

**Data Evaluation Report on the ECM and ILV of LGC-30473 in soil**  
EPA MRID Number 48535670 & 48535625

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**Data Requirement:** US EPA DP Barcode: 399085  
398866  
US EPA Guideline: OPPTS 850.6100

**Test material:**

Common name: Ethaboxam  
chemical name:  
IUPAC: N-( $\alpha$ -cyano-2-thenyl)-4-ethyl-2-(ethylamino)-5-thiazolecarboxamide  
CAS name:  
CAS No: 162650-77-3  
synonyms:

**Primary Reviewer (officer number):** H  l  ne Arsenault (2077)  
**PMRA**

**Secondary Reviewer:** **Date:** 11/13/13

**Andrew Shelby**  
EPA

**Signature:** 

**Company Code:** VAJ  
**Active Code:** EBX  
**Use Site Category:** 10, 11  
**EPA PC Code:** 090205

**Part 8.2.2 Analytical methodology (parent compound and transformation products)**

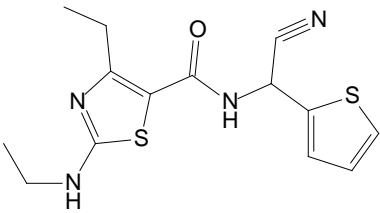
**Common Name:** Ethaboxam  
**Product Name:** Ethaboxam Technical  
**Submission Number:** 2011-4730  
**PCPA Reg. Number:** Not yet assigned  
**Source Code:** EBX-LGS-2

**Chemical structures:**

**Table 1. Chemical name, code and chemical structure for active and all major transformation products / metabolites**

| Chemical name | Code | Chemical structure |
|---------------|------|--------------------|
|---------------|------|--------------------|

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| <b>Table 1. Chemical name, code and chemical structure for active and all major transformation products / metabolites</b> |                    |   |
|---|--------------------|---|
| <i>N</i> -(cyano-2-thienylmethyl)-4-ethyl-2-(ethylamino)-5-thiazolecarboxamide  | LGC-30473 (parent) |  |

No major transformation products are expected.

**Data Submission and Review History:**

| <b>Table 2. Correspondence Dates, Data # and Content for Ethaboxam Technical</b> |        |   |                    |
|--|--------|---|--------------------|
| Date Received  | Data # | Content Summary                         | Reviewer Officer # |
| 03 Nov 2011  | 1      | Parts 8.2.2.1 and 8.2.2.2 study reports | 1930               |
|  |        |   |                    |

**Good Laboratory Practices Compliance Statement:**

The studies contained within this report were conducted in accordance with the Good Laboratory Practice Standards as specified in 40 CFR 160.

yes                       no                       not stated / applicable

Note: The original method validations do not specify GLP compliance, although the test facility is accredited by the UK monitoring authority and a study director was named and study protocol written. The ILV study was EPA GLP compliant.

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**8.2.2 Analytical Methodology (parent compound and transformation products)**

**8.2.2.1 Soil**

Reference:

- 1) PMRA # 2111119. EPA MRID 48535670. 2003, VALIDATION OF METHODOLOGY FOR THE POST-REGISTRATION MONITORING OF RESIDUES OF LGC-30473 IN SOIL, DACO: 8.2.2.1,8.2.2.2 (Data # 1)
- 2) PMRA # 2111120. EPA MRID 48535625. 2011, Independent Laboratory Validation for the Determination of V-10208 Residues in Soil and Water, DACO: 8.2.2.1,8.2.2.3 (Data # 1)

| <b>Items</b>           | <b>Details</b>   |
|------------------------|--|
| Details of sample used | Original validation: Sandy loam and clay loam soils, 4.1 % and 4.5 % organic carbon respectively<br>ILV: Loamy sand with 0.6 % organic matter  |
| Extraction method used | A sample of soil material (20 g) is weighed into a polyethylene bottle (sample is fortified at this point if required). 80 mL of extraction solvent (acetonitrile : water, 70:30) is added, and the sample shaken for 30 min. The sample is centrifuged and transferred to a 250 mL polyethylene bottle through a funnel with a glass wool plug. The sample is extracted a second time with 80 mL of extraction solvent, and the extracts combined and made up to 200 mL in extraction solvent.  |
| Sample clean-up method | A 10 mL aliquot of the combined extract is transferred to a 50 mL polypropylene tube. Aliquots of water (20 mL) and hexane (10 mL) are added and the samples shaken well. The hexane layer is removed and discarded, and the aqueous phase extracted again with 10 mL hexane, which is also discarded. A 10 mL aliquot of ethyl acetate is added, and the samples shaken well, and the ethyl acetate layer transferred to a 100 mL round bottom flask. The aqueous portion is extracted again with 10 mL ethyl acetate, and the ethyl acetate extracts are combined. The ethyl acetate is evaporated to dryness using rotary evaporation at 40 °C, and the residues are reconstituted in 5 mL methanol : water (50:50). Samples may be further diluted as required to be in calibration range. |

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| <b>Items</b>  | <b>Details</b>   |            |            |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |
|---|--|------------|------------|----|------|------|----|----|------------|------|---|-----|------------|-------|---|-----|------------|-------|----|----|------------|-------|----|----|------------|
| Method for identification and quantitative analysis of parent compound and transformation products      | <p>HPLC-MS (Electrospray positive ion mode )</p> <p>Instrument: HPLC with binary pump</p> <p>Detector: MS/MS</p> <p>Column: Phenomenex Luna C-8 15 cm x 2.0 mm i.d., 5µm particle size</p> <p>Mobile Phase: A) 80:20 (v/v) water : acetonitrile<br/>                     B) 20:80 (v/v) water : acetonitrile<br/>                     (both containing 0.01 M ammonium acetate / 0.1 % acetic acid)</p> <p>Gradient:</p> <table border="1"> <thead> <tr> <th>Time (min)</th> <th>% A</th> <th>%B</th> <th>Flow</th> </tr> </thead> <tbody> <tr> <td>0.00</td> <td>60</td> <td>40</td> <td>0.2 mL/min</td> </tr> <tr> <td>6.00</td> <td>0</td> <td>100</td> <td>0.2 mL/min</td> </tr> <tr> <td>12.00</td> <td>0</td> <td>100</td> <td>0.2 mL/min</td> </tr> <tr> <td>13.00</td> <td>60</td> <td>40</td> <td>0.2 mL/min</td> </tr> <tr> <td>25.00</td> <td>60</td> <td>40</td> <td>0.2 mL/min</td> </tr> </tbody> </table> <p>Retention time: 7.2 min. (LGC-30473 )</p> <p>Cycle time: 25 min.</p> <p>MS conditions:</p> <p>Ionization mode: ESI (positive ion mode)</p> <p>Acquisition type: MRM</p> <p>MRM (Q1) 321.00 → (Q3) 200.00 m/z<br/> <math>M^+ \rightarrow [M - 121]^+</math><br/>                     (probable loss of C<sub>6</sub>H<sub>3</sub>NS (α-cyano-2-thienyl), as the main peak in the MS (EI+) spectrum is 183 m/z</p> | Time (min) | % A        | %B | Flow | 0.00 | 60 | 40 | 0.2 mL/min | 6.00 | 0 | 100 | 0.2 mL/min | 12.00 | 0 | 100 | 0.2 mL/min | 13.00 | 60 | 40 | 0.2 mL/min | 25.00 | 60 | 40 | 0.2 mL/min |
| Time (min)  | % A  | %B         | Flow       |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |
| 0.00  | 60   | 40         | 0.2 mL/min |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |
| 6.00  | 0  | 100        | 0.2 mL/min |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |
| 12.00   | 0  | 100        | 0.2 mL/min |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |
| 13.00   | 60   | 40         | 0.2 mL/min |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |
| 25.00   | 60   | 40         | 0.2 mL/min |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |
| Chromatograms of spiked sample, control sample, blank and standard solution                             | <p>Chromatograms of standard solutions, spiked (fortified) soil samples and control soil samples (both clay and sandy loam soils) were provided in the original study.</p> <p>Chromatograms of standard solutions, spiked (fortified) soil samples and a control soil sample were provided in the ILV study.</p>   |            |            |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |
| Quantitation  | By method of external standards using linear regression on a 10 level (9 level for ILV) standard curve.  |            |            |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |
| Criteria for setting LOD and LOQ  | <p>The LOQ was defined as the lowest fortification level at which acceptable recovery data were obtained.</p> <p>The LOD was defined as the equivalent sample concentration of the lowest calibration standard chromatographed.</p>  |            |            |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |
| Stability of parent and transformation products at various stages of analysis                           | The stability of the parent at various stages of the analysis was not discussed. Recoveries of the active indicate that there were no stability issues in the timeframes used.   |            |            |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |
| Special problems encountered and/or precautions to be taken during analysis/handling/storage of samples | Centrifugation of the extracted samples may be required to separate the phases at the various solvent extraction steps.  |            |            |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |
| Total time for completion   | 8 – 10 hours to complete an extraction set of 12 soil samples  |            |            |    |      |      |    |    |            |      |   |     |            |       |   |     |            |       |    |    |            |       |    |    |            |

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The method validation data for the parent compound are summarized in Table 4.

| <b>Table 4. Method validation: Parent compound</b>  |  |  |  |
|---|--|--|--|
| <b>Parameter</b>  | <b>Parent compound</b>                               |  |  |
|   | <b>Validation study –clay loam soil <sup>1</sup></b> | <b>Validation study – sandy loam soil <sup>1</sup></b> | <b>ILV study loamy sand <sup>2</sup></b>     |
| % Recovery at spiking level-1<br>(n = 5 at 0.05 mg/kg)  | 91 (6.3 %RSD)  | 100.0 (4.8 %RSD)                                       | 101 (3.7 %RSD)                               |
| % Recovery at spiking level-2<br>(n = 5 at 0.5 mg/kg)   | 100 ( 6.3 % RSD)                                     | 92 (5.3% RSD)  | 101 (2.4 % RSD)                              |
| Mean % recovery   | 96 (n = 10)  | 96 (n = 10)  | 101 (n = 10)                                 |
| RSD %   | 7.5  | 6.6  | 3.0  |
| Method linearity  | 0, 1 – 50 ng/mL (9 levels and a blank)               | 0, 1 – 50 ng/mL (9 levels and a blank)                 | 1 – 50 ng/mL (9 levels, forced through zero) |
| Correlation coefficient   | 0.9996   | 0.9996   | 0.9994                                       |
| LOD   | 0.005 mg/kg  | 0.010 mg/kg  | 0.0125 mg/kg <sup>3</sup>                    |
| LOQ   | 0.05 mg/kg   | 0.05 mg/kg   | 0.05 mg/kg                                   |
| <sup>1</sup> data from Ref. 1 (pg 16 and 17, 25,26)<br><sup>2</sup> data from Ref. 2 (pg 21, 32)<br><sup>3</sup> based on the sample concentration equivalent to the lowest standard prepared – judging by the LOQ spike and unspiked control chromatograms, the actual LOD was estimated to be 50 – 100 times lower than this value (pg 32, 34)<br><sup>4</sup> calculated by reviewer |  |  |  |

**Conclusions/Other Comments:** An HPLC-MS method was developed for the determination of ethaboxam in soil and was validated in three control soils. The recovery data were acceptable (between 70-120%), and the LOQ was determined to be approximately 0.05 mg/kg. This method is acceptable for use as a post-registration monitoring method.

#### 8.2.2.2 Sediment

The method developed for soil is also applicable to sediment samples.

### Overall Summary of Data

## Part 8 Environmental Chemistry and Fate

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| Matrix          | Method   | Fortification level (n) | Parent compound   |         | LOQ        | Method accept-ability |
|-----------------|--|-------------------------|-------------------|---------|------------|-----------------------|
|                 |  |                         | Mean recovery (%) | RSD (%) |            |                       |
| Sandy Loam soil | LFK114   | 0.05 mg/kg              | 91                | 6.3     | 0.05 mg/kg | A                     |
|                 |  | 0.5 mg/kg               | 100               | 6.3     |            |                       |
| Clay Loam soil  |  | 0.05 mg/kg              | 100               | 4.8     |            |                       |
|                 |  | 0.5 mg/kg               | 92                | 5.3     |            |                       |
| Loamy Sand soil |  | 0.05 mg/kg              | 101               | 3.7     |            |                       |
|                 |  | 0.5 mg/kg               | 101               | 2.4     |            |                       |
| Sediment        | The method for soil can be extended to sediment – no additional data were provided |                         |                   |         |            | A                     |
| Surface water   | LFK115   | 1.0 µg/L (5)            | 91                | 3.0     | 1 µg/L     | A                     |
|                 |  | 10 µg/L (5)             | 94                | 5.0     |            |                       |
| Ground water    |  | 0.1 µg /L (5)           | 88                | 6.6     | 0.1 ug/L   |                       |
|                 |  | 1.0 µg /L (5)           | 95                | 9.7     |            |                       |
| Drinking water  |  | 0.1 µg /L (5)           | 82                | 11.7    | 0.1 ug/L   |                       |
|                 |  | 1.0 µg /L (5)           | 87                | 11.7    |            |                       |
| Tap water       |  | 1.0 µg/L (5)            | 109               | 2.9     | 1 µg/L     |                       |
|                 |  | 10 µg/L (5)             | 109               | 2.8     |            |                       |
| Plant           | reviewed by HED.   |                         |                   |         |            |                       |
| Animal matrix   |  |                         |                   |         |            | N                     |

**Conclusion:** The analytical methods developed for determination of ethaboxam in soil, sediment, and water have been validated and determined to be acceptable as post-registration monitoring methods. Methodology for the active ingredient in animal biota (preferably birds) is required by EAD and is still outstanding. This deficiency is included in the EAD level C deficiency memo, PMRA # 2144906.