

**Analytical method for PDMU and cPMU in water**

**Reports:** ECM: EPA MRID No.: 50595803. DeVellis, S.R. 2018. Validation of an Environmental Chemistry Method for the Determination of PDMU and cPMU in Surface Water. Report prepared by Smithers Viscient, Wareham, Massachusetts, and sponsored and submitted by ADAMA, Raleigh, North Carolina, and Tessenderlo Kerley, Inc., Phoenix, Arizona; 62 pages. Smithers Viscient Study No.: 14134.6113. Final report issued May 15, 2018.

ILV: EPA MRID No.: 50677003. Cashmore, A. 2018. Diuron - Independent Laboratory Validation of Analytical Method 14134.6113 for the Determination of PDMU and cPMU in Water. Report prepared by Smithers Viscient (ESG) Ltd., North Yorkshire, United Kingdom, monitored by Waterborne Environmental, Inc., Leesburg Virginia, and sponsored and submitted by ADAMA, Raleigh, North Carolina, and Tessenderlo Kerley, Inc., Phoenix, Arizona; 64 pages. Study No.: 3202043. Final report issued September 12, 2018 (p. 2).

**Document No.:** MRIDs 50595803 & 50677003

**Guideline:** 850.6100


**Statements:** ECM: The study was conducted in compliance with USEPA FIFRA GLP standards, as accepted by OECD GLP (1998; p. 3 of MRID 50595803). Signed and dated Data Confidentiality, GLP, and Quality Assurance statements were provided (pp. 2-4). An Authenticity statement was included with the Quality Assurance statement.

ILV: The study was conducted in compliance with United Kingdom (1999) GLP standards, as amended by GLP (2004) and OECD GLP (1998), as well as the United Kingdom Department of Health (p. 3; Appendix 3, p. 50 of MRID 50677003). The study was suitable for submission to US FDA, USEPA, and Japanese regulatory authorities. Signed and dated Data Confidentiality, GLP, Quality Assurance, and Authenticity statements were provided (pp. 2-5). An Authenticity statement was also included with the Quality Assurance statement (p. 4).


**Classification:** This analytical method is classified as **acceptable**. There are no aquatic toxicological data for degradates PDMU and cPMU with which to compare their lowest level of concern in water to the LOQ. However, these two analytes are not considered residues of concern.

**PC Code:** 035505

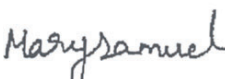
**EFED Final Reviewer:** William Gardner, Ph.D.,  
Environmental Scientist

Signature:   
Date: 12/17/2020

**CDM/CSS-Dynamac JV Reviewers:** Lisa Muto, M.S.,  
Environmental Scientist

Signature:   
Date: 05/15/2020

Mary Samuel, M.S.,  
Environmental Scientist

Signature:   
Date: 05/15/2020

*This Data Evaluation Record may have been altered by the Environmental Fate and Effects Division subsequent to signing by CDM/CSS-Dynamac JV personnel. The CDM/CSS-Dynamac Joint Venture role does not include establishing Agency policies.*

## Executive Summary

The analytical method, Smithers Viscient Study No. 14134.6113, is designed for the quantitative determination of PDMU and cPMU in water at the stated LOQ of 0.10 µg/L using LC/MS/MS. There are no aquatic toxicological data for degradates PDMU and cPMU with which to compare the lowest level of concern in water to the LOQ for these two analytes. However, these degradates are not considered residues of concern (USEPA 2020, DP 457224). Based on the performance data submitted by the ILV and ECM, the LLMV was equivalent to the reported method LOQ for the two analytes in the tested water matrices. The ECM and ILV validated the method using different surface water matrices; the test matrices appeared to represent difficult matrices based on the matrix effects and observed interferences. The ILV validated the method for PDMU and cPMU in water in the first trial for surface water with insignificant modifications to the analytical parameters and extending the calibration range. All ILV and ECM data regarding repeatability, accuracy, precision, linearity, and specificity were satisfactory for PDMU and cPMU, except that the specificity of the method for cPMU was not supported by ILV representative chromatograms of the quantitation ion transition where significant baseline noise interfered with peak integration and attenuation.

**Table 1. Analytical Method Summary**

Analyte(s) by Pesticide <sup>1</sup>	MRID		EPA Review	Matrix	Method Date (dd/mm/yyyy)	Registrant	Analysis	Limit of Quantitation (LOQ)
	Environmental Chemistry Method	Independent Laboratory Validation						
PDMU	50595803 <sup>2</sup>	50677003 <sup>3</sup>		Water	15/05/2018	ADAMA and Tessenderlo Kerley, Inc.	LC/MS/MS	0.10 µg/L
cPMU								

1 PDMU = 1,1-dimethyl-3-phenylurea; cPMU = 1-(3-chlorophenyl)-3-methylurea (p. 10 of MRID 50595803, and p. 12 of MRID 50677003).

2 In the ECM, surface water (SMV Lot No. 12July17Water-A; pH 6.2, dissolved oxygen concentration 5.92 mg/L) was collected from Weweantic River, Wareham, Massachusetts (p. 12 of MRID 50595803). The surface water was characterized by Smithers Viscient.

3 In the ILV, surface water (CS 14/18 Fountains Abbey surface water; pH 7.44, conductivity 154 µS/cm, dissolved organic carbon 11.2 mg/L; hardness 86 mg/L CaCO<sub>3</sub>) was collected by Smithers Viscient ESG at The Lake, Studley Royal, Ripon, United Kingdom (p. 12; Appendix 2, p. 49 of MRID 50677003). Water characterization was performed at the ILV.

## I. Principle of the Method

Water samples (8 mL) were fortified (0.08 mL or 0.80 mL of 0.01 mg/L fortification solution) and diluted with 2 mL of methanol (pp. 15-16 of MRID 50595803). The high fortification samples were further diluted by taking 2.50 mL of the sample and diluting to a final volume of 10.0 mL with methanol:surface water (20:80, v:v). An aliquot was taken for LC/MS/MS analysis.

Samples were analyzed for diuron using a Shimadzu LC-20AD HPLC coupled with an MDS Sciex API 5000 LC/MS/MS operated in the positive ion mode with multiple reaction monitoring (MRM; pp. 11, 16-17 of MRID 50595803). The following LC conditions were used: Waters XBridge C18 BEH column (2.1 mm x 50 mm, 2.5  $\mu$ m; column temperature 35°C), mobile phase of (A) 0.1% formic acid in water and (B) 0.1% formic acid in acetonitrile [mobile gradient phase of percent A:B (v:v) at 1.00 min. 90:10, 1.25 min. 50:50, 2.50-3.50 min. 0:100, 3.60-5.00 min. 90:10] and injection volume of 25  $\mu$ L. MS temperature was 450°C. Two ion pair transitions were monitored for each analyte (quantitation and confirmation, respectively):  $m/z$  165.2 $\rightarrow$ 72.0 and  $m/z$  165.2 $\rightarrow$ 45.9 for PDMU; and  $m/z$  185.1 $\rightarrow$ 92.9 and  $m/z$  185.1 $\rightarrow$ 127.9 for cPMU. Reported retention times were *ca.* 2.4 and 2.6 minutes for PDMU and cPMU, respectively.

The ILV performed the ECM methods as written, except for insignificant modifications to the analytical parameters and extending the calibration range (pp. 13, 15-17; Appendices 6-7, pp. 53-64 of MRID 50677003). Samples were analyzed for diuron using Nexera series HPLC coupled with an AB Sciex API 5000 Triple Quadrupole LC/MS/MS. The LC/MS/MS parameters were the same as those of the ECM. Two ion pair transitions were monitored for each analyte (quantitation and confirmation, respectively):  $m/z$  165.0 $\rightarrow$ 72.0 and  $m/z$  165.0 $\rightarrow$ 46.1 for PDMU; and  $m/z$  185.2 $\rightarrow$ 93.0 and  $m/z$  185.2 $\rightarrow$ 128.0 for cPMU. These ion transitions were similar to those of the ECM. Reported retention times were *ca.* 1.9 and 2.0 minutes for PDMU and cPMU, respectively. The ILV modifications did not warrant an updated ECM.

In the ECM and ILV, the Limit of Quantification (LOQ) was 0.10  $\mu$ g/L for PDMU and cPMU in water (pp. 9, 18-20 of MRID 50595803; pp. 20-21 of MRID 50677003). In the ECM, the Limit of Detection (LOD) was calculated as 0.000510-0.00307  $\mu$ g/L for PDMU and 0.00600-0.00696  $\mu$ g/L for cPMU. In the ILV, the LOD was calculated as 0.000802-0.00309  $\mu$ g/L for PDMU and 0.00674-0.0298  $\mu$ g/L for cPMU. Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ.

## II. Recovery Findings

ECM (MRID 50595803): Mean recoveries and relative standard deviations (RSDs) were within guidelines (mean 70-120%; RSD  $\leq$ 20%) for analysis of PDMU and cPMU at fortification levels of 0.10  $\mu\text{g/L}$  (LOQ) and 1.00  $\mu\text{g/L}$  (10 $\times$ LOQ) in one water matrix (Tables 1-4, pp. 27-30). Two ion pair transitions were monitored for the analytes; performance data was comparable between the quantitation and confirmation analyses. The surface water (SMV Lot No. 12July17Water-A; pH 6.2, dissolved oxygen concentration 5.92 mg/L) was collected from Weweantic River, Wareham, Massachusetts (p. 12). The surface water was characterized by Smithers Viscient.

ILV (MRID 50677003): Mean recoveries and RSDs were within guidelines for analysis of PDMU and cPMU at fortification levels of 0.10  $\mu\text{g/L}$  (LOQ) and 1.00  $\mu\text{g/L}$  (10 $\times$ LOQ) in one water matrix (Tables 1-4, pp. 25-28). Two ion pair transitions were monitored for the analytes; performance data was comparable between the quantitation and confirmation analyses. The surface water (CS 14/18 Fountains Abbey surface water; pH 7.44, conductivity 154  $\mu\text{S/cm}$ , dissolved organic carbon 11.2 mg/L; hardness 86 mg/L  $\text{CaCO}_3$ ) was collected by Smithers Viscient ESG at The Lake, Studley Royal, Ripon, United Kingdom (p. 12; Appendix 2, p. 49). Water characterization was performed at the ILV. The method for PDMU and cPMU in water was validated in the first trial for surface water with insignificant modifications to the analytical parameters and extending the calibration range (pp. 10, 21-22; Appendix 4, p. 51).

**Table 2. Initial Validation Method Recoveries for PDMU and cPMU in Water<sup>1,2</sup>**

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%) <sup>3</sup>	Relative Standard Deviation (%)
<b>Surface Water</b>						
Quantitation ion transition						
PDMU	0.10 (LOQ)	5	100-104	102	1.23	1.21
	1.00	5	96.4-103	99.2	2.19	2.21
cPMU	0.10 (LOQ)	5	101-109	105	3.08	2.94
	1.00	5	97.9-105	102	2.71	2.66
Confirmation ion transition						
PDMU	0.10 (LOQ)	5	95.4-104	99.5	3.21	3.22
	1.00	5	97.3-101	98.9	1.60	1.61
cPMU	0.10 (LOQ)	5	100-110	103	3.64	2.52
	1.00	5	97.8-103	101	2.30	2.27

Data (uncorrected recovery results; p. 19) were obtained from Tables 1-4, pp. 27-30 of MRID 50595803.

1 The surface water (SMV Lot No. 12July17Water-A; pH 6.2, dissolved oxygen concentration 5.92 mg/L) was collected from Weweantic River, Wareham, Massachusetts (p. 12). The surface water was characterized by Smithers Viscient.

2 Two ion pair transitions were monitored for each analyte (quantitation and confirmation, respectively):  $m/z$  165.2→72.0 and  $m/z$  165.2→45.9 for PDMU; and  $m/z$  185.1→92.9 and  $m/z$  185.1→127.9 for cPMU.

**Table 3. Independent Validation Method Recoveries for PDMU and cPMU in Water<sup>1,2,3</sup>**

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
<b>Surface Water</b>						
Quantitation ion transition						
PDMU	0.10 (LOQ)	5	92-98	96	2.5	2.6
	1.00	5	93-98	96	1.9	2.0
cPMU	0.10 (LOQ)	5	100-103	101	1.3	1.3
	1.00	5	85-92	88	2.8	3.2
Confirmation ion transition						
PDMU	0.10 (LOQ)	5	95-99	96	1.7	1.7
	1.00	5	95-98	96	1.3	1.4
cPMU	0.10 (LOQ)	5	96-102	100	2.4	2.4
	1.00	5	87-90	89	1.3	1.5

Data (uncorrected recovery results; p. 18) were obtained from Tables 1-4, pp. 25-28 of MRID 50677003.

1 The surface water (CS 14/18 Fountains Abbey surface water; pH 7.44, conductivity 154 µS/cm, dissolved organic carbon 11.2 mg/L; hardness 86 mg/L CaCO<sub>3</sub>) was collected by Smithers Viscient ESG at The Lake, Studley Royal, Ripon, United Kingdom (p. 12; Appendix 2, p. 49). Water characterization was performed at the ILV.

2 Two ion pair transitions were monitored for each analyte (quantitation and confirmation, respectively):  $m/z$  165.0→72.0 and  $m/z$  165.0→46.1 for PDMU; and  $m/z$  185.2→93.0 and  $m/z$  185.2→128.0 for cPMU. These ion transitions were similar to those of the ECM.

### III. Method Characteristics

In the ECM and ILV, the LOQ was 0.10 µg/L for PDMU and cPMU in water (pp. 9, 18-20 of MRID 50595803; pp. 19-21 of MRID 50677003). In the ECM and ILV, the LOQ was defined as the lowest fortification level validated. Also, in the ECM, the LOQ was defined as the level which the blank values did not exceed 30% of the LOQ. In the ECM, the LOD was calculated as 0.000510-0.00307 µg/L for PDMU and 0.00600-0.00696 µg/L for cPMU from the signal-to-noise response of each analyte in matrix at the LOQ level using the following equation:

$$\text{LOD} = (3 \times N_{\text{ctl}}) / (\text{Resp}_{\text{LS}}) \times \text{Conc}_{\text{LS}} \times \text{DF}_{\text{CNTL}}$$

Where, LOD is the limit of detection of the analysis,  $N_{\text{ctl}}$  is the mean signal to noise in height of the control samples (or blanks),  $\text{Resp}_{\text{LS}}$  is the mean response in height of the two low calibration standards,  $\text{Conc}_{\text{LS}}$  is the concentration of the low calibration standard, and  $\text{DF}_{\text{CNTL}}$  is the dilution factor of the control samples (1.25).

The LOD in water was estimated in the ILV as 0.000802-0.00309 µg/L for PDMU and 0.00674-0.0298 µg/L for cPMU at 3 x baseline noise for the primary and confirmatory transitions.

Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ.

**Table 4. Method Characteristics in Water**

		PDMU	cPMU
Limit of Quantitation (LOQ)*	ECM	0.10 µg/L	
	ILV		
Limit of Detection (LOD)	ECM (calc)	0.000510-0.00307 µg/L	0.00600-0.00696 µg/L
	ILV (calc)	0.000802-0.00309 µg/L	0.00674-0.0298 µg/L
Linearity (calibration curve r and concentration range)	ECM <sup>1</sup>	r = 0.9995 (Q & C)	
		0.05-0.5 ng/mL	
	ILV	r = 0.9979 (Q) r = 0.9978 (C)	r = 0.9991 (Q) r = 0.9993 (C)
		0.024-0.5 ng/mL	
Repeatable	ECM <sup>2</sup>	Yes at LOQ and 10×LOQ (one characterized water matrix –surface)	
	ILV <sup>3,4</sup>		
Reproducible		Yes for 0.10 µg/L (LLMV)* and 1.00 µg/L in surface water matrix	
Specific	ECM	Yes, no matrix interferences were observed. Minor peak tailing was observed.	Yes, no matrix interferences were observed. Baseline noise interfered with peak integration and attenuation.
	ILV	Yes, no matrix interferences were observed. Minor peak tailing was observed.	<b>No</b> for Q, matrix interferences were <11% of the LOQ (based on peak area); however, significant baseline noise interfered with peak integration and attenuation. <sup>5</sup> Yes for C, no matrix interferences were observed.

Data were obtained from pp. 9, 18-20 (LOQ/LOD); Tables 1-4, pp. 27-30 (recovery results); p. 21; Figures 11-14, pp. 45-48 (calibration curves); Figures 1-10, pp. 35-44 (chromatograms) of MRID 50595803; pp. 19-21 (LOQ/LOD); Tables 1-4, pp. 25-28 (recovery results); p. 20; Figures 1-2, p. 32; Figures 13-14, p. 38 (calibration curves); Figures 3-24, pp. 33-43 (chromatograms) of MRID 50677003. Q = quantitation ion transition; C = confirmation ion transition.

\* Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ. The lowest concentration tested with sufficiently accurate and precise recoveries is the LLMV.

- 1 Correlation coefficients (r) were reviewer-calculated based on r<sup>2</sup> values reported in the study report (p. 21 of MRID 50595803; DER Attachment 2). Matrix-matched calibration standards were used in the ECM and ILV (pp. 23-24 of MRID 50595803; p. 21 of MRID 50677003).
- 2 In the ECM, surface water (SMV Lot No. 12July17Water-A; pH 6.2, dissolved oxygen concentration 5.92 mg/L) was collected from Weweantic River, Wareham, Massachusetts (p. 12 of MRID 50595803). The surface water was characterized by Smithers Viscient.
- 3 In the ILV, surface water (CS 14/18 Fountains Abbey surface water; pH 7.44, conductivity 154 µS/cm, dissolved organic carbon 11.2 mg/L; hardness 86 mg/L CaCO<sub>3</sub>) was collected by Smithers Viscient ESG at The Lake, Studley Royal, Ripon, United Kingdom (p. 12; Appendix 2, p. 49 of MRID 50677003). Water characterization was performed at the ILV.
- 4 The ILV validated the method for PDMU and cPMU in water in the first trial for surface water with insignificant modifications to the analytical parameters and extending the calibration range (pp. 10, 21-22; Appendix 4, p. 51 of MRID 50677003).
- 5 Based on Figure 21, p. 42 (LOQ) and Figure 23, p. 43 (10×LOQ) of MRID 50677003.



#### IV. Method Deficiencies and Reviewer's Comments

1. Since the reported method LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ (pp. 9, 18-20 of MRID 50595803; pp. 19-21 of MRID 50677003). The lowest concentration tested with sufficiently accurate and precise recoveries is the LLMV. Based on the performance data submitted by the ILV and ECM, the LLMV was equivalent to the reported method LOQ for the two analytes in the tested water matrices.
2. The specificity of the method for cPMU was not supported by ILV representative chromatograms of the quantitation ion transition due to significant baseline noise interfered with peak integration and attenuation (Figure 21, p. 42; Figure 23, p. 43 of MRID 50677003.). The LOQ and 10×LOQ analyte peaks were not integrated to the baseline.
3. Only surface water matrices were used in the ECM and ILV. Based on the matrix effects and interferences observed in the ECM and ILV, the reviewer believed that the test matrices represented difficult matrices.
4. The ILV noted the following method issues: 1) stock solutions should be prepared and diluted directly into disposable glass vessels; and 2) the calibration range for cPMU could not include the 0.024 µg/L calibration standard due to background contamination (protocol deviation; p. 21; Appendix 7, p. 64 of MRID 50677003).
5. The communications between the ILV study author (Angela Cashmore) and ILV Study Monitor (Jennifer Gates, Waterborne Environmental, Inc.) were summarized (pp. 1, 20; Appendix 5, p. 52 of MRID 50677003). Reported communications included: protocol issue and the results of the first attempt of the ILV.
6. The determinations of the LOD and LOQ in the ECM and ILV were not based on scientifically acceptable procedures as defined in 40 CFR Part 136 (pp. 9, 18-20 of MRID 50595803; pp. 19-21 of MRID 50677003). In the ECM and ILV, the LOQ was defined as the lowest fortification level validated. Also, in the ECM, the LOQ was defined as the level which the blank values did not exceed 30% of the LOQ. No further justification of the LOQ was reported in the ECM or ILV. The LOD was calculated in the ECM using the following equation:  $LOD = (3 \times N_{ctl}) / (Res_{PLS}) \times Conc_{LS} \times DF_{CNTL}$ , where, LOD is the limit of detection of the analysis,  $N_{ctl}$  is the mean noise in height of the control samples (or blanks),  $Res_{PLS}$  is the mean response in height of the two low calibration standards,  $Conc_{LS}$  is the concentration of the low calibration standard, and  $DF_{CNTL}$  is the dilution factor of the control samples (1.25).. The LOD was estimated in the ILV using the following equation: 3 x baseline noise for the primary and confirmatory transitions. Detection limits should not be based on the arbitrarily selected lowest concentration in the spiked samples.

Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ.

The method detection limit (MDL) was calculated in the ECM and ILV as dependent upon the lowest concentration calibration standard and the dilution factor of the controls (p. 20 of



MRID 50595803; p. 21 of MRID 50677003). In the ECM, the MDL was equivalent to  $0.050 \mu\text{g/L} \times 1.25 = 0.0625 \mu\text{g/L}$ ; in the ILV, the MDL was equivalent to  $0.03 \mu\text{g/L}$  for PDMU ( $0.024 \mu\text{g/L} \times 1.25$ ) and  $0.0625 \mu\text{g/L}$  for cPMU ( $0.050 \mu\text{g/L} \times 1.25$ ).

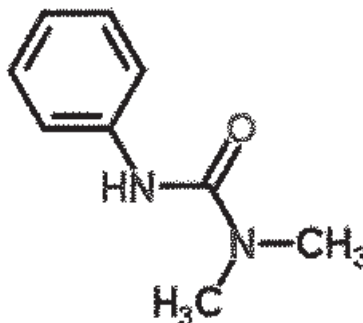
7. The reviewer noted a typographical error in the reported CAS# 20940-42-5 for cPMU in the ECM, which was reported as 2094-42-5 (p. 10 of MRID 50595803). The correct CAS# was verified by the reviewer in the Sigma Aldrich Chemical listing for 1-(3-chlorophenyl)-3-methylurea: <https://www.sigmaaldrich.com/catalog/search?term=20940-42-5&interface=CAS%20No.&N=0+&mode=partialmax&lang=en&region=US&focus=product>
8. The analyte PDMU is the herbicide fenuron (PC Code 035507) for which all U.S. registrations were cancelled in 1987.
9. The matrix interferences were determined to be significant (>20%) in the ECM and ILV; matrix-matched calibration standards were used in the ECM and ILV (pp. 23-24 of MRID 50595803; p. 21 of MRID 50677003).
10. The total time required to complete one set of samples was not reported in the ECM or ILV.

## V. References

- U.S. Environmental Protection Agency. 2020. Diuron: Draft Ecological Risk Assessment for Registration Review. DP 457224. Office of Chemical Safety and Pollution Prevention, Washington, DC. EPA 712-C-001.
- U.S. Environmental Protection Agency. 2012. Ecological Effects Test Guidelines, OCSPP 850.6100, Environmental Chemistry Methods and Associated Independent Laboratory Validation. Office of Chemical Safety and Pollution Prevention, Washington, DC. EPA 712-C-001.
- 40 CFR Part 136. Appendix B. Definition and Procedure for the Determination of the Method Detection Limit-Revision 1.11, pp. 317-319.

**Attachment 1: Chemical Names and Structures****PDMU (Fenuron; PC Code 035507)**

**IUPAC Name:** 1,1-Dimethyl-3-phenylurea  
**CAS Name:** N,N-Dimethyl-N'-phenylurea  
**CAS Number:** 101-42-8  
**SMILES String:** Not found

**cPMU**

**IUPAC Name:** 1-(3-Chlorophenyl)-3-methylurea  
**CAS Name:** Not reported  
**CAS Number:** 20940-42-5  
**SMILES String:** Not found

