buffer used in the main study reacted with some of the 724-ADTP produced, this separate study was conducted to determine the aqueous photolytic degradation rate of ^{14}C-742-ADTP in two buffer systems (pH 7 HEPES and TRIS) and water. Each solution was prepared at a nominal concentration of 5 mg/L, and samples were continuously irradiated or maintained in the dark for 15 DAT, equivalent to 39.5 days in 40° N summer sunlight.

4) Sampling: Describe sampling intervals and method of sampling in a tabular format.

Table 4: Sampling details (Table 4; p. 50).

Observations	Details
Sampling intervals for the parent/transformation products	0, 0.08, 0.17, 0.33, 0.83, 2, 4, 7 and 15 DAT (main experiment in HEPES buffer)
Sampling method	Sterility of samples checked, triplicate aliquots counted for mass balance, sample transferred to vial to check pH, sample injected directly into HPLC for analysis.
Method of sampling volatile compounds, if any	Purge and trap system shown in Figure 6 of the final report was used on duplicate samples only at 15 DAT.
Sampling intervals/times for: sterility check pH measurement	Sterility and pH checked at each sample time.
Sample storage before analysis, if any	Refrigerated
Other observation, if any (e.g.: precipitation, color change etc.)	None

C. ANALYTICAL METHODS: Briefly describe the methodology for:

Extraction/clean up/concentration methods: None

Total ^{14}C measurement: An aliquot of each ^{14}C-XDE-742 solution was analyzed directly by LSC and HPLC.

Derivatization method, if used: None.

Identification and quantification of parent compound: The primary HPLC system consisted of a Rheodyne 7125 manual sample injector, a Waters 500 pump controller with a 60F pump, a Watters 996 photodiode array (PDA) UV detector, and a Gilson 96-well-plate fraction collector. An XTerra MS column (C8, S-5, 120 A, 4.6 x 250 mm) was used for all separations. Fractions (0.1-minute) were collected in 96-well plates containing 200-µL MicroScint scintillator, and counted using a TopCount LSC (Packard Instrument Co.) and used to generate reconstructed radiochromatograms. A UV detector at 295 nm was used to determine the retention times of non-radiolabeled standards. Typical injection volume was 50 or 100 µL.

HPLC Method (Table 5, p. 51):

XTerra MS column (C8, S-5, 120 A, 4.6 x 250 mm)

Flow rate: 1.0 mL/minute

Solvent A = water:acetic acid:triethylamine, 99.0:0.5:0.5

Solvent B = acetonitrile:acetic acid:triethylamine, 99.0:0.5:0.5

Primary HPLC gradient method:

Time (minutes)	Composition	Description
0	85/15 A/B	Initial conditions
25	50/50 A/B	Linear gradient
30	5/95 A/B	Linear gradient
35	85/15 A/B	Begin re-equilibration
45	85/15 A/B	End run

Compound	Time (minutes)
742-ADTP	5.0
742-sulfinic acid	5.8
742-sulfonic acid	6.4
XDE-742	22.7

Polar HPLC gradient method (for improved separation of polar fraction)

Time (minutes)	Composition	Description
0	99/1 A/B	Initial conditions
20	50/50 A/B	Linear gradient
25	5/95 A/B	Linear gradient
35	99/1 A/B	Begin re-equilibration
45	99/1 A/B	End run

Compound	Time (minutes)
742-ADTP	15.3
742-sulfinic acid	15.3
742-sulfonic acid	16.1
XDE-742	25.4

Identification and quantification of transformation products: Samples of each radiolabel were prepared for degradate identification. Approximately 9 mg of non-radiolabeled XDE-742 was weighed into separate 10-mL quartz tubes. Radiolabeled XDE-742 (in acetonitrile) was added to each tube: 0.073 mg XDE-742-TP (6.2 µCi) to the TP-742-bulk sample and 0.097 mg XDE-742-PY (9.8 µCi) to the PY-742 bulk sample. The solvent was evaporated under a stream of nitrogen. The XDE-742 was dissolved in 9.0 mL pH 7 HEPES buffer for a final concentration of

approximately 1000 µg/mL. The samples were exposed to xenon light for approximately 24-hour intervals, totaling an equivalent of four (4) days of continuous irradiation.

Samples for identification purposes were not sterilized prior to their treatment with XDE-742 and no special care was taken to maintain sterility. The pH and mass balance were not monitored. These samples were not used to determine the transformation rate of XDE-742. Samples were analyzed by HPLC using the above gradient methods. Mass spectrometry was used to identify the transformation products.

Detection limits (LOD, LOQ) for the parent compound and transformation products: LOD = 10 dpm (disintegrations per minute) above background, LOQ = 40 dpm above background.

II. RESULTS AND DISCUSSION:

A. TEST CONDITIONS: The pH, sterility, temperature and other experimental conditions were maintained throughout the study. The pH ranged from pH 7.0 to pH 7.7 in the exposed samples (average pH 7.4 ± 0.2) and pH 6.7 to pH 7.3 in the dark controls (average pH 7.0 ± 0.2).

B. MASS BALANCE: Irradiated sample recoveries averaged 97.5 ± 4.6% (88.8 to 102%). Dark control sample recoveries averaged 101 ± 1.2% (98.4 to 103%). Through 7 DAT, mass balance in both labels was greater than 96.1%. There was a slight decline in the mass balance of the irradiated 15 DAT PY-labeled sample (88.8%). A duplicate 15 DAT irradiated PY-labeled sample was analyzed to determine if CO_2 or volatiles were produced. The majority of the radioactivity remained in the aqueous phase, 67.7% applied radioactivity (AR), a minimal amount was detected in the organic and caustic traps, 1.2% AR (combined traps), while 13.3% AR was recovered in organic rinses of the quartz glassware, for a combined mass balance of 82.2%. Acidification in preparation for trapping volatiles may have precipitated radioactivity from the aqueous solution.

Table 6: Phototransformation of XDE-742 in HEPES Buffer, expressed as percentage of the applied radioactivity (mean ± s.d., except as noted).[1]

Compound		Sampling times (DAT)								
		0	**0.08**	**0.17**	**0.34**	**0.83**	**1.8**	**3.8**	**6.8**	**14.9**
Parent compound	irradiated	99.0 ±1.7	94.8 ±0.2	85.4 ±4.0	75.2 ±1.2	50.4 ±2.1	19.9 ±0.8	4.2 ±0.1	0.6 ±0.4	ND
	dark	99.0 ±1.7	99.8 ±1.2	97.6 ±0.4	98.6 ±0.0	100 ±0.5	100 ±0.6	100 ±0.8	101 ±1.4	100 ±0.5
Transformation product GROUP 1 (polar components)	irradiated	ND	ND	ND	<LOQ	2.7	4.2 ±3.1	7.7 ±4.9	15.0 ±11	29.9 ±16
	dark	ND	ND	ND	ND	ND	ND	ND	ND	ND
Transformation product GROUP 2	irradiated	ND	0.7	1.9	4.5	9.5	11.2	19.4	11.1 ±11	±16.1 1.5
	dark	ND	ND	ND	ND	ND	ND	ND	ND	ND
Transformation product ADTP + HEPES	irradiated	ND	2.2	5.6	4.8	8.1	19.2	7.9	7.7	5.9
	dark	ND	ND	ND	ND	ND	ND	ND	ND	ND
Transformation product 742-ADTP	irradiated	ND	1.9	4.3	9.4	20.9	30.4	39.8	37.1	23.6
	dark	ND	ND	ND	ND	ND	ND	ND	ND	ND
Transformation product 742-sulfinic acid	irradiated	ND	5.4	15.2	23.4	46.1	70.3	79.2	73.1	45.0
	dark	ND	ND	ND	ND	ND	ND	ND	ND	ND
Unidentified product(s), (TP-top, PY-bottom)	irradiated	0.6 1.2	1.2 0.6	3.5 0.9	10.7 0.5	21.2 2.3	28.3 7.6	46.1 15.0	53.5 24.8	69.9 49.3
	dark	0.6 1.2	0.2 1.7	2.3 1.0	1.5 0.2	0.2 0.4	0.0 0.4	0.2 1.0	0.2 0.9	0.2 2.2
CO2 + volatile organics[2]	irradiated	ND	ND	ND	ND	ND	ND	ND	ND	1.2
	dark	ND	ND	ND	ND	ND	ND	ND	ND	ND
rinse of volatile glassware	irradiated	ND	ND	ND	ND	ND	ND	ND	ND	13.3
	dark	ND	ND	ND	ND	ND	ND	ND	ND	ND
Total % recovery	irradiated	99.9 ± 2.1	100.5 ±0.3	100.2 ±2.1	99.6 ± 0.5	99. 6± 1.0	97.2 ±1.5	97.1 ±1.2	97.8 ±0.8	93.3 ±6.4
	dark	99.9 ±2.1	100.7 ±0.1	99.2 ±0.5	99.5 ±0.9	100.6 ±0.3	100.2 ±0.9	101.0 ±1.4	101.8 ±0.9	102 ±1.9

[1] Raw data were not provided.
[2] Individual values of volatile organic compounds were not provided.

C. TRANSFORMATION OF PARENT COMPOUND: At study termination 100% of the applied radioactivity remained as the parent in the dark samples. No transformation occurred in the dark samples.

In the irradiated samples (HEPES buffer), the concentration of the parent compound decreased from 99 % at 0 DAT to 0.6 % of the applied radioactivity (AR) at 7 DAT. Significant levels of volatiles were not formed.

TRANSFORMATION PRODUCTS: One transformation product in the PY-label was found at greater than 10% AR, while two transformation products were formed above 10% AR in the TP label (eluting at approximately 13.5 minutes and 14.9 minutes by the Polar HPLC method). The three major photoproducts were the 742-sulfinic acid, 742-ADTP, and an adduct formed from 742-ADTP reacting with the HEPES buffer, with maximum concentrations of 79.2, 39.8 and 19.2% of the applied radioactivity observed on the 4th, 4th, and 2nd day of irradiation, respectively. These three major transformation products each decreased to 45.0, 23.6, and 5.9% of the applied radioactivity, respectively, by test termination (15 DAT). The reaction product of 742-ADTP and HEPES did not continue to increase, therefore 742-ADTP did not react completely with the buffer. Additional information on the photolytic degradation of 742-ADTP is provided.

Multiple unidentified minor peaks (less than 10% AR) were observed in irradiated samples throughout the study period. The 742-sulfonic acid was a minor transformation product in the PY-labeled irradiated samples but formed at levels too low to be quantified. The total unidentified radioactivity increased to 2.2% of the applied amount in the dark samples, and to 70% and 49% in the TP- and PY-labeled irradiated samples, respectively, by study termination. Unidentified radioactivity appeared to be multi-component with each component at low level. The Group 1 unidentified products were very polar and eluted at the solvent front when analyzed by HPLC. Group 2 unidentified products were slightly retained by the HPLC column (retention time approximately 4 minutes) on the main gradient system and were separated into multiple components using the Polar HPLC method. All transformation products formed in the irradiated samples could be attributed to phototransformation, as they did not appear in the dark samples.

PATHWAY: The phototransformation pathway likely proceeds through cleavage of the sulfonamide bridge, yielding the 742-sulfinic acid and the 742-ADTP. The 742-sulfonic acid is also formed but in very small quantities. All of these products transform further to multiple, low level components. The 742-ADTP appeared to be very reactive and formed an adduct with the HEPES buffer.

Table 7: Chemical names and CAS numbers for the transformation products of XDE-742 (pyroxsulam).

Applicant's Code Name	CAS Number	CAS and/or IUPAC Chemical Name(s)	Chemical formula	Mol. weight (g/mole)	SMILES string
742-ADTP	13223-43-3	5,7-dimethoxy [1,2,4]triazolo [1,5-α]pyrimidin-2-amine	$C_7H_9N_5O_2$	195.2	n1c(nc2n1c (cc(n2)OC) OC)N
742-sulfinic acid	not available	2-methoxy-4-(trifluoromethyl) pyridine-3-sulfinic acid	$C_7H_6F_3NO_3S$	241.19	c1(c(ccnc1O C)C(F)(F)F) S(O)=O

Applicant's Code Name	CAS Number	CAS and/or IUPAC Chemical Name(s)	Chemical formula	Mol. weight (g/mole)	SMILES string
742-sulfonic acid	not available	2-methoxy-4-(trifluoromethyl) pyridine-3-sulfonic acid	$C_7H_6F_3NO_4S$	257.19	c1(c(ccnc1O C)C(F)(F)F) S(O)(=O)=O

HALF-LIFE: The half- lives of XDE-742 for the dark and the irradiated samples were:

Test system	First-order half-life			$t_{1/2}$ (days)	$t_{9/10}$ (days)
	rate constant ($days^{-1}$)	Regression equation	r^2		
Dark	--	Y = 0.001 + 4.5976 (slight positive slope not significantly different from zero)	0.2229	--	--
Irradiated	0.76	Y = -0.7650x + 4.5402	0.9957	0.91	3.0

The photolytic rate constant (k_{phot}) and half-life, uncorrected for the intensity of the xenon lamp, were 0.76 $days^{-1}$ and 0.91 days, respectively (through 6.8 DAT) in HEPES buffer.

The environmental photolytic half-life and the $t_{9/10}$ values for XDE-742 photolysis at 40° N latitude in the summer sun were predicted to be 4.5 and 14.7 days, respectively. The environmental half-life from photolysis under field conditions will depend on location-specific factors including latitude and cloud cover.

D. SUPPLEMENTARY EXPERIMENT-RESULTS:

The rate of degradation did not change when a different buffer was used. The half-life in TRIS buffer was 0.80 days, which was equivalent to 2.1 days at 40° N summer sun (compared to 0.91 DAT and 3.0 days for HEPES buffer, respectively). The pH 7 TRIS buffer was insufficiently concentrated to buffer the irradiated samples and the pH decreased significantly through 14 DAT. At test termination, the pH remained approximately 7 in the dark samples but had declined to approximately 5.5 in the irradiated samples (Appendix F of study report). The TRIS buffer may have promoted the formation of oxidation products and thus the formation of a greater percentage of 742-sulfonic acid than 742-sulfinic acid, and multiple oxidized forms of 742-ADTP (proposed photoproducts). The different ratios of 742-sulfinic acid and 742-sulfonic acid and the oxidized 742-ADTP products in the two buffer systems may also be the result of a pH dependence.

In the irradiated ^{14}C-742-ADTP samples, the calculated half-life of ^{14}C-742-ADTP in 40° N

summer sunlight was 59.7, 59.7, and 61.0 days in pH 7 TRIS buffer, pH 7 HEPES buffer, and HPLC-grade water, respectively (based on reported $t_{1/2}$ of 22.3, 22.2 and 22.7 days, respectively). HPLC chromatograms from the 15 DAT samples are shown in Appendix G of the final report. The degradation route of ^{14}C-742-ADTP differs in the three test solutions. The combination of 742-ADTP + HEPES was not formed in this case perhaps because of a lack of an acid or other moiety that was formed from the XDE-742 photolysis in the main experiment. The supplemental ^{14}C-742-ADTP photolysis study showed that 742-ADTP can react with the test system buffer under some conditions and transforms more slowly than the parent XDE-742.

III. STUDY DEFICIENCIES:

No deficiencies were noted.

IV. REVIEWER'S COMMENTS:

1. The PMRA normally uses Day 0 concentrations and not % of nominal (applied) concentration as the basis for calculating % transformation. The recalculated values for the $t_{1/2}$ and $t_{9/10}$ reflect this, however the decision was made not to recalculate all the values on the tables as the day 0 concentrations in this case were almost 100% of the nominal value.
2. The PMRA and USEPA do not use ModelMaker. The $t_{1/2}$ and $t_{9/10}$ for the parent compound were recalculated using simple first-order kinetics. The fit to the curve of ln (% of applied radiation) *vs* time was excellent ($r^2 = 0.996$) so graphical determination of a DT_{50} and DT_{90} were not needed. The data point for 14.9 DAT was not used for this calculation, as the concentration of parent compound was below the detection limit at this time. The values calculated by the PMRA (4.5 and 14.7 days at 40°N latitude) are slightly longer than those calculated by the registrant (3.2 and 11 days).
3. The DT_{50} and DT_{90} calculations for the transformation products that were included in the original study template are not part of this review as they could not be verified. The values calculated for the further transformation of the major transformation products by the registrant (using ModelMaker) in any case are questionable in the light of the complications presented by the HEPES-adduct formation with the 742-ATDP transformation product. The values for the supplemental study on the 742-ADTP transformation product are reported but the calculated $t_{1/2}$ exceeded the total study time. The PMRA does not normally extrapolate from the data to reach a DT_{50} or use calculated $t_{1/2}$ that exceed the total study times. The PMRA-recalculated $t_{1/2}$ are similar to registrant-calculated values in terms of days but the light absorption rate constants for the individual buffers are not all given (they are not the same as that for the main study, which was 4.9 days equivalent summer sun per day irradiated nor the TRIS buffer study, which was 2.7 days). Back-calculation of the table on p. 137 of the main study indicates that they ranged from 1.45 to 1.5.
4. The quantum yield for the photolysis of XDE-742 was calculated by the registrant as 4.41×10^{-1}. The PMRA reviewer could not validate this result as the concentration of the XDE-742 solution did not appear to be stated explicitly, although the concentration of the actinometer PNAP standard was given in detail. The concentration of 0.01 M given on page

20 of the study appears to refer to the HEPES buffer and not to XDE-742 and the 0.025 M concentration used in the sample calculation on page 32 is not attributed. In any case both of these are well in excess of the solubility for the compound at pH 7, and even with the addition of 8% acetonitrile as a cosolvent, these concentrations are unlikely to have been the ones used The extinction coefficient and peak absorption wavelength given in DACO 8.2.1: Summary of Physicochemical Properties and the spectra shown in DACO 2.14.12 (Chemical and Physical Properties, UV/Visible Absorption Spectra) are consistent with the rapid photolysis observed.

5. Australian Reviewer's Comments: The Australian reviewer notes the above comments and notes that the results from the SFO model and that given by ModelMaker are not significantly different, thus the half lives were not recalculated.

V. REFERENCES:

1. Turner, B. J., "Determination of Water Solubility for XDE-742", 2004, NAFST806, unpublished report of Dow AgroSciences, LLC.

2. Madsen, S., "Determination of the Surface Tension, Density, and Vapour Pressure of the Pure Active Ingredient XDE-742," NAFST814, 2003, unpublished report of Dow AgroSciences LLC.

3. Sheets, J. J., Gast, R. E., Hanley, T. R., Krieger, M., Mayes, M. A. "Early Stage Registration Assessment of X666742: Phase I Weed Management Sulfonamide for European and Canadian Cereal Markets," DERBI No 79155, unpublished report of Dow AgroSciences LLC, 28 September 2000.

4. Turner, B. J., "Determination of Octanol/Water Partition Coefficient for XDE-742," NAFST807, 2004, unpublished report of Dow AgroSciences LLC.

5. Schaecker, M.; Foth, H.; Schlueter, J.; Kahl, R. Oxidation of Tris to one-carbon compounds in a radical-producing model system, in microsomes, in hepatocytes and in rats. Free Radical Res. Commun. 1991, 11(6), 339-47.

6. Koundal, K. R.; Sawhney, S. K.; Sinha, S. K. Oxidation of 2-Mercaptoethanol in the Presence of Tris Buffer. Phytochemistry 1983, 22(10), 2183-2184.

7. Taatjes, D. J.; Gaudiano, G.; Koch, T. H. Production of Formaldehyde and DNA-Adriamycin or DNA-Daunomycin Adducts, Initiated through Redox Chemistry of Dithiothreitol/Iron, Xanthion Oxidase/NADH/Iron, or Glutathione/Iron. Chem. Res. Toxicol. 1997, 10, 953-961.