European Commission

Renewal Assessment Report of the Inclusion of the Active Substance in Annex I of the Regulation (EC) 1107/2009

Oxamyl 10SL

Volume 3 (CP)
ANNEX B.5 Methods of analysis

Rapporteur Member State: Italy
Co-Rapporteur Member State: France

January 2018

VERSION HISTORY

Date	Data points containing amendments or additions	Document identifier or version number

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B.5 METHODS OF ANALYSIS

Introduction

Samples of the pure active substance and preparations as manufactured are available and can be provided upon request. Analytical standards for the pure active substance, reference standards for the quantitatively significant impurities (>1 g/kg), and for the relevant metabolites and other components included in the residue definition are available and can be provided upon request.

Oxamyl 10SL was not the representative formulation for the first EU approval review of oxamyl.

Unless specifically indicated, all reports in this section are submitted to address mandatory data requirements for the approval of active substance.

B.5.1 Methods used for the generation of pre-authorisation data

B.5.1.1 Analysis of the plant protection product

B.5.1.1.1 Methods for the determination of the active substance in plant protection products

Studies submitted to the EU for the first time in this submission.

B.5.1.1.1/01

Reference CP 5.1.1/01	**Report**	Pandey, S. (2015) Validation of the analytical method for determination of oxamyl (DPX- D1410) in technical grade oxamyl and oxamyl end-use products by reverse phase high performance liquid chromatography (RPLC) and ultra performance liquid chromatography (UPLC) **DuPont Report No.:** DuPont-36605 and DuPont-36605 Confidential attachment **GLP:** Yes

B.5.1.1.1/02

Reference CP 5.1.1/02	**Report**	Pandey, S., McNally, M.E.P. (2015) Determination of oxamyl (DPX-D1410) in technical grade oxamyl and end-use products **DuPont Report No.:** DuPont-42001 **GLP:** No

Description of the method

The method for assay of oxamyl in Oxamyl 10SL involves dissolution by ultrasonication of an Oxamyl 10SL sample in a solution of 5% methanol and 95% water adjusted to pH 3.0 with H_3PO_4. A known amount of acetanilide internal standard was added to each standard or sample. Samples were shaken well before weighing and filtered before analysis. Analysis was done by reversed-phase liquid chromatography (HPLC) and ultra-high pressure liquid chromatography (UPLC), with quantitation by ultraviolet absorbance at 240 nm. The column used was a 1.8-µm particle size, 4.6 mm × 100 mm Agilent Zorbax-XDB C18 column for UPLC and 5.0 µm particle size, 4.6 mm × 150 mm Agilent Zorbax-Aqua C18 column for HPLC. The mobile phase was a gradient mixture of acetonitrile and water that had been adjusted to pH 3.0. The weight percent of oxamyl in each sample was determined by comparing peak area ratios of oxamyl/acetanilide with a calibration curve generated from the analysis of standard solutions.

Specificity, linearity, accuracy, repeatability

The information reported below concerns the method for the determination of the active substance in Oxamyl 10SL.

Specificity

Details regarding the specificity of the method (DuPont-36605 Confidential attachment) are claimed as confidential and are included in Oxamyl EU Renewal Dossier, Document J, Part 1, DuPont-40926 EU. As the disclosure of this information would also disclose the impurity profile of the technical product, we request them to be treated as confidential information according to Article 63 of Regulation EC 1107/2009.

The method was evaluated for interferences from formulation inerts. None of the known formulation ingredients present in Oxamyl 10SL co-elute with oxamyl or the internal standard, acetanilide. Known impurities would not be present at concentration levels that would represent a chromatographic interference. Since the EU requires that any interference present does not contribute more than ±3% to the total quantity determined, this method satisfies the EU criteria for specificity.

Linearity

The linearity of the method proposed for the determination of the active substance, oxamyl, as manufactured was demonstrated. Linearity has been demonstrated for both HPLC and UPLC, by the analyses of seven standard solutions within the nominal ranges; 0.2–1.40 mg/mL for oxamyl. The resulting least square linear equations and correlation coefficients are as follows.

Table 1 Least square linear equations and correlation coefficients

System	Slope	y-intercept	Correlation coefficient (R^2)
HPLC	32.198	0.0042	0.9999
UPLC	32.004	0.0066	0.9999

Accuracy

For HPLC, the accuracy of this method for the analysis of oxamyl technical in Oxamyl 10SL as manufactured samples was evaluated by analysing standard material as surrogate samples using duplicate determinations at three concentrations, in the range of 75–125% of the nominal sample active concentration. The average percent recovery obtained was 96.56% with a standard deviation of 0.79%. The accuracy of this method is adequate for HPLC.

For UPLC, the accuracy of this method for the analysis of oxamyl technical in Oxamyl 10SL as manufactured samples was evaluated by analysing standard material as surrogate samples using duplicate determinations at three concentrations, in the range of 75–125% of the nominal sample active concentration. The average percent recovery obtained was 96.86% with a standard deviation of 0.79%. The accuracy of this method is adequate for UPLC.

Repeatability

Repeatability testing of the assay method was determined by calculating the standard deviation of the average percent oxamyl in Oxamyl 10SL obtained from the analysis of eight replicate test portions of the same sample of Oxamyl 10SL. The results were calculated from one analyst on one day.

For HPLC, the relative standard deviation was 0.51% for the analysis of Oxamyl 10SL as manufactured. The maximum allowable relative standard deviation calculated from the modified Horwitz equation is 1.90%. Therefore, the HPLC method fulfils the EU repeatability criteria.

For UPLC, the relative standard deviation was 0.51% for the analysis of Oxamyl 10 SL as manufactured. The maximum allowable relative standard deviation calculated from the modified Horwitz equation is also 1.90%. Therefore, the HPLC method fulfils the EU repeatability criteria.

There were no outliers during this testing.

Overall suitability for enforcement purposes

The method was successfully evaluated and meets the EU criteria with respect to linearity, precision (repeatability), accuracy (recovery), and specificity. The method requires instrumentation commonly available

in most well equipped analytical laboratories. No hazardous reagents are required. Therefore, this method is suitable for enforcement purposes.

Applicability of existing CIPAC methods

There is a CIPAC method for oxamyl, it is FAO specification 342/TK (April, 2008). The analytical method for determination of oxamyl (including identity tests) is based on reversed-phase HPLC with UV detection at 240 nm and internal standardization with acetanilide. The method was adopted by CIPAC, with provisional status in 2006, and full CIPAC method status in 2007. DuPont and CIPAC have noted that the method can also be used with external standardization. The method is applicable for technical concentrate, granules, and soluble concentrates.

RMS comments and conclusion

IT: the method presented is considered acceptable

B.5.1.1.2 Methods for the determination of impurities in the preparation

There are no impurities known to be of neither toxicological or environmental relevance, nor isomers in oxamyl as manufactured or formulating ingredients in Oxamyl 10SL that would justify the submission and disclosure of enforcement methods.

B.5.1.1.3 Methods for the determination of formulants or constituents of formulants in the plant protection product

There are no formulating ingredients in Oxamyl 10SL of toxicological or ecotoxicological concern that justify the need for the submission and disclosure of enforcement methods.

B.5.1.2 Methods for the determination of residues

All methods for the determination of oxamyl residues are included in the Oxamyl RAR Vol 3 (CA) B5.

B.5.2 Methods for post-authorisation control and monitoring purposes

All enforcement methods for the determination of oxamyl residues are included in the Oxamyl RAR Vol 3 (CA) B5.

B.5.3 References relied on

List of information, tests and studies which are considered as relied upon by the RMS for the evaluation with a view to the approval of the active substance.

Studies marked in yellow are submitted for the first time.

List of studies submitted sorted by Annex Point

Data Requirement No., Reference No.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data Protection Y/N	Justification if data protection is claimed	Owner
B.5.1.1.1/01	Pandey, S.	2015	Validation of the analytical method for determination of oxamyl (DPX- D1410) in technical grade oxamyl and oxamyl end-use products by reverse phase high performance liquid chromatography (RPLC) and ultra performance liquid chromatography (UPLC) Syngene DuPont-36605 and DuPont-36605 Confidential attachment GLP: Yes Published: No	N	Y	New method for the analysis of oxamyl technical and formulated product. The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or submitted.	DuPont
B.5.1.1.1/02	Pandey, S., McNally, M.E.P.	2015	Determination of oxamyl (DPX-D1410) in technical grade oxamyl and end-use products Syngene DuPont-42001 GLP: No Published: No	N	N		DuPont

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REFERENCE LIST, CP, SECTION 5, ANALYTICAL METHODS - DOCUMENTS SUBMITTED. VERTEBRATE STUDIES.

No vertebrate studies submitted.

REFERENCE LIST, CP, SECTION 5, ANALYTICAL METHODS - DOCUMENTS NOT SUBMITTED. PREVIOUSLY SUBMITTED AND RELIED UPON.

No studies previously submitted and relied upon.